遗传资源与进化国家重点实验室
State Key Laboratory of Genetic Resources and Evolution

2020年报
ANNUAL REPORT

中国科学院昆明动物研究所
KUNMING INSTITUTE OF ZOOLOGY .CAS

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主任致辞

征途漫漫，硕果累累。2020 年是国家决胜全面建成小康社会、决战脱贫攻坚之年，是中国科学院基本实现“四个率先”的关键年，也是全国人民勠力同心、艰难奋进的一年。在各级主管部门的领导与关怀下，遗传资源与进化国家重点实验室立足于我国西南和东南亚丰富的生物遗传多样性资源，坚持面向世界科技前沿及经济主战场，服务国家重大需求，在任务承担、科研成果、队伍建设、开放交流等各方面工作均取得了可喜进展。

在承担科研项目方面，实验室积极发挥集群优势，组织策划国家、国际重大科技任务，成效显著。2020 年，实验室新增科研项目 62 项，包括主持科技部重点研发计划 1 项，主持基金委重点项目 2 项等。承担研究项目共计 219 项，包括国家级项目 65 项，省部级项目 114 项，国际合作项目 6 项，横向协作项目 34 项。新增各类研究经费 9143.11 万元。在致力于基础研究的同时，实验室也积极结合国家和地区的战略与发展需求，为濒危物种的保护与繁育提供科学意见，并将基础理论应用于技术创新与推广应用。

在科研成果产出方面，实验室围绕三大研究方向，继续揭示生物多样性形成与演变的规律及其遗传机制，为遗传资源的保护和可持续利用提供理论依据。2020 年，发表 SCI 论文 180 篇，其中以第一完成单位发表论文 78 篇，以第一作者或通讯作者（含并列）在 *Science*、*Cell Research*、*Genome Biology*、*Advanced Science*、*Nature Communications* 等 $IF_{5\text{-}year}\geq 9$ 的国际知名期刊发表论文 28 篇，中国科学院期刊分区 1 区论文占总论文的 32.35%；独立或合作出版专著 4 部；申请发明专利 13 项，授权发明专利 4 项；获云南省自然科学一等奖 1 项。

在人才队伍建设方面，实验室继续采用“引进加培养”的方式，创新人才机制，激发队伍活力，取得明显成效。2020 年，新培养引进学术带头人王国栋研究员、刘振研究员，同时培养新增副研究员 8 人，实现了在学术领域方向研究表现突出的青年人才早挑重担的创新培养政策。在固定人员中，郑萍研究员新入选人社部百千万人才工程，张国捷研究员新入选国家海外高层次人才引进计划，孔庆鹏研究员荣获“享受国务院政府特殊津贴人选”，并新入选云南省高层次人才培养支持计划云岭学者，李学友、王晓爱、李玉春荣获中科院西部之光青年学者 B 类资助，和耀喜、马鹏程、罗鑫、尹婷婷新入选中科院青年创新促进会会员。培养输出博士研究生 21 人，硕士研究生 14 人，出站博士后 1 人。此外，还成功举办 2020 年“进化生物学”线上暑期班，吸引更多有志青年加入实验室。

实验室长期遵循“交流促进合作”的原则，在 2020 年开展了一系列合作交流活动。定期举办“遗传资源与进化青年学者论坛”共计 5 期，提升了室内青年学者学术表达能力并充分促进了室内外交流合作。不定期举办“遗传与进化前沿交叉论坛”，邀请 4 名国内外知名专家来室进行学术交流。此外，实验室还积极发挥国内相关研究领域的辐射和带动作用，对外设立开放课题 15 项，并将各科研平台开放共享。

乘风破浪，砥砺前行！ 2021 年是中国共产党建党 100 周年，也是国家“十四五”规划的开局之年。百年恰是风华正茂，立足过去，共创未来。我们在学术委员会指导下，力争在 2021 年做出更大贡献！在此，我谨代表实验室向给予实验室大力帮助的各级领导及社会各界朋友致以最诚挚的感谢，并期望能得到大家一如既往的关心和支持！

实验室主任：施鹏

实验室概况

一、实验室介绍

遗传资源与进化国家重点实验室依托于中国科学院昆明动物研究所，前身为中科院重点实验室“细胞与分子进化重点实验室”。2007 年 11 月经科技部批准筹建，2009 年 9 月通过验收。

实验室立足于我国西南和东南亚丰富的生物多样性遗传资源，面向战略生物资源的国家需求和世界科技前沿，围绕“遗传、发育与进化的统一”这一重大科学前沿问题，部署三个研究方向：遗传资源多样性的演化与保护、基因与基因组的进化、遗传发育与进化。

实验室积极发挥地域优势和资源特色，开展了大量动物和人类遗传资源收集工作，为生物多样性相关研究打下了坚实的基础。同时将资源优势与科学前沿有机结合，围绕遗传资源多样性的演变规律、自然 / 人工选择与生物适应的遗传机制等关键科学问题，在生物多样性演化的格局、过程与人工选择机制方面做出了具有影响力的代表性成果。近五年，实验室承担国家级、省部级、国际合作及横向项目共 354 项，到位研究经费共计 4.22 亿元。发表 SCI 论文共 861 篇，包括在 *Cell*、*Nature*、*Science*、*Nature Genetics*、*Cell Stem Cell*、*Cell Research*、*Genome Biology* 等 $IF_{5\text{-}year}$≥9 的国际顶级学术期刊上发表论文 172 篇。授权专利 22 项。农业农村部认定水产新品种 1 项。荣获云南省自然科学一等奖 3 项、二等奖 2 项，云南省科技进步三等奖 1 项，云南省专利二等奖、三等各 1 项。

实验室拥有研究组 21 个，支撑部门 3 个。目前固定工作人员 137 人，正高级职称 24 人，副高级职称 33 人，拥有博士学位 84 人。其中 40 岁以下研究骨干占比为 63.4%，青年研究骨干承担了实验室大部分的科研任务，发挥着创新探索的不竭动力。拥有中国科学院院士 1 人，欧洲科学院院士 1 人，发展中国家科学院院士 1 人，人社部百千万人才工程 5 人，中青年科技创新领军人才 3 人，教育部长江学者奖励计划 1 人，万人计划领军人才 3 人，万人计划青年拔尖人才 1 人，国家海外高层次人才引进计划 2 人，国家杰出青年科学基金获得者 5 人，国家优秀青年科学基金获得者 4 人。目前实验室在站博士后 9 人，在读博士研究生 108 人，硕士研究生 99 人。

实验室目前建设有 7 大平台：分子实验平台、显微影像与操作平台、生物信息学平台、功能基因发掘与分析平台、生物多样性考察平台、生命条形码平台、集成家猪平台。拥有大型仪器设备共计 100 余台 / 套，设备总价值 15257 万元。这些设施除了满足实验室在后基因组时代对基因组进化与基因功能研究的需求以外，所有大型设备还依托于昆明大型仪器区域中心，并通过“仪器设备共享管理网”对实验室内外乃至研究所内外全面开放共享。

另外，实验室还拥有无量山黑长臂猿监测站、哀牢山国家级自然保护区野生动物研究基地双柏监测站等野外观察站 4 个，云南土著鱼类养殖基地 3 个，嵩明小耳猪分子育种基地 1 个，为实验室的创新发展提供了重要支撑。

实验室积极开展与国内外的交流与合作，提高实验室在国内、国际学术界的知名度和影响力，促进实验室发展。在运行管理方面，严格按照科技部及中科院对国家重点实验室的要求，进一步完善“开放、流动、联合、竞争”的运行机制，实行依托单位领导下的主任负责制，加强规范化管理，营造出团结协作、

开放自主的科研氛围。

二、研究方向及内容

1. 遗传资源多样性的演化与保护

围绕我国西南及东南亚等生物多样性热点区域，建立世界一流的遗传资源库；研究遗传资源多样性形成和演变的规律，尤其是珍稀物种的濒危机制及其保护策略、野生和家养动物遗传资源的多样性和驯化演变关系，系统发掘农业动物基因，为我国农业可持续发展提供资源、理论和技术支撑，为遗传资源的保护和合理利用提供科学依据，为阐明基因和基因组进化的模式和规律、研究遗传、发育和进化的分子机制提供素材。

2. 基因与基因组的进化

以生命进化关键节点的物种和类群为研究对象，研究基因起源方式与进化规律、基因适应性进化与形态发生和环境适应的关系、基因互作网络形成的进化模式、基因组起源与多样化形成机制；探讨基因、基因互作网络和基因组的结构、功能多样性的起源与进化，阐明生命形态与功能多样化的基因组基础。

3. 遗传发育与进化

通过对不同进化地位和近缘物种的代表类群（如昆虫、头索动物、两栖类和哺乳类等）发育调控机制的研究与比较，从而解析进化中代表性和关键性性状的进化发育规律，进而在不同进化水平分析物种演化的发育生物学机制，如新基因、新的基因表达调控机制、表观遗传元件对物种形态演化与适应性的贡献等，阐明基因和基因组进化模式和规律的分子机制，最终实现遗传、发育与进化的统一。

三、组织结构

1. 现任实验室领导

主　任

施　鹏　研究员

副主任

文建凡　研究员

毛炳宇　研究员

焦保卫　研究员

2. 第三届学术委员会

主　任

张亚平　院　士，中国科学院

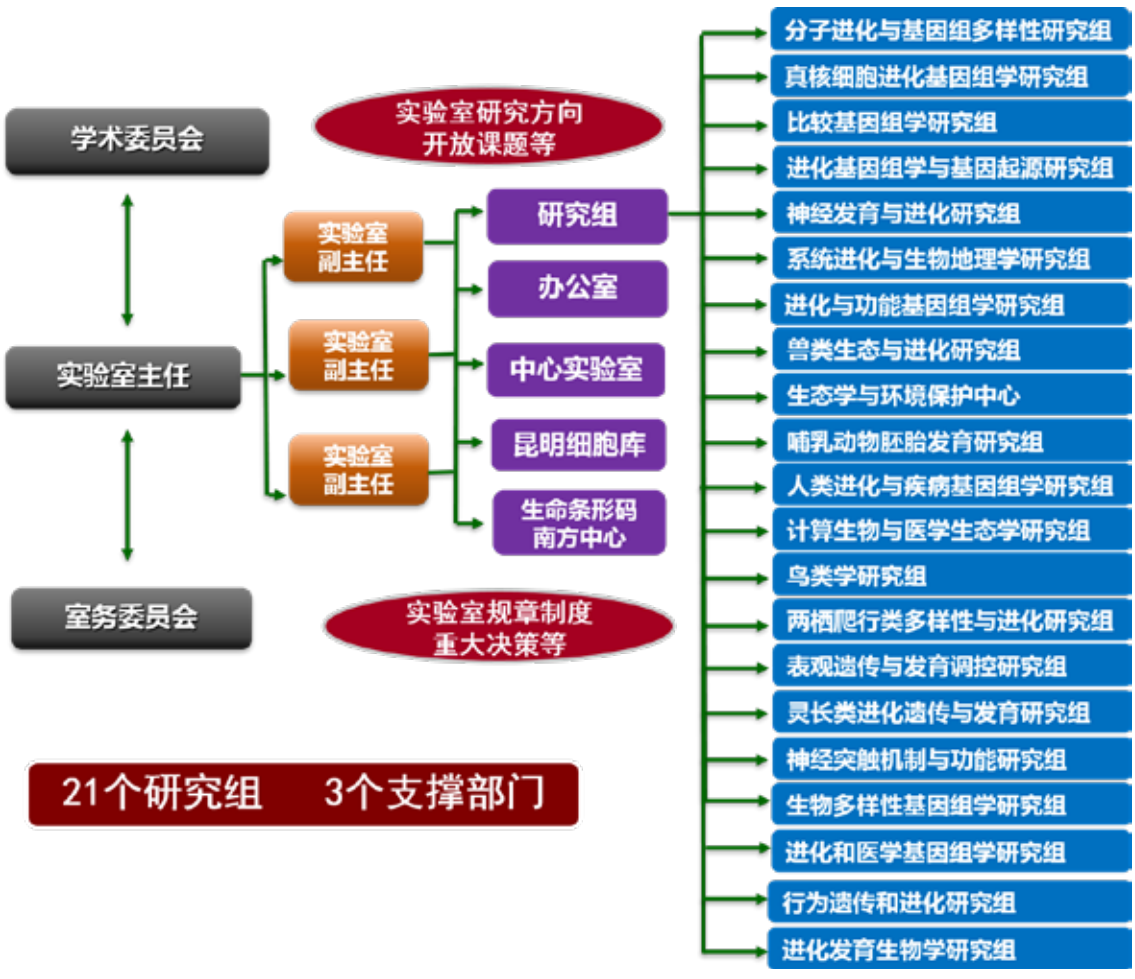
副主任

宿　兵　研究员，中国科学院昆明动物研究所

委　员

桂建芳　院　士，中国科学院水生生物学研究所
金　力　院　士，复旦大学
魏辅文　院　士，中国科学院动物研究所
吴仲义　院　士，中山大学
焦保卫　研究员，中国科学院昆明动物研究所
李德铢　研究员，中国科学院昆明植物研究所
施　鹏　研究员，中国科学院昆明动物研究所
汪小全　研究员，中国科学院植物研究所
王　文　研究员，中国科学院昆明动物研究所
杨　光　教　授，南京师范大学
张克勤　教　授，云南大学

3. 研究队伍



大事记



1 月 20 日，习近平总书记前往滇池星海半岛生态湿地，视察滇池保护治理情况，察看了杨君兴研究团队和昆明动物博物馆设计的滇池生态缸。滇池生态缸以“花 - 鱼 - 螺蚌”立体生态模式为主题，展示了滇池最具代表性的三类特有水生生物，分别是海菜花、滇池金线鲃、螺蛳，该生态缸展示的三类水生生物共生模式也是未来滇池水生态修复的努力方向。



2020 年，实验室举办第四届“青年学者论坛”共 5 场，为青年学者们提供展示分享科研进展的平台。每场邀请室内学术带头人及研究生或青年骨干进行学术报告，评选优秀报告，激发研究生以及青年骨干的科研创新思维，促进室内人员学术交流，并吸引了研究所内外广大师生积极参与。


2020 年，实验室不定期举办“遗传与进化前沿交叉论坛”共计 4 场，邀请到吴仲义院士、施苏华研究员、伦照荣教授等国内外知名学者到室进行学术报告，并开展线上报告直播，追踪研究领域热点前沿，积极与国内外一流机构开展学术交流及合作研究。

科学传播与科教融合

5 月 22 日至 23 日中国科学院公众科学日，实验室参与组织了研究所主题为 “ 云游昆明动物所，保护生物多样性 ” 的线上活动，部分学科组开放参观，展示了一线科研生活。学科组还撰写科普文章《汪星人的哲学思考》发表于中科院之声，并拍摄制作《别人家的狗子系列：汪星人居然那么配合采集 DNA ！》等科普公开课短视频。体现了实验室的开放和科教融合的运行特色。

8 月 5-7 日，实验室与研究生部联合举办了第十七届 “ 进化生物学 ” 线上暑期班，通过网络平台与 30 余名来自全国高校的优秀学员连线。暑期班安排有专家讲座、导师访谈、研究生科研生活直播等活动，通过线上讲座、访谈及参观等新尝试，为想要了解研究所的学生提供了便捷又能身临其境的新方式，普及科学知识的同时，吸引了优质大学生生源。

11 月，王国栋研究员受中央电视台科教频道邀请，参与录制科普节目《人类密友 — 犬之传奇》，系统介绍了家犬的驯化历史，与人类之间的密友关系等科研进展和科学知识。

12 月，施鹏研究团队罗杰博士再次接受中新社采访，介绍了人工珊瑚礁系统，并追溯了 2017 年首次采访后珊瑚礁研究和保护工作的进展和突破。同时，研究团队还拍摄了珊瑚礁相关纪录片。

第一章　科研工作进展

研究方向一：遗传资源多样性的演化与保护　代表性成果一

通过现生两栖爬行动物区系演化历史揭示喜马拉雅山脉隆升过程

Herpetological Phylogeographic Analyses Support a Miocene Focal Point of Himalayan Uplift and Biological Diversification

Xu W, Dong WJ, Fu TT, Gao W, Lu CQ, Yan F, Wu YH, Jiang K, Jin JQ, Chen HM, Zhang YP, David M Hillis*, **Che J***

Abstract

The Himalaya are among the youngest and highest mountains in the world, but the exact timing of their uplift and origins of their biodiversity are still in debate. The Himalayan region is a relatively small area but with exceptional diversity and endemism. One common hypothesis to explain the rich montane diversity is uplift-driven diversification—that orogeny creates conditions favoring rapid *in situ* speciation of resident lineages. We test this hypothesis in the Himalayan region using amphibians and reptiles, two environmentally sensitive vertebrate groups. In addition, analysis of diversification of the herpetofauna provides an independent source of information to test competing geological hypotheses of Himalayan orogenesis. We conclude that the origins of the Himalayan herpetofauna date to the early Paleocene, but that diversification of most groups was concentrated in the Miocene. There was an increase in both rates and modes of diversification during the early to middle Miocene, together with regional interchange (dispersal) between the Himalaya and adjacent regions. Our analyses support a recently proposed stepwise geological model of Himalayan uplift beginning in the Paleocene, with a subsequent rapid increase of uplifting during the Miocene, finally giving rise to the intensification of the modern South Asian Monsoon.

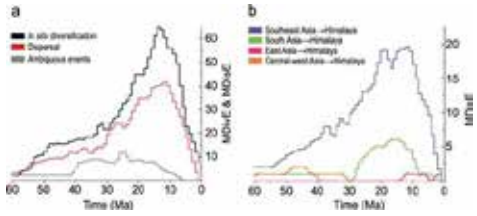
National Science Review, 2020, nwaa263

车静研究团队通过对喜马拉雅地区的长期考察研究，重建了该地区现生大部分两栖爬行动物类群的时空演化动态历史，并由此探讨了喜马拉雅山脉隆升及南亚季风发育等重要地质历史事件的假说，揭示了这些事件对生物分化、迁移的影响。

根据团队收集的一手数据，同时整合 GenBank 上已经发表的物种序列数据，最终收集到了 14 个科，1628 个两栖爬行动物的多基因序列片段数据，其中涉及到 182 个喜马拉雅山区物种，占该地区记录物种的 60% 左右。通过构建物种演化树，并结合时间校正点以及物种分布信息，探讨了喜马拉雅地区分布的两栖爬行动物的时空动态演化格局。首次对喜马拉雅山区两栖爬行动物区系的演化历史进行了整合和解析，并对不同的地质假说进行了探讨。在生物多样性保护角度，该研究也具有重要意义，其结果强烈支持喜马拉雅山地区是重要的物种形成、分化摇篮。喜马拉雅山脉在面积如此小的地区集中了如此多的特有物种，是世界级的生物基因宝库。我们理应加强对该地区生态环境及栖息地的保护，从而保护这些珍贵而独特的生物资源。

研究成果发表在 ***National Science Review*** 上。

喜马拉雅山区及代表两栖爬行动物示意图



喜马拉雅地区两栖爬行动物的演化过程
（a 总体演化模式，b 喜马拉雅和其它地区的扩散模式）

研究方向一：遗传资源多样性的演化与保护

代表性成果二

SCIENCE 发文建议调整中国大鲵保护策略及规范养殖产业管理

- **Giant salamanders: Farmed yet endangered**
- **Lu CQ, Chai J, Murphy RW, Che J***
- *Science,* 2020, 367(6481):989

中国大鲵（*Andrias davidianus s.l.*）是世界上现存最大的两栖动物，漫长的演化历史和极高的进化独特性使其在全球生物多样性资源保护中占据着重要地位。目前，中国大鲵被 IUCN 评估为极度濒危物种（CR），在我国为国家 II 级重点保护野生动物，采取建立保护区、人工繁殖和增殖放流等保护措施。然而，在商业化经济养殖的影响下，持续的低野外目击率意味着现行保护措施的失败。前期研究也发现，中国大鲵至少由 5 个物种组成，这一全新认识也提示现行的保护策略亟需重新调整。

图 1. 中国大鲵（Robert Murphy 摄）

车静研究团队持续开展野外科考和问卷调查，梳理现阶段中国大鲵的保护现状，发文指出现有保护策略存在的系列问题：在商业化经济养殖的影响下，中国大鲵陷入了保护悖论 —— 野外稀少、各类商业养殖场却大量囤积。而无序混乱的养殖模式极易造成潜在的生物病毒在自然水体中的传播，隐藏的水生生物资源及水生态环境风险长期被忽视。在经济利益的冲击下，涉及中国大鲵的保护区也不同程度的受到了养殖业的影响，还带来了病毒传播及养殖物种逃逸的风险，对保护区内原生物种种群及生态环境构成了严重威胁。另外，对比前期研究，发现的部分地方特有物种（地区特有的独立进化遗传谱系）不在保护区设置范围之内。此外，无序、盲目的放流活动已造成杂交种和非本地种流入野外。疾病筛查、放流点生态评估及效果评价等必要环节的缺失也在一定程度上导致了增殖放流活动较低的成功率。

中国大鲵的商业养殖看似“繁荣”，但其带来的各方面的影响却值得我们深思。如何平衡保护与利用的关系，是未来中国大鲵保护的关键。对此，文章提出如下建议：相关保护法律法规的严格执行，加强监管；商业养殖产业的规范管理（水生态安全隐患）；现阶段停止所有增殖放流；综合性科学调查研究，提升科学认识；加强公众文化教育。文章发表后，研究团队也通过中科院专报和人民日报内参提交了相关建议内容，为濒危物种保护和相关保护管理措施的调整提供科学意见。

研究成果发表在 ***Science*** 上。

研究方向一：遗传资源多样性的演化与保护

代表性成果三

在家养动物起源与驯化方面取得重要进展

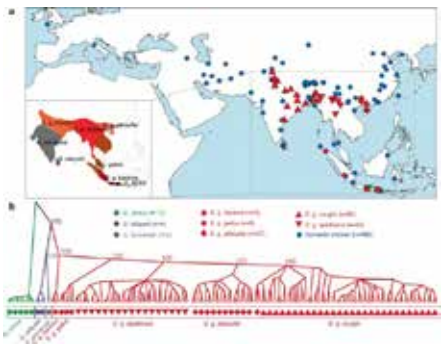
863 genomes reveal the origin and domestication of chicken

Wang MS[1], **Thakur M**[1], **Peng MS**[1], Jiang Y[1], **Frantz LAF**[1], Li M[1], **Zhang JJ, Wang S,** Peters J, **Otecko NO**, ……, **Jin JQ, Li ML, Liu YH, Chen HM, Ma C, Dai SS**, Bhuiyan AFH, Khan MS, Silva G, Le TT, Mwai OA, Ibrahim MNM, Supple M, Shapiro B, Hanotte O, **Zhang GJ,** Larson G, **Han JL*, Wu DD*, Zhang YP***

Abstract

Despite the substantial role that chickens have played in human societies across the world, both the geographic and temporal origins of their domestication remain controversial. To address this issue, we analyzed 863 genomes from a worldwide sampling of chickens and representatives of all four species of wild jungle fowl and each of the five subspecies of red jungle fowl (RJF). Our study suggests that domestic chickens were initially derived from the RJF subspecies *Gallus gallus spadiceus* whose present-day distribution is predominantly in southwestern China, northern Thailand and Myanmar. Following their domestication, chickens were translocated across Southeast and South Asia where they interbred locally with both RJF subspecies and other jungle fowl species. In addition, our results show that the White Leghorn chicken breed possesses a mosaic of divergent ancestries inherited from other subspecies of RJF. Despite the strong episodic gene flow from geographically divergent lineages of jungle fowls, our analyses show that domestic chickens undergo genetic adaptations that underlie their unique behavioral, morphological and reproductive traits. Our study provides novel insights into the evolutionary history of domestic chickens and a valuable resource to facilitate ongoing genetic and functional investigations of the world's most numerous domestic animal.

Cell Research, 2020, 30(8): 693-701



家鸡 (*Gallus gallus domesticus*) 是驯化最早的鸟类之一，根据不同的需求，人类已经培育数百种不同用途的家鸡品种。虽然已经确定红原鸡 (*Gallus gallus*) 是家鸡的主要祖先，但是红原鸡分为五个亚种，家鸡起源于哪个红原鸡亚种目前并不清楚。为系统性地解析家鸡的起源和驯化，张亚平、吴东东研究团队联合国内外研究人员，经过多年的努力，获得了全部 5 个红原鸡亚种的基因组数据，以及分布于东南亚、南亚、中东、东亚、欧洲等地区家鸡的全基因组数据，通过大量的群体遗传学分析，发现家鸡并不是以前认为的多地独立起源，印度、中国北方等并非家鸡的起源地。家鸡是由红原鸡滇南亚种（*Gallus gallus spadiceus*）驯化而来。目前 *Gallus gallus spadiceus* 亚种主要分布在中国西南、泰国北部、缅甸等地区，说明该地区很可能是家鸡的驯化中心。研究人员进一步分析了家鸡基因组中所受人工选择作用，发现大量生殖相关基因在家鸡驯化中受到人工选择作用，进一步支持人类驯化促进家养动物生殖行为的改变。

研究成果发表在 ***Cell Research*** 杂志上。同时，***Science*** 杂志 发表了题为 "The chicken first crossed the road in Southeast Asia, 'landmark' gene study finds" 的点评文章，系统介绍了该研究成果。

Cell Research

研究方向一：遗传资源多样性的演化与保护

代表性成果四

揭示澳洲野犬群体起源及野化机制

Genomic regions under selection in the feralization of the dingoes

Zhang SJ[1], **Wang GD**[1], **Ma PC**[1], Zhang LL, **Yin TT, Liu YH, Otecko NO**, Wang M, Ma YP, Wang L, **Mao BY***, Savolainen P*, **Zhang YP***

Abstract

Dingoes are wild canids living in Australia, originating from domestic dogs. They have lived isolated from both the wild and the domestic ancestor, making them a unique model for studying feralization. Here, we sequence the genomes of 10 dingoes and 2 New Guinea Singing Dogs. Phylogenetic and demographic analyses show that dingoes originate from dogs in southern East Asia, which migrated via Island Southeast Asia to reach Australia around 8300 years ago, and subsequently diverged into a genetically distinct population. Selection analysis identifies 50 positively selected genes enriched in digestion and metabolism, indicating a diet change during feralization of dingoes. Thirteen of these genes have shifted allele frequencies compared to dogs but not compared to wolves. Functional assays show that an A-to-G mutation in ARHGEF7 decreases the endogenous expression, suggesting behavioral adaptations related to the transitions in environment. Our results indicate that the feralization of the dingo induced positive selection on genomic regions correlated to neurodevelopment, metabolism and reproduction, in adaptation to a wild environment.

Nature Communications, 2020, 11(10): 671

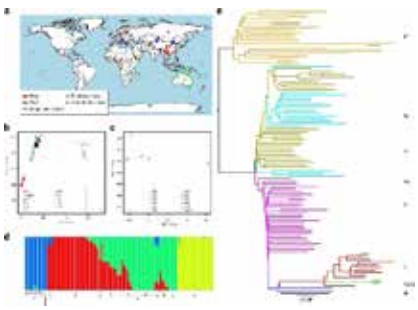


图 1. 澳洲野犬的群体结构

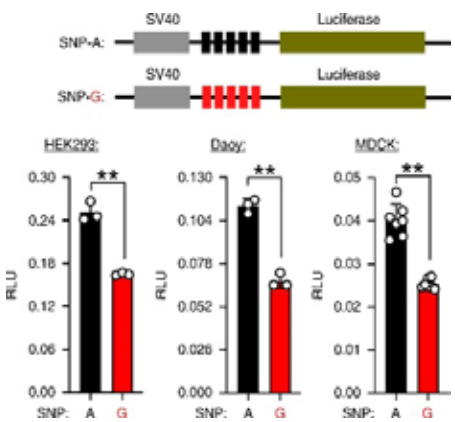


图 2. ARHGEF7 基因突变位点的功能验证

为了对澳洲野犬的起源和野化过程进行深入研究，张亚平院士领导的国际合作团队采集测序了 10 只野生的澳洲野犬和 2 只新几内亚歌唱犬，并且收集了 97 个家犬和灰狼的下载数据，组成了 109 个全基因组测序数据集。揭示证明了澳洲野犬的祖先是东亚已被驯化的家犬，在大约 9900 年前从中国南方出发，在大约 8300 年前到达了澳大利亚，并在澳大利亚迅速野化。同时发现了很多与神经发育，免疫，生殖和消化代谢有关的基因，这些功能都与家犬适应野外生存密切相关。最后分析了澳洲野犬的野化模式，发现了澳洲野犬的一些基因区域相比较家犬来说更像狼，这可能是由于澳洲野犬来自于还未被完全驯化的早期家犬。针对澳洲野犬一个和神经相关的基因 *ARHGEF7* 上的突变，设计了一个功能验证，发现这个澳洲野犬上的突变确实等影响 *ARHGEF7* 基因的表达。该工作利用了澳洲野犬的基因组推测出了它的群体历史，而且还提示了一次可能的古代人类迁移，又利用澳洲野犬的野化分析，推导出了他的野化模式，为今后人群迁移和野化研究提供了新的思路。

研究成果发表在 ***Nature Communications*** 上。

研究方向二：基因与基因组进化

代表性成果一

在家养动物高原适应进化机制方面取得新进展

Ancient Hybridization with an Unknown Population Facilitated High-Altitude Adaptation of Canids

Wang MS[1], **Wang S**[1], Li Y[1], Jhala Y[1], Thakur M[1], **Otecko NO**, Si JF, **Chen HM,** Shapiro B*, Nielsen R*, **Zhang YP*, Wu DD***

Abstract

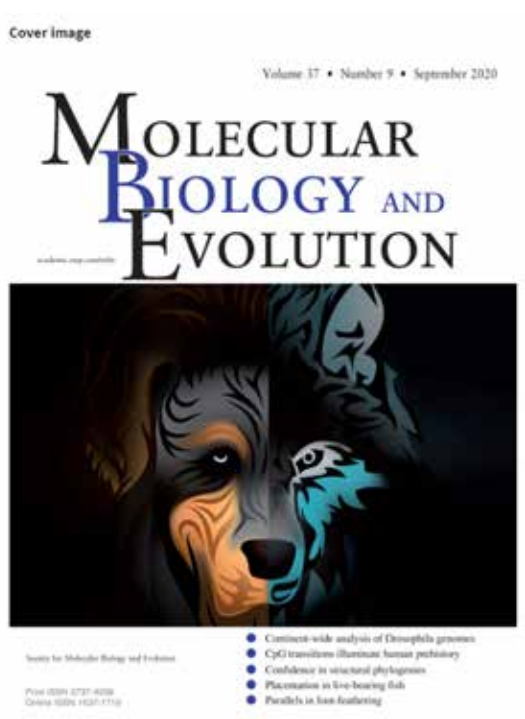
Genetic introgression not only provides material for adaptive evolution but also confounds our understanding of evolutionary history. This is particularly true for canids, a species complex in which genome sequencing and analysis has revealed a complex history of admixture and introgression. Here, we sequence 19 new whole genomes from high-altitude Tibetan and Himalayan wolves and dogs and combine these into a larger data set of 166 whole canid genomes. Using these data, we explore the evolutionary history and adaptation of these and other canid lineages. We find that Tibetan and Himalayan wolves are closely related to each other, and that ~39% of their nuclear genome is derived from an as-yet-unrecognized wolf-like lineage that is deeply diverged from living Holarctic wolves and dogs. The *EPAS1* haplotype, which is present at high frequencies in Tibetan dog breeds and wolves and confers an adaptive advantage to animals living at high altitudes, was probably derived from this ancient lineage. Our study underscores the complexity of canid evolution and demonstrates how admixture and introgression can shape the evolutionary trajectories of species.

Molecular Biology and Evolution, 2020, 37(9): 2616-2629

张亚平及吴东东研究团队长期基于大规模基因组学数据，综合各种生物学方法，揭示了青藏高原多个家养动物的适应性进化遗传机制，鉴定出一批以缺氧诱导通路为代表的高原适应候选基因，发现趋同进化和基因交流在环境适应中的重要性，总结归纳出了家养动物短期高原适应性进化的规律性认识。

为了进一步揭示基因交流在家养动物高原适应过程中的重要性和普遍性，研究人员综合分析了青藏高原藏獒和藏灰狼的群体基因组数据，发现两者之间存在大量的基因交流。以往的研究观点认为高原适应的明星基因 *EPAS1* 的高原适应突变通过基因交流从藏灰狼扩散至藏獒中，然而，综合各种群体遗传学分析以及群体历史模拟，研究人员认为藏獒和藏灰狼的 *EPAS1* 基因应该来自另外一个未知物种。因此，研究人员进一步与印度科学家 Yadvendradev Jhala、 Mukesh Thakur 教授合作，测得一个喜马拉雅狼的基因组，通过分析遗憾地发现，喜马拉雅狼并不是 *EPAS1* 高原适应突变的贡献者。因而，研究人员推测，青藏高原应该还存在一种至今我们未知甚至已经灭绝的犬科动物，藏獒和藏灰狼的 *EPAS1* 基因正是通过基因交流从该未知物种中获得。

研究成果发表在 ***Molecular Biology and Evolution*** 上。



MOLECULAR BIOLOGY AND EVOLUTION

研究方向二：基因与基因组进化

代表性成果二

利用多组学数据解析人类高原低氧适应的调控机制

Chromatin accessibility landscape and regulatory network of high-altitude hypoxia adaptation

Xin JX[1], **Zhang H**[1], **He YX**[1], Duren Z[1], Bai CJ[1], Chen L, **Luo X,** Yan DS, Zhang CY, Zhu X, Yuan QY, Feng ZY, Cui CY, **Qi XB,** Ouzhuluobu, Wong WH*, Wang Y*, **Su B***

Abstract

High-altitude adaptation of Tibetans represents a remarkable case of natural selection during recent human evolution. Previous genome-wide scans found many non-coding variants under selection, suggesting a pressing need to understand the functional role of non-coding regulatory elements (REs). Here, we generate time courses of paired ATAC-seq and RNA-seq data on cultured HUVECs under hypoxic and normoxic conditions. We further develop a variant interpretation methodology (vPECA) to identify active selected REs (ASREs) and associated regulatory network. We discover three causal SNPs of *EPAS1*, the key adaptive gene for Tibetans. These SNPs decrease the accessibility of ASREs with weakened binding strength of relevant TFs, and cooperatively down-regulate *EPAS1* expression. We further construct the downstream network of *EPAS1*, elucidating its roles in hypoxic response and angiogenesis. Collectively, we provide a systematic approach to interpret phenotype-associated noncoding variants in proper cell types and relevant dynamic conditions, to model their impact on gene regulation.

Nature Communications, 2020, 11(20): 4928

高原低氧环境适应的分子机制是进化和遗传领域的重要科学问题。为了系统解析藏族人群适应高原低氧的分子调控机制，宿兵研究团队与中科院数学与系统研究院王勇团队以及斯坦福大学和西藏大学合作，设计实验采集、测量、比较藏族适应型和汉族野生型两种脐带内皮细胞（HUVEC）在低氧和常氧条件下以及不同时间节点上的多组学数据，包括基因组、转录组、染色质可及性（ATAC-seq）和染色质空间构象（Hi-C）数据，并进一步发展了一种新的方法论框架：vPECA (Variants interpretation model by Paired Expression and Chromatin Accessibility data)，整合基因组 - 表观组 - 转录组 - 表型层面的数据，构建以受选择调控元件为核心的基因调控网络模型，对藏族高原低氧适应的调控机制进行了系统地分析。该模型可以检测位于非编码区变异位点是否在群体中受到选择，同时又位于具有调控活性的调控元件上，并在调控网络中影响下游基因表达水平。利用该模型研究揭示 *EPAS1* 基因表达由受选择和不受选择两类调控元件组合调控，发现了 3 个位于增强子区域的功能位点，这 3 个位点通过削弱所在区域的染色质开放程度（可及性），进而下调 *EPAS1* 的表达，从而避免藏族人群在高原低氧环境过高表达 *EPAS1* 带来的负效应。同时，研究人员还构建了 *EPAS1* 基因的下游调控网络，解析了下游受选择靶基因的调控机制，在网络中探索了高原适应相关表型的联系。

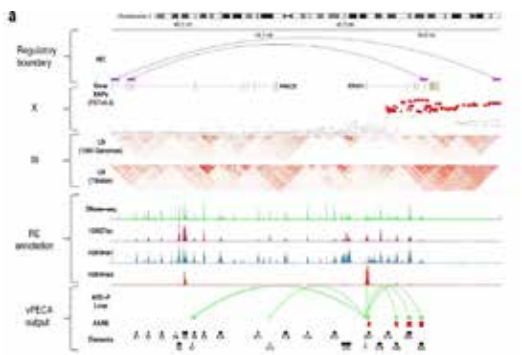


图 1. 利用 vPECA 新模型揭示 *EPAS1* 低氧适应的分子调控机制

该研究提供了一个群体遗传数据结合特定细胞环境多组学数据的研究范例，为今后多组学整合数据分析提供了一个非常有效的工具。同时进一步系统解析了低氧适应的调控网络，为今后高原适应的人群研究和低氧通路的代谢研究都提供了重要的数据。

研究成果发表在 ***Nature Communications*** 上。

研究方向二：基因与基因组进化

代表性成果三

古 DNA 研究发现新石器晚期青藏高原东北部存在热带大型哺乳动物

Ancient genomes reveal tropical bovid species in the Tibetan Plateau contributed to the prevalence of hunting game until the late Neolithic

Chen NB[1], Ren LL[1], Du LY[1], Hou JW[1], Mullin VE, Wu D, Zhao XY, **Li CM, Huang JH, Qi XB,** Capodiferro MR, Achilli A, Lei CZ, Chen FH, **Su B*,** Dong GH*, **Zhang XM***.

Abstract

Local wild bovids have been determined to be important prey on the northeastern Tibetan Plateau (NETP), where hunting game was a major subsistence strategy until the late Neolithic, when farming lifestyles dominated in the neighboring Loess Plateau. However, the species affiliation and population ecology of these prehistoric wild bovids in the prehistoric NETP remain unknown. Ancient DNA (aDNA) analysis is highly informative in decoding this puzzle. Here, we applied aDNA analysis to fragmented bovid and rhinoceros specimens dating ~5,200 y B.P. from the Neolithic site of Shannashuzha located in the marginal area of the NETP. Utilizing both whole genomes and mitochondrial DNA, our results demonstrate that the range of the present-day tropical gaur (Bos gaurus) extended as far north as the margins of the NETP during the late Neolithic from ~29°N to ~34°N. Furthermore, comparative analysis with zooarchaeological and paleoclimatic evidence indicated that a high summer temperature in the late Neolithic might have facilitated the northward expansion of tropical animals (at least gaur and Sumatran-like rhinoceros) to the NETP. This enriched the diversity of wildlife, thus providing abundant hunting resources for humans and facilitating the exploration of the Tibetan Plateau as one of the last habitats for hunting game in East Asia.

PNAS, 2020, 117:28150-28159

5,200 年前青藏高原东北部马家窑文化先民狩猎印度野牛和苏门答腊犀牛的场景复原图 （复原图由董广辉设计、张海岩绘制；版权所有）

史前人类向青藏高原扩散的历史及其对动植物资源利用的方式是国际学术界关注的热点科学问题。为研究史前人类向青藏高原扩散的历史及其对动植物资源利用的方式，宿兵研究团队与兰州大学、西北农林科技大学合作，对山那树扎遗址的10个大型牛科动物和2个犀牛科动物骨骼标本开展了古DNA研究。整合现生牛科动物和犀科动物群体大数据的系统分析、通过系统比较古气候和动物考古数据，研究团队提出约5,200年前较高的夏季温度和温暖湿润的宜人气候可能促使印度野牛和苏门答腊犀牛等许多热带动物分布于较高纬度的地区，丰富了该地区的野生动物多样性，为当时的先民提供了丰富的狩猎资源。此后，约五千到四千年前，在气候恶化和人类活动增强等多重影响下，青藏高原东北部野生动物多样性显著下降，牧业活动取代狩猎活动成为该地区先民主要生活方式。

该研究是青藏高原地区首次大型动物古DNA全基因组测序分析的工作，研究成果发表在 ***Proceedings of the National Academy of Sciences of the United States of America***，并被选为当期导读文章。同时该成果由开放课题（GREKF20-12）资助。

研究方向二：基因与基因组进化

代表性成果四

青藏高原周边人群的群体遗传学揭示吐蕃的扩张历史

Tracing the Genetic Legacy of the Tibetan Empire in the Balti

Yang XY[1], Rakha A[1], Chen W, Hou J, **Qi XB, Shen QK, Dai SS, Sulaiman X**, Abdulloevich NT, Afanasevna ME, Ibrohimovich KB, Chen X, Yang WK, Adnan A, **Zhao RH**, Yao YG, **Su B, Peng MS*, Zhang YP***

Abstract

The rise and expansion of Tibetan Empire in the 7th to 9th centuries AD affected the course of history across East Eurasia, but the genetic impact of Tibetans on surrounding populations remains undefined. We sequenced 60 genomes for four populations from Pakistan and Tajikistan to explore their demographic history. We showed that the genomes of Balti people from Baltistan comprised 22.6–26% Tibetan ancestry. We inferred a single admixture event and dated it to about 39–21 generations ago, a period that postdated the conquest of Baltistan by the ancient Tibetan Empire. The analyses of mitochondrial DNA, Y, and X chromosome data indicated that both ancient Tibetan males and females were involved in the male-biased dispersal. Given the fact that the Balti people adopted Tibetan language and culture in history, our study suggested the impact of Tibetan Empire on Baltistan involved dominant cultural and minor demic diffusion.

Molecular Biology and Evolution, 2020, 38(4):1529-1536

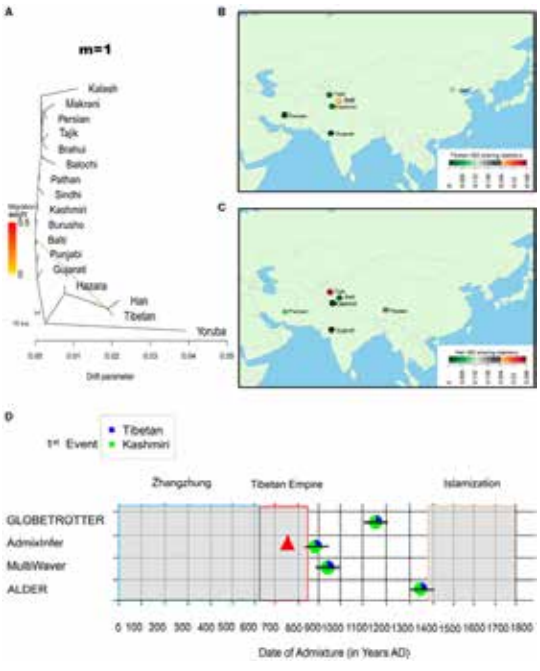


图 1. 巴尔蒂人群的遗传混合历史分析

青藏高原人群历史研究一直是人类学、历史学、考古学和民族学关注的议题。在公元 6 世纪，源于西藏山南地区雅砻河谷的吐蕃开始崛起，对邻近部落进行兼并。但吐蕃的扩张对青藏高原周边人群的影响如何，至今还不清楚。

张亚平院士团队与巴基斯坦健康科学大学开展了青藏高原周边人群的群体遗传学合作研究，从当代人群的 DNA 序列中追溯相关历史事件的影响。据史书记载，吐蕃和唐王朝为夺取西域的控制权，围绕勃律展开了半个多世纪的反复争夺。勃律位于今天巴基斯坦北部的吉尔吉特－巴尔蒂斯坦地区，扼守南亚、中亚和西藏之间的交通要道，是吐蕃进攻唐王朝安西四镇（碎叶、龟兹、于阗、疏勒）的要道。吐蕃最终在公元 757 年征服勃律，其统治及影响一直延续了几百年。为此，研究团队选取了生活在巴尔蒂斯坦的巴尔蒂人（Balti）的群体及其周边人群样本进行了基因组重测序；通过整合包括古代 DNA 在内的多种遗传变异数据，运用群体基因组学方法对巴尔蒂人群体历史进行了解析。

研究表明群体基因组学分析可以作为重要的历史研究方法，体现了学科交叉的重要作用。研究成果发表 ***Molecular Biology and Evolution*** 上。

研究方向二：基因与基因组进化

代表性成果五

在非洲白额长尾猴群体基因组方面取得重要进展

Population Genomics Reveals Incipient Speciation, Introgression, and Adaptation in the African Mona Monkey (*Cercopithecus mona*)

Ayoola AO[1], Zhang BL[1]*, Meisel RP, **Nneji LM, Shao Y,** Morenikeji OB, **Adeola AC, Ng'ang'a SI,** Ogunjemite BG, Okeyoyin AO, Roos C, **Wu DD***

Abstract

Guenons (tribe *Cercopithecini*) are the most widely distributed nonhuman primate in the tropical forest belt of Africa and show considerable phenotypic, taxonomic, and ecological diversity. However, genomic information for most species within this group is still lacking. Here, we present a high-quality de novo genome (total 2.90 Gb, contig N50 equal to 22.7 Mb) of the mona monkey (*Cercopithecus mona*), together with genome resequencing data of 13 individuals sampled across Nigeria. Our results showed differentiation between populations from East and West of the Niger River ~84 ka and potential ancient introgression in the East population from other mona group species. The *PTPRK*, *FRAS1*, *BNC2*, and *EDN3* genes related to pigmentation displayed signals of introgression in the East population. Genomic scans suggest that immunity genes such as *AKT3* and *IL13* (possibly involved in simian immunodeficiency virus defense), and *G6PD*, a gene involved in malaria resistance, are under positive natural selection. Our study gives insights into differentiation, natural selection, and introgression in guenons.

Molecular Biology and Evolution, 2020, 9;38(3):876-890

白额长尾猴主要分布于非洲的加纳、多哥、贝宁、尼日利亚和喀麦隆，是当地较为常见的灵长类。尽管目前所有灵长类被列为保护物种，但在非洲当地猎杀猴子作为食物的现象时有发生且屡禁不止。

吴东东研究团队主要聚焦在非洲尼日利亚境内的白额长尾猴，基于当地保护区多年以来缴获的样品，首先利用三代基因组测序技术构建了质量较好的白额长尾猴参考基因组，之后对来自不同地点的白额长尾猴样品进行基因组重测序，发现尼日利亚境内的长尾猴大致可以分为东（East）、中（WCb）、西（WCa）三个不同的地理遗传组分。东白额长尾猴与其他白额长尾猴遗传差异最大，且以尼日尔河为界和其他样品分开，分歧时间大约为 8.4 万年，这表明尼日尔河在白额长尾猴的种群分化中起着地理隔离的作用。另外对线粒体基因组的遗传进化分析，研究人员意外地发现东白额长尾猴与同域分布的冠毛长尾猴聚在一起，表明其在进化历史上可能与冠毛长尾猴发生过种间杂交，通过对基因组中发生渗透区域最长的片段进行分析发现其中的 3 个基因中有 2 个（*PTPRK* 和 *FRAS1*）被报道与毛色相关，表明毛色在性选择的过程中可能发挥重要作用。

研究成果发表在 ***Molecular Biology and Evolution*** 上。

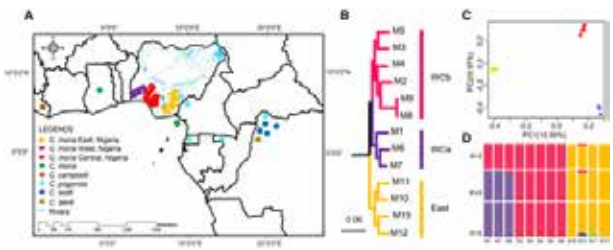


图 1. 采样范围和群体遗传结构分析

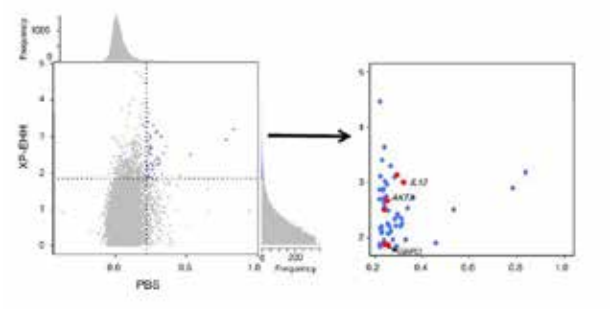


图 2. 候选的受选择基因

MOLECULAR BIOLOGY AND EVOLUTION

研究方向二：基因与基因组进化

代表性成果六

研究揭示非模式动物再生复杂性状遗传机制

Genome and single-cell RNA-sequencing of the earthworm *Eisenia andrei* identifies cellular mechanisms underlying regeneration

Shao Y[1], Wang XB[1], **Zhang JJ**[1], **Li ML**[1], Wu SS, **Ma XY**, Wang X, Zhao HF, Li Y, Zhu HH, **Irwin DM**, Wang DP, **Zhang GJ***, Ruan J*, **Wu DD***

Abstract

The earthworm is particularly fascinating to biologists because of its strong regenerative capacity. However, many aspects of its regeneration in nature remain elusive. Here we report chromosome-level genome, large-scale transcriptome and single-cell RNA-sequencing data during earthworm (*Eisenia andrei*) regeneration. We observe expansion of LINE2 transposable elements and gene families functionally related to regeneration (for example, *EGFR*, epidermal growth factor receptor) particularly for genes exhibiting differential expression during earthworm regeneration. Temporal gene expression trajectories identify transcriptional regulatory factors that are potentially crucial for initiating cell proliferation and differentiation during regeneration. Furthermore, early growth response genes related to regeneration are transcriptionally activated in both the earthworm and planarian. Meanwhile, single-cell RNA-sequencing provides insight into the regenerative process at a cellular level and finds that the largest proportion of cells present during regeneration are stem cells.

Nature Communications, 2020, 11(15)

动物的再生能力一直是一个令人着迷且非常复杂的生物学过程。在自然界中存在一些动物依然保留强大的再生能力，例如无脊椎动物 —— 蚯蚓，拥有极强的前 / 后部体节再生能力。

吴东东研究团队利用长读段 PacBio 平台 +Hi-C 辅助组装等策略测序并拼装了准染色体水平的高质量安德爱胜蚓（*Eisenia andrei*）基因组（Scaffold N50≈111Mb），并通过不同再生时期 bulk 转录组和单细胞转录组整合揭示蚯蚓再生的分子细胞学机制（图 1）。研究发现蚯蚓基因组中重复序列 LINE2 转座元件可能在蚯蚓再生中扮演重要调控角色，例如 LINE2 元件显著高比例地插入到蚯蚓早期再生相关的差异基因 locus；同时某些差异表达的 LINE2 元件（位于蛋白编码基因侧翼 5Kb 区域）和它们的邻近基因拥有极为相似的表达模式。同时，蚯蚓再生早期的单细胞转录组解析暗示蚯蚓再生早期 72h 后损伤愈合部位细胞的高比例组分是干细胞，暗示多能干细胞在蚯蚓再生早期过程中具有重要作用（图 2）。该研究提供了一些蚯蚓再生的候选分子细胞学机制，提出蚯蚓能够作为研究再生生物学或者再生医学的一个新的模型。

研究成果发表在 ***Nature Communications*** 上。

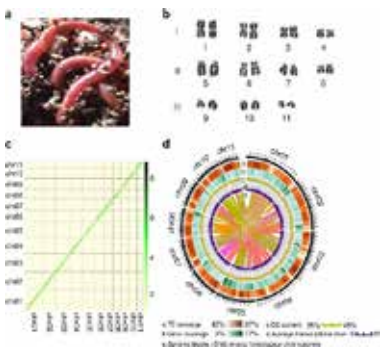


图 1. a 安德爱胜蚓（用于完成基因组测序物种）。b 安德爱胜蚓的核型分析。2n=22，根据染色体形态，初步分成三个亚类。核型分析源于蚯蚓环带的分裂中期细胞，该分析由昆明动物研究所细胞库完成。c Hi-C 互作图。d circos 展示蚯蚓基因组的特征。

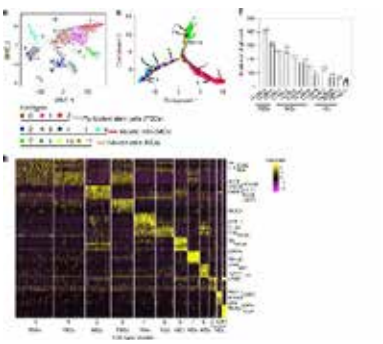


图 2. 单细胞 RNA-sequencing 揭示再生的细胞机制

研究方向三：遗传发育与进化

代表性成果一

在干细胞基因组稳定性调控机制研究中取得进展

Genome integrity and neurogenesis of postnatal hippocampal neural stem/progenitor cells require a unique regulator Filia

Li JZ, Shang YF, **Wang L, Zhao B, Sun CL**, Li JL, Liu SL, **Li C, Tang M,** Meng FL*, **Zheng P*.**

Abstract
Endogenous DNA double-strand breaks (DSBs) formation and repair in neural stem/progenitor cells (NSPCs) play fundamental roles in neurogenesis and neurodevelopmental disorders. NSPCs exhibit heterogeneity in terms of lineage fates and neurogenesis activity. Whether NSPCs also have heterogeneous regulations on DSB formation and repair to accommodate region-specific neurogenesis has not been explored. Here, we identified a regional regulator Filia, which is predominantly expressed in mouse hippocampal NSPCs after birth and regulates DNA DSB formation and repair. On one hand, Filia protects stalling replication forks and prevents the replication stress-associated DNA DSB formation. On the other hand, Filia facilitates the homologous recombination–mediated DNA DSB repair. Consequently, *Filia*$^{-/-}$ mice had impaired hippocampal NSPC proliferation and neurogenesis and were deficient in learning, memory, and mood regulations. Thus, our study provided the first proof of concept demonstrating the region-specific regulations of DSB formation and repair in subtypes of NSPCs.

Science Advances, 2020, 6(15): eaba0682

干细胞是机体发育和组织稳态维持的基础，基因组稳定是干细胞干性维持和再生医学应用的前提。研究干细胞如何维持基因组稳定有助于推动干细胞的安全应用，理解相关发育疾病的致病机理。郑萍研究团队长期关注干细胞维持基因组稳定性的独特机制。在前期工作中，鉴定了胚胎干细胞基因组稳定性调控的关键多功能因子Filia，揭示了其不同的作用途径，并发现人类同源基因的功能突变能导致胚胎发育失败和复发性流产。

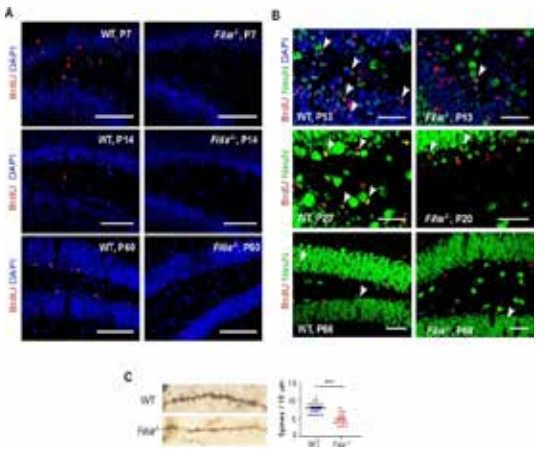


图 1. *Filia*$^{-/-}$ 小鼠海马中 NSPCs 的增殖和神经分化受损

和胚胎干细胞比较，组织干细胞仅具备组织特异的发育潜能。为了探究组织干细胞在基因组稳定性维持上存在共同调控机制，研究人员在小鼠神经干 / 祖细胞（neural stem/progenitor cells，NSPCs）中对 Filia 的表达和功能进行了研究。发现 Filia 仅特异表达在出生后的小鼠海马 NSPCs 中，且调控海马 NSPCs 的基因组稳定。海马区 Filia 缺失后，产生严重的 DNA 双链断裂及异常的神经发生。行为学实验进一步表明，海马相关的神经功能受损，小鼠表现出学习和空间记忆能力下降、焦虑。在猕猴 NSPCs 中也发现同源基因在猴 NSPCs 中具有保守功能，提示人类该基因的功能变异可能导致神经系统发育疾病。本研究揭示了 Filia 在调控海马正常神经发育和功能中的重要意义，也提出不同脑区 NSPCs 的基因组稳定性调控机制可能存在区域特异性，以适应不同的神经发生功能。

研究成果发表在国际期刊 ***Science Advances*** 上，同时该成果由开放课题（GREKF20-15）资助。

Science Advances

研究方向三： 遗传发育与进化

代表性成果二

揭示癌症演化中细胞表型适应性权衡和生态竞争造就肿瘤多样性和适应

Variation in the life history strategy underlies functional diversity of tumors

Li T[1], Liu JL[1], Feng J[1], Liu ZZ, Liu SX, Zhang MJ, Zhang YZ, Hou YL, Wu DF, Li CY, **Chen YB**, Chen H, **Lu XM***

Abstract

Classical *r*- vs. *K*-selection theory describes the trade-offs between high reproductive output and competitiveness and guides research in evolutionary ecology. While its impact has waned in the recent past, cancer evolution may rekindle it. Herein, we impose *r*- or *K*-selection on cancer cell lines to obtain strongly proliferative r cells and highly competitive K cells to test ideas on life-history strategy evolution. RNA-seq indicates that the trade-offs are associated with distinct expression of genes involved in the cell cycle, adhesion, apoptosis, and contact inhibition. Both empirical observations and simulations based on an ecological competition model show that the trade-off between cell proliferation and competitiveness can evolve adaptively. When the r and K cells are mixed, they exhibit strikingly different spatial and temporal distributions. Due to this niche separation, the fitness of the entire tumor increases. The contrasting selective pressure may operate in a realistic ecological setting of actual tumors.

National Science Review, 2020, nwaa124

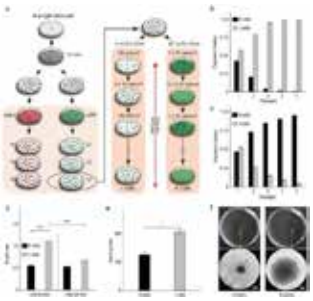


图 1. r-/K- 选择与肿瘤细胞适应性演化

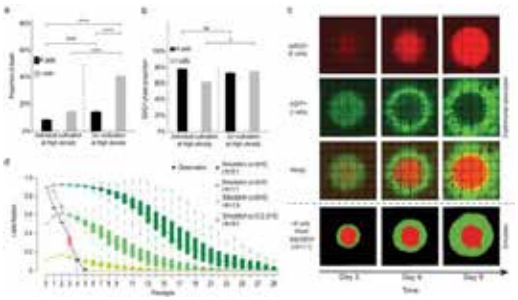


图 2. 混合种群中 r- 和 K- 细胞的种群间相互作用和时空生长

肿瘤是体细胞突变积累并进化而成，具有繁殖迅速、耐低氧、逃逸免疫、对化学药物或物理辐射还存在耐受性等多种适应性特征，使得癌症非常难以治愈，近乎于“全能”。

吕雪梅研究团队以密度依赖性选择中的经典理论——r-vs.K- 选择理论为基础，利用实验进化的手段，选择出 r 或 K 癌细胞系，获得了具有快速增殖能力的 r 细胞和具有高度竞争力的 K 细胞（图 1）。证实了癌症细胞群体中存在表型亚群分化，并系统地揭示了不同表型之间的适应性权衡。并且 RNA-seq 表明，这种权衡与细胞周期、粘附、凋亡和接触抑制相关基因的不同表达有关。此外，研究团队还建立了具有空间结构制约的肿瘤细胞系亚群竞争实验，当 r 细胞和 K 细胞混合时，它们表现出明显不同的时空分布。团队首次观察到癌症细胞不同表型亚群之间的生态位分离事件。由于这种生态位分离，整个癌症群体的适应性增加。实验观察和基于生态竞争模型的模拟计算都表明，癌症细胞群体中存在符合生态学原理的细胞增殖和竞争力之间的适应性权衡（图 2）。这项研究表明，癌症实质上是由癌症群体内部多种多样的具有不同表型特征的亚群共同组成的一个集合体，亚群之间是竞争关系。癌症群体内亚群的表型多样性以及生态学关系的确定，对癌症细胞群体的表型演化提供了新的认识，也为癌症治疗策略提供了新的思路。

研究成果发表在 ***National Science Review*** 上。

研究方向三：遗传发育与进化

代表性成果三

发现泌乳量和乳脂分泌的调控新机制

TDP-43 facilitates milk lipid secretion by post-transcriptional regulation of Btn1a1 and Xdh

Zhao LM[1], Ke H[1], Xu HB, Wang GD, Zhang HL, Zou L, Xiang S, Li MY, Peng L, Zhou MF, **Li LL,** Ao L, **Yang Q**, Shen CKJ, Yi P*, Wang L*, **Jiao BW***

Abstract
Milk lipid secretion is a critical process for the delivery of nutrition and energy from parent to offspring. However, the underlying molecular mechanism is less clear. Here we report that TDP-43, a RNA-binding protein, underwent positive selection in the mammalian lineage. Furthermore, TDP-43 gene (*Tardbp*) loss induces accumulation of large lipid droplets and severe lipid secretion deficiency in mammary epithelial cells to outside alveolar lumens, eventually resulting in lactation failure and pup starvation within three weeks postpartum. In human milk samples from lactating women, the expression levels of TDP-43 is positively correlated with higher milk output. Mechanistically, TDP-43 exerts post-transcriptional regulation of *Btn1a1* and *Xdh* mRNA stability, which are required for the secretion of lipid droplets from epithelial cells to the lumen. Taken together, our results highlights the critical role of TDP-43 in milk lipid secretion, providing a potential strategy for the screening and intervention of clinical lactation insufficiency.

Nature Communications, 2020, 11(15): 341

母乳喂养不仅有利于新生儿的成长和健康发育，同时也能降低产妇众多疾病如乳腺癌等的发病率。然而，人们对于泌乳的调控机制还知之甚少。

焦保卫研究团队通过比较哺乳类和非哺乳类的基因组序列，发现 RNA 结合蛋白中 TDP-43 可能在泌乳中发挥重要作用。利用乳腺特异性敲除小鼠，发现 TDP-43 敲除导致其喂养的幼鼠出现严重的营养不良甚至死亡，进一步实验证实 TDP-43 基因敲除的母鼠产奶量显著下降。TDP-43 敲除导致下游基因 *Xdh* 与 *Btn1a1* 的 RNA 稳定性下降，从而引起 TDP-43 敲除鼠的乳腺上皮细胞乳脂分泌异常，大量脂滴堆积在乳腺上皮细胞内，进而出现泌乳量显著下降，幼崽营养不良。为确定 TDP-43 表达是否与临床产妇泌乳不足相关，研究团队收集了临床产妇的乳汁样本，从而实现间接分析产妇乳腺上皮细胞中 TDP-43 的表达水平。结果显示，泌乳充足的产妇（纯母乳喂养组）的 TDP-43 表达显著高于泌乳量适中产妇（混合母乳喂养组），而泌乳缺乏产妇（奶粉喂养组）中 TDP-43 表达最低。说明 TDP-43 的低表达与产妇泌乳不足显著正相关（图 2）。该研究揭示了乳脂分泌的新机制，同时也为产后缺乳提供了可能的分子机制，为临床早期筛查和干预提供理论基础。

研究成果发表在 ***Nature Communications*** 上。

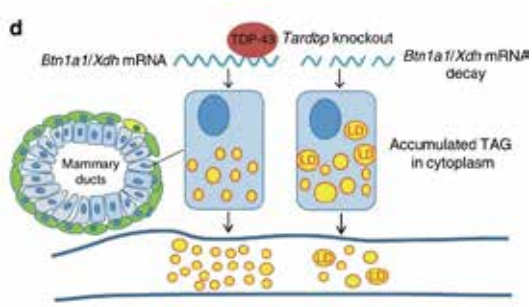


图 1. TDP-43 在乳脂分泌中的功能及其作用机制

图 2. TDP-43 低表达与产妇泌乳不足正相关

研究方向三： 遗传发育与进化

代表性成果四

合作发现乳腺癌干细胞的调控新机制

SGCE Promotes Breast Cancer Stem Cells by Stabilizing EGFR

Zhao LN[1], Qiu T[1], Jiang DW[1], **Xu HB, Zou L, Yang Q,** Chen CS*, **Jiao BW***

Abstract

Breast cancer stem cells (BCSCs) are responsible for resistance to chemotherapy, high degree of metastasis, and poor prognosis, especially in triple-negative breast cancer (TNBC). The $CD24^{low}CD44^{high}$ and high aldehyde dehydrogenase 1 (ALDH1) cell subpopulation ($CD24^{low}CD44^{high}$ $ALDH1^{+}$) exhibit very high tumor initiating capacity. In the current study, the upregulated genes are analyzed in both $CD24^{low}CD44^{high}$ and $ALDH1^{+}$ cell populations at single-cell resolution, and a highly expressed membrane protein, SGCE, is identified in both BCSC populations. Further results show that SGCE depletion reduces BCSC self-renewal, chemoresistance, and metastasis both in vitro and in vivo, partially through affecting the accumulation of extracellular matrix (ECM). For the underlying mechanism, SGCE functions as a sponge molecule for the interaction between epidermal growth factor receptor (EGFR) and its E3 ubiquitination ligase (c-Cbl), and thus inhibits EGFR lysosomal degradation to stabilize the EGFR protein. SGCE knockdown promotes sensitivity to EGFR tyrosine kinase inhibitors (TKIs), providing new clues for deciphering the current failure of targeting EGFR in clinical trials and highlighting a novel candidate for BCSC stemness regulation.

Advanced Science, 2020, 7(17)

三阴性乳腺癌 (TNBC) 缺少雌激素受体 (ER) 、孕激素受体 (PR) 和人表皮生长因子受体 2 （HER2）的表达，是恶性程度高、易转移、高复发和预后差的一类乳腺癌。

焦保卫研究团队结合 TNBC 单细胞测序数据，鉴定了一个在乳腺癌干细胞（BCSC）中高表达的基因 -SGCE。表型分析发现 SGCE 对于乳腺癌干细胞的自我更新不可或缺。在机制探讨上，发现 SGCE 与 E3 泛素连接酶 c-Cbl 相互结合，SGCE 缺失促进 c-Cbl 释放出来而泛素化其底物蛋白 EGFR，从而使得 EGFR 进入网格蛋白介导和巨胞饮途径的内化，内化的 EGFR 进而进入溶酶体降解。EGFR 的降解导致其下游通路被阻断并最终抑制 BCSC 自我更新和胞外基质 ECM 的累积。SGCE 在 BCSC 中高表达时，SGCE 与 c-Cbl 相互结合，EGFR 能够正常激活其下游信号通路 PI3K-AKT，促进 BCSC 干性维持、肿瘤细胞迁移、化疗药物和靶向 EGFR 抑制剂的耐药性（图 1）。

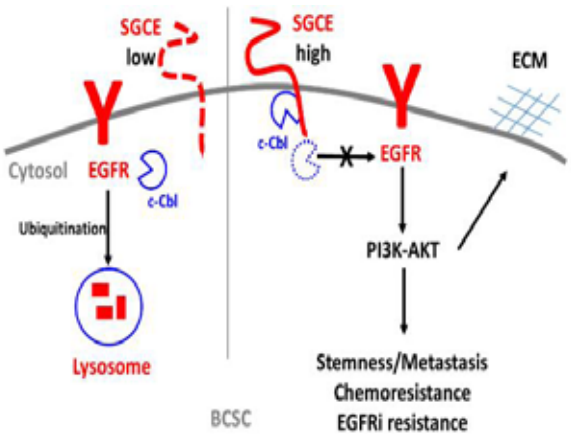


图 1. SGCE 通过调控 EGFR 而贡献于乳腺癌干细胞的自我更新

EGFR 在超过 50% TNBC 病人中高表达，与乳腺癌细胞增殖、转移和 BCSC 的干性维持密切相关，然而 EGFR 的抑制剂（如吉非替尼和拉帕替尼）在乳腺癌中的临床治疗效果并不显著 SGCE 分子帮助维持 BCSC 中 EGFR 高表达，去除 SGCE 的表达则可以促进 TNBC 中的 EGFR 靶向治疗的效果，从而为 EGFR 与其它靶点的联合治疗提供新策略。

研究成果发表在 ***Advanced Science*** 期刊上。

ADVANCED SCIENCE

系统进化与生物地理学

杨君兴，博士，研究员，博士生导师。研究方向包括：生物多样性的考察监测及评价、系统分类、系统发育与生物地理学；珍稀特有物种的生态学研究和保育；湿地生态系统的恢复研究。至今已主持项目 40 余项，发表论文 200 余篇，其中 SCI 论文 100 余篇，获得国家授权专利 20 项，云南省省级奖励 6 项。

重要成果及产出：

1. **Zhang YW, Pan XF , Wang XA, Fan W, Yang JX***. Restocking of *Anabarilius grahami* in Lake Fuxian, Southwest China: morphological and genetic effects[J]. Zoological Research, 2020, 41(6): 740 − 746.
2. **Zhang YW , Wang XA , Yang JX, Pan XF***.Growth performance and ploidy differences in reciprocal hybrids of Dianchi golden-line barbel (*Sinocyclocheilus grahami*) and barbless carp (*Cyprinus pellegrini*)[J]. Aquaculture Research, 2020, 10(10):78.
3. Qiu Y, Yin YH, Ruan ZQ, Gao Y, Bian C, Chen JM, **Wang XA, Pan XF, Yang JX*** , Shi Q* and Jiang WS*. Comprehensive transcriptional changes in the liver of Kanglang white minnow (*Anabarilius grahami*) in response to the infection of parasite Ichthyophthirius multifiliis[J]. Animals, 2020, 10(4):681.
4. Yu GH[1], Du LN[1], Wang JS, Rao DQ, Wu ZJ*, and **Yang JX***. From mainland to islands: colonization history in the tree frog *Kurixalus* (Anura: Rhacophoridae)[J]. Current Zoology, 2020,10(5):1-17.
5. **殷艳慧**，蒋万胜，**潘晓赋，杨君兴***. 水产养殖鱼类生长性状研究进展 [J]. 中国水产科学 ,2020,27(04):463-484.
6. **王晓爱，潘晓赋，杨君兴，刘倩** . 一种软鳍新光唇鱼肌肉细胞系的构建方法 . 专利号: 201510204471.9.(2020.1.3 授权)
7. **潘晓赋，王晓爱，杨君兴，刘倩** . 一种光倒刺鲃鳍细胞系的构建方法 . 专利号： 201610970091.0（2020.2.3 授权）
8. 杨坤凤，**王晓爱，张源伟，潘晓赋，杨君兴**，范伟 . 一种滇池金线鲃肌间刺的染色方法及其应用 . 专利号: 201811620374.8.（2020.7.2 授权）

1. 三种金线鲃鱼类全基因组

新增麦田河金线鲃 (*Sinocyclocheilus maitianheensis*)、无眼金线鲃 (*Sinocyclocheilus anophthalmus*) 全基因组测序，对比已发表的滇池金线鲃 (*Sinocyclocheilus grahami*)、安水金线鲃 (*Sinocyclocheilus anshuiensis*)、犀角金线鲃 (*Sinocyclocheilus rhinocerous*) 全基因组数据，进一步确定了五种金线鲃递进式的进化关系。转录组分析结果表明，基因突变可能是造成地表种与洞穴种色素差异的原因。同时，利用功能注释基因集筛选出金线鲃褪黑素合成酶、免疫、黑色素相关基因。另外，基于 RAD-seq 构建的遗传连锁图谱和 scaffold 水平基因组，构建了滇池金线鲃染色体水平基因组，该基因组包含 48 条染色体，36,924 个基因，约 1.49Gb。此外，基于该染色体水平基因组，结合 QTL-seq 和 BFR 参数（bulk frequency ratio），识别到两个生长相关的 QTLs，筛选到一些生长相关的候选基因，如 *map2k5, stat1, phf21a, cdkn1c, sox6, smad6*，这些基因与细胞增殖，神经发育，骨骼肌发育，软骨形成和免疫密切相关。

2. 滇池金线鲃与大头鲤远缘杂交

远缘杂交是指两个不同的物种、属或更高等级的类群之间的杂交，是将不同物种的基因组进行组合，实现后代杂种优势的有效途径。淡水鱼中，跨亚科间的远缘杂交，并不多见。滇池金线鲃和大头鲤 (*Cyprinus pellegrini*) 均为云南“四大名鱼”，其中，滇池金线鲃肉质鲜美，具有较高 DAA、EPA 和 DHA 含量，但其生长速度慢，个体小；大头鲤生长速度快、体型大，但其风味较差。通过远缘杂交获得了一个杂交品种，杂交品种生长速度较滇池金线鲃快，肌肉品质优于大头鲤。同时，首次证明了母本染色体数量少于父本染色体时，杂交后代也能够存活，并表明杂交过程中的染色体重排可能导致染色体损失。在水产养殖业中，该杂交品种可推广到更多的水产养殖地区，市场潜力巨大。

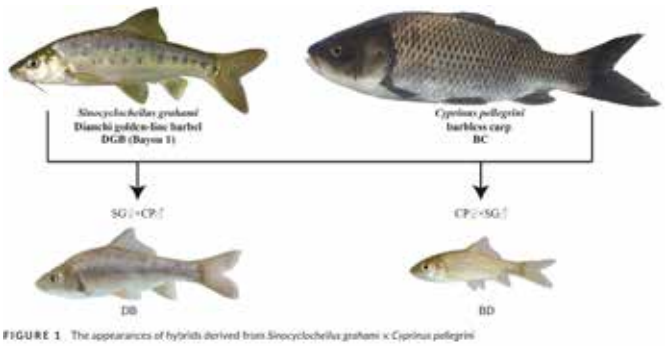


FIGURE 1 The appearances of hybrids derived from *Sinocyclocheilus grahami* × *Cyprinus pellegrini*

3. 云南珍稀特有鱼类的人工繁殖、养殖推广和野外种群复壮

目前，珍稀鱼类保育基地饲养有土著鱼类 60 余种，50 余万尾，无重大鱼病出现。单位养殖水体的养殖密度逐年提高。对西畴、曲靖、会泽、通海、芒市、保山、丽江、大理等养殖基地定期进行技术指导。

2020 年度在牛栏江流域放流滇池金线鲃 10 万余尾，短须裂腹鱼 5 万尾，金沙鲈鲤 3.5 万尾，云南光唇鱼 3 万尾，李仙江流域放流软鳍新光唇鱼 1 万尾，暗色唇鱼 1 万尾，抚仙湖放流抚仙金线鲃 2 万尾，云南光唇鱼 1 万尾，杞麓鲤 10 万尾。

Phylogenetics and Biogeography

Dr. Junxing Yang, Professor. The research team is mainly interested in biodiversity monitoring survey and evaluation, fauna taxonomic, phylogenetic and biogeographic; ecology and conservation research to rare and native species; especially focuses on the restoration of wetland ecosystem and application. Till now, presided over more than 40 projects, total of 200 papers have been published which more than 100 of them are SCI papers, and 6 books and 20 national invention patent have been published.

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1. Whole genome of three species of Sinocyclocheilus

Added the whole genome sequencing of *Sinocyclocheilus maitianheensis* and *Sinocyclocheilus anophthalmus* , and compared the published data of *Sinocyclocheilus grahami*, *Sinocyclocheilus anshuiensis*, and *Sinocerous rhinocerous*. Further confirmed the progressive evolutionary relationship of the five species of *Sinocyclocheilus*.The results of transcriptome analysis showed that gene mutation might be the cause of the difference of pigment between the surface species and cave species. Meanwhile, the gene set of functional annotation was used to screen out the melatonin related genes of *Sinocyclocheilus* melatonin synthase. In addition, we constructed chromosome-level genome based on previously constructed high-density genetic linkage map (unpublished) and assembled genome. Based on the previously constructed high-density genetic linkage map and genome, 48 pseudo-chromosomes were assembled. The final chromosome-level assembly covered 1.49 Gb, with 36,924 genes. By using QTL-seq strategy and BFR parameter, 2 QTL intervals were partially overlapped in full-sib family and mixed family. Meanwhile, some growth-related candidate genes, such as *map2k5*, *stat1*, *phf21a*, *cdkn1c*, *sox6*, *smad6*, were screened from the two major identified QTLs. These genes are closely related to cell proliferation, nerve development, skeletal muscle development, chondrogenesis and immunity.

2.Growth performance and ploidy differences in reciprocal hybrids of Dianchi golden-line barbel (Sinocyclocheilus grahami) and barbless carp (Cyprinus pellegrini)

Distant hybridization, which refers to crosses between two different species, genera or higher-ranking taxa, is an effective way to combine the genomes of different species and achieve heterosis in offspring. Distant hybridization across subfamilies is rare in freshwater fish. Both *Sinocyclocheilus grahami* and *Cyprinus pellegrini* are among the “four famous fish” in Yunnan. Among them, *Sinocyclocheilus grahami* have high content of delicious amino acids (DAA), eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA),However, its relatively small body size and slow growth rate; *Cyprinus pellegrini* have large body size and fast growth. But, its flavor is poor. A hybrid variety was obtained by far crossing. The growth rate of the hybrid was faster than that of *Sinocyclocheilus grahami*, and the muscle quality was better than *Cyprinus pellegrini* and demonstrated that when the number of maternal chromosomes is fewer but approach than that of paternal chromosomes, their hybridized offspring are able to survive. We also provided evidence suggesting that chromosome loss could occur via chromosomal rearrangements during fish hybridization. In aquaculture, the hybrid could be extended to more aquacultural areas, with huge market potential.

3. The artificial breeding, production and releasing in the wild of endangered fishes

In this year, we cultivated and produced more than 3 million fish fry of these fishes, including *Sinocyclocheilus grahami*, *Sinocyclocheilus tingi*, *Neolissochilus benasi*, *Percocypris retrodorslis*, *Schizothorax taliensis*, *Anabarilius liui chenghaiensis*, *Zacco platypus*, *Anabarilius grahami*, *Torqiaojiensis* and *Distoechodon macrophthalmus*. More than 0.36 million individuals were released in wild to rebuilt and restore the wild population of these fishes.

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工作人员（Staff）

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Yujiao He, Technician

研究生（Graduate Students）

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殷艳慧　Yanhui Yin 2017

潘晓赋　Xiaofu Pan 2018

黄新迪　Xindi Huang 2018

车星锦　Xingjing Che 2020

兽类生态与进化

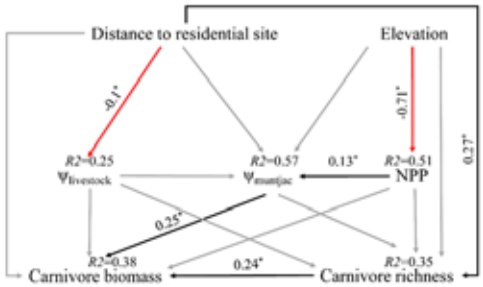
蒋学龙，博士，研究员。立足于东喜马拉雅 - 横断山地区开展哺乳动物生态与进化研究，主要研究内容包括哺乳动物分类、系统演化与生物地理，灵长类动物的生态行为，兽类资源考察、监测与保护，以揭示横断山地区哺乳动物多样性的形成机制及在特殊生态条件下的适应性进化与保护。近年来，主要以东喜马拉雅 - 横断山地区特有与常见小型哺乳动物、灵长类及地栖大中型兽类为研究对象，重点研究横断山区哺乳动物分布格局及其演化机制、西黑冠长臂猿的生态行为与适应性，并全面布局横断山区兽类资源监测网络与数据库建设，开展亚洲象生态学研究，为人象冲突防范与亚洲象保护提供科学对策。

重要成果及产出：

1. **Li XY**, Bleisch WV, **Liu XW**, **Hu WQ**, **Jiang XL** . 2020. Human disturbance and prey occupancy as predictors of carnivore richness and biomass in a Himalayan hotspot. ***Animal Conservation***, doi: 10.1111/acv.12600.
2. **Song WY**#, **Li XY**#, **Chen ZZ**, **Li Q**, **Onditi KO**, **He SW**, **Jiang XL** .2020. Isolated alpine habitats reveal disparate ecological drivers of taxonomic and functional beta-diversity of small mammal assemblages. ***Zoological Research***, doi: 10.24272/j.issn.2095-8137.2020.085.
3. **Chen ZZ**, **Li XY**, **Song WY**, **Li Q**, **Onditi KO**, Khanal L, **Jiang XL** .2020. Small mammal species richness and turnover along elevational gradient in Yulong Mountain, Yunnan, Southwest China. ***Ecology and Evolution***, 10:2545-58.
4. **Li XY**, Bleisch WV, **Liu XW**, **Jiang XL** .2020. Camera-trap surveys reveal high diversity of mammals and pheasants in Medog, Tibet. ***Oryx***, doi: 10.1017/S0030605319001467.
5. **Li XY**, Huang C, **Jiang XL** .2020. Spatiotemporal occurrence of Mishmi takin Budorcas taxicolor in Dulongjiang region, southwestern China. ***Mammalia***, 84, 513–519.
6. **Onditi KO**, Peterhans JK, Demos TC, Musila S, **Chen ZZ**, **Jiang XL**. 2020. Morphological and genetic characterization of Mount Kenya brush-furred rats (Lophuromys Peters 1874); relevance to taxonomy and ecology. Mammal Research, 65:387–400.
7. Chen SD, Qing J, Liu Z, **Jiang XL***, Liu SY*. 2020. Multilocus phylogeny and cryptic diversity of white-toothed shrews (Mammalia, Eulipotyphla, Crocidura) in China. BMC Evoluationary Biology, 20:29.
8. **李学友**，**胡文强**，**普昌哲**，**李权**，**于秋鹏**，**胡哲畅**，William V. Bleisch，**蒋学龙** .2020. 西南纵向岭谷区兽类及雉类红外相机监测平台: 方案、进展与前景 . 生物多样性，doi: 10.17520/biods.2020105

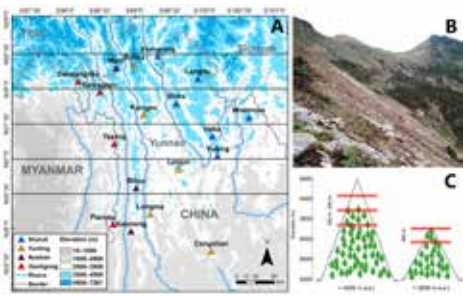
1. 人为干扰和猎物占域率对食肉类群落结构的影响

研究以保护关注度高的食肉类为研究对象，采用路径分析探讨猎物可得性、人类活动、相关环境变量与食肉类物种多样性及群落生物量间的直接或间接关联，结果显示，猎物可得性以及与居民点之间的距离是影响食肉类群落结构的关键因素，二者对食肉类物种多样性及群落功能性状（体重）具有直接和间接的显著关联：一方面，食肉类群落生物量和猎物可得性、食肉类物种多样性和人类活动强度间存在直接正关联；另一方面，人类活动对食肉类群落功能性状产生间接影响，距离居民点越近，群落平均体重越小，表明人类活动可能同时影响食肉类群落结构和功能。

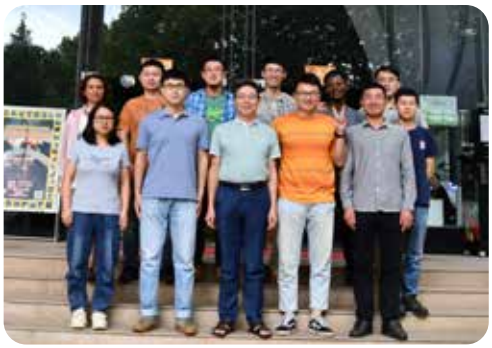


2. 高山隔离生境小型兽类群落物种和功能 β 多样性格局及其驱动因素

研究以非飞行小型兽类为研究对象，对高山栖息地的扩散限制过程促进物种分化，但栖息地相似性导致功能性状收敛的假说进行了验证。我们对三江并流区 18 个高山样点的非飞行小型兽类进行了标准化野外采样。计算了物种和功能 α 和 β 多样性，以及 β 多样性成分的相关指数。然后，我们分别评价了地理和环境因素对上述多样性指标的解释程度。结果并未显示局地尺度的功能结构比预期更加相似。但物种周转成分高于功能周转成分，且物种嵌套成分低于功能嵌套成分，说明不同高山样点间的物种组成差异是由功能相似的物种引起的。物种总 β 多样性及周转成分仅受地理隔离驱动，而功能总 β 多样性及周转成分主要受到低温等环境因子驱动。我们的结果证明，在特定情况下，同一区域内物种和功能 β 多样性及其成分可以由不同的生态机制驱动。该结果提示了通过 β 多样性分解可以极大程度加深我们对生物多样性格局及其驱动因素的理解。本研究还为极端环境中的陆生哺乳动物群落构建过程提供了实际案例。



Mammal Ecology and Evolution



Prof. Xuelong Jiang, Professor, The laboratory is mainly interested in specimen-based investigations of biodiversity inventory, taxonomy and systematics, phylogenetics and phylogeography of small mammals with a special focus in the Henduanshan Region, and also in spatial ecology of rare and cryptic mammal faunas, behavior and conservation of black crested gibbon, as well as conservation biology of Asian elephant and other large mammals.
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1. Camera-trap surveys reveal high diversity of mammals and pheasants in Medog, Tibet

Medog County lies within the Eastern Himalaya biodiversity hotspot, but biodiversity in the region remains largely unexplored as there was no permanent road access until 2014. Here we present data from camera-trap surveys in five areas of Medog County, to ascertain the occurrence and occupancy of threatened wildlife species. With a total survey effort of 4570 trap days we detected 23 medium and large terrestrial mammal species and six pheasant species,13 of which are categorized as Endangered, Vulnerable or Near Threatened in the IUCN Red List and 19 of which are categorized as regionally threatened on the China Species Red List. Carnivora was the most diverse order, with 15 species recorded. Our study produced the first camera-trap photographic evidence of the Bengal tiger *Panthera tigris tigris* in China. In addition, we detected the dhole *Cuon alpinus*,golden cat *Catopuma temminckii*,marbled cat *Pardofelismarmorata andmainland* clouded leopard *Neofelis nebulosa*, highlighting the conservation value of the region. The occupancy of muntjac *Muntiacus* spp. was high (52.7%), indicating prey for large carnivores was abundant. People, livestock and domestic dogs were also recorded frequently, suggesting the fauna are potentially threatened by human disturbance. In the light of recent development in the region, conservation efforts are urgently required, to prevent prey depletion and habitat degradation in this priority region for conservation.

2. Small mammal species richness and turnover along elevational gradient in Yulong Mountain, Yunnan, Southwest China

Understanding the species diversity patterns along elevational gradients is critical for biodiversity conservation in mountainous regions. We examined the elevational patterns of species richness and turnover, and evaluated the effects of spatial and environmental factors on nonvolant small mammals (hereafter “small mammal”) predicted a priori by alternative hypotheses (mid-domain effect [MDE], species–area relationship[SAR], energy, environmental stability, and habitat complexity]) proposed to explain the variation of diversity. We designed a standardized sampling scheme to trap small mammals at ten elevational bands across the entire elevational gradient on Yulong Mountain, southwest China. A total of 1808 small mammals representing 23 species were trapped. We observed the hump-shaped distribution pattern of the overall species richness along elevational gradient. Insectivores, rodents, largeranged species, and endemic species richness showed the general hump-shaped pattern but peaked at different elevations, whereas the small-ranged species and endemic species favored the decreasing richness pattern. The MDE and the energy hypothesis were supported, whereas little support was found for the SAR, the environmental stability hypothesis, and the habitat complexity. However, the primary driver(s) for richness patterns differed among the partitioning groups, with NDVI (the normalized difference vegetation index) and MDE being the most important variables for the total richness pattern. Species turnover for all small mammal groups increased with elevation, and it supported a decrease in community similarity with elevational distance. Our results emphasized for increased conservation efforts in the higher elevation regions of the Yulong Mountain.

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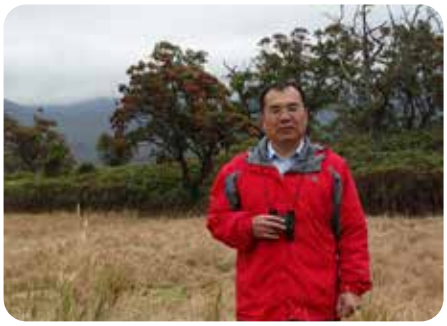

鸟类学研究组

杨晓君，研究员，主要从事西南地区鸟类分类区系、系统演化、生物地理、群落生态学及珍惜鸟类的行为生态学和保护生物学研究。近年来更关注青藏高原旗舰物种 — 黑颈鹤的保护及鸟类系统演化研究。目前已出版执行主编和副主编专著 9 部，发表论文 100 余篇。

重要成果及产出：

1. **Dong F**, Hung CM, **Yang XJ***. Secondary contact after allopatric divergence explains avian speciation and high species diversity in the Himalayan-Hengduan Mountains. Molecular Phylogenetics and Evolution. 143, 106671, 2020.
2. Dai CY, **Dong F**, **Yang XJ***. Morphotypes or distinct species? A multilocus assessment of two East Asian scimitar babblers (Aves, Timaliidae).Zoologica Scripta. 49(3): 256-279, 2020.
3. Kong DJ, Luo WX, Møller A.P., Zhang YY, **Yang XJ*.** Vigilance strategy differentiation between sympatric threatened and common crane species. Behavioural Processes.176, 104119, 2020.
4. **Dong F#**, Li ShH#, Chiu ChCh, Dong L, Yao ChT*, **Yang XJ***.Strict allopatric speciation of sky island Pyrrhula erythaca species complex. Molecular Phylogenetics and Evolution. 153, 106941,2020.

1. 两种同域分布受威胁鹤类的警戒策略区别

研究表明，与它们的近亲相比，受到威胁的物种可能表现出减少或提高的反捕食行为，但很少有研究揭示种群之间的行为差异。探索影响系统发育相关的常见物种和濒危物种行为的因素有助于理解这种差异。我们利用广义线性模型分析了在外部和内部的变量：包括月，每天的时间，栖息地类型、分布面积、族组成状态和群体大小，对警戒行为（包括组警戒频率和级别）同域分布的常见受胁的鹤类 -- 灰鹤与黑颈鹤。在群扫描水平上发现了明显的种间区别，灰鹤比黑颈鹤更加警觉。模型试验还表明，种群大小对两种鹤类的警戒频率有共同影响，分布区范围与黑颈鹤的警惕性显著相关，而在与黑颈鹤共生的区域，灰鹤更受时间和群落组成状况的影响。但当没有黑颈鹤时，时间对属于灰鹤的个体的行为没有影响，暗示存在种间竞争。

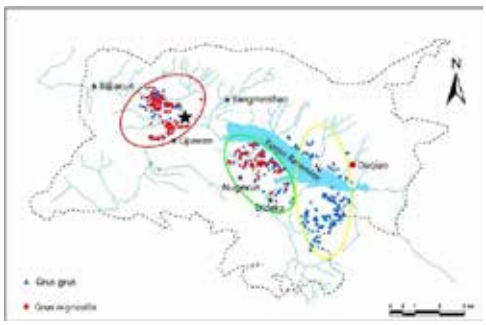

图 黑颈鹤和灰鹤分布

2. 严格异域成种灰头灰雀的物种形成

分化后物种间基因流动的证据越来越多，这改变了我们对物种形成模式的理解。在严格的异地物种形成仍然适用的情况下，出现了一个基本问题。独立岛种群可能会由于生态位保守性而减少向高原生境迁移的基因流，并以异地的方式跟随分化。在本研究中，我们通过对遗传和生态数据的统计分析，在独立岛屿的灰头灰雀(Pyrrhula erythaca)中验证了这一假说。基于聚类分析的多核位点分析结果表明，灰头灰雀可能是在中更新世冰期气候条件较差时迁居台湾岛的，之后是由分布于喜马拉雅 - 横断山脉和华北中部的灰头灰雀发生严格的异地辐散。生态位模拟结果表明，它们的形成可能是由于这些鸟类的生态位保守性和在随后较温和的冰期缺乏适宜的生态廊道所致。此外，根据遗传和行为证据，我们将传统定义的灰头灰雀划分为亚洲大陆的灰头灰雀和台湾的灰头灰雀。

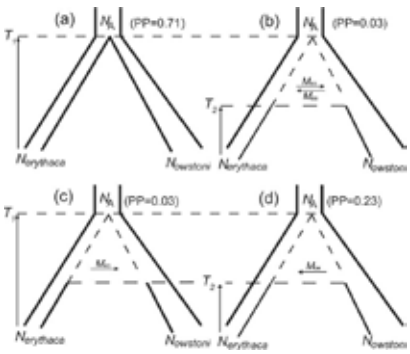

图 四种与后验概率相关的 *Pyrrhula erythaca* 和 *P. e. owstoni* 差异的系统地理模型。
(a) Allopatry 模型，(b) Island 模型，(c) EO 模型和 (d) OE 模型。

Ornithology

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1. Vigilance strategy differentiation between sympatric threatened and common crane species

Studies have indicated that threatened species may show reduced or elevated antipredator behavior compared with their close common relatives, but remarkably few studies revealed such differences in behavior among populations. Exploring factors affecting behavior between phylogenetically related common and threatened species could help understand such discrepancy. We tested for effects of external and internal variables including month, time of day, habitat type, distribution area, group composition status and group size on vigilance behavior (including group scan frequency and level) of two sympatric common Grus grus and threatened G. nigricollis cranes with generalized linear models. We detected significant species effect on group scan level, and grus was more vigilant than nigricollis. Model tests also indicated that group size had common effect on group scan frequency for both species, and distribution area significantly correlated with the vigilance of nigricollis, while grus was more affected by time of day and group composition status in areas of sympatry with nigricollis. But when nigricollis was absent, time had no effects on behavior by individuals belonging to grus, implying existence of inter-specific competition. We also found that grus decreased individual vigilance efforts by foraging with other species (e.g., Bar-headed Goose Anser indicus) to share large group alertness benefits (collective vigilance). As our results demonstrated, we argued that, with diverse antipredation tactics e.g., foraging with other species, alternating time rhythm or partitioning spatial utilization to mitigate inter-specific competition, reducing time allocation to preening while maintaining foraging efforts, common grus could maintain high level of vigilance, which may benefit their survival and population increase. Whereas less time spent vigilant antipredation strategy adopted by threatened nigricollis, this may have negative effects on their populations.

2. Strict allopatric speciation of sky island Pyrrhula erythaca species complex

Increasing evidence of post-divergence gene flow between taxa is shifting our understanding on the mode of speciation. A fundamental question arises concerning the circumstances under which strict allopatric speciation still holds true. Sky island populations might undergo reduced gene flow by niche conservatism to highland habitats and follow divergence in an allopatric manner. In this study, we tested this hypothesis in the sky island Grey-headed Bullfinch (Pyrrhula erythaca) species complex via statistical analyses of both genetic and ecological data. Results of coalescent-based analysis of multiple nuclear loci suggested that P. e. owstoni likely colonized Taiwan island during the severe mid-Pleistocene glacial climate followed by strictly allopatric divergence from P. e. erythaca distributed in Himalayas-Hengduan mountains and central North China. Results of ecological niche modeling suggested that their speciation may be attributed to the niche conservatism of these birds and the lack of a suitable ecological corridor during subsequent milder glacial episodes. In addition, we delimited the traditionally defined P. erythaca into two full species, P. erythaca in the Asian mainland and P. owstoni on the island of Taiwan, based on both genetic and behavioural evidences. These results suggest that ecology can have a dynamic role in allowing highland populations to expand their ranges and isolated by habitat barriers to diversify in a strictly allopatric manner.

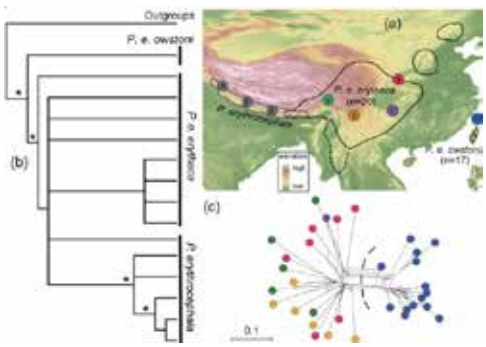

Fig. Sampling and molecular phylogenetics in the present study. (a) Sampling locations of Pyrrhula erythaca and P. erythrocephala are labeled with circles of a different color for each location. (b) Mitochondrial gene tree obtained from Bayesian analysis of the CYTB dataset. (c) Multilocus network based on combined mitochondrial and nuclear dataset. A scale was shown as relative indicator of distance because the matrices were standardized. Colors indicate individuals' sampling localities as marked in (a).

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Douglas W. Yu, 博士，研究员。生态学与环境保护中心负责人，首批云南省高端人才项目引进人才。主要关注两个方面的研究内容：生物多样性快速评估方法和互利共生研究。目前已发表超过 90 篇论文于国际期刊 *Nature, Science, PNAS, PLoS Biology, Ecology Letters, Ecological Monographs, Ecology, American Naturalist, Evolution* 等上。

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重要成果及产出：

1. Hughes, A.C.[1]*, Lechner, A.M., Chitov, A., Horstmann, A., Hinsley, A., Tritto, A., Chariton, A., Li, B.B., Ganapin, D., Simonov, E., Morton, K., Toktomushev, K., Foggin, M., Tan-Mullins, M., Orr, M.C., Griffiths, R., Nash, R., Perkin, S., Glémet, R., Kim, M., **Yu, D.W.** (2020) Horizon Scan of the Belt and Road Initiative (BRI) ***Trends in Ecology & Evolution.*** doi: 10.1016/j.tree.2020.02.005
2. Koster, J.[1]*, R. McElreath, K. Hill, **D. W. Yu**, G. Shepard, N. van Vliet, M. Gurven, B. Trumble, R. B. Bird, D. Bird, B. Codding, L. Coad, L. Pacheco-Cobos, B. Winterhalder, K. Lupo, D. Schmitt, P. Sillitoe, M. Franzen, M. Alvard, V. Venkataraman, T. Kraft, K. Endicott, S. Beckerman, S. A. Marks, T. Headland, M. Pangau-Adam, A. Sirén, K. Kramer, R. Greaves, V. Reyes-García, M. Guèze, R. Duda, Á. Fernández-Llamazares, S. Gallois, L. Napitupulu, R. Ellen, J. Ziker, M. R. Nielsen, E. Ready, C. Healey, and C. Ross. (2020) The life history of human foraging: Cross-cultural and individual variation. ***Science Advances*** 6:eaax9070.
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4. **Ji, Y.Q.**[1], Baker, C.C.M., **Li, Y.H.**, Popescu, V.D., **Wang, J.X.**, **Wang, L.**, Wen, Q.Z., **Yang, C.Y.**, Xu, C.C.Y., Pierce, N.E., **Yu, D.W***. Large-scale Quantification of Vertebrate Biodiversity in Ailaoshan Nature Reserve from Leech iDNA. bioRiv. doi:10.1101/2020.02.10.941336 https://www.scmp.com/lifestyle/health-wellness/article/3050703/how-leeches-could-help-prevent-future-coronavirus (in review)

1. “一带一路”的前景聚焦

“一带一路”倡议是人类历史上规模最大的基础设施建设和发展项目，也给生态系统、经济和社区带来了风险和机遇。有一些风险（比如栖息地的脆弱、修建公路导致动物死亡）是很明显的，但是更多的风险并不明显。我们这一次“一带一路”前景聚焦研讨会就是要考虑到“一带一路”建设所带来的风险和机遇。我们确定了 11 个可能会对环境和社会产生重大影响但尚未得到重视的前沿焦点问题，并对每一个前沿问题进行了描述。总体而言，“一带一路”将增强中国参与国际环境治理的能力。因此，需要新的合作治理模式来平衡地缘政治、社会和环境利益，提高和规范全球环境标准对于保护生态系统和人类社会来说至关重要。

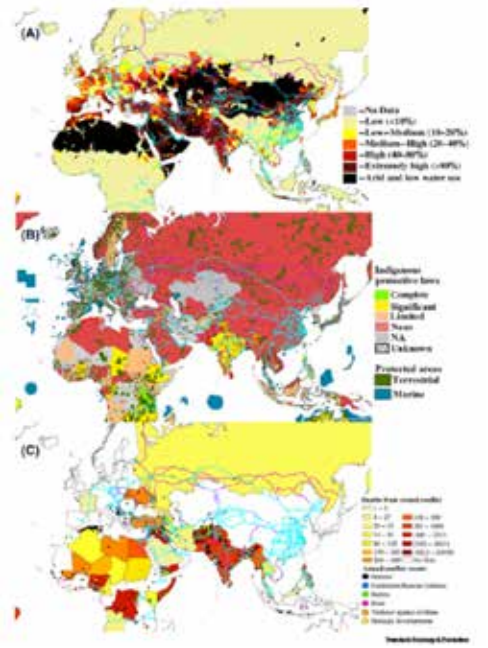

图 1. 在欧亚大陆和非洲，“一带一路”相关道路（浅紫色）和铁路（浅蓝色）空间重合

2. 人类觅食的生活史：跨文化与个体变异

人类的适应依赖于缓慢的生活史、复杂的生产技能和广泛的社会性的综合。精炼和测试人类生活历史和文化学习的进化模型得益于越来越精确的知识、技能和生产速度随年龄的增长。为了实现这一目标，我们从 40 个地点超过 1800 人的约 23,000 份狩猎记录中推断猎人技能的增长和下降。数据显示，尽管高技能在成年期的大部分时间里都保持着，但在 30 岁至 35 岁之间的平均生产力水平达到顶峰。此外，个体和地点之间也存在着很大的差异。在研究地点内，个体间的差异更多地取决于下降速率的异质性，而不是增长速率。这一分析使关于人类生命历史和文化适应共同进化的问题更加尖锐。

Ecology, Conservation, & Environment Center(ECEC)

Dr. Douglas W. Yu. Yu's research covers two fields, (1) game-theoretical models of symbiosis, and (2) rapid biodiversity assessment using genomics. In the first area, we have developed new genomics methods for biodiversity rapid assessment. In the second, we have been elucidating the mechanisms stabilizing cooperation among species, using in fig-wasp and ant-plant mutualisms as experimental models. Yu has 90 publications, including in *Nature, Science, PNAS, PLoS Biology, Ecology Letters, Ecological Monographs, Ecology.*
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1. Horizon Scan of the Belt and Road Initiative

The Belt and Road Initiative (BRI) represents the largest infrastructure and devel_x0002_opment project in human history, and presents risks and opportunities for ecosystems, economies, and communities. Some risks (habitat fragmentation, roadkill) are obvious, however, many of the BRI's largest challenges for develop_x0002_ment and conservation are not obvious and require extensive consideration to identify. In this first BRI Horizon Scan, we identify 11 frontier issues that may have large environmental and social impacts but are not yet recognised. More generally, the BRI will increase China's participation in international environmen_x0002_tal governance. Thus, new cooperative modes of governance are needed to balance geopolitical, societal, and environmental interests. Upgrading and standardising global environmental standards is essential to safeguard ecologi_x0002_cal systems and human societies.

2. The life history of human foraging: Cross-cultural and individual variation

Human adaptation depends on the integration of slow life history, complex production skills, and extensive sociality. Refining and testing models of the evolution of human life history and cultural learning benefit from increasingly accurate measurement of knowledge, skills, and rates of production with age. We pursue this goal by inferring hunters' increases and declines of skill from approximately 23,000 hunting records generated by more than 1800 individuals at 40 locations. The data reveal an average age of peak productivity between 30 and 35 years of age, although high skill is maintained throughout much of adulthood. In addition, there is substantial variation both among individuals and sites. Within study sites, variation among individuals depends more on heterogeneity in rates of decline than in rates of increase. This analysis sharpens questions about the coevolution of human life history and cultural adaptation.

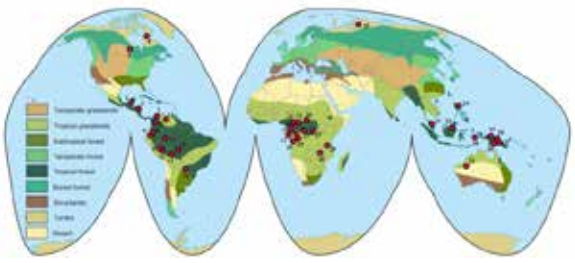

Figure 2. Distribution of study sites.

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两栖爬行类多样性与进化

车静，研究员，博士生导师。世界两栖爬行动物学大会执委，中国动物学会两栖爬行动物学分会副理事长，“中国两栖类”信息系统（http://www.amphibiachina.org/）负责人。2019 年度当选美国鱼类和两栖爬行动物联合学会（ASIH）终身外籍荣誉会员；入选中组部万人计划科技创新领军人才（2019 年度）；2017 年获国家基金委优秀青年基金。学科组 2012 年成立，立足中国及东南亚丰富的多样性资源，从宏观生物学问题出发，坚持多学科交叉，以整合的方法和进化的视角，瞄准两栖爬行动物多样性形成、演化、适应的前沿科学问题及濒危物种保护的重大需求开展工作。作为通讯（第一）作者在 *Science*、*PNAS*、*Syst Biol*、*Nati Sci Rev* 等一系列国际学术期刊发表 66 篇 SCI 论文。

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3. **Lu Chen-Qi**, **Chai J**, **Murphy RW**, **Che J***. 2020. Giant salamanders: Farmed yet endangered. ***Science***. 41(2): 194–198.
4. **Chen Jin-Min**[1], Prendinic E[1], **Wu YH**[1], **Zhang BL**, Suwannapoome C, **Chen HM** , **Jin JQ**, Lemmon ME, Lemmon AR, Stuarth BL, Raxworthy CJ, **Murphy RW**, Yuan ZY*, **Che J***. 2020. An integrative phylogenomic approach illuminates the evolutionary history of Old World tree frogs (Anura: Rhacophoridae). ***Molecular Phylogenetics and Evolution***. 145(2020): 106742.
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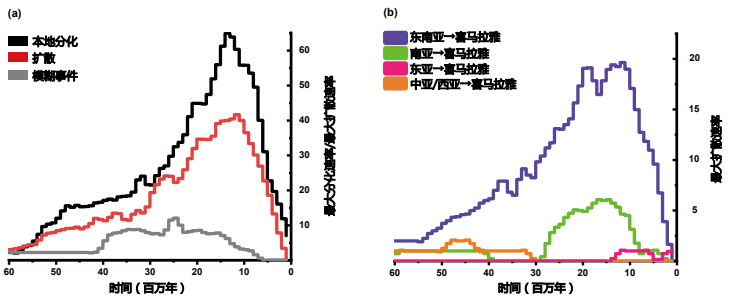
6. **Chen Jin-Min**[1],*, **Xu K**[1], Poyarkov Jr. NA, Wang K, Yuan ZY, Hou M, Suwannapoom C, Wang J, **Che J***. 2020. How little is known about “the little brown frogs” : description of three new species of the genus *Leptobrachella* (Anura: Megophryidae) from Yunnan Province, China. ***Zoological Research***. 41(3): 292 – 313.

1. 两栖爬行动物整合生物地理研究支持喜马拉雅渐进式隆升



通过重建该地区现生大部分两栖爬行动物类群的时空演化动态历史，探讨了喜马拉雅山脉隆升过程及南亚季风发育等重要地质历史事件假说并揭示其对生物分化、迁移的影响。喜山地区两栖爬行动物的演化动态模式更支持“渐进式隆升假说”，即喜马拉雅地区最早于古新世开始缓慢隆升，而在中新世早期快速隆升。其带来的一系列地质气候变化，促进了本地物种大量形成和与东南亚地区的频繁交流。这一研究成果从生物多样性保护角度具有重要的意义。建议加强对该地区生态环境及栖息地的保护，从而保护这些珍贵而独特的生物资源。

【Xu W et al. 2020. ***National Science Review***, 5 year IF= 15.209 】

2. 出版专著《西藏两栖爬行动物——多样性与进化》

该专著基于团队多年来在西藏考察及研究成果完成。与第一次科考相比，该书记录的两栖爬行动物增加了近 40% 的物种数目（增加两栖动物 14 种，爬行动物 26 种）。共记录两栖纲 2 目 8 科 22 属 60 种，爬行纲 1 目 9 科 43 属 79 种，同时展示 700 余张精美动物及环境彩色照片。第一次全面展示了西藏物种的系统演化地位，同时对近年来青藏高原两栖爬行动物的适应与进化研究进展进行了综述。从整合的方法、进化的视角看西藏两栖爬行动物多样性是本书的特点。该著作为深入理解西藏生物多样性起源、演化具有重要价值，为该地区的生物多样性保护提供了重要的一手数据。陈宜瑜院士及魏辅文院士为本书作序。

3. SCIENCE 发文建议调整中国大鲵保护策略及规范养殖产业管理

基于中国大鲵野外调查数据，撰文指出，在商业化经济养殖的影响下，中国大鲵陷入了保护悖论 —— 野外稀少、各类商业养殖场却大量囤积。现行的国家保护措施亟需调整优化，如何规范及监管当前庞大的大鲵养殖市场将是管理部门面临的一大挑战。该文针对中国大鲵保护提出了系列建议。

【Lu et al. 2020. ***Science*** (Letter), 5 year IF=44.372】

Herpetological Diversity and Evolution

Dr. Jing Che, Principal Investigator. Using amphibian and reptile as model, we often explore the biodiversity issue and evolutionary questions within a phylogenetic framework. We are interested in how historical and ongoing processes have shaped the patterns of biodiversity of amphibians and reptiles that exist today and how the species have adapted to and evolved.

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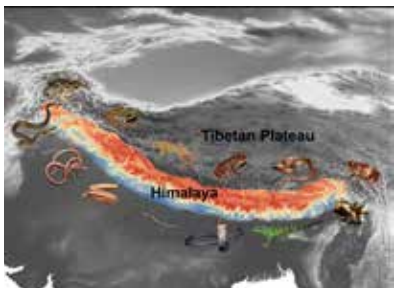
1. Herpetological phylogeographic analyses support a Miocene focal point of Himalayan uplift and biological diversification



Through reconstructing spatial-temporal history of most herpetofauna across the Himalaya, we examined two hypotheses about the uplift of the Himalaya and discussed the influence on biotic diversification. Our analyses support a recently proposed stepwise geological model of Himalayan uplift beginning in the Paleocene, with a subsequent rapid increase of uplifting during the Miocene, finally giving rise to the intensification of the modern South Asian Monsoon.

These series of geological and climatic events have left significant signal on the evolution of herpetofauna, boosting the *in situ* diversification and frequent interchange between the Himalaya and Southeast Asia. Our study is important for the conservation of the Himalayan biota, which is a world-class species treasure-house.

2. The book "the Tibetan Amphibians and Reptiles" has published

This book documents the diversity of amphibians and reptiles in Tibet, and further discusses the evolutionary processes and mechanisms for the Tibetan herpetofauna. It is based mainly on research conducted during the past nine years (2010–2018) . Compared with the first Scientific Expedition to the Qinghai-Tibetan plateau and its achievements made on the Tibetan herpetofauna (Hu, 1987), the book documents 23 additional species of amphibians and 26 more reptiles . This book is composed mainly of two sections: overview and monograph. A total of 60 amphibians (2 orders, 8 families, 22 genera), and 79 reptiles (1 order, 2 suborders, 9 families, 43 genera) species are reviewed herein. Supplemental files are presented in the form of electric QR code scans, with a total of ~200 pages and 60,812 words

3. Giant salamanders: Farmed yet endangered

Chinese giant salamanders (CGS) fall into a paradox of being extremely endangered in nature, but overstocked in farms. Profit speculation led to overstocking of millions of individuals for farm breed-stock and illegal poaching. The absence of genetic identification, habitat suitability, and disease quarantining has led to hybridization, low field survival of CGS, and ecological security issues.

Hence, considering the urgent need for adjustments, we offer suggestions for conservation, including unfailing supervision of the commercial market stringent law enforcement to stop commercial breeding farms in or near the reserves and illegal poaching, scientific evaluating of the current status of each species, ceasing of all releases until pure, native lines are propagated, and establishing ecotourism to develop local pride in resources.

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余传鑫 Chuanxin Yu
易木荣 Murong Yi
董文捷 Wenjie Dong
曹如君 Rujun Cao
冯小刚 Xiaogang Feng
于中斌 Zhongbin Yu
卢宸祺 Chenqi Lu
尹浩萍 Haoping Yin

分子进化与基因组多样性研究

张亚平，博士，研究员，中国科学院院士，发展中国家科学院院士，欧洲科学院院士。中国科学院副院长，遗传资源与进化国家重点实验室学术委员会主任，*Hum Mol Genet* 编委。近年来重点围绕家养动物起源与驯化历史、动物环境适应的基因组进化机制以及动物复杂性状形成的遗传基础开展研究工作。在 2020 年联合多家研究机构，组织开展合作研究系统解析了家鸡的起源和驯化历史、澳洲野犬的起源及野化机制、青藏高原多种家养动物的高原适应机制；运用多种基因组学手段揭示了穿山甲物种的濒危状况和群体历史，并以鲤亚科鱼类为对象探讨了脊椎动物异源多倍体亚基因组的动态演化过程。2020 年，在国际 SCI 刊物上发表了论文 19 篇，其中 IF>10 的 7 篇，包括 ***Cell Res*** (1)，***Nat Commun*** (1)，***Nat Sci Rev*** (2)，***Mol Biol Evol*** (2)，***Sci Adv*** (1) 等。

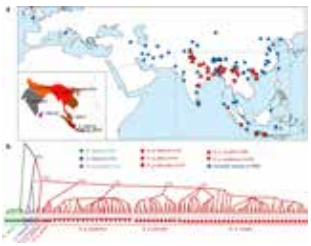
重要成果及产出：

1. Wang MS, Thakur M, **Peng MS**, Jiang Y, Frantz LAF, Li M, Zhang JJ, Wang S, Peters J, Otecko NO, Suwannapoom C, Guo X, Zheng ZQ, Esmailizadeh A, Hirimuthugoda NY, Ashari H, Suladari S, Zein MSA, Kusza S, Sohrabi S, Kharrati-Koopaee H, Shen QK, Zeng L, Yang MM, Wu YJ, Yang XY, Lu XM, Jia XZ, Nie QH, Lamont SJ, Lasagna E, Ceccobelli S, Gunwardana HGTN, Senasige TM, Feng SH, Si JF, Zhang H, Jin JQ, Li ML, Liu YH, Chen HM, Ma C, Dai SS, Bhuiyan AFH, Khan MS, Silva GLLP, Le TT, Mwai OA, Ibrahim MNM, Supple M, Shapiro B, Hanotte O, Zhang GJ, Larson G, Han JL, Wu DD, **Zhang YP**. 863 genomes reveal the origin and domestication of chicken. Cell Research, 2020,30(9):1-2. IF20.507
2. Wu DD, Yang CP, Wang MS, Dong KZ, Yan DW, Hao ZQ, Fan SQ, Chu SZ, Shen QS, Jiang LP, Li Y, Zeng L, Liu HQ, Xie HB, Ma YF, Kong XY, Yang SL, Dong XX, Esmailizadeh A, Irwin DM, Xiao X, Li M, Dong Y, Wang W, Shi P, Li HP, Ma YH, Gou X, Chen YB, **Zhang YP**. Convergent genomic signatures of high-altitude adaptation among domestic mammals. National Science Review, 2020, 7(6): 952-963. IF16.693
3. Hu JY, Hao ZQ, Frantz L, Wu SF, Chen W, Jiang YF, Wu H, Kuang WM, Li HP, **Zhang YP**, Yu L. Genomic consequences of population decline in critically endangered pangolins and their demographic histories. National Science Review, 2020, 7(4): 798-814. IF16.693
4. Luo J, Chai J, Wen YL, Tao M, Lin GL, Liu XC, Ren L, Chen ZY, Wu SG, Li SN, Wang YD, Qin QB, Wang S, Gao Y, Huang F, Wang L, Ai C, Wang XB, Li LW, Ye CX, Yang HM, Luo M, Chen J, Hu H, Yuan LJ, Zhong L, Wang J, Xu J, Du ZL, Ma ZS, Murphy RW, Meyer A, Gui JF, Xu P, Ruan J, Chen ZJ, Liu SJ, Lu XM, **Zhang YP**. From asymmetrical to balanced genomic diversification during rediploidization: Subgenomic evolution in allotetraploid fish. Science Advances, 2020, 6(22):1-11. IF13.116
5. Zhang SJ, Wang GD, Ma PC, Zhang LL, Yin TT, Liu YH, Otecko NO, Wang M, Ma YP, Wang L, Mao BY, Savolainen P, **Zhang YP**. Genomic regions under selection in the feralization of the dingoes. Nature Communications, 2020, 11(1)671. IF12.121
6. Yang XY, Rakha A, Chen W, Hou J, Qi XB, Shen QK, Dai SS, Sulaiman X, Abdulloevich NT, Afanasevna ME, Ibrohimovich KB, Chen X, Yang WK, Adnan A, Zhao RH, Yao YG, Su B, **Peng MS**, **Zhang YP**. Tracing the genetic legacy of the Tibetan Empire in the Balti. Molecular Biology and Evolution, 2020, doi: 10.1093/molbev/msaa313. IF11.062

1. 大规模基因组数据解析家鸡的驯化历史

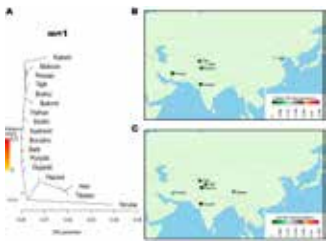
本课题组联合国内外研究人员，获得了不同原鸡、红原鸡亚种以及东南亚、南亚、中东、东亚、欧洲等地区家鸡的全基因组数据。大量的群体遗传学分析不支持家鸡多地区起源的模式；印度、中国北方等并非家鸡的起源地。家鸡是由红原鸡滇南亚种（*Gallus gallus spadiceus*）驯化而来。该亚种主要分布在中国西南、泰国北部以及缅甸，说明该地区很可能是家鸡的驯化中心。通过检测家鸡基因组中受人工选择作用的遗传信号，发现大量生殖相关基因，支持人类驯化促进家鸡生殖能力以及行为发生改变。 该工作引起国内外媒体的广泛关注，***Science*** 以 “Dawn of the chicken revealed in Southeast Asia” 为题做了专题报道。

【Wang MS et al. 2020 ***Cell Research***, IF= 20.507】



2. 巴尔蒂人群体基因组分析揭示吐蕃的扩张历史

为探讨吐蕃的扩张对青藏高原周边人群的影响，本课题组联合国内外研究人员，选取了生活在巴基斯坦北部巴尔蒂斯坦（古称勃律）的巴尔蒂人及其周边人群样本进行了基因组重测序。通过整合包括古代 DNA 在内的多种遗传变异数据，运用群体基因组学方法对巴尔蒂人群体历史进行了解析。结果显示，巴尔蒂人的形成受到一次藏族和克什米尔人的群体遗传混合事件的影响；其中藏族贡献了大约 22.6% – 26% 的遗传组分。混合时间估算为公元 869 – 1391 年间，时间发生在吐蕃控制勃律之后，但在巴尔蒂斯坦地区伊斯兰化之前。线粒体 DNA 和性染色体遗传标记的分析发现，源自藏族的男性和女性都参与了混合事件，并且男性贡献的比例要高于女性，符合男性主导的军事扩张的模式。



【Yang XY et al. 2020 ***Molecular Biology and Evolution***, IF= 11.062】

Molecular Evolution and Genome Diversity

Prof. Ya-Ping Zhang, Academician of Chinese Academy of Sciences (CAS), The World Academy of Sciences, and Academia Europaea. He serves as Vice President of CAS and the editorial board of ***Hum Mol Genet.*** He focuses on the origin, domestication and artificial selection of domestic animals, the local adaptation of animals, and the evolution of complex traits of animals. In 2020, Prof. Ya-Ping Zhang organized joint team to conduct series of evolutionary genomic researches on domestic animals, including the origins of chicken and dingo, as well as the high-altitude adaptation of livestock in the Tibetan Plateau. In addition, the joint team investigated pangolin conservation genomics and subgenomic evolution in allotetraploid fish. Prof. Ya-Ping Zhang published 19 SCI-indexed papers, including ***Cell Res*** **(1)**, ***Nat Commun*** **(1)**, ***Nat Sci Rev*** **(2)**, ***Mol Biol Evol*** **(2)**, and ***Sci Adv*** **(1)**.

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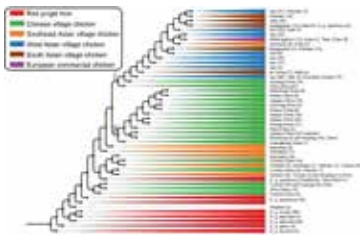
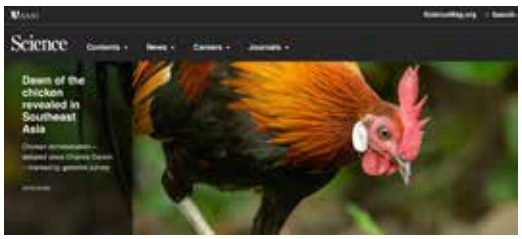
1. 863 genomes reveal the origin and domestication of chicken

We analyzed 863 genomes from a worldwide sampling of chickens and representatives of all four species of wild jungle fowl and each of the five subspecies of red jungle fowl (RJF). Our study suggests that domestic chickens were initially derived from the RJF subspecies *Gallus gallus spadiceus* whose present-day distribution is predominantly in southwestern China, northern Thailand and Myanmar. Following their domestication, chickens were translocated across Southeast and South Asia where they interbred locally with both RJF subspecies and other jungle fowl species. In addition, our results show that the White Leghorn chicken breed possesses a mosaic of divergent ancestries inherited from other subspecies of RJF. Despite the strong episodic gene flow from geographically divergent lineages of jungle fowls, our analyses show that domestic chickens undergo genetic adaptations that underlie their unique behavioral, morphological and reproductive traits.

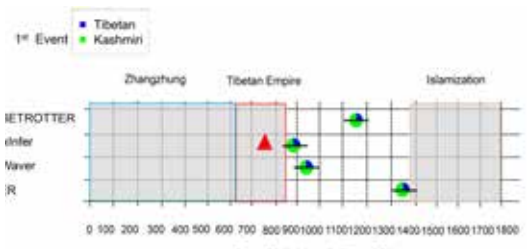
【Wang MS et al. 2020 ***Cell Research***, IF= 20.507】





2. Tracing the genetic legacy of the Tibetan Empire in the Balti

We sequenced 60 genomes for four populations from Pakistan and Tajikistan to explore their demographic history. We showed that the genomes of Balti people from Baltistan were comprised of 22.6% ~ 26% Tibetan ancestry. We inferred a single admixture event and dated it to about 39 to 21 generations ago, a period that postdated the conquest of Baltistan by the ancient Tibetan Empire. The analyses of mitochondrial DNA, Y, and X chromosome data indicated that both ancient Tibetan males and females were involved in the male-biased dispersal. Given the fact that the Balti people adopted Tibetan language and culture in history, our study suggested the impact of Tibetan Empire on Baltistan involved dominant cultural and minor demic diffusion.



【Yang XY et al. 2020 ***Molecular Biology and Evolution***, IF= 11.062】

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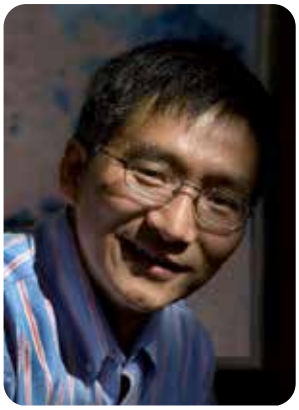
王凤娟　Wang,FJ
牛文静　Niu,WJ
姜香香　Jiang,XX
吴然燃　Wu,RR
David H Mauki



进化基因组学与基因起源

王 文，中国科学院昆明动物研究所，研究员、博士生导师，进化基因组学与基因起源学科组负责人。长期以来一直致力于进化基因组学的研究。目前已经在 *Science*、 *Nature Biotechnology*、*Nature Communications*、 *Nature ecology & evolution*、*Molecular plant* 等重要学术杂志上发表论文 210 余篇，2020 年在国际权威杂志上发表了论文 17 篇，其中 IF>10 的有 4 篇，包括 *Nature Communications* (2), *Science Advances* (1), *National Science Review* (1) 等。两项 973 项目首席科学家，国家基金委创新群体项目负责人，中科院战略性先导专项（B）两个首席科学家之一， 2012 年获得“国家自然科学二等奖”（第一完成人），2017 年获得两项“云南省自然科学二等奖”（分别为第一完成人和第二完成人），2019 年获得“云南省自然科学奖一等奖”（第三完成人）。

实验室主页：http://internal.kiz.ac.cn/wangw2013/WenWang_Labweb/page0002.htm

重要成果及产出：

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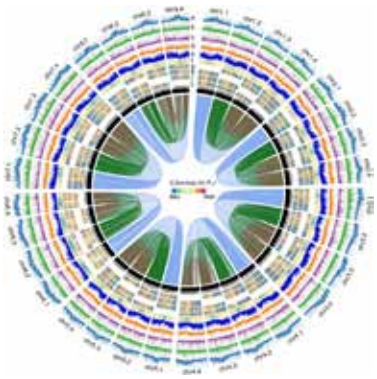
1. 苜蓿及水稻基因组资源的规模化挖掘及应用研究



通过大数据基因组资源挖掘与重要农艺性状相关的功能基因是现代作物遗传育种的重要方向。资源紫花苜蓿被称为“牧草之王”，但由于其同源四倍体、高杂合度及自交不亲和等特点，阻碍了其基因组及关键农艺性状相关的基因的挖掘以及新品种的培育。我们运用最新的测序技术，首次成功破译出我国地方特有品种“新疆大叶”的四倍体基因组，组装到 32 条染色体上，开发了基于 CRISPR/Cas9 的高效的基因编辑技术体系，通过精准敲除 *MsPALM1* 基因获得了一批多叶型新材料。而且杂交后代也稳定表现出多叶型性状且不含外源转基因片段。该成果对于通过大数据挖掘与优异农艺性状相关的基因以及加速培育优异紫花苜蓿新品种具有重大指导意义。水稻的 *OsTb1* 基因是玉米的驯化基因 *Tb1* 的直系同源基因，影响水稻分蘖。我们发现 *OsTb1* 在水稻驯化过程中不受到选择，但其重复基因 *OsTb2* 在陆稻适应陆地环境过程中受到人工选择，且该基因的自然变异与陆稻的分蘖数有关。过表达该基因的转基因稻的分蘖数增加。功能分析表明，*OsTb2* 蛋白通过与 *OsTb1* 蛋白相互作用正向调节分蘖，并抵消 *OsTb1* 蛋白在分蘖过程中的抑制效应。这些结果不仅展示了一个基因加倍以后形成相反新功能的案例，而且也表明在陆稻中 *Tb1* 基因的同源基因受到人工选择。

【Chen *et al*, 2020, ***Nature Communications***; Lyu *et al*, 2020, ***Nature Communications***.】

2. 昆虫重要表型特征（形态、生物荧光）适应性进化的遗传础研究

昆虫具有多样的形态特征来适应环境，我们以蝴蝶和发光甲虫为研究对象，通过整合形态、组学和功能实验等多层次数据，揭示了昆虫重要表型特征（形态、生物荧光）适应性进化的基因组基础。 以蝴蝶为例，在系统发育框架下利用 C 值探讨蝴蝶基因组大小进化的基础上，我们以枯叶蛱蝶为例，完成了首个包括 W 染色体的蝴蝶参考基因组，应用 CRISPR/Cas9 基因编辑技术证明多效基因 *ebony* 在生态适应中的重要意义，为探讨蝴蝶形态适应的遗传机制提供了重要的基因组资源。以发光甲虫为例，成功解析了两种萤火虫（云南扁萤、边褐端黑萤）高质量参考基因组，结合发光器官转录组和蛋白组数据、CRISPR/Cas9 基因编辑技术和三维形态构建等手段，提出更为完整的荧光素合成通路，并通过实验首次验证了萤火虫酰基辅酶 A 硫酯酶 1(ACOT1) 是荧光素构型（L- 荧光素转变成 D- 荧光素）转化的关键酶，为探讨荧光素和生物荧光的起源提供了新见解。

【Yang *et al*, 2020, ***Molecular Ecology Resources***; Zhang *et al*, 2020, ***Scientific Reports***.】

3. 棘皮动物发育过程中体型设计 (body plan) 的的遗传基础研究

棘皮动物具有非常特殊的体型结构，其在胚胎发育的早期展现出两侧对称的结构，而在发育后期转变成了辐射对称的结构。我们解析了海百合和绿海胆两种棘皮动物的高质量的参考基因组。比较基因组学和多组学数据分析的结果表明，棘皮动物具有较完整的 Hox 基因簇的分布，然而分析发现其辐射对称的成体结构并不是 Hox 基因簇造成其独特结构的原因。此外，我们发现棘皮动物体型结构确定的关键时期并不在其他动物保守的形态构建时期，暗示其并不遵守沙漏模型 (Hourglass model)，但是其辐射对称的构建却正常调用了其他两侧对称动物形态构建相似的一些关键基因。这些结果能够为我们更深入的理解动物复杂体型结构的演化奠定基础。【Li *et al*, 2020, ***Communications Biology***.】

Evolutionary Genomics and Origin of New Genes

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1. Large-scale exploration on genome resources in such crops as alfalfa and rice

Alfalfa (*Medicago sativa L.*), one of the most important crops, is challenging due to the lack of a reference genome and an efficient genome editing protocol, which mainly result from its autotetraploidy and self-incompatibility. We generate an allele-aware chromosome-level genome assembly for the cultivated alfalfa consisting of 32 allelic chromosomes by integrating high-fidelity single-molecule sequencing and Hi-C data. We further establish an efficient CRISPR/Cas9-based genome editing protocol on the basis of this genome assembly and precisely introduce tetra-allelic mutations into null mutants that display obvious phenotype changes. The mutated alleles and phenotypes of null mutants can be stably inherited in generations in a transgene-free manner by cross pollination. Our result will provide key foundations for accelerating research and molecular breeding of this important forage crop. The rice orthologue of maize domestication gene *Teosinte branched 1* (*Tb1*) affects tillering. But, unlike maize *Tb1* gene, it was not selected during domestication. Here, we report that an *OsTb1* duplicate gene (*OsTb2*) has been artificially selected during upland rice adaptation and that natural variation in *OsTb2* is associated with tiller number. Transgenic rice overexpressing *OsTb2* shows increased rather than decreased tillering. Functional analyses suggest that the *OsTb2* protein positively regulates tillering by interacting with the homologous *OsTb1* protein and counteracts the inhibitory effect of *OsTb1* on tillering. These results not only present an example of neo functionalization that generates an opposite function following duplication but also suggest that the *Tb1* homologue has been selected in upland rice.

2. Genomic basis of adaptive evolution of important phenotypic traits in insects

Insects are the most diverse group of animals on earth, and the adaptive evolution of their phenotypic traits is an important topic in biology. Due to their enigmatic phenotypic traits such as morphological diversity and bioluminescence, butterflies and luminous beetles have been one of the important groups for studying the adaptive evolution of species since the Darwin era. Using butterflies as case, we firstly investigated the evolution of genome size in a comprehensive phylogenetic context. Then, we assembled the chromosomal-level reference genome of dead butterfly *Kallima inachus*. This is the first butterfly genomes with all chromosomes including both candidate Z and W chromosomes assembled. The wings of adults with the pigmentary gene ebony knocked out using CRISPR/Cas9 showed mutated phenotypes in which the orange dorsal region and entire ventral surface darkened. Our results provide important genome resources for investigating the genetic mechanism underlying protective resemblance in dead-leaf butterflies and insights into the molecular basis of protective coloration. Fireflies are among the most charismatic insects for their spectacular bioluminescence, but the origin and evolution of bioluminescence remain elusive. Especially, the genic basis of luciferin (d-luciferin) biosynthesis and light patterns is largely unknown. Here, we present the high-quality reference genomes of two fireflies *Lamprigera yunnana* and *Abscondita terminalis* with great differences in both morphology and luminous behavior. We created the CRISPR/Cas9-induced mutants of *Abdominal B* gene without luminous organs in the larvae of *A. terminalis*. Combining gene expression analyses with comparative genomics, we propose a more complete luciferin synthesis pathway. Using experiments, the function of the firefly acyl-CoA thioesterase (ACOT1) to convert l-luciferin to d-luciferin was validated for the first time. Altogether, our results provide important resources for further exploring bioluminescence in insects.

3. Genetic basis of body plan transitions in echinoderms

Echinoderms are an exceptional group of bilaterians that develop pentameral adult symmetry from a bilaterally symmetric larva. Here we reported the green sea urchin (*L. variegatus*), a sea cucumber (*A. japonicus*) genome, and with particular emphasis on a sister group of the earliest-diverged echinoderms, the feather star (*A. japonica*). We learned that the last common ancestor of echinoderms retained a well-organized *Hox* cluster reminiscent of the hemichordate, and had gene sets involved in endoskeleton development. Further, unlike in other animal groups, the most conserved developmental stages were not at the body plan establishing phase, and genes normally involved in bilaterality appear to function in pentameric axis development. These results enhance our understanding of the divergence of protostomes and deuterostomes almost 500 Mya.

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比较基因组学

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实验室主页：http://159.226.149.45/compgenegroup/compgenegroup.htm

重要成果及产出：

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1、构建了藏族人群对高原低氧环境适应的染色质可及性全景图谱及其调控网络

对高原低氧环境适应的分子机制是进化和遗传领域的核心科学问题，自 2010 年以来，我们团队通过系统分析高原藏族人群生理表型和基因组学数据，挖掘了包括 EPAS1 和 EGLN1 在内的一系列与藏族高原适应相关的候选基因等特有遗传资源，并初步揭示了藏族人群对高原低氧环境的生理适应机制（Peng et al.2017; He et al.2018）。然而，鉴于已发现的绝大部分在藏族人群中富集的适应性突变都发生在非编码区域，为系统破译这些位点的分子调控机制和功能效应带来了极大挑战。随着多组学技术尤其是表观染色质状态和三维结构测序技术的发展和广泛应用，对解析这些非编码区域变异的调控机制带来了契机。为了系统解析藏族人群适应高原低氧的分子调控机制，中科院昆明动物所宿兵教授与中科院数学与系统研究院王勇教授、西藏大学崔超英教授等合作，利用脐带内皮细胞（HUVEC）的人工低氧环境模拟实验，采集了低氧处理不同时间节点上的细胞的多组学数据，包括基因组、转录组、染色质可及性（ATAC-seq）和染色质空间构象（Hi-C）数据，进一步发展了一种新型方法论框架：vPECA，即整合细胞的基因组 - 表观组 - 转录组 - 表型层面的数据，构建以受选择调控元件为核心的基因调控网络模型，对藏族人群对高原低氧环境适应的调控机制进行了系统分析。我们利用该模型进一步发现了 EPAS1 基因的 3 个位于增强子区域的功能位点，这 3 个位点通过削弱所在区域的染色质开放程度（可及性），进而下调 EPAS1 的表达，从而避免藏族人群在高原低氧环境红细胞的过度增生。同时，利用该模型还构建了 EPAS1 基因的下游调控网络，解析了下游受选择靶基因的调控机制。该研究提供了一个群体遗传数据结合特定细胞环境多组学数据的研究范例，包括基于多组学数据系统破译非编码区变异位点的调控方式和基于组学数据动态变化特征构建基因调控网络的统计模型，为今后利用多组学整合数据分析挖掘特定遗传资源提供了一个非常有效的工具。同时，该研究进一步揭示了 EPAS1 对藏族低氧适应的贡献，并系统解析了低氧适应的调控网络，为高原藏族人群中的特有遗传资源挖掘和低氧通路的调控机制研究提供了重要的基础数据。研究成果发表在 ***Nature Communications*** 11, 4928 (2020)。

2、古 DNA 研究发现新石器晚期青藏高原东北部存在热带大型哺乳动物的证据

史前人类向青藏高原扩散的历史及其对动植物资源利用的方式是国际学术界关注的热点科学问题。 宿兵研究员课题组张晓明副研究员与兰州大学环境考古团队（董广辉 - 教授 / 陈发虎 - 院士）和西北农林科技大学动物科技学院（雷初朝 - 教授）合作，对位于甘肃省岷县山那树扎遗址的 10 个大型牛科动物和 2 个犀牛科动物骨骼标本开展了古 DNA 研究。发现出土的 10 个大型牛科动物遗骸均属于现今只栖息于南亚和东南亚热带雨林地区的印度野牛，而 2 个犀牛遗骸属于现今野外大约只有 100 多头、只分布在印度尼西亚苏门答腊岛和婆罗洲的濒危动物苏门答腊犀牛，是亚洲现存唯一双角犀和体型最小的犀牛。群体动态变化历史分析显示，该古代印度野牛群体规模在约 2 万年前开始下降，与末次冰盛期的年代相符，并在约 5 千年前发生急剧下降并延续了较长的时间，与青海湖记录的 5,000-3,600 年前大幅度气候震荡的时间相吻合。物种间的基因流分析显示，此古代印度野牛群体与牦牛和西藏黄牛并不存在基因交流，从而推测前者与后两者可能存在时空上的生态位隔离。该研究首次表明，现今只分布在热带地区的野生大型哺乳动物约在 5 千多年前曾生活于青藏高原东北部，成为马家窑文化先民重要的狩猎资源。通过系统比较古气候和动物考古数据，研究团队提出约 5,200 年前较高的夏季温度和温暖湿润的宜人气候可能促使印度野牛和苏门答腊犀牛等许多热带动物分布于较高纬度的地区，丰富了该地区的野生动物多样性，为当时的先民提供了丰富的狩猎资源，使得新石器时代晚期的青藏高原东北部成为东亚地区最后的狩猎场之一。此后，约 5 千到 4 千年前，在气候恶化（寒冷 / 干燥）和人类活动增强等多重影响下，青藏高原东北部野生动物多样性显著下降，牧业活动取代狩猎活动成为该地区先民获取肉食资源的主要方式。研究成果发表在国际知名综合学术期刊 PNAS，并被选为当期导读文章。该成果系青藏高原地区首次大型动物古 DNA 全基因组测序分析的工作，是遗传学（古 DNA）、考古学、古气候学和地理学等多学科交叉合作的范例，对认识中晚全新世野生动物地理格局、气候变化和人类活动之间的互作关系具有重要的学术价值。

Comparative Genomics

Dr. Bing Su, principal investigator, The enlarged brain and highly developed cognitive skills are the most significant characteristics that set us apart from our relatives, the non-human primates. This evolutionary expansion is believed to be crucial to the highly developed cognitive abilities in humans, yet its genetic basis remains unsolved. our laboratory focuses on (1) the genetic mechanism underlying the dramatic enlargement of human brain and its highly developed cognitive skills during human evolution; (2) Origins and migration of modern human populations in East Asia and its adaptation to environmental stress.
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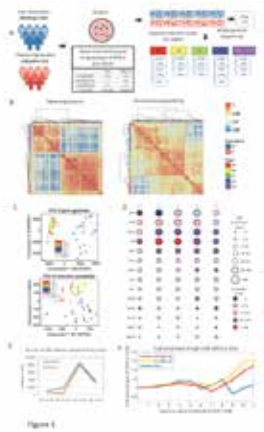
1. Chromatin accessibility landscape and regulatory network of high-altitude hypoxia adaptation



Tibetans' adaptation to high-altitude environment at the Qinghai-Tibetan plateau by a distinct suite of physiologic traits represents a remarkable case of natural selection during recent human evolution. Previous genome-wide scan found many genetic variants with the strongest selection signals lying within non-coding regions. This indicates the pressing need to reconstruct the process of regulatory element (RE) regulating gene expression with challenges in unknown cell type of action, relevant pathway, target gene, causality, and mechanism. We generated time series of paired ATAC-seq and RNA-seq data with WGS data in Tibetan and Han Chinese's umbilical endothelial cells from normoxia to hypoxia condition and presented the chromatin accessibility landscape and multi-stage dynamics under hypoxia. We further developed a variants interpretation model by Paired Expression and Chromatin Accessibility data (vPECA) to identify active REs (AREs) and active selected REs (ASREs) and their associated gene regulatory network. vPECA revealed the regulatory mechanism of EPAS1, the major-effect gene for high altitude adaptation, that three causal SNPs decrease the ASRE's accessibility, weaken the TF binding strength, and down-regulate EPAS1's expression. EPAS1's functional AREs and ASREs, validated by luciferase reporter assay and Hi-C experiments, cooperatively achieve delicate down-regulation pattern for high-altitude adaptation and causally interpret the positively selected SNPs. Furthermore, the reconstructed genome-wide network elucidates how EPAS1 drives down-stream TFs and genes via AREs for hypoxia response, angiogenesis, broad functional processes and pathways, and far reaching GWAS traits/phenotypes. Taken together, we have provided genome-wide hypoxia regulatory network with AREs and ASREs as a resource to characterize the effect of genetic variants in high-altitude adaptation, and suggested a systematic approach to understand the large-scale maps of noncoding variants by modeling omics data in proper cell types and dynamic condition for its act on gene regulation. (Figure 1). **Xin et al.** ***Nature Communications*** **11, 4928 (2020).**

2. Ancient genomes reveal tropical bovid species in the Tibetan Plateau contributed to the prevalence of hunting game until the late Neolithic

Local wild bovids have been determined to be important prey on the northeastern Tibetan Plateau (NETP), where hunting game was a major subsistence strategy until the late Neolithic, when farming lifestyles dominated in the neighboring Loess Plateau. However, the species affiliation and population ecology of these prehistoric wild bovids in the prehistoric NETP remain unknown. Ancient DNA (aDNA) analysis is highly informative in decoding this puzzle. Here, we applied aDNA analysis to fragmented bovid and rhinoceros specimens dating ~5,200 y B.P. from the Neolithic site of Shannashuzha located in the marginal area of the NETP. Utilizing both whole genomes and mitochondrial DNA, our results demonstrate that the range of the present-day tropical gaur (Bos gaurus) extended as far north as the margins of the NETP during the late Neolithic from ~29°N to ~34°N. Furthermore, comparative analysis with zooarchaeological and paleoclimatic evidence indicated that a high summer temperature in the late Neolithic might have facilitated the northward expansion of tropical animals (at least gaur and Sumatran-like rhinoceros) to the NETP. This enriched the diversity of wildlife, thus providing abundant hunting resources for humans and facilitating the exploration of the Tibetan Plateau as one of the last habitats for hunting game in East Asia (Figure 2). **Chen et al.** ***PNAS*** **117, 28150–28159 (2020).**

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进化与功能基因组学

施　鹏，研究员，中科院昆明动物研究所党委书记、副所长，遗传资源与进化国家重点实验室主任，进化与功能基因组学科组负责人。2013 年获国家杰出青年基金，2014 年获科技部中青年科技创新领军人才，2016 年入选中组部万人计划，2017 年入选人社部“国家百千万人才”，2019 年入选云南省“万人计划”- 云岭学者。长期从事进化基因组学和功能基因组学研究。本研究室的研究兴趣集中在以下两个方向：（1）利用新一代测序技术，运用自然选择理论在基因组范围内探讨基因型和表型的关系，结合生物信息学和功能实验的方法来研究动物适应环境的分子机制；（2）通过对非模式生物的基因组研究，从新的视角理解人类长寿、心血管疾病和肿瘤的发病机理及新的疾病相关基因资源的挖掘。

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1. 小丑鱼繁育平台搭建

为了进一步开展小丑鱼表型分化与斑纹形成机制的研究，我们搭建了全新的小丑鱼繁殖平台，采用并联的方式连接各个繁殖缸，通过一个统一的水质处理中心维持系统健康。水质处理中心利用红树和藻类完成主要的营养盐抹除工作，辅以蛋白质分离器确保水质保持最优。现已成功配对饲养了 8 种来自西太平洋和东印度洋海域的小丑鱼物种以及多个种内突变型，共计 25 对种鱼及部分未配对个体。在入冬前，白条双锯鱼已开始产卵，其余物种均有护巢和清理巢穴行为。该系统的搭建为将来深入研究小丑鱼表型形成机制提供了条件。待实验室各个物种小丑鱼实现稳定产卵后，可使用受精卵展开基因编辑的相关研究；同时，结合目前实验室的墨西哥脂鲤功能验证平台，以及繁殖的小丑鱼子代个体，可进行表型的遗传学分类和筛选，并利用 GWAS 和 AI 表型识别技术开展斑纹相关基因型和表型的关联研究。

图 1. 小丑鱼繁育平台

2. 青藏高原土著物种低氧适应的分子机制解析

为了阐明青藏高原特有的土著哺乳动物适应高寒、低氧、强辐射等严酷环境背后的分子机制，我们以高原鼢鼠和高原鼠兔等为研究对象，利用比较基因组学、群体基因组学、转录组学、宏基因组学及遗传操作等方法，解析不同遗传元件在高原适应中的作用及其调控关系。通过收集高原鼢鼠不同海拔群体的生理表型数据，我们发现高原鼢鼠在栖息于 3700 米以上时有显著的心脏体重比变化，在栖息于 4300 米左右时有红细胞表型的变化，进一步通过群体基因组学的方法，我们解析了这些适应性生理表型的遗传基础。利用二代及三代长读长测序技术，我们构建了高原鼢鼠及高原鼠兔的高质量参考基因组草图。结合已发表的牦牛、藏羚羊基因组，我们发现一些重要基因如视黄醇饱和酶 (RETSAT) 在这 4 个高原野生哺乳动物中发生了相同的（Q247R）趋同进化。通过构建携带此突变的 Knock-in 小鼠模型，我们发现 Knock-in 小鼠相较于野生型对照来说，具有更高的心脏体重比、更低的肺动脉压，且在急性低氧条件下存活时间更长，提示该突变对适应高原低氧环境可能具有重要作用。

3. 高原鼢鼠调控网络数据库的建立

以海拔 3300 米的高原鼢鼠的高质量基因组为蓝本，结合脑、心、肝、肾和肺中的转录谱数据，我们构建了一个集成的资源数据库 ZokorDB，用于高原鼢鼠的组织特异调控网络的注释。经由与其最近的基因和上游转录因子 motif 结合位点，我们对高原鼢鼠保守的非编码元件进行了注释。通过 ZokorDB，我们提供了一个通用的基因调控网络，即潜在转录因子与非编码的调控元件结合，继而调控靶基因的表达。此外，我们结合小鼠 ENCODE 项目中匹配的 RNA-seq 和 DNase-seq 数据，对高原鼢鼠基因调控网络进行了改进，重建了 5 个组织特异性调控网络。我们建立的高原鼢鼠非编码区域注释方案对其他非模式物种的研究具有重要的参考价值。为了方便地搜索、可视化和下载注释和数据，我们将该数据库免费向公众提供，所有数据可通过网站 (bigd.big.ac.cn/zokordb/) 免费获取。

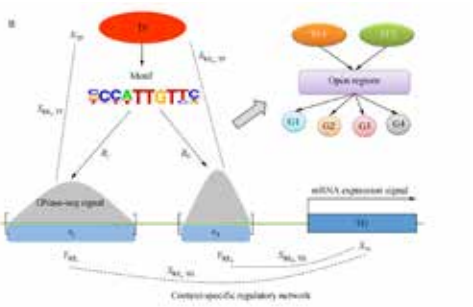

图 2. 高原鼢鼠非编码元件的调控示意图

重要成果及产出：

Xin JX[1], **Hao JJ**[1], Chen L, Zhang T, Li L, Chen LN, Zhao WM, Lu XM, **Shi P*** and Wang Y*(2020). ZokorDB: tissue specific regulatory network annotation for non-coding elements of plateau Zokor. ***Quant Biol*** , 8(1): 43–50.

Evolutionary and Functional Genomics

Prof. Peng Shi, Principal Investigator, has long been engaged to the researches on evolutionary and functional genomics. The work in Shi's laboratory covers two fields:

(1) molecular mechanism of adaptation to various environments in animals. We study the genotype-phenotype relationship at the genomic level under the guidance of natural selection theory, while combining multiple advanced techniques including NGS, bioinformatics and functional assays, etc.

(2) novel disease-related gene identification and the etiopathogenesis study. Through genomic analyses using non model organisms, we try to aid the comprehensive understanding of the etiopathogenesis in human longevity, cardiovascular diseases and tumors from a different angle.

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1.The setup of the breeding platform for clownfish

In order to further study the phenotypic differentiation and stripe formation mechanism of clownfish, we built a new clownfish breeding platform. The system connects each breeding tank in parallel, and there is a unified water treatment center to maintain the system healthy. The water treatment center completes the main part of nutrient removal work through mangrove and algae, and assists the protein skimmer to ensure the optimal water quality. Till now, eight species of clownfish from the Western Pacific and the eastern Indian Ocean have been successfully bred, including 25 pairs and several unpaired individuals. Before winter comes, the fish species *Amphiprion frenatus* have begun to lay eggs, and the rest species have exhibited nest protection and nest cleaning behaviors. The establishment of the breeding platform would benefit our future studies on the mechanism of phenotype formation in clownfish. Once the various species of clownfish bred in the laboratory can lay eggs stably, the fertilized eggs can be used to carry out gene editing experiments. Meanwhile, combining the *Astyanax spp.* raised in the laboratory as a functional verification platform and the offspring of clownfish, we can perform genetic classification and screening of phenotypes, and use GWAS and AI phenotype recognition technology to conduct the association studies of stripe-related genotypes and phenotypes.

2.The molecular mechanism underlying hypoxia adaptation of endemic species on Qinghai-Tibet Plateau

There are harsh environmental conditions such as extreme cold, hypoxia and high radiation on Qinghai-Tibetan plateau (QTP) whilst the indigenous species living on it adapted well to such extreme conditions. In order to dissect the molecular mechanism underlying their adaptation, we used plateau zokor and plateau pika as subjects and analyzed the role and regulatory relationship of different genetic components in plateau adaptation by means of comparative genomics, population genomics, transcriptomics, metagenomics and genetic operation. Collecting physiological data from groups of plateau zokor living at different altitudes, we found that zokor populations inhabit at 3700m or higher have significant elevation of the ratio of heart mass to body mass, while populations inhabit at extreme-high altitude (4300m) have phenotypic alteration related to red blood cells. We further identified the genetic components which possibly result in those phenotypic alterations.

By *de novo* assembling the draft genomes of plateau zokor and plateau pika and comparing with published yak and Tibetan antelope genomes, we identified that All-Trans-Retinol 13,14-Reductase (RETSAT) were convergently evolved in these four QTP endemic mammals. The knock-in mouse model with the modification of the single convergent nucleotide in RETSAT was constructed and it exhibited larger ratio of heart mass to body mass, lower pulmonary pressure and longer survival time under acute hypoxia. These results suggest that the convergent alteration possibly plays an important role in hypoxia adaptation on plateau.

3.Construction of an integrated database for zokor regulatory network annotation

Based on a high-quality draft genome of a plateau zokor at 3,300 m and its transcriptional profiles in brain, heart, liver, kidney and lung, we provided an integrated resource, ZokorDB, for tissue specific regulatory network annotation for zokor. The conserved non-coding elements of zokor were annotated by their nearest genes and upstream transcriptional factor motif binding sites. ZokorDB provides a general draft gene regulatory network, i.e., potential transcription factor binds to non-coding regulatory elements and regulates the expression of target genes. Furthermore, we refined the gene regulatory network by incorporating matched RNA-seq and DNase-seq data from mouse ENCODE project and reconstructed five tissue-specific regulatory networks. The pipeline of non-coding region annotation for zokor will be useful for other non-model species. As a web-based, open-access database for easily searching, visualizing, and downloading the annotation and data, ZokorDB is freely available at the website (bigd.big.ac.cn/zokordb/).

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真核细胞进化基因组学

文建凡，博士，研究员，遗传资源与进化国家重点实验室副主任。研究方向为“ 真核细胞进化基因组学 ”。以处在真核生物进化的关键地位的单细胞生物 (如贾第虫、衣藻、眼虫、领鞭毛虫等) 为主要研究对象，向下追溯到原核生物，向上扩展到多细胞生物，开展真核细胞的结构和功能，特别是基因、基因家族、功能途径基因群和基因组的多样性形成与进化研究，以及从适应性进化角度开展有害生物 (如寄生虫) 防治靶标的发掘利用，有益生物 (如藻类) 的高效、特异代谢途径的进化形成机制及其应用的基础研究。

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重要成果及产出：

1. **Feng J-M[1], Yang C-L[1], Tian H-F, Wang J-X, Wen J-F*.** Identification and evolutionary analysis of the nucleolar proteome of *Giardia lamblia*. ***BMC Genomics***. 2020. 21(1):269 .
2. **Lyu Z-X[1], Cheng J-N[1], Shao J-R, Ye Q-Q, Bai H-X, Wen J-F*.** An investigation of the prevalence of *Giardia agilis* in anuran amphibians from fourteen areas in China. ***International Journal for Parasitology: Parasites and Wildlife***. 2020. 12: 46–52.
3. **Lyu Z-X, Wen J-F*.** A rapid and inexpensive method for the isolation and identification of *Giardia*. ***MethodsX***. 2020. 7: 100998.

1. 三种宿主范围嵌套的贾第虫的比较基因组学研究

本实验室之前发现了一新种 —— 仓鼠贾第虫，通过单细胞测序技术测定其基因组。我们将宿主范围呈现宽窄嵌套的三种贾第虫的基因组进行系统的比较基因组学分析，发现它们的寄生适应性相关的一部分基因方面出现了分化，如：变异特异性表面蛋白家族、半胱氨酸蛋白酶家族、非有丝分裂激酶家族家族、锚蛋白重复蛋白家族、高半胱氨酸膜蛋白家族、高半胱氨酸蛋白家族、腹部吸盘蛋白和包囊壁蛋白；而三种贾第虫也有一部分与寄生适应性相关的基因未分化，如：贾第素家族、微管蛋白家族和鞭毛转运蛋白。通过系统的预测和比较了贾第虫的代谢途径，我们发现三种贾第虫的绝大多数代谢途径的基因在数量上都是一致的。有趣的是，仅有仓鼠贾第虫具有完整的脂肪酸从头合成的代谢途径，我们通过多种实验方法确证该代谢途径发挥了生理功能，并通过分析证明该代谢途径是在贾第虫线粒体退化的过程中被保留了下来的。在大量工作的基础上，我们总结了贾第虫的寄生策略在其物种进化形成过程中发生的多次分化，揭示了三种贾第虫在进化过程中它们各自基因组所发生的一系列变化。

图 1. 三种贾第虫宿主范围示意图

图 2. 三种贾第虫共有基因与特有基因

	蓝氏贾第虫	鼠贾第虫	仓鼠贾第虫
fabZ	-	-	+
fabI	-	-	+
fabD	-	-	+
fabG	-	-	+
fabH	-	-	+
fabF	-	-	+
accC	-	-	+
long-chain acyl-CoA synthetase	+	+	+

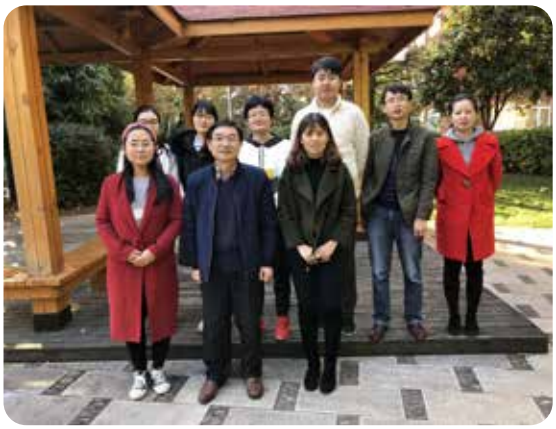
表 1. 三种贾第虫脂肪酸从头合成途径的基因

2. 绿藻混合营养和两栖营养的甄别与比较

微藻可以进行多种营养代谢方式，主要分为自养、异养和混合营养三种。长期以来，人们一直认为在光照条件下提供有机碳源时，藻细胞进行的就是混合营养生长，即自养和异养同时进行。绿藻 *Auxenochlorella protothecoides* 是一种高产油微藻，多数研究认为该藻具有混合营养生长的能力，然而还有研究表明该藻在外源葡萄糖存在时光合作用受到了抑制，只能进行异养生长，并称这种营养方式为两栖营养。那么这种两栖营养是否存在，与混合营养到底有怎样的区别，实际上仍不清楚。我们以最常用的两种有机碳源 —— 葡萄糖和乙酸对 *A. protothecoides* 进行了三种培养条件下的对比实验。通过比较不同碳源和光照条件下藻细胞的生长情况，我们发现在光照条件下添加乙酸时，藻细胞的生长速率和细胞干重均显著高于乙酸异养，且大于自养与乙酸异养之和；而在光照条件下添加葡萄糖时，藻细胞的生长速率和细胞干重与葡萄糖异养无显著差异。该结果表明，光照条件下同一种微藻在利用不同有机碳源时进行的营养方式可以是不同的：当碳源为乙酸时，*A. protothecoides* 进行的是混合营养生长；而当碳源是葡萄糖时，只能进行以异养生长为主的两栖营养。因此，微藻的营养方式不仅与藻的种类有关，还与有机碳源的种类有关，不能简单地认为某种微藻具有混合营养能力还是两栖营养能力。

Evolutionary Genomics of Eukaryotic Cells

Prof. Jian-Fan Wen, Principal Investigator, Vice Director of the State Key Laboratory of Genetic Resources and Evolution. His group is mainly interested in the origin and evolution of the eukaryotic cell. Taking the protists, which occupy key positions in the eukaryotic cell evolution, as models, and combining with the data of prokaryotes and multicellular organisms, they study the biodiversity and origin and evolution of the structures and functions, especially of genes, gene families, gene groups of functional pathways and genomes, of the eukaryotic cells. Based on these basic studies, they also explore the new ways for the control and treatment of some harmful organisms (e.g. parasitic protozoa and schistosomes) and the applications of the effective and specifc metabolic pathways.



1. Comparative genomic researches of three Giardia species with nesting host range

Our lab found a new species, *G. cricetidarum*. We sequenced the genome of *G. cricetidarum* using single-cell sequencing technique. Systematic comparative genomic analysis of the genomes of three *Giardia* species revealed that some of their genes showed diversification which were associated with parasitic adaptations of *Giardia*, including VSPs, CPs, NEKs, ARPs, HCMPs, HCPs, ventral disc proteins and cyst wall proteins; there is no diversification of the three *Giardia* species in giardins, microtubulins and flagellar transport proteins. We systematically predicted and compared the metabolic pathways of the three *Giardia* species, and found that the gene numbers of majority of core pathways were same in all three *Giardia* species. However, only *G. cricetidarum* has an intact metabolic pathway for de novo synthesis of fatty acids. We confirmed this metabolic pathway in *G. cricetidarum* are function physiologically by many experiments, and the phylogenetic analysis indicated that these genes are conserved during mitochondrial degradation during its evolution. Above all the works, we summarize diversifications about parasitic strategies of *Giardia* in the genomes during the evolution.

2. Distinguishment and comparison of mixotrophy and amphitrophy in green algae

Microalgae can carry out a variety of trophic modes, which are mainly divided into three types: autotrophy, heterotrophy and mixotrophy. It has long been held that algae cells grow mixotrophically when an organic carbon source is provided under light condition, that is, autotrophic and heterotrophic growth proceed simultaneously. The green algae *Auxenochlorella protothecoides* is an important oleaginous microalga. Most studies suggest that it can grow mixotrophically. However, some studies have shown that this alga cannot utilize light in the presence of exogenous glucose, a trophic mode which is called amphitrophy. It's still unclear whether this amphitrophy exists, and how it differs from mixotrophy. We conducted comparative experiments on *A. protothecoides* under three culture conditions with the two most commonly used organic carbon sources—glucose and acetate. By comparing the growth of algae cells under different carbon sources and light conditions, we found that when acetate was added under light conditions, the growth rate and cell dry weight were significantly higher than that of heterotrophic growth on acetate, even greater than the sum of those under photoautotrophic and heterotrophic conditions. When glucose was added under light conditions, the growth rate and dry cell weight were not significantly different from that of heterotrophic growth on glucose. These results show that an alga can perform different trophic modes when using different carbon sources under light condition: *A. protothecoides* performs mixotrophic growth with acetate as the organic carbon source, while when the organic carbon source is glucose, only amphitrophy in which heterotrophy plays the dominant role can be carried out. Therefore, the trophic mode of microalgae is not only depended on the species of algae, but also related to the type of organic carbon source. It cannot be considered simply that an alga has the ability of mixotrophy or amphitrophy.

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计算生物与医学生态学科组

马占山，研究员，博导，计算生物与医学生态学学科负责人。 2010 年 11 月中科院“百人计划(引进杰出技术人才)”引进。2011 年入选“云南省高端科技人才”和“百名海外高层次人才”计划；2015 年入选“云岭产业技术领军人才”; 2020 年获得美国哈佛大学 *Bullard Fellowship* 奖。美国 Idaho 大学计算机科学 (2008 年) 和昆虫学 (1997 年) 双博士、计算机科学和计算生物学研究科学家。并具有在硅谷等地长达八年多的涵盖电子、网络、软件、信息安全领域的计算机高级工程师经历。曾是美国“人类微生物菌群宏基因组研究计划 (HMP) 主要研发科学家之一 (2008-2010)，总部设在英国伦敦的 *Faculty 1000 of Biology & Medicine* 成员 (2008-2016)，并担任 *I. J. Network Science* 主编 (2015-2017)。现任 *PeerJ Computer Science* 和 *PeerJ* 编委。以第一或通讯作者在计算生物（生态）学、计算机科学、工程数学、计算智能、昆虫学、医学微生物学等领域发表近百篇论文。

重要成果及产出:

1. Ma ZS (2020) Predicting the Outbreak Risks and Inflection Points of COVID-19 Pandemic with Classic Ecological Theories. *Advanced Science*, 7(21):1-15
2. Ma ZS (2020) Critical network structures and medical ecology mechanisms underlying human microbiome-associated diseases. *iScience*, 2020 23(6):
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14. Ma ZS (2020) Assessing and interpreting the metagenome heterogeneity with power law. *Frontiers in Microbiology*, 10.3389/fmicb.2020.00648
15. Zhang Y, Zhang Z, Li LW , … Li JL (2020) Selective loss of 5hmC promotes neurodegeneration in the mouse model of Alzheimer's disease. *FASEB*
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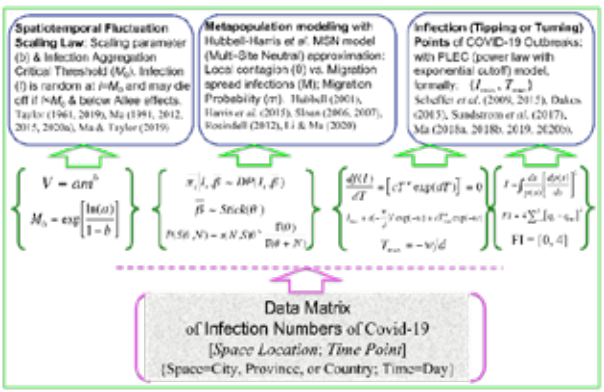
17. Luo J, Chai J, … Zhang YP (2020) From asymmetrical to balanced genomic versification during rediploidization: Subgenomic evolution in allotetraploid fish. *Science Advances*. DOI: 10.1126/sciadv.aaz7677

COVID-19“爆发拐点”及“聚集感染临界水平”等的预测

该研究主要解决了新冠肺炎流行预测领域如下三项难题：（1）流行拐点预测，即何时达到感染高峰拐点，高峰感染数量是多少？（2）聚集感染临界点，即如果超越临界点则可能导致流行爆发，控制在临界点之下则可能将其清零、从而避免大规模爆发。（3）评估社区接触传染与远程输入传染的相对重要性。 这些问题具有显而易见的实际意义，特别是流行拐点和聚集感染临界点的预测也是疫情期间人们通常所关注的问题 [Ma ZS (2020) Predicting the outbreak risks and inflection points of COVID-19… *Advanced Science*]



首次揭示由 SIV/HIV 感染所触发的肠道菌群迁移模式及概率

在正常情况下（也就是在健康人体中），肠道菌群会受到肠粘膜屏障的严密控制，同时免疫系统也严正以待，此时它们各司其职，表现得忠诚友善。然而，一旦受到宿主内外环境的影响，尤其是免疫系统出现漏洞或受到类似 HIV/SIV 病原体攻击时，肠粘膜屏障极易出现损伤，此时肠道菌群很可能会逃离“兵营”。其后果正像从战场上逃逸的士兵一样，当中的一些或许会掉转枪头，对“老东家”下手。

学科组博士生李文迪最新一项研究试图回答如下问题：（1）受 HIV/SIV 病毒感染后，肠道菌群中微生物逃逸（学术名词是“菌群易位”or microbial translocation) 是有计划、有组织的逃逸，还是近乎无序的随机游离？（2）可否从理论上估计出迁移概率以及迁移比例。研究通过理论建模分析，首次对以上问题作出了较为合理的回答。

当宿主感染了 SIV/HIV 后，胃肠道黏膜中的 CD4+ T 细胞会迅速衰减，黏膜免疫被过度激活，持续性的炎症反应诱发上皮细胞凋亡和紧密连接中断，从而使得黏膜上皮完整性被破坏（“肠漏”）；与此同时，肠道内环境紊乱也致使其内部栖息的菌群失调，益生菌数量骤减，机会性病原菌逐渐占据主导地位。这一系列的免疫病理过程最终导致胃肠道内微生物发生逃逸。通过分析 SIV 感染的猕猴的多组织（包括肠道、肠系膜淋巴结和肝脏）菌群数据，该项研究发现微生物从胃肠道逃逸到其他组织的过程类似于物理学中的随机游动 (random walk)。也就是说，虽然肠道微生物逃逸很可能是由于 SIV 感染导致的，但逃逸的过程是随机的、并非有组织地确定性迁移。此外，该研究还发现菌群从胃肠道逃逸至肠系膜淋巴结或肝脏的概率（即迁移率，在属水平均 >0.5）显著高于菌群在胃肠道内部的扩散率（在属水平 =0.01），并且胃肠道菌群中有接近 23% 的菌门和 55% 的菌属可能会从胃肠道逃逸至肠系膜淋巴结和肝脏。Li WD & Ma ZS (2020) A theoretic approach to the mechanism … *FEMS Microbiology Ecology*, Vol. 96(8).

Computational Biology and Medical Ecology Lab

Bio-sketch of the Lab Principal Investigator: **Zhanshan (Sam) Ma** received his double PhDs in Computer Science, and Entomology in 2008, and 1997, respectively, both from the University of Idaho (UI), USA. In November 2010, he was retained as Professor and Principal Investigator by Kunming Institute of Zoology (KIZ), the Chinese Academy of Sciences (CAS) through "The 100 Talents PI Program" of the CAS. Prior to joining in KIZ, he was a Research Scientist (in Computational Biology & Computer Science) at the UI. He was a senior network and software engineer from 1998 to 2006 in the computer industry in Silicon Valley, USA. Dr. Ma has been keeping dual track publishing in both Computer Science and Biology with over 100 peer-refereed papers in premier journals such as *IEEE Transactions on Reliability*, *Science Translational Medicine*, *The ISME Journal, Ecological Monographs,* and *Advanced Science*. He was a member of London-based "*Faculty 1000 of Biology and Medicine*". He is a recipient of the 2020 Bullard Fellowship Award from Harvard University in the USA.

揭示“非乳酸杆菌占优势”的女性抵御 BV 菌群失调的潜在机制

细菌性阴道炎（BV=Bacterial Vaginosis）系常见的女性生殖道疾病，据相关调查，其发生率可能高达 30%。BV 的潜在危害，除了施加于患者在生理和心理层面的生活质量影响外，还包括增加早产、性病传播、HIV 感染等的风险。然而，目前对于 BV 的发病机制仍无明确定论。早期的一些研究常将 BV 与一类生殖道菌群联系在一起，因为它们有着相似的群落结构：主要由厌氧和兼性厌氧的微生物组成，乳酸杆菌缺失或含量较低，整体具有较高的物种多样性，以及阴道 pH 值的升高。早期关于 BV 发病机制的研究还基于另一项经典认知：健康妇女的阴道环境应该是酸性，而正是阴道菌群中大量乳酸杆菌的存在维持了这种酸性的 pH。因此，传统上，乳酸菌的优势通常被认为是健康阴道菌群的标志之一，而乳酸菌的缺失则认为是 BV 风险的标志！近年来人类菌群宏基因计划研究计划（HMP）对以上提及的传统认知提出了严重挑战：首先，研究发现，许多健康妇女（非 BV 患者）阴道菌群并非乳酸杆菌占优，特别是非洲裔妇女。甚至有研究发现，各族裔妇女在阴道 pH 值也有差异。需要指出的是，在许多非人类灵长类动物中，酸性环境并非常态。然而，HMP 研究并不能解释为什么乳酸菌的缺失不一定代表 BV 高风险；换句话说，那些乳酸菌不占优的阴道菌群是如何抵御 BV 的?

针对这一关键问题，博士研究生李文迪利用 “ 优势度网络分析框架 (Ma & Eillson 2019: Ecological Monographs)” 从菌属和菌种两个水平，重新分析了 Doyle et al. (2019) 的数据。该研究发现在 “ 非乳酸菌占优的阴道菌群 ”nLDVM(non-*Lactobacillus* dominated vaginal microbiome) 中加德纳菌（*Gardnerella*）被 23 个菌属联合抑制，而乳酸杆菌则被 15 个菌属联合抑制。加德纳菌是与 BV 关系最为密切的病原菌之一，它与乳酸杆菌都有成为生殖道菌群优势物种的潜力。对它们二者抑制作用的存在可能是 nLDVM 杜绝菌群内部出现绝对优势物种、保持高物种多样性的潜在机制。该研究发现在 nLDVM 内，与加德纳菌和乳酸杆菌呈合作互惠关系的菌属极少，而它们二者是彼此间为数不多的同伴之一。具体到物种水平，与加德纳菌合作且被其他物种抑制的乳酸杆菌为 *Lactobacillus iners*。由此可见对于 nLDVM 而言，*Lactobacillus iners* 或许与加德纳菌一样都是潜在的 “ 敌人 ”，对它们的抑制作用或许是 nLDVM 维持稳定和健康的一种自我保护机制。 此外，该研究还找到了 nLDVM 优势度网络的骨架结构和由高显著骨架所组成的通路， 其中 *Finegoldia* 菌和 *Staphylococcus epidermidis* 是该骨架结构的核心，虽然目前关于它们的研究十分有限，但它们在 nLDVM 中所发挥的作用值得进一步探究。Li WD & Ma ZS (2020) Dominance network analysis of the healthy human vaginal microbiome not dominated by *Lactobacillus* species. *Computational and Structural Biotechnology Journal*

团队成员（Lab Member)

姓　名（学　位；早期背景；目前研究方向）

李连伟（博　士；特别研究助理；计算生物 | 生态学）

陈红菊（博士生；数学；进化博弈论）

肖琬蒙（博士生；林学；生物信息学）

杨　旭（硕士生；昆虫学；生物信息学）

李文迪（博士生；生物医学；医学生态学）

MD Motiur Rahman（博士生；概率统计；深度学习）

乔玉婷（硕士生；生物信息学；生物信息学）

人类菌群医学生态学理论框架初见雏形

医学生态学这一名词在文献中时有出现，并且（对其的定义）有不同版本。比较流行的版本包括已故微生物学家 Rene Dubos 于上世纪三十年代提出的 “ 研究直接影响人类健康的环境因素的交叉学科。例如清洁空气、优良饮水以及安全食物 ”，以及哥伦比亚大学公共卫生系所倡导的 “ 生态学、地球科学、公共卫生 ” 交叉学科。但这些工作大多都长期处于名词定义阶段。2010 年前后，马占山在为新成立的学科组命名时，将最初所构想的 “ 计算生物学与生物信息学 ” 最终定名为 “ 计算生物与医学生态学 ”。其初衷是强调 “ 计算生物学 ” 的理论以及更加具体的应用领域（人类菌群 — 宏基因组生物信息学分析）。 学科组成立后，除致力于三代基因测序算法和软件研制外（先后发布三项重要软件技术），其它主要研究精力基本集中在人类菌群与疾病关系的研究。学科组发现，除了计算生物信息学外，生态学（特别是理论生态学）为研究人类菌群相关疾病提供了极为重要的理论指导和分析方法。为此，过去 10 年间，学科组系统探索了理论生态学主要的经典理论和方法、并结合近年来新兴的复杂网络科学，从而为分析菌群宏基因大数据、特别是与人类疾病关系的机制方面提出了一系列理论、方法和技术（发表相关论文 50 余篇，申请发明专利 17 项）。并从 2019 年开始系统总结建立一门具有相对独立性、但仍处于探索阶段的交叉学科，也就是菌群医学生态学领域 (Medical Ecology of Human Microbiomes)。作为学科组所理解的医学生态学代表作包括 2019 年发表在权威期刊 *The ISME Journal*，*Ecological Monographs, Advanced Science* 的三篇重要研究结果，以及 2020 年发表在 *iScience* 两篇关于菌群与疾病机制的研究论文，以及 FEMES Microbiology Ecology 等杂志论文。这些论文整合了近年来学科组所提出的系列理论、方法和技术作出进一步系统整合，并对近 20 种常见的菌群相关疾病（例如肥胖、糖尿病、痛风、牙周炎、肠炎、老年痴呆症、阴道炎、直肠癌等）与菌群关系进行了机制性的深入分析。

Ma ZS (2020) Critical network structures and medical ecology mechanisms underlying human microbiome-associated diseases. *iScience.*

Ma ZS (2020) Testing the Anna Karenina Principle in human microbiome-associated diseases. *iScience*

Ma ZS (2020) Heterogeneity-disease relationship in the human microbiome associated diseases.
FEMS Microbiology Ecology, Vol. 96

Li WD & Ma ZS (2020) Population-level diversity-disease relationship (*P*-DDR) in the human microbiome associated diseases. (Under Review)

人类进化与疾病基因组学

孔庆鹏，中科院昆明动物所，研究员、博导。迄今在 *Am J Hum Genet*、*Genome Res*、*Mol Biol Evol*、*Natil Sci Rev*、 *PNAS*、*Theranostics* 及 *Hum Mol Genet* 等国际重要 SCI 期刊上发表论文 100 余篇，论文被各类 SCI 刊物累计引用 4000 余次，H 指数 31。主持有国家重点研发计划专项（任首席科学家）、国家基金委重点国际合作及优秀青年基金等项目；2013 年入选科技部科技创新中青年领军人才计划；2016 年入选国家“万人计划”领军人才；2020 年 3 月入选昆明市“春城科技领军人才”；2020 年 9 月入选“云岭学者”，现任 SCI 期刊 *Scientific Reports* 编委。研究组目前的主要研究方向：人群起源演化及健康长寿分子机制。

重要成果及产出：

1. **Jiang JJ**, **Kong QP***, Comparative analysis of long noncoding RNAs in long-lived mammals provides insights into natural cancer-resistance. ***RNA Biology***, 2020 Nov;17(11):1657-1665, IF=5.350
2. **Wang HT**, **Xiao FH**, **Li GH**, **Kong QP***, Identification of DNA N^6-methyladenine sites by integration of sequence features. ***Epigenetics & Chromatin***, 2020 Feb;13(1):8, IF=4.237
3. **Rahman ZU**, **Li YC**, **Tian JY**, **Kong QP***, Exploring European ancestry among the Kalash population: a mitogenomic perspective. ***Zoological Research***, 2020, 41(5): 552-556, IF=2.638
4. **Liu J**, **Li Y**, **Chen XQ**, Sun C, Sun XL, Yang Z, **Kong QP***, rs11046147 mutation in the promoter region of lactate dehydrogenase-B as a potential predictor of prognosis in triple-negative breast cancer. ***Cancer Communications,*** 2020 Jun;40(6):279-282, IF=5.627

1. lncRNA 在长寿物种天然抗癌机制中的比较分析

为了更好地了解长寿哺乳动物的抗癌机制，我们广泛鉴定了两种长寿哺乳动物的长非编码 RNA (lncRNA) 转录本，这两种长寿哺乳动物分别是北极露脊鲸 (BW, *Balaena mysticetus*) 和布氏鼠耳蝠 (BB, *Myotis brandtii*)，并进一步分析了 lncRNA 的序列特征、表达模式及其与癌症抗性的关系。利用 k-mers 聚类分析，发现 75-136 个 BW、 BB 和 裸鼹鼠 lncRNAs 与人类衰老性疾病相关 lncRNAs (HAR-Lncs) 密切相关 (Pearson's r ≥0.9, p < 0.01) (图 1)。此外，我们观察到 BB 和 BW 中很多 lncRNAs 与潜在的肿瘤抑制基因存在很强的共表达关系 (r > 0.8 或 r <-0.8，p < 0.01)，这表明 lncRNAs 可能参与长寿哺乳动物的抗癌调节。

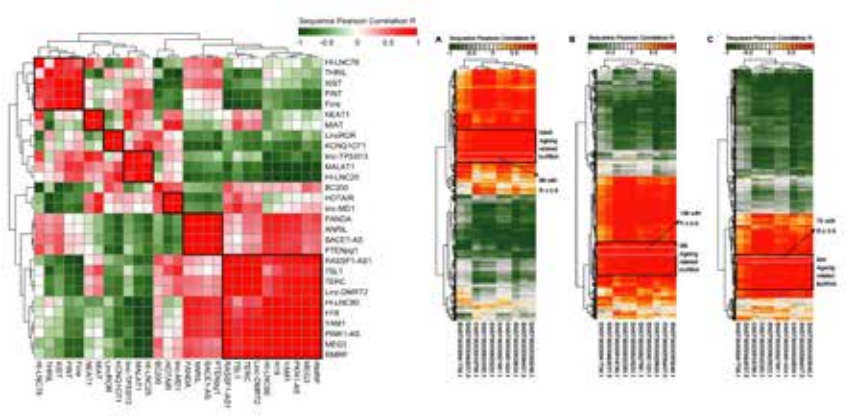


图 1. 利用 K-mer 方法预测长寿物种中的衰老相关 lncRNA

【Jiang JJ et al. 2020 ***RNA Biol***】

2. DNA N6- 甲基腺嘌呤（6mA）预测器 p6mA 的开发

近年来大量研究发现 DNA N6- 甲基腺嘌呤（6mA）具备表达调控功能且其具有重要的生物学意义，然而应用实验方法获取基因组水平该修饰状态耗费较多时间与物质资源。本课题组开发了预测器 p6mA，通过机器学习方法实现对于 DNA 腺嘌呤碱基 6mA 状态的预测。

p6mA 训练自四个物种（水稻、秀丽隐杆线虫、果蝇、人类）的 6mA 数据集，采用 PSTNP 等特征提取方法，利用 XGBoost 构建。其预测能力超过现存的几种预测器（如 MM-6mAPred，i6mA-Pred 等）。此外，其在拟南芥的 6mA 预测中也表现出了较为优秀的预测能力。

p6mA 可于 https://github.com/Konglab404/p6mA 获取。

Human Evolution and Disease Genomics

Dr. Qing-Peng Kong, Principal Investigator, Kunming Institute of Zoology, Chinese Academy of Sciences.

The main research interests of my laboratory are: (1) tracing the origin and evolutionary history of modern humans and (2) disclosing the molecular mechanism of healthy aging by studying longevity individuals. Our research group has already published over 100 papers on the international peer-reviewed journals such as *Am J Hum Genet, PNAS, Genome Res, Mol Biol Evol*, *Natil Sci Rev*, *Theranostics* with total citations over 4,000 times.

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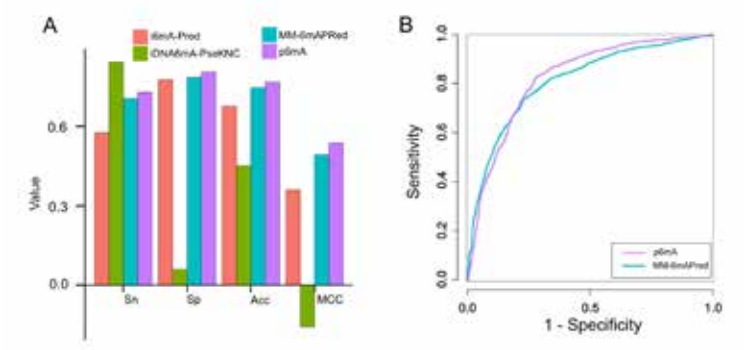
1. Comparative analysis of long noncoding RNAs in long-lived mammals provides insights into natural cancer-resistance

To better understand the underlying anti-cancer mechanisms in long-lived mammals, we genome widely identified long noncoding RNA (lncRNA) transcripts of two longevous mammals, bowhead whale (BW, *Balaena mysticetus*) and Brandt's bat (BB, *Myotis brandtii*) and featured their sequence traits, expression patterns, and their correlations with cancer-resistance. By utilizing k-mers clustering, 75–136 of BW, BB and NMR lncRNAs were found in close relation (Pearson's $r \geq 0.9$, $p < 0.01$) with human ageing diseases related lncRNAs (HAR-Lncs). In addition, we observed thousands of BB and BW lncRNAs strongly co-expressed ($r > 0.8$ or $r < -0.8$, $p < 0.01$) with potential tumour suppressors, indicating that lncRNAs are potentially involved in anti-cancer regulation in long-lived mammals. Our study provides the basis for lncRNA researches in perspectives of evolution and anti-cancer studies. **(Jiang JJ et al. 2020 RNA Biol)**

2. p6mA: Identification of DNA N6-methyladenine sites by integration of sequence features

An increasing number of nucleic acid modifications have been profiled with the development of sequencing technologies. DNA N^6-methyladenine (6mA). In this study, we constructed a multi-species 6mA predictor, p6mA, created from a series of sequence-based features, including physicochemical properties, position-specific triple-nucleotide propensity (PSTNP), and electron-ion interaction pseudopotential (EIIP).We showed that p6mA is a more robust and competitive 6mA predictor than other existing predictors, as determined using different benchmark datasets and independent validation. **(Wang HT et al. 2020 Epigenet. Chromatin)**



Results of independent validation by *A. thaliana* dataset.(A) The performance of the 4 predictors. (B) ROC curves of p6mA and MM-6mAPred.
【Wang HT et al. 2020 ***Epigenet. Chromatin***】

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郜宗亮 Zongliang Gao 2018
郭丽云 Liyun Guo 2018
韩一鸣 Yiming Han 2018
赵 龙 Long Zhao 2019
翁崇俊 Congjun Weng 2019
王霞燕 Xiayan Wang 2020
姚亚冬 Yadong Yao 2020

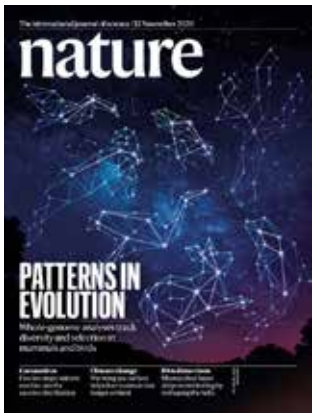
生物多样性基因组学研究

张国捷，中国科学院昆明动物研究所客座研究员，哥本哈根大学生物系终身教授，中国国家基因库副主任。长期担任 *Nature, Science, Genome Research, Current Biology* 等顶尖国际期刊和各国基金会评审委员。目前已在 *Science, Nature, Cell, Science Advances, Nature Communication, PNAS, Current Biology* 等国际高影响力杂志发表论文 140 余篇。2020 年，课题组报道了万种鸟类基因组计划（B10K）第二阶段（科级别）的研究结果，发表了 363 种鸟类基因组数据，建立了无参考序列下多基因组比对和分析的新方法；解析了法老蚁蚁后生殖功能成熟过程中大脑基因调控网络的重塑；通过结合二代三代测序，构建了高质量的染色体水平的法老蚁基因组和转录组，揭示了一系列与等级分化相关的可变剪接异构体及非编码 RNA 等。2020 年，在 ***Nature*** (2), ***Science Advances*** (1), ***Nature Communications*** (1), ***GigaScience*** (2) 等国际刊物发表 SCI 文章 13 篇。实验室主页： http://zhanggjlab.org/

重要成果及产出：

1. Nagel M[1], Qiu B[1], Brandenborg LE, Larsen RS, **Ning D**, Boomsma JJ, **Zhang G***. The gene expression network regulating queen brain remodeling after insemination and its parallel use in ants with reproductive workers, ***Science Advances***, 2020, 6(38), eaaz5772, IF14.094
2. **Shao Y**[1], Wang X-B[1], **Zhang J-J**[1], **Li M-L**[1], Wu S-S, **Ma X-Y**, Wang X, Zhao H-F, Li Y, Zhu HH, **Irwin DM**, Wang D-P, **Zhang G***, Ruan J*, **Wu D-D***. Genome and single-cell RNA-sequencing of the earthworm Eisenia andrei identifies cellular mechanisms underlying regeneration, ***Nature Communications***, 2020, 11:2656, IF13.61
3. **Feng S**[1], Stiller J[1], Deng Y[1], Armstrong J[1], Fang Q, Reeve AH, Xie D, Chen G, Guo C, Faircloth BC, Petersen B, Wang Z, Zhou Q, Diekhans M, Chen W, Andreu-Sanchez S, Margaryan A, Howard JT, Parent C, Pacheco G, Sinding MS, ……, Paten B*, **Zhang G***, Dense sampling of bird diversity increases power of comparative genomics, ***Nature***, 2020, 587, 252-257, IF46.488
4. Armstrong J[1], Hickey G, Diekhans M, Fiddes IT, Novak AM, Deran A, Fang Q, Xie D, **Feng S**, Stiller J, Genereux D, Johnson J, Marinescu VD, Alfoldi J, Harris RS, Lindblad-Toh K, Haussler D, Karlsson E, Jarvis ED, **Zhang G***, Paten B*. Progressive Cactus is a multiple-genome aligner for the thousand-genome era, ***Nature***, 2020, 587, 246-251, IF46.488
5. **Gao QH**[1], **Xiong ZJ**[1], **Larsen RS**, Zhou L, **Zhao J**, **Ding G**, **Zhao RP**, **Liu CY**, **Ran H**, **Zhang GJ***. High-quality chromosome-level genome assembly and full-length transcriptome analysis of the pharaoh ant *Monomorium pharaonis*, ***GigaScience***, 2020, 9, 1–14, IF7.715
6. **Zhang P**[1], Chen JS[1], Li QY[1], Sheng LX[1], Gao YX1, Lu BZ, Zhu WB, Zhan XY, Li Y, Yuan ZB, Xu G, Qiu BT, Yan M, Guo CX, Wang YQ, Huang YJ, Zhang JX, Liu FY, Tang ZW, Lin SZ, Cooper DN, Yang HM, Wang J, Gao YQ*, Yin W*, **Zhang GJ***, Yan GM*. Neuroprotectants attenuate hypobaric hypoxia-induced brain injuries in cynomolgus monkeys, ***Zoological Research***, 41 (1), 3-19

1. 万鸟基因组计划 (B10K) 第二阶段进展



2015 年由本课题组主导发起了万鸟基因组计划 (B10K)，旨在依据目科属种的分类阶元分阶段对所有现生鸟类进行基因组解读，重构鸟类演化历史，以研究物种分化的内在分子动力及物种宏观演化过程分子机制。2020 年，B10K 项目完成科阶元的测序分析工作，建立了全新的无参考序列下多基因组比对和分析方法，实现了获取更真实且全面的序列同源关系用于后续系统发生关系的解析和比较基因组学相关分析。该方法极大的提高了跨物种的比对效率，减少了由于与参考物种遗传距离差异引起的比对偏好和序列丢失（Armstrong et al., 2020, ***Nature***）。

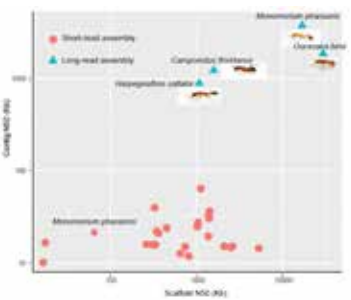
另一文章借助这一算法优势建立了更加完善的同源基因集合，还开发了一套鉴定任意演化分支特异获得和丢失序列的方法，从而完整描绘出鸟类物种谱系基因组动态演化图谱。研究发现这些动态变化的基因组区域往往存在一些分支特异基因或调控元件，可能与物种特异性状的起源和演化有关（Feng et al., 2020, ***Nature*** ）。

2. 解析雌性生殖蚁受精后大脑重塑基因调控网络

本课题组以法老蚁（*Monomorium pharaonis*）为模式，揭示了蚂蚁蚁后生殖功能分化过程中调控大脑可塑性的基因网络（Gene Regulatory Network, GRN）。通过比较基因组学分析发现，该机制在一些失去蚁后等级的蚂蚁物种平行存在，且被用于调控这些物种工蚁生殖潜能的重新激活。研究鉴定出两个关键的神经肽基因 *corazonin* 和 *neuroparsin A*，它们在神经分泌细胞表达，而且在 4 个代表性蚂蚁物种中，都同样的在生殖功能被抑制的个体中表达显著升高（Nagel et al., 2020, ***Science Advances*** ）。

3. 法老蚁高质量染色体水平基因组组装及全长转录组分析

本课题组通过结合 PacBio、Illumina、Hi-C 测序，从头组装了高质量的染色体水平法老蚁（*Monomorium pharaonis*）基因组。通过全长转录组 ISO-seq，获得了更完整的法老蚁各等级转录组，提高了法老蚁基因注释质量，精确检测到可变剪接异构体及蚂蚁保守的 lncRNA（Gao et al. 2020, ***GigaScience***）。



Biodiversity Genomics Lab

Dr. Guojie Zhang, Adjunct professor, head of Biodiversity Genomics Group, Kunming Institute of Zoology, CAS, full professor in University of Copenhagen and Associate Director of the China National GeneBank. Dr. Zhang has published more than 140 articles, including *Science, Nature, Cell, Science Advances, Nature Communications, PNAS* and *Current Biology*. In 2020, we reported the advances for phase II of the Bird 10,000 Genomes (B10K) Project. We analyzed 363 genomes from 92.4% of bird families—including 267 newly sequenced genomes and performed reference-free whole-genome alignment. We identified a far greater number of orthologous regions, revealed shared and lineage specific variations and improved the research on selection patterns. Besides, we revealed brain gene regulatory network changes accompanying queen reproductive role differentiation in pharaoh ants. We assembled and annotated a high quality pharaoh ant genome at chromosome level, a series of caste differentiation related transcript isoforms and non-coding RNAs were identified. 13 high profile SCI papers were published, including ***Nature*** (2), ***Science Advances*** (1), ***Nature Communications*** (1), ***GigaScience*** (2).

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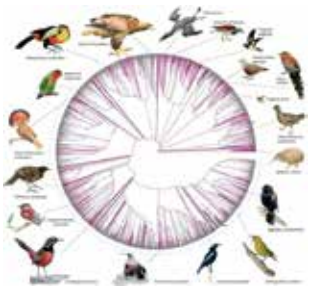
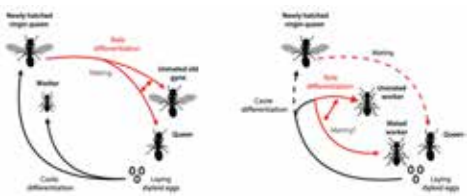
1. Bird 10,000 Genomes (B10K) phase II advances



We analyzed 363 genomes from 92.4% of bird families, including 267 newly sequenced genomes produced for phase II of the Bird 10,000 Genomes (B10K) Project. We used this comparative genome dataset in combination with a pipeline that leverages a reference-free whole-genome alignment to identify orthologous regions in greater numbers than has previously been possible, to recognize genomic novelties in particular bird lineages and to reveal selection patterns of genomic characteristics (Feng et al., 2020, *Nature*).

In another article, we created Progressive Cactus, which enables the reference-free alignment of tens to thousands of large vertebrate genomes while maintaining high alignment quality. We described results from an alignment of more than 600 amniote genomes, which is the largest multiple vertebrate genome alignment created so far (Armstrong et al., 2020, *Nature*).

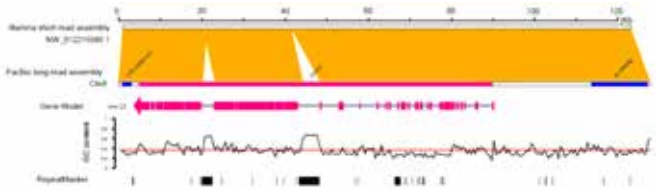
2. Gene regulatory network of ants queen brain remodeling after insemination



By comparative genomics analysis, we revealed a specific gene regulatory network (GRN) mediating both brain anatomy changes and behavioral modifications during queen reproductive role differentiation in pharaoh ants. This GRN appears to be also used by distantly related ants where workers became germline individuals after the queen caste was entirely or partially lost (Nagel et al., 2020, *Science Advances*).

3. Genome assembly and transcriptome analysis of Monomorium pharaonis

By combining Illumina, PacBio, and Hi-C sequencing technologies, we de novo assembled a high-quality chromosome-level genome for *Monomorium pharaonis*. By high-depth ISO-seq, we improved gene annotation quality and detected an unprecedented number of transcript isoforms and conserved long non-coding RNAs (lncRNAs) that were evolved specifically in ant lineages or conserved across insects (Gao et al., 2020, *GigaScience*).



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Mr. Hao Ran, Myrmecology Specialist
刘薇薇 博士 副研究员
Ms. Weiwei Liu, Associate Professor
高琼华 博士 博士后
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适应性进化与进化医学

吕雪梅，博士，研究员，博士生导师，适应性进化与进化医学学科组负责人。主要从事适应性进化的群体基因组学研究。以物种和细胞群体水平的变异和进化为核心，探讨中性进化和自然选择等进化驱动力的对群体动态演化相对作用，从而揭示从遗传和表观变异的累积、到适应性改变的形成和进化一系列过程的基本规律，成果发表在 *Genome Res*、*MBE*、*PNAS* 等著名期刊上。近年来关注肿瘤形成研究，其突变规律、群体动态、多样性形成和演变、适应性改变等进化规律仍有大量悬而未决的问题。在疫情期间，作为项目负责人，主持科技部重点研发计划新冠应急专项“新冠病毒基因组进化规律与动态演变研究技术体系创建与应用”，完成相关研究论文和动态追踪及分析的方法和数据库可视化建设，并为科技部等部门撰写多篇新冠相关咨询和研判报告。

重要成果及产出：

1. Li T[1], Liu JL[1], Feng J[1],Liu ZZ, Liu SX, Zhang MJ, Zhang YZ, Hou YL, Wu DF, Li CY, Chen YB, Chen H, **Lu XM***. Variation in the life history strategy underlies functional diversity of tumors. National Science Review, 2020, Accepted. IF15.209
2. Ruan YS[1], Luo ZD, Tang XL, Li GH, Wen HJ, He XL, **Lu XM***, Lu J *, Wu C-I*. On the founder effect in COVID-19 outbreaks – How many infected travelers may have started them all? National Science Review, 2020, Accepted. IF15.209
3. Luo J[1], Chai J[1], Wen YL[1], Tao M[1], Lin GL[1], Liu XC, Li R, Chen ZY, Wu SG, Li SN, Wang YD, Qin QB, Wang S, Gao Y, Huang F, Wang L, Ai C, Wang XB, Li LW, Ye CX, Yang HM, Luo M, Chen J, Hu H, Yuan LJ, Zhong L, Wang J, Xu J, Du ZL, Ma ZS (Sam), Robert W. Murphy, Axel Meyer, Gui JF, Xu P*, Ruan J*, Chen Z. Jeffrey*, Liu SJ*,**Lu XM***, **Zhang YP*.** From asymmetrical to balanced genomic diversification during rediploidization: subgen-omic evolution in allotetraploid fish. Science Advances, 2020, 6(22):eaaz7677, IF12.477
4. Liu QY[1], Wei JH[1], Li YW[1], Wang M, Su J, Lu YH, Mariana G. López, Qian XQ, Zhu ZQ, Wang HY, Gan MY, Jiang Q, Fu Y-X, Howard E.Takiff, Iñaki Comas, Li Feng*, **Lu XM *,** Sarah M. Fortune*, Gao Q *. Mycobacterium tuberculosis clinical isolates carry mutational signatures of host immune environments. Science Advances, 2020,6(22)：eaba4901. IF12.477
5. Ma FQ[1], Lu G-A[1], Chen QJ, Ruan YS, Li X, **Lu XM*,** Li CY*. Dynamic global analysis of transcription reveals the role of miRNAs in synergistic stabilization of gene expression. Science Bulletin, 2020, in press. IF5.143
6. Yin LD[1], Sharmi Banerjee[1], Fan JY , He JL, **Lu XM***, Xie HH*. Epigenetic regulation of neuronal cell specification inferred with single cell “Omics” data. Computational and Structural Biotechnology Journal, 2020, 18(942-52). IF4.962
7. Hou YL[1], Qi FR[1], Bai X[1], Ren T, Shen X, Chu Q, Zhang XQ* and **Lu XM*.** Genome-wide analysis reveals molecular convergence underlying domestication in 7 bird and mammals, BMC Genomics, 2020. 21(1): p. 204. IF3.684
8. Li T[1], Tang XL, Wu CC, Yao XM, Wang YR, **Lu XM*** and Lu J*. The use of SARS-CoV-2-related coronaviruses from bats and pangolins to polarize mutations in SARS-Cov-2, 2020, Science China_ Life Sciences, 2020，63(10):1608-1611. IF3.271

1. 揭示癌症演化中细胞表型适应性权衡和生态竞争造就肿瘤多样性和适应

该研究以密度依赖性选择中的经典理论——r-vs.K- 选择理论为基础，利用实验进化的手段，选择出 r 或 K 癌细胞系，获得了具有快速增殖能力的 r 细胞和具有高度竞争力的 K 细胞（图 1）。证实了癌症细胞群体中存在表型亚群分化，并系统地揭示了不同表型之间的适应性权衡。并且 RNA-seq 表明，这种权衡与细胞周期、粘附、凋亡和接触抑制相关基因的不同表达有关。此外，研究团队还建立了具有空间结构制约的肿瘤细胞系亚群竞争实验，当 r 细胞和 K 细胞混合时，它们表现出明显不同的时空分布。团队首次观察到癌症细胞不同表型亚群之间的生态位分离事件。由于这种生态位分离，整个癌症群体的适应性增加。实验观察和基于生态竞争模型的模拟计算都表明，癌症细胞群体中存在符合生态学原理的细胞增殖和竞争力之间的适应性权衡（图 2）。

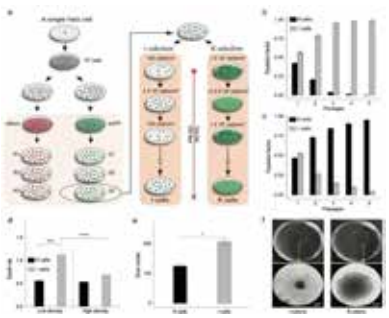

图 1. r-/K- 选择与肿瘤细胞适应性演化

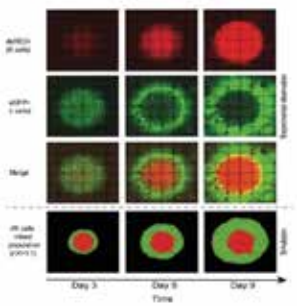

图 2. 混合种群中 r- 和 K- 细胞的种群间相互作用和时空生长

【Li T et al., 2020, ***National Science Review***, IF15.209】

2. 揭示脊椎动物异源多倍体亚基因组演化的动态历史

通过重建鲤亚科鱼类的多倍化演化历史，发现鲫鱼、鲤鱼和金线鲃共同起源于 13.8~15.1 百万年前的一次古异源多倍化事件。比较基因组学和多组织、多胚胎发育时期转录组和 DNA 甲基化的比较分析结果表明，红鲫与异源多倍体植物和爪蟾基因组中非对称的演化模式呈现明显不同：1）红鲫的父系和母系来源的亚基因组均没有显著的大规模非对称性丢失和演化速率偏向性，两个亚基因组在整个二倍化进程中一直经历交替的非对称性功能丢失；2）虽然两个亚基因组的同源基因对总体呈现平衡表达，有趣的是，两个基因拷贝随胚胎发育时间的推进发生表达优势的切换；3）同源基因拷贝的表达与 DNA 甲基化的变化呈负相关，但甲基化并不能解释同源基因对在胚胎发育进程中的表达优势切换模式，这提示可能存在更复杂的调控机制决定同源基因对的表达。

【Luo J et al., 2020, ***Science Advances***, IF12.477】

Adaptive Evolution and Evolutionary Medicine

Dr. Xuemei Lu, Professor, Principal Investigator, The recent studies of our group are about the fundamental paradigms of ecological and evolutionary biological processes such as speciation, adaptive evolution, adaptive phenotypic change of cells, etc. There are three scenes used for sparkling the research: 1) species level, 2) population level, and 3) cell population level. Basing on ecological and evolutionary theory and population genetics, together with system biology approaches and multi-omics methods, we have developed a somatic cell-based experimental evolutionary system to investigate the issues, which are hard to record and analyze in natural populations.

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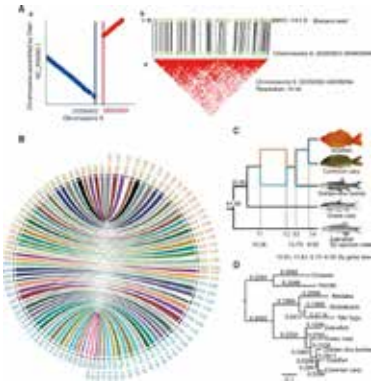
1. Variation in the life history strategy underlies functional diversity of tumors

Classical r- vs. K-selection theory describes the trade-offs between high reproductive output and competitiveness and guides research in evolutionary ecology. While its impact has waned in the recent past, cancer evolution may rekindle it. Herein, we impose r- or K- selection on cancer cell lines to obtain strongly proliferative r cells and highly competitive K cells to test ideas on life-history strategy evolution. RNA-seq indicates that the trade-offs are associated with distinct expression of genes involved in the cell cycle, adhesion, apoptosis, and contact inhibition. Both empirical observations and simulations based on an ecological competition model show that the trade-off between cell proliferation and competitiveness can evolve adaptively. When the r and K cells are mixed, they exhibit strikingly different spatial and temporal distributions. Due to this niche separation, the fitness of the entire tumor increases. The contrasting selective pressure may operate in a realistic ecological setting of actual tumors.

2. From asymmetrical to balanced genomic diversification during rediploidization: Subgenomic evolution in allotetraploid fish



A persistent enigma is the rarity of polyploidy in animals, compared to its prevalence in plants. Although animal polyploids are thought to experience deleterious genomic chaos during initial polyploidization and subsequent rediploidization processes, this hypothesis has not been tested. We provide an improved reference-quality de novo genome for allotetraploid goldfish whose origin dates to ~15 million years ago. Comprehensive analyses identify changes in subgenomic evolution from asymmetrical oscillation in goldfish and common carp to diverse stabilization and balanced gene expression during continuous rediploidization. The homoeologs are coexpressed in most pathways, and their expression dominance shifts temporally during embryogenesis. Homoeolog expression correlates negatively with alternation of DNA methylation. The results show that allotetraploid cyprinids have a unique strategy for balancing subgenomic stabilization and diversification. Rediploidization process in these fishes provides intriguing insights into genome evolution and function in allopolyploid vertebrates.

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冯　璥　Jing Feng
闫　凯　Kai Yan
魏昀旸　Yunyang Wei
张　昕　Xin Zhang
陶鑫灵　Xinling Tao
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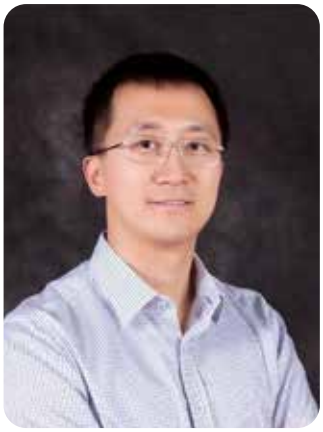
岳婷松　Tingsong Yue
陈　园　Yuan Chen
杨国兵　Guobing Yang



行为遗传和进化学科组

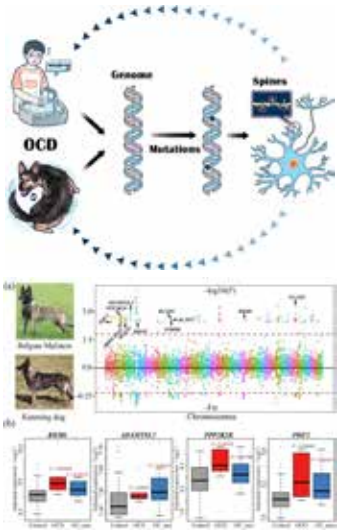
王国栋，博士，研究员，博士生导师。入选中组部万人计划青年拔尖人才，中国科学院青年促进会优秀会员，云南省中青年学术和技术带头人。获 2019 年度中国科学院青年科学家奖，作为发起人之一创建家犬基因组研究国际联盟。现任中国动物学会动物行为学分会第二届理事会理事（2019 年 11 月 -2023 年 11 月）和中国科学院昆明动物研究所人类疾病的家犬模型省创新团队带头人（2019- 至今）。主要研究方向为群体遗传、适应性进化、复杂表型和行为的遗传机制等研究。以第一作者和通讯作者（含并列）在 *Nat Genet*、*Nat Commun*、*Cell Res*、*PNAS*、*Mol Biol Evol* 和 *Nucl Acids Res* 等 SCI 杂志发表论文 28 篇。获 Sanofi-Cell Research 优秀论文和第三届中国科协优秀科技论文，研究结果被 *Nature*、*The New York Times*、*The Guardian*、*National Geographic*、*Scientific American* 等国际杂志报道。

重要成果及产出：

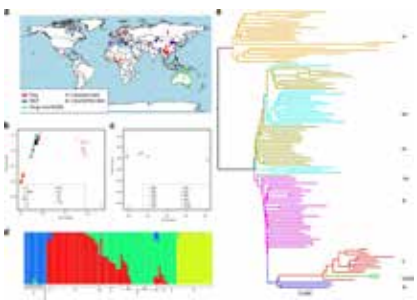
1. Ming Zhang, Guo-Ping Sun, Le-Le Ren, Hai-Bing Yuan, Guang-Hui Dong, Li-Zhao Zhang, Feng Liu, Peng Cao, AlbertMin- ShanKo, MelindaA. Yang, Songmei Hu*, **Guo-Dong Wang***, Qiao-Mei Fu*. 2020. Ancient DNA evidence from China reveals the expansion of Pacific dogs. Mol. Biol. Evol. 37(5).
2. **Shao-jie Zhang**[1], **Guo-Dong Wang**[1], **Peng-Cheng Ma**[1], Liang-Liang Zhang, **Ting-Ting Yin**, **Yan-Hu Liu**, **Newton O. Otecko**, Meng Wang, Ya-Ping Ma, Lu Wang, **Bing-Yu Mao***, Peter Savolainen*& **Ya-Ping Zhang***. 2020. Genomic regions under selection in the feralization of the dingoes. Nat. Commun. (2020) 11:671 .
3. Zeinab Amiri Ghanatsaman[1], **Guo-Dong Wang**[1], Hojjat Asadollahpour Nanaei, Masood Asadi Fozi, **Min-Sheng Peng**, **Ali Esmailizadeh*** and **Ya-Ping Zhang***. 2020. Whole genome resequencing of the Iranian native dogs and wolves to unravel variome during dog domesticatio. BMC Genomics (2020) 21:207 .
4. **Li-Min Zhao**[1], **Hao Ke**[1], **Hai-Bo Xu**, **Guo-Dong Wang**, **Hong-Lei Zhang**, **Li Zou**, Shu Xiang, Meng-Yuan Li, Li Peng, Ming-Fang Zhou, **Ling-Ling Li**, Lei Ao, **Qin Yang**, Che-Kun James Shen, Ping Yi*, Lu Wang* and **Bao-Wei Jiao***. 2020. TDP-43 Facilitates Milk Lipid Secretion by Post-Transcriptional Regulation of Btn1a1 and Xdh. Nat Commun 341 (2020).
5. **Xue Cao**[1], Wei-Peng Liu[1], Luguang Cheng, Hui-Juan Li, Hong Wu, Yanhu Liu,Chao Chen, Xiao Xiao, Ming Li*, **Guo-Dong Wang***, **Ya-Ping Zhang***. 2020. Whole genome analyses reveal significant convergence in obsessive-compulsive disorder between humans and dogs. Science Bulletin, https://doi.org/10.1016/j.scib.2020.09.021.
6. Xinchao Wang , Hu Feng , Yuxiao Chang, Chunlei Ma , Liyuan Wang , Xinyuan Hao ,A'lun Li , Hao Cheng , Lu Wang , Peng Cui , Jiqiang Jin , Xiaobo Wang , Kang Wei ,Cheng Ai, Sheng Zhao , Zhichao Wu , Youyong Li, Benying Liu , **Guo-Dong Wang***,Liang Chen *, Jue Ruan * & Yajun Yang*. 2020. Population sequencing enhances understanding of tea plant evolution. Nat. Commun. (2020) 11:4447.

1. 多组学研究揭示家犬和人强迫症之间显著的遗传趋同

本研究针对转圈行为这一家犬强迫症的代表性表型，在两个独立犬种中（比利时马里努阿犬和昆明犬）开展了表型鉴定和全基因组测序工作。通过群体分化和全基因组关联分析筛选到 11 个候选强迫症风险基因，且这些基因与人类全基因组关联研究揭示的强迫症关联基因有显著重叠（P<0.0001），证实了人类和家犬强迫症的显著遗传趋同性。进一步的基因表达分析和功能验证表明两个强迫症候选风险基因 PPP2R2B 和 ADAMTSL3 可显著影响树突棘的发育、密度和形态，提示树突棘发育与功能改变可能参与了人和家犬共享的强迫症发病机制。我们的研究揭示了人和家犬强迫症在遗传和细胞生物学方面的趋同性，提示家犬或可作为包括强迫症在内许多人类疾病研究的模型物种。
(B, D et al. 2020 ***Science Bulletin*** IF=9.511)



2. 澳洲野犬群体起源及野化机制



研究团队基于全基因组证据揭示证明了澳洲野犬的祖先是东亚已被驯化的家犬，在大约 9900 年前从中国南方出发，在大约 8300 年前到达了澳大利亚，并在澳大利亚迅速野化。并且这个时间与南岛扩散的时间不相符，可能是一次未知的古代人类到的澳洲的迁移活动。我们还利用澳洲野犬这一模型对野化进行了研究，发现了很多有趣的野化基因，这些基因大多与神经发育，免疫，生殖和消化代谢有关，这些功能都与家犬适应野外生存密切相关。最后我们分析了澳洲野犬的野化模式，发现了澳洲野犬的一些基因区域相比较家犬来说更像狼，这可能是由于澳洲野犬来自于还未被完全驯化的早期家犬。我们认为这些基因区域可能对野化和驯化来说都很重要，因此我们针对澳洲野犬一个和神经相关的基因 ARHGEF7 上的突变，设计了一个功能验证，发现这个澳洲野犬上的突变确实等影响 ARHGEF7 基因的表达。该工作利用了澳洲野犬的基因组推测出了它的群体历史，而且还提示了一次可能的古代人类迁移，又利用澳洲野犬的野化分析，推导出了它的野化模式，为今后人群迁移和野化研究提供了新的思路。
(Zhang, Wang et al. 2020 ***Nature Communications*** IF=12.121)

Molecular Evolution and Genome Diversity

Prof. Guodong Wang, researcher, Ph.D. Supervisor. The 2019 Young Scientist Award of the Chinese Academy of Sciences and as one of the initiators to create the Dog10K Consortium. Recently year we focused on genomic evolution, adaptive evolution, the genetic basis of complex traits and behavior. Research progress published on *Nat Genet, Nat Commun, Cell Res, PNAS, Mol Biol Evol, Nucl Acids Res* and other science citation index (SCI) journals.

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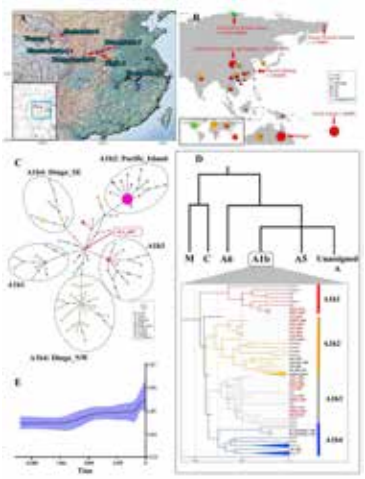
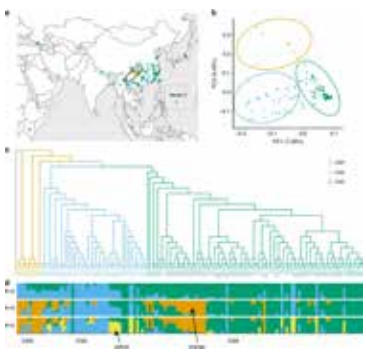
1. Ancient DNA evidence from China reveals the expansion of Pacific dogs



The ancestral homeland of Australian dingoes and Pacific dogs is proposed to be in South China. However, the location and timing of their dispersal and relationship to dog domestication is unclear. Here, we sequenced 7,000 to 2,000-year-old complete mitochondrial DNA (mtDNA) genomes of 27 ancient canids (one gray wolf and 26 domestic dogs) from the Yellow River and Yangtze River basins (YYRB). These are the first complete ancient mtDNA of Chinese dogs from the cradle of early Chinese civilization. We found that most ancient dogs (18/26) belong to the haplogroup A1b lineage that is found in high frequency in present-day Australian dingoes and pre-colonial Pacific Island dogs, but low frequency in present-day China. Particularly, a 7,000-year-old dog from the Tianluoshan site in Zhejiang province possesses a haplotype basal to the entire haplogroup A1b lineage. We propose that A1b lineage dogs were once widely distributed in the YYRB area. Following their dispersal to South China, and then into Southeast Asia, New Guinea and remote Oceania, they were largely replaced by dogs belonging to other lineages in the last 2,000 years in present-day China, especially North China.

(Zhang, Sun et al. 2020 ***Molecular Biology and Evolution*** IF=11.062)

2. Population sequencing enhances understanding of tea plant evolution



Tea is an economically important plant characterized by a large genome, high heterozygosity, and high species diversity. In this study, we assemble a 3.26-Gb high-quality chromosomescale genome for the 'Longjing 43' cultivar of Camellia sinensis var. sinensis. Genomic resequencing of 139 tea accessions from around the world is used to investigate the evolution and phylogenetic relationships of tea accessions. We find that hybridization has increased the heterozygosity and wide-ranging gene flow among tea populations with the spread of tea cultivation. Population genetic and transcriptomic analyses reveal that during domestication, selection for disease resistance and flavor in C. sinensis var. sinensis populations has been stronger than that in C. sinensis var. assamica populations. This study provides resources for marker-assisted breeding of tea and sets the foundation for further research on tea genetics and evolution.

(Wang, Feng et al. 2020 ***Nature Communications*** IF=12.121)

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神经发育与进化

毛炳宇，博士，研究员，中德马普青年科学家小组组长，遗传资源与进化国家重点实验室副主任。先后获得国家自然科学基金委杰出青年基金、重点项目等资助。实验室主要以小鼠、非洲爪蛙和文昌鱼为动物模型研究神经系统的早期发育机制及其演化。

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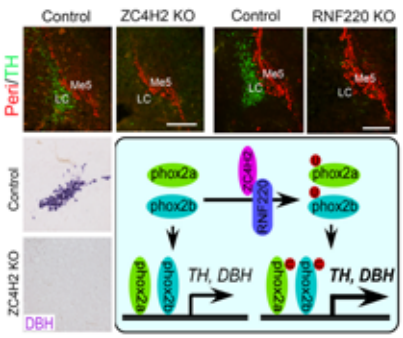
重要成果及产出：

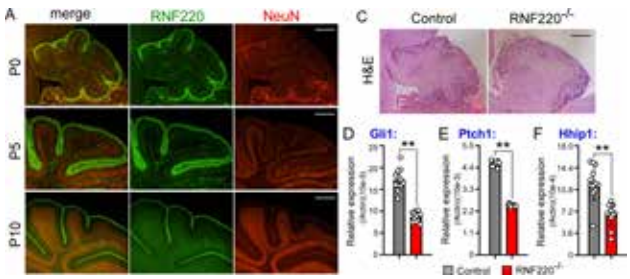
1. Guo X# , **Ma P#** , **Li Y** , Yang Y , Wang C, Xu T, **Wang H**, **Li C**, **Mao B***, Qi X* . (2020). Rnf220 mediates K63-linked poly-ubiquitination of Stat1 and promotes host defense. ***Cell Death Diff.*** DOI: 10.1038/s41418-020-00609-7.
2. Song NN#, **Ma P**#, Zhang Q, Zhang L, **Wang H**, **Zhang L**, **Zhu L**, He CH, **Mao B***, DingYQ*. (2020) Rnf220/Zc4h2-mediated monoubiquitylation of Phox2 is required for noradrenergic neuron development. ***Development***, 147: dev185199.
3. **Ma P**#, An T#, **Zhu L**, **Zhang L**, **Wang H**, **Ren B**, Sun B, Zhou X, Li Y*, **Mao B***. (2020) RNF220 is required for cerebellum development and regulates medulloblastoma progression through epigenetic modulation of Shh signaling. ***Development*** 147: dev188078.
4. **Zhang L**#, Ye M#, **Zhu L**, **Cha J**, **Li C**, Yao YG, **Mao B***. (2020). Loss of ZC4H2 and RNF220 inhibits neural stem cell proliferation and promotes neuronal differentiation. ***Cells***, 9:1600
5. **Wang X**, **Sun J**, Wang Z, **Li C**, **Mao B***. (2020) EphA7 is required for otic epithelial homeostasis by modulating Claudin6 in Xenopus. ***Biochem Biophys Res Commun***. 526:375-380
6. **Zhang SJ**#, **Wang GD**#, **Ma P**#, Zhang LL, **Yin TT**, **Liu YH**, **Otecko NO**, Wang M, Ma YP, Wang L, **Mao B***, Savolainen P*, **Zhang YP***. (2020). Genomic regions under selection in the feralization of the dingoes. ***Nature Commun.*** 11:671.

1. 揭示 RNF220/ZC4H2 调控中枢去甲肾上腺素能神经元分化的分子机制



脑的去甲肾上腺素能神经元主要分布于脑干的蓝斑核中。蓝斑核的去甲肾上腺素能神经元产生于胚胎发育 E10.5 天的第一菱脑节，并于胚胎发育后期迁移到脑桥。转录因子 Phox2a 和 Phox2b 对去甲肾上腺素能神经元的分化和维持起关键作用。本研究发现，RNF220/ZC4H2 泛素连接酶在蓝斑核发育中的去甲肾上腺素能神经元中特异高表达；在 RNF220 和 ZC4H2 敲除的小鼠中，蓝斑核的去甲肾上腺素能神经元均不能正常分化。生化实验表明，RNF220/ZC4H2 泛素连接酶复合体促进转录因子 Phox2a/2b 的单泛素化修饰，增强其转录活性。鸡胚电转实验在体内证明了 RNF220/ZC4H2 泛素连接酶复合体介导的 Phox2a/2b 的单泛素化修饰提高了其对下游靶基因 TH 和 DBH 的转录激活。本研究揭示了蓝斑去甲肾上腺素能神经元发育调控的一种新的分子机制，阐明了非经典的单泛素化修饰调控 Phox2a 和 Phox2b 蛋白转录活性的分子机制。

2. 揭示 RNF220 调控 Shh 信号与小脑发育的新机制



脊椎动物的小脑发育起源于后脑翼板背侧部的菱唇。在小脑发育过程中，浦肯野细胞分泌的 Shh 信号因子诱导位于外颗粒细胞层的颗粒神经元前体细胞增殖，促进小脑的发育。本研究发现，泛素连接酶 RNF220 在小鼠胚胎的小脑颗粒祖细胞中高表达；在 RNF220 敲除小鼠胚胎中，小脑颗粒祖细胞增殖受抑制，小脑发育异常，Shh 信号通路的靶基因下调；生化分析表明，RNF220 可以绕过对转录因子 Gli 的调控，通过对 PRC2 蛋白复合体成员 EED 的蛋白稳定性的调控，直接影响 Shh/Gli 信号通路靶基因的表观遗传修饰水平，正调控 Shh 信号通路，从而促进小脑颗粒祖细胞的增殖。该研究进一步揭示了脊椎动物早期胚胎发育过程中 Shh 信号通路精细调控的新机制，阐明了 RNF220 在小脑发育功能和作用机制。

Mechanisms of Neural Patterning and Evolution

Dr. Bingyu Mao, Principal Investigator, Ph. D. (1998, Shandong University, China). The molecular mechanisms of neural patterning and how these mechanisms evolved during vertebrate origin are the focuses of our lab. We use mouse, the amphibian *Xenopus* and the cephalochordate amphioxus as our model animals.
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1. RNF220/ZC4H2-mediated monoubiquitylation of Phox2 is required for noradrenergic neuron development

Noradrenaline belongs to the monoamine system and is involved in cognition and emotional behaviors. Phox2a and Phox2b play essential but non-redundant roles during development of the locus coeruleus (LC), the main noradrenergic (NA) neuron center in the mammalian brain. The ubiquitin E3 ligase RNF220 and its cofactor ZC4H2 participate in ventral neural tube patterning by modulating Shh/ Gli signaling, and ZC4H2 mutation is associated with intellectual disability, although the mechanisms for this remain poorly understood. Here, we report that ZC4H2 and RNF220 are required for the development of central NA neurons in the mouse brain. Both ZC4H2 and RNF220 are expressed in developing LC-NA neurons. Although properly initiated at E10.5, the expression of genes associated with LC-NA neurons is not maintained at the later embryonic stages in mice with a deficiency of either Rnf220 or ZC4H2. In addition, we show that the RNF220/ZC4H2 complex monoubiquitylates Phox2a/ Phox2b, a process required for the full transcriptional activity of Phox2a/Phox2b. Our work reveals a role for RNF220/ZC4H2 in regulating LC-NA neuron development, and this finding may be helpful for understanding the pathogenesis of ZC4H2 mutation-associated intellectual disability.

2. RNF220 is required for cerebellum development and regulates medulloblastoma progression through epigenetic modulation of Shh signaling

Sonic hedgehog (Shh) signaling is essential for proliferation of cerebellar granule neuron progenitors (CGNPs) and its mis-regulation is linked to various disorders, including cerebellar cancer medulloblastoma (MB). We recently identified RNF220, a ubiquitin E3 ligase promoting K63-linked polyubiquitylation and nuclear exportation of Gli transcription factors, as an Shh/Gli regulator involved in ventral neural patterning. Here, we report that RNF220 is required for the proliferation of CGNPs and Daoy cells (an Shh-grouped MB cell line), working as a positive regulator of Shh signaling. Mechanistic investigation demonstrated that RNF220 promotes Shh target gene expression by targeting the PRC2 component EED, and alters levels of epigenetic modification marks on Shh target promoters. We provided evidence that $RNF220^{+/-}$; $Ptch1^{+/-}$ mice showed lower spontaneous MB occurrence compared with $Ptch1^{+/-}$ mice. Furthermore, in human clinical MB samples, RNF220 expression correlated well with that of GAB1, an Shh-group MB marker. Our findings provide new insights into the epigenetic regulation of Shh signaling and identify RNF220 as a potential new diagnostic marker and therapeutic target for Shh-group MB.

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哺乳动物胚胎发育

郑　萍，博士，研究员，课题组长。2009 年入选中国科学院“百人计划”。云南省高端科技人才，中国科学院王宽诚人才奖“西部学者突出贡献奖”获得者。实验室主要研究方向包括：1）干细胞维持遗传物质稳定性的调控机制；2）生殖干细胞的基础生物学及其在动物基因修饰技术中的应用研究；3）灵长类早期胚胎发育。

重要成果及产出：

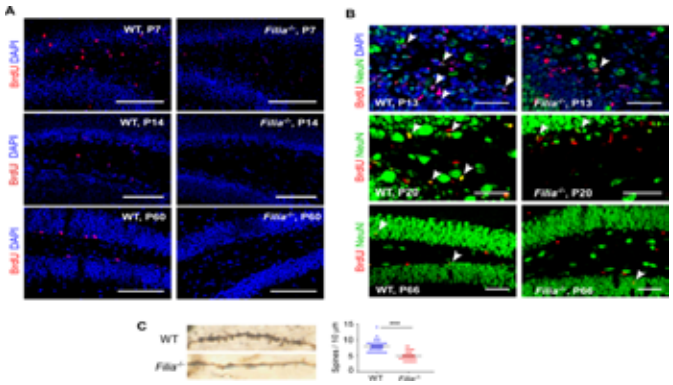
Li JZ, Shang YF, **Wang L**, **Zhao B**, **Sun CL**, Li JL, Liu SL, **Li C**, **Tang M**, Meng FL*, **Zheng P***. Genome integrity and neurogenesis of postnatal hippocampal neural stem/progenitor cells require a unique regulator Filia. ***Science Advances***, 2020, 6(44):eaba0682. 5 yr IF 14.09

发明专利：201610460383.X，一种建立可持续传代的树鼩精原干细胞细胞系的方法(郑萍，李朝晖，班文赞），2020 年授权。

1.Filia 调控海马神经干细胞基因组稳定性，维持海马正常神经发生和功能

干细胞是机体发育和组织稳态维持的基础，干细胞基因组不稳定常导致胚胎发育异常及组织器官的衰老和癌变。本研究鉴定了小鼠海马神经干 / 祖细胞（neural stem/progenitor cells，NSPCs）的基因组稳定性调控蛋白 Filia。Filia 缺失后，海马神经细胞产生严重的 DNA 双链断裂，海马神经发生和功能异常。猕猴 NSPCs 中，Filia 的同源基因具有保守功能，提示人类该基因的功能变异可能导致神经系统发育疾病。该工作揭示了 Filia 在调控海马正常神经发育和功能中的重要意义，也提出不同脑区 NSPCs 的基因组稳定性调控机制可能存在区域特异性，以适应不同的神经发生功能。

【***Science Advances***, 2020, 6(44) :eaba0682】



Filia$^{-/-}$ 小鼠海马中 NSPCs 的增殖和神经分化受损

2. 鉴定了调控干细胞基因组稳定性的全新 lncRNA

干细胞具很强的基因组稳定性维持能力，但机制远未清楚。通过转录组分析，我们在胚胎干细胞和多种成体干细胞中鉴定到一个尚未注释的 lncRNA，命名为 DISCN。DISCN 主要在干细胞中表达，且其表达响应 DNA 损伤处理。功能研究发现，DISCN 对维持胚胎干细胞和神经干细胞的基因组稳定性非常关键。在小鼠中敲除 DISCN，可导致新生鼠死亡。幸存的成年个体神经功能也严重受损，在学习记忆、情感及运动能力中表现出显著缺陷。机制分析发现，DISCN 定位于核仁中，通过 DISCN-Ncl-RPA 轴维持核质中自由 RPA 的蛋白量。RPA 蛋白是细胞 DNA 复制、DNA 损伤反应的限速因子。因此，干细胞通过高表达 DISCN，显著提升自由 RPA 的含量，从而显著增强其基因组稳定性。该工作揭示了基因组稳定性维持机制的进化。【已投稿】

Mammalian Embryonic Development

Dr. Ping Zheng, Principal Investigator, joined in Kunming Institute of Zoology, Chinese Academy of Sciences in 2009. The laboratory studies 1) how stem cells safeguard their genomic stability, 2) the biology of germ-line stem cells in male and female gonads, and 3) the early embryogenesis of non-human primates. We use mouse, monkey and tree shrew as animal models.
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1. Genome integrity and neurogenesis of postnatal hippocampal neural stem/progenitor cells require a unique regulator Filia

Endogenous DNA double strand breaks (DSBs) formation and repair in neural stem/progenitor cells (NSPCs) play fundamental roles in neurogenesis and neurodevelopmental disorders. NSPCs exhibit heterogeneity in terms of lineage fates and neurogenesis activity. Whether NSPCs also possess heterogeneous regulations on DSB formation and repair to accommodate region-specific neurogenesis has not been explored. Here we identified a regional regulator Filia, which is predominantly expressed in mouse hippocampal NSPCs after birth, and regulates DNA DSB formation and repair. On one hand, Filia protects stalling replication forks and prevents the replication-associated DSB formation. On the other hand, Filia facilitates the homologous recombination (HR)-mediated DNA DSB repair. Consequently, Filia-/- mice had impaired hippocampal NSPCs proliferation and neurogenesis, were deficient in learning, memory, and mood regulations. Thus, our study provided the first proof of concept demonstrating the region-specific regulations of DSB formation and repair in subtypes of NSPCs. (***Science Advances***, 2020, 6(44) :eaba0682)

2. A novel lncRNA DISCN safeguards genomic stability by sustaining RPA availability

Stem cells (SCs) possess superior stable genome compared to their differentiated progenies. The underlying mechanisms remain poorly defined. Here we identified an un-annotated lncRNA DISCN which is predominantly expressed in embryonic stem cells (ESCs) and tissue stem cells (e.g. neural stem/progenigor cells, NSPCs). Loss of DISCN led to massive genome instability in cultured mouse ESCs and NSPCs. Notably, knock out DISCN in mice resulted in newborn death as well as brain dysfunctions in survived adults due to the DNA double strand break accumulation and associated inflammatory reactions. Mechanistically, DISCN localizes in nucleolus where it binds to Ncl and sequesters Ncl at nucleolus. This prevents Ncl from translocating into nucleoplasm and avoids excessive Ncl-RPA association. Thus, DISCN sustains the RPA availability central to replication stress response. These findings have implications for understanding cancer cell biology and the evolution of genomic stability regulation. (**Submitted**)

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工作人员（Staff）

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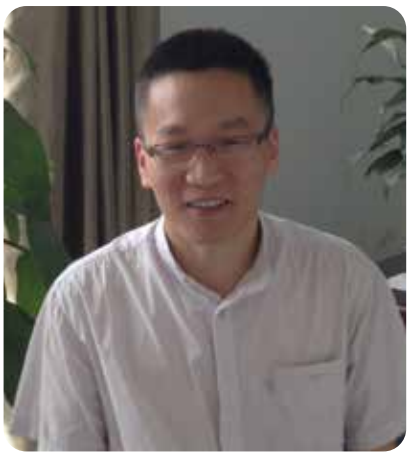
龚道华	Gong, Daohua	2018
唐　敏	Tang, Min	2018
谢　恒	Xie, Heng	2018
陶慧玲	Tao, Huiling	2019
孟夏朵	Meng, Xiaduo	2020
董玉萍	Dong, Yuping	2020
金　洁	Jin, jie	2020



表观遗传与发育调控

焦保卫，博士，研究员，博士生导师。“青年千人计划”引进人才。云南省细胞生物学学会第五届理事会秘书长。长期从事乳腺发育、乳腺癌、乳腺（癌）干细胞的研究。 鉴定了 RLIM 基因在乳腺发育中的关键作用，发现 X 染色体失活（XCI）在成体细胞中的新模式，阐明了 RLIM 基因在乳腺发育和胚胎发育早期的调控机制及其进化意义。研究团队发现 SGCE 在乳腺癌干细胞耐药中的新机制，以及 TAR DNA 结合蛋白 43 (TDP-43) 在乳脂分泌过程中的作用。目前已经在 *Cell*、*PNAS*、*Nature Communications*、*Advanced Science* 等国际期刊杂志发表论文 30 余篇。

重要成果及产出：

1. **Zhao L[1], Qiu T[1], Jiang D[1], Xu H, Zou L, Yang Q,** Chen C***, Jiao B*.** SGCE promotes breast cancer stem cells by stabilizing EGFR. ***Advanced Science.*** 2020. June 08; 7(14):1903700.
2. **Zhao L[1], Ke H[1], Xu H, Wang G, Zhang H, Zou L**, Xiang S, Li M, Peng L, Zhou M, Li L, Ao L, **Yang Q,** Shen C J, Yi P*, Wang L*, **Jiao B*.** TDP-43 facilitates milk lipid secretion by post-transcriptional regulation of Xdh and Btn1a1. ***Nature Communications.*** 2020. Jan 17;11(1):341.
3. **Xu H[1], Yang X[1],** Huang W[1], **Ma Y, Ke H, Zou L, Yang Q, Jiao B*.** Single-cell profiling of long noncoding RNAs and their cell lineage commitment roles via RNA-DNA-DNA triplex formation in mammary epithelium. ***Stem Cells.*** 2020. Sep 15.
4. **Xu H[1], Zhao L[1],** Feng X, Ma Y, Chen W, Zou L, Yang Q, Sun J, Yu H, **Jiao B*.** Landscape of genomic imprinting and its functions in the mouse mammary gland. ***J Mol Cell Biol.*** 2020 May 5: mjaa020.

1. SGCE 通过稳定 EGFR 促进乳腺癌干细胞的干性。

由肿瘤干细胞介导的耐药性是三阴性乳腺癌（TNBC）治疗的难点。结合 TNBC 单细胞测序数据，我们鉴定了一个在乳腺癌干细胞（BCSC）中高表达的基因 -SGCE。表型分析发现 SGCE 对于乳腺癌干细胞的自我更新不可或缺。在机制探讨上，发现 SGCE 与 E3 泛素连接酶 c-Cbl 相互结合，SGCE 缺失促进 c-Cbl 释放出来而泛素化其底物蛋白 EGFR，从而使得 EGFR 进入网格蛋白介导和巨胞饮途径的内化，内化的 EGFR 进而进入溶酶体降解。EGFR 的降解导致其下游通路被阻断并最终抑制 BCSC 自我更新和胞外基质 ECM 的累积。SGCE 在 BCSC 中高表达时，SGCE 与 c-Cbl 相互结合，EGFR 能够正常激活其下游信号通路 PI3K-AKT，促进 BCSC 干性维持、肿瘤细胞迁移、化疗药物和靶向 EGFR 抑制剂的耐药性。 EGFR 在超过 50% TNBC 病人中高表达，与乳腺癌细胞增殖、转移和 BCSC 的干性维持密切相关，然而 EGFR 的抑制剂在乳腺癌中的临床治疗效果并不显著。SGCE 分子帮助维持 BCSC 中 EGFR 高表达，去除 SGCE 的表达则可以促进 TNBC 中的 EGFR 靶向治疗的效果，从而为 EGFR 与其它靶点的联合治疗提供新策略。

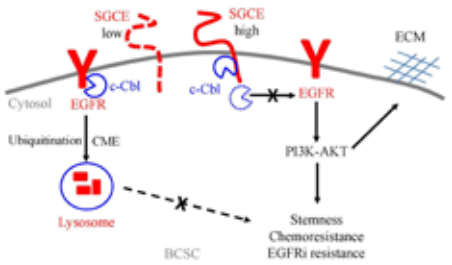


图 1. SGCE 通过调控 EGFR 而贡献于乳腺癌干细胞的自我更新

【Zhao LN et al., ***Advanced Science***. 2020, IF=15.840】

2. TDP-43 通过 Xdh 和 Btn1a1 的转录后调控促进乳脂分泌。

乳脂的分泌是将营养和能量从亲代传递给后代的关键过程。但是，潜在的分子机制尚不清楚。我们发现 RNA 结合蛋白 TDP-43 在哺乳动物进化中受到正向选择。乳腺特异性敲除小鼠模型中，发现 TDP-43 基因的缺失会导致乳脂上皮细胞中大量脂质液滴的积累，引起乳汁分泌异常，最终导致幼仔严重营养不良。在哺乳期妇女的人乳样品中，我们发现 TDP-43 的表达水平与较高的产奶量呈正相关。在分子机制上，TDP-43 通过转录后水平调控，稳定下游基因 Btn1a1 和 Xdh 的 mRNA 水平，从而影响乳脂分泌过程。我们的结果表明 TDP-43 在乳脂分泌中的关键作用，为临床泌乳不足的筛查和干预提供了潜在的策略。

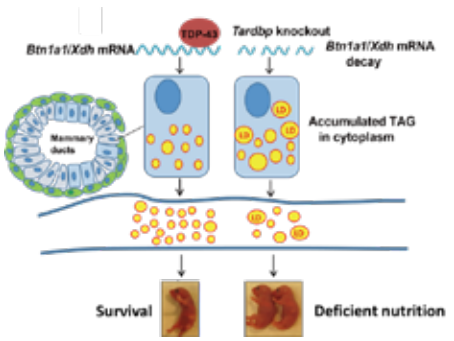


图 2. TDP-43 调控乳脂分泌的机制

【Zhao LM et al., ***Nature Communications***. 2020, IF= 12.121】

Epigenetic and Developmental Regulation

Dr. Baowei Jiao, Principal Investigator, doctoral supervisor. The research team is mainly interested in mammary gland development, breast cancer, normal and breast cancer stem cell. Research team a novel mechanism of SGCE in breast cancer stem cell chemoresistance and the role of TDP-43 in milk lipid secretion. Currently, over 30 papers have been published in international journals, such as *Cell*, *PNAS*, *Nature Communications*, *Advanced Science*.
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1. SGCE Promotes Breast Cancer Stem Cells by Stabilizing EGFR

Breast cancer stem cells (BCSCs) are responsible for resistance to chemotherapy, high degree of metastasis, and poor prognosis, especially in triple-negative breast cancer (TNBC). The $CD24^{low}CD44^{high}$ and high aldehyde dehydrogenase 1 (ALDH1) cell subpopulation ($CD24^{low}CD44^{high}ALDH1^{+}$) exhibit very high tumor initiating capacity. In the current study, the upregulated genes are analyzed in both $CD24^{low}CD44^{high}$ and $ALDH1^{+}$ cell populations at single-cell resolution, and a highly expressed membrane protein, SGCE, is identified in both BCSC populations. Further results show that SGCE depletion reduces BCSC self-renewal, chemoresistance, and metastasis both *in vitro* and *in vivo*, partially through affecting the accumulation of extracellular matrix (ECM). For the underlying mechanism, SGCE functions as a sponge molecule for the interaction between epidermal growth factor receptor (EGFR) and its E3 ubiquitination ligase (c-Cbl), and thus inhibits EGFR lysosomal degradation to stabilize the EGFR protein. SGCE knockdown promotes sensitivity to EGFR tyrosine kinase inhibitors (TKIs), providing new clues for deciphering the current failure of targeting EGFR in clinical trials and highlighting a novel candidate for BCSC stemness regulation.

2. TDP-43 facilitates milk lipid secretion by post-transcriptional regulation of Btn1a1 and Xdh

Milk lipid secretion is a critical process for the delivery of nutrition and energy from parent to offspring. However, the underlying molecular mechanism is less clear. Here we report that TDP-43, a RNA-binding protein, underwent positive selection in the mammalian lineage. Furthermore, TDP-43 gene (Tardbp) loss induces accumulation of large lipid droplets and severe lipid secretion deficiency in mammary epithelial cells to outside alveolar lumens, eventually resulting in lactation failure and pup starvation within three weeks postpartum. In human milk samples from lactating women, the expression levels of TDP-43 is positively correlated with higher milk output. Mechanistically, TDP-43 exerts post-transcriptional regulation of Btn1a1 and Xdh mRNA stability, which are required for the secretion of lipid droplets from epithelial cells to the lumen. Taken together, our results highlights the critical role of TDP-43 in milk lipid secretion, providing a potential strategy for the screening and intervention of clinical lactation insufficiency.

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灵长类进化遗传与发育

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重要成果及产出：

1. Adeola Oluwakemi Ayoola#, Bao-Lin Zhang#*, Richard P Meisel, Lotanna M Nneji, Yong Shao, Olanrewaju B Morenikeji, Adeniyi C Adeola, Said I Ng'ang'a, Babafemi G Ogunjemite, Agboola O Okeyoyin, Christian Roos, **Dong-Dong Wu***, Population Genomics Reveals Incipient Speciation, Introgression, and Adaptation in the African Mona Monkey (Cercopithecus mona). ***Molecular Biology and Evolution***,2020,doi.org/10.1093/molbev/msaa248.
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1. 白额长尾猴群体分化和适应性遗传性状解析

白额长尾猴主要分布于非洲的加纳、多哥、贝宁、尼日利亚和喀麦隆，是当地较为常见的灵长类，基于当地保护区多年以来缴获的样品，本研究首先利用三代基因组测序技术构建了质量较好的白额长尾猴参考基因组，获得的基因组组装大小为2.90 Gb，contig N50达到22.7 Mb。之后对来自不同地点的白额长尾猴样品进行基因组重测序，发现尼日利亚境内的长尾猴大致可以分为东（East）、中（WCb）、西（(WCa）三个不同的地理遗传组分（图1）。东白额长尾猴与其他白额长尾猴遗传差异最大，且以尼日尔河为界和其他样品分开，分歧时间大约为8.4万年，这表明尼日尔河在白额长尾猴的种群分化中起着地理隔离的作用。另外对线粒体基因组的遗传进化分析，研究人员意外地发现东白额长尾猴与同域分布的冠毛长尾猴聚在一起，表明其在进化历史上可能与冠毛长尾猴发生过种间杂交，通过对基因组中发生渗透区域最长的片段进行分析发现其中的3个基因中有2个（*PTPRK*和*FRAS1*）被报道与毛色相关，表明毛色在性选择的过程中可能发挥重要作用。此外，对不同种群的遗传分化分析发现与免疫相关的基因在不同的种群中发生了显著高分化，其中与抗猴免疫缺陷病毒（SIV）相关的基因（*AKT3* and *IL13*）和抗疟疾相关的基因（*G6PD*）被检测到了达尔文正选择信号。非洲多数灵长类动物是SIV病毒的天然宿主，它们与病毒的长期共处的过程中发生协同进化，因此即使它们感染了SIV病毒但在很多情况下并不致病。本研究提示白额长尾猴可能是研究SIV和疟疾的潜在动物模型。

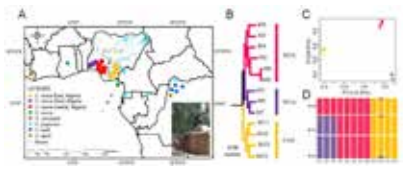

图1. 采样范围和群体遗传结构分析

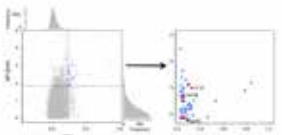

图2. 候选的受选择基因

2. 揭示低等无脊椎动物再生的分子细胞学机制

动物的再生能力一直是一个令人着迷且非常复杂的生物学过程。然而到目前为止，蚯蚓再生的分子细胞学机制还不是很清楚。我们利用长读段PacBio平台+Hi-C辅助组装等策略测序并拼装了准染色体水平的高质量安德爱胜蚓（Eisenia andrei）基因组（Scaffold N50≈111Mb），并通过不同再生时期bulk转录组和单细胞转录组整合揭示蚯蚓再生的分子细胞学机制（图3）。研究发现蚯蚓基因组中重复序列LINE2转座元件可能在蚯蚓再生中扮演重要调控角色，而在本研究中，我们发现EGR1不仅在蚯蚓再生过程中发生差异高表达，而且其侧翼的LINE2元件也发生显著差异表达上调，因此，我们推测这些显著差异表达的LINE2元件可能通过调控邻近基因的表达来参与蚯蚓再生过程。另一方面，我们在蚯蚓基因组中发现大量基因复制事件，进一步我们发现某些显著扩张的基因家族，可能通过增加其拷贝数剂量效应来调控蚯蚓再生过程。在转录激活水平，我们发现4个与早期再生显著相关的共表达网络模块和系列hub转录调控因子，富集分析显示它们可能参与再生早期细胞的增殖和分化。同时，蚯蚓再生早期的单细胞转录组解析暗示蚯蚓再生早期72h后损伤愈合部位细胞的高比例组分是干细胞，暗示多能干细胞在蚯蚓再生早期过程中具有重要作用（图4）。

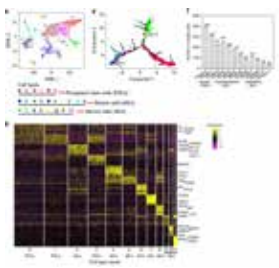

图4. 单细胞RNA-sequencing揭示再生的细胞机制

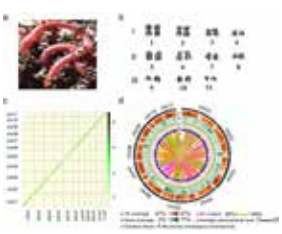

图3. a 安德爱胜蚓（用于完成基因组测序物种）。b 安德爱胜蚓的核型分析。2n=22，根据染色体形态，初步分成三个亚类。核型分析源于蚯蚓环带的分裂中期细胞，该分析由昆明动物研究所细胞库完成。c Hi-C 互作图。d circos 展示蚯蚓基因组的特征。

Primate Evolutionary Genetics and Development

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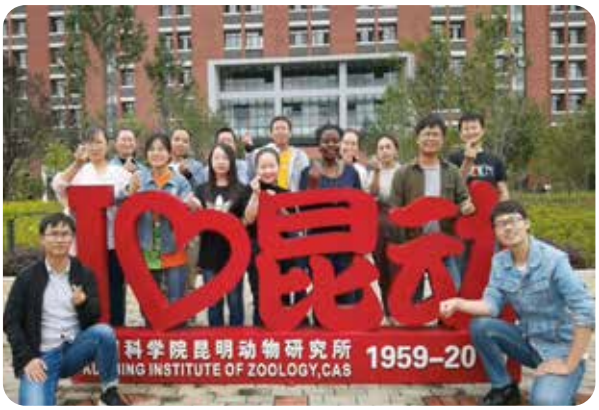

1. Origin and domestication of domestic chicken

Despite the substantial role that chickens have played in human societies across the world, both the geographic and temporal origins of their domestication remain controversial. To address this issue, we analyzed 863 genomes from a worldwide sampling of chickens and representatives of all four species of wild jungle fowl and each of the five subspecies of red jungle fowl (RJF). Our study suggests that domestic chickens were initially derived from the RJF subspecies Gallus gallus spadiceus whose present-day distribution is predominantly in southwestern China, northern Thailand and Myanmar. Following their domestication, chickens were translocated across Southeast and South Asia where they interbred locally with both RJF subspecies and other jungle fowl species. In addition, our results show that the White Leghorn chicken breed possesses a mosaic of divergent ancestries inherited from other subspecies of RJF. Despite the strong episodic gene flow from geographically divergent lineages of jungle fowls, our analyses show that domestic chickens undergo genetic adaptations that underlie their unique behavioral, morphological and reproductive traits. Our study provides novel insights into the evolutionary history of domestic chickens and a valuable resource to facilitate ongoing genetic and functional investigations of the world's most numerous domestic animal.

Fig 5. Sample distribution and phylogeny of Gallus taxa.

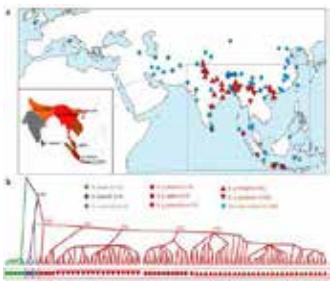

Fig 6. Science publishes an editorial titled "The chicken first crossed the road in Southeast Asia, 'landmark'gene study finds".

2.Ancient Hybridization with an Unknown Population Facilitated High-Altitude Adaptation of Canids

Genetic introgression provides material for adaptive evolution, but also confounds our understanding of evolutionary history. This is particularly true for canids, a species complex in which genome sequencing and analysis has revealed a complex history of admixture and introgression. Here, we sequence 19 new whole genomes from high-altitude Tibetan and Himalayan wolves and dogs and combine these into a larger data set of 166 whole canid genomes. Using these data, we explore the evolutionary history and adaptation of these and other canid lineages. We find that Tibetan and Himalayan wolves are closely related to each other, and that approximately 39% of their nuclear genome is derived from an as-yet unrecognized wolf-like lineage that is deeply diverged from living Holarctic wolves and dogs. The EPAS1 haplotype, which is present at high frequencies in Tibetan dog breeds and wolves and confers an adaptive advantage to animals living at high altitudes, was probably derived from this ancient lineage. Our study underscores the complexity of canid evolution and demonstrates how admixture and introgression can shape the evolutionary trajectories of species.

Fig 7. COVER ARTICLE of Molecular Biology and Evolution

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神经突触机制与功能

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1. 大脑进化发育调控的分子机制

在哺乳类动物的演化过程中，最显著的改变则是由大脑所决定的高级认知功能，大脑结构和功能调控的复杂性被认为是人类区别于其他物种的重要原因。我们研究组重点关注大脑皮层沟回结构、大脑半球对侧连接的重要结构胼胝体的进化发育的遗传机制，以及灵长类特异基因在皮层结构和神经突触环路进化发育中的作用机制。

皮层沟回结构是人类大脑的重要特征，其发育形成异常与诸多神经疾病密切相关。研究表明在哺乳类演化过程中，大脑皮层沟回形成经历多次起源。我们首先以非洲兽总目（Afrotheria）、劳亚兽总目（Laurasiatheria）和灵长目（Primate）三支哺乳类为研究对象，根据皱褶指数选取其中有脑回和无脑回的物种，采用趋同进化分析方法研究其基因组中受到共同正选择的基因，发现诸多分子与神经发育和功能相关。由于貂是目前研究沟回发育的主要动物模型，我们拟结合脑立体定位注射和 CRISPR 技术手段，在幼貂大脑皮层沟回形成过程中分别敲除上述基因，考察对大脑褶皱发育的影响。其次，我们分离了成年貂大脑沟与回组织，通过 RNA-seq、ChIP-seq、DNAase-seq 分析，考察沟与回之间基因表达和染色质调控区域的差异，相关数据正在分析中。同时，我们拟分别收集关键发育节点的貂大脑沟回组织，利用类似的组学分析，以进一步深入研究沟回进化发育的调控机制。

在演化过程中，胼胝体是从胎盘哺乳类开始出现的连接对侧大脑的神经纤维结构，在人类大脑中其缺失或发育异常往往导致认知功能障碍，与自闭症等神经精神疾病密切相关。研究表明，与单孔目和有袋类相比，胎盘哺乳类基因组中进化出约 600 个新的且保守的增强子。我们通过相关性基因功能分析发现，部分与胼胝体的发育调控相关。由于胼胝体主要是由皮层 2-3 层锥体神经元投射产生，因此我们通过 Cux2-Cre 和 Ai9 小鼠品系杂交，以特异标记此类神经元，收取不同胚胎发育和出生后皮层组织，通过 FACS 将这些细胞流式分选出来。结合 RNA-seq、ChIP-seq、ATAC-seq 组学分析，考察上述胎盘哺乳类特异增强子在胼胝体发育过程中的开放性。进一步结合 CRISPR 表观调控技术，增强或抑制其活性，研究对胼胝体发育的影响，以及调控的下游基因和作用机制。此外，我们也将利用上述组学分析技术，对比研究小鼠、树　和猕猴大脑皮层 2-3 层神经元中基因表达和调控的差异性，进一步研究进化过程中胼胝体形成的调控机制。

在演化过程中，包括人类的灵长类基因组中进化出诸多新基因，而其在大脑发育和功能调控中的作用不甚清楚。在我们前期工作中，我们发现了精神分裂症新易感基因 BTN3A2 是一个灵长类特异基因（**Wu Y et al. 2019 *EBioMedicine***），为了进一步研究其在神经突触进化和功能调控中的作用，我们构建了其条件性基因敲入小鼠，并于并与 Nestin-Cre 工具鼠杂交，以使在小鼠大脑中异位表达 BTN3A2 分子，通过神经行为学分析发现会影响小鼠焦虑行为和工作记忆。我们也利用该小鼠模型研究该灵长类特异基因对突触发育和传递的影响，以及其中的分子机制。

2. 神经突触传递调控与大脑功能

谷氨酸受体是大脑中兴奋性突触传递的重要接收器，在前期工作中，我们系统性研究了其家族成员红藻氨酸受体的突触转运和生理活性的调控机制，揭示了同质性 GluK1 和 GluK2 受体所依赖的不同的分子基础（**Sheng N et al. 2015 *Elife***，**Sheng N et al. 2017 *PNAS***，**Duan GF et al. 2018 *Nature Communications***）。我们进一步研究发现 GluK2/GluK4 和 GluK2/GluK5 异质性 KAR 受体，在海马神经突触转运调控过程是基于不同的分子机制，并且是由 GluK4 和 GluK5 亚基的胞外 ATD 结构域所决定。我们结合生化和细胞筛选系统，鉴定分别于其结合的 C1q 家族补体分子和跨突触分子复合物。在此基础上，我们将结合光遗传、CRIPSR 基因操作和神经电生理技术手段，深入研究该分子复合物在突触传递中的功能，并利用海马癫痫症模型研究在大脑功能调控中的作用。此外，我们正在开展精神疾病易感基因突变如 AUTS2、IQSEC 等在突触发育和传递中的作用和分子机制，以及对小鼠神经行为的影响，揭示突调控与大脑功能的内在联系。

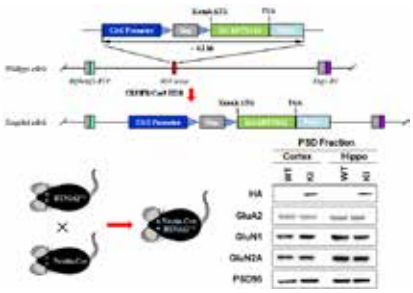

图 1. 灵长类特有基因 BTN3A2 人源化小鼠动物模型的构建

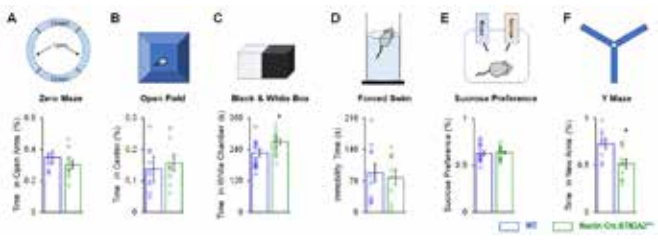

图 2. 大脑中表达 BTN3A2 对小鼠神经行为学的影响

Synaptic Function and Mechanism

Prof. Nengyin Sheng, Principal Investigator, joined in Kunming Institute of Zoology, Chinese Academy of Sciences in 2017. The research of Sheng's lab focuses on central nervous system (CNS) and will study the following topics using mice, ferret, shrew and rhesus monkey as model systems: (1) The regulatory mechanisms underlying synaptic physiological conditions; (2) The genetic bases underlying evolution and development of primate synapse; (3) The internal relationship between the evolution of human neural circuit and neuropsychiatric disorders.

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1.The molecular mechanism of brain evolution and development regulation

In the evolution of mammals, the most significant change is the acquirement of high-level cognitive abilities determined by the brain. The complexity of brain structure and function regulation is considered to be an important reason the most significant character to distinguish homo sapiens from other species. Our research group focuses on the genetic mechanisms underlying the evolution and development of gyrification structure of cerebral cortex and corpus callosum, an important structure of the contralateral connection of the cerebral hemisphere, as well as the role and mechanism of primate-specific genes in the evolution and development of the cortical structure and synaptic circuit.

The cortical folding is an important feature of the human brain, and its abnormal development is closely related to many neurological diseases. We first take the three branches of Afrotheria, Laurasiatheria and Primate as the research objects. According to the gyrification index, we selected species with and without brain gyrus, and used convergent evolution analysis to identify the genes subjected to common positive selection. The results found that many molecules are indeed related to neurodevelopment and function. Since ferret is currently the main animal model for studying the development of gyrification, we plan to combine brain stereotactic injection and CRISPR technologies to knock out the above genes during brain folding development of ferret cerebral cortex and investigated the impact on the development of brain gyrification. Secondly, we separated the sulcus and gyrus tissues of adult ferret brains. Through RNA-seq, ChIP-seq, and DNAase-seq analysis, we investigated the differences in gene expression and chromatin regulation regions between sulcus and gyrus. The relevant data is being analyzed. At the same time, we plan to collect the ferret sulcus and gyrus tissues of critical developmental stages and use similar omics analysis to further study the regulation mechanism of evolution and development of brain gyrification.

Corpus callosum is firstly evolved from placental mammals, and its absence or abnormal development in the human brain would cause cognitive dysfunction and neuropsychiatric diseases. Studies have shown that, compared with monotremes and marsupials, around 600 novel and conserved enhancers have been evolved in the placental mammalian genome. We crossed the Cux2-Cre and Ai9 mouse strains to specifically label the corpus callosum projection neurons, and used FACS to collect these neurons at different critical development stages. Different omics analyses including ATAC-seq are applied to examine the activities of these placental specific enhancers during corpus callosum development. We will further the role and mechanisms of these enhancers using CRISPR technology to enhance or inhibit their activities. In addition, we will also use the above-mentioned omics analysis techniques to identify the differential expressing genes and regulatory elements in cerebral cortical 2-3 layers neurons of mice, tree shrews, and macaques, and further study the molecular mechanisms of corpus callosum evolutionary development.

During evolution, many de novo genes have been evolved in the primate genome, but their roles in brain development and physiological function remain elusive. In our previous work, we identified BTN3A2, a primate-specific gene, as a new susceptibility gene for schizophrenia (Wu Y et al. 2019 EBioMedicine). In order to further study its role in synapse evolution and functional regulation, We constructed conditional gene knock-in mice and crossed them with Nestin-Cre mice to ectopically express BTN3A2 in the mouse brain. Through neurobehavioral analyses, we found that it would affect the anxiety behavior and work memory. We also used this mouse model to study the effect of this primate-specific gene on synapse development and transmission, and the underlying molecular mechanism.

2. Neural synaptic transmission regulation and brain function

Glutamate receptors are critical for excitatory synaptic transmission in the brain. In our previous work, we systematically studied the regulatory mechanism of synaptic trafficking and physiological activity of kainate receptors, and revealed that the homomeric GluK1 and GluK2 receptors are relied on different molecular basis (Sheng N et al. 2015 Elife, Sheng N et al. 2017 PNAS, Duan GF et al. 2018 Nature Communications). We further found that the synaptic trafficking of GluK2/GluK4 and GluK2/GluK5 heteromeric receptors are regulated by different molecular mechanisms and are determined by the extracellular ATD domains of GluK4 and GluK5 subunits. We combined biochemical and cellular screening systems to identify its transsynaptic complex wit the C1q complement molecules. On this basis, we will combine optogenetic, CRIPSR and electrophysiological techniques to deeply study the function of this molecular complex in synaptic transmission, and use hippocampal epilepsy model to study its role in brain function.

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李　熹	Li Xi	2020 硕士

进化发育生物学研究

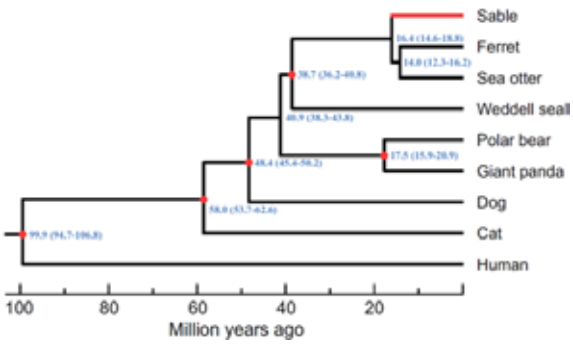
刘振，博士，研究员，博士生导师，国家基金委优秀青年基金获得者，云南省万人计划青年拔尖人才，2019 年成立进化发育生物学研究组，2020 年加入遗传资源与进化国家重点实验室。主要以非模式动物为研究对象，结合比较基因组学、进化遗传学和功能基因组学的理论和方法，从进化发育生物学的角度探讨动物适应性复杂性状的分子决定机制。目前，已在 *Science Advances, PNAS, Current Biology, Molecular Biology and Evolution* 等国际著名期刊发表研究论文十余篇。

1. 蝙蝠是研究非模式哺乳动物进化发育机制的独特模型

全世界大约有 1300 多种蝙蝠，是哺乳动物中仅次于啮齿目的第二大目。蝙蝠之所以成为演化最为成功的类群之一，与它们具有多种独特的适应性表型密切相关。例如，蝙蝠具有极端延长的前肢和宽大的翼膜，是哺乳动物中唯一会真正飞行的类群。食虫蝙蝠还拥有回声定位的能力，能够在夜晚捕食昆虫。目前对于蝙蝠适应性复杂表型起源和演化的分子机制的研究主要集中在基因组中蛋白质编码基因的进化和功能解析上，缺乏对基因组非编码区域、基因表达调控网络和发育机制的深入分析，因此无法全面系统回答蝙蝠适应性复杂表型是如何产生的问题。经过几年的积累，我们收集了三种蝙蝠全胚胎期的样品，获得了多种适应性表型的在不同发育期的数据，结合多种组学手段，争取在三年内对某些表型的发育机制开展系统全面的研究。

2. 第一个紫貂（Martes zibellina）的高质量基因组

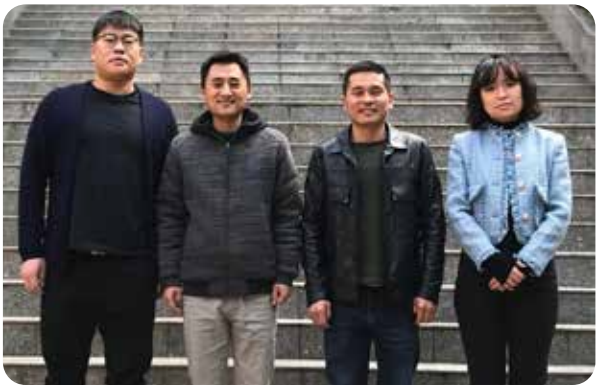
紫貂是貂属里面一个广泛分布的物种，在不同分布区域呈现出了群体分化和形态的多样性。为了对其适应性进化和适应性表型的进化发育机制的研究提供支持，我们对紫貂的基因组进行了深度解析。组装的基因组大小为 2.42Gb，scaffold 的 N50 达到了 5.2Mb，预测出了 19413 个蛋白质编码基因，完整性达到了 95.2%，因此，为后续的相关研究奠定了坚实的基础。



重要成果及产出：

1. **Guangshuai Liu**[1], Chao Zhao[1], **Dongming Xu**[1], Huanxin Zhang, Vladimir Monakhov, Shuai Shang, Xiaodong Gao, Weilai Sha, Jianzhang Ma, Wei Zhang, Xuexi Tang, Bo Li, Yan Hua, Xiaofang Cao*, **Zhen Liu***, and Honghai Zhang*. First Draft Genome of the Sable, *Martes zibellina*. ***Genome Biology and Evolution***. 12(3):59–65 (2020).

Evolutionary Developmental Biology



Prof. Zhen Liu, Principal Investigator. Evolutionary developmental biology is like a bridge to mediate the evolutionary biology and developmental biology for understanding the genetic basis of phenotypic changes macroevolutionarily. Using bats as a research model, we focus on the following major questions: (1) what are the roles of molecular variations on the developmental mechanisms for the origin and elaboration of adaptive phenotypes in evolutionary process? (2) what are the relative roles of chance and necessity in evolution for the developmental mechanisms of adaptive phenotypes?

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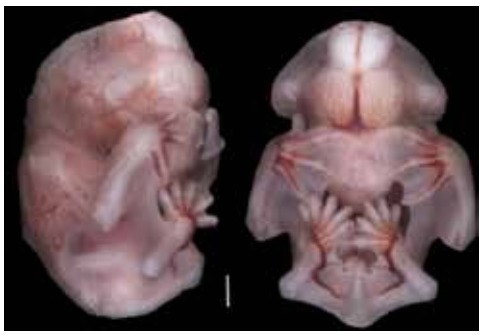
1. Bats are a unique model for researching the evolutionary developmental mechanisms of adaptive phenotypes in nonmodel mammals

To date, ~1300 bat species are discovered in the world, making them become the second biggest order in mammals except for rodents. It is because bats have evolved many adaptive complex traits that they represent one of most successful mammalian groups in evolution. For instance, bats own the extremely extended forelimbs and unique wing membranes and are the only mammals that can truly fly. Insectivorous bats have evolved laryngeal echolocation to prey insects at night. The current studies have been focusing on the evolutionary and functional analyses of protein-coding genes without comprehensively researching for the noncoding regions, gene expression regulatory networks, and developmental mechanisms at the genomic scale. Consequently, we cannot understand the molecular basis on how the adaptive complex traits of bats origin and elaborate during evolution.

We have collected embryonic samples across nearly all developmental time points of three bat species recent years, and measured the phenotypic data related to adaptive complex traits of bats, such as length of limbs and areas of wing membranes. Using multiple sequencing technologies, we are planning to investigate the evolutionary developmental mechanisms underlying the adaptive complex traits of bats.



2. First Draft Genome of the Sable, Martes zibellina

As one of the most widespread members in Martes, the sable shows distinct population differentiation and morphological variations across different distributions. To support further studies on the evolutionary developmental mechanisms of its adaptive traits, we present the first sable genome. The assembled genome is 2.42 Gb with a scaffold N50 of 5.20Mb and 95.15% of the curated single-copy orthologs were assembled as complete. A total of 19,413 protein-coding genes were predicted. Overall, our study provided the first reference genome for research in a broad range of areas including local adaptations, population evolution, conservation, and management for sable.

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昆明野生动物细胞库

昆明野生动物细胞库（简称昆明细胞库）成立于 1986 年，是以保存动物的遗传资源和遗传多样性为主要目的的细胞库。现已保存有 357 种动物的细胞系 2298 株 20000 余份。大多数为哺乳动物的细胞系，其中包括 60 种国家级重点保护动物的细胞系。目前，昆明细胞库是国家实验细胞资源共享服务平台、中国科学院生物遗传资源库、中国西南野生生物种质库的成员单位之一，也是遗传资源与进化国家重点实验室的成员单位之一。

重要成果及产出：

1. 苏伟婷，陈中正，万韬，王霞，周鸿艳，胡怡，王金焕，蒋学龙，佴文惠，何锴。2020。基于核型和分子系统学方法对中国猪尾鼠分类与分布的讨论。兽类学报，40 (3) : 239 - 248。

1. 细胞资源的收集和保藏

2020 年度，昆明细胞库利用从野外采集以及从其他途径获得的动物材料，共新建各类动物细胞系 62 株，其中包括龙蜥、斑飞蜥、尖吻蝮蛇、斑鸠等 8 种野生动物的细胞系 30 株，建立家养动物、人和实验动物的正常细胞系和肿瘤细胞系 32 株。复苏和扩增各类动物细胞系 451 株次。

2. 对外服务

在 2020 年度，昆明细胞库为全国各地的 402 家单位，其中高等院校 155 家，科研院所 92 家，企业 155 家的研究人员提供各类野生和家养动物细胞系、人及常见实验动物的各类正常组织来源的细胞系、肿瘤细胞系及培养液共计 520 株次。除提供细胞服务外， 我们还提供了核型分析和 STR 检测等技术服务 52 株次， 以及通过电话、邮件及现场指导等方式提供大量的细胞培养技术咨询。

3. 爬行动物细胞培养取得进展

爬行动物是真正适应陆栖生活的变温脊椎动物。由于没有成熟的细胞培养方法，已建系的爬行动物细胞系还很少。2020 年，我们利用获得的四种爬行动物材料，探索了爬行动物细胞培养的条件，成功建立了 16 株细胞系，为今后开展这个类群动物细胞资源的收集和保藏奠定了基础。

4. 北平顶猴不同组织来源细胞系的建立

平顶猴是国际上有报道唯一可感染艾滋病病毒（HIV-1）并伴有艾滋病样症状发生的灵长类动物。 利用一只病死的北平顶猴的组织材料， 我们成功建立了 8 株北平顶猴的不同组织来源的细胞系，并进行了核型分析为今后开展艾滋病的体外实验储备了材料。

Kunming Wild Animal Cell Bank

In order to conserve genetic resource and genetic diversity of animals, Kunming wild animal cell bank was established in Kunming Institute of Zoology, Chinese Academy of Science in 1986. Up to now 2298 cell lines from 357 species have been preserved in our cell bank. Most cell lines are derived from mammals. Among the species, 60 species are national protected wildlife in China. Now it is one branch of National Platform of Experimental Cell Resources for Sci-Tech, Biological Genetic Resource Bank of CAS, China Germplasm Bank of Wild Species, and State Key Laboratory of Genetic Resources and Evolution.

1. The collection and preservation of cell line

In 2020, 62 cell lines from various wild animals, domestic animals and humans had been established and frozen. Among these cell lines, 30 cell lines were derived from 8 species of wild animals such as Dragon Lizard, Spotted Flying Lizard, Great blind Snake, Spotted Doveetc; 32 cell lines were established from domestic animals, experimental animals and humans. Four hundred and fifty-one of frozen-stored cell lines were also resuscitated and subcultured.

2. Cell lines service and technical service

In this year, 520 cell lines and culture medium, 52 times of karyotype analysis and STR test had been provided for the researchers not only at State key laboratory of genetic resources and evolution, but also at other 155 Chinese universities, 155 enterprises, and 92 scientific research institutions. In addition, we also had provided a lot of cell culture technical advisory services by using the telephone and the email.

3. Advances have been made in reptile cell culture

Reptiles are really adapted to terrestrial life of the variable temperature vertebrates. There are few established reptile cell lines due to the lack of matured cell culture methods. In 2020, we explored the conditions for cell culture of reptiles by using the four kinds of reptile materials obtained, and successfully established 16 cell lines, laying a foundation for the collection and preservation of cell resources of this group of animals in the future.

4.The establishment of cell lines from Northern Pig-tailed Macaque

Pig-tailed macaque the only primate that has been reported to be infected with HIV-1 and has AIDS-like symptoms. Using the tissue materials of a dead Northern pig-tailed macaque, we successfully established 8 cell lines of different tissue sources of this monkey, and carried out karyotype analysis, so as to reserve materials for future in vitro experiments on AIDS.

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生命条形码南方中心

South China DNA Barcoding Center

生命条形码南方中心，于 2011 年 1 月成立，专门从事 DNA 条形码相关的科学研究、技术革新和应用推广。中国是国际生命条形码计划（iBOL）的核心成员，中国科学院昆明动物研究所顺应形势于 2011 年成立生命条形码南方中心，负责我国和东南亚地区野生动物 DNA 条形码数据的产出和管理，拥有完全访问国际生命条形码数据库 BOLD 系统的权限。生命条形码南方中心是专门从事 DNA 条形码技术的标准化、信息化和规模化，高通量条码实验的平台，并利用 DNA 条形码技术进行生物多样性评价和保护、濒危野生动物的物种识别，是国内首家面向 DNA 条形码研究和利用的综合性平台。

重要成果及产出：

1. Lotanna M. N , Adeniyi C. A , Moshood K. M, Segun O. O, Chabi A. M. S. D, Ifeanyi C. N, Babatunde E. A, Omotoso O, Adeola O. A, Agboola O. O, Odion O. I,Galadima F. U, Oluyinka A. I, Emmanuel O. F, Moise M. M, Wanze K. N, **Wang YY , Chen J, Wang WZ,** Jolly B. K, Obih A. U, Adiaha A. A. U & Christopher D.N. DNA Barcoding Silver ButterCatfish (Schilbe intermedius) Reveals Patterns of Mitochondrial Genetic Diversity Across African River Systems. ***Scientific Reports,*** (2020) 10:7097.
2. **Zhang HM**[1] & Hämäläinen M. Description of a new Caliphaea species from Yunnan, China (Odonata: Calopterygidae). ***Zootaxa*** 2020. 4895 (1): 103–110.
3. Dow R A, **Zhang HM**[1]. Two new species of Coeliccia Kirby from Yunnan, China (Odonata: Zygoptera: Platycnemididae). ***Zootaxa***, 2020. 4838 (4): 491–502
4. **张浩淼** . 常见蜻蜓野外识别手册 . 2020. 重庆：重庆大学出版社 .
5. **张浩淼** . 从水中诞生的空中芭蕾 — 蜻蜓 . 2020. 福州：海峡出版发行集团 .

1. 基于 DNA 条形码建立与重点口岸的快速鉴定互动机制

云南位于我国西南和东南亚地区是世界著名的生物多样性热点地区，随着“一带一路”战略的深入实施和国际贸易的日益频繁，许多入侵生物物种将不限于《名录》，且其形态的多样性，我国的分类学家不能很好的对其进行形态鉴定。物种鉴定是生物多样性认知的基础，是探讨生物分布与迁移规律的重要支撑，是有害生物防控的关键。而物种的准确鉴定离不开定名标本、分类学家以及关键分类技术的支持。因此，对口岸截获动物物种的准确鉴定、风险评估与有效防控，关键在于相关物种的有效的鉴定技术，以及可供口岸随时查阅和浏览的数据库信息平台。一般入侵害虫种类鉴定困难，分以下 3 种情况：1) 体型微小，形态观察不易；2) 外形近似的种类多；3) 成虫标本缺失。DNA 条形码回避了这 3 种情况，不受体型大小、外部形态、发育时期、标本性别以及标本完整性等的限制。该技术已被证实是比较通用、高效、精细的分子鉴定技术，1-3 个工作日的实验周期能一定程度满足口岸一线检验检疫工作者的需求。中心于 2019 年 -2020 年针对现有检验检疫重要有害物种的名录，与昆明动物博物馆、云南农业大学合作建立实体库和标准 DNA 条形码序列库，已构建基于 DNA 条形码技术的物种快速鉴定平台，建立与西南重点口岸的快速鉴定互动机制。

2. 蜻蜓目的分类学、系统学及数据库建立

中心张浩淼博士于 2020 年在云南德宏州铜壁关国家级自然保护区发现长腹扇属两个新种，分别为：铜壁关长腹扇 Coeliccia tongbiguan Dow & Zhang, 2020 和云南长腹扇蟌 Coeliccia yunnanensis Dow & Zhang, 2020。在云南楚雄州禄丰县发现闪色蟌属新种：赫曼闪色蟌 Caliphaea hermannkunzi Zhang & Hämäläinen, 2020。参与所级数据库平台建立中国蜻蜓网 “Odonata of China”, 计划于 2021 年 2 月开始正式运营。网站收录中国蜻蜓约 850 种，将成为世界最大的中国蜻蜓数据库。网站包括蜻蜓目的介绍、蜻蜓行为与生态、组学数据、分类系统及物种识别等板块，并涵盖中心正在进行的系统发育、基因组方面的研究数据。



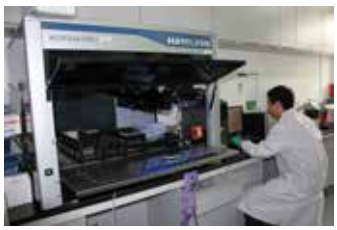
South China DNA Barcoding Center

China is a core member of the international Barcode of (IBOL). Kunming Institute of zoology, Chinese Academy of Sciences established the South China DNA Barcoding Center (SCDBC) in 2011, which is responsible for the production and management of DNA barcoding data of wild animals in China and Southeast Asia, and has full access to the international life barcoding database--BOLD SYSTEMS. SCDBC focus on establishing experimental platform which is high-throughput, standardized and informationalized. SCDBC also use DNA barcoding technology for biodiversity evaluation and protection, species identification of endangered wildlife. It is the first comprehensive platform for DNA barcoding research and utilization in China

Email: scdbc@mail.kiz.ac.cn

1. Rapid identification interaction mechanism with key department based on DNA barcoding

Yunnan province, is located in Southwest China and Southeast Asia. It is a hot spot in biodiversity in the world. With the in-depth implementation of the strategy of "one belt and one road" and frequent international trade, many invasive species will not be limited to the 'list'. The classification of Yunnan's species is not well identified by our taxonomists. Species identification is the basis of biodiversity cognition, an important support to explore the law of biological distribution and migration, and the key to pest control. The accurate identification of species can not be separated from the support of named specimens, taxonomists and key taxonomic techniques. Therefore, the key to accurate identification, risk assessment and effective prevention and control of animal species intercepted at ports lies in the effective identification technology of related species and the database information platform available for port to consult and browse at any time. Generally, it is difficult to identify invasive pest species in the following three situations: 1) small size, difficult to observe morphology; 2) many species with similar appearance; 3) lack of adult specimens. DNA barcoding avoids these three situations and is not limited by body size, external morphology, development period, specimen gender and specimen integrity. The technology has been proved to be a more general, efficient and fine molecular identification technology. The experimental cycle of 1-3 working days can meet the needs of frontier inspection and quarantine workers. From 2019 to 2020, the SCDBC cooperated with Kunming Animal Museum and Yunnan Agricultural University to establish a physical library and standard DNA barcoding sequence library for the existing list of important harmful species in inspection and quarantine. It has built a rapid species identification platform based on DNA barcoding technology and established an interactive mechanism for rapid identification with key ports in Southwest China.



2. Taxonomy, Phylogeny and Database of the order Odonata

Two new species of the genus Coeliccia Kirby, 1890 are found from Tongbiguan National Nature Reserve, Yingjiang County, Yunnan, named: Coeliccia tongbiguan Dow & Zhang, 2020 and Coeliccia yunnanensis Dow & Zhang, 2020. A new species of the genus Caliphaea Hagen in Selys, 1859 is found in Yunnan Province, Lufeng County, Chuxiong City, named: Caliphaea hermannkunzi Zhang & Hämäläinen, 2020. A website called"Odonata of China" is under establishing, which will be open around February 2021. The website contains about 850 species of dragonflies from China, being the largest database of the Chinese dragonfly worldwide. The database is divided into plates of Introduction, Ecology and Behavior, Phylogeny and Species Identification, also our ongoing study of phylogeny and genome will be shared.

团队成员（Lab Member）

工作人员（Staff）

王运宇 硕士 实验师
Yun-yu Wang, Engineer

张浩淼 博士 副研究员
Hao-miao Zhang, Associate Prof

中心实验室

中心实验室是隶属于遗传资源与进化国家重点实验室的公共技术服务平台，于 2008 年 11 月正式投入使用。目前，实验室共有基因组学分析平台、蛋白质组学分析平台、高性能计算平台三大技术平台，同时还涵盖一些中小型仪器设备。每个平台都配有专业技术人员，从实验设计，仪器操作，到数据分析，为仪器设备使用者提供全方位的技术支持与服务。

实验室主页：http://www.kiz.cas.cn/gre/gre6/gre61/

一、基因组学分析平台

1. Ion Torrent 测序系统

Ion Torrent 测序系统（Ion Proton 与 Ion PGM）主要用于基因组测序、转录组测序、外显子组测序、基因测序、ChIP 测序，线粒体基因组测序、甲基化分析等等。


2. Miseq 测序仪

Miseq 测序仪主要特点是测序精度高，读长长 (测序片段长度最长可达 2 X 300bp)，通量灵活，适合靶向和小型基因组测序。

3. 单细胞自动制备

C1™ 单细胞全自动制备系统是基于 Fluidigm 创新的微流体技术，能够快速可靠地分离单个细胞并进行基因组分析。

4. 高通量单细胞基因分型系统

BioMark HD 高通量单细胞基因分型系统整合了先进的微流控芯片和 qPCR 技术，通过独立的纳米级微型阀门控制溶液在阵列反应仓（Reaction Chamber）中的流动来实现生物样品的分液、qPCR 体系混合建立、qPCR 扩增。Fluidigm 的微流控 qPCR 芯片融合了芯片的高通量和 qPCR 的准确性。

5. 新一代实时定量 PCR 仪

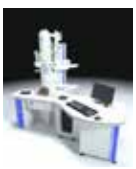
QuantStudio 12K Flex 实时荧光定量 PCR 仪在实现常规定量 PCR 仪功能的基础上，又可以满足 8 连管、96 孔板、384 孔板以及 OpenArray 芯片等不同通量的实验需求。

6. 高端定制型流式细胞仪

BD LSRFortessa™ 流式细胞分析仪兼顾了分析性能和可拓展性，可提供强大的扩展空间以满足不断发展的多色流式细胞仪实验的需求。

二、显微影像分析平台

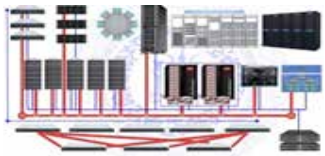
透射电子显微镜是观察细胞的超微结构和蛋白等生物大分子的细胞内定位等。在基因组进化的研究中，搞清楚细胞的细胞质、细胞器以及细胞核等超微结构，在重大疾病和新药研究领域中，通过对正常细胞和病变细胞的超微结构的对比观察，在干细胞研究领域中都是必备的研究工具。制样系统可以进行电镜样品前期处理，超薄切片机可以进行半薄和超薄切片，为透射电子显微镜提供较好的切片。






三、高性能计算平台

设计目标融合高性能计算和大数据分析于同一机群；系统双精度理论峰值计算能力 157.65 万亿次；4PB 容量读写带宽高达 20GB 每秒，单点带宽 >4GB 每秒；采用 cc-numa 架构 superdome flex 配置 16 路处理器 12TB 内存作为胖节点；3 台 4 路服务器厚节点配置 3TB 内存，50 台 2 路服务器计算节点配置 384GB 内存；4 块 volta 架构 Tesla v100 卡 的 GPU 服务器。

Core Facility

The Core Facility of the State Key Laboratory of Genetic Resources and Evolution is established in November 2008. Currently, the center contains three major technology platforms: Genomic Analysis Platform, Micro-imaging Analysis Platform , and High Performance Computing Platform. Each platform is supported by professional technicians, from the experimental design, instrument operation, to data analysis.

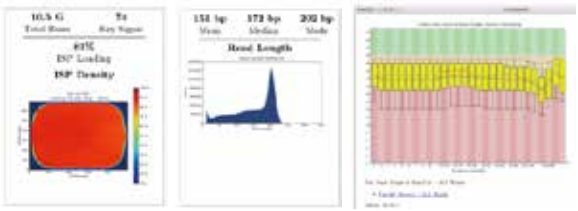
http://www.kiz.cas.cn/gre/gre6/gre61/

The Three Technical Platforms

I. Genomic Analysis Platform

1. Ion Torrent Sequencers

The Key applications of the Ion Torrent Sequencers (Ion Proton and Ion PGM) are genome sequencing, Whole transcriptome sequencing, Exome sequencing, Gene sequencing, ChIP sequencing, Mitochondrial sequencing, Methylation analysis, and so on.



2. Miseq Sequencer

The MiSeq desktop sequencer allows you to access more focused applications such as targeted gene sequencing, metagenomics, small genome sequencing, targeted gene expression, amplicon sequencing, and HLA typing.

3. Single-Cell Preparation System

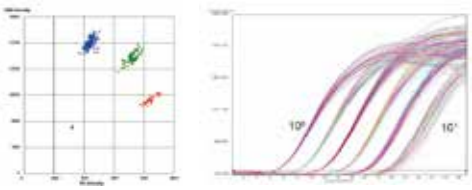
The C1 system enables cell capture, lysis, and preparation of individual cells for genomic applications. The system is an electrically and pneumatically operated desktop instrument. It has a built-in vacuum pump to hold the IFC in position. The embedded PC inside the system regulates all the functions and monitors the performance of the instrument. C1 uses a thermal stack to provide rapid, accurate, uniform heating and cooling.

4. Biomark HD Real-time PCR System

The BioMark HD System sets a new standard in high-throughput genotyping—it is the only multi-purpose real-time PCR system that performs genotyping, gene signature profiling, quantitative real-time digital PCR (qdPCR), and single-cell analysis. Its integrated fast-capable thermal cycler and four color detection provides even faster time to results and enough throughput for routine genomic testing applications.

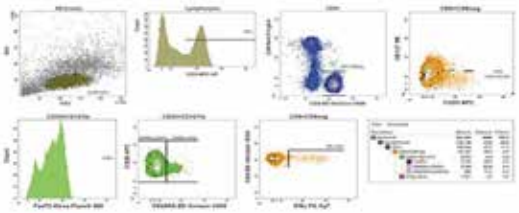
5. QuantStudio 12K Flex Real-Time PCR System

QuantStudio 12K Flex Real-Time PCR System is new level for qPCR, designed for maximum throughput, flexibility, and scalability. You can choose not only OpenArray®, 384-well, 96-well blocks for your experiments, but also digital PCR for high accuracy and sensitivity.



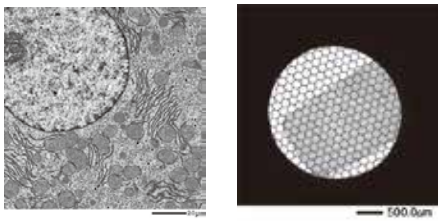
6.Miseq Sequencer

The BD LSRFortessa brand provides power, performance and consistency for your research. Designed to be affordable and expandable, BD LSRFortessa cell analyzers have the flexibility to support the growing needs of multicolor flow cytometry assays.



II. Micro-imaging Analysis Platform

The JEM-1400Plus is a transmission electron microscope (TEM) developed for application in a wide range of disciplines, from biology to materials researches, such as biological sections, polymers, nanomaterials and so on. With the JEM-1400Plus, images from the ultra LOWMAG mode (min. mag. ×10) to the MAG mode (max. mag. ×1.2 M) can be acquired with only one camera, resulting seamless observation with no switching of cameras or shifting one's gaze to a fluorescent screen. Using the auto montage function (provided as standard) makes it easy to acquire high-precision images of a wide field of view. 8M pixel camera (high-resolution camera) and a 1 M pixel cameras are selectable depending on user's purposes.



III. High Performance Computing Platform

It is a scalable linux platform with convergence of HPC and big data. The peak performance of the new Linux cluster is 157Tflops. One superfome flex from HPE with 16 way cpus and 12TB RAM serves as the fat node. The cluster consists of 50 inspur two-way servers with 384GB RAM as computing node and 3 four-way servers with 3TB RAM each as thick node. It is connected with 100Gbps infiniband communications link as computing network and Gbps LAN as administration network. DDN Inc supplies the 4PB file system storage volume with read/write aggregate throughput as high as 20GB/sec and over 4GB/sec single client throughput. We also have GPU platform with Nvidia Tesla v100 GPU for GPGPU computing applications.

重要在研项目

序号	项目名称	项目来源	项目类别	负责人	执行期	总经费（万元）	参与类型
1	第二次青藏高原综合科学考察研究任务五、生物多样性保护与可持续利用	科技部	科技基础资源调查专项	施　鹏	2019-2024	18993	主持
2	中国健康长寿人群多队列的系统研究	科技部	国家重点研发计划	孔庆鹏	2018-2022	2820	主持
3	中国长寿家系人群健康老龄调控因子甄别研究	科技部	国家重点研发计划	李功华	2019-2022	530	主持
4	新冠病毒基因组进化规律与动态演变研究技术体系创建与应用	科技部	国家重点研发计划	吕雪梅	2020-2022	450	主持
5	利用多组学技术解析社交与情感的遗传基础和调控网络	科技部	国家重点研发计划	王国栋	2019-2024	438	参与
6	动物多样性起源与地理格局形成机制及其进化动力	科技部	国家重点研发计划	蒋学龙	2017-2020	340	参与
7	企鹅物种进化树、进化格局以及对地质环境变迁的响应	科技部	国家重点研发计划	张国捷	2018-2021	228	参与
8	研发干预乳腺癌干细胞上皮间质相互转化预防乳腺癌的新技术和药物	科技部	国家重点研发计划	焦保卫	2020-2024	194.3	参与
9	基于多模态分子影像的移植后细胞生物行为的在体研究	科技部	国家重点研发计划	焦保卫	2016-2021	175	参与
10	继发性卵巢早衰致病因素及分子机制研究（参加课题 2）	科技部	国家重点研发计划	郑　萍	2017-2020	153	参与
11	灵长类大脑进化分子机制的转基因猕猴研究	基金委	重点项目	宿　兵	2018-2022	340	主持
12	多能干细胞高效调控 DNA 复制压力反应的关键 lncRNA 鉴定与功能分析	基金委	重点项目	郑　萍	2020-2024	312	主持
13	回声定位蝙蝠高频听力适应性进化的遗传发育机制	基金委	重点项目	施　鹏	2020-2024	303	主持
14	哺乳动物的趋同演化	基金委	优秀青年科学基金项目	刘　振	2020-2022	130	主持
15	高原湖泊水质变化过程中鲫鱼复合体种群体多样性变化及其生态适应性	基金委	联合基金项目	吕雪梅	2020-2023	231	主持
16	全球视角下全基因组数据解析家鸡的起源和扩散	基金委	联合基金项目	吴东东	2020-2023	230	主持
17	猕猴大脑发育调控的三维基因组解析与灵长类脑进化的遗传机制研究	基金委	联合基金项目	宿　兵	2021-2024	227	主持

序号	项目名称	项目来源	项目类别	负责人	执行期	总经费（万元）	参与类型
18	剪接因子 SFPQ 对三阴性乳腺癌中 Erα 的转录调控研究	基金委	联合基金项目	焦保卫	2019-2022	220	主持
19	阿尔茨海默症（AD）转基因树鼩模型的创建及有效性评价	基金委	联合基金项目	郑　萍	2018-2021	204	主持
20	鲤科鱼类肌间刺系统演化及其在滇池金线鲃遗传机制	基金委	联合基金项目	杨君兴	2018-2021	200	主持
21	基于线粒体基因组和 Y 染色体遗传信息追溯美洲印第安人的源流历史	基金委	国际合作	孔庆鹏	2017-2021	235	主持
22	猪、牛、羊肌肉生长和脂肪沉积性状重要育种价值基因的克隆及其功能验证	农业部	国家转基因重大专项	高　云	2016-2020	658.91	参与
23	万人计划青年拔尖人才项目	中组部	万人计划青年拔尖人才	王国栋	2019-2022	177	主持
24	驯化动植物对高寒环境的适应及基因资源利用	中科院	中科院 A 类先导专项	彭旻晟	2018-2022	1160	主持
25	高原湿地垫脚石式廊道生态修复技术与示范（子课题 2）	中科院	中科院 A 类先导专项	杨君兴	2019-2023	1145	主持
26	猪育种示范基地建设与完善	中科院	中科院 A 类先导专项	张亚平	2019-2024	1130	主持
27	关键区域的高通量、连续覆盖生物多样性监测与评估	中科院	中科院 A 类先导专项	Douglas W Yu	2018-2023	1094.23	主持
28	气候环境变化对典型动物及种群的影响	中科院	中科院 A 类先导专项	车　静	2018-2023	1060.29	主持
29	高原人群适应高寒环境的遗传资源发掘	中科院	中科院 A 类先导专项	孔庆鹏	2018-2022	686.31	主持
30	西南山地旗舰动物生态廊道设计技术与示范	中科院	中科院 A 类先导专项	蒋学龙	2019-2023	621.54	主持
31	国家公园旗舰动物生态廊道设计技术与示范	中科院	中科院 A 类先导专项	杨晓君	2019-2023	151.9	主持
32	两栖类生物多样性格局及其与季风气候的关系	中科院	中科院 B 类先导专项	周炜帏	2018-2023	398.72	主持
33	鸟类趋同演化及病毒协同演化机制	中科院	中科院 B 类先导专项	张国捷	2018-2023	300	主持
34	肿瘤的异质性演化理论指导下的新疗法研究	中科院	中科院重点部署项目	吕雪梅	2018-2020	350	主持
35	建立哀牢山自然保护区快速生物多样性监测方法	中科院	中科院前沿局重点项目	Douglas W Yu	2017-2022	400	主持

序号	项目名称	项目来源	项目类别	负责人	执行期	总经费（万元）	参与类型
36	过去 2500 年新疆民族融合遗传机制和模式研究	中科院	中国科学院院级项目	张亚平	2019-2020	900	主持
37	家犬强迫症疾病模型初探	中科院	中国科学院院级项目	王国栋	2019-2023	300	主持
38	西部之光引进人才项目 —— 吕雪梅	中科院	中科院西部之光	吕雪梅	2019-2021	200	主持
39	自闭症食蟹猴模型的创建	中科院	中科院西部之光交叉团队	郑　萍	2019-2021	200	主持
40	东非脊椎动物多样性格局及形成机制	中科院	国际合作项目	蒋学龙	2016-2020	500	主持
41	东非重要动物类群系统发育与进化	中科院	国际合作项目	彭旻晟	2016-2020	400	主持
42	现生鸟类多样性演化历史及机制研究	中科院	国际合作项目	张国捷	2019-2022	270	主持
43	健康长寿人群基因组表观修饰模式及功能利用研究	中科院	国际伙伴计划	孔庆鹏	2016-2020	250	主持
44	云南高原湖泊特有四大名鱼的保育及其深度发掘利用研究	云南省	云南科技厅对外科技合作专项	杨君兴	2020-2023	300	主持
45	云南省领军人才项目 —— 宿兵	云南省	云南省领军人才项目	宿　兵	2020-2024	920	主持
46	云南省云岭学者（2019）—— 施鹏	云南省	云南省高层次人才培养支持计划	施　鹏	2019-2024	200	主持
47	云南省云岭学者（2020）—— 孔庆鹏	云南省	云南省高层次人才培养支持计划	孔庆鹏	2020-2025	200	主持
48	云南省创新团队 —— 孔庆鹏	云南省	云南省创新人才计划	孔庆鹏	2018-2022	100	主持
49	云南省创新团队 —— 王国栋	云南省	云南省创新人才计划	王国栋	2020-2022	100	主持
50	昆明长水国际机场威胁性鸟类防控中心项目	企业合作	横向项目	杨晓君	2018-2021	295	主持

发表论文及专著

（蓝色标注：实验室为文章第一单位；加粗：标注实验室的人员；通讯作者 *；共同第一作者 [1]）

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专著

1. **车静**，蒋珂，颜芳，**张亚平**．西藏两栖爬行动物 —— 多样性与进化．科学出版社．2020.
2. **朱建国，饶定齐**．中国西南野生动物图谱 - 爬行动物卷．北京出版社．2020.
3. **张浩淼**．常见蜻蜓野外识别手册．重庆大学出版社．2020.
4. **张浩淼**．从水中诞生的空中芭蕾 - 蜻蜓．海峡书局．2020.

授权专利

专利号	专利名称	类别	授权日期	完成人（固定人员）
201510204471.9	一种软鳍新光唇鱼肌肉细胞系的构建方法	发明专利	2020-01-03	王晓爱，潘晓赋 杨君兴，刘　倩
201610460383.X	一种建立可持续传代的树鼩精原干细胞系的方法	发明专利	2020-01-14	郑萍，李朝晖，班文赞
201610970091.0	一种光倒刺鲃鳍细胞系的构建方法	发明专利	2020-02-03	潘晓赋，王晓爱 杨君兴，刘　倩
201811620374.8	一种滇池金线鲃稚鱼肌间的染色方法	发明专利	2020-07-02	杨坤凤，王晓爱 张源伟，潘晓赋 杨君兴，范　伟

获　奖

省部级奖励

序号	成果名称	成果类型	等级	完成人	排名
1	家养动物的起源与驯化	云南省自然科学奖	一等	张亚平，吴东东，王明山，彭旻晟，刘益平，陈善元，苗永旺	1

其它获奖

姓名	获奖年度	奖项	导师
车　静	2020	中国科学院 2020 年度青年科学家国际合作伙伴奖	国际合作奖

第二章 开放合作交流

开放课题

课题编号	申请人	职 称	申请人所在单位	项目名称	资助经费（万元）
GREKF20-01	华方圆	研究员	北京大学	土地利用变化和气候变化对横断山区森林生物多样性的影响研究	6
GREKF20-02	David M. Hillis	教　授	University of Texas at Austin	地质气候变化对青藏高原两栖爬行动物生物多样性格局形成的影响	6
GREKF20-03	黄　程	助理研究员（博士后）	中山大学	开阔地中亚洲象精细尺度运动选择	6
GREKF20-04	孙继红	主任医师	浙江大学医学院附属邵逸夫医院	印记基因在乳腺中的功能鉴定	6
GREKF20-05	张云霞	教　授	海南医学院	海南高龄人群肠道菌群分布模式及影响因素研究	6
GREKF20-06	刘　强	讲　师	红河学院	温泉微生物菌群网络分析	6
GREKF20-07	赵树华	副研究员	昆明医科大学	泛素连接酶 RNF220 在哺乳动物精子发生中的功能和作用机制	6
GREKF20-08	白　戈	研究员	浙江大学	BTN3A2 在突触发育和功能调控中作用机制研究	6
GREKF20-09	张同作	研究员	中国科学院西北高原生物研究所	沿海拔梯度高原鼢鼠低氧适应机制研究	6
GREKF20-10	杨国辉	高级实验师	大理大学	基于全基因组数据解析裂唇蜓科（蜻蜓目）的系统发育关系	6
GREKF20-11	毛秀光	副研究员	华东师范大学	基于基因组重测序研究渐渗杂交在菊头蝠属物种快速演化中的作用	6
GREKF20-12	陈宁博	副教授	西北农林科技大学	青藏高原史前牛科动物起源的古代 DNA 研究	6
GREKF20-13	杨召辉	讲　师	昆明理工大学	藏族人群肤色适应性进化的分子机制研究	6
GREKF20-14	杜小刚	副教授	四川农业大学	滇池金线鲃 Toll 样受体的分子鉴定及免疫功能分析	6
GREKF20-15	孟飞龙	研究员	中国科学院分子细胞科学卓越创新中心	Filia 调控神经干 / 祖细胞基因组稳定性及神经发育的研究	6

参加学术会议

序号	会议名称	参会人	地点	会议时间
1	云南省八学会 2020 年“新春联谊会暨学术交流会”	文建凡、薛　敏、白慧掀、程姣妮、邓　琪	云南　普洱	2020-1
2	中国两栖爬行动物红色名录更新评估会	陈进民	四川　成都	2020-6
3	生物安全与生物多样性科学研究主题沙龙	王国栋	山东　青岛	2020-8
4	“以家犬为模型解析社交与情感的生物学基础”项目启动会	王国栋	北京	2020-9
5	武汉第二届青年生命科学论坛	王国栋	湖北　武汉	2020-9
6	动物地理学术研讨会	吴　飞、董　锋	北京	2020-9
7	2020 年鹤类及栖息地保护学术研讨会	杨晓君	黑龙江　齐齐哈尔	2020-9
8	中国动物学会兽类学分会暨《兽类学报》创刊 40 周年学术研讨会	蒋学龙	青海　西宁	2020-10
9	第五届全国发育生物学大会	焦保卫	广东　广州	2020-10
10	第九届乳腺癌干细胞高峰论坛	焦保卫	山东　济南	2020-10
11	第五届全国发育生物学大会	马鹏程、李雨薇、王绘山	广东　广州	2020-10
12	中国干细胞第十届年会	郑　萍	贵州　贵阳	2020-10
13	第二届生物多样性前沿论坛暨《生物多样性》第六届编委会	车　静	宁夏　银川	2020-11
14	深圳先进院“青促会 - 生命科学”前沿交叉论坛	王国栋	广东　深圳	2020-11
15	中国动物学会动物行为学分会青年学者论坛	王国栋	湖北　武汉	2020-11

序号	会议名称	参会人	地点	会议时间
16	有害生物控制与资源利用国家重点实验室（中山大学）学术系列讲座（第 198 讲）	文建凡	广东　广州	2020-11
17	昆明医科大学交流会	文建凡	云南　昆明	2020-11

邀请学术报告

序号	专家姓名	单位	职称	报告题目	报告日期
1	伦照荣	中山大学	教　授	寄生虫的恶性化	11 月 13 日
2	吴仲义	中山大学	中研院院士 / 教授	The origin，spread and containment of SARS-CoV-2：An evolutionist's perspective	11 月 25 日
3	施苏华	中山大学	研究员	物种形成新理论模型与趋同演化的基因组机制	11 月 25 日
4	蔚鹏飞	深圳先进技术研究院	副研究员	基于机器学习的神经 - 行为学分析新技术与应用	12 月 21 日

第三章　人才队伍建设

新增人才称号

序号	姓名	荣誉称号	项目来源	获得年份
1	郑　萍	国家百千万人才工程	国家	2020
2	张国捷	国家海外高层次人才引进计划	国家	2020
3	孔庆鹏	享受国务院政府特殊津贴人选	国家	2020

序号	姓名	荣誉称号	项目来源	获得年份
4	和耀喜	青年创新促进会	中科院	2020
5	马怀孝	青年创新促进会	中科院	2020
6	李学友	西部之光青年学者 B 类	中科院	2020
7	李玉春	西部之光青年学者 B 类	中科院	2020
8	王晓爱	西部之光青年学者 B 类	中科院	2020
9	李学友	高层次人才培养支持计划 —— 青年拔尖人才	云南省	2020
10	李玉春	高层次人才培养支持计划 —— 青年拔尖人才	云南省	2020
11	张浩淼	高层次人才培养支持计划 —— 青年拔尖人才	云南省	2020
12	孔庆鹏	高层次人才培养支持计划 —— 云岭学者	云南省	2020
13	蔡　星	高层次人才引进计划 —— 青年人才	云南省	2020
14	马怀孝	高层次人才引进计划 —— 青年人才	云南省	2020
15	潘晓赋	技术创新人才培养对象	云南省	2020
16	李学燕	中青年学术和技术带头人后备人才	云南省	2020

在读研究生及博士后

序号	导师	硕士生	博士生	博士后
1	Douglas W Yu		杨洋、蔡望、李宗煦、罗明洁	李沅衡
2	车　静	ALEX PLIMO KARUNO、曹如君、董文捷、THET MYAT OO、冯小刚、卢宸祺、缪健军、于中斌	高伟、吴云鹤、张毅、付婷婷、侯绍兵、FELISTA KASYOKA KILUNDA、徐伟、余传鑫、易木荣	
3	佴文惠	吴甜甜、高简奥		
4	蒋学龙	ALOIS WAMBUA MWEU、胡哲畅、SAMSON MABEYA OURU、胡文豪、李弈仙、陈春妮	宋文宇、牛晓炜、KENNETH OTIENO ONDITI、于秋鹏、胡文强	
5	饶定齐	何圆圆		

序号	导师	硕士生	博士生	博士后
6	焦保卫	刁显红、刘霈、邵海莉、黄吉鹏、缪佳雨	郭璐、杨旭、邹丽	
7	孔庆鹏	顾康蜀云、郭荣慧、郜宗亮、韩一鸣、郭丽云、翁崇峻、赵龙、王霞燕	葛明侠、王昊天、尹藩乾、苏倩	
8	刘　振	国天日		
9	吕雪梅	陶鑫灵、魏婉宜、何晓艺、李丰邑、廖思洁	陈泽宇、冯璇、RAOGO BLAISE OUEDRAOGO、闫凯、REX FRIMPONG ANANE、魏昀旸、张昕	
10	马占山	乔玉亭、杨旭	李文迪、MD MOTIUR RAHMAN、陈红菊、肖琬蒙	
11	毛炳宇	茶靖美、杨陈成、陈锦芳、马玉竹	张龙龙、王绘山、朱良、李雨薇	
12	盛能印	唐杰、卜宇飞、万梨、易雅星、吴月春、易琳昀、赵阳、李熹、杨锐	叶雅馨、刘娅敏	
13	施　鹏	吕颜洁、陶乐、姚晓晴、华秦杨、李雪凤、马苑硕、周豪	朱磊、刘奇、张涛、白婧、陈杰、郭媛婷、蔡婉芷、华绒、周鑫、陈鹏	刘广帅 陈中正
14	王国栋	张湘泉、曾敏、冯馨瑶	戴珊珊、黎武略、周博闻	
15	王　文	李俊	陈海涛、王宝、刘威、毛初阳	胡平
16	文建凡	SULIAT ABIKE JIMOH	吕章夏、程姣妮、邓琪	
17	吴东东	VIOLET MAGOMA ONSONGO、陈勇璇、李彦旭、甘爽	ADEOLA OLUWAKEMI AYOOLA、田航宇、张佳进、张锦锦、SAID ISMAEL NG`ANG`A、庄晓琳	王胜、王坤
18	宿　兵	王永琴、张凤云、吴海旭、张悦、刘凯、罗文皓	袁佳妙、郑王山、郭永博、孟晓宇、岳天、周斌、曾雪芮	
19	祁学斌	黄家卉、徐嘉浩		
20	杨君兴	黄新迪	孙超、潘晓赋、殷艳慧、车星锦	
21	杨晓君	姚舜禹、赵岩、吴青琴	单鹏飞、王继山、王洁、高建云	
22	张国捷	李冀	张霞芳、戴学勤	高琼华
23	张亚平	路恒、LAMECK AJUMA ODONGO、郭超、母昌概、王凤娟、丁梦婷、吴然燃	李建波、DAVID HERIEL MAUKI、耿伟航、沈全宽、颜晨、许明敏、马成、张越东、汪轩、伍胤桥、李应菊、刘行、王蓉、孙伟杰、李婕	李锦秀

序号	导师	硕士生	博士生	博士后
24	高　云	施贤、牛文静、曹学娜		
25	彭旻晟	王雪琪、SUSAN MUTHONI MAINA、姜香香、李岩		
26	郑　萍	唐敏、谢恒、陶慧玲、董玉萍、孟夏朵	李竞争、姜方洁、孙春丽、龚道华、李聪、宁雨琪、金洁、黄晓妍	杨亚娟

毕业研究生一览表

序号	姓名	学位	攻读专业	导师姓名	毕业日期
1	王晓阳	博士	动物学	Douglas W Yu	2020.01
2	徐　婉	硕士	药学工程	黄京飞	2020.07
3	成　市	硕士	生态学	蒋学龙	2020.07
4	李　权	博士	动物学	蒋学龙	2020.01
5	宁文鹤	博士	动物学	蒋学龙	2020.07
6	成　美	硕士	细胞生物学	焦保卫	2020.07
7	徐海波	博士	遗传学	焦保卫	2020.07
8	杨　星	博士	细胞生物学	焦保卫	2020.07
9	赵丽娜	博士	细胞生物学	焦保卫	2020.07
10	殷利夺	博士	遗传学	吕雪梅	2020.09
11	李连伟	博士	遗传学	马占山	2020.07
12	陈艳艳	博士	遗传学	施　鹏	2020.01
13	雷孟龙	硕士	遗传学	施　鹏	2020.07
14	夏　尧	博士	遗传学	施　鹏	2020.07

序号	姓名	学位	攻读专业	导师姓名	毕业日期
15	杨　陆	硕士	药学	施　鹏	2020.07
16	郑智中	博士	遗传学	施　鹏	2020.07
17	祁飞燕	博士	细胞生物学	施　鹏、毛炳宇	2020.07
18	曾　严	博士	遗传学	王　文	2020.09
19	邱　兰	硕士	生物工程	文建凡	2020.01
20	李明莉	博士	遗传学	吴东东	2020.07
21	任小蝶	硕士	遗传学	吴东东	2020.09
22	曾雪芮	硕士	生物工程	宿　兵	2020.07
23	姜　瑾	博士	遗传学	宿　兵	2020.01
24	李丽雅	硕士	生物工程	宿　兵	2020.09
25	罗　鑫	博士	遗传学	宿　兵	2020.01
26	吴安丽	硕士	动物学	杨君兴	2020.07
27	GLADYS NYAKERU KUNG'U	硕士	动物学	杨晓君	2020.07
28	陈逸林	硕士	动物学	杨晓君	2020.07
29	袁兴海	硕士	动物学	杨晓君	2020.07
30	SABER KHEDERZADEH	博士	遗传学	张亚平	2020.01
31	胡靖扬	博士	遗传学	张亚平	2020.07
32	黄翠萍	博士	遗传学	张亚平	2020.07
33	马云飞	博士	遗传学	张亚平	2020.07
34	陈忠良	博士	细胞生物学	郑　萍	2020.01

研究生优秀论文奖

序号	姓名	获奖等级	期刊	IF	作者排序
1	徐　伟	二等奖	National Science Review	15.209	第一作者
2	李竞争	二等奖	Science advances	14.094	第一作者
3	Adeola Oluwakemi Ayoola	二等奖	Molecular Biology and Evolution	13.401	第一作者

工作人员名单

（按姓名拼音首字母排序）

学术带头人

Douglas W Yu	车　静	蒋学龙	焦保卫	孔庆鹏	刘　振
吕雪梅	马占山	毛炳宇	盛能印	施　鹏	王国栋
王　文	文建凡	吴东东	宿　兵	杨君兴	杨晓君
张国捷	张亚平	郑　萍			

工作人员

Adeniyi Charles Adeola	白慧掀	蔡　星	曾　琳	柴　静	常云艳
戴红娟	邓家坤	董　锋	董志巍	佴文惠	高建云
高　伟	高　云	郭　彦	郝军军	何水旺	何文彬
和耀喜	侯东敏	辉　洪	季吟秋	金洁琼	李朝翠
李春梅	李功华	李桂梅	李连伟	李梦雯	李　权
李欣然	李学燕	李学友	李玉春	李毓劲	廖爱文

刘贵春	刘鹤群	刘　倩	刘淑伟	刘薇薇	柳延虎
罗　杰	罗荣松	罗　鑫	吕　雪	马怀孝	马鹏程
潘晓赋	彭旻晟	彭　云	浦绍艳	祁学斌	饶定齐
邵　永	沈文菁	盛　丹	苏伟婷	谭玉莲	涂小龙
王洪娇	王　慧	王　洁	王金焕	王　林	王　林
王识之	王晓爱	王晓阳	王运梅	王运宇	王　壮
吴安丽	吴春莹	吴　飞	吴汝念	吴云鹤	伍和启
肖富辉	谢海兵	薛　敏	岩　道	杨春燕	杨　晖
杨利琴	杨　陆	杨敏敏	杨　钦	殷利夺	尹婷婷
余　琴	张宝林	张栋儒	张海林	张浩淼	张　慧
张树润	张　涛	张伟道	张晓明	张源伟	张　越
赵　洁	赵丽敏	赵丽娜	赵若含	赵若苹	赵士萍
郑俊娟	周其俊	周　鑫	周中银	朱春玲	朱建国
朱玮璟	邹　丽				

2020年度报告
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