UC San Diego Health

Researchers Map Thousands of MAPK Protein Interactions

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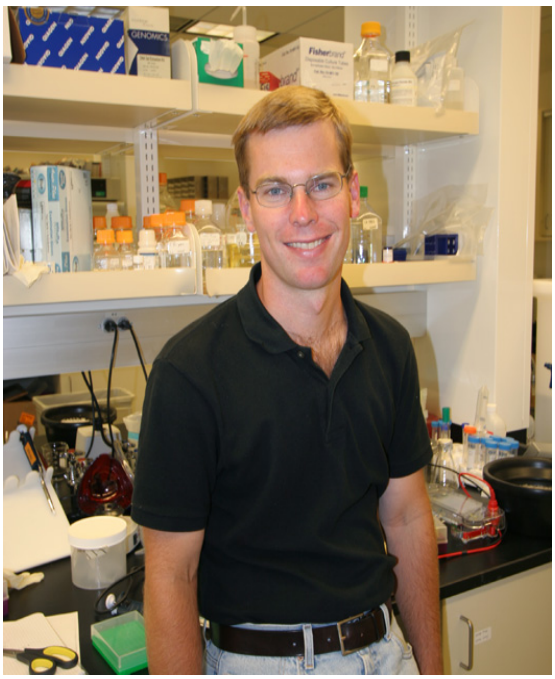
Investigators, led by researchers at the University of California, San Diego, have mapped a huge network of protein interactions involving Mitogen Activated Protein Kinase (MAPK) pathways. Their study will be published in the advanced online edition of *Nature Methods* on September 19.



Trey Ideker, PhD

"MAP kinases play an important role in human disease and as drug targets, so a better understanding of their thousands of interactions will likely identify new targets," said principal investigator Trey Ideker, PhD, chief of the Division of Genetics at UC San Diego.

Protein kinases transmit chemical signals within the cell to regulate a host of functions, such as cell growth or metabolism. Certain protein kinases have been implicated in the uncontrolled growth of cells, for example; their prolonged activation can lead to cardiac disease and breast cancer.

MAPK pathways – a collection of protein signaling cascades stimulated by a wide variety of extracellular signals, including growth factors, cytokines and environmental stresses – form the backbone of signal transduction within the mammalian cell. MAPK pathways regulate a large number of fundamental cellular functions including differentiation, proliferation and cell death through activation of specific transcription factors and other regulatory proteins.

"Because of their central role in signal transduction, MAPK proteins have been repeatedly implicated in the pathogenesis of cancer and autoimmune diseases, leading to their selection as targets for drug development," said Ideker. "It's very likely that many of the 2,269 interactors we have mapped will also be potential targets for new therapies."

Their work involved four steps: developing a screen for physical interactions between MAPK proteins and the rest of the proteome; an assessment of network quality and functional assessment of MAPK interactors through siRNA screening; analysis of the MAPK network to identify potential kinases scaffolds, thereby illustrating how the network can be used as a resource to guide the discovery of novel protein functions; and the identification of interaction modules and use of evolutionary conservation to aid in functional interpretation of the network.

Additional contributors to the study include Sourav Bandyopadhyay and Merril Gersten, UCSD Departments of Medicine and Bioengineering and Bioinformatics Program; Chih-yuan Chiang, and Suhaila White of the Genomics Institute of the Novartis Research Foundation; Jyoti Srivastava and Diane L. Barber, UCSF Department of Cell and Tissue Biology; Russell Bell, Sumit K. Chanda, Cornelia Kurschner, Christopher H. Martin, and Sudhir Sahasrabudhe, Sanford-Burnham Institute for Medical Research; and Mike Smoot, UCSD Department of Medicine and Bioengineering.

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