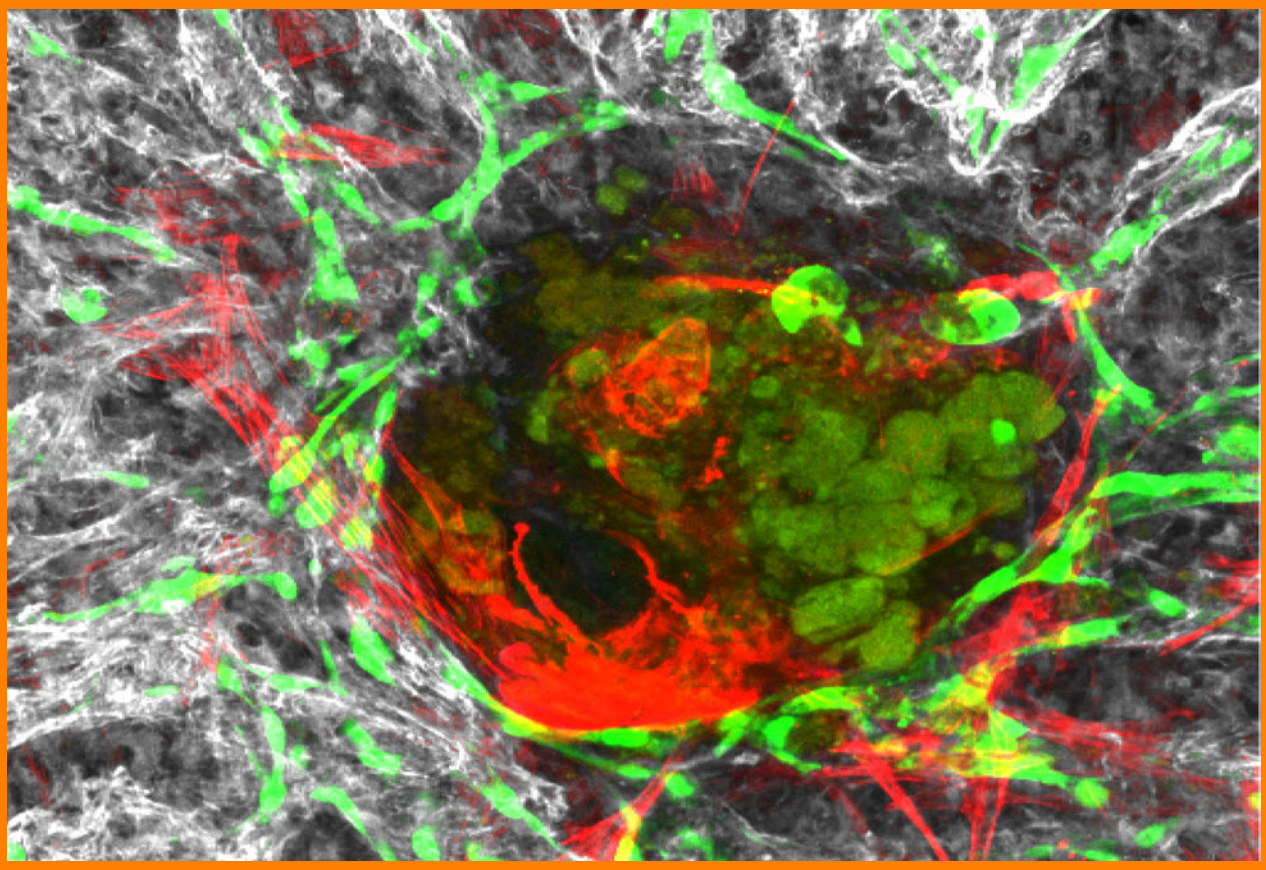
EDWIN L. STEELE LABORATORIES

DEPARTMENT OF RADIATION ONCOLOGY
MASSACHUSETTS GENERAL HOSPITAL
HARVARD MEDICAL SCHOOL



RESEARCH REPORT 2023

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PREFACE

A solid tumor is an organ composed of cancer cells and host stromal cells—nourished by blood vessels and drained by lymphatic vessels—all embedded in an extracellular matrix. The interaction among these cells, the surrounding matrix, and the local cellular microenvironment influences the expression of various genes, whose protein products control the pathophysiological characteristics of the tumor, govern tumor progression, and affect the tumor's response to various therapies. The overarching goal of our research is to dissect the role of tumor microenvironment in tumor progression and treatment resistance, and to translate this knowledge into improved cancer detection, prevention and treatment in humans. A tight integration between bench and bedside and the application of engineering principles to oncology is a hallmark of our research.

To unravel the complex biology of tumors, the Steele Laboratories have developed an array of optical technologies, mathematical models and sophisticated animal preparations. These include multiphoton microscopy and genetically engineered mice with surgically implanted transparent windows, which together permit the real-time visualization of gene expression and function in tumors and their surrounding host stroma. This undertaking has provided unprecedented molecular, cellular, anatomical and functional insights into the vascular, interstitial and cellular barriers to cancer treatment. Specifically, we demonstrated that the blood and lymphatic vasculature, fibroblasts, immune cells and the extracellular matrix associated with tumors are abnormal, which collaborate together to create a hostile tumor microenvironment characterized by hypoxia, low pH and high interstitial fluid pressure.

We next hypothesized that agents that induce "normalization" of the microenvironment should improve the treatment outcome. Our work in this area has come to fruition and led to two novel strategies: vascular and matrix normalization. The Steele Laboratories are now recognized worldwide for discovering that direct and indirect antiangiogenic therapies can "normalize" tumor vessels, thus improving blood perfusion, oxygenation and treatment efficacy in cancer patients. This revolutionary concept explained how bevacizumab (Avastin®)—the first antiangiogenic drug to receive FDA approval—works in patients and has spawned a number of basic and clinical studies. Indeed, we demonstrated that judicious use of antiangiogenic agents—originally designed to starve tumors—could transiently "normalize" tumor vasculature, alleviate hypoxia, increase delivery of drugs and anti-tumor immune cells, and improve the outcome of various therapies, including immunotherapy (Science 2005, 2019, 2020). In parallel, we provided compelling evidence for vascular normalization in cancer patients treated with antiangiogenic agents. In fact, vascular normalization and the resultant improvement in tumor perfusion and oxygenation associated with longer survival in patients. Our hypothesis has also been validated by several laboratories worldwide and has changed the thinking about how antiangiogenic agents work alone and in combination with conventional and emerging therapeutics. Our 2012 preclinical finding that vascular normalization can improve immunotherapy was confirmed by others in randomized phase III trials on combining antiangiogenic therapy with immune-checkpoint inhibitors for lung, kidney, liver, and endometrial cancers and led to the FDA approvals of seven such combinations of antiangiogenic therapy and immune-checkpoint inhibitors for these cancers.

The vascular normalization hypothesis also explained how bevacizumab and other anti-VEGF drugs improve vision in patients with wet age-related macular degeneration and opened doors to treating other non-malignant diseases harboring abnormal vasculature that afflict more than 500 million people worldwide. These include tuberculosis and neurofibromatosis-2 (NF2). In 2014, our clinical findings showing the reversal of hearing loss in NF2 patients by normalizing their blood vessels led to the approval of bevacizumab for these patients in the UK.

In parallel, by imaging collagen and measuring perfusion in tumors in vivo, we discovered that the extracellular matrix compresses blood vessels and impedes drug delivery in desmoplastic tumors (e.g., pancreatic cancer, hepatocellular carcinoma, certain breast cancers). We subsequently discovered that widely prescribed angiotensin blockers to control hypertension are capable of "normalizing" the extracellular matrix, opening compressed tumor vessels and improving the delivery and efficacy of therapy. This finding offers new hope for improving the

treatment of highly fibrotic tumors and led to a phase II clinical trial in 2013 at MGH on testing the benefit of adding losartan to the standard of care (chemotherapy and radiation followed by surgery) in patients with locally advanced pancreatic ductal adenocarcinoma (NCT01821729). This trial provided compelling evidence in support of this emerging concept and has spawned a multi-institutional randomized clinical trial (NCT03563248) in pancreatic ductal adenocarcinoma. If successful, this will represent a major paradigm shift in the treatment of this uniformly fatal disease and open doors for improving treatment of other malignant and non-malignant diseases.

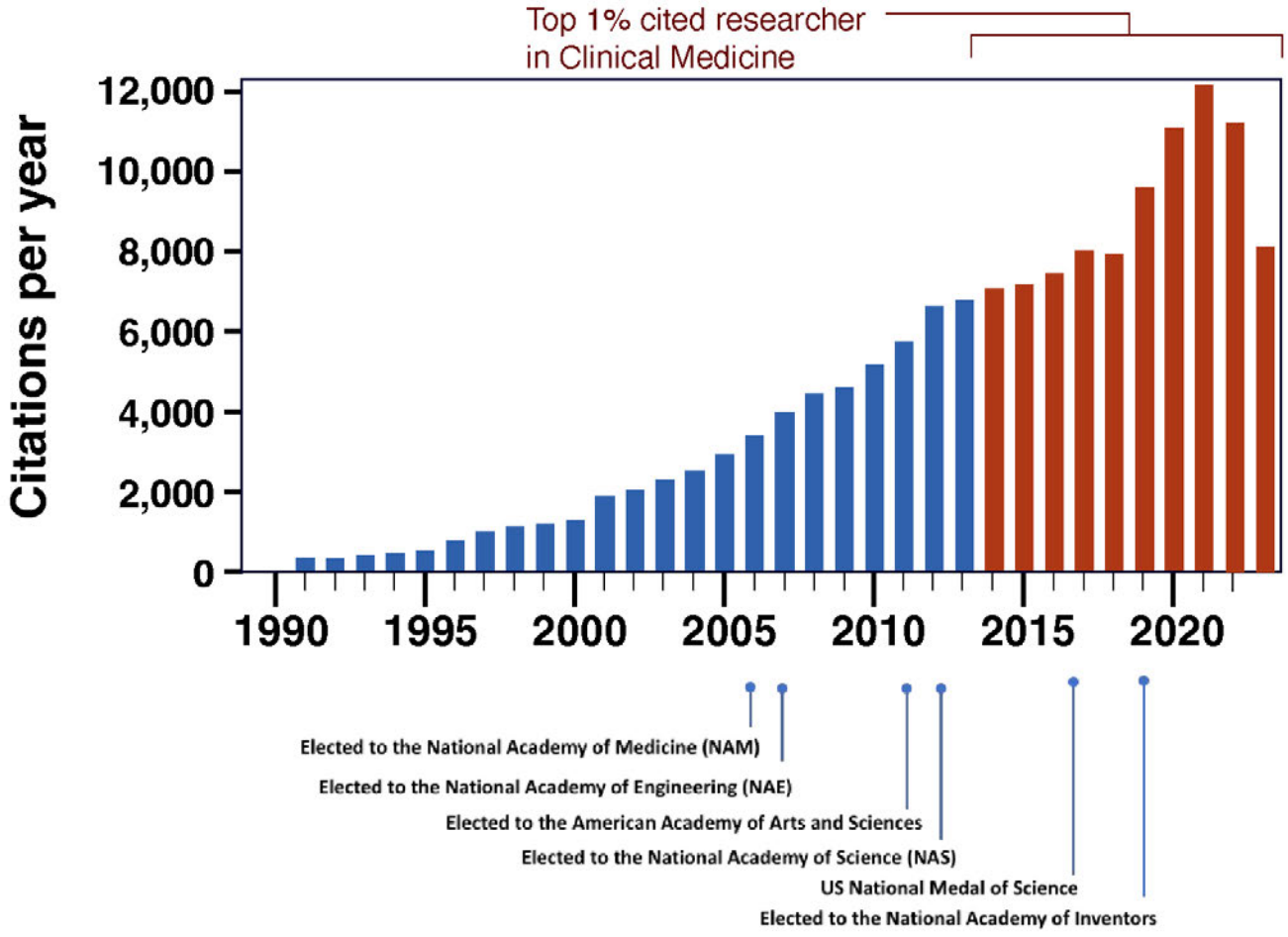
The Edwin L. Steele Laboratories for Tumor Biology were founded in 1975 with a generous gift by Mrs. Jane Bancroft Cook in memory of her late husband Edwin L. Steele. In addition, she endowed the Andrew Werk Cook Professorship of Radiation Oncology at Harvard University/MGH in honor of her second husband. Andrew Werk Cook. These donations to cancer research at MGH have been critical in the growth of tumor biology research at MGH, which over the years has led to improved understanding and treatment of cancer. The continued support of Ms. Elizabeth Steele (daughter of Mrs. Cook) and Jane's Trust Foundation has allowed us to translate our discoveries from bench to bedside. In September 1991, I was recruited to be the director of the Steele Laboratories. Starting with a small team of six people, we have since grown to approximately 65 members. The Steele Labs have fostered the careers of the 9 current faculty members, who collectively have trained over 220 graduate students and post-doctoral fellows from more than 25 countries. We have developed a leading, multidisciplinary research and education program in the integrative biology of cancer.

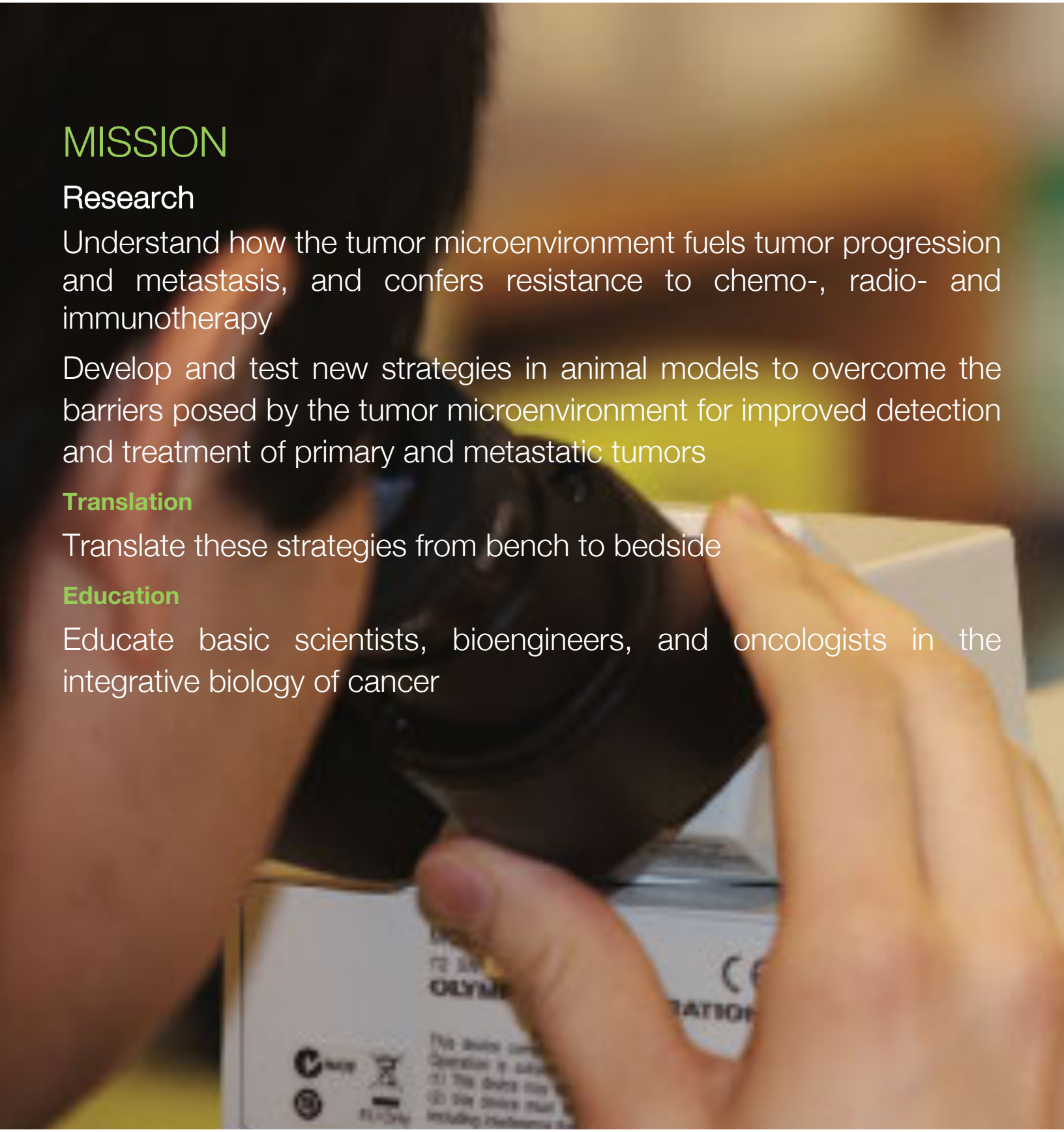
In addition to the research within our laboratory, we have several collaborative projects with clinicians and scientists at the MGH and other medical research centers worldwide. Results from the Steele Laboratories, as well as those from these collaborations, have been reported in more than 900 publications and have been presented at national and international meetings. In recognition of our past research accomplishments and future research plans, members of the research group have received more than 550 honors and awards, including membership in all three branches of the US National Academies – Medicine, Engineering and Sciences, US National Academy of Inventors, the 2013 US Medal of Science and more than 200 grants from various private and government agencies including the NCI Outstanding Investigator Grant (twice), the Advanced Medical Research Foundation, the Alex's Lemonade Stand Foundation, the American Association for Cancer Research, Brain Tumor Society, American Cancer Society, Burroughs Welcome Fund, Cancer Research Institute, the Charles A. King Trust, Children's Tumor Foundation, Cholangiocarcinoma Foundation, Damon Runyon Foundation, Ellison Foundation, Fat Disorders Research Society, Fund for Medical Discovery, the Bill and Melinda Gates Foundation, German Cancer Foundation, Goldhirsch Foundation, Humboldt Foundation, Jane's Trust Foundation, Lymphatic Education and Research Network, Ludwig Center at Harvard, Lustgarten Foundation, the National Institutes of Health, the National Foundation for Cancer Research, the National Science Foundation, Neuroendocrine Tumor Research Foundation, Susan Komen Foundation, United Negro College Fund, Innovator Award from the U.S. Army Breast Cancer Program, Yvonne Silverman Bequest and the Whitaker Foundation.

The Steele Laboratories are also dedicated to education, offering a bi-annual course in tumor pathophysiology to Harvard-MIT students. Annually, we also offer a continuing medical education course at Harvard Medical School on tumor microenvironment (angiogenesis, metastasis and Immunology) for national and international students, with the 39th offering scheduled for October 28 – November 1, 2024.

Rakesh K. Jain

Rakesh K. Jain, Ph.D.
Andrew Werk Cook Professor of Radiation Oncology (Tumor Biology)
Director, E.L. Steele Laboratories


Top 1% cited researcher
in Clinical Medicine
Citations per year
12,000
10,000
8,000
6,000
4,000
2,000
0
1990
1995
2000
2005
2010
2015
2020
Elected to the National Academy of Medicine (NAM)
Elected to the National Academy of Engineering (NAE)
Elected to the American Academy of Arts and Sciences
Elected to the National Academy of Science (NAS)
US National Medal of Science
Elected to the National Academy of Inventors



MISSION

Research

Understand how the tumor microenvironment fuels tumor progression and metastasis, and confers resistance to chemo-, radio- and immunotherapy

Develop and test new strategies in animal models to overcome the barriers posed by the tumor microenvironment for improved detection and treatment of primary and metastatic tumors

Translation

Translate these strategies from bench to bedside

Education

Educate basic scientists, bioengineers, and oncologists in the integrative biology of cancer

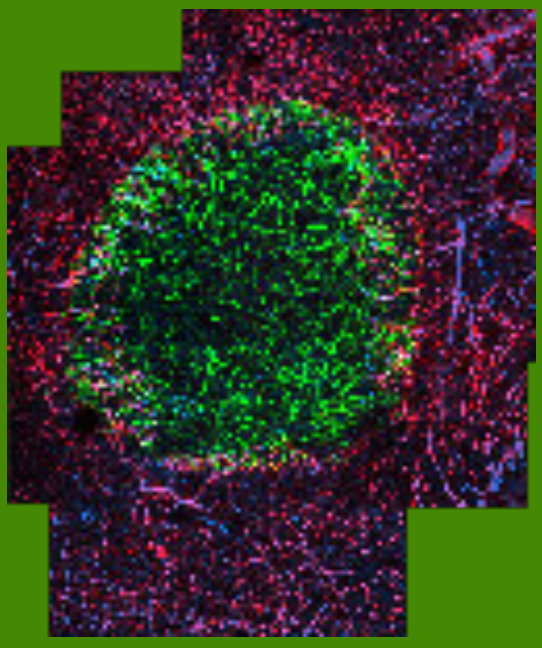
STRATEGIES

Research

- Unravel causal relationships between genetic and physiological function in various micro-environments using in vitro and in vivo microscopy, image analysis, genetic and pharmacological approaches.
- Analyze experimentally and mathematically the physical and physiological barriers and pharmacokinetics, and integrate the resulting information.
- Overcome barriers by creative manipulation of the tumor microenvironment.
- Emphasize multidisciplinary approaches, integration of engineering with tumor biology, and bench-to-bedside translation.

Education

- Develop and implement integrative tumor biology and bioengineering courses.
- Provide close mentorship by the faculty on individual research projects.



ACCOMPLISHMENTS

- Recruited and sustained a "critical" number of outstanding faculty, post-doctoral fellows, graduate students and technical staff to support core research.
- Initiated and continued collaborations with members of Massachusetts General Hospital, Harvard, MIT and other institutions.
- Established state-of-the-art intravital microscopy facilities.
- Developed unique in vivo tumor models.
- Published over 900 original and review articles in peer-reviewed journals, patents, and books in seven core research areas: Angiogenesis and blood flow, Tumor microenvironment, Transvascular transport, Interstitial and lymphatic transport, Cell mechanics and transport, Mathematical modeling, and Bench-to-bedside translation.
- Obtained research support from the National Cancer Institute and other government and private sources.
- Received more than 550 honors and awards from various scientific societies and academic institutions.
- Developed innovative courses in the integrative biology of cancer.
- Translated laboratory findings to cancer patients: e.g., the first treatment of schwannomas by bevacizumab and completion of more than three dozen multi-disciplinary clinical trials of anti-angiogenic therapy on cancer patients with brain, colorectal, liver, ovarian and connective tissue.
- Proposed the vascular normalization hypothesis that has changed the thinking in the field of oncology about how anti-VEGF targeted therapies work.
- Our preclinical work on the benefit of combining vascular normalization with immunotherapy laid the foundation of 7 FDA approvals of combining anti-VEGF/R agents with immune-checkpoint blockers for lung, liver, kidney and endometrial cancers.
- Proposed the matrix normalization hypothesis and showed the benefit of normalizing the tumor microenvironment using angiotensin system inhibitors in cancer in preclinical and clinical studies.

RESEARCH GRANTS AND AWARDS

1976-1999	National Science Foundation
1980-	National Institute of Health – Jain; Munn (2000 -); Fukumura (2002-); Boucher (2003-); Padera (2009-); Duda (2009-)
1980-	American Cancer Society – Jain; Burton (2000 - 2001); di Tomaso (2001-2003); Brown (2003-2004); Xu (2012-2016, 2020-)
1991-	Humboldt Fellowships - Leunig, Dellian, Sckell
1992-	National Research Service Awards - Berk, Munn, Litchtenbeld, Kadambi, Ramanujan, Koenig, Brown, Luong
1992	Kurt Wohl Lecturer (U. Delaware) - Jain
1992-1996	Howard Hughes Fellowship - Gazit, Ang
1992-1993	Hybritech-Lilly
1993-2000	Outstanding Investigator Grant, National Cancer Institute – Jain
1993, 1994	Instrumentation Awards, American Microcirculation Society - Berk, Leunig, Yuan, Jain
1994-1996	DuPont-Merck
1994-1996	Enzon
1994-2012	Deutsche Forschungsgemeinschaft - Patan, Hansen-Algenstaedt, Gralla, Kunert
1994	Outstanding Alumnus Award, Indian Institute of Technology – Jain
1995	Whitaker Award, Biomedical Engineering Society – Jain
1996-2002	US Army Breast Cancer Program
1996-2000	Whitaker Foundation (Munn)
1996-1999	Whitaker Junior Faculty Award - Berk, Munn
1996	Landis Award, Microcirculatory Society - Jain
1996-1998	Whitaker BERE Fellowship - Fukumura
1997-	National Science Foundation Fellowship – Padera, Lin, Pathak, Tong
1998-	National Foundation for Cancer Research
1998-	Election to Sigma Xi - Padera
1999-2000	Stewart Trust Award – Fukumura
1999	Kaplan Lecture (HMS), Berkeley Lecture (UCB) – Jain
2000	Pharmaceutical and Bioengineering Award, American Institute of Chemical Engineers – Jain
2000-2001	Human Science Foundation Fellowship –Izumi
2000-	Japanese Ministry of Health and Welfare Fellowship – Izumi, Kohno
2000-2001	Japanese Science and Technology Agency Fellowship – Ushiyama
2000-2002	Mildred-Scheel-Stiftung Deutsche Krebshilfe Fellowship – Bockhorn
2000-2001	Genentech
2000-2001	Miravant
2000-2001	ImClone
2000-2001	Whitaker Health Sciences Fund Fellowship – Padera
2000-2003	Biotechnology Training Program Fellow – McKee
2001-2002	Susan Komen Foundation Fellowship – Dolmans
2001-2003	University of Copenhagen Fellowship – Junker
2001-2003	Whitaker Foundation Graduate Fellowship – Cochran
2001	Honorary Fellow, Indian Institute of Chemical Engineers – Jain
2001-	Whitaker Foundation Graduate Fellowship – Tam
2001	Netherlands America Commission for Educational Exchange Fulbright Fellowship – Hagendoorn
2001-2003	Claflin Distinguished Scholar – Xu
2001-2003	University of Tsukuba, Ministry of Education Science and Culture of Japan - Koike
2001-2003	Foundation for Science and Technology of Portugal – Sousa
2002	Bioengineering Division Award of the American Institute for Chemical Engineers –Jain
2002-2006	The Goldhirsh Foundation
2002	Gerritsen Award, Microcirculatory Society – Jain
2002- 2005	Cancer Research Institute – Duda
2002-	Whitaker Foundation Graduate Fellowship – Mok
2003	Alumni Wall of Fame, University of Delaware - Jain
2003-2005	Emmy-Noether grant of the German Research Foundation – Winkler
2003-2005	Susan Komen Foundation Fellowship – Tong
2003-2008	NIH Research Career Development Award – Munn
2003	Institute of Medicine, the National Academy of Sciences – Jain
2003-2005	American Association for Cancer Research Career Development Award – Duda
2003-2005	Japan Society for the Promotion of Science – Nagano
2004	National Academy of Engineering, the National Academy of Sciences – Jain
2004	Robert Bras Lecturer, Princess Margaret Hospital and National Cancer Institute of Canada – Jain
2004-2024	NFCR Grant - Jain
2004-2005	National Defense Medical College Fellowship – Miyazaki
2005-2008	Damon Runyon Foundation Fellowship – Lahdenranta
2005	John S. Laughlin Lecturer, Memorial Sloan-Kettering Cancer Center, New York – Jain
2005	AstraZeneca
2005	French Medical Research Foundation Fellowship- LaCorre
2005	Academic Scientist of the Year, 2005 Pharmaceutical Achievement Awards – Jain
2006-2008	Brain Tumor Society
2006-2008	Claflin Distinguished Award – di Tomaso

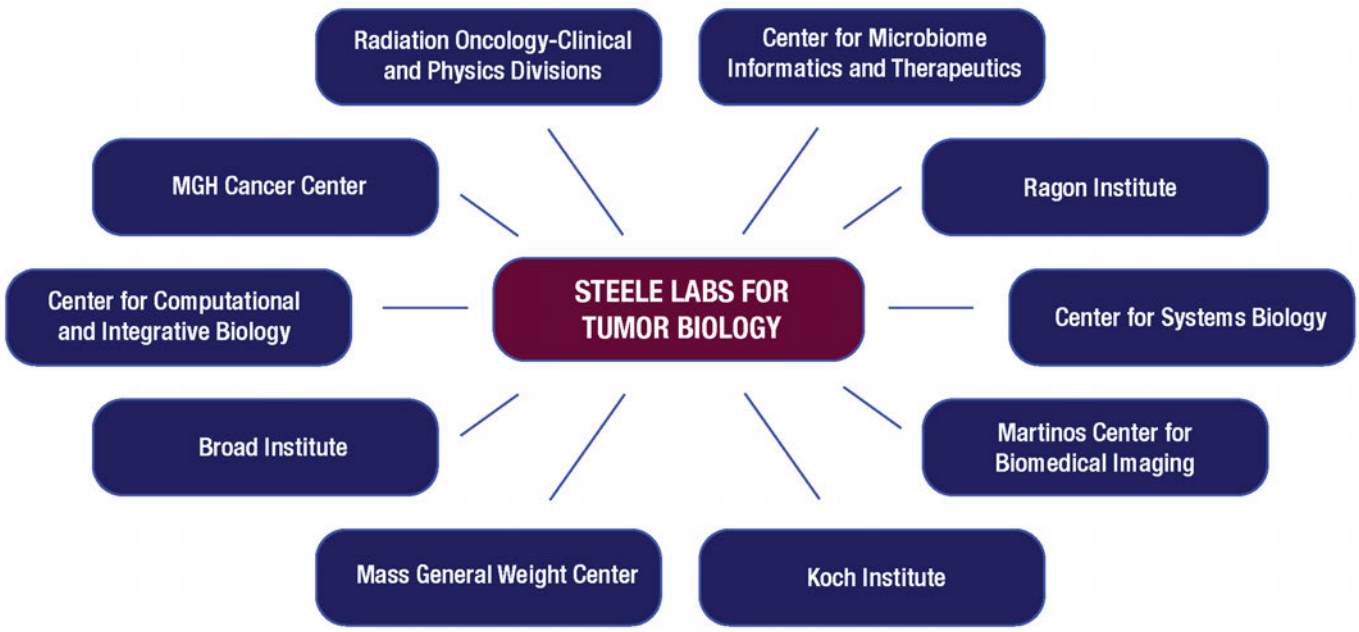
2006	Ford Foundation Diversity Fellowship – Dawson
2006-2009	Susan Komen Fellowship – Lacorre
2006-2009	Department of Defense Pre-doctoral Award – Lanning
2005-2008	Department of Defense Pre-doctoral Award – Pieters
2006	Distinguished Service Award, Nature Biotechnology - Miami Symposium on Angiogenesis – Jain
2006	Outstanding Achievement Award, Society of American Asian Scientists in Cancer Research – Jain
2006	Robert L. Krigel Lecture, Fox Chase Cancer Center, Philadelphia – Jain
2006	Alpha Chi Sigma Research Award, American Institute of Chemical Engineers – Jain
2006	Benjamin Zweifach Distinguished Lecture, The City College, New York – Jain
2007	Research Team Award, Clinical Research Day, MGH – Jain, di Tomaso, Duda, Kozak
2007	Uehara Memorial Foundation Fellowship – Yamashita
2007	Sam Gerson Leadership Chair of Research, Brain Tumor Society – Jain
2007	Drug Discovery Initiative Award, Children's Tumor Foundation – di Tomaso
2008	Sir Godfrey Hounsfield Lecture, Imperial College, London – Jain
2008	Richard D. Frisbee III Oncology Lecture, Yale University–Jain
2008	Sir Godfrey Hounsfield Lecture, Imperial College, London – Jain
2008	Peter C. Reilly Lecture, University of Notre Dame, Indiana–Jain
2008	Charles G. Moertel Lecture, Mayo Clinic, Rochester, Minnesota – Jain
2008	Ashland Distinguished Lecture, University of Kentucky, Lexington, Kentucky–Jain
2008	William E. Schiesser Lecture, Lehigh University, Bethlehem, Pennsylvania – Jain
2008	American Academy of Arts and Sciences–Jain
2008	Spiro Translational Research Award - Duda
2008	Susan Komen Fellowship - Kamoun
2008	Federal Share (Boucher)
2008	Tosteson Postdoctoral Fellowship Award from the Massachusetts Biomedical Research Corporation-Liao
2008	NIH Pathway to Independence Award-Padera
2009	National Academy of Sciences–Jain
2009	Dyax
2009	Zweifach Lecture, UCSD - Jain
2009	Susan Komen Fellowship - Stylianopoulos
2009	Merck Fellowship (Sodunke)
2009	Ruckenstein Lecture, University at Buffalo NY- Jain
2010	DoD Innovator Award (Jain)
2010	Pirkey Lecture, University of Texas at Austin - Jain
2010	Kelley Lectures, Purdue University - Jain
2010	William B. Lowrie Lecture, Ohio State Univ. - Jain
2010	Wagner Lecture, University of Michigan - Jain
2010	Spiro Translational Research Award - Duda
2010	Martin Research Prize for Excellence in Clinical Research-Padera, Tyrrell, Jain, di Tomaso
2011-	Federal Share (Boucher, Fukumura, Duda, Jain, Garkavtsev, Huang, Munn, Xu)
2011	Gates Foundation
2011	MedImmune (SRA)
2011	Roche (SRA)
2011	NIH Director's New Innovator Award - Padera
2011	Charles A. King Trust Fellowship Award - Liao
2011	Roland T. Lakey Award, Wayne State University - Jain
2011	American Cancer Society Basic Science Lecture, Society of Surgical Oncology - Jain
2011	Rous-Whipple Award, American Society of Investigative Pathology - Jain
2011	Irving O. Shoichet Lecture, University of Toronto, Canada – Jain
2011	Distinguished Research Lecturer, Carnegie Mellon - Jain
2012	NIH Pathway to Independence Award - Liao
2012	One of the 18 Indians Doing Cutting-Edge Research, Forbes (India) - Jain
2012	Herman Schwan Lecture, University of Pennsylvania-Jain
2012	ASCO Science of Oncology Award and Lecture, American Society of Clinical Oncology - Jain
2012	Election as an Honorary Member of the Academy of Medical Sciences of Romania - Duda
2012	2012 Children's Tumor Foundation – Clinical Research Award - Xu
2013	M. Gerritsen Award, Microcirculation Society - Fukumura, Duda, Munn, Jain
2013	Spiro Translational Research Award - Huang
2013	Max Kade Foundation - Reiberger
2013	Children's Tumor Foundation- Drug Discovery Initiative - Xu
2013	AACR-Boucher
2013-2023	Jane's Trust Foundation Grant - Jain
2014	M. Gerritsen Award, Microcirculation Society - Fukumura, Duda, Munn, Jain
2014-	One of the top 1% cited researchers in Clinical Medicine – Jain
2014	Earl Bakken Distinguished Lecture, Amer. Institute for Medical and Biological Engineering - Jain
2014	Spiro Translational Research Award - Huang
2014	AACR-Princess Takamatsu Lecture/Award, American Association for Cancer Research - Jain
2014	One of 50 Oncology Luminaries, American Society of Clinical Oncology (ASCO) - Jain

2014	Most cited paper (2013), Annals of Biomedical Engineering – Jain
2014	Fellow, American Association for the Advancement of Science (AAAS) - Jain
2014	Keio Medical Society Lecture, Japan - Duda
2014-2016	Warshaw Institute for Pancreatic Cancer Research Award - Duda
2015	NIH R01 - Munn, Padera, Jain
2015	Rice University Distinguished Alumnus Award – Munn
2015	Secretary General, IASGO – Duda
2015	"Eugene M. Landis Award" The Microcirculatory Society - Fukumura
2015	Honorary Doctorate, Katholieke Universiteit Leuven, Belgium – Jain
2015	MCS Landis Award Lecture, Annual Microcirculation Society Meeting, Boston
2015	Honorary Doctorate, Indian Institute of Technology (IIT), Kanpur, India - Jain
2015	Honorary Doctorate, Duke University -Jain
2015	Capussotti Award (International Association of Surgeons, Gastroenterologists, and Oncologists) – Duda
2015	Honoree of the One Hundred, Mass General Cancer Center – Duda
2015	Foreign Fellow, Indian National Science Academy (INSA) – Jain
2015	LE&RN/FDRS Lipedema Postdoctoral Fellowship - Bouta
2015	Schrodinger Fellowship by the Austrian Science Funds – Pinter
2015	Herman-Holtheusen Award of the German Societyfor Radiation Oncology - Askoxylakis
2015	Humboldt Foundation Feodor Lynen Research Fellowship – Schanne
2015	Susan G. Komen Foundation Postdoctoral Grant; FSQ Fellowship; FMD ECOR - Ferraro
2015	Tufts Graduate School of Arts and Sciences Travel Award, School of Engineering Travel Award, AACR Scholar in Training Award - Datta
2015	Poster of Distinction Award at MGH ECOR SAC Meeting - Ferraro, Datta
2015	De Beaumont Bonelli Foundation Travel Award, Lorini Foundation Award - Seano
2015	ABTA Fellowship - Chatterjee
2015	Keynote Speaker, Wolfsberg/ESTRO Radiation Biology Meeting - Duda
2015	AACR-Aflac, Incorporated Scholar in Training Award, Keystone Global Helath Award - Jung
2015	Tohoku Medical Society Lecture, Japan - Duda
2015	Award of the State Scholarship Fund by the China Scholarship Council (CSC) - Zhao
2015	Spiro Award - Padera, Xu
2015	Merrimack Pharma SRA - Duda
2015	Warshaw Institute for Pancreatic Cancer Research Award - Fukumura
2015	Nikon Small World Competition, 5th place - Seano
2015	Keynote Speaker, Neurooncology Group (NOA) Winterschool, Germany - Duda
2015	SPARC SRA - Garkavstev
2015	North America Vascular Biology Organization Outstanding Poster Award - Bazou
2015	Pierre Gilles de Gennes Fondation pour la Recherche Fellowship, Consejo Superior de Investigaciones Cientificas Award - Bazou
2015	Children's Tumor Foundation Drug Discovery Award - Xu
2015	NIH Outstanding Investigator Award - Jain
2015	Bill and Melinda Gates Foundation Grand Challenges: New Interventions in Global Health Award -Jain
2015	Ludwig Institute Grant - Jain
2015	Bayer, BMS SRAs - Duda
2015	Rice University Distinguished Alumnus Award – Munn
2016	Inductee, American Institute of Medical and Biological Engineeering - Munn
2016	Heroes of Hope Award Granara-Skerry Trust for Pancreatic Cancer Research - Duda
2016	Won Partners in Excellence Award - Roberge
2016	DoD New Investigator Award – Xu
2016	2016 AACR-GYRIG Scholar-in-Training Award – Jung
2014, 14, 16	One of the top 1% cited researchers in Clinical Medicine, Thomson Reuters - Jain
2016	Princess Takamatsu Cancer Research Fund International Lecturer, Japan - Jain
2016	SRA - Xu
2016	One of the Most Influential/Cited Authors on the 75th Anniversary of *Cancer Research* – Jain
2016	R. B. Trull Lecture, University of Texas, Austin – Jain
2016	United States National Medal of Science (for 2013) – Jain
2016	NIH F31 Fellowship – Datta
2016	AACR Postdoctoral Fellowship – Wong
2016	Tosteson Postdoctoral Fellowship – Nia
2016	Uehara Foundation Postdoctoral Fellowship – Shigeta
2016	NIH R01 – Padera, Munn
2016	Feodor-Lynen Postdoctoral Research Fellow – Ghosh
2016	The Kyoto Univ. Foundation – Kawaguchi
2016	Resource Center for Health Science (RECHS) – Kawaguchi
2017	2017 NIH R01 BRG – Fukumura/Jain
2017	NIH U01 – Jain/Pittet

2017	NIH R41 – Duda
2017	NCI/NIAID R01 BRG, Supplement – Jain/Pittet
2017-2021	Exelixis – Duda
2017-2019	Leap Tx SRA – Duda
2017	ECOR ISF Grants – Fukumura, Duda
2017	Lifetime Achievement Award, American Assoc. of Indian Scientists in Cancer Research – Jain
2017	Ramzi Cotran Lecture, Harvard Medical School – Jain
2017	Plenary Lecture, Hong Kong International Oncology Forum 2017 (HKIOF 2017) – Duda
2017	New England Choice Award – Jain
2017	Elected to the National Academy of Inventors - Jain
2017	Election to College of Fellows of American Institute of Medical and Biological Engeineering - Fukumura
2017	Swedish Research Council Fellowship - Andersson
2017	Keio Medical Society Lecture, Japan - Duda
2017-2025	Ludwig Center at Harvard Grant - Jain
2018	Maud Menten Lecture, University of Pittsburgh - Jain
2018	NIH Training Grant - Posada
2018	Cancer Research Institute Postdoctoral Fellowship - Talele
2018	One of the top 1% cited researchers in Clinical Medicine - Jain
2018	Totally "Rad" Researcher Employee of the year in Research - Huang
2018	IASGO Achievement Award - Duda
2018	NETF Pilot Grant – Duda
2018	Earl Benditt Award, North American Vascular Biology Organization -Jain
2018	One of the top 1% cited researchers in Clinical Medicine - Jain
2018	Cholangiocarcinoma Foundation – Aoki
2018	R21 - Padera
2018	Excellence Award, Romania-USA Chamber of Commerce - Duda
2018	Children's Tumor Fundation Drug Discovery Award - Xu
2019	Election to College of Fellows of American Institute of Medical and Biological Engeineering - Padera
2019	One of the top 1% cited researchers in Clinical Medicine – Jain, Fukumura
2019	Judah Folkman Lecture, Harvard Medical School/Boston Children's Hospital - Jain
2019	Jeffrey M. Isner Memorial Lecture, Tufts University School of Medicine – Jain
2019	ECOR ISF Grants - Xu
2019	ACR-Loxo Oncology Pediatric Cancer Research Fellowship - Datta
2019	Cancer Research Institute Postdoctoral Fellowship- Ren
2019	MGH Cancer center excellence award - Amoozgar
2019	DOD Horizon award - Krishnan
2019-2022	DOD Impact Award - Duda
2019-2021	DOD Idea Award - Duda
2019	Tosteson Fellowship – Ren
2019	German Cancer Aid DAAD Fellowship - Hauth
2019	Nile Albert Research Foundation Grant -Jain
2020	Election to College of Fellows of American Institute of Medical and Biological Engeineering - Duda
2020	Election as AACR Academy Fellow - Jain
2020-2022	NF Therapeutics SRA - Xu
2020-2023	DOD Investigator-Initiated Research Award - Xu
2020	One of the top 1% cited researchers in Clinical Medicine – Jain, Fukumura
2020	Excellence Award – World Ambassador of Romanian Medicine, Romanian Academy and Tarus Media - Duda
2021-2026	NIH R01 (x2) - Duda
2021-2026	NIH R01 – Munn/Duda
2021	NIH R01- Jain/Vander Heiden
2021	NIH U01- Munn/Jain
2021-2023	NIH R03 - Duda
2021-2024	DOD Idea Award - Duda
2021-2026	Rullo Family MGH Research Scholar - Padera
2021	One of the top 1% cited researchers in Clinical Medicine – Jain, Fukumura
2021	Doctor Honoris Causa, University of Medicine Iasi, Romania - Duda
2021-2023	Japan Society for the Promotion of Science Fellowship - Morita
2022	Election Fellow of the American Association for the Advancement of Science (AAAS) - Duda
2022	NIH R01 – Jain
2022-2023	Warshaw Institute for Pancreatic Cancer Research Award - Duda
2022	One of the top 1% cited researchers in Clinical Medicine – Jain, Fukumura
2022	Szent-Györgyi Prize for Progress in Cancer Research from The National Foundation for Cancer Research (NFCR) - Jain
2022-2027	NIH R01 - Jain
2022	Inaugural Dr. Youcef Rustum Lecture, Roswell Park Cancer Center, Buffalo - Jain
2022	Keio Medical Society Lecture, Japan - Duda
2022	International Honorary Member, Japanese Cancer Association - Jain
2022	Seiki Matsuno State-of-the-Art Lecture Joint Congress – 26th IAP and 53rd JSP Meetings, Kyoto, Japan - Duda

2022	Team Science – Honorable Mention, MGH Clinical Research Day – Jain, Duda
2022-2024	DOD Impact Award - Xu
2022-2024	Children's Tumor Foundation Award - Xu
2022	Erudite Scholar-in-Residence Kerala State Higher Education Council (KSHEC), India - Duda
2023	One of the top 1% cited researchers in Clinical Medicine – Jain
2023	Smith Family Foundation Lecture, MD Anderson Cancer Center - Jain
2023	Induction into the College of IASGO Fellows (FASGO) - Duda
2023	Election Fellow of the American Association for the Advancement of Science (AAAS) - Padera
2023	Appointed to the Congressionally mandated National Commission on Lymphatic Diseases - Padera

2023	Children's Tumor Foundation Young Investigator Award - Yin
2023-2024	Children's Tumor Foundation Award - Xu
2023	Foreign Member, Academia Europaea (The Academy of Europe) - Duda
2023-2027	Takeda Science Foundation Fellowship - Ando
2023	MGH ECOR Fund for Medical Discovery (FMD) Fundamental Research Fellowship - Morita
2023	MGH ECOR Fund for Medical Discovery (FMD) Fundamental Research Fellowship - Subudhi
2023-2028	NIH R01 – Munn/Padera
2023-2028	NIH R01 - Padera
2023-2028	NIH R01 (x2) – Xu
2023	Honorary Doctorate, University of Delaware - Jain
2023	"Best Scientist" by Research.com - Jain



RESEARCH GOALS

The long-term goal of our research is to reveal the role of host-tumor interactions in the biology and therapeutic response of tumors and to translate this insight into improved cancer detection, prevention and treatment. A quantitative understanding of pathophysiology of solid tumors is developed using five unique yet complementary approaches in our research

1 a microscopic approach to directly visualize gene expression, physiological function and delivery of therapeutics *in vivo*.

2 a macroscopic approach using tissue-isolated tumors to access and monitor arterial and venous blood in rodent and human tumors.

3 in vitro characterization of deformability, permeability, migration, adhesion and force generation in cells

4 molecular and genetic approaches as well as the development of transgenic cell lines and animals

5 mathematical modeling to integrate existing data and to guide new clinical and experimental studies.

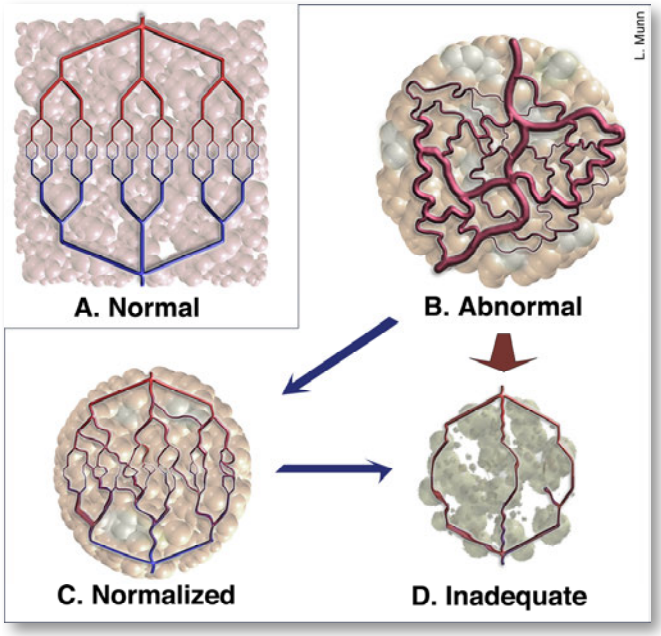
These five approaches are intertwined in seven multi-disciplinary projects

1. tumor angiogenesis and blood flow
2. metabolic microenvironment
3. transvascular transport
4. interstitial and lymphatic transport
5. cell mechanics and transport;
6. mathematical modeling
7. translation of laboratory findings to the clinic

The goals of the first project are to understand the molecular and physical mechanisms underlying the temporal and spatial heterogeneities in tumor vasculature; and to develop strategies for manipulating these parameters to "normalize" the tumor vasculature.
The goals of the second project are to determine molecular and cellular mechanisms that lead to the abnormal tumor microenvironment and to develop strategies to "normalize" the microenvironment.
The goals of the third project are to characterize transvascular transport pathways in tumors, to identify molecular mechanisms that govern transport of molecules across the vessel wall, and to develop molecular and physiological strategies for improved transport.
The goals of the fourth project are to characterize transport in the interstitium and relate it to the interstitial structure, to determine the causes of interstitial hypertension, to develop strategies to alter pressure in solid tumors, and to examine the diagnostic and prognostic value of tumor interstitial pressure in the management of cancer. Since lack of functioning lymphatics is a major cause of interstitial hypertension, a related goal is to further our understanding of lymph transport, and to identify inhibitors of lymphangiogenesis and lymphatic function in tumors.
The goals of the fifth project are to quantify the structural rigidity, force generation, and motility of cancer cells and of various lymphocyte subpopulations, to measure the adhesive interactions among lymphocytes, endothelial cells and tumor cells, to define the mechanisms which control these structural and functional properties, to relate these biophysical parameters with the in vivo movement of lymphocytes and cancer cells and to develop novel technologies for separating rare cells from blood based on this understanding.

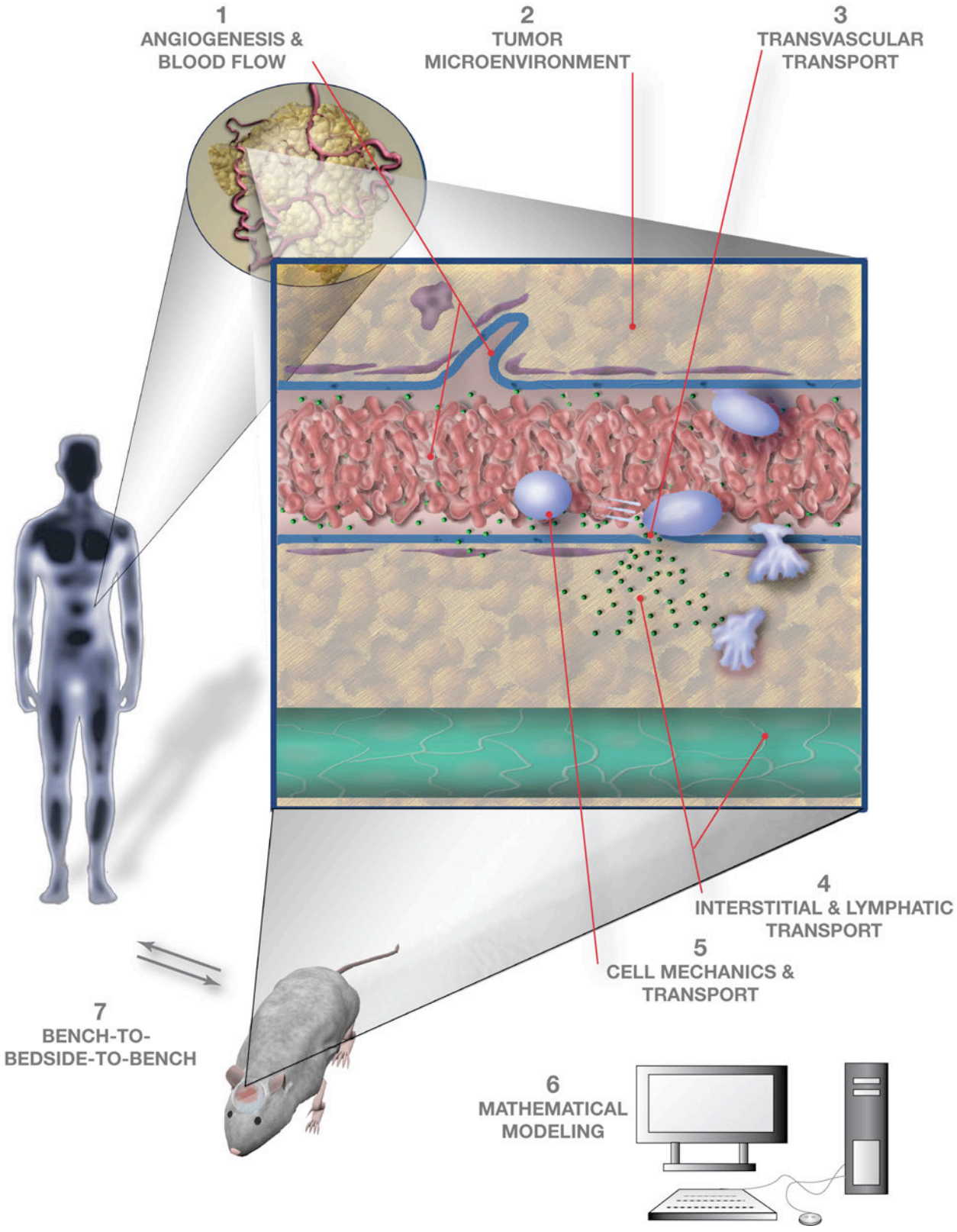
Vascular cast of human colon tumor vessels used to study vascular abnormalities. The plastic material was injected and polymerized after the surgical resection of a tumor from the colon of a patient.

The goal of the sixth project is to bring together the knowledge generated in the first five projects by developing appropriate mathematical models. Current efforts are focused on improving the delivery of therapeutic agents to tumors using various approaches, scale-up of rodent data to humans, fractal analysis of vascular networks, mathematical modeling of angiogenesis and leukocyte-endothelial interactions and development of new transport and growth equations for solid tumors based.
The goal of the seventh project is to translate our laboratory findings in the clinic with the goal of improving current therapies and to develop new molecular and cellular biomarkers for individualizing cancer treatment.
We believe that our work will continue to provide valuable insight into tumor pathophysiology and suggest novel strategies for improved detection, prevention and treatment of solid tumors.



Normalization hypothesis: Anti-angiogenesis drugs cause abnormal tumor vessels (B) to become more normal with better function (C), allowing uniform drug delivery and more effective radiation therapy.

RESEARCH HIGHLIGHTS



RESEARCH HIGHLIGHTS

1 Angiogenesis and Blood Flow

- Developed sophisticated animal models for studies of tumor angiogenesis, microcirculation, progression, metastases and treatments including dorsal window (Leunig et al., 1992b, Leunig et al., 1995, Leunig et al., 1997), cranial window (Yuan et al., 1994b), liver ((Fukumura et al., 1997b), gallbladder (Gohongi et al., 1999), pancreas (Tsuzuki et al., 2001), mammary fat pad (Monsky et al., 2002), tissue-isolated tumor (Kristjansen et al., 1994, Kristjansen et al., 1996).
- Developed state of the art imaging techniques for in vivo studies including multiphoton laser-scanning microscopy (Brown et al., 2001; Padera et al, 2002), Quantum dots (Stroh et al., 2005; Allen et al, 2010; Liu et al., 2010; Chen et al., 2013), Life time imaging (Kumar et al., 2009), OFDI (Vakoc et al, 2009), (Kim et al., 2010), (Kamoun et al., 2010), video-rate MPLSM (Kirkpatrick et al., 2012),
- Developed a noninvasive model to visualize angiogenesis and adipogenesis and found provocative reciprocal regulation between them, suggesting a novel therapy for obesity related diseases including cancer (Fukumura et al., 2003; Tam et al., 2009b). Established a physiologically based mathematical model to study body weight balance (Tam et al., 2009a).
- Provided the first quantitative measurements of geometric resistance to blood flow and of branching patterns in the rat and human tumor vasculature (Less et al., 1991).
- Established and tested a network model to explain the effect of vasoactive agents on tumor blood flow and interstitial fluid pressure (Zlotecki et al., 1995).
- Developed a novel scheme to quantify the vascular architecture in a tumor (Gazit et al., 1995, Gazit et al., 1997). This analysis has allowed us to calculate the role of vascular heterogeneity in nutrient and drug delivery of tumors (Baish et al., 1997, 2011, Baish and Jain, 2000, 2001).
- Utilized tissue-isolated tumors for residence time distribution studies to examine the accuracy of models used to estimate blood flow (Eskey et al., 1994) and for drug uptake studies to investigate barriers to drug delivery (Kristjansen et al., 1996, Heijn et al., 1999).
- Discovered new mechanisms of tumor angiogenesis (Patan et al., 1996) and vascular anastomosis (Cheng et al., 2011).
- Discovered a new mechanism of intermittent blood flow in tumors (Netti et al., 1996, 2001).
- Demonstrated roles of nitric oxide (Fukumura and Jain, 1998; Fukumura et al., 2006) on the regulation of tumor blood flow (Kristensen et al., 1997; Fukumura et al., 1997a), angiogenesis (Fukumura et al., 2001) and pericyte recruitment (Kashiwagi et al., 2005), and that perivascular nitric oxide gradients normalize tumor vasculature (Kashiwagi et al., 2008) and Tie-2 activation potentiate it (Goel et al., 2013).
- Measured the stress generated by tumor growth to explain vascular collapse (Helmlinger et al., 1997b; Koike et al., 2002) and showed that relieving stress by inducing tumor cell apoptosis could open vessels (Griffon-Etienne et al., 1999; Padera et al., 2004).
- Demonstrated the importance of host organ in tumor angiogenesis, microcirculation (Fukumura et al., 1997b; Tsuzuki et al., 2001; Monsky et al., 2002) and VEGF/bFGF induced vessels (Dellian et al., 1996a), suppression of secondary angiogenesis (Sckell et al., 1998, Gohongi et al., 1999; Hartford et al., 2000) and response to anti-VEGF and HER2 therapies (Bockhorn et al., 2003; Kodack et al., 2012).
- Discovered that tumor induces VEGF-promoter activity in the host fibroblasts (Fukumura et al., 1998), these activated fibroblasts play an active role in angiogenesis (Brown et al., 2001) and the host cells contribute significantly to VEGF production (Tsuzuki et al., 2000) and compensate tumor cells' production (Izumi et al., 2002)
- Discovered indirect pro-/anti-angiogenic effects such as hormone therapy/withdrawal (Jain et al., 1998a; Kristensen et al., 1999b) on blood flow and microcirculation in tumors angiogenesis. Anti-HER2 therapies (Izumi et al., 2002; Kodack et al., 2012)
- Demonstrated that VEGF produced by endothelial cells in oxygen gradients can lead to vascular network formation in vitro (Helmlinger et al., 2000).
- Quantified the frequency of mosaic vessels in tumors (Chang et al., 2000).
- Demonstrated that anti-VEGF and anti -VEGF-R2 antibodies potentiate radiation-induced short- and long-term tumor control (Lee et al., 2000; Kozin et al., 2001).
- Demonstrated that decorin inhibits angiogenesis in vitro (Davies et al., 2001).
- Proposed that judiciously applied anti-angiogenic therapy can normalize tumor vasculature (Jain, 2001).
- Discovered the mechanism of blood flow shutdown by PDT (Dolmans et al., 2002a,b).
- Demonstrated that VEGF blockade can retard the growth of spontaneous autochthonus tumors (Izumi et al., 2003).
- Created long-lasting blood vessels in vivo using endothelial cells and mesenchymal precursor cells (Koike et al., 2004), hES cells (Wang et al., 2007), EPCs (Au et al., 2008a), MSCs (Au et al., 2008b), human iPS cells (Samuel et al., 2013).
- Discovered the differential transplantability of tumor stromal cells and stromal cell metastasis (Duda et al., 2004, 2010).
- Demonstrated normalization of tumor vasculature by an anti-angiogenic therapy (Tong et al., 2004; Winkler et al., 2004; Kashiwagi et al., 2008; Kamoun et al., 2009; Huang et al., 2012)
- Characterized nanoparticle transport (Stroh et al., 2005) and the effect of size (Popović et al., 2010; Chauhan et al., 2012), charge (Campbell et al., 2002; Stylianopoulos et al., 2010 & 2013; Han et al., 2013), shape (Chauhan e al., 2011), multistage system (Wong et al., 2011), and vascular normalization (Chauhan et al., 2012)
- Discovered Ang-2 as a potential target for anti-VEGF therapy reistance (Chae et al., 2010; Peterson et al., 2016; Kloepper et al., 2016).
- Demonstrated that CXCR4 promotes metastasis via Gr-1+ BMDC recruitment (Hiratsuka et al., 2011a).
- Discovered that tumors prime metastatic "soil" by inducing focal hyperpermeability in the lungs (Hiratsuka et al., 2011b).
- Determined how fluid forces and VEGF cooperate to control angiogenic sprouting (Song & Munn, 2011)
- Discovered PlGF/NRP1 as a novel therapeutic target in pediatric medulloblastoma (Snuderl et al., 2013)
- Discovered obesity induces anti-VEGF therapy resistance via IL-6 and bFGF (Incio et al., 2018).
- Used experimental and computational analyses to reveal the dynamics of tumor vessel cooption and optimal treatment strategies to prevent brain tumor escape from antiangiogenic therapy (Vouturi et al., 2019).
- Demonstrated that normalizing tumor blood vessels may improve immunotherapy against brain cancer (Dong et al., 2023)

2 Tumor Microenvironment

- Adapted and developed fluorescence ratio imaging microscopy (FRIM) to measure pH in vivo in normal and tumor microcirculation in the rabbit ear chamber and mouse dorsal chamber (Martin and Jain, 1993, Martin and Jain, 1994, Dellian et al., 1996b).
- Provided the first combined measurement of pH and pO2 profiles in human tumor xenografts (Helmlinger et al., 1997a).
- Demonstrated that VEGF produced by endothelial cells in oxygen gradients can lead to vascular network formation in vitro via an autocrine mechanism (Helmlinger et al., 2000).
- Measured oxygen consumption of endothelial cells in vitro (Helmlinger et al., 2000) and during various treatments (Hansen-Algenstaedt et al., 2000).
- Delineated the mechanisms of low pH in tumors (Helmlinger et al., 2002).
- Measured glucose metabolism and vascular parameters in lung cancer patients using PET and MRI (Hunter et al., 1998).
- Measured the effect of creatine and cyclocreatine on energy levels in tumors (Kristensen et al., 1999a).
- Determined increase in tumor pO2 by modified hemoglobins (Nozue et al., 1996).
- Examined the feasibility of the Eppendorf histograph for pO2 measurements (Nozue et al., 1997a,1997b).
- Demonstrated a lack of universal correlation between pO2 and IFP (Boucher et al., 1995).
- Discovered that HIF1α deletion leads to lower VEGF expression, angiogenesis and oxygenation, yet the tumors grow more rapidly (Carmeliet et al., 1998), and H1F1α (-/-) cells localize in hypoxic regions (Brown et al, 2001).
- Discovered that low pH and pO2 independently regulate VEGF (Fukumura et al, 2001), and delineated the signaling pathways for low pH induced VEGF upregulation (Xu et al., 2002).
- Demonstrated signaling pathways in hypoxia-induced IL-8 expression (Xu et al., 2004).
- Demonstrated that HIF-2α acts as a tumor suppressor (Acker et al., 2005).
- Discovered that the judicious application of anti-angiogenic therapy alleviates hypoxia in tumors (Winkler et al, 2004).
- Developed "smart" nanoparticles that become smaller in size once they enter the tumor microenvironment and penetrate deeper into tumors (Wong et al, 2011)
- Discovered that medulloblastoma cells stimulate stromal granule cells via Shh to produce PlGF, which promotes medulloblastoma cell growth and spread (Snuderl et al., 2013)
- Discovered that reprogramming liver tumor microenvironment using CXCR4 inhibition can facilitate immunotherapy (Chen et al, 2015)
- Discovered that obesity induces inflammation, desmoplasia and resistance to anti-angiogenic therapy in breast cancer via IL-6 and bFGF (Incio et al., 2018) and chemotherapy in pancreatic cancer via IL-1 (Incio et al., 2016).
- Demonstrated the role of the liver immune microenvironment in colon cancer resistance to immunotherapy (Ho et al., 2020)
- Demonstrated the role of the brain metabolic microenvironment in breast cancer resistance to therapy (Ferraro et al., 2021)

3 Transvascular Transport

- Found that decompressing vessels with angiotensin inhibition can enhance oxygen delivery to tumors (Chauhan et al., 2013)
- Provided the first measurement of microvascular permeability in a human tumor xenograft using intravital fluorescence microscopy (Yuan et al., 1993).
- Demonstrated that the local microenvironment of tumors can control permeability (Yuan et al., 1994b; Fukumura et al., 1997b).
- Showed that anti-VEGF antibody or hormone withdrawal can lower tumor permeability and lead to vascular regression (Yuan et al., 1996, Jain et al., 1998a, Lichtenbeld et al., 1999, Jain et al., 1998), yet VEGF showed no correlation with vascular permeability in different sites (Fukumura et al., 1997b).
- Measured the molecular weight and charge dependencies of vascular permeability (Yuan et al., 1994a, 1995; Dellian et al., 2000; Campbell et al., 2002) and discovered that the pore size cut-off for transvascular pathways depends on tumor-host interaction and changes in response to therapy (Hobbs et al., 1998).
- Discovered that hyperpermeability of tumor vessels coupled with high interstitial pressure can lead to vascular stasis (Netti et al., 1996, Baish et al., 1997).
- Measured the hydraulic conductivity (Sevick and Jain, 1991a) and distribution of water channel protein (AQP1) in tumors (Endo et al., 1999).
- Discovered that increase in vascular permeability by VEGF depends on the host-origin of endothelium (Chang et al., 2000) and host-tumor interaction (Monsky et al., 1999).
- Demonstrated that the gaps between endothelial cells cause hyperpermeability in tumors (Hashizume et al., 2000).
- Measured the effect of PlGF and VEGF on the hydraulic conductivity of endothelium in vitro (Dull et al, 2001).
- Demonstrated induction of vascular permeability by nitric oxide in tumors and VEGF-induced angiogenic vessels (Fukumura et al., 1997a and 2001).
- Demonstrated that anti-VEGFR2 antibody reduces vascular permeability and normalizes tumor vasculature (Tong et al., 2004; Winkler et al., 2004).
- Examined how focal vessel hyperpermeability can influence network flow patterns (Sun et al., 2008).
- Found that modulating nanoparticle shape can enhance the penetration of tumors (Chauhan et al., 2011)
- Determined that vascular normalization can enhance the penetration of small but not large nanomedicines in tumors (Chauhan et al., 2012)
- Discovered that inhibiting VE-PTP, which itself inhibits the vessel maturation activities of Tie-2, matures vessels in primary and metastatic lesions to prevent disease progression and enhance radiation sensitivity (Goel et al., 2013)
- Demonstrated focused ultrasound-induced BTB distruction and enhanced drug delivery in brain metastasis (Arvanitisa et al., 2018)
- Demonstrated that optimized exercise therapy induces vessel normalization, boosts antitumor effector cell infiltration and function, and delays tumor growth in a CXCR3 pathway/CD8+ T cell- dependent manner (Gomes-Santos et al., Cancer Immunol Res 2021).

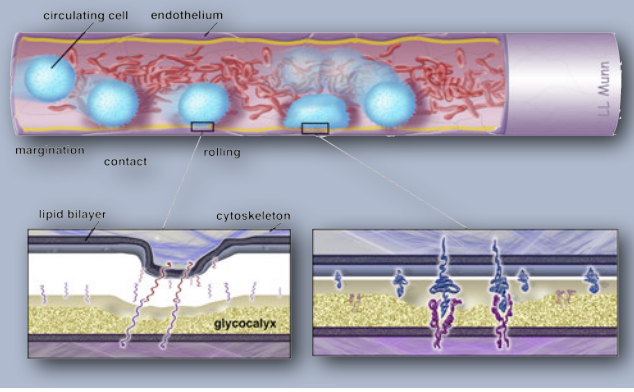
4 Interstitial and Lymphatic Transport

- Provided evidence that microvascular pressure is the principal driving force for interstitial hypertension in tumors (Boucher et al., 1992, Zlotecki et al., 1993, 1995), and that interstitial pressure goes up with the onset of angiogenesis (Boucher et al., 1996).
- Theoretically predicted and experimentally confirmed the time constants of transvascular and interstitial fluid exchange in tumors (Netti et al., 1995) and developed a novel strategy for improving drug delivery based on these findings (Netti et al., 1999).
- Demonstrated that it is possible to lower tumor pressure using nicotinamide (Lee et al., 1992), dexamethasone (Kristjansen et al., 1993), pentoxifylline (Lee et al., 1994a), hemodilution (Lee et al., 1994b), TNFα (Kristensen et al., 1996, Kristensen et al., 1997), taxanes (Griffon-Etienne et al., 1999), radiation (Znati et al., 1996) and various vasoactive agents (Zlotecki et al., 1995).
- Suggested the possibility that pressure could be used as a prognostic marker (Leunig et al., 1992a, Leunig et al., 1994a).
- Demonstrated a lack of universal correlation between pO2 and IFP (Boucher et al., 1995).
- Adapted fluorescence recovery after photobleaching (FRAP) to thick samples (Beck et al., 1993) and used it to measure the effect of charge, molecular weight and configuration on diffusion in gels (Johnson et al., 1995, Johnson et al., 1996a, Johnson et al., 1996b, Pluen et al., 1999).
- Measured the hydraulic conductivity of the tumor interstitial matrix (Boucher et al., 1998).
- Discovered that collagen network contributes to resistance (Netti et al., 2000; Davies et al., 2002; Ramanujan et al., 2002), and to host-organ dependence of interstitial transport in tumors (Pluen, et al, 2001).
- Adapted FRAP to measure binding kinetics between antibody and tumor associated antigens in vitro (Kaufman et al., 1991, Kaufman et al., 1992a, Kaufman et al., 1992b) and in vivo (Berk et al., 1997).
- Demonstrated that VEGF-C, the first lymphangiogenic molecule, leads to lymphatic hyperplasia in skin (Jeltsch et al., 1997), in the tumor margin (Padera et al, 2002), and angiogenesis in tumors (Kadambi et al, 2001).
- Developed a new model for lymphatic transport (Leu et al., 1994) and measured flow velocities in lymph capillaries of the tail skin of mice using RTD and FRAP (Swartz et al., 1996, Berk et al., 1996).
- Provided the first measurements of oncotic pressure in tumors (Stohrer et al, 2000).
- Demonstrated the absence of functional lymphatics in tumors despite the presence of VEGF-C and its receptors (Leu et al., 2000; Padera et al., 2002).
- Demonstrated that LYVE-1 is not specific to lymphatics, and LYVE-1 Prox1 structures, presumably lymphatics are absent in primary and secondary tumors in livers of patients (Mouta-Carreira, et al, 2001)
- Developed a new model for acute lymphedema in the tail and alleviated edema using a flap transfer (Slavin et al., 1999, Losken et al, 2001).
- Developed a technique for optically imaging collagen in tumors in vivo using second harmonic generation (Brown et al., 2003).
- Quantified the dynamics of collagen modification after pharmacologic intervention and provided mechanistic insight into improved diffusive transport induced by the hormone relaxin (Brown et al., 2003).
- Demonstrated that radiation enhances the production of collagen I and reduces fluid flow in tumors (Znati et al., 2003).
- Developed a two-photon correlation microscopy technique and found two-phase nature of interstitial transport in tumors (Alexandrakis et al., 2004).
- Demonstrated that compressive mechanical forces generated by proliferating cancer cells can cause the collapse of intratumor blood and lymphatic vessels (Padera et al., 2004).
- Demonstrated that VEGF-C overexpression leads to the formation of lymphatic vessels that demonstrate retrograde flow and implies that the VEGF-C alone can not produce mature, functional lymphatic vessels (Isaka et al., 2004).
- Demonstrated that nitric oxide and eNOS act on the collecting lymphatic vessels, but not the initial lymphatic vessels, of the mouse tail and alters the rate of lymph flow in these vessels (Hagendoorn et al., 2004).
- Demonstrated that VEGF signaling blockade reduces the tumor interstitial fluid pressure in experimental tumors (Lee et al., 2000; Tong et al., 2004).
- Evaluated tadpole model as a novel system to study lymphangiogenesis (Ny et al., 2005)
- Discovered elevated IFP and abnormal lymphatics in premalignant lesions (Hagendoorn et al., 2006).
- Imaged each step in the process of lymphatic metastasis and found that VEGF-C increases cancer cell arrival in the lymph node and thereby increases metastasis formation (Hoshida et al., 2006).
- Demonstrated a lack of efficacy of VEGFR TKIs against lymphatic metastasis in the adjuvant setting (Padera et al., 2008)
- Demonstrated the critical function of NO in the autonomous contraction of collecting lymphatic vessels (Liao et al., 2011).
- Discovered that the widely prescribed anti-hypertensive drugs can "normalize" the collagen matrix and improve the delivery and efficacy of drugs in desmoplastic tumors (Diop-Frimpong et al, 2011).
- Found that TGF-beta inhibition can enhance the penetration and efficacy of nanomedicines in tumors (Liu et al., 2012)
- Discovered that VEGF-C sensitizes lymphatic endothelial cells to radiation (Kesler et al., 2014)
- Found that lymph node metastasis do not require sprouting angiogenesis in order to grow (Jeong, Jones et al., 2015).
- Developed mathematical model to characterize the role of mechanobiological inputs in driving lymphatic pumping (Kunert et al., 2015).
- Demonstrated the first dynamic lymph flow measurement without injected contrast in vivo (Blatter et al., 2016).
- Showed that MRSA infections permenantly impair lymphatic pumping by killing lymphatic muscle cells (Jones et al., 2018).
- Showed that lymph node metastasis can invade lymph node blood vessels, escape the lymph node, and colonize distant metastatic sites (Pereira et al 2018).
- Showed that tumor draining lymphatic vessels have impaired pumping (Liao et al 2019)
- Demonstrated that cancer-related solid stress impairs lymphocyte infiltration into lymph-node metastases (Jones et al., 2021).
- Simulated the effects of gravity on lymphatic pumping (Li et al., 2022).
- Showed that cancer cells in metastatic lymph nodes can cause the formation of immune suppressive regulatory T cells by expressing MHCII molecules (Lei et al., 2023).

- Adapted and further developed rectangular and cylindrical systems to quantify deformation, rolling and adhesion of lymphocytes (Munn et al., 1994, Yuan et al., 2000).
- Developed a new technology to measure membrane-associated antigen in intact cell monolayers (Munn et al., 1995).
- Demonstrated that interleukin-2 (IL-2) increases the rigidity of NK cells (Melder and Jain, 1992) and that thioglycollate can reduce the rigidity of IL-2 activated NK cells without affecting their cytotoxicity or adhesiveness (Melder and Jain, 1994), and thus avoid entrapment in the lungs (Melder et al, 2001)
- Discovered that RBCs augment selectin and integrin mediated rolling and adhesion of lymphocytes to the vascular endothelium both in vitro and in vivo (Melder et al., 1995b, Munn et al., 1996, Melder et al., 2000; Yuan et al., 2001).
- Demonstrated that rolling in the dorsal skin is reduced but not eliminated in P-selectin deficient mice (Yamada et al., 1995a), and that rolling increases with age (Yamada et al., 1995b).
- Discovered that rolling is normal, but adhesion is reduced in E-selectin Mice (Milstone et al., 1998).
- Demonstrated using three different in vivo tumor models that IL-2 activated NK cells preferentially adhere to the tumor vasculature (Ohkubo et al., 1991, Sasaki et al., 1991, Melder et al., 1993, Melder et al., 1994, Melder et al., 1995a), even though the leukocyte-endothelial interaction in tumors is heterogeneous (Fukumura et al., 1995) and differs among subpopulations of lymphocytes (Melder et al., 1997, Koenig et al.,2000).
- Discovered the connection between angiogenesis and leukocyte adhesion (Melder et al., 1996, Detmar et al., 1998, Moulton et al., 1999).
- Discovered that VEGF upregulates while bFGF downregulates adhesion molecules in vascular endothelium in vitro and in vivo (Melder et al., 1996, Detmar et al., 1998, Jain et al., 1998) and PKCγ, PLD and PKC signaling is involved in inhibition by bFGF (Koenig et al., 2000).
- Developed a physiologically based model of cell biodistribution in mice and humans (Zhu et al., 1996).
- Developed a new method for labeling cells for in vivo biodistribution studies using PET and MRI (Melder et al., 1993, Melder et al., 1994, Schoeph et al., 1998).

Cell adhesion to vascular endothelium can be facilitated by specific adhesion molecules.

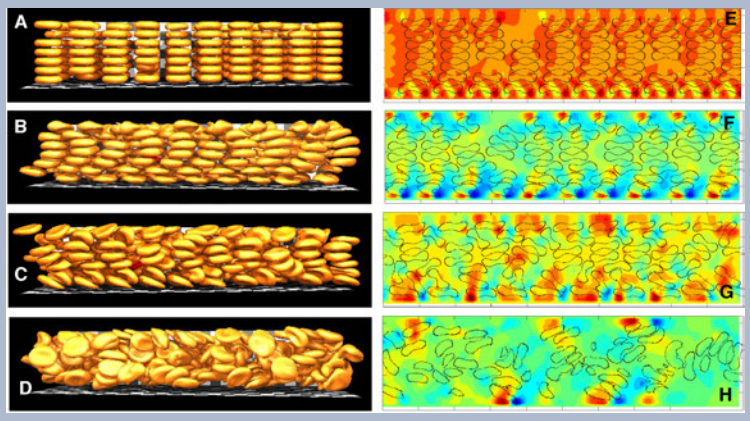
- Using a chorioallantoic membrane model and in vivo microscopy, characterized the early events in metastasis and examined the induction of metastasis-related genes (Shioda et al., 1997).
- Showed increased rate of lymphocyte turnover in SIV-injected macaques (Rosenzweig et al., 1998), and differential proliferation in lymphocytes in acute SIV infection (Kaur et al., 2000).
- Demonstrated tumor targeting by salmonella and showed that salmonella accumulation in tumors is due to selective growth in necrotic regions rather than active migration (Forbes et al., 2003).
- Demonstrated that bone marrow stem cells can be labeled with quantum dots for improved in vivo detection (Stroh et al., 2005).
- Quantified bone-marrow cell-derived neovascularization in transplanted and spontaneous tumors and demonstrated its dependence on mouse strain and tumor site (Duda et al., 2005)
- Demonstration that telopeptide-free collagen I enhances RhoA activity and the invasion of a metastatic breast tumor cell line (Demou et al., 2005).
- Demonstrated that platelets play a role in angiogenesis (Kisucka et al., 2006).
- Evaluated circulating endothelial cells (CECs) as a biomarker for antiangiogenic therapy in cancer patients, and characterized the phenotype of CECs (Willett et al., 2004; Willett et al., 2005; Duda et al., 2006).
- Discovered that mechanical compressive stresses can make cancer cells more invasive (Tse et al, 2011).
- Identified the components of tumors that contribute to compressive mechanical stresses in tumors (Stylianopoulos et al., 2012) and anti-VEGF therapy and obesity induces ECM deposition and mechanical stress that compress blood vessels (Rahbari et al, 2016; Incio et al, 2015 & 2016)
- Desmonstrated that targeting cancer-associated fibroblast activity can reduce compressive mechanical stresses in tumors to decompress vessels, increase perfusion, and enhance chemotherapy efficacy (Chauhan et al., 2013) and targeting fibroblasts by angiotensin receptor blocker (ARB) significantly improved pancreatic cancer surgery (Liu et al, 2017; Murphy et al, 2018)
- Reported that patients with hypertension who were concomitantly taking a renin–angiotensin–aldosterone system (RAAS) inhibitor during immune checkpoint inhibitor therapy had better overall survival (Drobni et al, 2022)



RESEARCH HIGHLIGHTS

6 Mathematical Modeling

- Developed macro- and microscopic distributed models for antibody distribution in tumors to demonstrate the role of binding (Baxter and Jain, 1991a, Baxter and Jain, 1991b).
- Developed lumped and distributed models for bifunctional antibodies and haptens and described the data available in the literature (Yuan et al., 1991; Baxter et al., 1992).
- Developed a physiologically based pharmacokinetic model for antibody using one- and two-step approaches. The model described the data in mice (Baxter et al., 1994) and predicted the human data (Baxter et al., 1995), and allowed dose estimations (Zhu et al., 1997, Zhu et al., 1998).
- Developed a physiologically based model of cell biodistribution in mice and humans (Zhu et al., 1996; Melder et al., 2002; Friedrich et al., 2002).
- Response to anti-VEGF treatment in rectal cancer. Top: before treatment; bottom: after treatment. Arrow shows location of shrinking, paler tumor.
- Developed a distributed parameter model for microscopic distribution of drugs in ADEPT approach (Baxter and Jain, 1996).
- Developed a poro-elastic model of tumors and suggested a novel strategy to improve the drug delivery to solid tumors (Netti et al., 1995, 1997, 1999).
- Developed the theoretical framework to calculate residual stress in tumors (Skalak et al., 1996).
- Calculated solid stress generated by tumor spheroids (Helmlinger et al., 1997b) and proposed the hypothesis that the tumors lack functional lymphatics due to their collapse by solid stress.
- Developed a novel scheme to quantify the vascular architecture in a tumor (Gazit et al., 1995, 1997). This analysis has allowed us to calculate the role of vascular heterogeneity in nutrient and drug delivery to tumors (Baish et al., 1997, Baish and Jain, 1998, 2000).
- Developed a poro-elastic model for interstitial lymphatic transport (Swartz et al., 1999a).
- Developed a mathematical model for necrosis and dormancy in primary tumors and suppression of angiogenesis in distal tumors based on the transport and generation of angiogenic and anti-angiogenic molecules (Ramanujan et al., 2000).
- Developed a lattice Boltzmann model if leukocyte-RBC-endothelial interaction (Migliorini et al., 2002)
- Developed a linear poroelasticity model for the solid stress generated by spheroid growth as a model of tumor expansion (Roose et al., 2003).
- Developed a mathematical model of the contribution of endothelial progenitor cells to angiogenesis in tumors (Stoll et al., 2003).
- Developed a model for temporal heterogeneities of tumor blood flow (Mollica et al., 2003).
- Used microfluidics to separate blood components (Shevkoplyas et al., 2005).
- Analyzed blood rheology based on the particulate nature of blood using lattice Boltzmann analysis (Sun et al. Biophys. J., 2005).
- Analyzed the effect of erythrocytes in the margination of leukocytes in vessel expansions (Sun et al., Physica A, 2005).
- Provided the first measurements of interstitial hypertension in various human tumors (Boucher et al., 1991, Roh et al., 1991, Gutmann et al., 1992, Less et al., 1992, Jain, 1994c, Boucher et al., 1997, Padera et al., 2002, Willett et al., 2004).
- Analyzed the effects of fiber geometry and charge on drug transport (Stylianopoulos et al Biophys J 2010a, 2010b).
- Developed a 2-parameter model to describe network efficiency (Baish et al., PNAS 2011).
- Predicted that combining 'vascular normalization' and 'stress normalization' can greatly enhance chemotherapy delivery in tumors (Stylianopoulos et al., 2013)
- Demonstrated that modelling of COVID-19 pathobiology can suggest biomarkers that predict optimal response to a given immunomodulatory treatment (Subudhi et al, 2022).

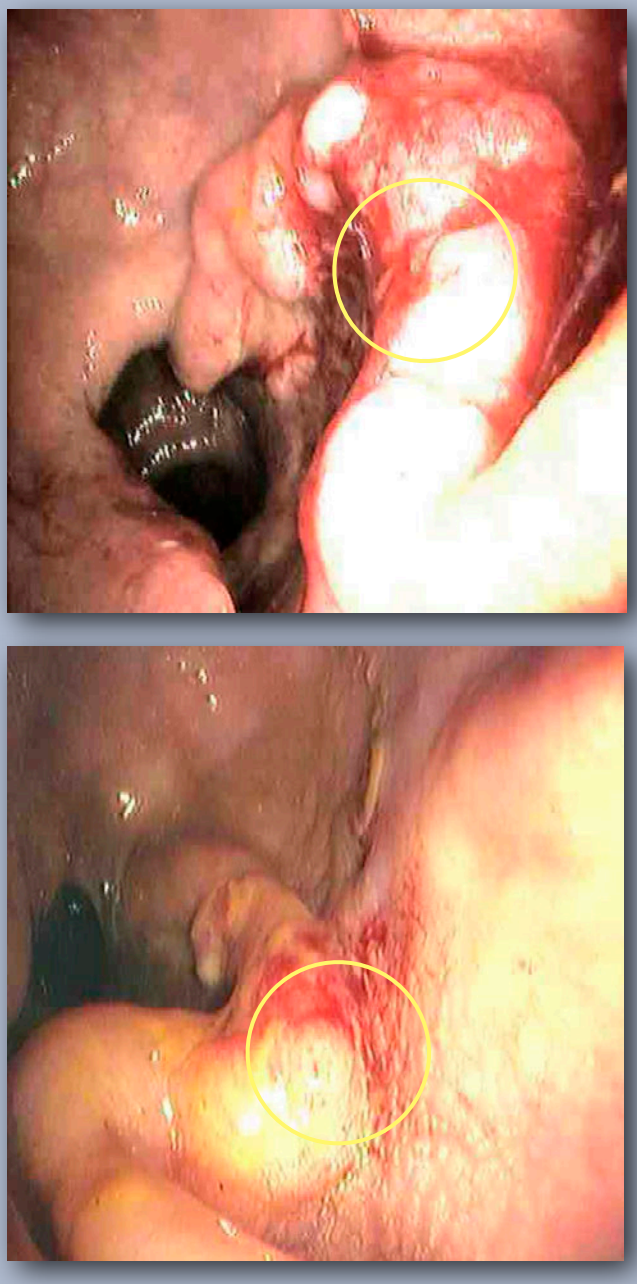


Mathematical modeling of blood flow. Erythrocytes flow from left to right (time sequence--A-D). E-H give the corresponding pressure profiles in the plasma.

- **Mathematical modeling of blood flow. Erythrocytes flow from left to right (time sequence--A-D). E-H give the corresponding pressure profiles in the plasma.**

7 Bench-to-bedside translation

- Provided the first quantitative measurements of geometric resistance to blood flow and of branching patterns in the rat and human tumor vasculature (Less et al., 1997).
- Provided the first glimpse of how anti-angiogenic drug Avastin works in cancer patients (Willett et al., 2004, 2005, 2007).
- Provided the first evidence for vascular normalization by an antiangiogenic agent in rectal carcinoma patients (Willett et al., 2004).
- Demonstrated that VEGF signaling blockade reduces the tumor interstitial fluid pressure in human rectal cancer (Willett et al., 2004; 2005).
- Provided the first evidence that Avastin increases the level of VEGF and PlGF in patients' circulation (Willett et al., 2005).
- Found the presence of PDGFR-β on the lymphatic vessels of Gorham's lymphangiomatosis (Hagendoorn et al., 2006)
- Provided the first evidence that an oral antiangiogenic agent creates a window of normalization in recurrent gliomas and alleviates edema in the brain of these patients (Batchelor et al., 2007). This has led to the recently completed pivotal trial of cediranib in glioblastoma patients.
- Discovered that glioblastoma re-growth after antiangiogenic treatment is associated with increases in plasma levels of bFGF, stromal-derived factor 1 alpha (SDF1α), and blood circulating endothelial cells (CECs) (Batchelor et al., 2007).
- Discovered that liver cancer response may be predicted by MRI and plasma measurements of interleukin 6, and that re-growth after antiangiogenic treatment is associated with increases in plasma levels of interleukin 6, stromal-derived factor 1 alpha (SDF1α), and blood circulating progenitor cells (CPCs) (Zhu et al., 2009).
- Discovered that antiangiogenic therapy with bevacizumab benefits patients with benign tumors (schwannomas) (Plotkin et al., 2009).
- Established a "vascular normalization index" in glioblastoma patients that might predict response to anti-VEGF therapy as early as 1 day after treatment (Sorensen et al., 2009).
- Discovered that blocking VEGF increases SDF1α, CXCR4, NRP-1 and CXCL6 in rectal cancer by laser-capture microdissection in serial patient biopsies (Xu et al., 2009).
- Demonstrated that the brain tumor patients whose tumor blood perfusion improved due to vascular normalization by anti-angiogenic therapy survive longer (Sorensen et al, 2011; Emblem et al, 2013; Batchelor et al, 2013).
- Demonstrated that vascular normalization and not pruning after antiangiogenic therapy with chemotherapy is the mechanism of benefit in breast and lung cancer patients (Heist et al., 2015; Tolaney et al., 2015)
- Dicovered that the anti-VEGFR2 agent cabozantinib has immunomodulatory effects in breast cancer patients (Tolaney et al., 2017)
- Demonstrated that adding losartan – to normalize the tumor matrix – to chemoradiotherapy was associated with high complete resection rates in locally advanced pancreatic ductal adenocarcinoma patients (Murphy et al., 2018; Saulnier-Sholler et al 2022; Plotkin et al 2023).



Response to anti-VEGF treatment in rectal cancer. Top: before treatment; bottom: after treatment. Arrow shows location of shrinking, more pale tumor.

We are pleased with our progress, which is a result of the hard work, dedication, innovation, organization, and cooperation of the members of the Steele Laboratories, as well as the collaborative support of various members of the MGH/Harvard/MIT community.

Faculty Research Summaries

Normalizing the Tumor Microenvironment to Improve Cancer Treatment: Bench to Bedside & Back

Rakesh K. Jain, PhD, A.W. Cook Professor of Radiation Oncology (Tumor Biology) & Director, Steele Laboratories

My research goals are (i) to understand how the abnormal tumor microenvironment confers resistance to various cancer treatments (e.g., chemotherapies, targeted therapies, nanomedicine, radiation and immunotherapy), (ii) to develop innovative strategies for manipulating the tumor microenvironment to overcome this resistance, and (iii) to translate these strategies from bench to bedside through multi-disciplinary clinical trials. This tight integration between bench and bedside, and application of engineering/physical science principles to oncology is a hallmark of my research.

To unravel the complex biology of tumors, we developed an array of imaging technologies, mathematical models, and sophisticated animal preparations. This undertaking has provided unprecedented molecular, cellular, anatomical, and functional insights into the barriers in the tumor microenvironment and how to overcome them.

In 2001, I proposed the hypothesis that "normalizing" the tumor microenvironment should improve the treatment outcome. Indeed, our team demonstrated that judicious use of antiangiogenic agents—originally designed to starve tumors—could transiently "normalize" the tumor vasculature, improve perfusion, alleviate hypoxia, increase delivery of drugs and anti-tumor immune cells, polarize macrophages to anti-tumor phenotype, and improve the outcome of radiation, chemotherapy, and immunotherapy in multiple animal models. Moreover, the trials - led by our clinical collaborators - on antiangiogenics in brain, liver, colorectal and breast cancer patients supported this concept. They revealed that the patients whose tumor blood perfusion/oxygenation increased in response to anti-VEGF therapy survived longer than those whose blood perfusion/oxygenation did not increase.

In parallel, by imaging the extracellular matrix and perfusion in tumors in vivo, we discovered that the extracellular matrix could compress blood vessels and impede drug and oxygen delivery in tumors. We also discovered that blocking TGFb-signaling using losartan, an angiotensin receptor blocker, can "normalize" the extracellular matrix by reprogramming carcinoma associated fibroblasts, opening compressed tumor vessels, activating both innate and adoptive immune pathways, and improving the delivery and efficacy of various treatments, including immunotherapy, in multiple murine models of cancer.

These discoveries have led to 40+ clinical trials in the past 20 years and underpinned the approval of bevacizumab for NF2-associated schwannomas in UK in 2014 as well as the US FDA approval of 7 different combinations of anti-VEGF drugs and immune-checkpoint blockers for kidney, lung, liver and endometrial cancers since 2018.

I have had the good fortune of mentoring more than 225 doctoral and postdoctoral fellows from diverse backgrounds including engineering, mathematics, physics, chemistry, molecular and cellular biology, immunology, pathology, radiology, radiation-, medical-, neuro- and surgical-oncology. I have also had productive collaborations with a similar number of basic scientists and clinicians from all over the world. Many of my trainees are now leaders in academia, government and industry.

For our multi-disciplinary contributions to tumor biology and therapy, I have received more than 90 awards and honors, including election to all three US National Academies—Science (NAS), Engineering (NAE) and Medicine (NAM) – and National Academy of Inventors. Since 2014, I am among the top 1% cited researchers (Web of Science). I received the 2013 US National Medal of Science from President Obama – "For pioneering research at the interface of engineering and oncology, including tumor microenvironment, drug delivery, and imaging; and for discovering groundbreaking principles guiding the development and novel use of drugs for cancer and non-cancerous diseases."

Selected Publications

- Nia H, Munn LL and Jain RK. Physical Traits of Cancer. Science 370, eaaz0868 (2020).
- Munn LL and Jain RK. "Vascular regulation of anti-tumor immunity. Science 365: 544-545 (2019).
- D Fukumura, J Kloepper, Z Amoozgar, DG Duda and RK Jain. Enhancing Cancer Immunotherapy Using Antiangiogenics: Opportunities and Challenges. Nature Reviews Clinical Oncology. 15: 325-340 (2018).
- Naxerova K, et al. Origins of lymphatic and distant metastases in human colorectal cancer. Science 357: 55-60 (2017).
- M Pinter and RK Jain. Targeting the renin-angiotensin system to improve cancer treatment: Implications for immunotherapy. Science Translational Medicine 9: eaan5616 (2017).
- Jain RK. Antiangiogenesis strategies revisited: From starving tumors to alleviating hypoxia. Cancer Cell 26: 605–622 (2014).
- Jain RK. Normalizing tumor microenvironment to treat cancer: Bench to bedside to biomarkers. J Clinical Oncology 2013; 31:2205-18.
- Snuderl M et al. Targeting placental growth factor/neuropilin 1 pathway inhibits growth and spread of medulloblastoma. Cell 2013; 152: 1065–1076.
- Jain RK. Normalization of the tumor vasculature: An emerging concept in anti-angiogenic therapy. Science 2005; 307:58-62
- Padera TP, et al. Lymphatic metastasis in the absence of functional intratumor lymphatics. Science 2002; 296:1883 1886.
- Izumi Y, et al. Herceptin acts as an anti-angiogenic cocktail. Nature 2002; 416: 279-280.
- Carmeliet P and Jain RK. Angiogenesis in Cancer and Other Diseases. Nature, 407: 249-257 (2000).
- Fukumura D, et al. Tumor induction of VEGF promoter activity in stromal cells. Cell 1998; 94:715-725.

Dan G. Duda, DMD, PhD
Associate Professor of Radiation Oncology

New Therapy Approaches for Hepato-Biliary-Pancreatic (HBP) Malignancies and Metastatic Diseases

Dr. Duda obtained a DMD from the University of Medicine Iasi, Romania, in 1993 and then earned a PhD in Medical Sciences from Tohoku University Graduate School of Medicine, Sendai, Japan, in 2001. After graduation, he pursued postdoctoral training with Professor Rakesh K. Jain in the Steele Laboratories for Tumor Biology, Department of Radiation Oncology, MGH, and Harvard Medical School in Boston for 3 years. In 2004, Dr. Duda became a Junior Faculty member at Harvard (Instructor). He then rose through the ranks to Full Investigator at MGH Research Institute in 2016 and Associate Professor of Tumor Biology (Radiation Oncology) in 2012. In 2016, Dr. Duda was appointed Director of Translational Research in Gastrointestinal Radiation Oncology at MGH. In 2021, he received the honorary degree "Doctor Honoris Causa" from the University of Medicine Iasi, Romania, his Alma Mater.

Over the last decade and a half, Dr. Duda has built a productive Liver Cancer Research Program. The translational goal of this program is to increase the durability of response to the most effective available therapies. The approach is to identify new cellular and molecular mechanisms of local and metastatic tumor progression and treatment resistance and validate them as new targets for combination therapies for these cancers.

His group studies the activity of agents targeting the tumor microenvironment (antiangiogenic or antifibrotic agents) or targeting the cancer cells (radiotherapy, chemotherapy, targeted agents) combined with immunotherapy approaches. To this end, they developed preclinical models that reproduce hallmarks of human cancers, including genetically engineered models of primary hepatocellular carcinoma and cholangiocarcinoma, and metastatic pancreatic, breast, and prostate carcinomas. In parallel, they are conducting correlative studies of biomarkers of response to the same approaches in clinical trials in cancer patients in a CLIA-certified environment. Dr. Duda's research is supported by multiple National Cancer Institute (NCI) grants, and Department of Defense (DoD) awards.

Dr. Duda has authored 261 publications, including basic research published in *Nature, Nature Medicine, Nature Biotechnology, Nature Genetics, Nature Communications, Cell, Cancer Cell, Science Translational Medicine, JNCI, Gut*, and *Hepatology,* and clinical reports published in *Journal of Clinical Oncology, npj Precision Oncology,* and *JAMA Oncology*. Over the last two decades, he has been invited to present our results at over 250 local, national, and international meetings, including in Grand Rounds (Harvard, Mayo Clinic, Yale, Fred Hutchinson Cancer Center, UPMC), Plenary and State-of-the-art Talks (AACR, ISSCR, IASGO, IAP), and Keynote Lectures. Dr. Duda has received multiple awards for his research, including from the AACR, Cancer Research Institute (CRI), IASGO, and MGH. He became an Honorary Member of the Academy of Medical Sciences of Romania in 2012, was inducted into the College of Fellows of the American Institute for Medical and Biomedical Engineering (AIMBE) in 2020, was elected as a 2021 American Association for the Advancement of Science (AAAS) Fellow in 2022, and was elected as an IASGO Fellow (FASGO) in 2023. He was elected a Foreign Member of the Academy of Europe in 2023.

Dr. Duda has been a chartered or ad-hoc Member and Chair of multiple expert panels (currently Chair of the Cancer Diagnostics and Treatments Study Section since 2022). Since 2015, he has been serving as the Secretary-General of the IASGO. Dr. Duda is Chair of the SWOG Translational Medicine GI Committee. Dr. Duda chaired the Forbeck Forum on "*The Biology and Treatment of Hepatocellular Carcinoma*" in 2023 and will chair the "*Boston Angiogenesis Meeting*" (BAM) in 2024.

Dr. Duda teaches tumor biology and translational oncology through the daily supervision of 50+ postdoctoral research fellows and graduate and undergraduate students. As a passionate supporter of IASGO's mission to globalize the best medical practice and knowledge worldwide, he has been coordinating, teaching, and directing Postgraduate Courses in 29 countries in Asia, Europe, Africa, and the Americas since 2013.

Selected Publications

Gkika E, Firat E, Adebahr S, Graf E, Popp I, Radicioni G, Lo SS, Nestle U, Nicolay NH, Niedermann G, Duda DG, Grosu AL. Systemic immune modulation by stereotactic radiotherapy in early-stage lung cancer. NPJ Precis Oncol. 2023;7(1):24.

Chen S, Huang C, Liao G, Sun H, Xie Y, Liao C, Wang J, He M, Hu H, Dai Z, Ren X, Zeng X, Lin Z, Zhang GP, Xie W, Shen S, Li S, Peng S, Kuang DM, Zhao Q, Duda DG, Kuang M. Distinct single-cell immune ecosystems distinguish true and de novo HBV-related hepatocellular carcinoma recurrences. Gut. 2023;72(6):1196-1210.

Kikuchi H, Matsui A, Morita S, Amoozgar Z, Inoue K, Ruan Z, Staiculescu D, Wong JS, Huang P, Yau T, Jain RK, Duda DG. Increased CD8+ T-Cell Infiltration and Efficacy for Multikinase Inhibitors after PD-1 Blockade in Hepatocellular Carcinoma. J Natl Cancer Inst. 2022;114(9):1301-1305.

Xiao Y, Chen J, Zhou H, Zeng X, Ruan Z, Pu Z, Jiang X, Matsui A, Zhu L, Amoozgar Z, Chen DS, Han X, Duda DG, Shi J. Combining p53 mRNA nanotherapy with immune checkpoint blockade reprograms the immune microenvironment for effective cancer therapy. Nat Commun. 2022;13(1):758 - PMID: 35140208.

Aoki S, Inoue K, Klein S, Halvorsen S, Chen J, Matsui A, Nikmaneshi MR, Kitahara S, Hato T, Chen X, Kawakubo K, Nia HT, Chen I, Schanne DH, Mamessier E, Shigeta K, Kikuchi H, Ramjiawan RR, Schmidt TC, Iwasaki M, Yau T, Hong TS, Quaas A, Plum PS, Dima S, Popescu I, Bardeesy N, Munn LL, Borad MJ, Sassi S, Jain RK, Zhu AX, Duda DG. Placental growth factor promotes tumour desmoplasia and treatment resistance in intrahepatic cholangiocarcinoma. Gut. 2021;71(1):185-193.

Dai Fukumura, MD, PhD
Associate Professor of Radiation Oncology

Angiogenesis and Tumor Microenvironment

I have three decades of research experience and teaching in the areas of vascular biology and tumor microenvironment (TME) and two decades of experience in serving as PI in NIH grants (P01, R01s, R24s). I joined the Steele Laboratories in 1994 rose through the ranks at MGH and Harvard, and I am currently a Full Investigator (MGH Research Institute), Deputy Director of the Steele Laboratories for Tumor Biology (MGH), and an Associate Professor at Harvard Medical School (HMS). In 2019, 2020, 2021, and 2022 I was ranked among the top 1% Highly Cited Researchers by the Web of Science. I received multiple awards and honors including Eugene M. Landis Award (2015) and election to the American Institute for Medical and Biological Engineering (AIMBE) College of Fellows (2017). The long-term goal of my research is to advance fundamental understanding of vascular biology and TME, exploit this new knowledge for uncovering mechanisms of TME-induced resistance to various cancer treatments, and develop novel strategies to overcome these barriers.

Role of obesity and exercise in TME and treatment response.

Obesity is world-wide pandemic causing and/or aggravating many diseases, including cancer. Using my expertise in vascular biology, anti-angiogenic therapy, and immunotherapy, I have been revealing the mechanisms of, and strategies to overcome, obesity-induced resistance to cancer treatments. I revealed provocative reciprocal regulation of adipogenesis and angiogenesis, and resistance to diet-induced obesity. Then, I uncovered cellular and molecular mechanisms – inflammatory and immune pathways – underlying induced cancer aggravation and demonstrated improvement of pancreatic and breast cancer treatment by targeting these pathways. Exercise is a standard of care for obesity and recommended to cancer patients. However, its effect and mechanisms are not known. To uncover underlying mechanisms and fact-promote fact-based integration of exercise into cancer treatment, I have been studying the role of exercise in tumor vasculature, TME and its effect on immunotherapy. Indeed, I found normalization of vasculature and immune profile in breast cancers following exercise. I have been dissecting molecular mechanisms.

Role of tumor-host interactions in angiogenesis, tumor growth and metastasis

Using sophisticated animal models and imaging techniques, we found for the first time that nontransformed stromal cells –including activated fibroblasts, bone marrow derived cells – are a major inducer of tumor angiogenesis and mediate the formation of abnormal microenvironment. Furthermore, various anti-angiogenic or molecularly targeting treatments result in the activation of host stromal cells leading to treatment resistance. We also showed that stromal cells in the primary tumor travel with tumor cells and facilitate survival and growth of metastatic tumors. Controlling tumor-host interaction is a promising approach to facilitate tumor treatment. For example, dual blockade of angiopoietin 2 and vascular endothelial growth factor signaling can normalize tumor vasculature, reprogram immune cells, and prolong survival in glioblastoma.

Role of NO in tumor vasculature

Nitric oxide (NO) is a highly reactive mediator with a variety of physiological and pathological functions. NO increases and/or maintains tumor blood flow, decreases leukocyte-endothelial interactions, and increases vascular permeability. Furthermore, NO mediates angiogenesis and vessel maturation predominantly through endothelial NO synthase (eNOS). We also found that eNOS mediates lymph-angiogenesis, lymphatic function, and metastasis. On the other hand, we also found that tumor cell-derived NO disrupts perivascular NO gradients resulting in abnormal structure and function of tumor vasculature. We have shown that targeting tumor cell NO production to restores perivascular NO gradients and improves TME.

Probing tumor microenvironment using nanotechnology

To characterize transport properties of nanoparticles in tumors, we did imaging studies of nanoparticles with different characteristics. We found that relatively large nanoparticles – size of current nanomedicine – can take advantage of enhanced permeability and retention effect for transvascular transport but are unable to penetrate tumor tissues. We also found superior transvascular transport of rod-shape over spherical nanoparticles. Furthermore, we discovered that neutral charge is the best for interstitial transport. These findings led us to develop multistage nanotherapeutics that shrink upon the entry to the tumor microenvironment to facilitate interstitial transport.

Engineering blood vessels

A major limitation of tissue engineering is the lack of functional blood and lymph vessels. We established, for the first time, a model of tissue engineered blood vessels that generates durable functional blood vessels from endothelial cells and perivascular cell precursors *in vivo* which last the rest of host animal life. Using this tissue engineered blood vessel model, we further successfully generated endothelial cells from human ES cells and cord blood and peripheral blood-derived progenitor cells, perivascular cells from human bone marrow derived mesenchymal stem cells, and functional blood vessels using them. Finally, we could generate functional blood vessels endothelial cells and perivascular cells both derived from the same iPS cells.

Selected Publications

- Fukumura D, – Jain RK. Enhancing cancer immunotherapy using antiangiogenics: opportunities and challenges. *Nature Reviews Clinical Oncology* 2018;15(5):325-340.
- Gomes-Santos – Fukumura D. Exercise training improves tumor control by increasing infiltration of CD8+ T cells via CXCR3 signaling and sensitizes breast cancer to immune checkpoint blockade. *Cancer Immunology Research* 2021;9(7):765–78.
- Incio J, – Fukumura D, Jain RK. Obesity promotes resistance to anti-VEGF therapy in breast cancer by upregulating IL-6 and FGF-2. *Sci Transl Med* 2018;10. pii: eaag0945.
  Jung K, – Fukumura D. Ly6Clo monocytes drive immunosuppression and confer resistance to anti-VEGFR2 cancer therapy. *JCI* 2017;127:3039-51.

Spontaneous Tumors and their Isograft Models: Histopathology/Pathophysiology Studies and Applications in Experimental Cancer Therapy

Peigen Huang, MD, MS
Assistant Professor of Radiation Oncology

First, our research focuses on the development of spontaneous tumors in mice and on how the age, genetic background, and immune status of the mice - as well as the presence or absence of specific genes affect the histopathological characteristics of the tumors.

We study the incidence of spontaneous tumors and their pathological pattern in the natural setting of aged mice, which are kept alive for nearly their full normal life span. The animals are raised within a gnotobiotic colony that is free of life-shortening intercurrent infectious diseases. We have found a high incidence of subcutaneous sarcoma in our aging C3Hf/Sed female mice.

In our aging, retired FVB/N breeder mice, tumors are most commonly found in the lungs. The incidence of spontaneous T-cell thymic lymphomas in severe combined immunodeficient (SCID) mice is strikingly high. We have also published the first comprehensive report of spontaneous nonthymic tumors, including 8 myoepitheliomas and 3 rhabdomyosarcomas, from our SCID retired breeders. Our results show that the incidence of spontaneous tumors and their morphological changes are markedly strain dependent, and are immune status and age associated. We are also documenting the development, growth, and histopathological characteristics of spontaneous tumors in the GFP transgenic mice with FVB background (such as VEGF-GFP/FVB, and Tie2-GFP/FVB mice). Our goal is to test the hypotheses that (a) the insertion of GFP reporter genes affects the incidence of spontaneous tumors in aging FVB genotobiotic mice, as well as changes their pathological patterns, and (b) spontaneous tumors developed in FVB-GFP transgenic mice exhibit different biological and molecular biological characteristics, such as different growth and metastatic potential, and different GFP expression in tumors as compared to the tumors in wild-type FVB mice.

Second, we are interested in developing novel tumor lines that are derived from the spontaneous tumors found in our laboratory. These tumor lines are used to study tumor pathophysiology in specific strains of transgenic mice derived from the same genetic background as the spontaneous tumors. One of our tumor lines, Os-P0107, is derived from a spontaneous osteosarcoma in a VEGF-GFP transgenic mouse; each of the cells in an Os-P0107 tumor expresses green fluorescent protein (GFP), which makes them easy to locate and track with intravital microscopy. Another tumor line, LAP0297, is a lung adenocarcinoma with a high incidence of distant lung metastases. This line, which is ideal for the study of metastasis, is derived from a spontaneous lung tumor in an FVB/N mouse. For pre-clinical studies of antiangiogenesis therapy, we have used spontaneous autochthonous tumors and their isografts, implanted in aged C3Hf/Sed mice, to more accurately simulate the clinical conditions that affect many human cancer patients.

Most recently, we established and characterized two novel in vitro and in vivo tumor models (MCa-M3C and MCa-PSTC) from the spontaneous adenocarcinomas arising in MMTV-PyVT/FVB transgenic mice. MCa-M3C is a high-selected HER2/neu-positive metastatic mammary tumor line, which has been considered a very useful model for several new research projects in our laboratory. We have made significant progress in the studies of combining Losartan with radiotherapy for the treatment of MCa-M3C metastatic breast cancer, resulting significantly decreased MCa-M3C MFP-to-lung macro metastases and increased host survival.

During the last decades, several novel tumor lines have been established and characterized, including Os-P0107, MCaP0008, LAP0297, MCa-M3C, MCa-PSTC, and MCa-P1362 from spontaneous tumors in our laboratories. These novel tumor lines have been widely used for the study of tumor pathophysiology and experimental treatment in our Steele laboratories and many other institutes around the world.

Selected Publications

- Jana S, Li W, Lei PJ, Wang Z, Huang P, Jones D. Isolation and characterization of a novel hormone receptor positive mammary adenocarcinoma MCa-P1362 with stromal drivers of tumor growth, metastasis, and drug resistance. bioRxiv. 2023 Jun 06. PMID: 37333242; PMCID: PMC10274631.
- Li W, Li S, Chen IX, Liu Y, Ramjiawan RR, Leung C-H, Gerweck LE, Fukumura D, Loeffler JS, Jain RK, Duda DG, and Huang P. Combining losartan with radiotherapy increases tumor control and inhibits lung metastases from a HER2/neu-positive orthotopic breast cancer model. Radiat Oncol. 2021; 16 (1): 48. DOI: https://doi.org/10.1186/s13014-021-01775-9. PMID: 33663521.
- Jones D, Wang Z, Chen IX, Zhang S, Banerji R, Lei P, Zhou H, Xiao V, Kwong C, Wijnbergen JWMv, Pereira ER, Vakoc BJ, Huang P, Nia HT, and Padera TP. Solid stress impairs lymphocyte infiltration into lymph-node metastases. Nat Biomed Eng. 2021; 12: 1426-1436. DOI: 10.1038/s41551-021-00766-1. PMID: 34282290.
- Li W, Liu Y, Yang W, Han X, Li S, Liu H, Gerweck LE, Fukumura D, Loeffler JS, Yang BB, Jain RK, and Huang P. MicroRNA-378 enhances radiation response in ectopic and orthotopic implantation models of glioblastoma. J Neuro-Oncol. 2018; 136: 63-71. DOI:10.1007/s11060-017-2646-y. PMID: 29081036.
- Nia Ht, Datta M, Seano G, Huang P, Munn LL, and Jain RK. Quantifying solid stress and elastric energy from excised or in situ rumors. Nat Protoc. 2018; 13: 1091-1105. DOI: 10.1038/nprot 2018.020. PMID: 29674756.
- Gerweck LE, Huang P, Lu HM, Paganetti H, Zhou Y. Lifetime increased cancer risk in mice following exposure to clinical proton beam-generated neutrons. Int J Radiat Oncol Biol Phys. 2014; 89(1):161-6. PMID: 24725699; PMCID: PMC4298825.
- Chauhan VP, Martin JD, Liu H, Lacorre DA, Jain SR, Kozin SV, Stylianopoulos T, Mousa AS, Han X, Adstamongkonkul P, Popovic Z, Huang P, Bawendi MG, Boucher Y, Jain RK. Angiotensin inhibition enhances drug delivery and potentiates chemotherapy by decompressing tumour blood vessels. Nat Commun. 2013; 4:2516. PMID: 24084631; PMCID: PMC3806395.

Lance L. Mun, PhD,
Associate Professor of Radiation Oncology

Tumor Mechanobiology and Vascular Physiology

The Munn Laboratory focuses on mechanobiology of cancer and the vascular systems:

Lymphatic Pumping

Flow of fluid within the lymphatic system is central to many aspects of physiology, including fluid homeostasis and immune function, and poor lymphatic drainage results in significant morbidity in millions of patients each year. We are investigating the mechanisms of lymphatic pumping, considering the nitric oxide and calcium dynamics driven by mechanobiological mechanisms.

Vascular Anastomosis

To form new, patent blood vessels, angiogenic sprouts must connect. The process by which this happens - anastomosis – is poorly understood, but represents new targets for vascular therapy. Using intravital microscopy and engineered vascular devices, we are following the steps of anastomosis to identify cellular and molecular mechanisms that may eventually be targeted for enhancing wound healing or inhibiting pathological angiogenesis.

Blood Vessel Remodeling

In many normal physiological responses, endothelial cells and the blood vessel networks they form undergo dramatic changes in morphology and function. Examples include angiogenesis in wound healing, vessel dilation/hyperpermeability in inflammation, and endometrial angiogenesis in the female reproductive cycle.

Endothelial cells, in cooperation with other stromal cells, have to accomplish these diverse changes by responding to a limited number of growth factors including VEGF, PlGF and bFGF. We are using a systems biology approach to understand how the various growth factors and cells cooperate to produce these seemingly diverse functions. Because tumor angiogenesis relies on many of these same growth factors and cellular mechanisms (but in an abnormal, poorly controlled way), these studies will allow a better understanding of tumor angiogenesis and anti-angiogenic therapy.

Cancer Cell Invasion

During the initial stage of metastasis, cancer cells must breach the vessel wall and enter the circulation. Despite intense research in this area, the cellular mechanisms by which this occurs are poorly understood. Some tumors seem to metastasize as single rogue cells, while others travel in groups or clusters; some seem to actively migrate into the vessel, while others may be passively pushed. Using gene array analysis and carefully designed coculture systems, we are assessing the mechanical and cellular determinants of the initiation of metastasis.

Angiogenic Sprouting

During angiogenesis, endothelial cells abandon their normal arrangement in the vessel wall to migrate into the extravascular matrix. This process is controlled by mul-tiple signals and is necessary for tissue regeneration and tumor growth. Using in vitro models and microfluidic devices, we are investigating the biochemical and mechanical determinants of this morphogenic transformation.

Mathematical Modeling

With sufficient understanding of the underlying mechanisms, mathematical models can be assembled to validate existing hypotheses and generate new ones.

Selected Publications

- Cheng G, Liao S, Wong HK, Lacorre DA, di Tomaso E, Au P, Fukumura D, Jain RK, Munn LL Engineered blood vessel networks connect to host vasculature via wrapping-and-tapping anastomosis. Blood 2011; 118:4740-4749.
- Tse, JM, Cheng, G, Tyrrell, JA, Wilcox-Adelman, SA, Boucher, Y, Jain RK, Munn, LL. Mechanical compression drives cancer cells toward invasive phenotype PNAS 2011.
- Bazou D, Maimon N, Gruionu G, Grahovac J, Seano G, Liu H, Evans CL, Munn LL. Vascular beds maintain pancreatic tumor explants for ex vivo drug screening. Journal of Tissue Engineering and Regenerative Medicine. 2017; 1–5.
- Nia HT, Liu H, Seano G, Datta M, Jones D, Rahbari N, Incio J, Chauhan VP, Jung K, Martin JD, Askoxylakis V, Padera TP, Fukumura D, Boucher Y, Hornicek FJ, Grodzinsky AJ, Baish JW, Munn LL, Jain RK. Solid stress and elastic energy: new measures of tumor mechanopathology. Nature Biomedical Engineering. 2017; 1:0004.
- Bazou D, Maimon N, Gruionu G, Munn LL. Self-assembly of vascularized tissue to support tumor explants in vitro. Integrative Biology. 2016b; 8:1301-11.
- Subudhi S, Verma A, Patel AB, Hardin CC, Khandekar MJ, Lee H, McEvoy D, Stylianopoulos T, Munn LL, Dutta S, Jain RK. Comparing Machine Learning Algorithms for Predicting ICU Admission and Mortality in COVID-19. NPJ Digital Medicine 2021.
- Nikmaneshi MR, Jain RK, Munn LL. Computational simulations of tumor growth and treatment response: Benefits of high-frequency, low-dose drug regimens and concurrent vascular normalization. PLOS Computational Biology 2023 19 (6), e1011131.
- Nikmaneshi MR, Baish JW, Zhou H, Padera TP, Munn LL, Transport Barriers Influence the Activation of Anti-Tumor Immunity: A Systems Biology Analysis. Adv. Sci. 2023.
- Wang X, Shen Y, Shang M, Liu X, Munn LL, Endothelial mechanobiology in atherosclerosis, Cardiovascular Research, 2023.
- Nia HT, Munn LL, Jain RK. Physical traits of cancer. Science, 370, 2020.
- Nikmaneshi MR, Jain RK, Munn LL. Computational simulations of tumor growth and treatment response: Benefits of high-frequency, low-dose drug regimens and concurrent vascular normalization. PLOS Computational Biology 2023 19 (6), e1011131.
- Nikmaneshi MR, Baish JW, Zhou H, Padera TP, Munn LL, Transport Barriers Influence the Activation of Anti-Tumor Immunity: A Systems Biology Analysis. Adv. Sci. 2023, 2304076. https://doi.org/10.1002/advs.202304076.
- Nia HT, Munn LL, Jain RK. Physical traits of cancer. Science, 370, 2020.

The lymphatic system in disease processes and cancer progression

Timothy P. Padera, PhD
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Lymphatic vessels are responsible for draining interstitial fluid from tissues and for transporting immune cells to lymph nodes to maintain the body's immune surveillance. Thus, lymphatic vessels are important in maintaining both tissue fluid balance and proper function of the immune system. Predictably, disruptions of the lymphatic system lead to lymphedema and set the conditions for chronic infections. Lymphatic vessels also facilitate the dissemination of cancer cells from a primary tumor to regional lymph nodes. My research group looks to understand the mechanisms behind the growth, maturation and function of lymphatic vessels and how these mechanisms can contribute to the pathogenesis of lymphedema, chronic infections and cancer dissemination. Currently, there are no FDA approved drugs indicated to alter lymphatic function, which presents an important opportunity to develop such drugs for the first curative treatments for lymphedema and other lymphatic related disorders.

In order to study the role of the lymphatic system in a variety of disease states, we have developed novel animal models which mimic certain aspects of human disease. Using intravital microscopy, we have investigated the individual steps of lymphatic metastasis. We can monitor the lymphatic vessels in the tumor margin, observe tumor cells moving in lymphatic vessels, measure lymph flow and quantify the number of tumor cells that arrive in the draining lymph node. Our studies have shown that tumors lack functional intratumor lymphatic vessels due to compressive forces inside tumors that cause their collapse. Our studies have also shown that VEGF-C, which is associated with lymphatic metastasis in patients, increases the size of the tumor margin lymphatic vessels, making them more vulnerable to invasion. Our data suggests that VEGF-C needs to be blocked very early in the metastatic process to be able to reduce VEGF-C enhanced lymphatic metastasis.

To further study the growth of metastasis in the lymph node, we have developed a novel model that allows chronic imaging of a tumor draining lymph node. Using our model, we have shown that lymph node metastases do not require sprouting angiogenesis in order to grow anddo not respond to anti-angiogenic therapies, identifying one possible mechanism of the lack of efficacy of anti-angiogenic therapy in patients. We have also shown that cancer cells from lymph node metastases can invade lymph node blood vessels, escape the lymph node and colonize distant metastatic sites. Thus, lymph node metastases can be a source of distant metastases.

Lymph nodes are the critical organs for the generation of adaptive immune responses and these responses must be suppressed in order for cancer cells to grow in the lymph nodes. We have shown that metastatic cancer cells remodel lymph node blood vessel, preventing lymphocytes from entering the metastatic lesions. Further, we showed that cancer cells in metastatic lymph nodes can induce the formation of immune suppressive regulatory T cells by expressing MHCII molecules.

In addition, we have begun to study the pathogenesis of lymphedema by unraveling the molecular underpinnings of autonomous contraction of collecting lymphatic vessels using a novel animal model. We have shown that the spatial and temporal gradients of nitric oxide, which are disrupted during inflammation, are critical for lymphatics to drive lymph forward. Furthermore, when lymphatic contractions are disrupted, the immune response to a foreign antigen is muted. Thus, disruption of lymphatic function has consequences for the overall immune function. We have also shown the *s. aureus* infections permanently impair lymphatic pumping and flow by destruction of lymphatic muscle cells. We have identified a bacterial regulatory element in *s. aureus* that controls the toxins responsible for this lymphatic muscle cell death.

In order to better understand the relationship between lymphatic vessel contraction and lymph flow, we have developed the first method to measure dynamic lymph flow *in vivo* without the need for injected contrast. Our future studies will continue to dissect the physical and molecular determinants of lymphatic vessel function, lymph flow, lymphangiogenesis and lymphatic metastasis. Through the use of our novel imaging technologies and animal models, we will answer timely questions that can lead to the development of treatments for lymphedema, chronic infections and lymphatic metastasis.

Selected Publications

- P.J. Lei#, E.R. Pereira#, P. Andersson, Z. Amoozgar, J.W. Van Wijnbergen, M. O'Melia, H. Zhou, S. Chatterjee, W.W. Ho, J.M. Posada, A.S. Kumar, S. Morita, L. Menzel, C. Chung, I. Ergin, D. Jones, P. Huang, S. Beyaz*, T.P. Padera*. "Cancer cell plasticity and MHC-II-mediated immune tolerance promote breast cancer metastasis to lymph nodes." Journal of Experimental Medicine, 2023; doi: 10.1084/jem.20221847.
- D. Jones, Z. Wang, I.X. Chen, S. Zhang, R. Banerji, P. Lei, H. Zhao, V. Xiao, C. Kwong, J.W.M. van Wijnbergen, E.R. Pereira, B.J Vakoc, P. Huang, H.T. Nia, T.P. Padera. "Solid stress remodels high endothelial venules and impairs lymphocyte infiltration into lymph node metastases." Nature Biomedical Engineering, 2021; 5:1426-1436Jul 19. doi: 10.1038/s41551-021-00766-1.
- E.R. Pereira, D. Kedrin, G. Seano, O. Gautier, E.F.J. Meijer, D. Jones, S.M. Chin, S. Kitahara, E.M. Bouta, J. Chang, E. Beech, H.S. Jeong, M.C. Carroll, A.G. Taghian, T.P. Padera. "Lymph node metastases can invade local blood vessels, exit the node and colonize distant organs in mice." Science, 2018; 359: 1403-1407.
- D Jones, EFJ Meijer, C Blatter, S Liao, ER Pereira, EM Bouta, K Jung, SM Chin, P Huang, LL Munn, BJ Vakoc, M Ottto, TP Padera. "Methicillin-resistant *Staphylococcus aureus* causes sustained collecting lymphatic vessel dysfunction." Sci. Trans. Med. 2018; pii: eaam7964
- Blatter C, Meijer EFJ, Nam AS, Jones D, Bouma BE, Padera TP*, Vakoc BJ*. "In vivo label-free measurement of lymph flow velocity and volumetric flow rates using Doppler optical coherence tomography." Sci. Rep. 2016; Jul 5;6:29035. doi: 10.1038/srep29035 .
- Jeong HS*, Jones D*, Liao S, Wattson DA, Cui CH, Duda DG, Willett CG, Jain RK, Padera TP. "Investigation of the lack of angiogenesis in the formation of lymph node metastases." JNCI. 2015; 107 (9): djv155 (2015). doi: 10.1093/jnci/djv155.
- Liao S, Cheng G, Conner D, Huang Y, Kucherlapati R, Munn L, Ruddle N, Jain RK, Fukumura D, Padera TP. Impaired lymphatic contraction associated with immunosuppression. PNAS. 2011; 108: 18784- 18789..
- Padera TP, Stoll BR, Tooredman JB, Capen D, di Tomaso E, Jain RK. Pathology: cancer cells compress intratumour vessels. Nature. 2004; 427:695.
- Padera TP, Kadambi A, di Tomaso E, Carreira CM, Brown EB, Boucher Y, Choi NC, Mathisen D, Wain J, Mark EJ, Munn LL, Jain RK. Lymphatic metastasis in the absence of functional intratumor lymphatics. Science. 2002; 296:1883-6.

Computational and Experimental Approaches in Cancer Immunopathology and Metabolism

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The synergy between cutting-edge computational tools and experimental efforts can delve deep into the complex landscape of cancer biology. In my research program, I would integrate computational biology, clinical informatics, immunopathology, cancer biology and metabolism to identify and evaluate novel cancer therapies with the goal of improving patient care.

Transcriptomics analysis of human diseases to understand pathogenesis

The pathophysiology of Non-alcoholic fatty liver disease (NAFLD) is complex and disease pathogenesis of distinct stages is challenging to study. By leveraging next generation sequencing techniques and computation biology tools, I identified new pathways pathways that were altered in the early stages of NAFLD, which is beneficial to develop therapeutic interventions accordingly. Extending this approach into cancer, we investigated Pancreatic Ductal Adenocarcinoma (PDAC). The focus was to understand the impact of losartan in a neoadjuvant setting.

Role of the immune system in chronic viral hepatitis

Using extensive computational pipelines, we analyzed the specific T cells in hepatitis C virus infection. Towards the goal of understanding T cell behavior, I studied the recovery of functionality of specific T cells after removal of chronic HCV infection, as this is critical to understand the dynamics of HCV re-infection. Analyzing the RNA-seq data indicated that T cells partially recover from exhaustion after virus antigen is removed. Additionally, we characterized the immune landscape of normal human liver using single-cell RNA sequencing, which helps to understand the biology of immune cells in liver vs blood.

Application of computational biology on clinical data to predict disease outcomes

Using bioinformatic skills, I applied my knowledge of machine learning model development and predicted severity of COVID-19 using clinical parameters. Ensemble-based algorithms outperformed other algorithms in predicting COVID-19 disease severity and mortality. We also developed a treatment score to predict therapeutic outcomes in a COVID-19 mathematical model which demonstrated a potential method of minimizing heterogeneity in clinical trials.

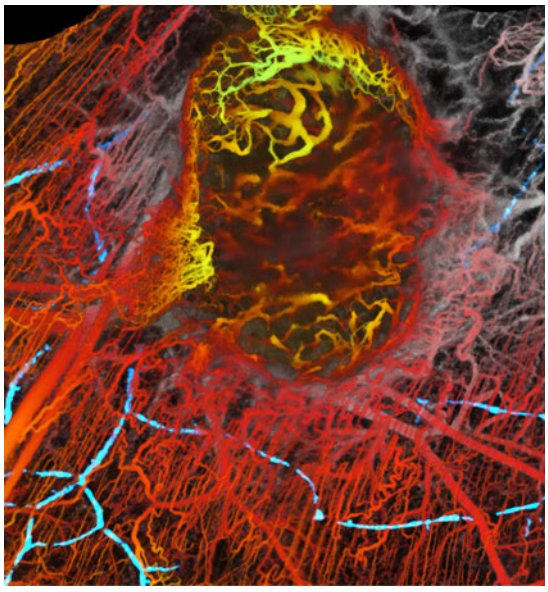
Exploiting metabolic vulnerabilities of cancer for therapy

Cancer metabolism and particularly immunometabolism is an exciting emerging area of research. Breast cancer brain metastasis is a significant clinical problem as existing therapies targeting the genetic drivers of breast cancer often prove ineffective against brain metastases. This ineffectiveness can be attributed to two main factors: limited drug penetration through the blood-brain barrier and the influence of external factors within the brain tumor environment. We discovered that metastatic breast cancer cells in the brain increase the production of critical metabolites through elevated *de novo* synthesis. Selective disruption of key biosynthetic enzymes allow us to pinpoint genes vital for the survival and proliferation of breast cancer cells within brain. Our ongoing hypothesis is that such tissue specific metabolic adaptations exists in other cancer types and the same also affects immune cell populations in the tumor microenvironment.

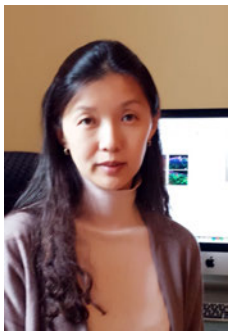
An interdisciplinary approach which combines bioinformatics, molecular biology and immunopathology, has the potential to accelerate translational research and make meaningful impact on patient care and public health.

Selected Publications

- Boucher Y, Posada JM, Subudhi S, et al. Addition of losartan to FOLFIRINOX and chemoradiation reduces immunosuppression-associated genes, Tregs and FOXP3+ cancer cells in locally advanced pancreatic cancer. Clin Cancer Res 2023.
- Genshaft AS, Subudhi S, Keo A, et al. Single-cell RNA sequencing of liver fine-needle aspirates captures immune diversity in the blood and liver in chronic hepatitis B patients. Hepatology 2023.
- Subudhi S, Voutouri C, Hardin CC, et al. Strategies to minimize heterogeneity and optimize clinical trials in Acute Respiratory Distress Syndrome (ARDS): Insights from mathematical modelling. EBioMedicine 2022;75:103809.
- Osganian SA, Subudhi S, Masia R, et al. Expression of IGF-1 receptor and GH receptor in hepatic tissue of patients with nonalcoholic fatty liver disease and nonalcoholic steatohepatitis. Growth Horm IGF Res 2022;65:101482.
- Subudhi S, Drescher HK, Dichtel LE, et al. Distinct Hepatic Gene-Expression Patterns of NAFLD in Patients With Obesity. Hepatol Commun 2022;6:77-89.
- Subudhi S, Verma A, Patel AB, et al. Comparing Machine Learning Algorithms for Predicting ICU Admission and Mortality in COVID-19. NPJ Digit Med 2021.
- Tonnerre P, Wolski D, Subudhi S, et al. Differentiation of exhausted CD8+ T cells after termination of chronic antigen stimulation stops short of achieving functional T cell memory. Nature Immunology 2021;22:1030-41.



Tumor-Host Interaction in Tumor Angiogenesis and Metastasis



Lei Xu, MD, PhD
Assistant Professor, Radiation Oncology

The goals of my research team are to develop innovative strategies to enhance treatment efficacy and improve patient quality of life. My current research is focused on three diseases:

Neurofibromatosis type 2

Neurofibromatosis type 2 (NF2) is a genetic disorder characterized by non-malignant tumors grown on the hearing nerve, disrupting hearing, and causing social impairment and clinical depression. No drug is FDA-approved to treat the tumor or the associated hearing loss.

The NF2 research is limited by i) the lack of orthotopic mouse models that reproduce tumor-induced hearing loss, ii) the lack of patient-derived cell lines, and iii) the lack of a targeted therapy that can simultaneously prevent hearing loss and control tumor growth.

I have made several contributions to advance NF research and management. First, my group established novel mouse models that faithfully reproduce schwannoma-induced hearing loss and neurologic deficit (*PNAS 2015; Nature Protocol 2019, Experimental Neurology 2018, NeuroMethods 2021*). In mice, the short length and small caliber of the vestibular nerves, and their encasement in the bony internal auditory canal pose significant technical challenges for orthotopic tumor implantation. My group developed a novel cerebellopontine angle (CPA) model that allows the measurement of hearing function in tumor-bearing mice. This model addresses a major bottleneck in the NF field and provides the NF research and clinical community with a robust and biologically relevant tool to explore new therapeutic targets to tackle this devastating disease. Using this new model, we identified cMET and angiotensin signaling are potential targets for NF2 (*PNAS 2018; Science Translational Medicine 2021*). Based on our compelling data, the Department of Radiation Oncology at MGH has amended the current ongoing clinical trial (NCT01199978), to include 10 patients to be treated with losartan concurrently with fractionated proton therapy, with follow-up evaluations for hearing function.

Ovarian cancer

Ovarian cancer (OvCa) is the most lethal gynecologic malignancy. My ovarian cancer research is focused on: i) deciphering mechanisms of treatment resistance, ii) identifying novel strategies to enhance treatment efficacy, and iii) reducing malignant ascites, which contribute to poor quality of life in patients with OvCa.

I discovered that normalizing the ovarian cancer tumor microenvironment by targeting TGF-b (*Clinical Cancer Research 2011; PNAS 2012*) and angiotensin signaling (*PNAS 2019*) not only enhances the delivery and efficacy of chemotherapy but also improves the diaphragm lymphatic vessel drainage function, leading to reduced ascites. These findings suggest a potential treatment to improve patients' quality of life. In collaboration with MGH Gynecological Oncologists, I further demonstrated that in ~300 ovarian cancer patients treated at two Harvard Medical School-affiliated teaching hospitals (MGH and Brigham and Women's Hospital) who received losartan survived 30 months longer than those taking other anti-hypertension drugs (*PNAS 2019*).

Schwannomatosis

Schwannomatosis (SWN), a type of neurofibromatosis, is a rare genetic disorder characterized by multiple non-malignant schwannomas growing on the spine and peripheral nerves. Patients with SWN overwhelmingly present with intractable, debilitating chronic pain severe enough to cause permanent disability.

Recognizing that one of the biggest challenges in finding a cure for SWN is the lack of clinically relevant models, I collected patient samples and successfully established a biobank of patient-derived SWN cells. I also developed the first orthotopic patient-derived xenograft (PDX) SWN spine model in mice. Currently, using my novel PDX models, I'm investigating the etiology of tumor-induced pain response and testing the treatment efficacy of potential targets.

Selected Publications

- Wu, L., Vasilijic, S., Sun, Y., Chen, J., Landegger, L.D., Zhang, Y., Zhou, W., Ren, J., Early, S., Yin, Z., Ho, W.W., Zhang, N., Gao, X., Lee, G.Y., Datta, M., Sagers, J.E., Brown, A., Muzikansky, A., Stemmer-Rachamimov, A., Zhang, L., Plotkin, S.R., Jain, R.K., Stankovic, K.M., and Xu, L**.** Losartan prevents tumor-induced hearing loss and augments radiation efficacy by normalizing the tumor microenvironment in NF2 schwannoma.*Science Translational Medicine***.** 2021, 13(602):eabd4816.
- Zhao, Y., Cao, J., Melamed, A., Worley, M., Gockley, A., Jones, D., Nia, H.T., Zhang, Y., Stylianopoulos, T., Kumar, A.S., Mpekris, F., Datta, M., Sun, Y., Wu, L., Gao, X., Yeku, O., del Carmen, M., Spriggs, D.R., Jain, R.K., and Xu, L. Losartan treatment enhances chemotherapy efficacy and reduces ascites in ovarian cancer models by normalizing the tumor stroma. Proceedings of National Academy of Science USA. (2019); 116(6): 2210-2219.
- Zhao Y, Liu P, Zhang N, Chen J, Landegger LD, Wu L, Zhao F, Zhao Y, Zhang J, Fujita T, Stemmer-Rachamimov A, Ferraro GB, Liu H, Muzikansky A, Plotkin SR, Stankovic KM, Jain RK, Xu L. Targeting the cMET pathway augments radiation response without adverse effect on hearing in NF2 schwannoma models. Proceedings of National Academy of Science. USA. 115(9): E2077-E2084. 2018
- Chen J, Landegger LD, Sun Y, Ren J, Maimon N, Wu L, Ng MR, Chen JW, Zhang N, Zhao Y, Gao X, Fujita T, Roberge S, Huang P, Jain RK, Plotkin SR, Stankovic KM, Xu L. A cerebellopontine angle mouse model for the investigation of tumour biology, hearing and neurological function in NF2-related vestibular schwannoma. Nature Protocols. 2019. 1, 541-555.

PUBLICATIONS

1991 Publications

Original Articles

1. J. Less, T. Skalak, E.M. Sevick, and R.K. Jain, Microvascular Architecture in a Mammary Carcinoma: Branching Patterns and Dimensions, *Cancer Research*, **51**:265-273 (1991).
2. E. M. Sevick and R.K. Jain, Measurement of Capillary Filtration Coefficient in a Solid Tumor, *Cancer Research*, **51**:1352-1355 (1991a).
3. C. Ohkubo, D. Bigos and R.K. Jain, IL-2 Induced Leukocyte Adhesion to the Normal and Tumor Microvascular Endothelium *In Vivo* and its Inhibition by Dextran Sulfate: Implications for Vascular-Leak-Syndrome, *Cancer Research*, **51**:1561-1563 (1991).
4. E. M. Sevick and R.K. Jain, Effect of RBC Rigidity on Tumor Blood Flow: Increase in Viscous Resistance During Hyperglycemia, *Cancer Research*, **51**:2727-2730 (1991b).
5. F. Yuan, L.T. Baxter and R.K. Jain, Pharmacokinetic Analysis of Two-step Approaches Using Bifunctional and Enzyme-conjugated Antibodies, *Cancer Research*, **51**:3119-3130 (1991).
6. K.A. Ward, D.J. DiPette, T.N. Held and R.K. Jain, Effect of I.V. Versus I.P. Glucose Injection on Systemic Hemodynamics and Blood Flow Rate in Normal and Tumor Tissues in Rats, *Cancer Research*, **51**:3612-3616 (1991).
7. Y. Boucher, J. Kirkwood, D. Opacic, M. Desantis and R.K. Jain, Interstitial Hypertension in Superficial Metastatic Melanomas in Humans, *Cancer Research*, **51**:6691-6694 (1991).
8. H.D. Roh, Y. Boucher, S. Kalnicki, R. Buchsbaum, W.D. Bloomer and R.K. Jain, Interstitial Hypertension in Carcinoma of Uterine Cervix in Patients: Possible Correlation with Tumor Oxygenation and Radiation Response, *Cancer Research*, **51**:6695-6698 (1991).
9. A. Sasaki, R.J. Melder, T.L. Whiteside, R.B. Herberman, and R.K. Jain, Preferential Localization of Human A-LAK Cells in Tumor Microcirculation: A Novel Mechanism of Adoptive Immunotherapy, *Journal of National Cancer Institute*, **83**:433-437 (1991).
10. L.T. Baxter and R.K. Jain, Transport of Fluid and Macromolecules in Tumors. III. Role of Binding and Metabolism, *Microvascular Research*, **41**:5-23 (1991a).
11. L.T. Baxter and R.K. Jain, Transport of Fluid and Macromolecules in Tumors. IV. A Microscopic Model of the Perivascular Distribution, *Microvascular Research*, **41**:252-272 (1991b).
12. E.N. Kaufman and R.K. Jain, Measurement of Mass Transport and Reaction Parameters in Bulk Solution Using Photobleaching: Reaction Limited Binding Regime, *Biophysical Journal*, **60**:596-610 (1991).

Books

13. P. Vaupel and R.K. Jain (editors), Tumor Blood Supply and Metabolic Microenvironment: Characterization and Therapeutic Implications, Gustav Fischer Publications, Stuttgart (1991).

Reviews, Commentaries and Book Chapters

14. R.K. Jain, Parameters Governing Tumor Blood Flow, *In: Tumor Blood Supply and Metabolic Microenvironment: Characterization and Therapeutic Implications*, P. Vaupel and R.K. Jain, Eds., Fischer Publications, Stuttgart (1991).
15. L.T. Baxter and R.K. Jain, Vascular and Interstitial Transport in Tumors, *In: Tumor Blood Supply and Metabolic Microenvironment: Characterization and Therapeutic Implications*, P. Vaupel and R.K. Jain, Eds., Fischer Publications, Stuttgart (1991).
16. E.M. Sevick and R.K. Jain, Viscous Resistance to Blood Flow in the Tumor Microcirculation: Clinical Implications, *In: Tumor Blood Supply and Metabolic Microenvironment:* Characterization *and Therapeutic Implications*, P. Vaupel and R.K. Jain, Eds., Fischer Publications, Stuttgart (1991).
17. K.A. Ward and R.K. Jain, Blood Flow Response to Hyperglycemia, *In: Tumor Blood Supply and Metabolic Microenvironment: Characterization and Therapeutic Implications*, P. Vaupel and R.K. Jain, Eds., Fischer Publications, Stuttgart (1991).
18. R.K. Jain, Hemodynamic and Transport Barriers to the Treatment of Solid Tumors, *International Journal of Radiation Biology*, **60**:85-100 (1991).
19. R.K. Jain, Therapeutic Implications of Tumor Physiology, *Current Opinion in Oncology*, **3**:1105-1108 (1991).

1992 Publications

Original Articles

20. M. Leunig, A.E. Goetz, M. Dellian, G. Zetterer, F. Gamarra, R.K. Jain and K. Messmer, Interstitial Fluid Pressure in Solid Tumors Following Hyperthermia: Possible Correlation with Therapeutic Response, Cancer Research, 52:487-490 (1992a).
21. R. Gutmann, M. Leunig, J. Feyh, A.E. Goetz, K. Messmer, E. Kastenbauer and R.K. Jain, Interstitial Hypertension in Head and Neck Tumors in Patients: Correlation with Tumor Size, Cancer Research, 52:1993-1995 (1992).
22. I. Lee, Y. Boucher, and R.K. Jain, Nicotinamide Can Lower Tumor Interstitial Fluid Pressure: Mechanistic and Therapeutic Implications, Cancer Research, 52:3237-3240 (1992).
23. E.N. Kaufman and R.K. Jain, Effect of Bivalent Interaction Upon Apparent Antibody Affinity: Experimental Confirmation of Theory Using Fluorescence Photobleaching and Implications for Antibody Binding Assays, Cancer Research, 52:4157-4167 (1992a).
24. Y. Boucher and R.K. Jain, Microvascular Pressure Is the Principal Driving Force for Interstitial Hypertension in Solid Tumors: Implications for Vascular Collapse, Cancer Research, 52:5110-5114 (1992).
25. L.T. Baxter, F. Yuan, and R.K. Jain, Pharmacokinetic Analysis of the Perivascular Distribution of Bifunctional Antibodies and Haptens, Cancer Research, 52:5838-5844 (1992).
26. C.J. Eskey, A.P. Koretsky, M.M. Domach and R.K. Jain, 2H NMR Imaging of Tumor Blood Flow: Spatial and Temporal Heterogeneity in a Tissue-isolated Mammary Adenocarcinoma, Cancer Research, 52:6010-6019 (1992).
27. J.R. Less, M.C. Posner, Y. Boucher, D. Borochovitz, N. Wolmark and R.K. Jain, Interstitial Hypertension in Human Breast and Colorectal Tumors, Cancer Research, 52:6371-6374 (1992).
28. R. J. Melder and R.K Jain, Kinetics of Interleukin - 2 Induced Changes in Rigidity of Human Natural Killer Cells, Cell Biophysics, 20:161-176 (1992).
29. M. Leunig, F. Yuan, M. Menger, Y. Boucher, A. Goetz, K. Messmer and R.K. Jain, Angiogenesis, Microvascular Architecture, Microhemodynamics and Interstitial Fluid Pressure During Early Growth of Human Adenocarcinoma LS174T in SCID Mice, Cancer Research, 52:6553-6560 (1992b).
30. E.N. Kaufman and R.K. Jain, In Vitro Measurement and Screening of Monoclonal Antibody Affinity Using Fluorescence Photobleaching, J. Immunol. Methods, 155:1-17 (1992b).

1993 Publications

Original Articles

31. C.J. Eskey, A.P. Koretsky, M.M. Domach and R.K. Jain, Role of Oxygen versus Glucose in Energy Metabolism in a Mammary Carcinoma Perfused Ex Vivo: Direct Measurement by 31P NMR, Proc. Natl. Acad. Sci., 90:2646-2650 (1993).
32. F. Yuan, M. Leunig, D. Berk and R.K. Jain, Microvascular Permeability of Albumin, Vascular Surface Area and Vascular Volume Measured in Human Adenocarcinoma LS174T Using Dorsal Chamber in SCID Mice, Microvascular Research, 45:269-289 (1993).
33. R. Zlotecki, Y. Boucher, I. Lee, L.T. Baxter and R.K. Jain, Effect of Angiotensin II Induced Hypertension on Tumor Blood Flow and Interstitial Fluid Pressure, Cancer Research, 53:2466-2468 (1993).
34. G.R. Martin and R.K. Jain, Fluorescence Ratio Imaging of pH Gradients: Calibration and Application in Normal and Tumor Tissues, Microvascular Research, 46:216-230 (1993).
35. D. Berk, F. Yuan, M. Leunig and R.K. Jain, Fluorescence Photobleaching with Spatial Fourier Analysis: Measurement of Diffusion in Light-Scattering Media, Biophysical Journal, 65:2428-2436 (1993).
36. P.E.G. Kristjansen, Y. Boucher and R.K. Jain, Dexamethasone Reduces the Interstitial Fluid Pressure in a Human Colon Adenocarcinoma Xenograft, Cancer Research, 53:4764-4766 (1993).
37. R.J. Melder, A.L. Brownell, T.M. Shoup, G.L. Brownell and R.K. Jain, Imaging of Activated Natural Killer Cells in Mice by Positron Emission Tomography: Preferential Uptake in Tumors, Cancer Research, 53:5867-5871 (1993).

Reviews, Commentaries and Book Chapters

38. R.K. Jain and L.T. Baxter, Extravasation and Interstitial Transport in Tumors, In: Biological Barriers to Protein Delivery, K.L. Audus and T.J. Raub, Eds., Chapter 15, pp. 441-465, Plenum Press, New York (1993).
39. R.K. Jain, Physiological Resistance to the Treatment of Solid Tumors, In: Drug Resistance in Oncology, B. Teicher, Ed., Chapter 4, pp. 87-105, M. Dekker, New York (1993).
40. R.J. Melder and R.K. Jain, Delivery of Effector Cells to Tumors, In: '93 Recent Advances in Cancer Research, J.G. Park, Ed., pp. 202-217, Seoul National University, Seoul, (1993).

1994 Publications

Original Articles

41. I.P. Torres-Filho, M. Leunig, F. Yuan, M. Intaglietta, and R.K. Jain, Non-invasive Measurement of Microvascular and Interstitial p02 Profiles in a Human Tumor in SCID Mice, Proc. Natl. Acad. Sci., 91:2081-2085 (1994).
42. M. Leunig, A.E. Goetz, F. Gamarra, G. Zetterer, K. Messmer and R.K Jain, Photodynamic Therapy-induced Alterations in Interstitial Fluid Pressure, Volume and Water Content of an Amelanotic Melanoma in the Hamster, British Journal of Cancer, 69:101-103 (1994a).
43. L.T. Baxter, H. Zhu, D. Mackensen and R.K. Jain, Physiologically Based Pharmacokinetic Model for Specific and Nonspecific Monoclonal Antibodies and Fragments in Human Tumor Xenograft in Nude Mice, Cancer Research, 54:1517-1528 (1994).
44. C.J. Eskey, N. Wolmark, C.L. McDowell, M.M. Domach and R.K. Jain, Residence Time Distributions of Various Tracers in Tumors: Implications for Drug Delivery and Blood Flow Measurement, Journal of the National Cancer Institute, 86:293-299 (1994).
45. I. Lee, Y. Boucher, T. J. Demhartner and R.K. Jain, Changes in Tumour Blood Flow, Oxygenation and Interstitial Fluid Pressure Induced by Pentoxifylline, British Journal of Cancer, 69:492-496 (1994a).
46. F. Yuan, M. Leunig, S.K. Huang, D.A. Berk, D. Papahadjopoulos and R.K. Jain, Microvascular Permeability and Interstitial Penetration of Sterically Stabilized (Stealth) Liposomes in a Human Tumor Xenograft, Cancer Research, 54:3352-3356 (1994a).
47. M. Leunig, F. Yuan, D. Berk, L.E. Gerweck and R.K. Jain, Angiogenesis and Growth of Isografted Bone: Quantitative In Vivo Assay in Nude Mice, Laboratory Investigations, 71:300-307 (1994b).
48. I. Lee, T.J. Demhartner, Y. Boucher, R.K. Jain and M. Intaglietta, Effect of Hemodilution and Resuscitation on Tumor Interstitial Fluid Pressure, Blood Flow and Oxygenation, Microvascular Research, 48:1-12 (1994b).
49. P.E.G. Kristjansen, S. Roberge, I. Lee and R.K. Jain, Tissue-Isolated Human Tumor Xenografts in Athymic Nude Mice, Microvascular Research, 48:389-402 (1994).
50. F. Yuan, H.A. Salehi, Y. Boucher, U.S. Vasthare, R.F. Tuma and R.K. Jain, Vascular Permeability and Microcirculation of Gliomas and Mammary Carcinomas Transplanted in Rat and Mouse Cranial Windows, Cancer Research, 54:4564-4568 (1994b).
51. A.J. Leu, D.A. Berk, F. Yuan and R.K. Jain, Flow Velocity in the Superficial Lymphatic Network of the Mouse Tail, American Journal of Physiology, 267:H1507-H1513 (1994).

Original Articles

52. I.P. Torres-Filho, M. Leunig, F. Yuan, M. Intaglietta, and R.K. Jain, Non-invasive Measurement of Microvascular and Interstitial p02 Profiles in a Human Tumor in SCID Mice, Proc. Natl. Acad. Sci., 91:2081-2085 (1994).
53. M. Leunig, A.E. Goetz, F. Gamarra, G. Zetterer, K. Messmer and R.K Jain, Photodynamic Therapy-induced Alterations in Interstitial Fluid Pressure, Volume and Water Content of an Amelanotic Melanoma in the Hamster, British Journal of Cancer, 69:101-103 (1994a).
54. L.T. Baxter, H. Zhu, D. Mackensen and R.K. Jain, Physiologically Based Pharmacokinetic Model for Specific and Nonspecific Monoclonal Antibodies and Fragments in Human Tumor Xenograft in Nude Mice, Cancer Research, 54:1517-1528 (1994).
55. C.J. Eskey, N. Wolmark, C.L. McDowell, M.M. Domach and R.K. Jain, Residence Time Distributions of Various Tracers in Tumors: Implications for Drug Delivery and Blood Flow Measurement, Journal of the National Cancer Institute, 86:293-299 (1994).
56. I. Lee, Y. Boucher, T. J. Demhartner and R.K. Jain, Changes in Tumour Blood Flow, Oxygenation and Interstitial Fluid Pressure Induced by Pentoxifylline, British Journal of Cancer, 69:492-496 (1994a).
57. F. Yuan, M. Leunig, S.K. Huang, D.A. Berk, D. Papahadjopoulos and R.K. Jain, Microvascular Permeability and Interstitial Penetration of Sterically Stabilized (Stealth) Liposomes in a Human Tumor Xenograft, Cancer Research, 54:3352-3356 (1994a).
58. M. Leunig, F. Yuan, D. Berk, L.E. Gerweck and R.K. Jain, Angiogenesis and Growth of Isografted Bone: Quantitative In Vivo Assay in Nude Mice, Laboratory Investigations, 71:300-307 (1994b).
59. I. Lee, T.J. Demhartner, Y. Boucher, R.K. Jain and M. Intaglietta, Effect of Hemodilution and Resuscitation on Tumor Interstitial Fluid Pressure, Blood Flow and Oxygenation, Microvascular Research, 48:1-12 (1994b).
60. P.E.G. Kristjansen, S. Roberge, I. Lee and R.K. Jain, Tissue-Isolated Human Tumor Xenografts in Athymic Nude Mice, Microvascular Research, 48:389-402 (1994).
61. F. Yuan, H.A. Salehi, Y. Boucher, U.S. Vasthare, R.F. Tuma and R.K. Jain, Vascular Permeability and Microcirculation of Gliomas and Mammary Carcinomas Transplanted in Rat and Mouse Cranial Windows, Cancer Research, 54:4564-4568 (1994b).
62. A.J. Leu, D.A. Berk, F. Yuan and R.K. Jain, Flow Velocity in the Superficial Lymphatic Network of the Mouse Tail, American Journal of Physiology, 267:H1507-H1513 (1994).
63. G.R. Martin and R.K. Jain, Noninvasive Measurement of Interstitial pH Profiles in Normal and Neoplastic Tissue Using Fluorescence Ratio Imaging Microscopy, Cancer Research, 54:5670-5674 (1994).
64. L. Hamberg, P.E.G. Kristjansen, G.J. Hunter, G.L. Wolf and R.K. Jain, Spatial Heterogeneity in Tumor Perfusion Measured with Functional Computed Tomography at 0.05ml Resolution, Cancer Research, 54:6032-6036 (1994).

1994 Publications

65. L.L. Munn, R.J. Melder and R.K. Jain, Analysis of Cell Flux in the Parallel Plate Flow Chamber: Implications for Cell Capture Studies, Biophysical Journal, 67:889-895 (1994).

66. R.J. Melder and R.K. Jain, Reduction of Rigidity in Human Activated Natural Killer Cells by Thioglycollate Treatment, Journal of Immunological Methods, 175:69-77 (1994).
67. R.J. Melder, D. Elmaleh, A. L. Brownell, G. L. Brownell and R.K. Jain, A Method for Labeling Cells for Positron Emission Tomography (PET) Studies, Journal of Immunological Methods, 175:79-87 (1994).

Reviews, Commentaries and Book Chapters

68. R.K. Jain, Transport Phenomena in Tumors, Advances in Chemical Engineering, 20:129-200 (1994a).
69. R.K Jain, Tumor Microcirculation: Role in Cancer Diagnosis and Treatment, In: Progress in Microcirculation Research, H. Niimi, et al, Eds., pp. 29-36, Pergamon Press, Tarrytown (1994b).
70. R.K. Jain, Barriers to Drug Delivery in Solid Tumors, Scientific American, 271:58-65 (1994c).

1995 Publications

Original Articles

71. E.M. Johnson, D.A. Berk, R.K. Jain and W.M. Deen, Diffusion and Partitioning of Proteins in Charged Agarose Gels, Biophysical Journal, 68:1561-1568 (1995).
72. R.J. Melder, H.A. Salehi, and R.K. Jain, Interaction of Activated Natural Killer Cells with Normal and Tumor Vessels in Cranial Windows in Mice, Microvascular Research, 50:35-44 (1995a).
73. F. Yuan, M. Dellian, D. Fukumura, M. Leunig, D.A. Berk V.P. Torchilin and R.K. Jain, Vascular Permeability in a Human Tumor Xenograft: Molecular Size-dependence and Cut-off Size, Cancer Research, 55:3752-3756 (1995).
74. Y. Boucher, I. Lee and R.K. Jain, Lack of General Correlation between Interstitial Fluid Pressure and Oxygen Partial Pressure in Solid Tumors, Microvascular Research, 50:175-182 (1995).
75. L.L. Munn, G.C. Koenig, R.K. Jain and R.J. Melder, Kinetics of Adhesion Molecule Expression and Spatial Organization Using Targeted Sampling Fluoremetry, BioTechniques, 19:622-631 (1995).
76. Y. Gazit, D.A. Berk, M. Leunig, L.T. Baxter and R.K. Jain, Scale-Invariant Behavior and Vascular Network Formation in Normal and Tumor Tissue, Physical Review Letters, 75:2428-2431 (1995).
77. L.T. Baxter, H. Zhu, D.G. Mackensen, W.F. Butler and R.K. Jain, Biodistribution of Monoclonal Antibodies: Scale-up from Mouse to Human Using a Physiologically Based Pharmacokinetic Model, Cancer Research, 55:4611-4622 (1995).
78. D. Fukumura, H. Salehi, B. Witwer, R.F. Tuma, R.J. Melder and R.K. Jain, TNFα-Induced Leukocyte-Adhesion in Normal and Tumor Vessels: Effect of Tumor Type, Transplantation Site and Host, Cancer Research, 55:4824-4829 (1995).
79. S. Yamada, T. Mayadas, F. Yuan, D. Wagner, R. Hynes, R. Melder and R.K. Jain, Rolling in P-Selectin Deficient Mice is Reduced but Not Eliminated in the Dorsal Skin, Blood, 86:3487-3492 (1995a).
80. R.J. Melder, L.L. Munn, S. Yamada, C. Ohkubo and R.K. Jain, Selectin and Integrin Mediated T Lymphocyte Rolling and Arrest on TNFα-activated Endothelium is Augmented by Erythrocytes, Biophysical Journal, 69:2131-2138 (1995b).
81. R.A. Zlotecki, L.T. Baxter, Y. Boucher and R.K. Jain, Pharmacologic Modification of Tumor Blood Flow and Interstitial Fluid Pressure in a Human Tumor Xenograft: Network Analysis and Mechanistic Interpretation, Microvascular Research, 50:429-443 (1995).
82. M. Leunig, F. Yuan, L. E. Gerweck, D.A. Berk and R.K. Jain, Quantitative Analysis of Angiogenesis and Growth of Bone: Consequences of Indomethacin Exposure in a Combined In Vitro - In Vivo Approach, Res. Exp. Medicine, 195:275-288 (1995).
83. P.A. Netti, L.T. Baxter, Y. Boucher, R. Skalak and R.K. Jain, Time Dependent Behavior of Interstitial Pressure in Solid Tumors: Implications for Drug Delivery, Cancer Research, 55:5451-5458 (1995).
84. S. Yamada, R. J. Melder, M. Leunig, C. Ohkubo and R.K. Jain, Leukocyte-rolling Increases with Age, Blood, 86:4707-4708 (1995b).

1996 Publications

Original Articles

85. M.A. Swartz, D.A. Berk and R.K. Jain, Transport in Lymphatic Capillaries: I. Macroscopic Measurements Using Residence Time Distribution Theory, American Journal of Physiology, 270:H324-H329 (1996).
86. D.A. Berk, M.A. Swartz, A.J. Leu and R.K. Jain, Transport in Lymphatic Capillaries: II. Microscopic Velocity Measurement with Fluorescence Recovery After Photobleaching, American Journal of Physiology, 270:H330-H337 (1996).
87. P.E.G. Kristjansen, T.J. Brown, L.A. Shipley and R.K. Jain, Intratumor Pharmacokinetics, Flow Resistance, and Metabolism During Gemcitabine Infusion in Ex Vivo Perfused Human Small Cell Lung Cancer, Clinical Cancer Research, 2:359-367 (1996).
88. C.A. Znati, M. Rosenstein, Y. Boucher, M.W. Epperly, W.D. Bloomer and R.K. Jain, Effect of Radiation on Interstitial Fluid Pressure and Oxygenation in a Human Colon Carcinoma Xenograft, Cancer Research, 56:964-968 (1996).
89. L.T. Baxter and R.K. Jain, Pharmacokinetic Analysis of the Microscopic Distribution of Enzyme-conjugated Antibodies and Prodrugs: Comparison with Experimental Data, British Journal of Cancer, 73:447-456 (1996).
90. S. Patan, L. Munn and R.K. Jain, Intussusceptive Microvascular Growth in Solid Tumors: A Novel Mechanism of Tumor Angiogenesis, Microvascular Research, 51:260-272 (1996).

1996 Publications

91. E.M. Johnson, D.A. Berk, R.K. Jain and W.M. Deen, Hindered Diffusion in Agarose Gels: Test of Effective Medium Model, Biophysical Journal, 70:1017-1026 (1996a).
92. M. Leunig, F. Yuan, D.A. Berk, L. Gerweck and R.K. Jain, Heating or Freezing Bone: Effects on Angiogenesis Induction and Growth Potential in Mice, Acta Orthop Scand., 67:383-388 (1996).
93. J.W. Baish, Y. Gazit, D.A. Berk, M. Nozue, L.T. Baxter and R.K. Jain, Role of Tumor Vascular Architecture in Nutrient and Drug Delivery: An Invasion Percolation Model, Microvascular Research, 51:327-346 (1996).
94. M. Dellian, B.P. Witwer, H.A. Salehi, F. Yuan and R.K. Jain, Quantitation and Physiological Characterization of bFGF and VEGF/VPF Induced Vessels in Mice: Effect of Microenvironment on Angiogenesis, American Journal of Pathology, 149:59-71 (1996a).
95. L.L. Munn, R.J. Melder and R.K. Jain, Role of Erythrocytes in Leukocyte-endothelial Interactions: Mathematical Model and Experimental Validation, Biophysical Journal, 71:466-478 (1996).
96. M. Nozue, I. Lee, J.M. Manning, L. R. Manning and R.K. Jain, Oxygenation in Tumors by Modified Hemoglobins, Journal of Surgical Oncology, 62:109-114 (1996).
97. P.A. Netti, S. Roberge, Y. Boucher, L.T. Baxter, and R.K. Jain, Effect of Transvascular Fluid Exchange on Arterio-Venous Pressure Relationship: Implication for Temporal and Spatial Heterogeneities in Tumor Blood Flow, Microvascular Research, 52:27-46 (1996).
98. C.A. Kristensen, M. Nozue, Y. Boucher and R.K. Jain, Reduction of Interstitial Fluid Pressure After TNF-α Treatment of Human Melanoma Xenografts, British Journal of Cancer, 74:533-536 (1996).
99. H. Zhu, R. Melder, L. Baxter and R.K. Jain, Physiologically Based Kinetic Model of Effector Cell Biodistribution in Mammals: Implications for Adoptive Immunotherapy, Cancer Research, 56:3771-3781 (1996).
100. Y. Boucher, M. Leunig and R.K. Jain, Tumor Angiogenesis and Interstitial Hypertension, Cancer Research, 56:4264-4266 (1996).
101. R.J. Melder, G. Koenig, B.P. Witwer, N. Safabakhsh, L.L. Munn and R.K. Jain, During Angiogenesis, Vascular Endothelial Growth Factor and Basic Fibroblast Growth Factor Regulate Natural Killer Cell Adhesion to Tumor Endothelium, Nature Medicine, 2:992-997 (1996).
102. R. Skalak, S. Zargaryan, P. Netti, R.K. Jain and A. Hoger, Compatibility and the Genesis of Residual Stress by Volumetric Growth, Journal of Mathematical Biology, 34:889-914 (1996).
103. M. Dellian, G. Helmlinger, F. Yuan and R.K. Jain, Fluorescence Ratio Imaging and Optical Sectioning: Effect of Glucose on Spatial and Temporal Gradients, British Journal of Cancer, 74:1206-1215 (1996b).
104. M.E. Johnson, D.A. Berk, D. Blankschtein, D.E. Golan, R.K. Jain and R. Langer, Lateral Diffusion of Small Compounds in Human Stratum Corneum and Model Lipid Bilayer Systems, Biophysical Journal, 71:2656-2668 (1996b).
105. F. Yuan, Y. Chen, M. Dellian, N. Safabakhsh, N. Ferrara and R.K. Jain, Time-dependent Vascular Regression and Permeability Changes in Established Human Tumor Xenografts Induced By an Anti-VEGF/VPF Antibody, Proceedings of the National Academy of Sciences, 93:14765-14770 (1996).
106. H.C. Lichtenbeld, F. Yuan, C.C. Michel and R.K. Jain, Perfusion of Single Tumor Microvessels: Application to Vascular Permeability Measurement, Microcirculation, 3:349-357 (1996).

Reviews, Commentaries and Book Chapters

107. R.K. Jain, Delivery of Molecular Medicine to Solid Tumors, Science, 271:1079-1080 (1996).
108. W. M. Saltzman and R.K. Jain, Drug Delivery: Barriers to Drug Transport and the Design of Novel Therapeutic Agents, Molecular Medicine Today, 1:4 (1996).
109. R.K. Jain, 1995 Whitaker Lecture: Delivery of Molecules, Particles and Cells to Solid Tumors, Annals of Biomedical Engineering, 24:457-473 (1996).
110. R.K. Jain, G. Koenig, M. Dellian, D. Fukumura, L.L. Munn and R.J. Melder, Leukocyte-Endothelial Adhesion and Angiogenesis in Tumors, Cancer and Metastasis Reviews, 15:195-204 (1996).
111. R.K. Jain, Solid Tumor Barriers to Anticancer Drugs, Cope, 12:22-23 (1996).

1997 Publications

Original Articles

112. G. Helmlinger, F. Yuan, M. Dellian and R.K. Jain, Interstitial pH and pO2 Gradients in Solid Tumors In Vivo: High-Resolution Measurements Reveal a Lack of Correlation, Nature Medicine, 3:177-182 (1997a).
113. C.A. Kristensen, S. Roberge and R.K. Jain, Effect of Tumor Necrosis Factor-a on Vascular Resistance, Nitric Oxide Production, Glucose and Oxygen Consumption in Perfused, Tissue-Isolated Human Melanoma Xenografts, Clinical Cancer Research, 3:319-324 (1997).
114. D. Fukumura, F. Yuan, M. Endo and R. K. Jain, Role of Nitric Oxide in Tumor Microcirculation: Blood Flow, Vascular Permeability, and Leukocyte-endothelial Interactions, American Journal of Pathology, 150:713-725 (1997a).
115. J. R. Less, M.C. Posner, T.C. Skalak, N. Wolmark and R.K. Jain, Geometric Resistance and Microvascular Network Architecture of Human Colorectal Carcinoma, Microcirculation, 4:25-33 (1997).
116. Y. Boucher, H. Salehi, B. Witwer, G.R. Harsh, IV and R.K, Jain, Interstitial Fluid Pressure in Intracranial Tumors in Patients and in Rodents, British Journal of Cancer, 75:829-836 (1997).
117. P.A. Netti, L.T. Baxter, Y. Boucher, R. Skalak and R.K. Jain, Macro- and Microscopic Fluid Transport in Living Tissues: Application to Solid Tumors, AIChE Journal, 43:818-834 (1997).
118. R.J. Melder, G. Koenig, L.L. Munn and R.K. Jain, Adhesion of Activated Natural Killer Cells to TNF-beta Treated Endothelium Under Physiological Flow Conditions, Natural Immunity, 15:154-163 (1997).

1997 Publications

119. H. Zhu, L. Baxter, and R.K. Jain, Potential and Limitations of Radioimmunodetection and Radioimmunotherapy with Monoclonal Antibodies: Evaluation Using a Physiologically-Based Pharmacokinetic Model, Journal of Nuclear Medicine, 38:731-741 (1997).

120. D.A. Berk, F. Yuan, M. Leunig and R.K. Jain, Direct in vivo Measurement of Targeted Binding in a Human Tumor Xenograft, Proceedings National Academy of Sciences USA, 94:1785-1790 (1997).
121. J.W. Baish, P.A. Netti and R.K. Jain, Transmural Coupling of Fluid Flow in Microcirculatory Network and Interstitium in Tumors, Microvascular Research, 53:128-141 (1997).
122. M. Jeltsch, A. Kaipainen, V. Joukov, X. Meng, M. Lakso, H. Rauvala, M. Swartz, D. Fukumura, R.K. Jain, and K. Alitalo, Hyperplasia of Lymphatic Vessels in VEGF-C Transgenic Mice, Science, 276:1423-1425 (1997).
123. M. Leunig, F. Yuan, L. Gerweck and R.K. Jain, Effect of bFGF on Angiogenesis and Growth of Isografted Bone: Quantitative in vitro -in vivo Analysis in Mice, International Journal of Microcirculation, 17:1-9 (1997).
124. T. Shioda, L.L Munn, R.K. Jain and K.J. Isselbacher, Early Events of Metastasis in the Microcirculation Involve Changes in Gene Expression of Cancer Cells, American Journal of Pathology, 150:2099-2112 (1997).
125. G. Helmlinger, P.A. Netti, H.C. Lichtenbeld, R.J. Melder and R.K. Jain, Solid Stress Inhibits the Growth of Multicellular Tumor Spheroids, Nature Biotechnology, 15:778-783 (1997b).
126. D. Fukumura, F. Yuan, W. L. Monsky, Y. Chen and R.K. Jain, Effect of Host Microenvironment on the Microcirculation of Human Colon Adenocarcinoma, American Journal of Pathology, 150:679-688 (1997b).
127. G. Griffon-Etienne, Y. Boucher, R.K. Jain and H.D. Suit, Effects of Needle Insertion in Tumors on Interstitial Fluid Pressure, Microvascular Research, 54:174-177 (1997).
128. M. Nozue, I. Lee, F. Yuan, B. Teicher, D. M. Brizel, M.W. Dewhirst, C. G. Milross, L. Milas, C.W. Song, C.D. Thomas, M. Guichard, S.M. Evans, C.J. Koch, E.M. Lord, R.K. Jain and H.D. Suit, Interlaboratory Variation in Oxygen Tension Measurement by Eppendorf Histograph and Comparison With Hypoxic Marker, Journal of Surgical Oncology, 66:30-38 (1997a).
129. Y. Gazit, J.W. Baish, N. Safabakhsh, M. Leunig, L.T. Baxter and R.K. Jain, Fractal Characteristics of Tumor Vascular Architecture During Tumor Growth and Regression, Microcirculation, 4:395-402 (1997).
130. M. Nozue, I. Lee, A. Hartford, S. Tanda, H.D. Suit and R.K. Jain, p02 Measurements in Murine Tumors Using Eppendorf Histograph: Calibration, Reproducibility and Comparison with Diamond-General Device, International Journal of Oncology, 9:955-962 (1997b).

Reviews, Commentaries and Book Chapters

131. R.K. Jain, 1996 Landis Award Lecture: Delivery of Molecular and Cellular Medicine to Solid Tumors, Microcirculation, 4:1-23 (1997).
132. D.M. Briscoe, P. Ganz, S.I. Alexander, R.J. Melder, R.K. Jain, R.S. Cotran and A.H. Lichtman, The Problem of Chronic Rejection: Influence of Leukocyte-Endothelial Interactions, Kidney International, 51:S-22-S-27 (1997).
133. R.K. Jain, Vascular and Interstitial Physiology of Tumours: Role in Cancer Detection and Treatment, In: Tumor Angiogenesis, R. Bicknell, C. Lewis and N. Ferrara, Eds., Oxford University Press, Oxford, pp. 45-59 (1997).
134. R.K. Jain, Delivery of Molecular and Cellular Medicine to Solid Tumors, Advanced Drug Delivery Reviews, 26:71-90 (1997).
135. R.K. Jain, K. Schlenger, M. Höckel and F. Yuan, Quantitative Angiogenesis Assays: Progress and Problems, Nature Medicine, 3:1203-1208 (1997).
136. R.K. Jain, Delivery of Molecular Medicine to Solid Tumors, In: Microcirculation Annual 1997, M. Tsuchiya, M. Asano and N. Sato, Eds., Nihon-Igakukan, Tokyo, 13:1-5 (1997).
137. R.K. Jain, Tumor Microcirculation: Role in Drug and Nutrient Delivery, In: Advances in Blood Substitutes, Eds., R.M. Winslow, K. D. Vandegriff, and M. Intaglietta, Birkhäuser, Boston, pp. 46-70 (1997).

1998 Publications

Original Articles

138. H. Zhu, R.K. Jain and L.T. Baxter, Tumor Pretargeting for Radioimmunodetection and Radioimmunotherapy: Evaluation Using a Physiologically-Based Pharmacokinetic Model, Journal of Nuclear Medicine, 39:65-76 (1998).
139. S. Hobbs, W. Monsky, F. Yuan, G. Roberts, L. Griffiths, V.P. Torchilin and R.K. Jain, Regulation of Transport Pathways in Tumor Vessels: Role of Tumor Type and Microenvironment, Proceedings National Academy of Sciences USA, 95:4607-4612 (1998).
140. G.J. Hunter, L.M. Hamberg, N. Choi, R.K. Jain, T. McCloud and A.J. Fischman, Dynamic T1-weighted Magnetic Resonance Imaging and Positron Emission Tomography in Patients with Lung Cancer: Correlating Vascular Physiology with Glucose Metabolism, Clinical Cancer Research, 4:949-955 (1998).
141. M. Rosenzweig, M. DeMaria, D. Harper, S. Friedrich, R.K. Jain and R. P. Johnson, Increased Rates of CD4+ and CD8+ T Lymphocyte Turnover in Simian Immunodeficiency Virus-infected Macaques, Proceedings National Academy of Sciences USA, 95:6388-6393 (1998).
142. U. Schoeph, E.M. Marecos, R.J. Melder, R.K. Jain and R. Weissleder, Intracellular Magnetic Labeling of Lymphocytes for in vivo Trafficking Studies, Biotechniques, 24:642-651 (1998).
143. M. Detmar, L.F. Brown, M.P. Schön, B.M. Elicker, L. Richard, P. Velasco, D. Fukumura, W. Monsky, K.P. Claffey and R.K. Jain, Increased Microvascular Density and Enhanced Leukocyte Rolling and Adhesion in the Skin of VEGF Transgenic Mice, Journal of Investigative Dermatology, 3:1-6 (1998).

1998 Publications

144. P. Carmeliet, Y. Dor, J.M. Herbert, D. Fukumura, K. Brusselmans, M. Dewerchin, M. Neeman, F. Bono, R. Abramovitch, P. Maxwell, C.J. Koch, P. Ratcliffe, L. Moons, R.K. Jain, D. Collen and Eli Keshet, Role of HIF-1αin Hypoxia-mediated Apoptosis, Cell Proliferation and Tumor Angiogenesis, Nature, 394:485-490 (1998).
145. D. Fukumura, R. Xavier, T. Sugiura, Y. Chen, E.C. Parks, N. Lu, M. Selig, G. Nielsen, T. Taksir, R.K. Jain and B. Seed, Tumor Induction of VEGF Promoter Activity in Stromal Cells, Cell, 94:715-725 (1998).
146. R.K. Jain, N. Safabakhsh, A. Sckell, Y. Chen, L.A. Benjamin, F. Yuan and E. Keshet, Endothelial Cell Death, Angiogenesis, and Microvascular Function Following Castration in an Androgen-dependent Tumor: Role of VEGF, Proceedings of the National Academy of Sciences USA, 95:10820-10825 (1998a).
147. D.S. Milstone, D. Fukumura, R.C. Padget, P.E. O'Donnell, V.M. Davis, O.J. Benavidez, R.J. Melder, R.K. Jain and M.A. Gimbrone, Mice Lacking E-Selectin Show Normal Rolling But Reduced Arrest of Leukocytes on Cytokine-Activated Microvascular Endothelium, Microcirculation, 5:153-171 (1998).
148. Y. Boucher, C. Brekken, P.A. Netti, L.T. Baxter and R.K. Jain, Intratumoral Infusion of Fluid: Estimation of Hydraulic Conductivity and Implications for the Delivery of Therapeutic Agents, British Journal of Cancer, 78:1442-1448 (1998).
149. A. Sckell, N. Safabakhsh, M. Dellian and R.K. Jain, Primary Tumor Size-Dependent Inhibition of Angiogenesis at a Secondary Site: An Intravital Microscopic Study in Mice, Cancer Research, 58:5866-5869 (1998).
150. Review, Commentaries and Book Chapters
151. R.K. Jain, The Next Frontier of Molecular Medicine: Delivery of Therapeutics, Nature Medicine, 4:655-657 (1998a).
152. R.K. Jain, Integrative Pathophysiology of Solid Tumors: Role in Detection and Treatment, The Cancer Journal from Scientific American, 4:48-57 (1998b).
153. R.K. Jain, Delivery of Molecular and Cellular Medicine to Solid Tumors, Journal of Controlled Release, 53:49-67 (1998).
154. D. Fukumura and R.K. Jain, Role of Nitric Oxide in Angiogenesis and Microcirculation in Tumors, Cancer and Metastasis Reviews, 17:77-89 (1998).
155. J.W. Baish and R.K. Jain, Cancer, Angiogenesis and Fractals, Nature Medicine, 4:984 (1998).
156. R.K. Jain, Tumor Microcirculation: Role in Delivery of Molecular and Cellular Medicine, In: The Biology of Tumors, Proceedings of the Ninth Annual Pezcoller Symposium on the Biology of Tumors, Rovereto, Italy, June 4-7, 1997, 319-345 (1998).
157. R.K. Jain, Delivery of Monoclonal Antibodies to the Tumor Cell, In: Monoclonal Antibody-Based Therapy of Cancer, M.L. Grossbard, Ed., Marcel Dekker, Inc., New York, pp. 23-52 (1998).
158. R.K. Jain, Microcirculation and Transport Phenomena in Tumours, In: Connective Tissue Biology: Integration and Reductionism. R.K. Reed and K. Rubin Eds., Portland Press Ltd., London, 71:269-293 (1998).
159. R.K. Jain, L.L. Munn, D. Fukumura and R.J. Melder, In vitro and In vivo Quantification of Adhesion Between Leukocytes and Vascular Endothelium, In: Methods in Molecular Medicine - Methods in Tissue Engineering, J.R. Morgan and M.L. Yarmush, Eds., Humana Press, Totowa, pp. 553-575 (1998b).

1999 Publications

Original Articles

160. P.A. Netti, L.M. Hamberg, J.W. Babich, S. Roberge, D. Kierstead, W. Graham, G.J. Hunter, G.L. Wolf, A. Fischman, Y. Boucher and R.K. Jain, Enhancement of Fluid Filtration Across Tumor Vessels: Implication for Delivery of Macromolecules, Proceedings of the National Academy of Sciences USA, 96:3137-3142 (1999).
161. C.A. Kristensen, N. Askenasy, R.K. Jain and A.P. Koretsky, Creatine and Cyclocreatine Treatment of Human Colon Adenocarcinoma Xenografts:31P and 1H Magnetic Resonance Spectroscopic Studies, British Journal of Cancer, 79:278-285 (1999a).
162. S.A. Slavin, A.D. van den Abbeele, A. Losken, M. Swartz and R.K. Jain, Return of Lymphatic Function Following Flap Transfer for Acute Lymphedema, Annals of Surgery, 229:421-427 (1999).
163. H.C. Lichtenbeld, N. Ferrara, R.K. Jain and L. L. Munn, Effect of Anti-VEGF Antibody on Tumor Microvessel Permeability, Microvascular Research, 57:357-362 (1999).
164. A. Pluen, P.A. Netti, R.K. Jain and D.A. Berk, Diffusion of Macromolecules in Agarose Gels: Comparison of Linear and Globular Configurations, Biophysical Journal, 77:542-552 (1999).
165. G. Griffon-Etienne, Y. Boucher, C. Brekken, H.D. Suit and R.K. Jain, Taxane-Induced Apoptosis Decompresses Blood Vessels and Lowers Interstitial Fluid Pressure in Solid Tumors: Clinical Implications, Cancer Research, 59:3776-3782 (1999).
166. W.L. Monsky, D. Fukumura, T. Gohongi, M. Ancukiewcz, H.A. Weich, V.P, Torchilin, F. Yuan and R.K. Jain, Augmentation of Transvascular Transport of Macromolecules and Nanoparticles in Tumors Using Vascular Endothelial Growth Factor, Cancer Research, 59:4129-4135 (1999).
167. M. Heijn, S. Roberge and R.K Jain, Cellular Membrane Permeability of Anthracyclines Does Not Effect Their Delivery in a Tissue Isolated Tumor, Cancer Research, 59:4458-4463 (1999).
168. M. Endo, R.K. Jain, B. Witwer and D. Brown, Water Channel (Aquaporin 1) Expression and Distribution in Mammary Carcinomas and Glioblastomas, Microvascular Research , 58:89-98 (1999).
169. M.A. Swartz, A. Kaipainen, P. Netti, C. Brekken, Y. Boucher, A.J. Grodzinsky and R.K. Jain, Mechanics of Interstitial-Lymphatic Fluid Transport: Theoretical Foundation and Experimental Validation, Journal of Biomechanics , 32: 1297-1303 (1999a).
170. M.A. Swartz, C.A. Kristensen, R.J. Melder, S. Roberge, E. Calautti, D. Fukumura, and R.K. Jain, Cells Shed from Tumors Show Reduced Clonogenicity, Resistance to Apoptosis, and in vivo Tumorigenicity, British Journal of Cancer, 81:756-759 (1999b).

1999 Publications

171. K.S. Moulton, R.J. Melder, V. Dharnidharka, J. Hardin-Young, R.K. Jain, and D.M. Briscoe, Angiogenesis in the huPBL-SCID Model of Human Transplant Rejection, Transplantation, 67:1626-1631 (1999).
172. T. Gohongi, D. Fukumura, Y. Boucher, C. Yun, G.A. Soff, C. Compton, T. Todoroki and R.K. Jain, Tumor-host Interactions in the Gallbladder Suppress Distal Angiogenesis and Tumor Growth: Role of TGFβ, Nature Medicine, 5:1203-1208 (1999).
173. C. A. Kristensen, L. M. Hamberg, G. J. Hunter, S. Roberge, D. Kierstead, G. L. Wolf and R.K. Jain, Changes in Vascularization of Human Breast Cancer Xenografts Responding to Estrogen Withdrawal and Tamoxifen Therapy, Neoplasia, 1:518-525 (1999b).
174. P. Somasundaran, S. Simpson, I. Ivanov, R.K. Jain, and D. Sarkar, Thinning and Rupture of Aqueous Surfactant Films on Silica, Langmuir, 15:7658-7661 (1999).

Reviews, Commentaries and Book Chapters

175. R.K. Jain, Understanding Barriers to Drug Delivery: High Resolution In vivo Imaging is Key, Clinical Cancer Research, 5:1605-1606 (1999).
176. R.K. Jain, Transport of Molecules, Particles, and Cells in Solid Tumors, Annual Reviews of Biomedical Engineering, 1:241-263 (1999).

2000 Publications

Original Articles

177. S. Ramanujan, G.C. Koenig, T.P. Padera, B.R. Stoll and R.K. Jain, Local Imbalance of ProAngiogenic and AntiAngiogenic Factors: A Potential Mechanism of Focal Necrosis and Dormancy in Tumors, Cancer Research, 60:1442-1448 (2000).
178. R.J. Melder, J. Yuan, L.L. Munn, R.K. Jain, Erythrocytes Enhance Lymphocyte Rolling and Arrest in Vivo, Microvascular Research, 59: 316-322 (2000).
179. Y.S. Chang, L.L. Munn, M.V. Hillsley, R. O. Dull, T.W. Gardner, R.K. Jain and J.M. Tarbell, Effect of Vascular Endothelial Growth Factor on Cultured Endothelial Cell Monolayer Transport Properties, Microvascular Research, 59:265-277 (2000).
180. H. Hashizume, P. Baluk, S. Morikawa, J.W. McLean, G. Thurston, S. Roberge, R.K. Jain and D.M. McDonald, Openings Between Defective Endothelial Cells Contribute to Tumor Vessel Leakiness, American Journal of Pathology, 156:1363-1380 (2000).
181. M. Dellian, F. Yuan, V.S. Trubetskoy, V.P. Torchilin and R.K. Jain, Vascular Permeability in a Human Tumor Xenograft: Molecular Charge Dependence, British Journal of Cancer, 82:1513-1518 (2000).
182. A.C. Hartford, T. Gohongi, D. Fukumura and R.K. Jain, Irradiation of a Primary Tumor, Unlike Surgical Removal, Enhances Angiogenesis Suppression at a Distal Site: Potential Role of Host-Tumor Interaction, Cancer Research, 60:2128-2131 (2000).
183. P.A. Netti, D.A. Berk, M.A. Swartz, A.J. Grodzinsky and R.K. Jain, Role of Extracellular Matrix Assembly in Interstitial Transport in Solid Tumors, Cancer Research, 60:2497-2503 (2000).
184. G. Helmlinger, M. Endo, N. Ferrara, L. Hlatky and R.K. Jain, Formation of Endothelial Cell Networks, Nature, 405:139-141 (2000).
185. A. Kaur, C.L. Hale, S. Ramanujan, R.K. Jain and R.P. Johnson. Differential Dynamics of CD4+ and CD8+ T Lymphocyte Proliferation and Activation in acute Simian Immunodeficiency Virus Infection, Journal of Virology, 74:8413-8424 (2000).
186. M. Stohrer, Y. Boucher, M. Stangassinger and R.K. Jain, Oncotic Pressure in Solid Tumors is Elevated, Cancer Research, 60:4251-4255 (2000).
187. A.J. Leu, D.A. Berk, A. Lymboussaki, K. Alitalo and R.K. Jain, Absence of Functional Lymphatics within a Murine Sarcoma: a Molecular and Functional Evaluation, Cancer Research, 60:4324-4327 (2000).
188. N. Hansen-Algenstaedt, B.R. Stoll, T.P. Padera, D.J. Hicklin, D. Fukumura and R.K. Jain, Tumor Oxygenation in Hormone-Dependent Tumors during VEGFR-2 Blockade, Hormone Ablation, and Chemotherapy, Cancer Research , 60:4556-4560 (2000).
189. P. Somasundaran, S. Simpson, R.K. Jain, I. Ivanov, V. Raghuraman, Investigation of Thin Aqueous Films on Silica Using a Modified Interferometric Technique, Journal of Colloid and Interface Science, 225:243-246 (2000).
190. C.G. Lee, M. Heijn, E. di Tomaso, G. Griffon-Etienne, M. Ancukiewicz, C. Koike, K.R. Park, N. Ferrara, R.K. Jain, H.D. Suit and Y. Boucher, Anti-VEGF Treatment Augments Tumor Radiation Response Under Normoxic or Hypoxic Conditions, Cancer Research, 60:5565-5570, (2000).
191. Y. Tsuzuki, D. Fukumura, B. Oosthuyse, C. Koike, P. Carmeliet and R.K. Jain. VEGF Modulation by Targeting HIF-1α→HRE→ VEGF Cascade Differentially Regulates Vascular Response and Growth Rate in Tumors, Cancer Research, 60:6248-6252, (2000).
192. Y.S. Chang, E. di Tomaso, D.M. McDonald. R. Jones, R.K. Jain and L.L. Munn. Mosaic Blood Vessels in Tumors: Frequency of Cancer Cells in Contact with Flowing Blood, Proceedings of the National Academy of Sciences USA, 97:14608-14613 (2000).

Reviews

193. R.K. Jain and L.L. Munn Leaky vessels? Call Ang! Nature Medicine, 6:131-32 (2000).
194. D.M. McDonald, L. Munn and R.K. Jain, Vasculogenic Mimicry: How Convincing, How Novel, and How Significant?, American Journal of Pathology, 156: 383-388 (2000).
195. R.K. Jain, Delivery of Biologic Molecules and Cells to Tumors, In: Biologic Therapy of Cancer: Principles and Practice, S. Rosenberg, Ed., Lippincott, Williams and Watkins, Philadelphia, pp. 865-874 (2000).
196. J.W. Baish and R.K. Jain, Fractals and Cancer, Cancer Research, 60:3683-88 (2000).
197. P. Carmeliet and R.K. Jain, Angiogenesis in Cancer and Other Diseases, Nature, 407:249-257 (2000).

2001 Publications

Original Articles

198. D. Fukumura, T. Gohongi, A Kadambi, J. Ang, C. Yun, D.G. Buerk, P.L. Huang and R.K. Jain, Predominant Role of Endothelial Nitric Oxide Synthase in VEGF-induced Angiogenesis and Vascular Permeability, PNAS, 98:2604-2609 (2001).
199. Pluen, Y. Boucher, S. Ramanujan, T.D. McKee, T. Gohongi, E. di Tomaso, E.B. Brown, Y. Izumi, R.B. Campbell, D.A. Berk, and R.K. Jain, Role of Tumor-Host Interactions in Interstitial Diffusion of Macromolecules: Cranial vs. subcutaneous tumors, PNAS, 98:4628-4633 (2001).
200. J. Yuan, R.J. Melder, R.K. Jain and L.L. Munn, A Lateral View Flow System for Studies of Cell Adhesion and Deformation under Flow Conditions, Biotechniques, 30:388-394 (2001).
201. S.V. Kozin, Y. Boucher, D.J. Hicklin, P. Bohlen, R.K. Jain and H.D. Suit., VEGF Receptor-2 Blocking Antibody Potentiates Radiation-Induced Long Term Control of Human Tumor Xenografts, Cancer Research, 61:39-44 (2001).
202. A. Kadambi, C.M. Carreira, C.-O. Yun, T.P. Padera, D.E.J.G.J. Dolmans, P. Carmeliet, D. Fukumura and R.K. Jain. Vascular Endothelial Growth Factor (VEGF)-C Differentially Affects Tumor Vascular Function and Leukocyte Recruitment: Role of VEGF-Receptor 2 and Host VEGF-A, Cancer Research, 61:2404-2408 (2001).
203. R.O. Dull, J. Yuan, Y.S. Chang, J. Tarbell, R.K. Jain, and L.L. Munn, Kinetics of Placenta Growth Factor/Vascular Endothelial Growth Factor Synergy in Endothelial Hydraulic Conductivity and Proliferation, Microvascular Research, 61:203-210 (2001).
204. R.J. Melder, C.A. Kristensen, L.L. Munn, and R.K. Jain, Modulation of A-NK Cell Rigidity: In Vitro Characterization and In Vivo Implications for Cell Delivery, Biorheology, 38:151-159 (2001).
205. E.B. Brown, R.B. Campbell, Y. Tsuzuki, L. Xu, P. Carmeliet, D. Fukumura, and R.K. Jain, In vivo Measurement of Gene Expression, Angiogenesis and Physiological Function in Tumors Using Multiphoton Laser Scanning Microscopy, Nature Medicine, 7:864-868 (2001).
206. C.L. Davies, R.J. Melder, L.L. Munn, C. Mouta-Carreira, R.K. Jain, and Y. Boucher, Decorin Inhibits Endothelial Migration and Tube-Like Structure Formation: Role of Thrombospondin-1, Microvascular Research, 62:26-42 (2001).
207. Losken, M.A. Swartz, A.D. Van Den Abbeele, R.K. Jain, and S.A. Slavin, A Potential Murine Model for Flap-Related Investigations, Plastic Reconstruction Surgery, 107:1504-1508 (2001).
208. D. Fukumura, L. Xu, Y. Chen, T. Gohongi, B. Seed, and R.K. Jain, Hypoxia and Acidosis Independently Up-Regulate VEGF Transcription in Brain Tumors In Vivo, Cancer Research, 61:6020-6024 (2001).
209. S. Patan, L.L. Munn, S. Tanda, S. Roberge, R.K. Jain, and R.C. Jones, Vascular Morphogenesis and Remodeling in a Model of Tissue Repair: Blood Vessel Formation and Growth in the Ovarian Pedicle after Ovariectomy, Circulation Research 89::23-731 (2001).
210. S. Patan, S. Tanda, S. Roberge, R.C. Jones, R.K. Jain and L.L. Munn, Vascular Morphogenesis and Remodeling in a Model of Tissue Repair: Blood Vessel Formation and Growth after Ovariectomy and Tumor Implantation, Circulation Research 89:732-739 (2001).
211. Y. Tsuzuki, C.M. Carreira, M. Bockhorn, L. Xu, R.K. Jain, D. Fukumura, Pancreas Microenvironment Promotes VEFG Expression And Tumor Growth: Novel Window Models for Pancreatic Tumor Angiogenesis And Microcirculation, Lab Investigations 81:1439-1451 (2001).
212. C. Mouta Carreira, S.M. Nasser, E. diTomaso, T.P. Padera, Y. Boucher, S.I. Tomarev, and R.K. Jain, LYVE-1 is not Restricted to the Lymph Vessels: Expression in Normal Liver Blood Sinusoids and Down-regulation in Human Liver Cancer and Cirrhosis, Cancer Research, 61:8079-8084 (2001).

Reviews, Commentaries and Book Chapters

213. R.K. Jain, Clearing the Smoke on Nicotine and Angiogenesis, Nature Medicine, 7:775-777 (2001).
214. R.K. Jain. Delivery of Molecular and Cellular Medicine to Solid Tumors, Adv Drug Deliv Rev, 46:149-168 (2001).
215. R.K. Jain, L.L. Munn, and D. Fukumura, Transparent Window Models and Intravital Microscopy: Imaging Gene Expression, Physiological Function and Drug Delivery in Tumors, In: Tumor Models in Cancer Research, B. Teicher, Ed., Humana Press, Inc., Totowa, NJ, Chapter 34:647-672 (2001).
216. R.K. Jain, Delivery of Molecular Medicine to Solid Tumors: Lessons from In Vivo Imaging of Gene Expression and Function, J Controlled Release, 74:7-25 (2001).
217. R.K. Jain, Normalizing Tumor Vasculature with Anti-Angiogenic Therapy: A New Paradigm for Combination Therapy, Nature Medicine, 7:987-989 (2001).
218. J.W. Baish and R.K. Jain, Correspondence Regarding Fractals and Cancer, Cancer Research 61:8348-8350, (2001).
219. R.K. Jain, In Memoriam: Pietro M. Gullino (1919-2001) Cancer Research, 61:930-8931 (2001).
220. R.K. Jain and N. Forbes, Can Engineered Bacteria Help Control Cancer?, PNAS, 98:14748-14750 (2001).
221. R.K. Jain and P. Carmeliet, Vessels of Death or Life, Scientific American, 258:38-45 (2001).

2002 Publications

222. T.P. Padera, B.R. Stoll, P.T.C. So, and R.K. Jain, Conventional and High-Speed Intravital Multiphoton Laser Scanning Microscopy of Microvasculature, Lymphatics, and Leukocyte-Endothelial Interactions, Molecular Imaging, 1:9-15 (2002).
223. L. Xu, D. Fukumura, R.K. Jain, Acidic extracellular pH induces vascular endothelial growth factor (VEGF) in human glioblastoma cells via ERK1/2 MAPK signaling pathway. Mechanism of low pH induced VEGF. J Biol Chem., 277:11368-11374 (2002).
224. Y. Izumi, L. Xu, E. di Tomaso, D. Fukumura, and R.K. Jain, Herceptin Acts as an Anti-angiogenic Cocktail, Nature, 416:279-280 (2002).

225. D.E.J.G.J. Dolmans, A. Kadambi, J.S. Hill, C.A. Waters, B.C. Robinson, J.P. Walker, D. Fukumura, and R.K. Jain, Vascular Accumulation of a Novel Photosensitizer, MV6401, Causes Selective Thrombosis in Tumor Vessels following Photodynamic Therapy, Cancer Research, 62:2151-2156 (2002).
226. W.L. Monsky, C. Mouta Carreira, Y. Tsuzuki, T. Gohongi, D. Fukumura, and R.K. Jain, Role of Host Microenvironment in Angiogenesis and Microvascular Functions in Human Breast Cancer Xenografts: Mammary Fat Pad vs. Cranial Tumors, Clinical Cancer Research, 8:1008-1013 (2002).
227. G. Helmlinger, A. Sckell, M. Dellian, N.S. Forbes, and R.K. Jain, Acid Production in Glycolysis-Impaired Tumors Provides New Insights into Tumor Metabolism, Clinical Cancer Research, 8:1284-1291 (2002).
228. S. Morikawa, Peter Baluk, T. Kaidoh, A. Haskell, R.K. Jain, and D.M. McDonald, Abnormalities In Pericytes on Blood Vessels and Endothelial Sprouts In Tumors, American Journal of Pathology, 160:985-1000 (2002).
229. R.J. Melder, L.L. Munn, B.R. Stoll, E.M. Marecos, L.T. Baxter, R. Weissleder, and R.K. Jain, Systemic Distribution And Tumor Localization Of Adoptively Transferred Lymphocytes In Mice: Comparison With Physiologically Based Pharmacokinetic Model, Neoplasia, 4:3-8 (2002).
230. T.P. Padera, A. Kadambi, E. di Tomaso, C. Mouta Carreira, E.B. Brown, Y. Boucher, N.C. Choi, D. Mathisen, J. Wain, E.J. Mark, L.L. Munn, R.K. Jain, Lymphatic Metastasis in the Absence of Functional Intratumor Lymphatics, Science, 296:1883-1886 (2002).
231. C. Koike, T.D. McKee, A. Pluen, S. Ramanujan, K. Burton, L.L. Munn, Y. Boucher, and R.K. Jain, Solid Stress Facilitates Spheroid Formation: Potential Involvement of Hyaluronan, BJC, 86:947-953 (2002).
232. C. de L. Davies, D.A. Berk, A. Pluen, and R.K. Jain, Comparison of IgG Diffusion and Extracellular Matrix Composition in Rhabdomyosarcomas Grown in Mice Versus In Vitro as Spheroids Reveals the Role of Host Stromal Cells, BJC, 86:1639-1644 (2002).
233. D.E.J.G.J. Dolmans, A. Kadambi, J.S. Hill, K. Flores, J. Gerber, J.P. Walker, I.H.M. Borel Rinkes, R.K. Jain, D. Fukumura, Targeting Tumor Vasculature and Cancer Cells in Orthotopic Breast Tumor by Fractionated Photosensitizer Dosing Photodynamic Therapy, Cancer Research, 62:4289-4294 (2002).
234. S. Ramanujan, A. Pluen, R.D. McKee, E.B. Brown, Y. Boucher, R.K. Jain, Diffusion and Convection in Collagen Gels: Implications for Transport in the Tumor Interstitium, Biophysical Journal, 83:1650-1660 (2002).
235. S.W. Friedrich, S.C. Lin, B.R. Stoll, L.T. Baxter, L.L.Munn and R.K. Jain, Antibody Directed Effector Cell Therapy of Tumors: Analysis and Optimization Using a Physiologically Based Pharmacokinetic Model, Neoplasia, 4:449-463 (2002).
236. C. Migliorini, Y.H. Qian, H. Chen, E.B. Brown, R.K. Jain and L.L. Munn, Red Blood Cells Augment Leukocyte Rolling in a Virtual Blood Vessel, Biophysical Journal, 83:1834-1841 (2002).
237. R.B. Campbell, D. Fukumura, E.B. Brown, L.M. Mazzola, Y. Izumi, R.K. Jain, V.P. Torchilin, and L.L. Munn, Cationic Charge Determines the Distribution of Liposomes between the Vascular and Extravascular Compartments of Tumors, Cancer Research, 62:6831-6836(2002).

Reviews

238. R.K. Jain, L.L. Munn, and D. Fukumura, Dissecting Tumor Pathophysiology using Intravital Microscopy, Nature Reviews Cancer, 2:266-276 (2002).
239. R.K. Jain and B.T. Fenton, Intratumoral Lymphatic Vessels: A Case of Mistaken Identity or Malfunction? JNCI, 94:417-421 (2002).
240. R.K. Jain and T.P. Padera, Prevention and Treatment of Lymphatic Metastasis by Anti-Lymphangiogenic Therapy, JNCI, 94:785-787 (2002).
241. R.K. Jain, Tumor Angiogenesis and Accessibility: Role of Vascular Endothelial Growth Factor, Seminars in Oncology, 29:3-9 (2002).
242. R.K.Jain, Angiogenesis and Lymphangiogenesis in Tumors: Insights from Intravital Microscopy, Cold Spring Harbor Symposia on Quantitative Biology, 67:239-248 (2002).

2003 Publications

Original Articles

243. H. Schmidt, EB. Brown, B. Schwaller and J. Eilers, Diffusional mobility of parvalbumin in spiny dendrites of cerebellar purkinje neurons quantified by fluorescence recovery after photobleaching. Biophys. J., 84:2599-2608, (2003).
244. Y. Izumi, E. di Tomaso, A. Hooper, P. Huang, J. Huber, DJ Hicklin, D Fukumura, R.K. Jain and H.D. Suit, Responses to Anti-Angiogenesis Treatment of Spontaneous Autochthonous Tumors and Their Isografts, Cancer Research, 63:747-751 (2003).
245. F. Mollica, R.K. Jain and P.A. Netti, A Model for Temporal Heterogeneities of Tumor Blood Flow, Microvascular Research, 65:56-60 (2003).
246. E. Brown, T. McKee, E. di Tomaso, B. Seed, Y. Boucher and R.K. Jain, Dynamic Imaging of Collagen and its Modulation in Tumors in vivo using Second Harmonic Generation. Nature Medicine, 9:796-801 (2003).
247. X. Wei, VG Henke, C Strübing, EB Brown and DE Clapham, Real-time imaging of nuclear permeation by EGFp in single intact cells. Biophys. J., 84:1317-1327, 2003.
248. P.A. Netti, F. Travascio, R.K. Jain, Coupled Macromolecular Transport and Gel Mechanics: Poroviscoelastic Approach, AIChE Journal, 49:1580-1596 (2003)

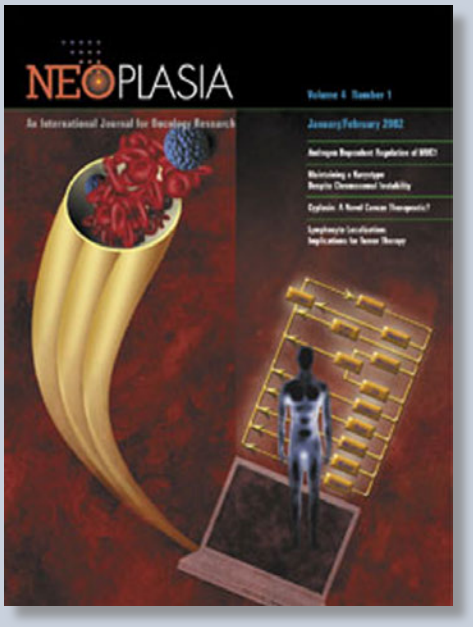
249. B.R. Stoll, C. Migliorini, A. Kadambi, L.L. Munn and R.K. Jain, A Mathematical Model of the Contribution of Endothelial Progenitor Cells to Angiogenesis in Solid Tumors: Implications for Anti-Angiogenic Therapy, Blood, 102:2555-2561.
250. N.S. Forbes, L.L. Munn, D. Fukumura and R.K. Jain, Sparse initial entrapment of systemically injected salmonella typhimurium leads to heterogeneous accumulation within tumor necrosis. Cancer Research, 63:5188-5193(2003).
251. A. Abdul-Karim, K, Al-Kofahi, E. Brown, R.K. Jain and B. Roysam Automated tracing and change analysis of angiogenic vasculature from in vivo multiphoton image time series. Microvascular Research, 66:113-125(2003).
252. C. Sun, C. Migliorini and L.L. Munn, Red blood cells initiate leukocyte rolling in postcapillary expansions: a lattice-Boltzmann analysis. Biophysical Journal, 85:208-222(2003).
253. D. Fukumura, A. Ushiyama, D. G. Duda, L. Xu, J. Tam, V. K. K. Chatterjee, I. Garkavtsev, and R.K. Jain. Paracrine Regulation of Angiogenesis and Adipocyte Differentiation during In Vivo Adipogenesis. Circulation Research, 93:E88-E97(2003).
254. M. Bockhorn, Tsuzuki Y, Xu L, Frilling A., Broelsch CE, and Fukumura D. Differential vascular and transcriptional responses to anti-vascular endothelial growth factor antibody in orthotopic human pancreatic cancer xenografts. Clin Cancer Res, 9:4221-4226(2003).
255. E.B. Friedrich, A.M. Tager, E. Liu, A. Pettersson, C. Owman, L. Munn, A.D. Luster, R.E. Gerszten. Mechanisms of leukotriene b4-triggered monocyte adhesion. Arterioscler Thromb Vasc Biol, 23:1761-1767(2003).
256. T. Roose, P.A. Netti, L.L. Munn, Y. Boucher and R.K. Jain, Solid stress generated by spheroid growth estimated using a linear poroelastisity model. Microvascular Research, 66:204-212(2003).
257. C.A. Znati, M. Rosenstein, T.D. Mckee, E. Brown, D. Turner, W.D. Bloomer, S. Watkins, R.K. Jain and Y. Boucher, Irradiation Reduces Interstitial Fluid Transport and Increases the Collagen Content in Tumors. Clinical Cancer Research, 9:5508-5513(2003).

Reviews

258. R.K. Jain and T. P. Padera, Lymphatics Make the Break, Science, 299:209-210 (2003).
259. D.E.J.G.J. Dolmans, D. Fukumura, R.K. Jain, Photodynamic Therapy for Cancer Nature Rev. Cancer 3:380-387 (2003).
260. R.K. Jain, Molecular Regulation of Vessel Maturation, Nature Medicine, 9:685-693 (2003).
261. L.L. Munn, Aberrant Vascular Architecture in Tumors and its Importance in Drug-based Therapies. Drug Discovery Today 8:396-403 (2003).
262. P.A. Netti and R.K. Jain, Interstitial Transport in Solid Tumors, In: Cancer Modeling and Simulation (Editor: L Preziosi) Chapman & Hall, Boca Raton, FL, Chapter 3, pp. 51-74 (2003).
263. R.K. Jain, Molecular Pathophysiology of Tumors, In: Principles and Practice of Radiation Oncology, 4th Edition (Editors: C. A. Parez, L. W. Brady, E. C. Halperin, and R. Schmidt-Ullrich), Lippincott, Williams & Wilkins, New York, Chapter 4, pp- 163-179(2003).
264. R.K. Jain and M. F. Booth, What brings pericytes to tumor vessels? Journal of Clinical Investigation 112:1134-1136(2003).
265. R.K. Jain and D. G. Duda, Role of bone marrow-derived cells in Tumor Angiogenesis and Treatment, Cancer Cell 3:515-516(2003).

2004 Publications

Original Articles



266. C. Willett, Boucher Y, diTomaso E, Duda D, Munn LL, Tong R, Chung D, Sahani D, Kalva S, Kozin S, Mino M, Cohen K, Scadden D, Hartford A, Fischman A, Clark J, Ryan D, Zhu A, Blaszkowsky L, Chen H, Shellito P, Lauwers G, Jain R.K. Direct evidence that the VEGF-specific antibody bevacizumab has antivascular effects in human rectal cancer, Nature Medicine, 10:145-147 (2004).
267. G. Alexandrakis, Brown E, Tong R, McKee T, Campbell R, Boucher Y, Jain R.K. Two-photon correlation spectroscopy reveals the two-phase nature of transport in tumors, Nature Medicine, 10:203-207 (2004).
268. T. Padera, Stoll B., Tooredman J., Capen D., diTomaso E., Jain R.K. Cancer cells compress intratumour vessels, Nature, 427:625(2004).
269. N. Koike, Fukumura D., Gralla O., Schechner J., Jain R.K. Creation of long-lasting blood vessels Nature, 428:138-139(2004).
270. I. Garkavtsev, Kozin, S, Chernova, O, Xu, L, Winkler, F, Brown, E, Barnett G, Jain R.K. The candidate tumour suppressor protein ING4 regulates brain tumour growth and angiogenesis. Nature, 428:328-332(2004).
271. T. Gohongi, T. Todoroki, D. Fukumura and R.K. Jain, Influence of the site of human gallbladder xenograft (Mz-ChA-1) on angiogenesis at the distant site Oncology Reports, 11:803-807 (2004).
272. M. Bockhorn, S. Roberge, C. Sousa, R.K. Jain and L. L. Munn, Differential Gene Expression in Metastasizing Cells Shed from Kidney Tumors, Cancer Research, 64:2469-2473 (2004).
273. E.B. Brown, Y. Boucher, S. Nasser, and R.K. Jain, Measurement of Macromolecular Diffusion Coefficients in Human Tumors, Microvascular Research, 67:231-236 (2004).
274. N. Isaka, T. P. Padera, J. Hagendoorn, D. Fukumura, and R.K. Jain, Peritumor lymphatics induced by vascular endothelial growth factor-C exhibit abnormal function, Cancer Research, 64:4400-4404 (2004).
275. R.T. Tong, Y. Boucher, S.V. Kozin, D.J. Hicklin, and R.K. Jain, Vascular normalization by VEGFR2 blockade induces a pressure gradient across the vasculature and improves drug penetration in tumors, Cancer Research, 64:3731-3736 (2004).
276. D.G. Duda, D. Fukumura, L.L. Munn, M.F. Booth, E.B. Brown, P. Huang, B. Seed and R.K. Jain, Differential transplantability of tumor-associated stromal cells, Cancer Research, 63:5920-5924(2004).
277. J. Hagendoorn, T.P. Padera, S. Kashiwagi, N. Isaka, F. Noda, M.I. Lin, P.L.Huang, W.C. Sessa, D. Fukumura, and R.K. Jain. Endothelial nitric oxide synthase regulates microlymphatic flow via collecting lymphatics, Circulation Research, 95:204-209 (2004).
278. L. Xu, P.S. Pathak and D. Fukumura, Hypoxia-induced activation of p38 MAPK and PI3K signaling pathways contributes to expression of interleukin-8 in human ovarian carcinoma cells: Mechanism of hypoxia induced interleukin 8. Clinical Cancer Research, 10:701-707 (2004).
279. Y.T. Chan, J.P. Zimmer, M. Stroh, J.S. Steckel, R.K. Jain, & M.G. Bawendi, Incorporation of luminescent nanocrystals into monodisperse core-shell silica microspheres, Advanced Materials, 16:23-24 (2004).
280. F. Winkler, S. Kozin, R. Tong, S. Chae, M. Booth, I. Garkavstev, L. Xu, D. J. Hicklin, D. Fukumura, E. di Tomaso, L.L. Munn, R.K. Jain, Kinetics of vascular normalization by VEGFR2 blockade governs brain tumor response to radiation: Role of oxygenation, Angiopoietin-1, and matrix metallproteinases, Cancer Cell, 6:553-562 (2004).

Reviews

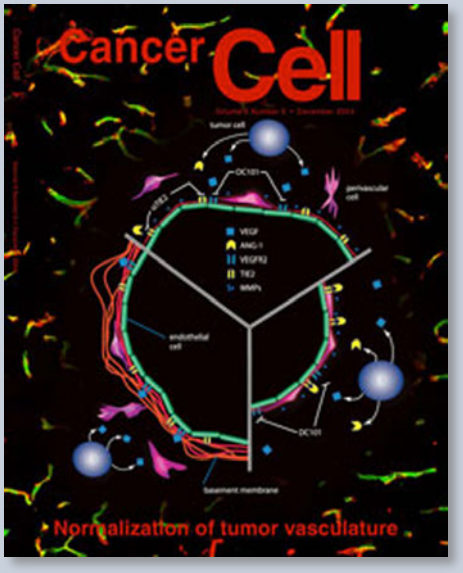
281. D.G. Duda, D. Fukumura and R.K. Jain. Role of eNOS in neovascularization: NO for EPCs, Trends in Molecular Medicine 10:143-145 (2004).
282. R.K. Jain, Recognition of tumor blood vessel normalization as a new antiangiogenic concept Nature Medicine 10:329-330 (2004).
283. C.G. Willett, D.G. Duda, A. Fischman and R.K. Jain, Correspondence: PET concerns in bevacizumab treatment, Nature Medicine, 10:561 (2004).
284. R.K. Jain, E.B. Brown, L.L. Munn, and D. Fukumura, Intravital microscopy of normal and diseased tissues in the mouse. In: Live Cell Imaging: A Laboratory Manual (Editors: R. D. Goldman and D. L. Spector). Cold Spring Harbor Laboratory Press, Cold Spring Harbor, New York, Chapter 24, pp. 435-466 (2004).
285. R.K. Jain Vascular and Interstitial Biology of Tumors, In: Clinical Oncology, 3rd Edition (Editors: M. Abeleff, J. Armitage, J. Niederhuber, M. Kastan and G. McKenna), Elsevier, Philadelphia, PA, Chapter 9, pp. 153-172 (2004).
286. R.K. Jain, & M. Stroh, Zooming in and out with quantum dots. Nature Biotechnology, 22:959-960 (2004).

2005 Publications

Original articles

287. M. Stroh, Zimmer JP, Duda DG, Levchenko TS, Cohen KS, Brown EB, Scadden DT, Torchilin VP, Bawendi MG, Fukumura D, Jain RK. Quantum Dots spectrally distinguish multiple species within the tumor milieu in vivo. Nature Medicine, 11:678-682 (2005).
288. S.S. Shevkoplyas, Yoshida T, Munn LL, Bitensky MW. Biomimetic autoseparation of leukocytes from whole blood in a microfluidic device. Analytical Chemistry Analytical Chemistry, 77:933-937 (2005).
289. C. Sun, Munn LL. Particulate nature of blood determines macroscopic rheology: a 2-D lattice Boltzmann analysis. Biophysical Journal, 88:1635-1645 (2005).
290. Z.N. Demou, M. Awad, T. McKee, J. Y. Perentes, X. Wang, L. L. Munn, R.K. Jain and Y. Boucher, Lack of Telopeptides in Fibrillar Collagen I Promotes the Invasion of a Metastatic Breast Tumor Cell Line. Cancer Research, 65:5674-5682 (2005).
291. E. di Tomaso, D. Capen, A. Haskell, J. Hart, D.M. McDonald, R.K. Jain, R.C. Jones and L.L. Munn, Mosaic tumor vessels: cellular basis and ultrastructure of focal regions lacking endothelial markers, Cancer Research, 65:5740-5749 (2005).
292. L. Xu, R. Tong, D. M. Cochran and R.K. Jain, Blocking PDGF-D/PDGFR? Signaling Inhibits Human Renal Cell Carcinoma Progression in an Orthotopic Mouse Model, Cancer Research, 65:5711-5719 (2005).
293. S. Kashiwagi, Izumi Y, Gohongi T, Demou ZN, Xu L, Huang PL, Buerk DG, Munn LL, Jain RK, Fukumura D. NO mediates mural cell recruitment and vessel morphogenesis in murine melanomas and tissue-engineered blood vessels, Journal of Clinical Investigation, 115:1816-127 (2005).
294. P. Huang, T. D. McKee, R.K. Jain and D. Fukumura, Green fluorescence protein (GFP)-expressing model derived from a spontaneous osteosarcoma in a VEGF-GFP expressing mouse, Comparative Medicine, 55:236-243 (2005).

295. A. Ny, M. Koch, M. Schneider, E. Neven, R.T. Tong, S. Maity, C. Fischer, S. Plaisance, D. Lambrechts, C. Héligon, S. Terclavers, M. Ciesiolka, R. Kälin, W.Y. Man, I. Senn, S. Wyns, L. Marconcini, K. Vleminckx, S. Oliviero, F. Lupu, J. Wood, A. Brändli, D. Collen, E. M. Conway, M. Dewerchin, L. Moons, R.K. Jain and P. Carmeliet, A genetic Xenopus Laevis tadpole model to study lymphangiogenesis, Nature Medicine, 11:998-1004 (2005).
296. C.G. Willett, Y. Boucher, E. di Tomaso, D.G. Duda, L.L. Munn, R. Tong, D. Chung, D. Sahani, S. Kalva, S. Kozin, M. Mino, K. Cohen, D. Scadden, A. Hartford, A. Fischman, J. Clark, D. Ryan, A. Zhu, L. Blaszkowsky, P. Shellito, G. Lauwers, and R.K. Jain. Surrogate markers for antiangiogenic therapy and dose limiting toxicities for bevacizumab with radio-chemotherapy: Continued experience of a Phase I trial in rectal cancer patients, Journal of Clinical Oncology, 31:8136-9 (2005).
297. J. A. Tyrrell, V. Mahadevan, R. T. Tong, E. B. Brown, R.K. Jain and B. Roysam, A 2-D/3-D model-based method to quantify the complexity of microvasculature imaged by in vivo multiphoton microscopy, Microvascular Research, 70:165-178 (2005).
298. D.G. Duda, Cohen KS, Kozin SV, JY Perentes, Fukumura D, Scadden DT & Jain RK. Evidence for bone marrow-derived endothelial cells incorporation into perfused blood vessels in tumors. Blood, First Edition December 8, p-3210 (2005).
299. T. Acker, T. Diez, J. Aragones, M. Tjwa, K. Brusselmans, D. Fukumura, J. M. Herbert, A. Burger, J. Riedel, G. Elvert, I. Flamme, P. Maxwell, D. Collen, R.K. Jain, K. H. Plate and P. Carmeliet, Genetic evidence for a tumor suppressor Role of HIF-2 a , Cancer Cell 8:131-141 (2005).



Reviews

300. R.K. Jain. Normalization of tumor vasculature: An emerging concept in antiangiogenic therapy of breast cancer. Science, 307:58-62 (2005).
301. R.K. Jain, Antiangiogenic therapy of cancer: Current and emerging concepts, Oncology (Supplement), 19:7-16 (2005).
302. D.G. Duda and R.K. Jain Pleiotropy of tissue-specific growth factors: from neurons to vessels via the bone marrow, Journal of Clinical Investigation, 115:596-598 (2005).
303. R.K. Jain, P. Au, J. Tam, D. G. Duda and D. Fukumura, Engineering vascularized tissue, Nature Biotechnology, 23: 821-823 (2005).
304. J. Hagendoorn, Padera T.P., Fukumura D., Jain R.K. Molecular regulation of microlymphatic formation and function: role of nitric oxide. Trends in Cardiovascular Medicine, 15:169-173 (2005).
305. E. Brown, A. Majewska, R.K. Jain, FRAP and Multiphoton FRAP. In: Yuste R, Konnerth A. (eds). Imaging in Neuroscience and Development: A Laboratory Manual. Cold Spring Harbor Laboratory Press, Cold Spring Harbor, New York, Chapter 56, pages 429-438 (2005).

2005 Publications

306. E. Brown, L.L. Munn, D. Fukumura, R.K. Jain. A Practical Guide to in vivo Imaging of Tumors. In: Yuste R, Konnerth A. (eds). Imaging in Neuroscience and Development: A Laboratory Manual. Cold Spring Harbor Laboratory Press, Cold Spring Harbor, New York. Chapter 92, pages 695-700 (2005).
307. D. Fukumura. Role of microenvironment on gene expression, angiogenesis and microvascular functions in tumors. In: Meadows GG. editor. Integration/Interaction of Oncologic Growth, Vol. 15. In: Hans Kaiser H. series editor. Cancer Growth And Progression series, Springer Science + Business Media B.V., Dordrecht, the Netherlands Chapter 2, 23-36 (2005).

2006 Publications

Original articles

308. D.G. Duda, Cohen K.S. di Tomaso E., Au P., Klein R.J., Scadden D.T., Willett C.G. & Jain R.K. Differential CD146 expression on circulating versus tissue endothelial cells in cancer patients: Implications for circulating endothelial cells as biomarker for antiangiogenic therapy. Journal of Clinical Oncology, 107:2774-2776 (2006).
309. J. Kisucka, Butterfield CE, Duda DG, Eichenberger SC, Saffaripour S, Ware J, Ruggeri ZM, Jain RK, Folkman J and Wagner DD. Platelets and platelet adhesion support angiogenesis while preventing excessive hemorrhage. Proceedings of the National Academy of Sciences USA, 103:855-860 (2006).
310. J. Hagendoorn, Tong R, Fukumura D, Lin Q, Lobo J, Padera TP, Xu L, Kucherlapati R, Jain RK. Onset of abnormal blood and lymphatic vessel function and interstitial hypertension in early stages of carcinogenesis. Cancer Research 66:8065-75 (2006).
311. T. McKee, P Grandi, W Mok, G Alexandrakis, N Insin, JP Zimmer, MG Bawendi, Y Boucher, XO Breakefield and RK Jain, Degradation of fibrillar collagen in a human melanoma xenograft improves the efficacy of an oncolytic HSV vector, Cancer Research 66:3360-3364 (2006).
312. L. Xu, D.M. Cochran, R.T. Tong, F. Winkler, S. Kashiwagi, R.K. Jain and D. Fukumura, PlGF Overexpression Inhibits Tumor Growth, Angiogenesis and Metastasis by Depleting VEGF Homodimers in Orthotopic Mouse Models, Cancer Research ,66:3971-3977 (2006).
313. J. Hagendoorn, TP Padera, TI Yock, GP Nielsen, E di Tomaso, TF Delaney, HA Gaissert, AE Rosenberg, RK Jain and DH Ebb, Platelet-derived growth factor receptor-β in Gorham's disease, Nature Clinical Practice Oncology, 3:693-697 (2006).
314. T. Hoshida, N. Isaka, J. Hagendoorn, E. di Tomaso, Y.L. Chen, B. Pytowski, D. Fukumura, T.P. Padera, R.K. Jain, Imaging steps of lymphatic metastasis reveals that vascular endothelial growth factor-C increases metastasis by increasing delivery of cancer cells to lymph nodes: therapeutic implications., Cancer Res., 66:8065-75 (2006).
315. L.E. Gerweck, Vijayappa S, and Kozin S. Tumor pH controls the in vivo efficacy of weak acid and base chemotherapeutics. Molecular Cancer Therapy, 5:1275-1279 (2006).
316. Y. Saito, Sunamura M, Motoi F, Abe H, Egawa S, Duda DG, Hoshida T, Fukuyama S, Hamada H, Matsuno S. Oncolytic replication-competent adenovirus suppresses tumor angiogenesis through preserved E1A region. Cancer Gene Therapy, 13:242-52. (2006).
317. C.H. Sun, Munn LL. Influence of erythrocyte aggregation on leukocyte margination in postcapillary expansions: a lattice-Boltzmann analysis, Physica A, 362:191-196 (2006).
318. R. Jones, Capen D, Jacobson M, Munn L. PDGF and microvessel wall remodeling in adult rat lung: Imaging PDGF-AA and PDGF-Ra molecules in progenitor smooth muscle cells developing in experimental pulmonary hypertension. Cell and Tissue Research, 16794827 (2006).
319. D.M. Cochran, Fukumura D, Carmeliet P, Jain RK, Evolution of oxygen and glucose concentration profiles in a tissue-mimetic culture system of embryonic stem cells. Annals of Biomedical Engineering, 34:1247-1258 (2006).
320. S.T. Reddy, D.A. Berk, R.K. Jain and M.A. Swartz, A sensitive in vivo model for quantifying interstitial convective transport of injected macromolecules and nanoparticles, Journal of Applied Physiology, 101:1162-1169 (2006).

Reviews

321. R.K. Jain, D.G. Duda, J. W. Clark & L.S. Loeffler. Lessons from Phase III clinical trials of anti-VEGF therapy for cancer. Nature Clinical Practice Oncology, 3:24-40 (2006).
322. C.G. Willett, Kozin SV, Duda GD, di Tomaso E, Kozak KR, Boucher Y, and Jain RK Combined vascular endothelial growth factor-targeted therapy and radiotherapy for rectal cancer: Theory and clinical practice. Seminars in Oncology, 33:S35-S40. (2006).
323. D.G. Duda. Anti-angiogenesis and drug delivery in tumors: Bench to bedside and back. Cancer Research, 66:3967-70 (2006).
324. R.K. Jain, Seminal findings and an allergy to black flies. In: Reflections from the Frontiers, Explorations for the Future: Gordon Research Conferences, 1931-2006 (Editors: Arthur A. Daemmrich, Nancy Ryan Gray and Leah Shaper), Gordon Research Conferences and Chemical Heritage Foundation, Philadelphia, pp 70-71 (2006).
325. D.G. Duda. Angiogenesis and vascular targeting agents drug discovery & development. Investigational Drugs Database (IDdb) and Thomson Pharma, September (2006).
326. D.S. Hoon, M. Kitago, J. Kim, T. Mori, A. Piris, K. Szyfelbein, M.C. Mihm Jr., S.D. Nathanson, T.P. Padera, A.F. Chambers, S.A. Vantyghem, I.C. MacDonald, S.C. Shivers, M. Alsarraj, D.S. Reintgen, B. Passlick, W. Sienel, K. Pantel. Molecular mechanisms of metastasis. Cancer and

2006 Publications

Metastasis Reviews, 25:203-220 (2006).

327. L.L. Munn. Analytical approaches to leukocyte-endothelium interactions. In: Shepro D, editor. Microvascular Research: Biology and Pathology, Elsevier Press; Amsterdam, Chapter 117, pp. 791-794.(2006).
328. D. Fukumura. Window Models. In: D. Shepro Editor. Microvascular Research: Biology and Pathology, Elsevier Science, San Diego, CA: Chapter 24:151-157 (2006).
329. D. Fukumura, Kashiwagi S, Jain RK. Role of nitric oxide in tumour progression. Nature Reviews Cancer, 6:521-534 (2006).

2007 Publications

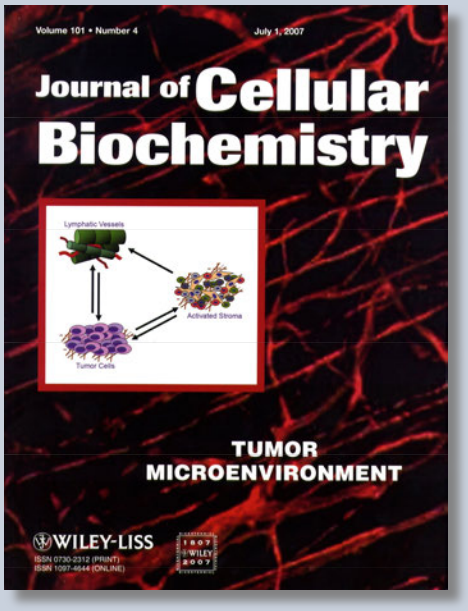
Original articles

330. T.T. Batchelor, Sorensen AG, di Tomaso E, Zhang W-T, Duda DG, Cohen KS, Kozak KR, Cahill DP, Chen P-J, Zhu M, Ancukiewicz M, Mrugala MM, Plotkin S, Drappatz J, Louis DN, Ivy P, Scadden DT, Benner T, Loeffler JS, Wen PY, Jain RK. AZD2171, a pan-VEGF receptor tyrosine kinase inhibitor, normalizes tumor vasculature and alleviates edema in glioblastoma patients, Cancer Cell, 11:83-95 (2007).
331. D.G. Duda, Cohen KS, Au P, Scadden DT, Willett CG, Jain RK. Detection of circulating endothelial cells: CD146- based magnetic separation enrichment or flow cytometric assay? Journal of Clinical Oncology, 25:e3-e5 (2007).
332. C.G. Willett, Duda DG, di Tomaso E, Boucher Y, Czito BG, Bendell J, Hurwitz HI, Bentley R, Wong TZ, Paulson E, Jain, RK. Complete pathological response in T4 locally advanced rectal cancer after treatment with bevacizumab and standard radio-chemotherapy. Nature Clinical Practice Oncology, 4:316-321 (2007).
333. R.K. Jain, Tong R, Munn LL. Effect of vascular normalization by anti-angiogenic therapy on interstitial hypertension, peri-tumor edema and lymphatic metastasis: insights from a mathematical model. Cancer Research, 67:2729-2735 (2007).
334. J.A. Tyrrell, E. di Tomaso, D. Fuja, R. Tong, K. Kozak, R.K. Jain and B. Roysam, Robust 3-D modeling of vasculature imagery using superellipsoid, IEEE Transactions on Medical Imaging, 26:223-237 (2007).
335. Z.Z. Wang, P. Au, T. Chen, Y. Shao, L. M. Daheron, H. Bai, M. Arzigian, D. Fukumura, R.K. Jain and D. Scadden, Human ES cell-derived endothelial cells form durable functional blood vessels in vivo, Nature Biotechnology 25,317-318 (2007).
336. D.G. Duda, K. S. Cohen, D. Scadden and R.K. Jain, A protocol for detection and enumeration of blood circulating endothelial cells and progenitor cells in human blood, Nature Protocols, 4:805-810 (2007).
337. L. Xu and R.K. Jain, Downregulation of Placenta Growth Factor by Promoter Hypermethylation in Human Lung and Colon Carcinoma, Molecular Cancer Research, 5:873-880 (2007).
338. S.V. Kozin, F. Winkler, I. Garkavtsev, D.J. Hickliin, R.K. Jain, Y. Boucher, Human tumor xenografts recurring after radiotherapy are more sensitive to anti–vascular endothelial growth factor receptor-2 treatment than treatment-naive tumors. Cancer Research, 67:5076-82 (2007).
339. C. Sun, R.K. Jain and L.L. Munn, Non-uniform plasma leakage affects local hematocrit and blood flow: Implications for inflammation and tumor perfusion, Annals of Biomedical Engineering, 35:2121-29 (2007).
340. C. Sun and L.L. Munn. "Lattice-Boltzmann simulation of blood flow in digitized vessel networks," Computers & Mathematics with Applications; 55:1594-1600 (2007).
341. M.M. Dupin, I. Halliday, C.M. Care and L.L. Munn. "Modeling the flow of dense suspensions of deformable particles in three dimensions," PRE; 75:066707 (2007).
342. G.M. Nelson, T. P. Padera, I. Garkavtsev, T. Shioda and R.K. Jain, Differential gene expression of primary cultured lymphatic and blood vascular endothelial cells, Neoplasia, 9:1038-1045 (2007).
343. W. Mok, Y. Boucher and R.K. Jain, MMP-1 and -8 improve the distribution and efficacy of an oncolytic virus, Cancer Research, 67:10664-10668 (2007).
344. B.D. Lawenda, Smith DE, Xu L, Niemierko A, Silverstein JR, Boucher Y, Kashiwagi S, Held KD, Jain RK, Loeffler JS, Eisenberg DM, Blumberg JB. Do the dietary supplements epigallocatechin gallate or vitamin E cause a radiomodifying response on tumors in vivo? A pilot study with murine breast carcinoma. J Soc Integr Oncol., 5:11-7 (2007).

2007 Publications

Reviews

345. C.G. Willett, D. G. Duda, R.K. Jain, Surrogate biomarkers for anti-angiogenic therapy for advanced colorectal cancer, Current Colorectal Cancer Reports, 3:94-98 (2007).
346. D.G. Duda, T. Batchelor, C.G. Willett and R.K. Jain, The current progress, hurdles and future prospects in anti-VEGF targeted cancer therapy strategies. Trends in Molecular Medicine, 13:222-230 (2007).
347. D. Fukumura and R.K. Jain, Tumor microenvironment abnormalities: causes, consequences, and strategies to normalize. Journal of Cellular Biochemistry, 101:937-949 (2007).
348. R.K. Jain & D.G. Duda, Angiogenesis in Solid Tumors. In: Antiangiogenic Cancer Therapy (Editors: James L. Abbruzzese, Darren W. Davis and Roy S. Herbst), CRC Press, Boca Raton, pp. 43-90 (2007).
349. R.K. Jain and D.G. Duda, Normalization of tumor vasculature and microenvironment by antiangiogenic therapy. In: Angiogenesis: Mechanisms and Cancer Therapy (Editors: Dieter Marmé and Norbert E. Fusenig), Springer-Verlag, Berlin, pp. 577-92 (2007).
350. R.K. Jain, T. T. Batchelor, D.G. Duda, C.G. Willett, Normalization of tumor vasculature and microenvironment, In: Antiangiogenic Agents in Cancer Therapy. (Editors: Beverly Teicher and Lee Ellis), Humana Press, pp. 261-76 (2007).
351. C.G. Willett, D.G. Duda, B.G. Czito, J.C. Bendell, J.W. Clark, R.K. Jain, Targeted therapy in rectal cancer, Oncology, 21:1055-65 (2007).
352. D.G. Duda, R.K. Jain, C.G. Willett, Antiangiogenics: The potential role of integrating this novel treatment modality with chemoradiation for solid cancers, Journal of Clinical Oncology, 225:4033-42 (2007).
353. P. Au, J. Tam, D. Fukumura, R.K. Jain, Small blood vessel engineering, Methods in Molecular Medicine, 140:183-195 (2007).
354. R.K. Jain and L.L. Munn, Vascular normalization as rationale for combining chemotherapy with antiangiogenic agents, PPO Updates, 21:1-7 (2007).
355. R.K. Jain, D. Fukumura, L. Munn and E. Brown, Optical Microscopy in Small Animal Research. In: Imaging of Vertebrates (Editors: Tavitian B, Leroy-Willig A & Ntziachristos V). Wiley, London, pp 183-187 (2007).



356. R.K. Jain, D. Fukumura, L. Munn and E. Brown, Tumor Angiogenesis and Blood Flow. In: Imaging of Vertebrates (Editors: Tavitian B, Leroy-Willig A & Ntziachristos V). Wiley, London, pp 199-201 (2007).
357. M. Bockhorn, R.K. Jain and L.L. Munn, Active versus passive mechanisms in metastasis: do cancer cells crawl into vessels, or are they pushed? Lancet Oncology 8:444-8 (2007).
358. R.K. Jain, E. diTomaso, D.G. Duda, J.S. Loeffler, A.G. Sorensen and T.T. Batchelor, Angiogenesis in brain tumors, Nature Reviews Neuroscience, 8:610-622 (2007).
359. R.K. Jain, A.V. Finn, F.D. Kolodie, H.K. Gold and R. Virmani, Antiangiogenic therapy for normalization of atherosclerotic plaque vasculature: A potential strategy for plaque stabilization, Nature Clinical Practice Cardiovascular Medicine, 4:491-502 (2007).
360. D.G. Duda, Endothelial cell–based therapy for hematopoiesis, Blood 109:2272-3 (2007).
361. D. Fukumura, Jain RK. Novel function of RANKL: eNOS activator. Blood 109:1339-1340 (2007).
362. R.K. Jain and L. Xu, αPlGF: A new kid on the antiangiogenic block, Cell, 131: 443-445 (2007).
363. E.R. Gerstner, Duda DG, di Tomaso E, Sorensen G, Jain RK, Batchelor TT. Antiangiogenic agents for the treatment of glioblastoma, Expert Opin Investig Drugs, 16:1895-1908 (2007).
364. D. Fukumura and R.K. Jain, Tumor microvasculature and microenvironment: Targets for anti-angiogenesis and normalization, Microvascular Research, 74:72-84 (2007).
365. T.P. Padera, M. Ancukiewicz, T. Hoshida, D. Fukumura and R.K. Jain, Data do not support benefits of anti-VEGFR3 therapy, Cancer Research, 67:5055 (2007).

2008 Publications

Original articles

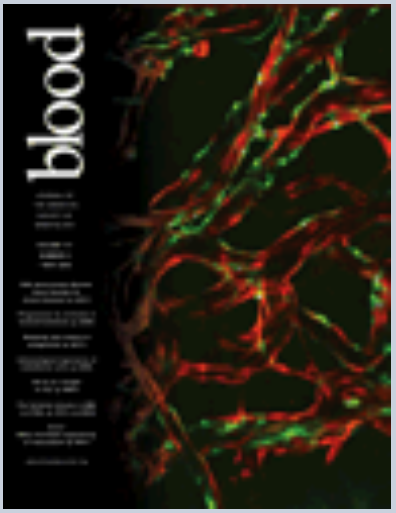
366. P. Au, L.M. Daheron, D.G. Duda, K.S. Cohen, J.A. Tyrrell, R.M. Lanning, D. Fukumura, D.T. Scadden, and R.K. Jain, Differential in vivo potential of endothelial progenitor cells from human umbilicalcord blood and adult peripheral blood to form functional long-lasting vessels, Blood 111:1302-1305 (2008).
367. P. Au, J. Tam, D. Fukumura and R. K. Jain, "Bone marrow-derived mesenchymal stem cells facilitate engineering of long-lasting functional vasculature," Blood 114: 255- 257 (2008).
368. R. Jones, D. Capen, K. S. Cohen, L. L. Munn, R. K. Jain, D. G. Duda. "A protocol for phenotypic detection and characterization of vascular cells in a lung neovascularization model in rodents," Nature Protocols, 3:378-87 (2008).
369. R. Jones, D. Capen, B. Petersen, R. K. Jain, D.G. Duda, "A protocol for a lung neovascularization model in rodents," Nature Protocols, 3:388-97 (2008).

2008 Publications

370. S. Kashiwagi, K. Tsukada, L. Xu, J. Miyazaki, S. V. Kozin, J. A. Tyrrell, W. C. Sessa, L. E. Gerweck, R. K. Jain and D. Fukumura, "Perivascular nitric oxide gradients normalize tumor vasculature," Nature Medicine 14: 255-257 (2008).
371. P. Huang, D. G. Duda, R. K. Jain and D. Fukumura, "Histopathological findings and establishment of novel tumor lines from spontaneous tumors in FVB/N mice," Comparative Medicine 58: 253-263 (2008).
372. S. Nagano, J. Y. Perentes, R. K. Jain and Y. Boucher, "Cancer cell death enhances the penetration and efficacy of oncolytic herpes simplex virus in tumors," Cancer Research 68: 3795-802 (2008).
373. T. P. Padera, A. H. Kuo, T. Hoshida, S. Liao, J. Lobo, K. R. Kozak, D. Fukumura and R. K. Jain, "Differential response of primary tumor versus lymphatic metastasis to VEGFR-2 and -3 kinase inhibitors cediranib and vandetanib," Molecular Cancer Therapeutics 7: 2272-2279 (2008).
374. L.L. Munn and M.M. Dupin. "Blood cell interactions and segregation in flow," Annals of Biomedical Engineering; 36: 534-544 (2008).
375. M.M. Dupin, I. Halliday, C.M. Care and L.L. Munn, "Lattice Boltzmann modelling of blood cell dynamics," International Journal of Computational Fluid Dynamics; 22: 481-492 (2008).

Reviews

376. R.K. Jain, Taming vessels to treat cancer, Scientific American, 298:56-63 (2008).
377. R. K. Jain, "Lessons from multidisciplinary translational trials on antiangiogenic therapy of cancer," Nature Reviews Cancer 8:309-316 (2008).
378. R.K. Jain, "Judah Folkman," Journal of Clinical Investigation 118: 823 (2008).
379. E. Brown, A. Majewska and R. K. Jain, "Photobleaching and recovery with nonlinear microscopy." In: Handbook of Biomedical Nonlinear Optical Microscopy (Editors: B. R. Masters and P. T. C. So). Oxford University Press, New York, Chapter 26, pp. 673-688 (2008).
380. R. K. Jain, M. F. Booth, T. P. Padera, L. L. Munn, D. Fukumura and E. Brown, "Applications of nonlinear intravital microscopy in tumor biology." In: Handbook of Biomedical Nonlinear Optical Microscopy (Editors: B. R. Masters and P. T. C. So). Oxford University Press, New York, Chapter 29, pp. 735-756 (2008
381. R.K. Jain and K. Kozak, "Molecular Pathophysiology of Tumors," In: Principles and Practice of Radiation Oncology, 5th Edition (Editors: E. C. Halperin, C. A. Parez, L. W. Brady), Lippincott, Williams & Wilkins, New York, Chapter 4, pp. 126-141 (2008).
382. R. K. Jain, D. G. Duda, T. T. Batchelor, A. G. Sorensen and C. G. Willett, "Normalization of tumor vasculature and microenvironment," In: Angiogenesis: An Integrative Approach from Science to Medicine (Editors: W. D. Figg and J. Folkman), Springer, pp. 273-282 (2008).
383. D. Fukumura and R. K. Jain," Imaging angiogenesis and the microenvironment," APMIS 116:695-715 (2008).
384. A. G. Sorensen, T. T. Batchelor, P. Y. Wen, W. T. Zhang and R. K. Jain, "Response criteria for glioma," Nature Clinical Practice Oncology 5:634-44 (2008).
385. E. R. Gerstner, A. G. Sorensen, R. K. Jain and T. T. Batchelor, "Advances in neuroimaging techniques for the evaluation of tumor growth, vascular permeability, and angiogenesis in gliomas," Current Opinion in Neurology 21:728-35 (2008).
386. T. P. Padera and R. K. Jain, "VEGFR3: A new target for anti-angiogenesis therapy?" Developmental Cell 15:178-179 (2008).
387. R. K. Jain, J. Lahdenranta and D. Fukumura, "Targeting Platelet-Derived Growth Factor Signaling in Carcinoma-Associated Fibroblasts Controls Cervical Cancer in Mouse Model," PLoS Medicine 5(1): e24 (2008); doi:10.1371/journal.pmed.0050024.



2009 Publications

Original articles

388. J. Tam, D. Fukumura and R. K. Jain, "A mathematical model of murine metabolic regulation by leptin: energy balance and defense of a stable body weight," Cell Metabolism 9:52-63 (2009).
389. J. Y. Perentes, T. D McKee, C. D. Ley, H. Mathiew, M. Dawson, T. P. Padera, L. L Munn, R. K. Jain and Y. Boucher, "In vivo imaging of extracellular matrix remodeling by tumor-associated fibroblasts," Nature Methods 6:143-145 (2009).
390. P. Y. Wen, W.K. A. Yung, K. R. Lamborn, A. D. Norden, T. F. Cloughesy, L. M. DeAngelis, H. A. Fine, S. M. Chang, H. I. Robins, K. Fink, L. E. Abrey, A. B. Lassman, M. Mehta, J. Drappatz, E. Di Tomaso, K. Ligon, K. Aldape, Rakesh K. Jain, R. Capdeville, C. Stiles, R. Kaplan, M. J. Egorin, A. J. Murgo, M. D. Prados, "Phase II study of Imatinib Mesylate (Gleevec®) for recurrent meningiomas (North American Brain Tumor Consortium Study 01-08)," Neuro-Oncology 11:853-860 (2009).

391. G. Cheng, J. Tse, R. K. Jain and L. L. Munn, "Micro-environmental Mechanical stress controls tumor spheroid size and morphology by suppressing proliferation and inducing apoptosis in cancer cells," PLoS One 4:e4632 (2009).
392. M. X. Luong, J. T. Q. Lin, J. Hagendoorn, K. J. Moore, T. P. Padera, B. Seed, D. Fukumura, R. Kucherlapati, and R. K. Jain "Lack of lymphatic vessel phenotype in LYVE-1/CD44 double knock out mice," Journal of Cellular Physiology 219:430-437 (2009).
393. W. Mok, T. Stylianopoulos, Y. Boucher, R.K. Jain, "Mathematical modeling of herpes simplex virus distribution in solid tumors: Implications for cancer gene therapy," Clinical Cancer Research 15:2352-2360 (2009).
394. J. Lahdenranta, J. Hagendoorn, T.P. Padera, T. Hoshida, G. Nelson, S. Kashiwagi, R.K. Jain, D. Fukumura, "Endothelial nitric oxide synthase mediates lymphangiogenesis and lymphatic metastasis," Cancer Research 69:2801-8 (2009).
395. E. Chung, H. Yamashita, P. Au, BA Tannous, D. Fukumura, R.K. Jain, "Secreted Gaussia Luciferase as a biomarker for monitoring tumor progression and treatment response of systemic metastases," PLoS One 4:e8316 (2009).
396. A.T.N. Kumar, E. Chung, S.B. Raymond, J.A.J.M. van de Water, K. Shah, D. Fukumura, R.K. Jain, B.J. Bacskai, D.A. Boas, "Feasibility of in vivo imaging of fluorescent proteins using lifetime contrast," Optics Letters 34:2066-2068 (2009).
397. R. Jones, D. Capen, M. Jacobson, K.S. Cohen, D.T. Scadden, D.G. Duda, "VEGFR2+PDGFRβ+ circulating precursor cells participate in lung capillary repair after hyperoxia-induced lung injury (HALI)," Journal of Cellular and Molecular Medicine 9b: published online May 6, 2009 as doi:10.1111/j.1582-4934.2009.00785.x. (2009).
398. Zhu AX, Sahani DV, Duda DG, di Tomaso E, Ancukiewicz M, Catalano OA, Sindhwani V, Blaszkowsky LS, Yoon SS, Lahdenranta J, Bhargava P, Meyerhardt J, Clark JW, Kwak EL, Hezel AF, Miksad R, Abrams TA, Enzinger PC, Fuchs CS, Ryan DP, Jain RK. 2009, "Efficacy, safety, and potential biomarkers of sunitinib monotherapy in advanced hepatocellular carcinoma: a phase II study." Journal of Clinical Oncology, 27(18):3027-35. PMC2702235
399. Willett CG, Duda DG, di Tomaso E, Boucher Y, Ancukiewicz M, Sahani DV, Lahdenranta J, Chung DC, Fischman AJ, Lauwers GY, Shellito PC, Czito BG, Wong TZ, Paulson E, Poleski M, Vujaskovic Z, Bentley R, Chen HX, Clark JW, Jain RK. "Efficacy, safety and biomarkers of neoadjuvant bevacizumab, radiation therapy and 5-Fluorouracil in rectal cancer: A multidisciplinary phase II study," Journal of Clinical Oncology 27:3020-3026 (2009).
400. P. Au, J. Tam, D. G. Duda, D. Fukumura, R. K. Jain, "Paradoxical effects of PDGF-BB overexpression in endothelial cells on engineered blood vessels in vivo," American Journal of Pathology 175:294-302 (2009).
401. Sorensen AG, Batchelor TT, Zhang W-T, Chen P-J, Yeo P, Wang M, Jenning D, Wen PY, Ancukiewicz M, Lahdenranta J, di Tomaso E, Duda DG, Jain RK, "A "Vascular Normalization Index" as potential mechanistic biomarker to predict survival after a single dose of cediranib in recurrent glioblastoma patients," Cancer Research 69:5296-5300 (2009).
402. Dawson MR, Duda DG, Fukumura D, Jain RK. "VEGFR1-activity-independent metastasis formation," Nature 461:E4-E5 (2009).
403. Dawson MR, Duda DG, Chae S-S, Fukumura D, Jain RK, "VEGFR1 activity modulates myeloid cell infiltration in growing lung metastases but is not required for spontaneous metastasis formation," PLoS One 4:e6525 (2009).
404. Xu L, Duda DG, di Tomaso E, Ancukiewicz M, Chung DC, Lauwers GY, Samuel R, Shellito PC, Czito B, Poleski M, Bentley R, Clark JW, Willett CG, Jain RK, "Direct evidence that bevacizumab, an anti-VEGF antibody, upregulates SDF1α, CXCR4, CXCL6 and neuropilin 1 in tumors in rectal cancer patients," Cancer Research 69: 7905-7910 (2009).
405. J. Tam, D. G. Duda, J. Y. Perentes, R. S. Quadri, D. Fukumura and R. K. Jain, "Blockade of VEGFR2 and not VEGFR1 can limit diet-induced fat tissue expansion: Role of local versus bone-marrow derived endothelial cells," PLoS One 4: e4974 (2009).
406. E. di Tomaso, N. London, D. Fuja, J. Logie, J. A. Tyrrell, W. Kamoun, L. L. Munn and R. K. Jain, "PDGF-C induces maturation of blood vessels in a model of glioblastoma and attenuates the response to anti-VEGF treatment," PLoS One 4:e5123 (2009).
407. V. P. Chauhan, R. M. Lanning, B. Diop-Frimpong, W. Mok, E. B. Brown, T. P. Padera, Y. Boucher, and R. K. Jain, "Multiscale measurements distinguish cellular and interstitial hindrances to diffusion in vivo," Biophysical Journal 97: 330-336 (2009).
408. W. S. Kamoun, C. D. Ley, C. T. Farrar, A. M. Duyverman, J. Lahdenranta, D. A. Lacorre, T. T. Batchelor, E. di Tomaso, D. G. Duda, L. L. Munn, D. Fukumura, A. G. Sorensen and R. K. Jain, "Edema control by cediranib, a VEGF targeted kinase inhibitor, prolongs survival despite persistent brain tumor growth in mice," Journal of Clinical Oncology 27: 2542-2552 (2009).
409. S. R. Plotkin, A. O. Stemmer-Rachamimov, F. G. Barker II, C. Halpin, T. P. Padera, A. Tyrell, A. G. Sorensen, R. K. Jain and E. di Tomaso, "Hearing improvement after bevacizumab in patients with neurofibromatosis 2," New England Journal of Medicine 361:358-369 (2009).
410. B. J. Vakoc, R. M. Lanning, J. A. Tyrrell, T. P. Padera, L. A. Bartlett, T. Stylianopoulos, L. L. Munn, G. J. Tearney, D. Fukumura, R. K. Jain and B. E. Bouma, "Three-dimensional microscopy of the tumor microenvironment in vivo using optical frequency domain imaging," Nature Medicine 15:1219-1224 (2009).

Reviews

411. R. K. Jain, "A new target for tumor therapy," New England Journal of Medicine 360:2669-2671 (2009).
412. J. Y. Perentes, D. G. Duda and R. K. Jain, "Visualizing anti-tumor immune responses in vivo," Disease Models and Mechanisms 2:107-110 (2009).
413. Gerstner ER, Duda DG, di Tomaso E, Ryg PA, Loeffler JS, Sorensen AG, Ivy P, Jain RK, Batchelor TT, "The potential utility of anti-VEGF agents to normalize tumor vasculature and alleviate edema in brain and spinal cord tumor patients," Nature Clinical Practice Oncology 6:229-236 (2009).

2009 Publications

414. R. K. Jain, J. Tam, P. Au, D. Fukumura, "Angiogenesis in Development, Disease and Regeneration," In: Santin M, editor. Strategies in Regenerative Medicine: Integrating Biology with Materials Design. Chapter 6. Springer, New York (2009).
415. Gerstner ER, Sorensen AG, Jain RK, Batchelor TT, "Anti-vascular endothelial growth factor therapy for malignant glioma," Current Neurology Neuroscience Report 9:254-262 (2009).
416. Jain RK, Duda DG, Willett CG, Sahani DV, Zhu AX, Loeffler JS, Batchelor TT, Sorensen AG, "Biomarkers of response and resistance to antiangiogenic therapy in cancer," Nature Reviews Clinical Oncology 6:327-338 (2009).
417. A. S. Chi, A. G. Sorensen, R. K. Jain, T. T. Batchelor, "Angiogenesis as a therapeutic target in malignant gliomas," Oncologist 14:621-636 (2009).
418. Zhu AX, Duda DG, Sahani DV, Jain RK. Development of sunitinib in hepatocellular carcinoma: Rationale, early clinical experience and correlative studies. Cancer Journal 2009; 15: 263-8.
419. Duda DG, Ancukiewicz MA, Jain RK. Biomarkers of antiangiogenic therapy: How do we move from candidate biomarkers to valid biomarkers? Journal of Clinical Oncology 2009; 28: 183-5.
420. Woodward WA, Bristow RG, Clarke MF, Coppes R, Cristofanilli M, Duda DG, Fike JR, Hambardzumyan D, Hill R, Jordan CT, Milas L, Pajonk F, Curran W, Dicker A, Chen Y. "Radiation Therapy Oncology Group Translational Research Program Stem Cell Symposium: Incorporating stem cell hypothesis into clinical trials," International Journal of Radiation Oncology, Biology and Physics 74: 1580-91 (2009).

2010 Publications

Original articles

421. Kirsch DG, Santiago PM, di Tomasso E, Sullivan JM, Hou W-S, Dayton T, Jeffords LB, Sodha P, Mercer K, Cohen R, Tekeyushi O, Korsmeyer S, Bronson R, Kim CF, Haigis KM, Jain RK, Jacks T. "p53 controls radiation-induced gastrointestinal syndrome in mice independent of apoptosis," Science. 327:593-6 (2010).
422. Liu W, Greytak AB, Lee J, Wong CR, Park J, Marshall LF, Jiang W, Curtin PN, Ting AY, Nocera DG, Fukumura D, Jain RK, Bawendi MG. Compact Biocompatible Quantum Dots via RAFT-Mediated Synthesis of Imidazole-Based Random Copolymer Ligand. J Am Chem Soc. 132:472-83 (2010).
423. Allen PM, Liu W, Chauhan VP, Lee J, Ting AY, Fukumura D, Jain RK, Bawendi MG. InAs(ZnCdS) Quantum Dots Optimized for Biological Imaging in the Near-Infrared. J Am Chem Soc. 132: 470-1 (2010).
424. C. T. Farrar, W. S. Kamoun, C. D. Ley, Y. R. Kim, S. J. Kwon; G. Dai, B. R. Rosen, E. di Tomaso; R. K. Jain, A. G. Sorensen , "In vivo validation of MRI vessel caliber index measurement methods with intravital optical microscopy in a U87 mouse brain tumor model," Neuro-Oncology 12:341-50 (2010).
425. E. R. Gerstner, P. J. Chen, P. Y. Wen, R. K. Jain, T. T. Batchelor, and G. Sorensen, " Infiltrative patterns of glioblastoma spread detected via diffusion MRI after treatment with cediranib," Neuro-Oncology, 12:466-72 (2010).
426. H. K. Wong, J. Lahdenranta, W. S. Kamoun, A. W. Chan, A. I. McClatchey, S. R. Plotkin, R. K. Jain and E. di Tomaso, "Anti-vascular endothelial growth factor therapies as a novel therapeutic approach to treating neurofibromatosis-related tumors," Cancer Research 70:3483-93 (2010).
427. P. Kim, E. Chung, H. Yamashita, K. E. Hung, A. Mizoguchi, R. Kucherlapati, D. Fukumura, R. K. Jain and S. H. Yun, "In vivo wide-area cellular imaging by side-view endomicroscopy", Nature Methods 7:303-5 (2010).
428. T. T. Batchelor, D. G. Duda, E. di Tomaso, M. Ancukiewicz, S. R. Plotkin, E. Gerstner, A. F. Eichler, J. Drappatz, F. H. Hochberg, D. N. Louis, K. S. Cohen, H. Chea, A. Exarhopoulos, M. A. Moses, P. Ivy, A. G. Sorensen, P. Y. Wen and R. K. Jain, "Phase II study of cediranib, an oral pan-VEGF receptor tyrosine kinase inhibitor, in patients with recurrent glioblastoma," Journal of Clinical Oncology, 28: 2817-23 (2010).
429. Kamoun, W., Chae, S.-S., Lacorre, D., Tyrrell, J., Mitre, M., Gillissen, M., Fukumura, D., Jain, R., and Munn, LL. Simultaneous measurement of RBC velocity, flux, hematocrit and shear rate in vascular networks in vivo. Nature Methods, 15:845–851 (2010).
430. Duda DG, Willett CG, Ancukiewicz M, di Tomaso E, Shah M, Czito BG, Bentley R, Poleski M, Lauwers GY, Carroll M, Tyler D, Mantyh C, Shellito PC, Clark JW, Jain RK. Plasma Soluble VEGFR1 is a Potential Dual Biomarker of Response and Toxicity for Bevacizumab with Chemoradiation in Locally Advanced Rectal Cancer. Oncologist, 15: 577-83 (2010).
431. Willett CG, Duda DG, Ancukiewicz M, di Tomaso E, Shah M, Czito BG, Bentley R, Poleski M, Lauwers GY, Carroll M, Tyler D, Mantyh C, Shellito PC, Clark JW, Jain RK. A Safety and Survival Analysis of Neoadjuvant Bevacizumab with Standard Chemoradiation in a Phase I/II Study Compared to Standard Chemoradiation in Locally Advanced Rectal Cancer. Oncologist, 15:845–851 (2010).
432. Sergey V. Kozin, Walid S. Kamoun, Yuhui Huang, Michelle R. Dawson, Rakesh K. Jain, and Dan G. Duda, "Recruitment of Myeloid but not Endothelial Precursor Cells Facilitates Tumor Regrowth after Local Irradiation," Cancer Research 70: 5679-85 (2010).
433. Chae SS, Kamoun WS, Farrar CT, Kirkpatrick ND, Niemeyer E, de Graaf AM, Sorensen AG, Munn LL, Jain RK, Fukumura D, "Angiopoietin-2 Interferes with Anti-VEGFR-2- Induced Vessel Normalization and Survival Benefit in Mice Bearing Gliomas," Clinical Cancer Research 16:3618-27 (2010).
434. R. Mounzer, O. Svendsen, P. Baluk, C. Bergman, T. Padera, H. Wiig, R. K. Jain, D. McDonald, N. Ruddle, "Lymphotoxin α contributes to lymphangiogenesis," Blood 116:2173-82 (2010).
435. Z. Popović, W. Liu, V. P. Chauhan, J. Lee, C. Wong, A. B. Greytak, N. Insin, D. G. Nocera, D. Fukumura, R. K. Jain and M. G. Bawendi, "A nanoparticle size series for in vivo fluorescence imaging, " Angewandte Chemie Intl Ed Engl, 49:8649-52 (2010).
436. Stylianopoulos T, Poh M-Z, Insin N, Bawendi MG, Fukumura D, Munn LL, Jain RK," Diffusion of Particles in the Extracellular Matrix: the Effect of Repulsive Electrostatic Interactions," Biophysical Journal 99:1342-9 (2010).

2010 Publications

437. T. Stylianopoulos, B. Diop-Frimpong, L. L. Munn and R. K. Jain, "Diffusion anisotropy in collagen gels and tumors: the effect of fiber network orientation," Biophysical Journal 99:3119-3128 (2010).
438. D. G. Duda, A. M. M. J. Duyvermana, M. Kohno, M. Snuderl, E. J. A. Steller, D. Fukumura and R. K. Jain, "Malignant cells facilitate lung metastasis by bringing their own soil," Proceedings of the National Academy of Science U S A 107: 21677-21682 (2010).

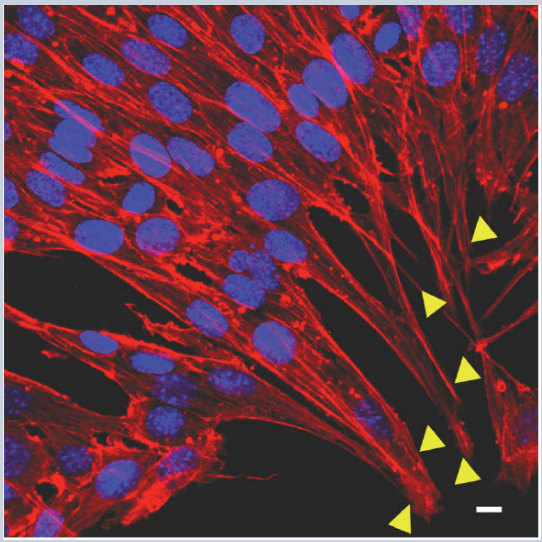
Reviews

439. D. G. Duda, M. Ancukiewicz, and R. K. Jain, "Biomarkers of antiangiogenic therapy: How do we move from candidate biomarkers to valid biomarkers?" Journal of Clinical Oncology 28:183-5 (2010).
440. R. K. Jain, L. L. Munn and D. Fukumura, "Intravital microscopy of normal and diseased tissues in the mouse. In: Live Cell Imaging: A Laboratory Manual, 2nd Edition, Chpater 26, pp 475-521 (R. D. Goldman, J. R. Swedlow and D. L. Specter, Eds.), CSH Press, Cold Spring Harbor, NY (2010).
441. A. K. Finn, R. K. Jain, "Coronary plaque neovascularization and hemorrhage: a potential target for plaque stabilization?," JACC Cardiovasc Imaging. 3:41-4 (2010).
442. D. Fukumura, D. G. Duda, L. L. Munn and R. K. Jain, "Tumor microvasculature and microenvironment: Novel insights through intravital imaging in pre-clinical models," Microcirculation 17:206-25 (2010).
443. Duda DG, Jain RK, "Pre-metastatic lung "niche": Is VEGFR1 activation a requirement?" Cancer Research 70: 5670-3 (2010).
444. Brown E, Munn LL, Fukumura D, Jain RK. In vivo imaging of tumors. Cold Spring Harb Protoc. 2010 Jul 1; 2010:pdb.prot5452. doi: 10.1101/pdb.prot5452.
445. S. Liao, T. P. Padera and R. K. Jain, "Notch leads lymphatics and connects to blood vessels," Arteriosclerosis, Thrombosis and Vascular Biology 30:1682-3 (2010).
446. R. K. Jain and T. Stylianopoulos, "Delivering nanomedicine to solid tumors," Nature Reviews Clinical Oncology 7:653-64 (2010).

2011 Publications

Original articles

447. Dawson MR, Chae S-S, Jain RK, Duda DG. Direct evidence for lineage-dependent effects of bone marrow stromal cells on tumor progression. American Journal of Cancer Research 1: 144-54 (2011).
448. di Tomaso E, Snuderl M, Kamoun W, Duda DG, Auluck PK, Fazlollahi L, Andronesi OC, Frosch MP, Wen PY, Plotkin SR, Hedley-Whyte T, Sorensen AG, Batchelor TT, Jain RK. Glioblastoma recurrence after cediranib therapy in patients: Lack of "rebound" revascularization as mode of escape. Cancer Research 71: 17-28 (2011).
449. Hiratsuka S, Duda DG, Huang Y, Goel S, Sugiyama T, Nagasawa T, Fukumura D, Jain RK. C-X-C receptor type 4 promotes metastasis by activating p38 mitogen-activated protein kinase in myeloid differentiation-antigen (Gr-1) positive cells. Proceedings of the National Academy of Science U S A. 108: 302-7 (2011).
450. Gerstner ER, Eichler AF, Plotkin SR, Drappatz J, Doyle CL, Xu L, Duda DG, Wen PY, Jain RK, Batchelor TT. Phase I trial with biomarker studies of vatalanib (PTK787) in patients with newly diagnosed glioblastoma treated with enzyme inducing anti-epileptic drugs and standard radiation and temozolomide. Journal of Neuro-oncology 103: 325-32 (2011).
451. Zhu AX, Duda DG, Ancukiewicz M, di Tomaso E, Clark JW, Miksad RA, Fuchs CS, Ryan DP, Jain RK. Exploratory analysis of sunitinib toxicity in advanced hepatocellular carcinoma: Kinetics and potential biomarker value. Clinical Cancer Research 17: 918-27 (2011).



452. Hiratsuka S, Goel S, Kamoun W, Fukumura D, Duda DG, Jain RK. Endothelial focal adhesion kinase mediates cancer cell homing to discrete foci in lungs. Proceedings of the National Academy of Science U S A 108: 3725-30 (2011).
453. C. Wong, T. Stylianopoulos, J. Cuia, J. Martin, V. P. Chauhan, W. Jiang, Z. Popovic, R. K. Jain, M. G. Bawendi and D. Fukumura, "Multistage nanoparticle delivery system for deeppenetration into tumor tissue," Proceedings of the National Academy of Science U S A, 108: 2426-2431 (2011).
454. Horowitz NS, Penson RT, Duda DG, di Tomaso E, Boucher Y, Ancukiewicz M, Cohen KS, Berlin S, Krasner C, Moses MA, Jain RK. Safety, efficacy and biomarker exploration in a phase II study of bevacizumab, oxaliplatin and gemcitabine in recurrent Müllerian carcinoma. Clin Ovarian Cancer Other Gynecol Malig 4: 26-33 (2011).
455. J. Baish, T. Stylianopoulos, R. M. Lanning, W. S. Kamoun, D. Fukumura, L. L. Munn, and R. K. Jain, "Scaling rules for diffusive drug delivery in tumor and normal tissues," Proceedings of the National Academy of Science U S A 108: 1799-1803 (2011).
456. B. Diop-Frimpong, V. P. Chauhan, S. Krane, Y Boucher, and R. K. Jain, "Losartan inhibits collagen I synthesis and improves the distribution and efficacy of nanotherapeutics in tumors," Proceedings of the National Academy of Science U S A, 108:2909-14 (2011).

457. S. Liao, J. Liu, P. Lin, T. Shi, R. K. Jain and Lei Xu, "TGF-beta blockade controls ascites by preventing abnormalization of lymphatic vessels in orthotopic human ovarian carcinoma model," Clinical Cancer Research, 17:1415-24 (2011).
458. I. Garkavtsev, V. Chauhan, H. K.Wong, A. Mukhopadhyay, M. Glicksman, R. Peterson and R. K. Jain, "Dehydro-α-lapachone, a plant product with antivascular activity," Proceedings of the National Academy of Science U S A 108: 11596-601 (2011).
459. Yoon SS, Duda DG, Karl DL, Kim T-M, Kambadakone AR, Chen Y-L, Rothrock C, Rosenberg AE, Nielsen GP, Kirsch DG, Choy E, Harmon DC, Hornicek FJ, Dreyfuss J, Ancukiewicz M, Sahani DV, Park PJ, Jain RK, DeLaney DF. Phase II study of neoadjuvant bevacizumab and radiation therapy for resectable soft tissue sarcomas. International Journal of Radiation Oncology, Biology and Physics 81: 1081-90 (2011).
460. J. Liu, S. Liao, Y. Huang, R. Samuel, T. Shi, K. Naxerova, P. Huang, W. Kamoun, R. K. Jain, D. Fukumura and L. Xu, "PDGF-D improves drug delivery and efficacy via vascular normalization, but promotes lymphatic metastasis by activating CXCR4 in breast cancer," Clinical Cancer Research 17: 3638-48 (2011).
461. C. T. Farrar, W. S. Kamoun, C. D. Ley, Y. R. Kim, C. Catana, S. J. Kwon, B. R. Rosen, R. K. Jain, A. G. Sorensen, "Sensitivity of MRI Tumor Biomarkers to VEGFR Inhibitor Therapy in an Orthotopic Mouse Glioma Model." PLoS One 6(3): e17228 (2011).
462. H. Kim, C. Catana, E. M. Ratai, O. C. Andronesi, D. Jennings, T. T. Batchelor, R. K. Jain, A. G. Sorensen, "Serial Magnetic Resonance Spectroscopy Reveals a Direct Metabolic Effect of Cediranib in Glioblastoma," Cancer Research 71:3745-52 (2011).
463. K. E. Emblem, A. Bjornerud, K. Mouridsen, R. J. Borra, T. T. Batchelor, R. K. Jain, A. G. Sorensen, "T(1)- and T(2)(*)-dominant extravasation correction in DSC-MRI: Part II predicting patient outcome after a single dose of cediranib in recurrent glioblastoma patients," J Cereb Blood Flow Metab. 31(10): 2054-64 (2011).
464. J.Y. Perentes, N. Kirkpatrick, S. Nagano, E. Y. Smith, C. M. Shaver, D. Sgroi, I. Garkavstev, L. L. Munn, R. K. Jain and Y. Boucher, "Cancer cell-associated MT1-MMP promotes blood vessel invasion and distant metastasis in triple-negative mammary tumors," Cancer Research 71: 4527-38 (2011).
465. Zhao W, Schafer S, Choi J, Yamanaka YJ, Lombardi ML, Bose S, Carlson AL, Phillips JA, Teo W, Droujinine IA, Cui CH, Jain RK, Lammerding J, Love JC, Lin CP, Sarkar D, Karnik R, Karp JM, "Cell-surface sensors for real-time probing of cellular environments," Nat Nanotechnol. 6:524-31 (2011).
466. G. Cheng, S. Liao, H. K. Wong, D. A. Lacorre, E. di Tomaso, P. Au, D. Fukumura, R. K. Jain and L. L. Munn, "Engineered blood vessel networks connect to host vasculature via wrapping-and-tapping anastomosis." Blood 118:4740-9 (2011).
467. Liao S, Cheng G, Conner DA, Huang Y, Kucherlapati RS, Munn LL, Ruddle NH, Jain RK, Fukumura D and Padera TP, "Impaired lymphatic contraction associated with immunosuppression." Proceedings of the National Academy of Science U S A 108:18784-9 (2011).
468. Chauhan VP, Popović Z, Chen O, Cui J, Fukumura D, Bawendi MG, Jain RK, "Fluorescent Nanorods and Nanospheres for Real-Time In Vivo Probing of Nanoparticle Shape-Dependent Tumor Penetration," Angew Chem Int Ed Engl. 50:11417-11420 (2011).
469. Jain A, Munn LL Biomimetic postcapillary expansions for enhancing rare blood cell separation on a microfluidic chip. Lab Chip 11(17): 2941-7 (2011).
470. Song JS, Munn LL Fluid forces control endothelial sprouting. Proceedings of the National Academy of Science U S A 2011; 108(37): 15342-7.
471. Faber A, Corcoran RB, Ebi H, Sequist LV, Waltman BA, Chung E, Incio J, Digumarthy SR, Pollack SF, Song Y, Muzikansky A, Lifshits E, Roberge S, Coffman EJ, Benes C, Gómez H, Baselga J, Arteaga CL, Rivera MN, Dias-Santagata D, Jain RK, Engelman JA. BIM expression in treatment naïve cancers predicts responsiveness to kinase inhibitors. Cancer Discov. 1(4): 352-365 (2011).
472. P. Huang, S. V. Westmoreland, R. K. Jain and D. Fukumura, "Spontaneous Nonthymic Tumors in SCID Mice." Comp Medicine 61:227-34 (2011).

Reviews

473. Y. Huang, M. Snuderl, and R. K. Jain, "Polarization of tumor-associated macrophages: A novel strategy for vascular normalization and antitumor immunity," Cancer Cell 19: 1-2 (2011).
474. E. Van Cutsem, D. Lambrechts, H. Prenen, R. K. Jain and P. Carmeliet. Lessons From the Adjuvant Bevacizumab Trial on Colon Cancer: What Next? J Clin Oncol, 29:1-4 (2011).
475. D. G. Duda, S. V. Kozin, N. D. Kirkpatrick, L. Xu, D. Fukumura, and R. K. Jain. CXCL12 (SDF1a) – CXCR4/CXCR7 Pathway Inhibition: An Emerging Sensitizer for Anti-Cancer Therapies? Clinical Cancer Research 17:2074-2080 (2011).
476. A. X. Zhu, D. G. Duda, D. V. Sahani and R. K. Jain, "HCC and angiogenesis: possible targets and future directions," Nature Reviews Clinical Oncology 8: 292-301 (2011).
477. P. Carmeliet and R. K. Jain, "Molecular mechanisms and clinical applications of angiogenesis," Nature 473: 298-307 (2011).
478. P. Carmeliet and R. K. Jain, "Principles and mechanisms of vessel normalization for cancer and other angiogenic diseases," Nature Reviews Drug Discovery 10:417-27 (2011).
479. S. Goel, D. G. Duda, L. Xu, L.L. Munn, Y. Boucher, D. Fukumura and R. K. Jain. Normalization of the vasculature for treatment of cancer and other diseases. Physiological Reviews 91: 1071–121 (2011).

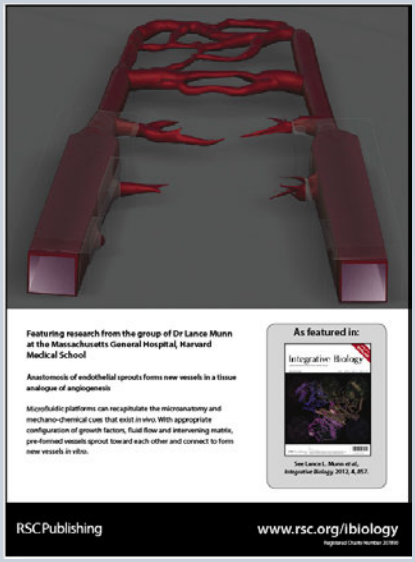
2011 Publications

480. A. F. Eichler, E. Chung, D. P. Kodack, J. S. Loeffler, D. Fukumura and R. K. Jain. The biology of brain metastases—translation to new therapies. Nature Reviews Clinical Oncology 8: 344-56 (2011).
481. Duda DG. Targeting Tumor Angiogenesis: Biomarkers of Angiogenesis and Antiangiogenic Therapy in Cancer. e-publication, Angiogenesis Foundation, CME, August 30, 2011 (2011).
482. V. P. Chauhan, T. Stylianopoulos, Y. Boucher and R. K. Jain. Delivery of molecular and nanoscale medicine to tumors: Transport barriers and strategies. Annual Review of Chemical and Biomolecular Engineering 2: 281–98 (2011).
483. Kozin SV, Duda DG, Munn LL, Jain RK. Is vasculogenesis crucial for the regrowth of irradiated tumours? Nat Rev Cancer 11(7): 532 (2011).

2012 Publications

Original articles

484. Tse, JM, Cheng, G, Tyrrell, JA, Wilcox-Adelman, SA, Boucher, Y, Jain RK, Munn, LL. Mechanical compression drives cancer cells toward invasive phenotype. Proceedings of the National Academy of Science U S A 109(3): 911-6 (2012).
485. Saylor PJ, Kozak RK, Smith MR, Ancukiewicz M, Efstathiou JA, Zietman AL, Jain RK, Duda DG. Changes in biomarkers of inflammation and angiogenesis during androgen deprivation therapy for prostate cancer. Oncologist 17(2): 212-9 (2012).
486. Duyverman AMMJ, Kohno M, Roberge S, Fukumura D, Duda DG, Jain RK. Studying stromal cell involvement in cancer metastasis using an isolated tumor perfusion model in mice. Nature Protocols 7(4): 749-55 (2012).
487. Duyverman AMMJ, Steller JA, Fukumura D, Jain RK, Duda DG. Studying carcinoma-associated fibroblast involvement in cancer metastasis in mice. Nature Protocols 7(4): 756-62 (2012).
488. Duyverman AMMJ, Kohno M, Duda DG, Jain RK, Fukumura D. Studying stromal cell involvement in cancer metastasis in mice using skin transplantation by transient parabiosis. Nature Protocols 7(4): 763-70 (2012).
489. Raut CP, Boucher Y, Duda DG, Morgan JA, Quek R, Ancukiewicz M, Lahdenranta J, Eder JP, Demetri GD, Jain RK. Effects of sorafenib on intra-tumoral interstitial fluid pressure and circulating biomarkers in patients with refractory sarcomas (NCI Protocol 6948). PLoS One 7(2): e26331 (2012).
490. Sorensen AG, Emblem KE, Polaskova P, Jennings D, Kim H, Ancukiewicz M, Wang M, Wen PY, Ivy P, Batchelor TT, Jain RK. Increased survival of glioblastoma patients who respond to antiangiogenic therapy with elevated blood perfusion. Cancer Res. 72(2): 402-7 (2012).
491. Wong HK, Shimizu A, Kirkpatrick ND, Garkavtsev I, Chan AW, di Tomaso E, Klagsbrun M, Jain RK. Merlin/NF2 regulates angiogenesis in schwannomas through a Rac1/semaphorin 3F-dependent mechanism. Neoplasia 14(2): 84-94 (2012).
492. ND. Kirkpatrick, E Chung, DC.Cook, XHan, G Gruionu, S Liao, LL Munn, TP Padera, D Fukumura and RK Jain, Video-rate resonant scanning multiphoton microscopy: An emerging technique for intravital imaging of the tumor microenvironment. IntraVital, 1: 60-68 (2012)..
493. Stylianopoulos T, Wong C, Bawendi MG, Jain RK, Fukumura D. Multistage nanoparticles for improved delivery into tumor tissue. Methods Enzymol. 508: 109-30 (2012).
494. Chauhan VP, Stylianopoulos T, Martin JD, Popović Z, Chen O, Kamoun WS, Bawendi MG, Fukumura D, Jain RK. Normalization of tumour blood vessels improves the delivery of nanomedicines in a size-dependent manner. Nat Nanotechnol. Epub on Apr 8, 2012 as doi: 10.1038/nnano.2012.45 (2012).
495. Plotkin SR, Bredella MA, Cai W, Kassarjian A, Harris GJ, Esparza S, Merker VL, Munn LL, Muzikansky A, Askenazi M, Nguyen R, Wenzel R, Mautner VF. Quantitative assessment of whole-body tumor burden in adult patients with neurofibromatosis. PLoS One 7(4): e35711 (2012).
496. Duyverman AMMJ, Kohno M, Roberge S, Fukumura D, Duda DG, Jain RK. Studying stromal cell involvement in cancer metastasis using an isolated tumor perfusion model in mice. Nature Protocols 7:749-55 (2012).
497. Duyverman AMMJ, Steller JA, Fukumura D, Jain RK, Duda DG. Studying carcinoma-associated fibroblast involvement in cancer metastasis in mice. Nature Protocols 7:756-62 (2012).
498. Duyverman AMMJ, Kohno M, Duda DG, Jain RK, Fukumura D. Studying stromal cell involvement in cancer metastasis in mice using skin transplantation by transient parabiosis. Nature Protocols 7:763-70 (2012).
499. Chauhan VP, Stylianopoulos T, Martin JD, Popović Z, Chen O, Kamoun WS, Bawendi MG, Fukumura D, and Jain RK. Normalization of tumour blood vessels improves the delivery of nanomedicines in a size dependent manner. Nature Nanotechnology 7: 383-8 (2012).
500. Stylianopoulos T, Martin JD, Chauhan VP, Jain SR, Diop-Frimpong B, Bardeesy N, Smith BL, Ferrone CR, Hornicek FJ, Boucher Y, Munn LL and Jain RK. Causes, consequences and remedies for growth-induced solid stress in murine and human tumors. PNAS 109:15101-8 (2012)



Reviews

501. Vacok B, Fukumura D, Jain RK and Bouma B. Cancer imaging by optical coherence tomography: preclinical progress and clinical potential. Nature Reviews Cancer 12:363-8 (2012).
502. Meyerhardt JA, Ancukiewicz M, Abrams TA, Schrag D, Enzinger PC, Chan JA, Kulke MH, Wolpin BM, Goldstein M, Blaszkowsky L, Elliott M, Regan E, Jain RK, Duda DG. Phase I study of cetuximab, irinotecan, and vandetanib (ZD6474) as therapy for patients with previously treated metastastic colorectal cancer. PLoS One (In press).
503. Somers RC, Lanning RM, Snee PT, Greytak AB, Jain RK, Bawendi MG and Nocera DG. A Nanocrystal-based Ratiometric pH Sensor for Natural pH Ranges. Chemical Science (2012).

2012 Publications

504. Stylianopoulos T, Soteriou K, Fukumura D, and Jain RK. Cationic nanoparticles have superior transvascular flux into solid tumors: Insights from a mathematical model. Annals of Biomedical Engineering 41:68-77 (2012).
505. Liu J, et al. TGF-b blockade improves the distribution and efficacy of therapeutics in breast carcinoma by normalizing the tumor stroma. PNAS 109:16618-23 (2012).
506. Huang Y, et al. Vascular normalizing doses of antiangiogenic treatment reprogram the immunosuppressive tumor microenvironment and enhance immunetherapy. PNAS, 109:17561-6 (2012).
507. Kodack DP, et al. Combined targeting of HER2 and VEGFR2 for effective treatment of HER2-amplified breast cancer brain metastases. PNAS, 109: E3119–E3127 (2012).
508. Jain RK, Munn LL, Fukumura D. Measuring Interstitial pH and pO2 in Mouse Tumors. Cold Spring Harb Protoc. 2013;2013(7):675-7 - PMID: 23818669
509. Jain RK, Munn LL, Fukumura D. Measuring interstitial diffusion, convection, and binding parameters in mouse tumors. Cold Spring Harb Protoc. 2013;2013(7):678-80 - PMID: 23818670
510. Jain RK, Munn LL, Fukumura D. Measuring leukocyte-endothelial interactions in mice. Cold Spring Harb Protoc. 2013;2013(6):561-3 - PMID: 23734020
511. Jain RK, Munn LL, Fukumura D. Measuring vascular permeability in mice. Cold Spring Harb Protoc. 2013;2013(5):444-6 - PMID: 23637370
512. Jain RK, Munn LL, Fukumura D. Measuring angiogenesis and hemodynamics in mice. Cold Spring Harb Protoc. 2013;2013(4):354-8 - PMID: 23547161
513. Jain RK, Munn LL, Fukumura D. Lung window preparation in mice. Cold Spring Harb Protoc. 2013;2013(1):ePub - PMID: 23282642
514. Jain RK, Munn LL, Fukumura D. Pancreatic tumor preparation in mice. Cold Spring Harb Protoc. 2012;2012(12):ePub - PMID: 23209145
515. Jain RK, Munn LL, Fukumura D. Liver tumor preparation in mice. Cold Spring Harb Protoc. 2012;2012(12):ePub - PMID: 23209146
516. Jain RK, Munn LL, Fukumura D. Lymphangiography of the mouse tail. Cold Spring Harb Protoc. 2012;2012(11):1177-8 - PMID: 23118364
517. Jain RK, Munn LL, Fukumura D. Lymphangiography of the mouse ear. Cold Spring Harb Protoc. 2012;2012(11):1179-80 - PMID: 23118365
518. Jain RK, Munn LL, Fukumura D. Mammary fat pad chamber preparation in mice. Cold Spring Harb Protoc. 2012;2012(10):1113-4 - PMID: 23028075
519. Jain RK, Munn LL, Fukumura D. Mammary fat pad tumor preparation in mice. Cold Spring Harb Protoc. 2012;2012(10):1115-6 - PMID: 23028076
520. Jain RK, Munn LL, Fukumura D. Corneal pocket assay in rabbits. Cold Spring Harb Protoc. 2012;2012(9):1017-8 - PMID: 22949714
521. Jain RK, Munn LL, Fukumura D. Rabbit ear chambers. Cold Spring Harb Protoc. 2012;2012(7):813-14 - PMID: 22753607
522. Jain R.K. and Duda DG. Molecular Pathophysiology of Tumors. In: Principles and Practice of Radiation Oncology, 6th Edition (Editors: E. C. Halperin, C. A. Parez, L. W. Brady), Lippincott, Williams & Wilkins, New York, Chapter 4; in press (2012).
523. Goel S, Wong AH, Jain RK. Vascular normalization as a therapeutic strategy for malignant and nonmalignant disease. Cold Spring Harb Perspect Med. 2(3): a006486 (2012).
524. Goel S, Fukumura D, Jain RK. Normalization of the tumor vasculature through oncogenic inhibition: An emerging paradigm in tumor biology. Proc Natl Acad Sci U S A. Epub on May 1, 2012 (2012).
525. Kozin SV, Duda DG, Munn LL and Jain RK. Neovascularization after irradiation: What is the source of newly formed vessels in recurring tumors? JNCI, 104: 899-905 (2012).
526. Jain RK, Carmeliet P. SnapShot: Tumor Angiogenesis. Cell, 149:1408-1408.e1 (2012).

2013 Publications

Original articles

527. H-S Han, JD Martin, J Lee, DK. Harris, D Fukumura, RK. Jain, and M Bawendi, Spatial Charge Configuration Regulates Nanoparticle Transport and Binding Behavior In Vivo. Angew Chem Int Ed Engl. 52:1414-9 (2013).
528. M Snuderl, A Batista, ND Kirkpatrick, CR de Almodovar, L Riedemann, EC Walsh, R Anolik, Y Huang, JD Martin, W Kamoun, E Knevels, T Schmidt, CT Farrar, BJ Vakoc, N Mohan, E Chung, S Roberge, T Peterson, C Bais, BH Zhelyazkova, S Yip, M Hasselblatt, C Rossig, E Niemeyer; N Ferrara, M Klagsburn, DG Duda, D Fukumura, L Xu, P Carmeliet and RK Jain. Targeting placental growth factor/neuropilin 1 pathway inhibits growth and spread of medulloblastoma. Cell, 152: 1065–1076 (2013). [Highlighted in Nature Reviews Cancer, Cancer Discovery, The New England Journal of Medicine].
529. Zhu AX, Ancukiewicz M, Supko JG, Sahani DV, Blaszkowsky LS, Meyerhardt JA, Abrams TA, Jackson McCleary N, Bhargava P, Muzikansky A, Sheehan S, Regan E, Vasudev E, Knowles M, Fuchs CS, Ryan DP, Jain RK, Duda DG. Efficacy, safety, pharmacokinetics and biomarkers of cediranib monotherapy in advanced hepatocellular carcinoma: A phase II study. Clin Cancer Res. 19: 1557-66 (2013).
530. O Chen, J Zhao, VP Chauhan, J Cui, C Wong, DK Harris, H Wei, H-S Han, D Fukumura, RK Jain & MG Bawendi. Compact high-quality "CdS core" shell nanocrystals with narrow emission linewidths and suppressed blinking. Nature Materials. 12: 445-51 (2013).
531. Y Huang, S Goel, DG Duda, D Fukumura and RK Jain. Vascular normalization as an emerging strategy to enhance cancer immunotherapy. Cancer Research 73: 2943-2948 (2013).
532. T Stylianopoulos, JD Martin, M Snuderl, F Mpekris, SR Jain and RK Jain. Co-evolution of solid stress and interstitial fluid pressure in tumors during progression: Implications for vascular collapse. Cancer Research 73: 3833-3841 (2013).
533. C Lu-Emerson, M Snuderl, ND Kirkpatrick, J Goveia, C Davidson, Y Huang, L Riedemann, J Taylor, P Ivy, DG Duda, M Ancukiewicz, SR Plotkin, AS Chi, ER Gerstner, AF Eichler, J Dietrich, AO Stemmer-Rachamimov, TT Batchelor and RK Jain. Increase in tumor-associated macrophages after antiangiogenic therapy is associated with poor survival in recurrent glioblastoma patients. Neuro-Oncology 15:1079-87, 2013.

534. R Samuel, L Daheron, S Liao, T Vardam, WS Kamoun, A Batista, C Buecker, R Schäfer, X Han, P Au, DT Scadden, DG Duda, D Fukumura and RK Jain. Generation of functionally competent and durable engineered blood vessels from human induced pluripotent stem cells. PNAS 110:12774-9, 2013.
535. T Batchelor, P Mulholland, B Neyns, L Nabors, M Campone, A Wick, W Mason, T Mikkelsen, S Phuphanich, L Ashby, J DeGroot, R Gattamaneni, L Cher, M Rosenthal, F Payer, J Jurgensmeier, RK Jain, GA Sorensen, J Xu, Q Liu and M van den Bent. Phase III randomized trial comparing the efficacy of cediranib as monotherapy, and in combination with lomustine, versus lomustine alone in patients with recurrent glioblastoma. Journal of Clinical Oncology 31(26):3212-3218 (2013).
536. DV Sahani, T Jiang, K Hayano, DG Duda, OA Catalano, M Ancukiewicz, RK Jain and AX Zhu. Magnetic resonance imaging biomarkers in hepatocellular carcinoma: Association with response and circulating biomarkers after sunitinib therapy. Journal of Hematology & Oncology July 10, 2013. [Epub ahead of print].
537. S Goel, N Gupta, BP Walcott, M Snuderl, CT Kesler, ND Kirkpatrick, T Heishi, Y Huang, JD Martin, E Ager, R Samuel, S Wang, J Yazbek, BJ Vakoc, RT Peterson, TP Padera, DG Duda, D Fukumura, and RK Jain. Effects of Vascular-Endothelial Protein Tyrosine Phosphatase Inhibition on Breast Cancer Vasculature and Metastatic Progression. JNCI 105 (16): 1188-1201 (2013). [See accompanying editorial: doi: 10.1093/jnci/djt199].
538. M Thunemann, L Wen, M Hillenbrand, IA Vachaviolos, S Feil, T Ott, X Han, D Fukumura, RK Jain, M Russwurm, C de Wit and R Feil. Transgenic Mice for cGMP Imaging. Circulation Research 113:365-71 (2013).
539. KE Emblem, K Mouridsen, A Bjornerud, CT Farrar, D Jennings, RJ H. Borra, PY Wen, P Ivy, TT Batchelor, BR Rosen, RK Jain and AG Sorensen. Vascular architecture imaging identifies patient responders to anti-angiogenic therapy. Nature Medicine 19:1178-1183 (2013).
540. VP Chauhan, JD Martin, H Liu, DA Lacorre, SR Jain, SV Kozin, T Stylianopoulos, AS Mousa, X Han, P Adstamongkonkul, Z Popović, P Huang, MG Bawendi, Y Boucher and RK Jain. Angiotensin inhibition enhances drug delivery and potentiates chemotherapy by decompressing tumor blood vessels. Nature Communications 4: 2516 (2013).
541. Chen Y, Huang P, Reiberger T, Duyverman AM, Samuel R, Hiddingh L, Roberge S, Koppel C, Lauwers GY, Zhu AX, Jain RK, Duda DG. Differential effects of sorafenib on liver versus tumor fibrosis mediated by SDF1α/CXCR4 axis and Gr-1+ myeloid cell infiltration in mice. Hepatology; doi: 10.1002/hep.26790 (2013).
542. Zhu AX, Finn RS, Mulcahy M, Gurtler J, Sun W, Schwartz JD, Dalal RP, Joshi A, Hozak RR, Xu Y, Ancukiewicz M, Jain RK, Nugent FW, Duda DG, Stuart K. A phase II and biomarker study of ramucirumab, a fully human monoclonal antibody targeting the vascular endothelial growth factor receptor-2, as first-line monotherapy in patients with advanced hepatocellular carcinoma. Clinical Cancer Research (in press).
543. Batchelor TT, Gerstner ER, Emblem KE, Duda DG, Kalpathy-Cramer J, Snuderl M, Ancukiewicz M, Polaskova P, Pinho M, Jennings D, Plotkin SR, Chi AS, Eichler AF, Dietrich J, Hochberg FH, Lu-Emerson C, Bo-Moon C, Iafrate AJ, Rosen B, Loeffler JS, Wen PY, Sorensen AG, Jain RK. Improved perfusion and oxygenation due to vascular normalization improves survival in glioblastoma patients treated with cediranib and chemoradiation. Proceedings of the National Academy of Science USA (in press).
544. T Stylianopoulos and RK Jain. Combining two strategies to improve perfusion and drug delivery in solid tumors. Proceedings of the National Academy of Science USA (in press).
545. Kesler CT, Kuo AH, Wong H-K, Masuck DJ, Shah JL, Kozak KR, Held KD, Padera TP. Vascular endothelial grow th factor-C enhances radiosensitivity of lymphatic endothelial cells. Angiogenesis, In Press.

546. Qazi H, Palomino R, Shi Z-D, Munn LL, Tarbell JM. Cancer Cell Glycocalyx Mediates Mechanostransduction and Flow-Regulated Invasion. Integr. Biol., 2013, DOI: 10.1039/C3IB40057C.
547. Munn LL. Dynamics of tissue topology during cancer invasion and metastasis. Physical Biology 2013, 10(6):065003 (13pp).

Reviews

548. U Prabhakar, H Maeda, RK Jain, EM Sevick-Muraca, W Zamboni, OC Farokhzad, ST Barry, A Gabizon, P Grodzinski and DC Blakey. Challenges and key considerations of the enhanced permeability and retention (EPR) effect for nanomedicine drug delivery in oncology. Cancer Research 73: 2412-2417 (2013).
549. RK Jain. Normalizing tumor microenvironment to treat cancer: Bench to bedside to biomarkers. J Clinical Oncology 31:2205-18 (2013).
550. DG Duda, LL Munn and RK Jain. Can we identify predictive biomarkers for anti-angiogenic therapy of cancer using mathematical modeling? JNCI 105:762-5 (2013).
551. Munn LL, Kunert C, Tyrrell JA, Modeling Tumor Blood Vessel Dynamics, in Mathematical Methods and Models in Biomedicine-- Lecture Notes on Mathematical Modelling in the Life Sciences, Urszula Ledzewicz, Heinz Schättler, Avner Friedman, Eugene Kashdan ed. (2013), pp 117-147
552. Kesler CT, Liao S, Munn LL, Padera TP Lymphatic vessels in health and disease. Wiley Interdisciplinary Reviews: Systems Biology and Medicine, (2013).
553. Huang Y, Goel S, Duda DG, Fukumura D, Jain RK. Vascular normalization as an emerging strategy to enhance cancer immunotherapy. Cancer Research 73: 2943-8 (2013).
554. Huang Y, Stylianopoulos T, Duda DG, Fukumura D, Jain RK. [Letter] Benefits of vascular normalization are dose- and time-dependent. Re: Bevacizumab Hampers Antibody Uptake. Cancer Research doi:10.1158/0008-5472.CAN-13-1989 (2013).
555. Jain RK, Fukumura D, Duda DG. Modes of neovascularization in tumors and clinical translation of antiangiogenic therapy. In: Pathobiology of Human Disease: A Dynamic Encyclopedia of Disease Mechanisms. First Edition, Elsevier Inc. McManus LM and Mitchell RN, editors. 12:958-962 (2013).
556. Liao S, Padera TP. Lymphatic function and immune regulation in health and disease. Lymphatic Research and Biology, 11(3):136-143 (2013).

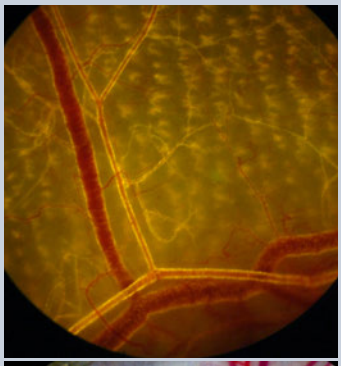
2013 Publications

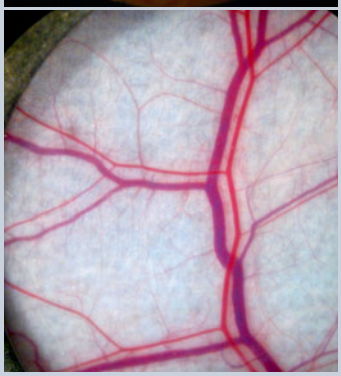
PMC3780287.

557. Jain RK, Chauhan V, Duda DG. Vascular and interstitial biology of tumors. In: Clinical Oncology Fifth Edition, Elsevier, Philadelphia. Abeloff M, Armitage J, Niederhuber J, Kastan M, McKenna WG, editors. 2013; in press.
558. VP Chauhan and RK Jain. Size matters in cancer nanomedicine. Nature Materials (in press).
559. Hagendoorn J, Yock TI, Borel Rinkes IHM, Padera TP, Ebb DH. Novel molecular pathways in Gorham's disease: implications for treatment. Pediatric Blood and Cancer, In Press.

2014 Publications

Original articles





560. Faber AC, Coffee EM, Costa C, Dastur A, Ebi H, Hata AN, Yeo AT, Edelman EJ, Song Y, Tam AT, Boisvert JL, Milano RJ, Roper J, Kodack DP, Jain RK, Corcoran RB, Rivera MN, Ramaswamy S, Hung KE, Benes CH, Engelman JA. mTOR Inhibition Specifically Sensitizes Colorectal Cancers with KRAS or BRAF Mutations to BCL-2/BCL-XL inhibition by Suppressing MCL-1. Cancer Discovery 4:42-52 (2014).
561. Kesler CT*, Kuo AH*, Wong H-K, Masuck DJ, Shah JL, Kozak KR, Held KD, Padera TP. "Vascular endothelial growth factor-C enhances radiosensitivity of lymphatic endothelial cells." Angiogenesis, 17(2):419-27 (2014)
562. MC Pinho, P Polaskova, J Kalpathy-Kramer, D Jennings, K Emblem, RK Jain, BR Rosen, PY Wen, AG Sorensen, TT Batchelor and ER Gerstner. Anti-VEGF therapy suppresses GBM pseudoprogression. Oncologist 19:75-81 (2014).
563. CM Lemon, PN Curtin, RC Somers, AB Greytak, RM Lanning, RK Jain, MG Bawendi and DG Nocera. Metabolic Tumor Profiling with pH, Oxygen, and Glucose Chemosensors on a Quantum Dot Scaffold. Inorg Chem. 53:1900-15 (2014).
564. RK Jain. An indirect way to tame cancer. Scientific American 310: 46-53 (2014). [Link to the podcast about this article, posted on January 27, 2014
565. Naxerova K, Brachtel E, Salk JJ, Seese AM, Power K, Abbasi B, Snuderl M, Chiang S, Kasif S, and Jain RK. Hypermutable DNA chronicles the evolution of human colon cancer. PNAS 111(18): E1889-98 (2014).
566. Liao S, Jones D, Cheng G, Padera TP. "Method for the quantitative measurement of collecting lymphatic vessel contraction in mice." Journal of Biological Methods, 1(2):e6 1-9. (2014)
567. Hong TS, Ryan DP, Borger DR, Blaszkowsky LS, Yeap BY, Ancukiewicz M, Deshpande V, Shinagare S, Wo JY, Boucher Y, Wadlow RC, Kwak EL, Allen JN, Clark JW, Zhu AX, Ferrone CR, Mamon HJ, Adams J, Winrich B, Grillo T, Jain RK, DeLaney TF, Fernandez-Del Castillo C, Duda DG. A Phase 1/2 and Biomarker Study of Preoperative Short Course Chemoradiation With Proton Beam Therapy and Capecitabine Followed By Early Surgery for Resectable Pancreatic Ductal Adenocarcinoma. Int J Radiat Oncol Biol Phys. 89:830-8 (2014).
568. G Seano, G Chiaverina, PA Gagliardi, L di Blasio, A Puliafito, C Bouvard, R Sessa, G Tarone, L Sorokin, D Helley, RK Jain, G Serini, F Bussolino and L Primo. Endothelial podosome rosettes regulate vascular branching in tumor angiogenesis. Nature Cell Biology 16:931-941 (2014).
569. O Chen, L Riedemann, F Etoc, H Herrmann, M Coppey, M Barch, C Farrar, J Zhao, O Bruns, H Wei, P Guo, J Cui, R Jensen, Y Chen, D Harris, J Cordero, Z Wang, A Jasanoff, D Fukumura, R Reimer, M Dahan, RK Jain, and M Bawendi. Magneto-fluorescent core-shell supernanoparticles. Nature Communications 5:5093 (2014). doi: 10.1038/ncomms6093.

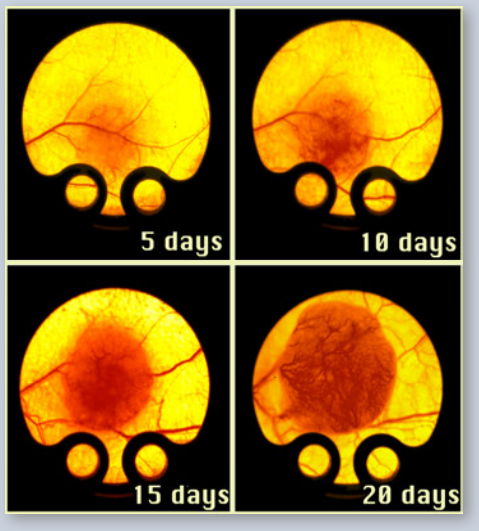
Reviews

570. Hagendoorn J, Yock TI, Borel Rinkes IHM, Padera TP, Ebb DH. "Novel molecular pathways in Gorham's disease: implications for treatment." Pediatric Blood and Cancer, 61:401-6 (2014).
571. VP Chauhan, Y Boucher, CR Ferrone, S Roberge, JD Martin, T Stylianopoulos, N Bardeesy, RA DePinho, TP Padera, LL Munn, and RK Jain. Compression of pancreatic tumor blood vessels by hyaluronan is caused by solid stress and not interstitial fluid pressure. Cancer Cell 26:14-15 (2014).
572. DG Duda, M Ancukiewicz, SJ Isakoff, IE Krop, RK Jain. Seeds and soil: How does local tumor stroma mediate distant metastasis? JNCI 106(8) pii: dju187 (2014).
573. Munn LL, Padera TP. "Imaging the lymphatic system." Microvascular Research, 96:55-63 (2014).
574. RK Jain, JD Martin and T Stylianopoulos,. The role of physical forces in tumor growth and therapy. Annual Reviews of Biomedical Engineering 16: 321-46 (2014).
575. K Emblem, C Farrar, E Gerstner, T Batchelor, R Borra, B Rosen, AG Sorensen, and RK Jain. Vessel caliber - a potential MRI biomarker of tumour response in clinical trials. Nature Reviews Clinical Oncology. 11:566-584 (2014).
576. E Chung, C Yeon, RK Jain and D Fukumura. Uncovering tumor biology by intravital microscopy. In: Comprehensive Biomedical Physics, Volume: IV "Optical molecular imaging" (Editor: Kiessling Alves & Anders Brahme). Elsevier Press (In press).
577. Jain RK, Netti PA. Letter to the editor regarding recent article by Wu et Al. [journal of Theoretical Biology, 355, 194-207 (2014)].
578. RK Jain, D Fukumura and DG Duda. Modes of neovascularization in tumors and clinical translation of antiangiogenic therapy. In: Pathobiology of Human Disease: A Dynamic Encyclopedia of Disease Mechanisms (Editor: LM McManus & RN Mitchell). Elsevier Press, San Diego, p. 2926-2957 (2014).
579. Jain RK. Antiangiogenesis strategies revisited: From starving tumors to alleviating hypoxia. Cancer Cell 26: 605–622 (2014).

2015 Publications

Original articles

580. Han HS, Niemeyer E, Huang Y, Kamoun WS, Martin JD, Bhaumik J, Chen Y, Roberge S, Cui J, Martin MR, Fukumura D, Jain RK, Bawendi MG, Duda DG. Quantum dot/antibody conjugates for in vivo cytometric imaging in mice. PNAS 112(5): 1350-5 (2015).
581. Ladra MM, Mandeville HC, Niemierko A, Padera TP, Friedmann AM, MacDonald SM, Ebb DH, Chen YL, Tarbell NJ, Yock TI. "Local failure in parameningeal rhabdomyosarcoma correlates with poor response to induction chemotherapy." Int J Radiat Oncol Biol Phys, Apr 8. pii: S0360-3016(15)00155-8. doi: 10.1016/j.ijrobp.2015.01.049 (2015)
582. Kuo AH, Ancukiewicz M, Kozak KR, Yock TI, Padera TP. "Cardiac and inflammatory biomarkers do not correlate with volume of heart or lung receiving radiation." Radiation Oncology, 10:5 1-5 (2015)
583. Heist RS, Duda DG, Sahani DV, Ancukiewicz M, Fidias P, Sequist LV, Temel JS, Shaw AT, Pennell NA, Neal JW, Gandhi L, Lynch TJ, Engelman JA, Jain RK. Improved tumor vascularization after anti-VEGF therapy with carboplatin and nab-paclitaxel associates with survival in lung cancer. PNAS 112(5): 1547-52 (2015).
584. Datta M, Via LE, Kamoun WS, Liu C, Chen W, Seano G, Weiner DM, Schimel D, England K, Martin JD, Gao X, Xu L, Barry CE III, and Jain RK. Anti-vascular endothelial growth factor treatment normalizes tuberculosis granuloma vasculature and improves small molecule delivery. PNAS 112(6): 1827-32 (2015).
585. Cho JK, Hyun SH, Choi N, Kim MJ, Padera TP, Choi JY, Jeong HS. "Significance of lymph node metastasis in cancer dissemination of head and neck cancer." Translational Oncology, 8:119-25 (2015).
586. Kodack DP, Askoxylakis V, Ferraro GB, Fukumura D and Jain RK. Emerging strategies for treating brain metastases from breast cancer. Cancer Cell 27: 163–175 (2015).
587. Kesler CT, Pereira ER, Cui CH, Nelson GM, Masuck DJ, Baish JW, Padera TP. "Angiopoietin-4 increases permeability of blood vessels and promotes lymphatic dilation." FASEB Journal, 29:3668-77 (2015)..
588. Ager EI, Kozin S, Kirkpatrick ND, Seano G, Kodack DP, Askoxylakis V, Huang Y, Goel S, Snuderl M, Muzikansky A, Finkelstein D, Dransfield DT, Devy L, Boucher Y, Fukumura D, Jain RK. Blockade of MMP14 activity in murine breast carcinomas: implications for macrophages, vessels, and radiotherapy. JNCI 107(4). pii: djv017. doi: 10.1093/jnci/djv017 (2015).



589. Stylianopoulos T, Economides E-A, Baish JW, Fukumura D and Jain RK. Towards optimal design of cancer nanomedicines: Multi-stage nanoparticles for the treatment of solid tumors. Annals of Biomedical Engineering 43: 2291-2300 (2015).
590. Chen Y, Ramjiawan RR, Reiberger T, Ng MR, Hato T, Huang Y, Ochiai H, Kitahara S, Unan EC, Reddy TP, Fan C, Huang P, Bardeesy N, Zhu AX, Jain RK, Duda DG. CXCR4 inhibition in tumor microenvironment facilitates anti-programmed death receptor-1 immunotherapy in sorafenib-treated hepatocellular carcinoma in mice. Hepatology 61(5): 1591-602 (2015).
591. H-S Jeong, D Jones, S Liao, DA Wattson, C Cui, DG Duda, CG Willett, RK Jain and TP Padera. Investigation of the lack of angiogenesis in the formation of lymph node metastases. JNCI 2015;107(9) pii: djv155. doi: 10.1093/jnci/djv155.
592. Lee EQ, Kaley TJ, Duda DG, Schiff D, Lassman AB, Wong ET, Mikkelsen T, Purow B, Muzikansky A, Ancukiewicz M, Huse JT, Ramkissoon SH, Drappatz J, Norden AD, Beroukhim R, Weiss SE, Alexander BM, McCluskey CS, Gerard M, Smith KH, Jain RK, Batchelor T, Ligon KL, Wen PY. A multicenter, phase II, randomized, non-comparative clinical trial of radiation and temozolomide with or without vandetanib in newly-diagnosed glioblastoma patients. Clin Cancer Res. 21(16): 3610-8 (2015).
593. Gerstner ER, Ye X, Duda DG, Levine MA, Mikkelsen T, Kaley TJ, Olson JJ, Nabors BL, Ahluwalia MS, Wen PY, Jain RK, Batchelor TT, Grossman S. A phase I study of cediranib in combination with cilengitide in patients with recurrent glioblastoma. Neuro Oncol. 17:1386-92 (2015).
594. Reiberger T, Chen Y, Ramjiawan RK, Hat T, Fan C, Samuel R, Roberge S, Huang P, Lauwers GY, Zhu AX, Bardeesy N, Jain RK, Duda DG. An orthotopic mouse model of hepatocellular carcinoma with underlying liver cirrhosis. Nature Protocols 10:1264-1274 (2015).
595. Jain, RK, Duda DG and Fukumura, D. Role of Tumor Microenvironment in Tumor Progression and Treatment Response: A 30 Years Journey. Cancer J. 21: 235-236 (2015).
596. Batista A, Riedemann L, Vardam T, and Jain, RK. Targeting the Tumor Microenvironment to Enhance Pediatric Brain Cancer Treatment. Cancer J. 21: 307-313 (2015).
597. Lemon CM, Karnas E, Han X, Bruns OT, Kempa TJ, Fukumura D, Bawendi MG, Jain RK, Duda DG, Nocera DG. Micelle-Encapsulated Quantum Dot-Porphyrin Assemblies as in Vivo Two-Photon Oxygen Sensors. J Am Chem Soc. 137:9832-42 (2015).
598. Zou HY, Friboulet L, Kodack DP, Engstrom LD, Li Q, West M, Tang RW, Wang H, Tsaparikos K, Wang J, Timofeevski S, Katayama R, Dinh DM, Lam H, Lam JL, Yamazaki S, Hu W, Patel B, Bezwada D, Frias RL, Lifshits E, Mahmood S, Gainor JF, Affolter T, Lappin PB, Gukasyan H, Lee N, Deng S, Jain RK, Johnson TW, Shaw AT, Fantin VR, Smeal T. PF-06463922, an ALK/ROS1 Inhibitor, Overcomes Resistance to First and Second Generation ALK Inhibitors in Preclinical Models. Cancer Cell 28:70-81 (2015).
599. R Samuel, DG Duda, D Fukumura and RK Jain. Vascular diseases await translation of blood vessels engineered from stem cells. Science Translational Medicine 7, 309rv6 (2015). doi: 10.1126/scitranslmed.aaa1805
600. Stylianopoulos T and Jain RK. Design considerations for nanotherapeutics in oncology. Nanomedicine: Nanotechnology, Biology and Medicine 11: 1893-1907 (2015).

2015 Publications

601. Datta M, Via LE, Chen W, Baish JW, Xu L, Barry CE, and Jain RK. Mathematical Model of Oxygen Transport in Tuberculosis Granulomas. Annals of Biomedical Engineering (in press).
602. Sara M. Tolaney Yves Boucher, Dan G. Duda, John D. Martin, Giorgio Seano, Marek Ancukiewicz, William T. Barry, Shom Goel, Johanna Lahdenrata, Steven J. Isakoff, Eren Yeh, Saloni R. Jain, Mehra Golshan, Jane Brock, Matija Snuderl, Eric P. Winer, Ian E. Krop, Rakesh K. Jain. Potential Role of Vascular Density and Vascular Normalization in Response to Neoadjuvant Bevacizumab and Chemotherapy in Breast Cancer Patients. PNAS, 112: 14325-14330 (2015).
603. X Gaoa, Y Zhao, AO Stemmer-Rachamimovd, H Liu, Peigen Huang, SM China, M Selig, S Plotkin, RK Jain and L Xu. Anti-VEGF treatment improves neurological function and augments radiation response in NF2 schwannoma model. PNAS, 112: 14676-81 (2015).
604. Askoxylakis V, Ferraro GB, Kodack DP, Badeaux M, Shankaraiah RC, Seano G, Kloepper J, Vardam T, Martin JD, Naxerova K, Bezwada D, Qi X, Selig M, Brachtel E, Duda DG, Huang P, Fukumura D, Engelman JA and Jain RK. Preclinical efficacy of ado-trastuzumab emtansine in the brain microenvironment. JNCI Nov 7; 108(2). pii: djv313. Print 2016 Feb.
605. Kunert C, Baish JW, Liao S, Padera TP, Munn LL. Mechanobiological oscillators control lymph flow, PNAS 2015. doi:10.1073/pnas.
606. J Incio, P Suboj, SM Chin, T Vardam-Kaur, H Liu, T Hato, S Babykutty, I Chen, V Deshpande, RK Jain, and D Fukumura. Metformin reduces desmoplasia in pancreatic cancer by reprogramming stellate cells and tumor-associated macrophages. PLoS One 10(12): e0141392 (2015). doi: 10.1371/journal.pone.0141392.
607. Whitley MJ, Cardona DM, Lazarides AL, Spasojevic I, Ferrer JM, Cahill J, Lee CL, Snuderl M, Blazer III DG, Hwang SE, Greenup RA, Mosca PJ, Mito JK, Cuneo KC, Larrier NA, O'Reilly EK, Riedel RF, Eward WC, Strasfeld DB, Fukumara D, Jain RK, Lee WD, Griffith LG, Bawendi MG, Kirsch DG, and Brigman BE. A Mouse-human Phase I co-clinical trial of a protease-activated fluorescent probe for imaging cancer. Science Translational Medicine (In Press)
608. PK Singhal, S Sassia, L Lana, P Au, SC Halvorsena, D Fukumura, RK Jain, and B Seed. Mouse Embryonic Fibroblasts Exhibit Extensive Developmental and Phenotypic Diversity. PNAS, 113:122-7 (2016). doi/10.1073/pnas.1522401112.
609. J Incio, P Suboj, SM Chin, T Vardam-Kaur, H Liu, T Hato, S Babykutty, I Chen, V Deshpande, RK Jain, and D Fukumura. Metformin reduces desmoplasia in pancreatic cancer by reprogramming stellate cells and tumor-associated macrophages. PLoS One 10(12): e0141392 (2015). doi: 10.1371/journal.pone.0141392.

Reviews

610. Naxerova K, Jain RK Using tumour phylogenetics to identify the roots of metastasis in humans. Nat Rev Clin Oncol. 12: 258-272 (2015).
611. Pereira ER, Jones D, Jung K, Padera TP. "The lymph node microenvironment and its role in the progression of metastatic cancer." Seminars in Cell and Developmental Biology, 38:98-105 (2015).
612. C Lu-Emerson, DG Duda, KE Emblem, JW Taylor, ER Gerstner, JS Loeffler, TT Batchelor, and RK Jain. Lessons from Anti-VEGF/VEGFR Trials in Glioblastoma Patients. Journal of Clinical Oncology 33:1197-1213. (2015).
613. Song JW, Bazou D, Munn LL. Microfluidic Model of Angiogenic Sprouting. In Vascular Morphogenesis, Springer, NY. (2015) pp 243-254.
614. Munn LL. Mechanobiology of lymphatic contractions. Seminars in Cell & Developmental Biology (2015), 38:67-74.
615. Jain RK, Fukumura D, Duda DG. Lessons From 30 Years of Teaching About the Microenvironment of Tumors. Cancer J. 21:137 (2015)
616. Duda DG, Heist RS, Sahani DV, Stylianopoulos T, Engelman JA, Jain RK. Reply to Ciccolini et al.: Using mathematical modeling to predict response to antiangiogenic therapy in cancer patients. PNAS 112(27): E3454 (2015).

2016 Publications

Original articles

617. Askoxylakis V, Ferraro GB, Kodack DP, Badeaux M, Shankaraiah RC, Seano G, Kloepper J, Vardam T, Martin JD, Naxerova K, Bezwada D, Qi X, Selig M, Brachtel E, Duda DG, Huang P, Fukumura D, Engelman JA and Jain RK. Preclinical efficacy of ado-trastuzumab emtansine in the brain microenvironment. JNCI Nov 7; 108(2). pii: djv313. Print 2016 Feb.
618. PK Singhal, S Sassia, L Lana, P Au, SC Halvorsena, D Fukumura, RK Jain, and B Seed. Mouse Embryonic Fibroblasts Exhibit Extensive Developmental and Phenotypic Diversity. PNAS, 113:122-7 (2016). doi/10.1073/pnas.1522401112.
619. Whitley MJ, Cardona DM, Lazarides AL, Spasojevic I, Ferrer JM, Cahill J, Lee CL, Snuderl M, Blazer III DG, Hwang SE, Greenup RA, Mosca PJ, Mito JK, Cuneo KC, Larrier NA, O'Reilly EK, Riedel RF, Eward WC, Strasfeld DB, Fukumara D, Jain RK, Lee WD, Griffith LG, Bawendi MG, Kirsch DG, and Brigman BE. A Mouse-human Phase I co-clinical trial of a protease-activated fluorescent probe for imaging cancer. Science Translational Medicine, 8(320):320ra4 (2016).
620. Park KR, Monsky WL, Lee CG, Song CH, Kim DH, Jain RK, Fukumura D. Mast Cells Contribute to Radiation-Induced Vascular Hyperpermeability. Radiat Res. 185:182-9 (2016).
621. D Fukumura, J Incio, R Shankaraiah, RK Jain, Obesity and cancer: an angiogenic and inflammatory link. Microcirculation 23:191-206 (2016).
622. Datta M, Via LE, Chen W, Baish JW, Xu L, Barry CE, and Jain RK. Mathematical Model of Oxygen Transport in Tuberculosis Granulomas. Annals of Biomedical Engineering 44: 863-872 (2016).

623. Peterson TE, Kirkpatrick ND, Huang Y, Farrar CT, Marijt KA, Kloepper J, Datta M, Amoozgar Z, Seano G, Jung K, Kamoun WS, Vardam T, Snuderl M, Goveia J, Chatterjee S, Batista A, Muzikansky A, Leow CC, Xu L, Batchelor TT, Duda DG, Fukumura D, Jain RK. Dual inhibition of Ang-2 and VEGF receptors normalizes tumor vasculature and prolongs survival in glioblastoma by altering macrophages. PNAS 113:4470-5 (2016).
624. Kloepper J, Riedemann L, Amoozgar Z, Seano G, Susek K, Yu V, Dalvie N, Amelung RL, Datta M, Song JW, Askoxylakis V, Taylor JW, Lu-Emerson C, Batista A, Kirkpatrick ND, Jung K, Snuderl M, Muzikansky A, Stubenrauch KG, Krieter O, Wakimoto H, Xu L, Munn LL, Duda DG, Fukumura D, Batchelor TT, Jain RK. Ang-2/VEGF bispecific antibody reprograms macrophages and resident microglia to anti-tumor phenotype and prolongs glioblastoma survival. PNAS 113:4476-81 (2016).
625. Blatter C, Meijer EFJ, Nam AS, Jones D, Bouma BE, Padera TP*, Vakoc BJ*. "In vivo label-free measurement of lymph flow velocity and volumetric flow rates using Doppler optical coherence tomography." Scientific Reports, Jul 5;6:29035. doi: 10.1038/srep29035 (2016). *Equal contribution corresponding authors. PMC4932526.

626. Incio J, Tam J, Rahbari NN, Suboj P, McManus DT, Chin SM, Vardam TD, Batista A, Babykutty S, Jung K, Khachatryan A, Hato T, Ligibel J, Krop IE, Puchner SB, Schlett CL, Hoffmman U, Ancukiewicz M, Shibuya M, Carmeliet P, Soares R, Duda DG, Jain RK, Fukumura D. PlGF/VEGFR-1 signaling promotes macrophage polarization and accelerated tumor progression in obesity. Clinical Cancer Research 22: 2993-3004 (2016).
627. Blakeley JO, Ye X, Duda DG, Halpin CF, Bergner AL, Muzikansky A, Merker VL, Gerstner ER, Fayad LM, Ahlawat S, Jacobs MA, Jain RK, Zalewski C, Dombi E, Widemann BC, Plotkin SR. Efficacy and Biomarker Study of Bevacizumab for Hearing Loss Resulting From Neurofibromatosis Type 2-Associated Vestibular Schwannomas. J Clin Oncol. 34:1669-75 (2016).
628. Incio J, Liu H, Suboj P, Chin SM, Chen IX, Pinter M, Ng MR, Nia HT, Grahovac J, Kao S, Babykutty S, Huang Y, Jung K, Rahbari NN, Han X, Chauhan VP, Martin JD, Kahn J, Huang P, Desphande V, Michaelson J, Michelakos TP, Ferrone CR, Soares R, Boucher Y, Fukumura D & Jain RK. Obesity-induced inflammation and desmoplasia promote pancreatic cancer progression and resistance to chemotherapy. Cancer Discovery 6: 852–869 (2016). [Commentaries by V Bronte and G Tortora, Cancer Discovery 6: 821-3 (2016); MC Arkan, Nature 536:157-8 (2016).]
629. Nia HT, Liu H, Seano G, Datta M, Jones D, Rahbari N, Incio J, Chauhan VP, Jung K, Martin JD, Askoxylakis V, Padera TP, Fukumura D, Boucher Y, Hornicek FJ, Grodzinsky AJ, Baish JW, Munn LL and Jain RK. Solid stress and elastic energy as measures of tumour mechanopathology. Nature Biomedical Engineering 1: 4 (2016). doi:10.1038/s41551-016-0004. [Accomanying News & Views by Daniele M. Gilkes and Denis Wirtz - 'Tumour mechanopathology: Cutting the stress out' doi: 10.1038/s41551-016-0012; Peter Sidaway, Solid stress indicates tumour pathology, Nature Reviews Clinical Oncology (2016) doi:10.1038/nrclinonc.2016.209].
630. Hajjarian Z, Nia HT, Ahn S, Grodzinsky AL, Jain RK, and Nadkarni S. Laser Speckle Rheology for evaluating the viscoelastic properties of hydrogel scaffolds. Scientific Reports 6:37949 (2016). doi: 10.1038/srep37949.
631. Emblem KE and Jain RK. Improving Treatment of Liver Metastases by Targeting Non-angiogenic Mechanisms. Nature Medicine 22: 1209-1210 (2016).
632. Menter AR, Carroll NM, Sakoda LC, Delate T, Hornbrook MC, Jain RK, Kushi LH, Quinn VP and Ritzwoller DP. Effect of Angiotensin System Inhibitors on Survival in Patients Receiving Chemotherapy for Advanced Non-Small Cell Lung Cancer. Clinical Lung Cancer 2016, Aug 20. pii: S1525-7304(16)30188-7. doi: 10.1016/j.cllc.2016.07.008.

633. Meijer EFJ, Baish JW, Padera TP, Fukumura D. "Measuring vascular permeability in vivo." Methods in Molecular Biology, 1458:71-85 (2016).
634. Rahbari N, Kedrin D, Incio J, Liu H, Nia HT, Edrich C, Dubroix J, Chen I, Heishi T, Martin JD, Huang Y, Grodzinsky AJ, Duda DG, Jain RK & Fukumura D. Extracellular matrix remodeling after anti-VEGF therapy contributes to therapeutic resistance in colorectal cancer liver metastases. Science Translational Medicine 8: 360ra135 (2016). doi:10.1126/scitranslmed.aaf5219. [Highlighted in Cancer Discovery, Nature Reviews Cancer, Nature Reviews Gastroenterology].
635. Kalpathy-Cramer J, Chandra V, Da X, Ou Y, Emblem KE, Muzikansky A, Cai X, Douw L, Evans JG, Dietrich J, Chi AS, Wen PY, Stufflebeam S, Rosen B, Duda DG, Jain RK, Batchelor TT, Gerstner ER Phase II study of tivozanib, an oral VEGFR inhibitor, in patients with recurrent glioblastoma. J Neurooncol. 2016 Nov 16.
636. Baish JW, Kunert C, Padera TP, Munn LL. Synchronization and random triggering of lymphatic vessel contractions. PLOS Computational Biology. 2016; 12: e1005231. doi: 10.1371/journal.pcbi.1005231.
637. Gruionu GG, Bazou D, Maimon N, Onita-Lenco M, Gruionu LG, Huang P, Munn LL. Implantable Tissue Isolation Chambers for Analyzing Tumor Dynamics In Vivo. Lab Chip. 2016; 16:1840-51.
638. Qazi H, Shi ZD, Song JW, Cancel LM, Huang P, Zeng Y, Roberge S, Munn LL*, Tarbell JM.* Heparan Sulfate Proteoglycans Mediate Renal Carcinoma Metastasis. International Journal of Cancer. 2016; 139:2791-2801. *Equal contributions.
639. Bazou D, Ng MR, Song JW, Chin SM, Maimon N, Munn LL. Flow-induced HDAC1 phosphorylation and nuclear export in angiogenic sprouting. Nature Scientific Reports. 2016; 6:34046.
640. Bazou D, Maimon N, Gruionu G, Munn LL. Self-assembly of vascularized tissue to support tumor explants in vitro. Integrative Biology. 2016; 8:1301-11.

2016 Publications

641. Nia HT, Liu H, Seano G, Datta M, Jones D, Rahbari N, Incio J, Chauhan VP, Jung K, Martin JD, Askoxylakis V, Padera TP, Fukumura D, Boucher Y, Hornicek FJ, Grodzinsky AJ, Baish JW, Munn LL, Jain RK. "Solid stress and elastic energy as measures of tumour mechanopathology." Nature Biomedical Engineering, 1: 0004 (2016)
642. Setia N, Agoston AT, Han HS, Mullen JT, Duda DG, Clark JW, Deshpande V, Mino-Kenudson M, Srivastava A, Lennerz JK, Hong TS, Kwak E, Lauwers GY. A protein and mRNA expression based classification of gastric cancer. Modern Pathology 2016; 29: 772-84.
643. Batchelor TT, Gerstner ER, Ye X, Desideri S, Duda DG, Peereboom D, Lesser GJ, Chowdhary S, Wen PY, Grossman S, Supko JG. Feasibility, phase I, and phase II studies of tandutinib, an oral platelet-derived growth factor receptor-β tyrosine kinase inhibitor, in patients with recurrent glioblastoma. Neuro-Oncology 2016; Epub ahead of print on Sept 23, 2016 as doi: 10.1093/neuonc/now185.
644. Patil MD, Bhaumik J, Babykutty S, Banerjee UC, Fukumura D. Arginine dependence of tumor cells: targeting a chink in cancer's armor. Oncogene 2016;35:4957–4972. PMCID: PMC5457742

Reviews

645. Munn LL and Jain, RK. The forces of cancer. The Scientist 30: 52-57 (2016).
646. Ferraro GB, Kodack DP, Askoxylakis V and Jain RK. Closing the gap between astrocytes and brain metastases. Cell Research 26: 973-4 (2016).
647. Martin JD, Fukumura D, Duda DG, Boucher Y, Jain RK Reengineering the tumor microenvironment to alleviate hypoxia and overcome cancer heterogeneity. Cold Spring Harbor Perspectives in Medicine 6:a027094 (2016). doi: 10.1101/cshperspect.a027094
648. Kumar V, Boucher Y, Liu H, Ferreira D, Hooker J, Catana C, Jain RK and Guimaraes AR. Noninvasive assessment of losartan-induced increase in functional microvasculature and drug delivery in pancreatic ductal adenocarcinoma. Tranlational Oncology 9:431-437 (2016).
649. Ng RM and Jain RK. Hypoxia–induced DNA hypermethylation: Another reason to normalize tumor vessels. Translational Cancer Research 5(Suppl 7):S1358-S1362 (2016). doi: 10.21037/tcr.2016.12.72.
650. Munn LL. Cancer and Inflammation. WIREs Systems Biology and Medicine. 2016; doi:10.1002/wsbm.1370.
651. Padera TP, Meijer EFJ, Munn LL. "The lymphatic system in disease processes and cancer progression." Annual Reviews in Biomedical Engineering, 18:125-58 (2016).
652. Gupta N, Duda DG. Role of Stromal Cell-Derived Factor 1 α Pathway in Bone Metastatic Prostate Cancer. Journal of Biomedical Research 2016; 30: 181-185.
653. Hato T, Zhu AX, Duda DG. Rationally combining anti-VEGF therapy with checkpoint inhibitors in hepatocellular carcinoma. Immunotherapy 2016; 8: 299-313.
654. Popp I, Niedermann G, Grosu AL, Duda DG. Immune modulation by hypofractionated stereotactic radiation therapy: Therapeutic implications. Radiotherapy and Oncology 2016; 120: 185-94.
655. Pantziarka P, Hutchinson L, André N, Benzekry S, Bertolini F, Bhattacharjee A, Chiplunkar S, Duda DG, Gota V, Gupta S, Joshi A, Kannan S, Kerbel R, Kieran M, Palazzo A, Parikh A, Pasquier E, Patil V, Prabash K, Shaked Y, Saulnier Sholler G, Sterba J, Waxman D, Banavali S. Next Generation Metronomic Chemotherapy – Report from the 5th Biennial International Metronomic and Anti-angiogenic Therapy Meeting, 6th – 8th May 2016, Mumbai. eCancer 2016; 10: 689.
656. Meijer EFJ, Baish JW, Padera TP, Fukumura D. Measuring vascular permeability *in vivo*. Methods in Molecular Biology. Springer press. 2016, Chapter 6. p. 71-85. PMCID: PMC5435480

2017 Publications

Original articles

657. Tolaney SM, Ziehr DR, Guo H, Ng MR, Barry WR, Higgins MJ, Isakoff SJ, Brock JE, Ivanova EV, Paweletz CP, Demeo MK, Ramaiya NH, Overmoyer BA, Jain RK, Winer EP and Duda DG. Phase 2 and biomarker study of cabozantinib for metastatic triple-negative breast cancer patients. Oncologist 2017: 22: 25-32
658. Andronesi O, Esmaeili M, Borra R, Emblem K, Gerstner E, Pinho M, Plotkin S, Chi A, Eichler A, Dietrich J, Ivy P, Wen PY, Duda DG, Jain RK, Rosen B, Sorensen AG, Batchelor TT. Early changes in glioblastoma metabolism measured by MR Spectroscopic Imaging during combination of antiangiogenic cediranib and chemoradiation therapy are associated with survival. Nature Precision Oncology 2017 (in press).
659. Pinter M, Weinmann A, Wörns MA, Hucke F, Bota S, Marquardt JU, Duda DG, Jain RK, Galle PR, Trauner M, Peck-Radosavljevic M, Sieghart W. Use of inhibitors of the renin-angiotensin system is associated with longer survival in patients with hepatocellular carcinoma. United European Gastroenterol J. 2017;5(7):987-996
660. Rowlands CJ, Park D, Bruns OT, Piatkevich KD, Fukumura D, Jain RK, Bawendi MG, Boyden ES, So PT. Wide-field three-photon excitation in biological samples. Light Sci Appl. 2017;6:e16255.
661. Bruns OT, Bischof TS, Harris DK, Franke D, Shi Y, Riedemann L, Bartelt A, Jaworski FB, Carr JA, Rowlands CJ, Wilson MWB, Chen O, Wei H, Hwang GW, Montana DM, Coropceanu I, Achorn OB, Kloepper J, Heeren J, So PTC, Fukumura D, Jensen KF, Jain RK, Bawendi

MG. Next-generation in vivo optical imaging with short-wave infrared quantum dots. Nat Biomed Eng. 2017;1.
662. Li W, Yang W, Liu Y, Chen S, Chin S, Qi X, Zhao Y, Liu H, Wang J, Mei X, Huang P, Xu D. MicroRNA-378 enhances inhibitory effect of curcumin on glioblastoma. Oncotarget. 2017;8(43):73938-73946.
663. Li S, Kumar T P, Joshee S, Kirschstein T, Subburaju S, Khalili JS, Kloepper J, Du C, Elkhal A, Szabó G, Jain RK, Köhling R, Vasudevan A. Endothelial cell-derived GABA signaling modulates neuronal migration and postnatal behavior. Cell Res. 2017;:ePub - PMID: 29086765
664. Li W, Liu Y, Yang W, Han X, Li S, Liu H, Gerweck LE, Fukumura D, Loeffler JS, Yang BB, Jain RK, Huang P. MicroRNA-378 enhances radiation response in ectopic and orthotopic implantation models of glioblastoma. J Neurooncol. 2017;:ePub - PMID: 29081036
665. Askoxylakis V, Badeaux M, Roberge S, Batista A, Kirkpatrick N, Snuderl M, Amoozgar Z, Seano G, Ferraro GB, Chatterjee S, Xu L, Fukumura D, Duda DG, Jain RK. A cerebellar window for intravital imaging of normal and disease states in mice. Nat Protoc. 2017;12(11):2251-2262 .

666. Zhang N, Chen J, Ferraro G, Wu L, Datta M, Jain RK, Plotkin SR, Stemmer-Rachamimov A, Xu L. Anti-VEGF treatment improves neurological function in tumors of the nervous system. Exp Neurol. 2017;:ePub - PMID: 28911884
667. Jung K, Heishi T, Incio J, Huang Y, Beech EY, Pinter M, Ho WW, Kawaguchi K, Rahbari NN, Chung E, Kim JK, Clark JW, Willett CG, Yun SH, Luster AD, Padera TP, Jain RK, Fukumura D. Targeting CXCR4-dependent immunosuppressive Ly6C(low) monocytes improves antiangiogenic therapy in colorectal cancer. Proc Natl Acad Sci U S A. 2017;114(39):10455-10460.
668. Wang X, Freire Valls A, Schermann G, Shen Y, Moya IM, Castro L, Urban S, Solecki GM, Winkler F, Riedemann L, Jain RK, Mazzone M, Schmidt T, Fischer T, Halder G, Ruiz de Almodóvar C. YAP/TAZ Orchestrate VEGF Signaling during Developmental Angiogenesis. Dev Cell. 2017;42(5):462-478.e7.
669. Blatter C, Meijer EFJ, Padera TP, Vakoc BJ. Simultaneous measurements of lymphatic vessel contraction, flow and valve dynamics in multiple lymphangions using optical coherence tomography. J Biophotonics. 2017;:ePub - PMID: 28700145
670. Jung K, Heishi T, Khan OF, Kowalski PS, Incio J, Rahbari NN, Chung E, Clark JW, Willett CG, Luster AD, Yun SH, Langer R, Anderson DG, Padera TP, Jain RK, Fukumura D. Ly6Clo monocytes drive immunosuppression and confer resistance to anti-VEGFR2 cancer therapy. J Clin Invest. 2017;127(8):3039-3051.
671. Naxerova K, Reiter JG, Brachtel E, Lennerz JK, van de Wetering M, Rowan A, Cai T, Clevers H, Swanton C, Nowak MA, Elledge SJ, Jain RK. Origins of lymphatic and distant metastases in human colorectal cancer. Science. 2017;357(6346):55-60.
672. Meijer EFJ, Jeong HS, Pereira ER, Ruggieri TA, Blatter C, Vakoc BJ, Padera TP. Murine chronic lymph node window for longitudinal intravital lymph node imaging. Nat Protoc. 2017;12(8):1513-1520.
673. Jusakul A, Cutcutache I, Yong CH, Lim JQ, Huang MN, Padmanabhan N, Nellore V, Kongpetch S, Ng AWT, Ng LM, Choo SP, Myint SS, Thanan R, Nagarajan S, Lim WK, Ng CCY, Boot A, Liu M, Ong CK, Rajasegaran V, Lie S, Lim AST, Lim TH, Tan J, Loh JL, McPherson JR, Khuntikeo N, Bhudhisawasdi V, Yongvanit P, Wongkham S, Totoki Y, Nakamura H, Arai Y, Yamasaki S, Chow PKH, Chung AYF, Ooi LLPJ, Lim KH, Dima S, Duda DG, Popescu I, Broet P, Hsieh SY, Yu MC, Scarpa A, Lai J, Luo DX, Carvalho AL, Vettore AL, Rhee H, Park YN, Alexandrov L, Gordan R, Rozen SG, Shibata T, Pairojkul C, Teh BT, Tan P. Whole-Genome and Epigenomic Landscapes of Etiologically Distinct Subtypes of Cholangiocarcinoma. Cancer Discov. 2017;7(10):1116-1135.
674. Levin VA, Chan J, Datta M, Yee JL, Jain RK. Effect of angiotensin system inhibitors on survival in newly diagnosed glioma patients and recurrent glioblastoma patients receiving chemotherapy and/or bevacizumab. J Neurooncol. 2017;:ePub - PMID: 28631191
675. Liu H, Naxerova K, Pinter M, Incio J, Lee H, Shigeta K, Ho WW, Crain JA, Jacobson A, Michelakos T, Dias-Santos D, Zanconato A, Hong TS, Clark JW, Murphy JE, Ryan DP, Deshpande V, Lillemoe KD, Fernandez-Del Castillo C, Downes M, Evans RM, Michaelson J, Ferrone CR, Boucher Y, Jain RK. Use of Angiotensin System Inhibitors is Associated with Immune Activation and Longer Survival in Non-Metastatic Pancreatic Ductal Adenocarcinoma. Clin Cancer Res. 2017;23(19):5959-5969 .

676. Li W, Yang W, Liu Y, Chen S, Chin S, Qi X, Zhao Y, Liu H, Wang J, Mei X, Huang P, Xu D. MicroRNA-378 enhances inhibitory effect of curcumin on glioblastoma. Oncotarget. 2017;:ePub - PMID: 28575858
677. Kodack DP, Askoxylakis V, Ferraro GB, Sheng Q, Badeaux M, Goel S, Qi X, Shankaraiah R, Cao ZA, Ramjiawan RR, Bezwada D, Patel B, Song Y, Costa C, Naxerova K, Wong CSF, Kloepper J, Das R, Tam A, Tanboon J, Duda DG, Miller CR, Siegel MB, Anders CK, Sanders M, Estrada MV, Schlegel R, Arteaga CL, Brachtel E, Huang A, Fukumura D, Engelman JA, Jain RK. The brain microenvironment mediates resistance in luminal breast cancer to PI3K inhibition through HER3 activation. Sci Transl Med. 2017;9(391): eaal4682
678. Meijer EF, Blatter C, Chen IX, Bouta E, Jones D, Pereira ER, Jung K, Vakoc BJ, Baish JW, Padera TP. Lymph node effective vascular permeability and chemotherapy uptake. Microcirculation. 2017;:ePub - PMID: 28510992
679. Nastase A, Teo JY, Heng HL, Ng CC, Myint SS, Rajasegaran V, Loh JL, Lee SY, Ooi LL, Chung AY, Chow PK, Cheow PC, Wan WK, Azhar R, Khoo A, Xiu SX, Alkaff SM, Cutcutache I, Lim JQ, Ong CK, Herlea V, Dima S, Duda DG, Teh BT, Popescu I, Lim TK. Genomic and proteomic characterization of ARID1A chromatin remodeller in ampullary tumors. Am J Cancer Res. 2017;7(3):484-502.

2017 Publications

680. Chen Y, Liu YC, Sung YC, Ramjiawan RR, Lin TT, Chang CC, Jeng KS, Chang CF, Liu CH, Gao DY, Hsu FF, Duyverman AM, Kitahara S, Huang P, Dima S, Popescu I, Flaherty KT, Zhu AX, Bardeesy N, Jain RK, Benes CH, Duda DG. Overcoming sorafenib evasion in hepatocellular carcinoma using CXCR4-targeted nanoparticles to co-deliver MEK-inhibitors. Sci Rep. 2017;7:44123.
681. Goyal L, Zheng H, Yurgelun MB, Abrams TA, Allen JN, Cleary JM, Knowles M, Regan E, Reardon A, Khachatryan A, Jain RK, Nardi V, Borger DR, Duda DG, Zhu AX. A phase 2 and biomarker study of cabozantinib in patients with advanced cholangiocarcinoma. Cancer. 2017;123(11):1979-1988.
682. Mpekris F, Baish JW, Stylianopoulos T, Jain RK. Role of vascular normalization in benefit from metronomic chemotherapy. Proc Natl Acad Sci U S A. 2017;114(8):1994-1999.
683. Gupta N, Badeaux M, Liu Y, Naxerova K, Sgroi D, Munn LL, Jain RK, Garkavtsev I. Stress granule-associated protein G3BP2 regulates breast tumor initiation. Proc Natl Acad Sci U S A. 2017;114(5):1033-1038.
684. N Lippok, M Villiger, A Albanese, EFJ Meijer, K Chung, TP Padera, SN Bhatia, BE Bouma. Depolarization signatures map gold nanorods within biological tissue. Nature Photonics, July 31, 2017 doi:10.1038/nphoton.2017.128.
685. Pinter M, Weinmann A, Wörns MA, Hucke F, Bota S, Marquardt JU, Duda DG, Jain RK, Galle PR, Trauner M, Peck-Radosavljevic M, Sieghart W. Use of inhibitors of the renin-angiotensin system is associated with longer survival in patients with hepatocellular carcinoma. United European Gastroenterol Journal: 5(7): 987-996 (2017).
686. Kozin SV, Maimon N, Wang R, Gupta N, Munn LL, Jain RK, Garkavtsev I. Secretory leukocyte protease inhibitor (SLPI) as a potential target for inhibiting metastasis of triple-negative breast cancers. Oncotarget. 2017; 8(65): 108292–108302.
687. DA Reardon, A Lassman, D Schiff, Shakeeb Yunus; Elizabeth Gerstner; Timothy Cloughesy; Eudocia Quant Lee; Sarah C. Gaffey; Jennifer Barrs; Jennifer Bruno; Alona Muzikansky, Dan G. Duda; Rakesh K. Jain; Patrick Y. Wen. Phase II and biomarker study of trebananib, an angiopoietin blocking peptibody, with and without bevacizumab for recurrent glioblastoma patients. Cancer 2017; 124: 1438–48.

Reviews

688. Aoki S, Cobbold M, Zhu AX, Duda DG. Can smart nanomedicine deliver effective targeted cytotoxic treatments to hepatocellular carcinomas while reducing the liver damage? Hepatology. 2017;:ePub - PMID: 29077214
689. Mitchell MJ, Jain RK, Langer R. Engineering and physical sciences in oncology: challenges and opportunities. Nat Rev Cancer. 2017;17(11):659-675.
690. Pinter M, Jain RK. Targeting the renin-angiotensin system to improve cancer treatment: Implications for immunotherapy. Sci Transl Med. 2017;9(410):ePub - PMID: 28978752.
691. Ali MA, Lacin S, Abdel-Wahab R, Uemura M, Hassan M, Rashid A, Duda DG, Kaseb AO. Nonalcoholic steatohepatitis-related hepatocellular carcinoma: is there a role for the androgen receptor pathway? Onco Targets Ther. 2017;10:1403-1412
692. Askoxylakis V, Arvanitis CD, Wong CSF, Ferraro GB, Jain RK. Emerging Strategies for Delivering Antiangiogenic Therapies to Primary and Metastatic Brain Tumors. Adv Drug Deliv Rev. 2017;119:159-174.
693. Ramjiawan RR, Griffioen AW, Duda DG. Anti-angiogenesis for cancer revisited: Is there a role for combinations with immunotherapy? Angiogenesis. 2017;20(2):185-204.
694. Zhang N, Gao X, Zhao Y, Datta M, Liu P, Xu L. Rationally combining anti-VEGF therapy with radiation in NF2 schwannoma. J Rare Dis Res Treat. 2017;1(2):51-55.
695. Askoxylakis V, Kodack DP, Ferraro GB, Jain RK. Antibody-based therapies for the treatment of brain metastases from HER2-positive breast cancer: time to rethink the importance of the BBB? Breast Cancer Res Treat. 2017;165(2):467-468.
696. De Palma M, Jain RK. CD4(+) T Cell Activation and Vascular Normalization: Two Sides of the Same Coin? Immunity. 2017;46(5):773-775.
697. Wang N, Jain RK, Batchelor TT. New Directions in Anti-Angiogenic Therapy for Glioblastoma. Neurotherapeutics. 2017;14(2):321-332.
698. Munn LL. Cancer and Inflammation. WIREs Systems Biology and Medicine. (2017) 9:e1370 doi:10.1002/wsbm.1370.

2018 Publications

Original articles

699. Sung Y-C, Liu Y-C, Chao P-H, Chang C-C, Lin T-T, Lin J-A, Cheng H-T, Wang J, Lai CP, Chen L-H, Jin P, Wu AY, Chiang T, Gao D-Y, Duda DG, Chen Y. Combined delivery of sorafenib and a MEK inhibitor using CXCR4-targeted nanoparticles reduces hepatic fibrosis and prevents tumor development. Theranostics 2018; 8: 894–904.
700. Bouta EM, Blatter C, Ruggieri TA, Meijer EFJ, Munn LL, Vakoc BJ, Padera TP. Lymphatic function measurements influenced by contrast agent volume and body position. 2018; JCI Insight. 3(2):e96591. J
701. Jones D, Meijer EFJ, Blatter C, Liao S, Pereira ER, Bouta EM, Jung K, Chin SM, Huang P, Munn LL, Vakoc BJ, Otto M, Padera TP. Methicillin-resistant Staphylococcus aureus causes sustained collecting lymphatic vessel dysfunction. 2018; Science Translational Medicine. 10(424), eaam7964. OI:10.1126/scitranslmed.aam7964.
702. Bazou D, Maimon N, Gruionu G, Grahovac J, Seano G, Liu H, Evans CL, Munn LL. Vascular beds maintain pancreatic tumor explants for ex vivo drug screening. Journal of Tissue Engineering and Regenerative Medicine. 2018; 12(1): e318-e322.
703. E.R. Pereira, D. Kedrin, G. Seano, O. Gautier, E.F.J. Meijer, D. Jones, S.M. Chin, S. Kitahara, E.M. Bouta, J. Chang, E. Beech, H.S. Jeong, M.C. Carroll, A.G. Taghian, T.P. Padera. "Lymph node metastases can invade local blood vessels, exit the node and colonize distant organs in mice." Science, 359: 1403-1407 (2018).

2018 Publications

704. A. Bourquard, A.P. Trinidad, I. Butterworth, Á. Sánchez-Ferro, C.C. Canales, K. Humala, M.F. Urdiola, C. del Rio, B. Valles, J.M. Tucker-Schwartz, E.S. Lee, B.J. Vakoc, T.P. Padera, M.J. Ledesma-Carbayo, Y.-B. Chen, E.P. Hochberg, M.L. Gray, C. Castro-González "Non-invasive detection of severe neutropenia in chemotherapy patients by optical imaging of nailfold microcirculation." Scientific Reports, Mar 28;8(1):5301. doi: 10.1038/s41598-018-23591-0. (2018).
705. K Dixon, M Schorer, J Nevin, Y Etminan, Z Amoozgar, T Kondo, S Kurtulus, N Kassam, RA Sobel, D Fukumura, RK Jain, AC Anderson, VK Kuchroo, N Joller. Functional anti-TIGIT antibodies regulate development of autoimmunity and anti-tumor immunity. Journal of Immunology. 200: 3000-3007 (2018).
706. D.J. Firl, S.E. Degn, T. Padera, M.C. Carroll. "Capturing change in clonal composition amongst single mouse germinal centers." eLife, Aug 1;7. pii: e33051. doi: 10.7554/eLife.33051 (2018).
707. S Li, P Kumar T, S Joshee, T Kirschstein, S Subburaju, J Khalili, J Kloepper, C Du, A Elkhal, G Szabo, RK Jain, R Koehling and A Vasudevan. Endothelial Cell Derived GABA Signaling Modulates Neuronal Migration and Postnatal Behavior. Cell Research, 28:221-248 (2018).
708. MJ Khandekar and RK Jain. Smooth sailing for immunotherapy for unresectable stage III Non-small cell lung cancer: The PACIFIC study. Translational Cancer Research 7: S16-S20 (2018).
709. DA Reardon, A Lassman, D Schiff, Shakeeb Yunus; Elizabeth Gerstner; Timothy Cloughesy; Eudocia Quant Lee; Sarah C. Gaffey; Jennifer Barrs; Jennifer Bruno; Alona Muzikansky, Dan G. Duda; Rakesh K. Jain; Patrick Y. Wen. Phase II and biomarker study of trebananib, an angiopoietin blocking peptibody, with and without bevacizumab for recurrent glioblastoma patients. Cancer (Online on December 19, 2017). doi: 10.1002/cncr.31172. 124:1438-1448 (2018).
710. W Li, Y Liu, W Yang, X Han, S Li, H Liu, LE Gerweck, D Fukumura, JS Loeffler, BB Yang, RK Jain and P Huang. MicroRNA-378 enhances radiation response in ectopic and orthotopic implantation models of glioblastoma. Journal of Neuro-Oncology 136: 63-71 (2018).
711. Y Zhao, P Liu, N Zhang, J Chen, LD Landegger, L Wu, F Zhao, Y Zhang, J Zhang, T Fujita, A Stemmer-Rachamimov, GB Ferraro, H Liu, A Muzikansky, SR Plotkin, KM Stankovic, RK Jain and L Xu. Targeting the cMET pathway augments radiation response without adverse effect on hearing in NF2 schwannoma models. PNAS (online on Feb 9, 2018) 115: E2077-E2084 (2018).
712. J Incio, JA Ligibel, DT McManus, P Suboj, K Jung, K Kawaguchi, M Pinter, S Babykutty, SM Chin, TD Vardam, Y Huang, NN Rahbari, S Roberge, D Wang, IL Gomes-Santos, SB Puchner, CL Schlett, U Hoffmman, M Ancukiewicz, SM Tolaney, IE Krop, DG Duda, Y Boucher, D Fukumura and RK Jain. Obesity promotes resistance to anti-VEGF therapy in breast cancer by upregulating IL-6 and potentially FGF-2. Science Translation Medicine, 10: eaag0945. Published online on March 14, 2018.
713. JA Carr, D Frankea, JR Carama, CF Perkinsona, V Askoxylakis, M Datta, D Fukumura, RK Jain, MG Bawendi and OT Bruns. Shortwave Infrared Fluorescence Imaging with the Clinically Accessible Near-Infrared Dye Indocyanine Green. PNAS 115:4465-4470 (2018).
714. HT Nia, M Datta, G Seano, P Huang, LL Munn, and RK Jain. Quantifying solid stress and elastic energy from excised or in situ tumors. Nature Protocols 13(5):1091-1105 (2018). https://rdcu.be/LZEV
715. A Griveau, G Seano, SJ Shelton R Kupp, A Jahangiri, K Obernier, S Krishnan, OR Lindberg, TJ Yuen, A-C Tien, JK Sabo, N Wang, I Chen, J Kloepper, L Larrouquere, M Ghosh, It Tirosh, E Huillard, A Alvarez-Buylla, MC Oldham, Al Persson, WA Weiss, TT Batchelor, A Stemmer-Rachamimov, ML Suva, JJ Phillips, M Aghi, S Mehta, RK Jain and DH Rowitch. A glial signature and Wnt7 signaling regulate glioma-vascular interactions and tumor microenvironment. Cancer Cell 33 (5): 874-889 (2018).
716. M Binnewies, E Roberts, V Chan, K Kersten, DF Fearon, M Merad, LM Coussens, D Gabrilovich, S Ostrand-Rosenberg, CC Hedrick, RH Vonderheide, M Pittet, RK Jain, W Zou, K Howcroft, E Woodhouse, The TiME Working Group, R Weinberg, M Krummel. The Tumor Immune Microenvironment (TIME): The Future of Understanding Tumor-Tissue Biology for Key Insights and Cures. Nature Medicine 24(5): 541-550 (2018).
717. Grassberger C, Hong TS, Hato T, Yeap BY, Wo JY, Tracy M, Bortfeld T, Wolfgang JA, Eyler CE, Goyal L, Clark JW, Crane CH, Koay EJ, Cobbold M, DeLaney TF, Jain RK, Zhu AX and Duda DG. Differential Association Between Circulating Lymphocyte Populations with Outcome after Radiation Therapy in Subtypes of Liver Cancer. Int J Radiat Oncol Biol Phys. 101(5):1222-1225 (2018).
718. EQ Lee, DG Duda, A Muzikansky, ER Gerstner, JG Kuhn, DA Reardon, L Nayak, AD Norden, L Doherty, J Stefanik, D LaFrankie, J Armitage, T Vardam, D Stokes, KH Smith, C McCluskey, S Gaffey, TT Batchelor, RK Jain and, PY Wen. Phase I and biomarker study of plerixafor and bevacizumab in recurrent high-grade glioma. Clinical Cancer Research 24(19):4643-4649 (2018).
719. CD Arvanitis, V Askoxylakis, Y Guo, M Datta, J Kloepper, GK Ferraro, MO Bernabeu, D Fukumura, N McDannold and RK Jain. Mechanisms of enhanced drug delivery in brain metastases with focused ultrasound-induced transient blood-tumor barrier disruption. PNAS 115(37): E8717-E8726 (2018).
720. Ina Ly K, Vakulenko-Lagun B, Emblem KE, Ou Y, Da X, Betensky RA, Kalpathy-Cramer J, Duda DG, Jain RK, Chi AS, Plotkin SR, Batchelor TT, Sorensen G, Rosen BR, Gerstner ER. Probing tumor microenvironment in patients with newly diagnosed glioblastoma during chemoradiation and adjuvant temozolomide with functional MRI. Science Reports 8(1):17062 (2018).
721. S Li, W Li, C-H Leung, S Kitahara, Y Liu, S Klein, D Fukumura, JS Loeffler, RK Jain, DG Duda, and P Huang. Combining Angiotensin Receptor Blocker Losartan and the CXCR4 Inhibitor AMD3100 Increases the Efficacy of Radiotherapy in a Metastatic Osteosarcoma Mouse Model. J Cancer Sci Ther 10: 351-365 (2018). doi: 10.4172/1948-5956.1000570.
722. S.D. Nathanson, D. Krag, H.M. Kuerer, L.A. Newman, M. Brown, D. Kerjaschki, E.R. Pereira, T.P. Padera. "Breast cancer metastasis through the lympho-vascular system." Clinical and Experimental Metastasis, May 13, 2018 https://doi.org/10.1007/s10585-018-9902-1

Reviews

723. D Fukumura, J Kloepper, Z Amoozgar, DG Duda and RK Jain. Enhancing Cancer Immunotherapy Using Antiangiogenics: Opportunities and Challenges. Nature Reviews Clinical Oncology. 15: 325-340 (2018).
724. RK Jain and A. Batista. A physical view of cancer. Trends in Cancer 4: 257 (2018).

2018 Publications

725. T Stylianopoulos, LL Munn and RK Jain. Reengineering the tumor vasculature: Improving drug delivery and efficacy. Trends in Cancer 4: 258-259 (2018).
726. T Stylianopoulos, LL Munn and RK Jain. Reengineering the physical microenvironment of tumors to improve drug delivery and efficacy: From math modeling to bench to bedside. Trends in Cancer 4: 292-319 (2018).
727. M Pinter, WJ Kwanten and RK Jain. Renin-angiotensin system inhibitors to mitigate cancer treatment-related adverse events. Clinical Cancer Research 24: 3803-12 (2018).
728. Nowak-Sliwinska P, Alitalo K, Allen E, Anisimov A, Aplin AC, Auerbach R, Augustin HG, Bates DO, van Beijnum JR, Bender RHF, Bergers G, Bikfalvi A, Bischoff J, Böck BC, Brooks PC, Bussolino F, Cakir B, Carmeliet P, Castranova D, Cimpean AM, Cleaver O, Coukos G, Davis GE, De Palma M, Dimberg A, Dings RPM, Djonov V, Dudley AC, Dufton NP, Fendt SM, Ferrara N, Fruttiger M, Fukumura D, Ghesquière B, Gong Y, Griffin RJ, Harris AL, Hughes CCW, Hultgren NW, Iruela-Arispe ML, Irving M, Jain RK, Kalluri R, Kalucka J, Kerbel RS, Kitajewski J, Klaassen I, Kleinmann HK, Koolwijk P, Kuczynski E, Kwak BR, Marien K, Melero-Martin JM, Munn LL, Nicosia RF, Noel A, Nurro J, Olsson AK, Petrova TV, Pietras K, Pili R, Pollard JW, Post MJ, Quax PHA, Rabinovich GA, Raica M, Randi AM, Ribatti D, Ruegg C, Schlingemann RO, Schulte-Merker S, Smith LEH, Song JW, Stacker SA, Stalin J, Stratman AN, Van de Velde M, van Hinsbergh VWM, Vermeulen PB, Waltenberger J, Weinstein BM, Xin H, Yetkin-Arik B, Yla-Herttuala S, Yoder MC, Griffioen AW. Consensus guidelines for the use and interpretation of angiogenesis assays. Angiogenesis. 2018; ePub - PMID: 29766399 - DOI: 10.1007/s10456-018-9613-x
729. Munn LL, Garkavtsev I. SLPI: a new target for stopping metastasis. Aging. 2018;10(1): 13–14.
730. D. Jones, E.R. Pereira, T.P. Padera. "Growth and immune evasion of lymph node metastasis." Frontiers in Oncology, Feb 21;8:36. doi: 10.3389/fonc.2018.00036. (2018).

2019 Publications

Original articles

731. Li H, Mei Y, Maimon N, Padera TP, Baish JW, Munn LL. The effects of valve leaflet mechanics on lymphatic pumping assessed using numerical simulations. Scientific Reports 2019; 9(1): 10649.
732. L Goyal, H Zheng, T Abrams, R Miksad, A Bullock, J Allen, M Yurgelun, J Clark, A Muzikansky, M Knowles, A Galway, A Afflitto, C Dinicola, E Regan, T Hato, E Mamessier, K Shigeta, RK Jain, DG Duda, and A Zhu. A Phase II and Biomarker Study of Sorafenib Combined with FOLFOX in Patients with Advanced Hepatocellular Carcinoma. Clinical Cancer Research 25: 80-89 (2019).
733. I Keklikoglou, C Cianciaruso, E Güç, M L Squadrito, S Tazzyman, L Lambein, A Poissonnier, GB Ferraro, C Baer, A Cassará, A Guichard, ML Iruela-Arispe, CE Lewis, LM Coussens, A Bardia, LM Spring, RK Jain, JW Pollard and M DePalma. Chemotherapy elicits pro-metastatic extracellular vesicles in breast cancer models. Nature Cell Biology 21(2):190-202 (2019).
734. S Liao, EM Bouta, LM Morris, D Jones, RK Jain and TP Padera. Inducible nitric oxide synthase and CD11b+Gr1+ cells impair lymphatic contraction of tumor draining lymphatic vessels. Lymphatic Research and Biology 17: 294-300 (2019).
735. G Seano, HT Nia, KE Emblem, M Datta, J Ren, J Kloepper, S Krishnan, M Ghosh, MC Pinho, V Askoxylakis, GB Ferraro, L Riedemann, ER Gerstner, TT Batchelor, PY Wen, NU Lin, AJ Grodzinsky, D Fukumura, P Huang, JW Baish, TP Padera, LL Munn and RK Jain. Solid stress in brain tumours causes neuronal loss and neurological dysfunction and can be reversed by lithium. Nature Biomedical Engineering 3: 230-245 (2019).
736. Lee EQ, Muzikansky A, Duda DG, Gaffey S, Dietrich J, Nayak L, Chukwueke UN, Beroukhim R, Doherty L, Laub CK, LaFrankie D, Fontana B, Stefanik J, Ruland S, Caruso V, Bruno J, Ligon K, Reardon DA, Wen PY. Phase II trial of ponatinib in patients with bevacizumab-refractory glioblastoma. Cancer Med. 8(13): 5988-5994 (2019).
737. J Chen, L Landegger, Y Sun, J Ren, N Maimon, L Wu, M Ng, J Chen, N Zhang, Y Zhao, X Gao, T Fujita, S Roberge, P Huang, RK Jain, S Plotkin, K Stankovic and L Xu. A cerebellopontine angle mouse model for the investigation of tumour biology, hearing and neurological function in NF2-related vestibular schwannoma. Nature Protocols 14(2):541-555 (2019).
738. V Askoxylakis, GB Ferraro, M Badeaux, DP Kodack, I Kirst, RC Shankaraiah, CSF Wong, DG Duda, D Fukumura and RK Jain. Dual endothelin receptor inhibition enhances T-DM1 efficacy in brain metastases from HER2-positive breast cancer. NPJ Breast Cancer 5: 4 (2019).
739. Moran H, Cancel LM, Mayer MA, Qazi H, Munn LL, Tarbell JM. The cancer cell glycocalyx proteoglycan glypican-1 mediates interstitial flow mechanotransduction to enhance cell migration and metastasis. Biorheology. 56(2-3):151-161 (2019)
740. Saftoiu A, Bhutani MS, Itoi T, Arcidiacono PG, Bories E, Cazacu IM, Constantin A, Coronel E, Dietrich CF, Duda DG, Garcia JI, Hocke M, Ignee A, Jenssen C, Jinga M, Khor C, Oppong KW, Pereira S, Petrone MC, Santo E, Seicean A, Seo DW, Siyu S, Vilmann P, Waxman I, Yeaton P. Changes in tumor vascularity depicted by contrast-enhanced EUS as a predictor of prognosis and treatment efficacy in patients with unresectable pancreatic cancer (PEACE): A study protocol. Endosc Ultrasound 8(4):235-240 (2019)
741. Li H, Mei Y, Maimon N, Padera TP, Baish JW, Munn LL. The effects of valve leaflet mechanics on lymphatic pumping assessed using numerical simulations. Sci Rep. 9(1):10649 (2019)
742. Richter C, Andronesi OC, Borra RJH, Voigt F, Löck S, Duda DG, Guimaraes AR, Hong TS, Bortfeld TR, Seco J. Inter-patient variations of radiation-induced normal-tissue changes in Gd-EOB-DTPA-enhanced hepatic MRI scans during fractionated proton therapy. Clin Transl Radiat Oncol. 18:113-119 (2019)

2019 Publications

743. Shvedova M, Litvak MM, Roberts JD, Fukumura D, Suzuki T, Sencan İ, Li G, Reventun P, Buys ES, Kim HH, Sakadžić S, Ayata C, Huang PL, Feil R, Atochin DN. cGMP-dependent protein kinase I in vascular smooth muscle cells improves ischemic stroke outcome in mice. J Cereb Blood Flow Metab. 39(12): 2379-2391 (2019)
744. Munn LL, Nia HT. Mechanosensing tensile solid stresses. Proc Natl Acad Sci U S A. 116(44):21960-21962 (2019)
745. Plotkin SR, Duda DG, Muzikansky A, Allen J, Blakeley J, Rosser T, Campian JL, Clapp DW, Fisher MJ, Tonsgard J, Ullrich N, Thomas C, Cutter G, Korf B, Packer R, Karajannis MA. Multicenter, Prospective, Phase II and Biomarker Study of High-Dose Bevacizumab as Induction Therapy in Patients With Neurofibromatosis Type 2 and Progressive Vestibular Schwannoma. J Clin Oncol. 37(35):3446-3454 (2019)
746. Granoff MD, Johnson AR, Lee BT, Padera TP, Bouta EM, Singhal D. A Novel Approach to Quantifying Lymphatic Contractility during Indocyanine Green Lymphangiography. Plast Reconstr Surg. 144(5):1197-1201 (2019)
747. Kong N, Tao W, Ling X, Wang J, Xiao Y, Shi S, Ji X, Shajii A, Gan ST, Kim NY, Duda DG, Xie T, Farokhzad OC, Shi J Synthetic mRNA nanoparticle-mediated restoration of p53 tumor suppressor sensitizes p53-deficient cancers to mTOR inhibition. Sci Transl Med. 11(523) (2019)
748. Y Zhao, J Cao , A Melamed , M Worley , A Gockley , D Jones , HT Nia , Y Zhang , T Stylianopoulos , AS Kumar , F Mpekris , M Datta , Y Sun , L Wu , X Gao , O Yeku , MG del Carmen , DR Spriggs , RK Jain and L Xu. Losartan treatment enhances chemotherapy efficacy and reduces ascites in ovarian cancer models by normalizing the tumor stroma. PNAS 116: 2210-2219 (2019)
749. C Voutouri, ND Kirkpatrick, E Chung, F Mpekris, JW Baish, LL Munn, D Fukumura, T Stylianopoulos and RK Jain. Experimental and computational analyses reveal dynamics of tumor vessel cooption and optimal treatment strategies. PNAS 116: 2662-2671 (2019)
750. IX Chen, VP Cauhan, J Posada, MR Ng, MW Wu, P Adstamongkonkul, P Huang, N Lindeman, R Langer and RK Jain. Blocking CXCR4 alleviates desmoplasia, increases T-lymphocyte infiltration, and improves immunotherapy in metastatic breast cancer. PNAS 116 (10) 4558-4566 (2019) www.pnas.org/cgi/doi/10.1073/pnas.1815515116 [Accompanying Commentary by George Sledge 116 (11) 4769-4771 (2019) https://doi.org/10.1073/pnas.1900368116] [NCI Blog: https://www.cancer.gov/news-events/cancer-currents-blog/2019/transplant-drug-immunotherapy-metastatic-breast-cancer]
751. VP Chauhan, IX Chen, R Tong, MR Ng, JD Martin, K Naxerova, MW Wu, Y Boucher, DS Kohane, R Langer and RK Jain. Reprogramming the microenvironment with tumor-selective angiotensin blockers enhances cancer immunotherapy. PNAS 116: 10674-10680 (2019).
752. JE Murphy, JY Wo, DP Ryan, JW Clark, W Jiang, BY Yeap, LC Drapek, LS Blaszkowsky, CR Ferrone, M Qadan, D Berger, A Parikh, CD Weekes, R Nipp, EL Kwak, JN Allen, RB Corcoran, DT Ting, JE Faris, AX. Zhu, L Goyal, KD Lillemoe, RK Jain, TF DeLaney, DG Duda, Y Boucher, C Fernandez-del Castillo and TS Hong. Total Neoadjuvant Therapy with Folfirinox in Combination with Losartan Followed by Chemoradiotherapy for Locally Advanced Pancreatic Cancer: A Phase II Clinical Trial. JAMA Oncology 5(7):1020-1027 (2019). Doi: 10.1001./jamaoncol.2019.0892.
753. JM Cleary, NK Horick, NJ McCleary, TA Abrams, MB Yurgelun, CG Azzoli, DA Rubinson, G Brooks, JA Chan, LS Blaszkowsky, JW Clark, L Goyal, JA Meyerhardt, K Ng, D Schrag, DMF Savarese, C Graham, KA Gibb, Y Boucher, DG Duda, RK Jain, CS Fuchs, and PC Enzinger. FOLFOX plus ziv-aflibercept or placebo in first-line metastatic esophagogastric adenocarcinoma (ZAMEGA): a double blind randomized multi-center phase 2 trial. Cancer 125: 2213-2221 (2019). https://doi.org/10.1002/cncr.32029
754. CJ Rowland, OT Bruns, D Franke, D Fukumura, RK Jain, MG Bawendi and PTC So. Increasing the penetration depth of temporal focusing multiphoton microscopy for neurobiological applications. Journal of Physics D: Applied Physics (2019).
755. K Shigeta, M Datta, Tai Hato, S Kitahara, I Chen, A Matsui, H Kikuchi, E Mamessier, S Aoki, P Huang, M Cobbold, AX Zhu, RK Jain and DG Duda. Dual PD-1 and VEGFR-2 blockade promotes vascular normalization and enhances anti-tumor immune responses in HCC. Hepatology Published online on Aug 5, 2019. doi: 10.1002/hep.30889.
756. C Fernandez-Martos, C Pericay, F Losa, R García-Carbonero, L Layos, N Rodríguez-Salas, M Martin-Richard, V Alonso, R Vera, J Gallego, J Capdevila, A Salud, M Nogué, J Maurel, I Guash, C Montagut, C Lopez, I Macias RK Jain, and X Garcia-Albeniz. Effect of Adding Aflibercept to Induction Chemotherapy Followed by Chemoradiotherapy and Surgery in High-Risk Rectal Cancer. GEMCAD 1402 Study. A Randomized Clinical Trial. JAMA Oncology. 5(11):1566-1573 (2019).
757. JP Leone, DG Duda, J Hu, WT Barry, L Trippa, ER Gerstner, RK Jain, STan, E Lawler, EP Winer, NU Lin, and SM Tolaney. A phase II study of cabozantinib alone or in combination with trastuzumab in breast cancer patients with brain metastases. Breast Cancer Research and Treatment. https://doi.org/10.1007/s10549-019-05445-z

Reviews

758. JD Martin, G Seano and RK Jain. Normalizing Function of Tumor Vessels: Progress, Prospects and Challenges. Annual Reviews of Physiology 81: 505-534 (2019). https://doi.org/10.1146/annurev-physiol-020518-114700
759. H Nia, LL Munn and RK Jain. Mapping physical tumor microenvironment and drug delivery. Clinical Cancer Research 25: 2024-6 (2019). http://clincancerres.aacrjournals.org/content/25/7/2024.full
760. Z Amoozgar, RK Jain and D Duda. Role of apelin in glioblastoma vascularization and invasion after anti-VEGF therapy: What is the impact on the immune system? Cancer Research 79: 2104-2106 (2019).
761. Tamburini BAJ, Padera TP, Lund AW. Editorial: Regulation of Immune Function by the Lymphatic Vasculature. Front Immunol. 10:2597 (2019)
762. Ruscic KJ, Padera TP. Silence of the Lymphs: Some anaesthetic regimens inhibit lymphatic pumping. J Physiol. 597(11):2827-2828 (2019)
763. M Datta, LM Coussens, H Nishikawa, FS Hodi and RK Jain. Reprogramming the Tumor Microenvironment to Improve Immunotherapy: Emerging Strategies and Combination Therapies. Am Soc Clin Oncol Educ Book. 39:165-174 (2019). doi: 10.1200/EDBK_237987.
764. CD Arvanitis, GB Ferraro and RK Jain. The blood–brain barrier and blood–tumor barrier in brain tumors and metastases. 20: 26-41 (2020).LL Munn and RK Jain. Vascular regulation of anti-tumor immunity. Science 365: 544-545 (2019). DOI: 10.1126/science.aaw7875.

2019 Publications

765. JD Martin, H Cabral, T Stylianopoulos and RK Jain. Improving cancer immunotherapy using nanomedicine: Progress, opportunities and challenges. Nature Reviews Clinical Oncology (2019).
766. Datta M, Coussens LM, Nishikawa H, Hodi FS, Jain RK. Reprogramming the Tumor Microenvironment to Improve Immunotherapy: Emerging Strategies and Combination Therapies. Am Soc Clin Oncol Educ Book. 39:165-174 (2019)
767. Johnson AR, Granoff MD, Lee BT, Padera TP, Bouta EM, Singhal D. The Impact of Taxane-based Chemotherapy on the Lymphatic System. Ann Plast Surg. 82(4S Suppl 3):S173-S178 (2019)

2020 Publications

Original articles

768. E Gerstner, K Emblemn, K Chang, B Vakulenko-Lagun, Y-F Yen, A Beers, J Dietrich, S Plotkin, C Catana, J Hooker, D Duda, B Rosen, J Kalpathy-Cramer, RK Jain, and TB Batchelor. Bevacizumab reduces permeability and concurrent temozolomide delivery in a subset of patients with recurrent glioblastoma. Clinical Cancer Research 26 :206-212 (2020).
769. JA Flores-Toro, D Luo, A Gopinath, MR Sarkisian, JJ. Campbell, IF Charo, R Singh, TJ Schall, M Datta, RK Jain, DA Mitchell and JK Harrison. CCR2 inhibition reduces tumor myeloid cells and unmasks a checkpoint inhibitor effect to slow progression of resistant murine gliomas. PNAS 117(2):1129-1138 (2020).
770. JP Leone, DG Duda, J Hu, WT Barry, L Trippa, ER Gerstner, RK Jain, STan, E Lawler, EP Winer, NU Lin, and SM Tolaney. A phase II study of cabozantinib alone or in combination with trastuzumab in breast cancer patients with brain metastases. Breast Cancer Research and Treatment 179(1):113-123 (2020).
771. F Mpekris, C Voutouri, JW Baish, DG Duda, LL Munn, T Stylianopoulosa and RK Jain. Combining microenvironment normalization strategies to improve cancer immunotherapy. PNAS 117: 3728-37 (2020).

    [Accompanying Commentary by AS Popel, Immuno-activating the tumor microenvironment enhances immunotherapy as predicted by integrative computational model. PNAS 117 (9) 4447-4449 (2020).
772. JD Martin, H Cabral, T Stylianopoulos and RK Jain. Improving cancer immunotherapy using nanomedicine: Progress, opportunities and challenges. Nature Reviews Clinical Oncology. 17(4):251-266 (2020).
773. DG Millar, N Gupta, RR Ramjiawan, LT Morton, S Zhang, F Shi, JM Heather, K Shigeta, S Sepulveda, L Wan, R Joseph, E Minogue, A Khatri, A Bardia, LW Ellisen, RB Corcoran, A Hata, SI Pai, RK Jain, D Fukumura, DG Duda and M Cobbold. Reprogramming antigenicity through selective delivery of peptide payload corrects antigen-repertoire mismatch in cancer. Nature Biotechnology. 38(4):420-425 (2020)
774. K Shigeta, M Datta, Tai Hato, S Kitahara, I Chen, A Matsui, H Kikuchi, E Mamessier, S Aoki, P Huang, M Cobbold, AX Zhu, RK Jain and DG Duda. Dual PD-1 and VEGFR-2 blockade promotes vascular normalization and enhances anti-tumor immune responses in HCC. Hepatology 71(4):1247-126 (2020).
775. Meijer EF, Bouta EM, Mendonca C, Skolny MN, Salama LW, Taghian AG, Padera TP. A retrospective analysis of commonly prescribed medications and the risk of developing breast cancer-related lymphedema. Clin Res Trials. 2020;6(1):ePub - PMID: 32864167 (2020)
776. Nagalo BM, Breton CA, Zhou Y, Arora M, Bogenberger JM, Barro O, Steele MB, Jenks NJ, Baker AT, Duda DG, Roberts LR, Russell SJ, Peng KW, Borad MJ. Oncolytic Virus With Attributes of Vesicular Stomatitis Virus and Measles Virus in Hepatobiliary and Pancreatic Cancers.
777. Mol Ther Oncolytics. 18:546-555 (2020)
778. Goyal L, Sirard C, Schrag M, Kagey MH, Eads JR, Stein S, El-Khoueiry AB, Manji GA, Abrams TA, Khorana AA, Miksad R, Mahalingam D, Zhu AX, Duda DG. Phase I and Biomarker Study of the Wnt Pathway Modulator DKN-01 in Combination with Gemcitabine/Cisplatin in Advanced Biliary Tract Cancer. Clin Cancer Res. 26(23):6158-6167 (2020)
779. Abdel-Wahab R, Hassan MM, George B, Carmagnani Pestana R, Xiao L, Lacin S, Yalcin S, Shalaby AS, Al-Shamsi HO, Raghav K, Wolff RA, Yao JC, Girard L, Haque A, Duda DG, Dima S, Popescu I, Elghazaly HA, Vauthey JN, Aloia TA, Tzeng CW, Chun YS, Rashid A, Morris JS, Amin HM, Kaseb AO
780. Impact of Integrating Insulin-Like Growth Factor 1 Levels into Model for End-Stage Liver Disease Score for Survival Prediction in Hepatocellular Carcinoma Patients. Oncology. 98(12):836-846 (2020)
781. Nikmaneshi MR, Firoozabadi B, Mozafari A, Munn LL. A multi-scale model for determining the effects of pathophysiology and metabolic disorders on tumor growth. Sci Rep. 10(1):3025 (2020)
782. Sagers JE, Beauchamp RL, Zhang Y, Vasilijic S, Wu L, DeSouza P, Seist R, Zhou W, Xu L, Ramesh V, Stankovic KM. Combination therapy with mTOR kinase inhibitor and dasatinib as a novel therapeutic strategy for vestibular schwannoma. Sci Rep 10(1): (2020)
783. Nikmaneshi MR, Firoozabadi B, Munn LL. A mechanobiological mathematical model of liver metabolism. Biotechnol Bioeng 117(9):2861-2874 (2020)
784. M Saif, WJ Kwanten, JA Carr, IX Chen, JM Posada, A Srivastava, J Zhang, Y Zheng, M Pinter, S. Chatterjee, S Softic, CR Kahn, KV Leyen, OT Bruns, RK Jain and MG Bawendi. NIR/SWIR Imaging Establishes Endogenous Lipofuscin as a Biomarker for Monitoring Chronic Liver Disease Noninvasively. Nature Biomedical Engineering 4(8):801-813 (2020).

2020 Publications

785. Ngo B, E Kim, V Osorio-Vasquez, S Doll, S Bustraan, RJ Liang, A Luengo, SM Davidson, A Ali, GB Ferraro, GM Fischer, R Eskandari, DS Kang, J Ni, A Plasger, VK.Rajasekhar, ER Kastenhuber, S Bacha, RK Sriram, BD Stein, SF Bakhoum, M Snuderl, P Cotzia, JH Healey, N Mainolfi, V Suri, A Friedman, M Manfredi, DM Sabatini, DR Jones, M Yu, JJ Zhao, RK Jain, KR Keshari, MA Davies, MG Vander Heiden, E Hernando, M Mann, LC Cantley and ME Pacold. Limited Environmental Serine and Glycine Confer Brain Metastasis Sensitivity to PHGDH Inhibition. Cancer Discovery. 10:1352–73 (2020).
786. HT Nia, M Datta, G Seano, S Zhang, WW Ho, S Roberge, P Huang, LL Munn and RK Jain. In vivo compression and imaging in the brain to measure the effects of solid stress. Nature Protocols 15(8):2321-2340 (2020).
787. M Valiente, A Van Swearingen, C Anders, A Bairoch, A Boire, P Bos, D Cittelly, N Erez, G Ferraro, D Fukumura, B Gril, M Herlyn, S Holmen, RK Jain, J Joyce, M Lorger, J Massague, J Neman, N Sibson, P Steeg, F Thorsen, L Young, D Varešlija, A Vultur, F Weiss-Garcia, and F Winkler. Brain Metastasis Cell Lines Panel: a public resource of organotropic cell lines. Cancer Research 80(20):4314-4323 (2020).
788. IX Chen, K Newcomer, K Pauken, VR Juneja, K Naxerova, MW Wu, M Pinter, M Singer, AH Sharpe and RK Jain. A bilateral tumor model identifies transcriptional programs that associated with patient response. PNAS. 117: 23684-94 (2020).
789. S Subburaju, S Kaye, YK Choi, J Baruah, D Datta, J Ren, A S Kumar, G Szabo, D Fukumura, RK Jain, A Elkha and A Vasudevan. NAD+ Mediated Rescue of Prenatal Forebrain Angiogenesis Restores Postnatal Behavior. Science Advances 6(41): eabb9766 (2020).
790. X Jin, Z Demere, K Nair, A Ali, GB Ferraro, T Natoli, A Deik, L Petronio, A Tang, C Zhu, L Wang, D Rosenberg, V Mangena, J Roth, K Chung, RK Jain, C Clish, M Vander Heiden and TR Golub. MetMap: a map of metastatic potential of human cancer cell lines. Nature 588: 331-336 (2020).
791. K Shigeta, A Matsui, H Kikuchi, S Klein, E Mamessier, I Chen, S Aoki, S Kitahara, K Inoue, A Shigeta, T Hato, RR Ramjiawan, D Staiculescu, D Zopf, L Fiebig, GS. Hobbs, A Quaas, S Dima, I Popescu, P Huang, LL Munn, M Cobbold, L Goyal, AX Zhu, RK.Jain and DG Duda. Regorafenib combined with PD1 blockade increases CD8 T-cell infiltration by inducing CXCL10 expression in hepatocellular carcinoma. Journal for ImmunoTherapy of Cancer 8(2): 8:e001435 (2020)
792. Gerstner ER, Emblem KE, Yen Y-F, Dietrich J, Jordan JT, Catana C, Wenchin KL, Hooker J, Duda DG, Rosen BR, Kalpathy-Cramer J, Jain RK, Batchelor TT. Vascular Dysfunction Promotes Regional Hypoxia after Bevacizumab Therapy in Recurrent Glioblastoma Patients. Neuro-Oncology Advances, 2(1):vdaa157 (2020).Kongpetch S, Jusakul A, Lim JQ, Ng CCY, Chan JY, Rajasegaran V, Lim TH, Lim KH, Choo SP, Dima S, Popescu I, Duda DG, Kukongviriyapan V, Khuntikeo N, Pairojkul C, Rozen SG, Tan P, Teh BT. Lack of Targetable FGFR2 Fusions in Endemic Fluke-Associated Cholangiocarcinoma. JCO Glob Oncol. 6:628-638 (2020)
793. Duda DG, Dima SO, Cucu D, Sorop A, Klein S, Ancukiewicz M, Kitahara S, Iacob S, Bacalbasa N, Tomescu D, Herlea V, Tanase C, Croitoru A, Popescu I. Potential Circulating Biomarkers of Recurrence after Hepatic Resection or Liver Transplantation in Hepatocellular Carcinoma Patients. Cancers (Basel) 12(5) PMID: 32443546 (2020).

Reviews

794. CD Arvanitis, GB Ferraro and RK Jain. The blood–brain barrier and blood–tumor barrier in brain tumors and metastases. 20: 26-41 (2020).
795. Sahai E, Astsaturov I, Cukierman E, DeNardo DG, Egeblad M, Evans RM, Fearon D, Greten FR, Hingorani SR, Hunter T, Hynes RO, Jain RK, Janowitz T, Jorgensen C, Kimmelman AC, Kolonin MG, Maki RG, Powers RS, Puré E, Ramirez DC, Scherz-Shouval R, Sherman MH, Stewart S, Tlsty TD, Tuveson DA, Watt FM, Weaver V, Weeraratna AT, Werb Z. A framework for advancing our understanding of cancer-associated fibroblasts. Nature Reviews Cancer 20(3):174-186 (2020).
796. JD Martin, DG Duda and RK Jain. Going beyond VEGF pathway inhibition for antiangiogenic cancer therapy: Is inhibition of the PP2A/B55a complex the answer? Circulation Research 127(6):724-726 (2020).
797. JD Martin and RK Jain. Normalizing the tumor microenvironment for radiosensitization. In "Molecular Targeted Radiosensitizers: Opportunities and Challenges." Editors: Henning Willers & Iris Eke. Cancer Drug Discovery and Development. Chapter 12 pp 301-338 (2020).
798. H Nia, LL Munn and RK Jain. Physical Traits of Cancer. Science 370: eaaz0868 (2020).
799. Chen J, Duda DG. Overcoming sorafenib treatment-resistance in hepatocellular carcinoma: A future perspective at a time of rapidly changing treatment paradigms. EBioMedicine 52:102644 (2020)
800. G. Seano and RK Jain. Vessel co-option in glioblastoma: emerging insights and opportunities. Angiogenesis 23: 9–16 (2020).

2021 Publications

Original articles

801. L Nayak, AM Molinaro, KB Peters, JL Clarke, JT Jordan, JF de Groot, PL Nghiemphu, TJ Kaley, H Colman, C McCluskey, S Gaffey, T Smith, DJ Cote, M Severgnini, JH Yearley, Q Zhao, WM Blumenschein, DG Duda, A Muzikansky, RK Jain, PY Wen and DA Reardon. Phase II and biomarker study of pembrolizumab or pembrolizumab plus bevacizumab for recurrent glioblastoma patients. Clinical Cancer Research, 27: 1048-1057 (2021).
802. S Krishnan, Z Amoozgar, D Fukumura and RK Jain. Implications of a granulocyte-high glioblastoma microenvironment in immune suppression and therapy resistance. Journal of Pathology, 253: 160–173 (2021).
803. C Voutouri, MR Nikmaneshi, CC Hardin, AB Patel, A Verma, MJ Khandekar, S Dutta, T Stylianopoulos, LL Munn and RK Jain. In silico dynamics of COVID-19 phenotypes for optimizing clinical management. PNAS. 118 (3): e2021642118 (2021).

804. W Li, S Li IX Chen, Y Liu, RR Ramjiawan, C-Ho Leung1, LE Gerweck, D Fukumura, JS Loeffler, RK Jain, DG Duda, and P Huang. Combining Losartan with Radiotherapy Increases Tumor Control and Inhibits Lung Metastases from a HER2/neu-positive Orthotopic Breast Cancer Model. Radiation Oncology. 6:48 (2021). doi: 10.1186/s13014-021-01775-9.
805. LL Munn, T Stylianopoulos, NK Jain, CC Hardin, M Khandekar, and RK Jain. Vascular normalization to improve treatment of COVID-19: Lessons from treatment of cancer. Clinical Cancer Research. 27 (10): 2706-2711 (2021).
806. G Ferraro, Ali A, Luengo A, Kodack DP, Deik A, Abbott KL, Bezwada D, Blanc L, Prideaux B, Jin X, Possada JM, Chen J, Chin CR, Amoozgar Z, Ferreira R, Chen IX, Naxerova K, Ng C, Westermark AM, Duquette M, Roberge S, Lindeman NI, Lyssiotis CA, Nielsen J, Housman DE, Duda DG, Brachtel E, Golub TR, Cantley LC, Asara JM, Davidson SM, Fukumura D, Dartois VA, Clish CB, Jain, RK and Vander Heiden MG. Fatty acid synthesis is required for breast cancer brain metastasis. Nature Cancer 2: 414–428 (2021). [Accompanying News & Views: Vogel, F.C.E., Schulze, A. Fatty acid synthesis enables brain metastasis. Nature Cancer 2, 374–376 (2021).]
807. IG dos Santos, Z Amoozgar, A Kumar, W Ho, K Roh, N Talele, H Curtis, K Kawaguchi, RK Jain, and D Fukumura. Exercise training improves tumor control by increasing infiltration of CD8+ T cells via CXCR3 signaling and sensitizes breast cancer to immune checkpoint blockade. Cancer Immunology Research 9:765–778 (2021) [Featured on the journal Cover.]
808. Z Amoozgar, J Kloepper, J Ren, RE Tay, SW Kazer, E Kiner, S Krishnan, JM Posada, M Ghosh, E Mamessier, C Wong, GB Ferraro, A Batista, N Wang, M Badeaux, S Roberge, L Xu, P Huang, AK Shalek, D Fukumura, HJ Kim and RK Jain. Targeting Treg cells with GITR activation alleviates resistance to immunotherapy in murine glioblastomas. Nature Communications 12: 2582 (2021).
809. RK Jain, WP Skelton, GR Pond, M Naqvi, Y Kim, C Curran, D Freeman, PV Nuzzo, SAAlaiwi, A Nassar, RK Jain, and G Sonpavde. Angiotensin blockade modulates the activity of PD1/L1 inhibitors in metastatic urothelial carcinoma. Clinical Genitourinary Cancer, ePub on April 20, 2021.
810. S Subudhi, A Verma, AB Patel, CC Hardin, MJ Khandekar, H Lee, D McEvoy, T Stylianopoulos, LL Munn, S Dutta and RK Jain. Comparing Machine Learning Algorithms for Predicting ICU Admission and Mortality in COVID-19. npj Digital Medicine, 4(1):87 (2021).
811. Y Boucher, A Kumar, J Posada, E Gjini, K Pfaff, M Lipschitz, A Lako, DG Duda, S Rodig, FS Hodi and RK Jain. Bevacizumab Improves Tumor Infiltration of Mature Dendritic Cells and Effector T-cells in Triple-Negative Breast Cancer Patients. npj Precision Oncology. 6:52 (2021)
812. M Sewicki, Gort-Freitas NA, Messemaker M, Bill R, Gungabeesoon J, Engblom C, Zilionis R, Garris C, Gerhard GM, Kohl A, Lin Y, Zou AE, Cianciaruso C, Bolli E, Pfirschke C, Lin YJ, Piot C, Mindur JE, Talele N, Kohler RH, Iwamoto Y, Mino-Kenudson M, Pai SI, deVito C, Koessler T, Merkler D, Coukos A, Wicky A, Fraga M, Sempoux C, Jain RK, Dietrich PY, Michielin O, Weissleder R, Klein AM, Pittet MJ. Resident Kupffer cells and neutrophils drive liver toxicity in cancer immunotherapy. Science Immunology 6(61) (2021).
813. L Wu, S Vasilijic, Y Sun, J Chen, LD Landegger, Y Zhang, W Zhou, J Ren, S Early, Z Yin, WW Ho, N Zhang, X Gao, GY. Lee, M Datta, JE Sagers, A Brown, A Muzikansky, A Stemmer-Rachamimov, L Zhang, SR Plotkin, RK. Jain, KM. Stankovic, and L Xu. Losartan prevents tumor-induced hearing loss and augments radiation efficacy by normalizing the tumor microenvironment in NF2 schwannoma models. Science Translational Medicine 13(602): eabd4816 (2021). doi: 10.1126/scitranslmed.abd4816
814. W Ho et al. Dendritic cell paucity in mismatch repair-proficient colorectal cancer liver metastases limits immune checkpoint blockade efficacy. PNAS 118: e2105323118 (2021).
815. Silva M, Kato Y, Melo MB, Phung I, Freeman BL, Li Z, Roh K, Van Wijnbergen JW, Watkins H, Enemuo CA, Hartwell BL, Chang JYH, Xiao S, Rodrigues KA, Cirelli KM, Li N, Haupt S, Aung A, Cossette B, Abraham W, Kataria S, Bastidas R, Bhiman J, Linde C, Bloom NI, Groschel B, Georgeson E, Phelps N, Thomas A, Bals J, Carnathan DG, Lingwood D, Burton DR, Alter G, Padera TP, Belcher AM, Schief WR, Silvestri G, Ruprecht RM, Crotty S, Irvine DJ. A particulate saponin/TLR agonist vaccine adjuvant alters lymph flow and modulates adaptive immunity. Sci Immunol 6(66):eabf1152 (2021)
816. Gkika E, Adebahr S, Brenner A, Schimek-Jasch T, Radicioni G, Exner JP, Rühle A, Spohn SKB, Popp I, Zamboglou C, Sprave T, Firat E, Niedermann G, Nicolay NH, Nestle U, Grosu AL, Duda DG. Changes in Blood Biomarkers of Angiogenesis and Immune Modulation after Radiation Therapy and Their Association with Outcomes in Thoracic Malignancies. Cancers (Basel) 13(22): ePub - PMID: 34830880 (2021)
817. Keahey P, Si P, Razavi M, Yu S, Lippok N, Villiger M, Padera TP, de la Zerda A, Bouma B. Spectral- and Polarization-Dependent Scattering of Gold Nanobipyramids for Exogenous Contrast in Optical Coherence Tomography. Nano Lett 21(20):8595-8601 (2021)
818. Jones D, Wang Z, Chen IX, Zhang S, Banerji R, Lei PJ, Zhou H, Xiao V, Kwong C, van Wijnbergen JWM, Pereira ER, Vakoc BJ, Huang P, Nia HT, Padera TP. Solid stress impairs lymphocyte infiltration into lymph-node metastases. Nat Biomed Eng 5(12):1426-1436 (2021)
819. Mohamed YI, Lee S, Xiao L, Hassan MM, Qayyum A, Hiatia R, Pestana RC, Haque A, George B, Rashid A, Duda DG, Elghazaly H, Wolff RA, Morris JS, Yao J, Amin HM, Kaseb AO. Insulin-like growth factor 1/Child-Turcotte-Pugh composite score as a predictor of treatment outcomes in patients with advanced hepatocellular carcinoma treated with sorafenib. Oncotarget 12(8):756-766 (2021)
820. Ajdari A, Xie Y, Richter C, Niyazi M, Duda DG, Hong TS, Bortfeld T. Toward Personalized Radiation Therapy of Liver Metastasis: Importance of Serial Blood Biomarkers. JCO Clin Cancer Inform 5:315-325 (2021)
821. Pfister D, Núñez NG, Pinyol R, Govaere O, Pinter M, Szydlowska M, Gupta R, Qiu M, Deczkowska A, Weiner A, Müller F, Sinha A, Friebel E, Engleitner T, Lenggenhager D, Moncsek A, Heide D, Stirm K, Kosla J, Kotsiliti E, Leone V, Dudek M, Yousuf S, Inverso D, Singh I, Teijeiro A, Castet F, Montironi C, Haber PK, Tiniakos D, Bedossa P, Cockell S, Younes R, Vacca M, Marra F, Schattenberg JM, Allison M, Bugianesi E, Ratziu V, Pressiani T, D'Alessio A, Personeni N, Rimassa L, Daly AK, Scheiner B, Pomej K, Kirstein MM, Vogel A, Peck-Radosavljevic M, Hucke F, Finkelmeier F, Waidmann O, Trojan J, Schulze K, Wege H, Koch S, Weinmann A, Bueter M, Rössler F, Siebenhüner A, Dosso S, Mallm JP, Umansky V, Jugold M, Luedde T, Schietinger A, Schirmacher P, Emu B, Augustin HG, Billeter A, Müller-Stich B, Kikuchi H, Duda DG, Kütting F, Waldschmidt DT, Ebert MP, Rahbari N, Mei HE, Schulz AR, Ringelhan M, Malek N, Spahn S, Bitzer M, Ruiz de Galarreta M, Lujambio A, Dufour JF, Marron TU, Kaseb A, Kudo M, Huang YH, Djouder N, Wolter K, Zender L, Marche PN, Decaens T, Pinato DJ, Rad R, Mertens JC, Weber A, Unger K, Meissner F, Roth S, Jilkova ZM, Claassen M, Anstee QM, Amit I, Knolle P, Becher B, Llovet JM, Heikenwalder M. NASH limits anti-tumour surveillance in immunotherapy-treated HCC. Nature 592(7854):450-456 (2021)

2021 Publications

822. L Blank, G Ferraro, M Tuck, B Prideaux, V Dartois, RK Jain and N Desbenoit. A Kendrick Mass Defect variation to decipher isotopic labeling in brain metastases studied by mass spectrometry imaging. Analytical Chemistry. 93, 49, 16314–16319 (2021)

Reviews

823. M Pinter, RK Jain, DG Duda. The current landscape of immune checkpoint blockade in hepatocellular carcinoma. JAMA Oncology. 7(1):113-123 (2021).
824. Klein S, Duda DG. Machine Learning for Future Subtyping of the Tumor Microenvironment of Gastro-Esophageal Adenocarcinomas. Cancers (Basel) 13(19):ePub - PMID: 34638408 (2021)
825. Hauth F, Ho AY, Ferrone S, Duda DG. Radiotherapy to Enhance Chimeric Antigen Receptor T-Cell Therapeutic Efficacy in Solid Tumors: A Narrative Review. JAMA Oncol 7(7):1051-1059 (2021)
826. Zhou H, Lei PJ, Padera TP. Progression of Metastasis through Lymphatic System. Cells 10(3):ePub - PMID: 33808959 (2021)
827. Nathanson SD, Detmar M, Padera TP, Yates LR, Welch DR, Beadnell TC, Scheid AD, Wrenn ED, Cheung K. Mechanisms of breast cancer metastasis. Clin Exp Metastasis 39(1):117-137 (2021)

2022 Publications

Original articles

828. Aoki S, Inoue K, Klein S, Halvorsen S, Chen J, Matsui A, Nikmaneshi MR, Kitahara S, Hato T, Chen X, Kawakubo K, Nia HT, Chen I, Schanne DH, Mamessier E, Shigeta K, Kikuchi H, Ramjiawan RR, Schmidt TC, Iwasaki M, Yau T, Hong TS, Quaas A, Plum PS, Dima S, Popescu I, Bardeesy N, Munn LL, Borad MJ, Sassi S, Jain RK, Zhu AX, Duda DG. Placental growth factor promotes tumour desmoplasia and treatment resistance in intrahepatic cholangiocarcinoma. Gut. 71(1):185-193 (2022)
829. S Subudhi, C Voutouri, CC Hardin, MR Nikmaneshi, AB Patel, A Verma, MJ Khandekar, S Dutta, T Stylianopoulos, RK Jain and LL Munn. Strategies to minimize heterogeneity and optimize clinical trials in acute respiratory distress syndrome (ARDS): Insights from mathematical modeling. EBioMedicine. 75: 103809 (2022).
830. ZD Drobni, O Michielin, T Quinaglia, DA Zlotoff, L Zubiri, B Merkely, V Muller, RJ Sullivan, KL Reynolds, MJ Pittet, RK Jain and TG Neilan. Renin-Angiotensin-Aldosterone System Inhibitors and Survival in Patients with Hypertension Treated with Immune Checkpoint Inhibitors. European Journal of Cancer. 163, 108-118 (2022).
831. H Kikuchi, A Matsui, S Morita, Z Amoozgar, K Inoue, Z Ruan, D Staiculescu, J Wong, P Huang, T Yau, RK Jain, and DG Duda. Increased CD8+ T-cell infiltration and efficacy for multikinase inhibitors after PD-1 blockade in HCC. JNCI, djac051 (2022).
832. A Agrud, S Subburaju, P Goel, J Ren, A S Kumar, B Caldarone, W Dai, Je Chavez, D Fukumura, RK Jain, RA Kloner and A Vasudevan. Gabrb3 endothelial cell-specific knockout mice display abnormal blood flow, schizophrenia-like behavior, and hypertension. Scientific Reports 12:4922 (2022).
833. W Hwang, Jagadeesh KA, Guo JA, Hoffman HI, Yadollahpour P, Reeves JW, Mohan R, Drokhlyansky E, Van Wittenberghe N, Ashenberg O, Farhi SL, Schapiro D, Divakar P, Miller E, Zollinger DR, Eng G, Schenkel JM, Su J, Shiau C, Yu P, Freed-Pastor WA, Abbondanza D, Mehta A, Gould J, Lambden C, Porter CBM, Tsankov A, Dionne D, Waldman J, Cuoco MS, Nguyen L, Delorey T, Phillips D, Barth JL, Kem M, Rodrigues C, Ciprani D, Roldan J, Zelga P, Jorgji V, Chen JH, Ely Z, Zhao D, Fuhrman K, Fropf R, Beechem JM, Loeffler JS, Ryan DP, Weekes CD, Ferrone CR, Qadan M, Aryee MJ, Jain RK, Neuberg DS, Wo JY, Hong TS, Xavier R, Aguirre AJ, Rozenblatt-Rosen O, Mino-Kenudson M, Castillo CF, Liss AS, Ting DT, Jacks T, Regev A. Single-nucleus and spatial multi-omics of frozen pancreatic cancer reveals multi-compartment reprogramming and enrichment of a neuronal-like phenotype after neoadjuvant treatment. Nature Genetics 54(8):1178-1191 (2022).
834. PV Nuzzo, E Adib, N Weise, C Curran, T Stewart, D Freeman, AH Nassar, SA Alaiwi, Z Bakouny, BA McGregor, TK Choueiri, RK. Jain, RR McKay and G Sonpavde. Impact of renin-angiotensin system inhibitors on outcomes in patients with metastatic renal cell carcinoma treated with immune-checkpoint inhibitors. Clinical Genitourinary Cancer, 20(4):301-306 (2022).
835. van den Bent L, Frenkel NC, Poghosyan S, Molenaar IQ, Padera TP, Kranenburg O, Borel Rinkes IHM, Hagendoorn J. Liver lymphatic drainage patterns follow segmental anatomy. Br J Surg. 109(6):559-560 (2022)
836. Li H, Wei H, Padera TP, Baish JW, Munn LL. Computational simulations of the effects of gravity on lymphatic transport. PNAS Nexus 1(5):pgac237 (2022)
837. Mohamed YI, Duda DG, Awiwi MO, Lee SS, Altameemi L, Xiao L, Morris JS, Wolff RA, Elsayes KM, Hatia RI, Qayyum A, Chamseddine SM, Rashid A, Yao JC, Mahvash A, Hassan MM, Amin HM, Kaseb AO. Plasma growth hormone is a potential biomarker of response to atezolizumab and bevacizumab in advanced hepatocellular carcinoma patients. Oncotarget 13:1314-1321 (2022)
838. Sasaki T, Shigeta K, Kitahara S, Suzuki Y, Matsui S, Seishima R, Okabayashi K, Duda DG, Kitagawa Y. Inhibition of STAT3 Promotes Effector T Cell Infiltration But also Immunosuppression in the HCC Tumor Microenvironment. Anticancer Res 42(11):5205-5215 (2022)
839. Nagalo BM, Zhou Y, Loeuillard EJ, Dumbauld C, Barro O, Elliott NM, Baker AT, Arora M, Bogenberger JM, Meurice N, Petit J, Uson Junior PLS, Aslam F, Raupach E, Gabere M, Basnakian A, Simoes CC, Cannon MJ, Post SR, Buetow K, Chamcheu JC, Barrett MT, Duda DG, Jacobs B, Vile R, Barry MA, Roberts LR, Ilyas S, Borad MJ. Characterization of Morreton Virus (MORV) as a Novel Oncolytic Virotherapy Platform for Liver Cancers. Hepatology 77(6):1943-1957 (2022)

2022 Publications

840. Katagiri W, Yokomizo S, Ishizuka T, Yamashita K, Kopp T, Roessing M, Sato A, Iwasaki T, Sato H, Fukuda T, Monaco H, Manganiello S, Nomura S, Ng MR, Feil S, Ogawa E, Fukumura D, Atochin DN, Choi HS, Kashiwagi S. Dual near-infrared II laser modulates the cellular redox state of T cells and augments the efficacy of cancer immunotherapy. FASEB J 36(10):e22521 (2022)
841. Munoz NM, Dupuis C, Williams M, Dixon K, McWatters A, Zhang J, Pavuluri S, Rao A, Duda DG, Kaseb A, Sheth RA. Immune modulation by molecularly targeted photothermal ablation in a mouse model of advanced hepatocellular carcinoma and cirrhosis. Sci Rep 12(1):14449 (2022)
842. How J, Ren S, Lombardi-Story J, Bergeron M, Foster J, Amrein PC, Brunner AM, Fathi AT, Hock H, Khachatryan A, Kikuchi H, Ng MR, Moran J, Narayan R, Neuberg D, Ramos A, Som T, Vartanian M, Chen YB, Duda DG, Hobbs GS. A nonrandomized phase I and biomarker trial of regorafenib in advanced myeloid malignancies. EJHaem 3(2):434-442 (2022)
843. Pu Z, Duda DG, Zhu Y, Pei S, Wang X, Huang Y, Yi P, Huang Z, Peng F, Hu X, Fan X. VCP interaction with HMGB1 promotes hepatocellular carcinoma progression by activating the PI3K/AKT/mTOR pathway. J Transl Med 20(1):212 (2022)
844. Zhao F, Chen Y, Li SW, Zhang J, Zhang S, Zhao XB, Yang ZJ, Wang B, He QY, Wang LM, Xu L, Liu PN. Novel patient-derived xenograft and cell line models for therapeutic screening in NF2-associated schwannoma. J Pathol 257(5):620-634 (2022)
845. Baish JW, Padera TP, Munn LL. The effects of gravity and compression on interstitial fluid transport in the lower limb. Sci Rep 12(1):4890 (2022)
846. Chamseddine I, Kim Y, De B, El Naqa I, Duda DG, Wolfgang J, Pursley J, Paganetti H, Wo J, Hong T, Koay EJ, Grassberger C. Predictive Modeling of Survival and Toxicity in Patients With Hepatocellular Carcinoma After Radiotherapy. JCO Clin Cancer Inform 6:e2100169 (2022)
847. Xiao Y, Chen J, Zhou H, Zeng X, Ruan Z, Pu Z, Jiang X, Matsui A, Zhu L, Amoozgar Z, Chen DS, Han X, Duda DG, Shi J. Combining p53 mRNA nanotherapy with immune checkpoint blockade reprograms the immune microenvironment for effective cancer therapy. Nat Commun 13(1):758 (2022)
848. Moran H, Cancel LM, Huang P, Roberge S, Xu T, Tarbell JM, Munn LL. Glycocalyx mechanotransduction mechanisms are involved in renal cancer metastasis. Matrix Biol Plus 13:100100 (2022)
849. JD Martin, Lanning RM, Chauhan VP, Martin MR, Mousa AS, Kamoun WS, Han HS, Lee H, Stylianopoulos T, Bawendi MG, Duda DG, Brown EB, Padera TP, Fukumura D, Jain RK. Multiphoton phosphorescence quenching microscopy reveals kinetics of tumor oxygenation during anti-angiogenesis and angiotensin signaling inhibition. Clinical Cancer Research, 28: 3076-90 (2022).
850. Saulnier-Sholler, Duda DG, Bergendahl G, Ebb D, Snuderl M, Laetsch TW, Michlitsch J, Hanson D, Isakoff MS, Bielamowicz K, Kraveka JM, Ferguson W, Carmeliet P, De Deene A, Gijsen L, Jain RK. A Phase I Trial of TB-403 in Relapsed Medulloblastoma, Neuroblastoma, Ewing Sarcoma, and Alveolar Rhabdomyosarcoma. Clinical Cancer Research 28 (18): 3950–3957 (2022).

Reviews

851. F Mpekris, C Voutouri, M Panagi, JW Baish, RK Jain and T Stylianopoulos. Normalizing the tumor microenvironment with nanomedicine and metronomic therapy: Implications for immunotherapy. J Contolled Release. 345: 190-199 (2022).
852. WH Ho, MJ Pittet, D Fukumura and RK Jain. The local microenvironment matters in preclinical studies of cancer immunology and immunotherapy. Cancer Cell 40: 701-702 (2022).
853. DG Duda and RK Jain. Revisiting Antiangiogenic Multikinase Inhibitors in the Era of Immune Checkpoint Blockade: The Case of Sorafenib. Cancer Research 82:3665-3667 (2022).
854. Dima SO, Dumitrascu T, Popescu I, Duda DG. Using Molecular Subtyping of Pancreatic Ductal Adenocarcinoma for Multimodal Treatment Selection in Resectable Disease. Chirurgia (Bucur). 117(4):407-414 (2022)
855. Morita S, Duda DG. Refining genetic and molecular classifications to facilitate breakthrough treatments in intrahepatic cholangiocarcinoma: are we there yet? Gut 72(4):608-610 (2022)
856. Souri M, Soltani M, Moradi Kashkooli F, Kiani Shahvandi M, Chiani M, Shariati FS, Mehrabi MR, Munn LL. Towards principled design of cancer nanomedicine to accelerate clinical translation.
857. Mater Today Bio 13:100208 (2022)
858. Hauth F, Roberts HJ, Hong TS, Duda DG. Leveraging Blood-Based Diagnostics to Predict Tumor Biology and Extend the Application and Personalization of Radiotherapy in Liver Cancers. Int J Mol Sci 23(4):ePub - PMID: 35216045 (2022)
859. D G Kirsch; C Willett; H Paganetti; J Schuemann; KD. Held; and RK Jain. Herman D. Suit, MD, DPhil (1929–2022): A Giant of Modern Radiation Oncology. Radiat Res 198 (5): 536–543 (2022).

2023 Publications

Original articles

860. V Voutouri, Hardin CC, Naranbhai V, Nikmaneshi MR, Khandekar MJ, Gainor JF, Stylianopoulos T, Munn LL, Jain RK. Mechanistic model for booster doses in healthy, cancer and immunosuppressed patients infected with SARS-CoV-2. PNAS 20 (3) e2211132120 (2023).
861. M. Datta, Chatterjee S, Perez EM, Gritsch S, Roberge S, Duquette M, Chen IX, Naxerova K, Kumar AS, Ghosh M, Emblem KE, Ng MR, Ho WW, Kumar P, Krishnan S, Dong X, Speranza MC, Neagu MR, Iorgulescu JB, Huang RY, Youssef G, Reardon DA, Sharpe AH, Freeman GJ, Suvà ML, Xu L, Jain RK. Losartan controls immune checkpoint blocker-induced edema and improves survival in glioblastoma PNAS 120: e2219199120 (2023).

2023 Publications

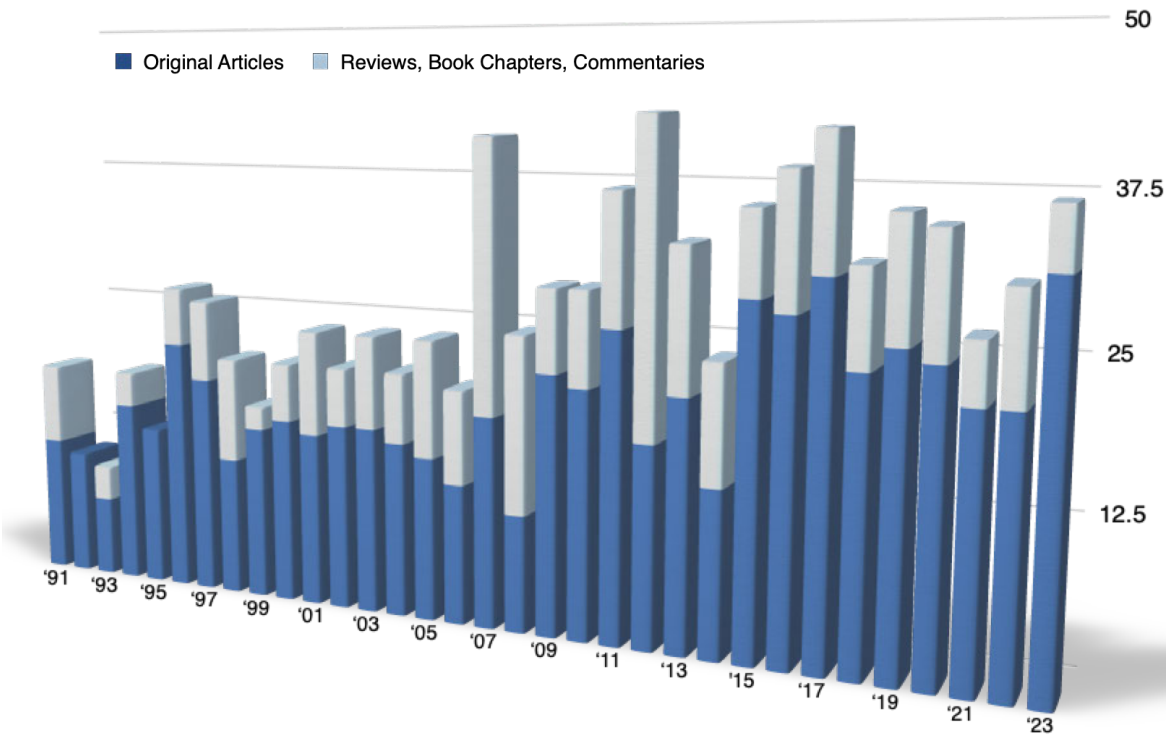
862. N Gupta, H Ochiai, Y Hoshino, S Klein, J Zustin, RR Ramjiawan, S Kitahara, N Maimon, D Bazou, S Chiang, S Li, DH Schanne, RK Jain, LL Munn, P Huang, SV Kozin and DG Duda. Inhibition of CXCR4 Enhances the Efficacy of Radiotherapy in Metastatic Prostate Cancer Models. Cancers 15(4): 1021 (2023).
863. Y. Boucher, Posada JM, Subudhi S, Kumar AS, Rosario SR, Gu L, Kumra H, Mino-Kenudson M, Talele NP, Duda DG, Fukumura D, Wo JY, Clark JW, Ryan DP, Fernandez-Del Castillo C, Hong TS, Pittet MJ, Jain RK. Addition of losartan to FOLFORINOX and chemoradiation downregulates pro-invasion and immunosuppression-associated genes in locally advanced pancreatic cancer. Clinical Cancer Research, 29 (8): 1605–1619 (2023).
864. X. Dong, Ren J, Amoozgar Z, Lee S, Datta M, Roberge S, Duquette M, Fukumura D, Jain RK. Anti-VEGF therapy improves EGFR-vIII-CAR-T cell delivery and efficacy in syngeneic glioblastoma models in mice. Journal of Immunotherapy of Cancer 11: e005583 (2023).
865. S. Plotkin, Allen J, Dhall G, Campian JL, Clapp DW, Fisher MJ, Jain RK, Tonsgard J, Ullrich NJ, Thomas C, Edwards LJ, Korf B, Packer R, Karajannis MA, Blakeley JO. Maintenance bevacizumab for children and adults with NF2-related schwannomatosis and progressive vestibular schwannoma: NF104. Neuro-Oncology 25(8):1498-1506 (2023).
866. BE Wolf, Weydandt L, Dornhöfer N, Hiller GGR, Höhn AK, Nel I, Jain RK, Horn LC, Aktas B. Desmoplasia in cervical cancer is associated with an aggressive tumor phenotype. Scientific Reports 13:18946 (2023).
867. MR Nikmaneshi, RK Jain and LL Munn. Optimizing vessel normalization and chemotherapy to control angiogenesis and tumor growth. PLoS Computational Biology 19(6): e1011131 (2023).
868. Zhang Q, Gerweck LE, Cascio E, Gu L, Yang Q, Dong X, Huang P, Bertolet A, Nesteruk KP, Sung W, McNamara AL, Schuemann J. Absence of Tissue-Sparing Effects in Partial Proton FLASH Irradiation in Murine Intestine. Cancers (Basel). 15(8): DOI: 10.3390/cancers15082269 (2023)
869. Jana S, Li W, Lei PJ, Wang Z, Huang P, Jones D. Isolation and characterization of a novel hormone receptor positive mammary adenocarcinoma MCa-P1362 with stromal drivers of tumor growth, metastasis, and drug resistance. bioRxiv. DOI: 10.1101/2023.06.02.543434 (2023)
870. Munn LL, Bazou D. A Self-Assembly Method for Creating Vascularized Tumor Explants Using Biomaterials for 3D Culture. Methods Mol Biol 2645: 211-220 (2023)
871. Lei PJ, Pereira ER, Andersson P, Amoozgar Z, Van Wijnbergen JW, O'Melia MJ, Zhou H, Chatterjee S, Ho WW, Posada JM, Kumar AS, Morita S, Menzel L, Chung C, Ergin I, Jones D, Huang P, Beyaz S, Padera TP. Cancer cell plasticity and MHC-II-mediated immune tolerance promote breast cancer metastasis to lymph nodes. J Exp Med 220(9) DOI: 10.1084/jem.20221847 (2023)
872. Chamseddine S, Mohamed YI, Lee SS, Yao JC, Hu ZI, Tran Cao HS, Xiao L, Sun R, Morris JS, Hatia RI, Hassan M, Duda DG, Diab M, Mohamed A, Nassar A, Datar S, Amin HM, Kaseb AO. Clinical and Prognostic Biomarker Value of Blood Circulating Inflammatory Cytokines in Hepatocellular Carcinoma. Oncology 101(11):730-737 (2023)
873. Chivu-Economescu M, Herlea V, Dima S, Sorop A, Pechianu C, Procop A, Kitahara S, Necula L, Matei L, Dragu D, Neagu AI, Bleotu C, Diaconu CC, Popescu I, Duda DG. Soluble PD-L1 as a diagnostic and prognostic biomarker in resectable gastric cancer patients. Gastric Cancer 26(6):934-946 (2023)
874. Kashiwagi R, Funayama R, Aoki S, Matsui A, Klein S, Sato Y, Suzuki T, Murakami K, Inoue K, Iseki M, Masuda K, Mizuma M, Naito H, Duda DG, Unno M, Nakayama K. Collagen XVII regulates tumor growth in pancreatic cancer through interaction with the tumor microenvironment. Cancer Sci 114(11):4286-4298 (2023)
875. Zhou H, Baish JW, O'Melia MJ, Darragh LB, Specht E, Czapla J, Lei PJ, Menzel L, Rajotte JJ, Nikmaneshi MR, Razavi MS, Heiden MGV, Ubellacker JM, Munn LL, Boland GM, Cohen S, Karam SD, Padera TP. Cancer immunotherapy responses persist after lymph node resection.bioRxiv DOI: 10.1101/2023.09.19.558262 (2023)
876. Nikmaneshi MR, Baish JW, Zhou H, Padera TP, Munn LL. Transport Barriers Influence the Activation of Anti-Tumor Immunity: A Systems Biology Analysis. Adv Sci (Weinh). DOI: 10.1002/advs.202304076 (2023)
877. Morita S, Kikuchi H, Birch G, Matsui A, Morita A, Kobayashi T, Ruan Z, Huang P, Hernandez A, Coyne EM, Shin SM, Yarchoan M, Mino-Kenudson M, Romee R, Ho WJ, Duda DG. Preventing NK cell activation in the damaged liver induced by cabozantinib/PD-1 blockade increases survival in hepatocellular carcinoma models. bioRxiv. DOI: 10.1101/2023.10.20.563378 (2023)
878. Lei PJ, Ruscic KJ, Roh K, Rajotte JJ, O'Melia MJ, Bouta EM, Marquez M, Pereira ER, Kumar AS, Arroyo-Ataz G, Razavi MS, Zhou H, Menzel L, Kumra H, Duquette M, Huang P, Baish JW, Munn LL, Ubellacker JM, Jones D, Padera TP. Lymphatic muscle cells are unique cells that undergo aging induced changes. bioRxiv DOI: 10.1101/2023.11.18.567621 (2023)
879. Pal R, K M, Matsui A, Kang H, Morita S, Taniguchi H, Kobayashi T, Morita A, Choi HS, Duda DG, Kumar ATN. In vivo quantification of programmed death-ligand-1 expression heterogeneity in tumors using fluorescence lifetime imaging. Res Sq. DOI: 10.21203/rs.3.rs-3222037/v1 (2023)
880. Yin Z, Wu L, Zhang Y, Sun Y, Chen JW, Subudhi S, Ho W, Lee GY, Wang A, Gao X, Ren J, Zhu C, Zhang N, Ferraro GB, Muzikansky A, Zhang L, Stemmer-Rachamimov A, Mao J, Plotkin SR, Xu L. Co-Targeting IL-6 and EGFR signaling for the treatment of schwannomatosis and associated pain.bioRxiv DOI: 10.1101/2023.02.06.527377 (2023)
881. Chen S, Huang C, Liao G, Sun H, Xie Y, Liao C, Wang J, He M, Hu H, Dai Z, Ren X, Zeng X, Lin Z, Zhang GP, Xie W, Shen S, Li S, Peng S, Kuang DM, Zhao Q, Duda DG, Kuang M. Distinct single-cell immune ecosystems distinguish true and de novo HBV-related hepatocellular carcinoma recurrences. Gut 72(6):1196-1210 (2023)
882. Li Z, Huang S, He Y, van Wijnbergen JW, Zhang Y, Cottrell RD, Smith SG, Hammond PT, Chen DZ, Padera TP, Belcher AM. A new label-free optical imaging method for the lymphatic system enhanced by deep learning. bioRxiv ePub - PMID: 36711668 (2023)
883. Zhang Q, Gerweck LE, Cascio EW, Yang Q, Huang P, Niemierko A, Bertolet A, Nesteruk KP, McNamara AL, Schuemann J. Proton FLASH effects on mouse skin at different oxygen tensions. Phys Med Biol 68(5) DOI: 10.1088/1361-6560/acb888 (2023)

2023 Publications

884. Chamseddine I, Kim Y, De B, Naqa IE, Duda DG, Wolfgang JA, Pursley J, Wo JY, Hong TS, Paganetti H, Koay EJ, Grassberger C. Predictive Model of Liver Toxicity to Aid the Personalized Selection of Proton vs Photon Therapy in Hepatocellular Carcinoma. Int J Radiat Oncol Biol Phys 116(5): 1234-1243 (2023)
885. Gkika E, Firat E, Adebahr S, Graf E, Popp I, Radicioni G, Lo SS, Nestle U, Nicolay NH, Niedermann G, Duda DG, Grosu AL. Systemic immune modulation by stereotactic radiotherapy in early-stage lung cancer. NPJ Precis Oncol 7(1):24 (2023)
886. Wang Y, Drum DL, Sun R, Zhang Y, Yu L, Jia L, Isakoff SJ, Kehlmann AM, Dal AE, Dotti G, Zheng H, Ferrone CR, Taghian AG, DeLeo AB, Zhang H, Jounaidi Y, Fan S, Huang P, Wang C, Yang J, Boland GM, Sadreyev RI, Wong L, Ferrone S, Wang X. Stressed target cancer cells drive nongenetic reprogramming of CAR T cells and tumor microenvironment, overcoming multiple obstacles of CAR T therapy for solid tumors. Res Sq DOI: 10.21203/rs.3.rs-2595410/v1 (2023)
887. McCullum L, Shin J, Xing S, Beekman C, Schuemann J, Hong T, Duda D, Mohan R, Lin S, Correa-Alfonso CM, Domal S, Withrow J, Bolch W, Paganetti H, Grassberger C. Predicting Severity of Radiation Induced Lymphopenia in Individual Proton Therapy Patients for Varying Dose Rate and Fractionation Using Dynamic 4D Blood Flow Simulations. Int J Radiat Oncol Biol Phys 116(5): 1226-1233 (2023)
888. Sun Y, Yin Z, Wu L, Yue C, Zhang Y, Subudhi S, Lei P, Muzikansky A, Zhang L, Rueda BR, Jain RK, Xu L. Losartan rewires ovarian cancer tumor-immune microenvironment and suppresses IGF-1 to amplify chemo-immunotherapy sensitivity. bioRxiv. 2023 Sept 3.
889. Z. Amoozgar et al. Combined blockade of VEGF, Angiopoietin-2, and PD1 reprograms glioblastoma endothelial cells into quasi-antigen presenting cells.

Reviews

890. S Patel, M Nilsson, X Le, T Cascone, RK Jain and JV Heymach. Molecular Mechanisms and Future Implications of VEGF/VEGFR in Cancer Therapy. Clinical Cancer Research 29(1):30-39 (2023)
891. Franses JW, Duda DG. Scirrhous HCC: Another 'omic thread in the HCC tapestry. Hepatology. DOI: 10.1097/HEP.0000000000000609 (2023)
892. Wang X, Shen Y, Shang M, Liu X, Munn LL. Endothelial mechanobiology in atherosclerosis. Cardiovasc Res 119(8):1656-1675 (2023)
893. Gok Yavuz B, Datar S, Chamseddine S, Mohamed YI, LaPelusa M, Lee SS, Hu ZI, Koay EJ, Tran Cao HS, Jalal PK, Daniel-MacDougall C, Hassan M, Duda DG, Amin HM, Kaseb AO. The Gut Microbiome as a Biomarker and Therapeutic Target in Hepatocellular Carcinoma. Cancers (Basel) 15(19): ePub - PMID: 37835569 (2023)
894. Singhal D, BörnerK, Chaikof EL, Detmar M, Hollmén M, Iliff JJ, Itkin M, Makinen T, Oliver G, Padera TP, Quardokus EM, Radtke AJ, Suami H, Weber GM, Rovira II, Muratoglu SC, Galis ZS. Mapping the lymphatic system across body scales and expertise domains: A report from the 2021 National Heart, Lung, and Blood Institute workshop at the Boston Lymphatic Symposium. Front Physiol 14:1099403 (2023)



PATENTS

R.K. Jain, Y. Boucher, A. Stacey-Clear, R. Moore and D. Kopans, "Method for Locating Tumors Prior to Needle Biopsy," U.S. Patent Number 5, 396, 897, March 14, 1995.

P. Netti and R.K. Jain, "Method of Enhancing Delivery of a Pharmaceutical Formulation," U.S. Patent Number 5, 888, 530, March 30, 1999.

R.K. Jain, R.J. Melder, G.C. Koenig, and L.L. Munn. "Therapeutic Use of bFGF to Treat Conditions Involving Adhesion of Cytotoxic White Cells to Endothelium," U.S. Patent Number 6, 101, 712, January 4, 2000.

G. Helmlinger, P. Netti, R.J. Melder, H. Lichtenbeld-Dubois, and R.K. Jain. "Modulation of Multicellular Aggregates by Pressure from Growth in a Matrix," U.S. Patent Number 6,368,858, April 9, 2002.

R. B. Campbell and R. K. Jain, "Drug Delivery Formulations and Targeting," U.S. Patent Number 6,860,068, January 20, 2004.

B. Seed and R. K. Jain. "Methods to Potentiate Cancer Therapies", Patent number US 6,719,977, April 13, 2004.

R.K. Jain, S. Kozin, D. Fukumura, D.G. Duda. "Anti-CXCR4 As A Sensitizer to Cancer Therapeutics" US Patent No. 9,155,723, Oct 13, 2015

Duda D.G., Tolaney S. "Triple Negative Breast Cancer Treatment Method". US Patent WO2017184597A1, 2017.

R. K. Jain, V. Chauhan, B. Diop-Frimpong, Y. Boucher, S. M. Krane and A. L. Crane. "Novel Composition and Uses of Anti-hypertension agents for Cancer Therapy." Foreign Patent No. 030258-069094-AU, April 13, 2017.

C. R. Wong, M. G. Bawendi, D. Fukumura, and R. K. Jain. "Multistage nanoparticle drug delivery system for the treatment of solid tumors," U.S. Patent No. 9,919,059, March 20, 2018.

R. K. Jain, V. Chauhan, B. Diop-Frimpong, Y. Boucher, S. M. Krane and A. L. Crane. "Novel Composition and Uses of Anti-hypertension agents for Cancer Therapy." Foreign Patent No. 030258-069094-AU, April 13, 2017.

C. R. Wong, M. G. Bawendi, D. Fukumura, and R. K. Jain. "Multistage nanoparticle drug delivery system for the treatment of solid tumors," U.S. Patent No. 9,919,059, March 20, 2018.

Duda D.G., Lauwers G. Y. "A Protein and mRNA Expression Based Classification of Gastric Cancers" US Patent 2019 49 453A1, 2019.

Vasileios Askoxylakis; Dai Fukumura; David Kodack; Qing Sheng; Gino B. Ferraro; Jeffrey A Engelman; Rakesh Kumar Jain. "Treatment of Breast Cancer Brain Metastases." EPO Patent No. 3229803. January 29, 2020.

Vasileios Askoxylakis; Dai Fukumura; David Kodack; Qing Sheng; Gino B. Ferraro; Jeffrey A Engelman; Rakesh Kumar Jain. "Treatment of Breast Cancer Brain Metastases." U.S. Patent No. 10,689,459. June 23, 2020.

Vasileios Askoxylakis; Dai Fukumura; David Kodack; Qing Sheng; Gino B. Ferraro; Jeffrey A Engelman; Rakesh Kumar Jain. "Treatment of Breast Cancer Brain Metastases." India Patent No. 4047/DEL/2015. September 25, 2020.

Vasileios Askoxylakis; Dai Fukumura; David Kodack; Qing Sheng; Gino B. Ferraro; Jeffrey A Engelman; Rakesh Kumar Jain. "Treatment of Breast Cancer Brain Metastases." Japan Patent No. 6847835. March 3, 2021.

Gabriel Gruionu; Lance L Munn; Lucian Gruionu; Rakesh Kumar Jain. "System and Method for Measuring Solid Stress in Tissues". U.S. Patent No. 11,259,714. March 1, 2022.

Igor Garkavtsev and Rakesh Kumar Jain. "Compounds for Inhibiting Secretory Leukocyte Protease Inhibitor (SLPI)". U.S. Patent No. 11,351,144 June 7, 2022.

Igor Garkavtsev and Rakesh Kumar Jain. "Compounds for Targeting Cancer Stem Cell". US Patent No. 11,427,543 August 30, 2022.

Dan G Duda and Jinjun Shi. "Lipid-based Composition and Methods Thereof". Application Number: PCT/US22/52158, filed on December 7, 2022.

RESEARCH TEAM (2023)

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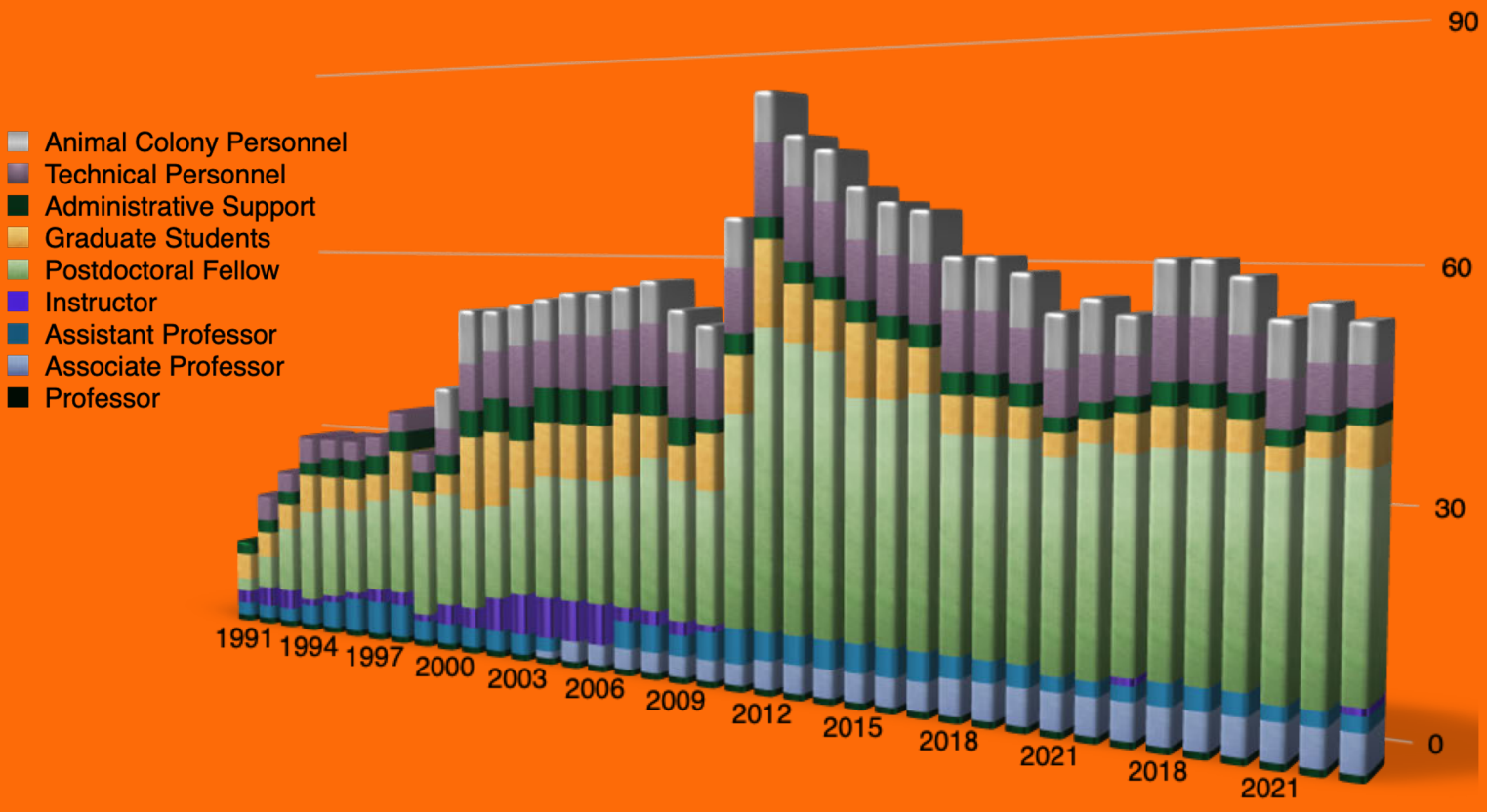
Graduate Students	Ashwin Kumar Ahmed Al-Azzam Marc Holl Franciele Filardi Cimino Silva Noel Hollosi Julia Linke Atsuyo Morita Jacob Olondo Kuba
Technical Assistants	Mark Duquette Ya Li (Sandy) Guan Julia Kahn Anna Khachatryan Brigido Lopez YanFang Lu Carolyn Smith Tsion Tale Penny Woo Marla Marquez
Administrative support	Lisa Purter Elizabeth Garzon Zeina Chaptini

RESEARCH TEAM

In September 1991, we started with a small team of six people, and we have since grown to approximately 60 members, and have developed a leading, multidisciplinary research and education program in the integrative biology of cancer. We have trained more than 230 graduate and post-graduate students - several of them have become leaders in academia, government, and industry.



ALUMNI

Associate Professor	
Yves Boucher	1987 – 2023
Assistant Professors	
Robert J. Melder	1989 – 98
Fan Yuan	1990 – 96
Laurence T. Baxter	1991 – 98
David Berk	1992 – 98
Emmanuelle diTomaso	1998 – 09
Igor Garkavtsev	2002 – 21
Instructors	
Intae Lee	1991 – 94
Hera Lichtenbeld	1994, 1997 – 99
Ping Jiang	1997 – 98
Kevin Burton	1999 – 2001
Fellows	
Cindy Znati	1990 – 95
Michael Leunig	1991 – 93
Robert Zlotecki	1992 – 93
Paul Kristjansen	1992 – 94
Anders Leu	1993 – 94
Manfred Stohrer	1993 – 94
Shige Yamada	1993 – 94
Marc Dellian	1993 – 95
Mutsumi Nozue	1993 – 95
Shigeru Tanda	1994 – 96
Mit Endo	1994 – 97
Gabriel Helmlinger	1994 – 97
Paolo Netti	1994 – 97
Sybil Patan	1994 – 99
Stuart Freidrich	1996 – 97
Axel Sckell	1996 – 97
Lance Wilsey	1996 – 97
Genevieve Griffon	1996 – 98
Wayne Monsky	1996 – 98
Takeshi Gohongi	1997 – 00
Alain Pluen	1997 – 00
Jin Yuan	1997 – 00
Nils Hansen	1997 – 98
Keiichi Ohtaka	1997 – 98
Marc Heijn	1997 – 99
Chang Geol Lee	1997 – 99
Kyung Ran Park	1997 – 99
Saroja Ramanujan	1998 – 00
Yoshikazu Tsuzuki	1998 – 01
Chieko Koike	1998 – 00
Ananth Kadambi	1998 – 01
Yong Chang	1998 – 00
Chae – Ok Yun	1998 – 00
Randal Dull	1998 – 99
Sergey Kozin	1998 – 15
Yotaro Izumi	1999 – 02
Vincent Moutardier	1999 – 00
Carla Mouta – Carreira	1999 – 01
Robert Campbell	1999 – 02
Edward Brown	1999 – 05
Brenda Fenton	2000 – 01
Oliver Gralla	2000 – 01
Cristiano Migliorini	2000 – 01
Akira Ushiyama	2000 – 01
Xaioye Wang	2000 – 01
Maximilian Bockhorn	2000 – 02
Dennis Dolmans	2000 – 02
Neil Forbes	2000 – 02
Tiina Roose	2001 – 02
Naoto Koike	2001 – 03
George Alexandrakis	2001 – 04
Zoe Demou	2001 – 04
Naohide Isaka	2002 – 04
Mark Stroh	2002 – 04
Chenghai Sun	2002 – 05
Patrick Au	2002 – 09
Frank Winkler	2003 – 04
Jeroen Hagendoorn	2003 – 05
Mitsutomo Kohno	2003 – 05
Michael Booth	2003 – 06
Tohru Hoshida	2003 – 06
Satoshi Kashiwagi	2003 – 06
Mai Luong	2003 – 07
Aaron Mulivor	2003 – 07
Sung Suk Chae	2004 – 10
Junichi Miyazaki	2004 – 05
Michael Dupin	2004 – 07
Aaron Mulivor	2004 – 07
Greg Nelson	2004 – 07
Jean Yannis Perentes	2004 – 07
Satoshi Nagano	2004 – 09
Cimona Hinton	2005
Carsten Ley	2005
Delphine Lacorre	2005 – 11
Kevin Kozak	2005 – 07
Carsten Ley	2005 – 07
Michelle Dawson	2005 – 08
Johanna Lahdrenranta	2005 – 08
Mai Luong	2005 – 08
Gang Cheng	2005 – 09
Walid Kamoun	2006 – 11
Annique Pieters	2006 – 10
Kevin Kozak	2006 – 07
J. Alex Tyrrell	2006 – 08
Angera Kuo	2006 – 09
Euiheon Chung	2007 – 10
Sachie Nakamura	2007 – 10
Hiroshi Yamashita	2007 – 10
Kosuke Tsukada	2007 – 09
Andus Wong	2007 – 09
Shan Liao	2007 – 13
Rekha Samuel	2008 – 11
T. Stylianopoulos	2008 – 10
Ned Kirkpatrick	2008 – 13
Matija Snuderl	2008 – 12
Jonathan Song	2008-14
Han – Sing Jeong	2009 – 11
Temitope Sondunke	2009 – 10
Jayeeta Bhaumik	2010 – 11
Christian Kunert	2010-15
David Kodack	2010-14
Christina Kesler	
Becky Chen	2010 – 13
Christine Lu-Emerson	2010 – 12
Janet Tse	2010 – 11
Ana Batista	2010 – 15
Robin Amelung	
Lars Riedemann	2011-15
Eleanor Ager	2011- 13
Despina Bazou	2011- 16
Tatiana Demidova-Rice	2011 – 13
Nuh Rahbari	2011- 13
Gabriel Gruionu	2011-15
Julien Daubriac	
Rouxu Dou	
Vikash Chauhan	2012-15
Nir Maimon	2012 -19
Mark Badeaux	2012 -17
Dennis Jones	2012- 18
Echoe Bouta	2012- 17
Jennie Taylor	2012 -14
Trupti Vardam	2012-15
Vera Verbuggen	
Xiaoxing Han	2012 -15
Jonas Kloepper	2012 -16
Daniel Schanne	2013- 17
Tai Hato	2013- 16
Giorgio Seano	2013 -18
Rosa Ng	2013 -18
Shuang Yan	2014 -15
Shuji Kitahara	2014- 17

Sen Li	2014 - 16
Hadi Nia	2014 - 18
Louis Larrouquere	2015 - 17
Yingchao Zhao	2015 - 16
Eelco Meijer	2015 - 17
Yuhui Zhao	2015 - 17
Matthias Pinter	2015 - 17
Ivy Chen	2015 - 19
Mitrajit Ghosh	2016 - 17
Emilie Mamessier	2016 - 17
Keehoon Jung	2016 - 18
Christina Wong	2016 - 18
Kohei Shigeta	2016 - 18
Kosuke Kawaguchi	2016 - 18
Shuichi Aoki	2016 - 19
Nojiri Takashi	2017 - 18
Som Nath Pandey	2019 - 21
Patrik Andersson	2017 - 22
Zohreh Amoozgar	2015 - 21
Jiang Chen	2018 - 21
Sampurna Chaterjee	2014 - 21
Yoon Sun Choi	2018 - 19
Meenal Datta	2018 - 21
Gino Ferraro	2013 - 21
Lei Gao	
Koetsu Inoue	2018 - 21
Kazumichi Kawakubo	2019 - 20
Hiroto Kikuchi	2018 - 21
Sergey Kozin	1998 - 23
Shanmugarajan Krishnan	2016 - 21
Huabing Li	
Chong Liu	
Aya Matsui	2015 - 20
Bhushan Patel	
Ethel Perreira	
Nilesh Talele	2017 - 21
Mina Kim	2017 - 18
Jesica Posada	2018 - 21
Nick (Xiaoling) Qi	
Jun Ren	2016 - 20
Kangsan Roh	2019 - 21
Zhiping Ruan	2019 - 21
Ze-Long Liu	2019 - 22
Franziska Hauth	2020 - 22
Yao Sun	
Wei Yang	
Weining Yang	
Changli Yue	2017 - 19
Yanxia Zhao	2015 - 17
Gustavo Cruzeiro	2019 - 20
Xinyue Dong	2020 - 22
Hans Prufer	2019 - 21
Yue Shi	2021 - 22
Evelin Krajnc	2022 - 23
Si Chen	2021 - 23

Medical Students

Thomas Demhartner	1992
Hassan Salehi	1993 – 94
Brian Witwer	1994 – 95
Daniel Greif	1995
Albert Loskin	1995 – 96
Nina Safabakhsh	1995 – 96
Jennifer Ang	1998 – 99
Aloke Finn	2005 – 06
Michael Awad	2001 – 03
Toshiya Miyauchi	2013 – 14
Sebastian Klein	2014 – 15
Takuya Suematsu	2014 – 15
Glenn Geidel	2015 – 16
Kevin Koch	2016 – 17
Mie Yamanaka	2018 - 19
Masako Miyamoto	2018 - 19
Shiho Hirose	2019
Masaaki Iwasaki	2019 - 20
Kanshiro Suzuki	2019 - 20
Tyge Schmidt	2019 - 20
Max Meyer	2021 - 22
Lennard Weide	2022 - 23
Maxence Galvan	2022 - 23

Technical Assistants

Houng Pham	-
Beatrice Sonntag	1991 - 93
Yi Chen	1994 - 99
Daniel Ross	1992 - 93
Feng Zhou	1999 - 2000
Chelsea Swandal	2000 - 04
Amy Alt	2000 - 01
Naran Bao	2001 - 02
Yenong Zhou	2001 - 19
Peter Vitello	2002 - 04
James Logie	2003 - 04
Jessica Tooredman	2002 - 04
Chris Van Wart	2002 - 03
Damon Hobson	2003 - 05
Lucine Petit	2004 - 06
Melanie Fortier	2004 - 06
Michelle Riley	2003 - 06
Song Xu	2006 - 07
PeiChun Lin	2006 - 08
MaryGrace Gorospe	2006 - 08
MingTau Lee	2006 -
Marlana Yee	2008 - 09
Dan Nguyen	2008 - 09
Kathryn Kinzel	2008 - 11
Dannie Wang	2009 - 11
Christina Koppel	2009 - 13
Aurea Aguasvivas	
Nghia Pham	
Sylvie Roberge	1991 - 23
Daniel Staiculescu	2019 - 21

Graduate Students

Cliff Eskey	1992
Hui Zhu	1992 - 96
Yuval Gazit	1993 - 96
Sue Hobbs	1993 - 98
Cecilia Capello	1994
G. Ray Martin	1994
Christian Brekken	1994 - 95, 1997
Melody Swartz	1994 - 98
Brian Stoll	1998 - 2003
Trevor McKee	2000 - 05
David Cochran	2001 - 05
Ricky Tong	2001 - 05
Wilson Mok	2002 - 07
Josh Tam	2002 - 08
Ryan Lanning	2003 - 09
Irene Chen	2008
Vikash Chauhan	2006 - 12
Benjamin Diop-Frimpong	2007 - 10
Ming - Zer Poh	2007 - 09
Janet Tse	2007 - 11
Abhishek Jain	2008 - 12
Yuhui Huang	2008-13
Shom Goel	2009 - 12
Jieqion (Jane) Liu	2009 - 12
Chun Li	2009
John Martin	2009-15
Kamila Naxerova	2009 -13
Teresa Peterson	2009 -15
Joao Incio	2010 -16
Elisabeth Niemeyer	2010 – 11
Koen Marijt	
Rakesh Ramjiawan	2012-18
Nisha Gupta	2012-17
Li Chong	2012 -15
Meenal Datta	2013 -18
William Ho	
Jan Willem vanWijnbergen	2018-20
Mohammad Nikmaneshi	2019 - 21
Linling Zhu	2019 - 21
Zhangya Pu	2019 - 21

Research Assistants	
Eric Kaufman	1988 - 92
Patrick Yoon	1993
Peter Khalifah	1993 - 93
Luke Wang	1995

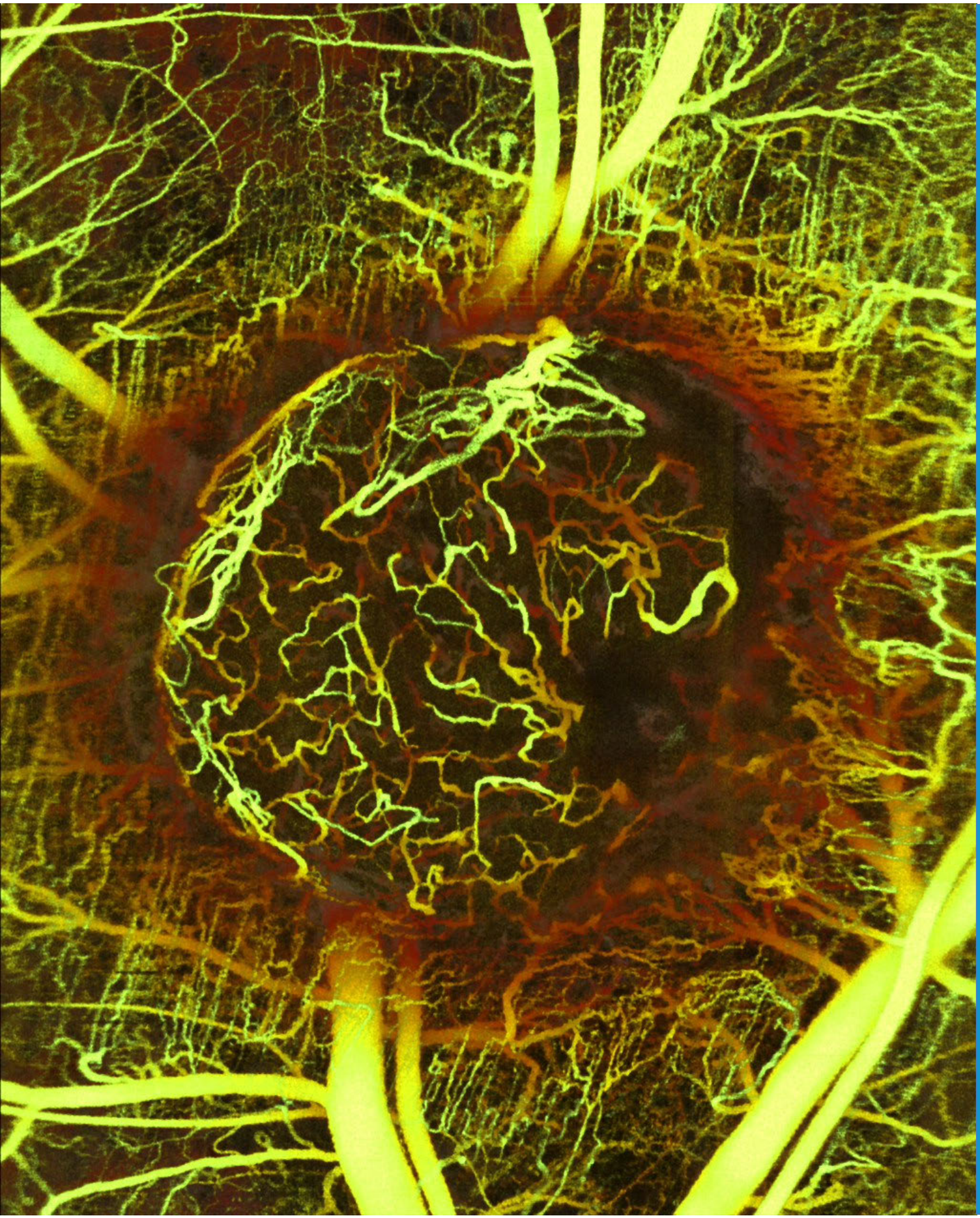
Valerie Verdier	1995 - 96
Visiting Scholars	
James Baish	1994, 2013, 2017
Catharina Davies	1997 - 98

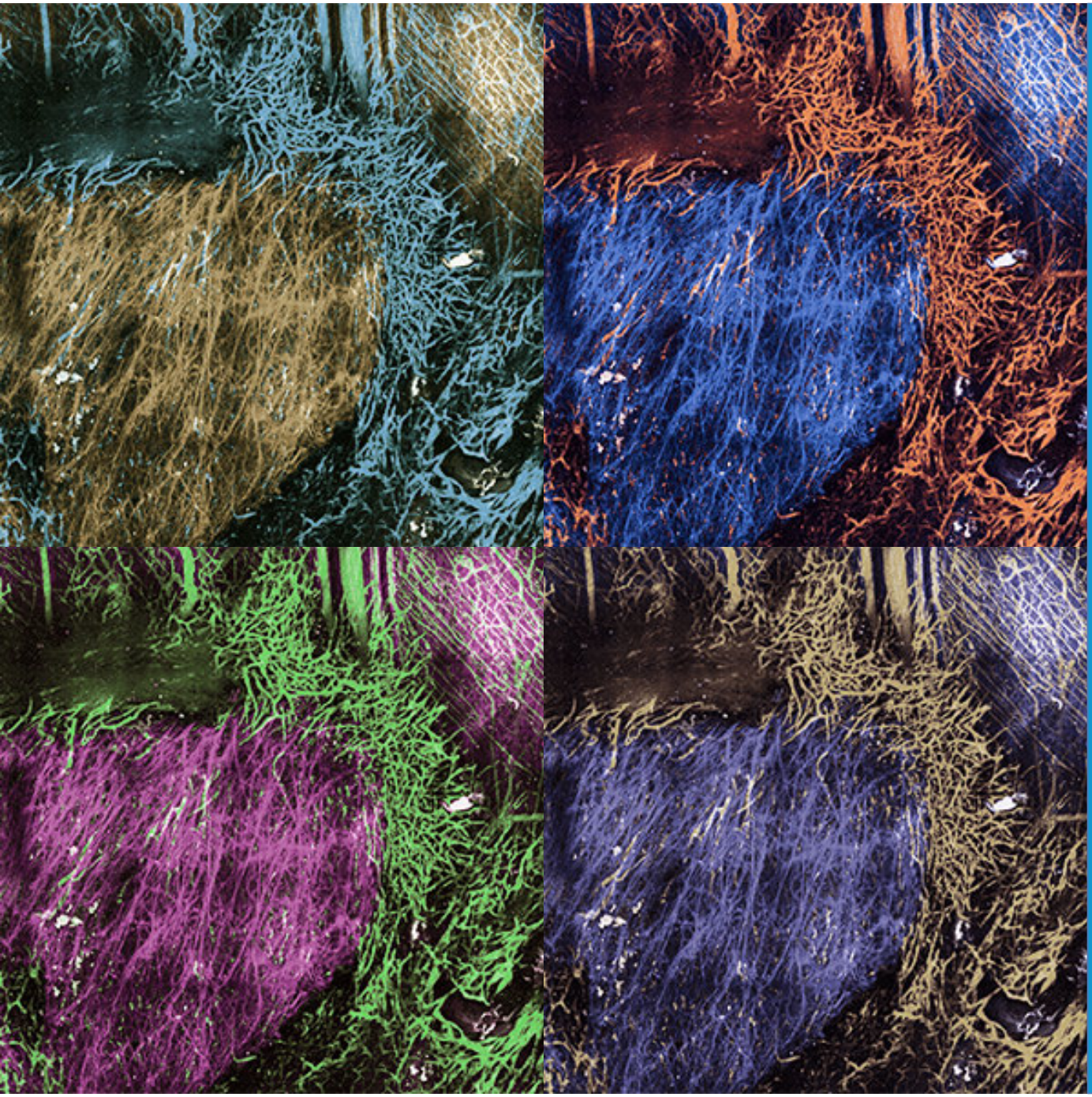
John Tarbell	1997 - 98
Donald Buerk	1998 - 99
Robert Feil	2012 - 13

RESOURCES AND ENVIRONMENT

The Steele Laboratories are located at two different sites. A facility for defined flora and immunodeficient rodents and about 1500 ft^2 of laboratory space, including two microscopy suites and multipurpose bench area and offices, are located at the Massachusetts General Hospital (MGH). Additional laboratory space (approximately 5,000 ft^2) which includes a microscopy suite, tissue culture facility, surgical area, clinical research studies, multipurpose bench space and offices, is located at the MGH-East facility in Charlestown. Investigators divide their time between these sites via a shuttle system.

Facility	Use
Intravital fluorescence microscopy laboratory #1	In vivo quantitative fluorescence microscopy measurement of hemodynamics and transport in tissues
Intravital fluorescence microscopy laboratory #2	In vivo quantitative fluorescence microscopy, including fluorescence photobleaching
Intravital fluorescence microscopy laboratory #3	In vivo quantitative fluorescence microscopy, on-line digitization of images and digital image analysis, and optical measurement of pH, pO_2, etc.
Intravital fluorescence microscopy laboratory #4	In vivo quantitative fluorescence microscopy for single vessel perfusion
Intravital fluorescence microscopy laboratory #5	In vivo two-photon laser scanning microscopy/ Animal colony
Intravital fluorescence microscopy laboratory #6	Video rate multiphoton microscopy
Intravital fluorescence microscopy laboratory #7	Multiphoton microscopy with oxygen sensing and permeability measurement capabilities
Optical frequency domain microscope suite	Imaging of tissue and blood vessels with high depth penetration base on doppler optical frequency domain technology; high frequency ultrasound imaging.
Histology facility	Serial sections, immunohistology, etc.
Pathophysiology laboratory	In vivo and ex vivo perfusion of isolated tumors and measurement of blood flow, blood pressure, interstitial fluid pressure, pO_2, etc.
Cellular biophysics laboratory	Measurement of cell deformability and dynamic adhesion; Time-lapse live cell imaging
Molecular biology laboratory	Molecular techniques
Cell culture facility	Mammalian cell culture
Tumor metabolism	Measurement of blood flow, pO_2, pH
Computing facilities	Various computer workstations, desktop and portable computers; 32 node cluster for parallel computation
Cox Animal facility	Gnotobiotic mice (33 strains)
Clinical research laboratory	Measurement in cancer patients of blood and urine markers, interstitial fluid pressure, pO_2, immunohistology, molecular and cellular studies etc





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