BIOGRAPHICAL SKETCH

NAME: Ideker, Trey

eRA COMMONS USER NAME: TIDEKER

POSITION TITLE: Professor of Medicine

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Massachusetts Institute of Technology	B.S.	1994	Elec. Eng. & Comp. Sci.
Massachusetts Institute of Technology	M.Eng.	1995	Elec. Eng. & Comp. Sci.
University of Washington	Ph.D.	2001	Molecular Biotechnology
Whitehead Institute for Biomedical Research		2003	Whitehead Fellow

A. Personal Statement

I am a Professor in the Departments of Medicine and Bioengineering at UC San Diego. Research in my laboratory focuses on mapping molecular networks and using these networks to guide the development of novel therapies and diagnostics. I am Co-Director of the Cancer Genomics and Networks program at the UCSD Moores Cancer Center, and Director of the Cancer Cell Map Initiative (CCMI), the San Diego Center for Systems Biology (SDCSB) and the National Resource for Network Biology (NRNB). I am on the Executive and Admissions Committees for the UCSD PhD Program in Bioinformatics and Systems Biology, and I have mentored students in numerous departments campus-wide, including Biomedical Sciences, Biology, Bioengineering and Computer Science. In the past 10 years teaching as a professor at UC San Diego, I have trained 22 postdoctoral scholars, 25 graduate students, and 25 undergraduate students.

For network analysis I created the Cytoscape platform, a very widely used software resource, which is supported by a vibrant open-source community of software developers. We have also demonstrated many key ideas for building and using network models of cells, including network alignment and evolutionary comparison; the identification of 'differential' network interactions across conditions; and the central use of networks for interpreting gene expression profiles. Recently, we published two key bioinformatics advances. First, we introduced the technique of Network-Based Stratification, where we use prior knowledge of cell biology captured in maps of molecular networks to stratify a population of tumors based on the somatic mutations in their genomes. Second, we developed an approach called Network Extracted Ontologies (NeXO), which analyzes molecular interaction data to identify a hierarchy of modular machines, in a manner that reconstructs and greatly extends the hierarchy of biological processes curated by the Gene Ontology.

1. Shannon P, et al. Cytoscape: A software environment for integrated models of biomolecular interaction networks. Genome Research. 2003 Nov;13(11):2498-504. PMCID: PMC403769
2. Gross AM, et al. Multi-tiered genomic analysis of head and neck cancer ties TP53 mutation to 3p loss. Nature Genetics. 2014 Sep;46(9):939-43. PMCID: PMC4146706.
3. Pratt D, et al. NDEx: The Network Data Exchange. Cell Systems. 2015 Oct 28;1(4):302-305. PMCID: PMC4649937
4. Srivas R, et al. A Network of Conserved Synthetic Lethal Interactions for Exploration of Precision Cancer Therapy. Molecular Cell. 2016 S1097-2765(16)30280-5. PMID: 27453043.

B. Positions and Honors

Employment

2003 - 2006 Assistant Professor, Department of Bioengineering, UC San Diego, La Jolla, CA
2006 - 2010 Associate Professor, Department of Bioengineering, UC San Diego, La Jolla, CA
2009 - 2014 Division Chief, Genetics, Department of Medicine, UC San Diego, La Jolla, CA
2006 - present Adjunct Professor, Computer Science & Engineering, UC San Diego, La Jolla, CA
2006 - present Member, Moores Cancer Center, UC San Diego, La Jolla, CA

2010 - present Professor, Department of Medicine, UC San Diego, La Jolla, CA
2010 - present Professor, Department of Bioengineering, UC San Diego, La Jolla, CA

Advisory Boards and Consulting

2001 - 2003 Consultant, Pfizer Inc., Cambridge, MA and Groton, CT
2001 - 2003 Scientific Advisory Board, Metabolon Inc., Cambridge, MA
2001 - 2010 Scientific Advisory Board, Genstruct, Cambridge, MA (now Selventa)
2007 - 2013 Consultant, Monsanto, St. Louis, MO
2007 - 2015 Scientific Advisory Board, Mendel Biotechnology, Antioch, CA
2014 - present Data4Cure, co-Founder and Chair of Scientific Advisory Board
2015 - present Scientific Advisory Board, IDEAYA Biosciences, Menlo Park, CA

Review Panels

2002 - 2006 Ad-hoc Reviewer, NIH BISTI, GCAT, MABS, and BDMA Study Sections
2005 - 2006 Standing Member, European Commission (EU) Sixth Framework Grant Programme
2007 - 2012 Standing Member, NIH Biodata Management and Analysis Study Section (BDMA)
2004 - present Ad-hoc Reviewer, NSF (e.g., Biochem. Engineering, J. Lee and FIBR Program)
2006 - present Program & Organizing Committees, ISMB, PSB and RECOMB Bioinformatics Conferences
2016 - present Standing Member, NIGMS Advisory Council

Editorial Boards

2006 - 2013 Editorial Board, *Bioinformatics*
2008 - present Editorial Board, *PLoS Computational Biology*
2011 - present Editorial Board, *Cell Reports*
2013 - present Editorial Board, *DNA Repair*
2013 - present Editorial Board, *Scientific Data*
2013 - present Editorial Board, *Molecular Systems Biology*
2013 - present Editorial Board, *Cell*

Honors

2004 David and Lucille Packard Fellowship
2005 Technology Review Top 35 Young Innovators of 2005
2006 Technology Review Top 10 Innovators of 2006
2009 Overton Prize, International Society for Computational Biology (ISCB)
2014 Elected Fellow, American Institute for Medical and Biological Engineering (AIMBE)
2015 Elected Fellow, American Association for the Advancement of Science (AAAS)

C. Contribution to Science

1. **Open-source software for analyzing biological networks.** My laboratory develops several bioinformatics resources to promote network biology. These efforts first included Cytoscape, an open-source software package for analysis and visualization of biomolecular interaction networks which quickly became a standard tool in the field (~10,000 downloads per month, >200 Apps). More recently, we have been leveraging the infrastructure and community we established through Cytoscape to develop the Network Data Exchange (NDEx; ndexbio.org), a new online database and community for sharing networks. Under the first two years of NCI funding for NDEx, we have built and released a first-generation prototype which was simultaneously described in a publication in *Cell Systems*. We are now in the process of connecting NDEx to Cytoscape; maturing this resource along several version releases; and using NDEx as a platform to build network biology communities, including important links to publishing houses such as Elsevier which are embedding Cytoscape/NDEx figures in journal articles.

    a. Shannon P, et al. Cytoscape: A software environment for integrated models of biomolecular interaction networks. *Genome Research*. 2003 Nov;13(11):2498-504. PMCID: PMC403769
    b. Smoot M. E., et al. Cytoscape 2.8: new features for data integration and network visualization. *Bioinformatics*, 2011 27(3), 431-432.
    c. Saito R, et al. A travel guide to Cytoscape plugins. *Nature Methods*. 2012 Nov;9(11):1069-76. PMCID: PMC3649846
    d. Pratt D, et al. NDEx: The Network Data Exchange. *Cell Systems.* 2015 Oct 28;1(4):302-305. PMCID: PMC4649937

2. **Stratifying tumor mutations and genetic variants using knowledge of molecular networks.** Many forms of cancer have multiple subtypes with different causes and clinical outcomes. Tumor genome sequences provide a rich new source of data for uncovering these subtypes but have proven difficult to compare, as two tumors rarely share the same mutations. Recently my laboratory introduced network-based stratification (NBS), a method to integrate somatic tumor genomes with knowledge of hallmark cancer pathways encoded in gene networks. This approach allows for stratification of cancer into informative subtypes by clustering together patients with mutations in similar network regions (i.e. distinct mutations in the same hallmark pathway). We demonstrated NBS in ovarian, uterine and lung cancer cohorts: for each tissue, NBS identified subtypes that are predictive of clinical outcomes such as patient survival, response to therapy or tumor histology. This recent success is the latest in a progression of work from my lab demonstrating that the most effective biomarkers are often networks, not individual genes or proteins. The key idea is that complex diseases are hard to analyze because they can invoke different genetic causes in different patients, but these causes frequently integrate at levels of organization higher than individual genes. My lab first introduced this idea in 2007, through an approach that integrates network/pathway knowledge with gene expression profiles to classify patient subtypes; this approach was translated to the clinic in 2012. These works have stimulated studies by many research groups who have further advanced the methods or networks underlying a variety of diseases including neurodegeneration.

    a. Chuang HY, et al. Network-based classification of breast cancer metastasis. *Mol Syst Biol.* 2007 Nov;10(11):1108-15. PMCID: PMC2063581
    b. Chuang HY, et al. Subnetwork-based analysis of chronic lymphocytic leukemia identifies pathways that associate with disease progression. *Blood.* 2012 Sep 27;120(13):2639-49. PMCID: PMC3460686
    c. Hofree M, et al. Network-based stratification of tumor mutations. *Nature Methods* 2013 10(11):1108-15. PMCID: PMC3866081
    d. Hofree M, et al. Challenges in identifying cancer genes by analysis of exome sequencing data. *Nature Communications.* 2016 7:12096 PMID: 27417679

3. **Foundational work in Systems Biology.** Leroy Hood and I published one of the founding papers in the field of Systems Biology during the time I was a graduate student in his laboratory (~2000 citations). It was proof-of-principle for what we called the 'systems approach': a methodology for interrogating biological systems by "perturbing them systematically (biologically, genetically, or chemically); monitoring the global cellular response at multiple molecular levels (gene, protein, or metabolite); integrating these data; and, ultimately, formulating mathematical models that describe the structure of the system and its response to perturbation." Using this framework we built and iteratively revised a model of the gene regulatory network underlying galactose metabolism, leading us to suggest new mechanisms for transcriptional control of this pathway as well as physical interactions with many other metabolic pathways. It was the first work to vertically integrate multiple omics data sets (mRNA profiles, quantitative proteomics, and transcriptional and protein networks). It was also the first to show how genome-wide data can be used not only in a 'discovery-driven' mode to identify new gene functions, but in a 'hypothesis-driven' mode in which the predicted outputs of a mechanistic model of the system could be tested systematically by additional genome-wide profiles. This work directly inspired many subsequent studies seeking to infer pathway structure from global data sets.

    a. Ideker T, et al. Integrated Genomic and Proteomic Analyses of a Systematically Perturbed Metabolic Network. *Science*. 2001 May 4;292(5518):929-34. PMID: 11340206
    b. Ideker T, et al. A new approach to decoding life: systems biology. *Annual Review of Genomics and Human Genetics.* 2001; 2:343-72. PMID: 11701654

4. **Inferring the Gene Ontology entirely through systematic 'omics analysis.** This recent line of work from my laboratory seeks to unify two major, but so far separate, efforts in biology. The first is analysis of large-scale 'omics' data sets which, to this day, is driven by methods related to clustering. The second is creation of the Gene Ontology, a widely-used resource which curates expert knowledge and literature to unify knowledge about the hierarchy of functions carried out by a cell. Our work demonstrates that 'omics' data and GO are in fact reflections of the same underlying cell biology. Based on this idea, we have demonstrated an approach by which the wealth of omics data are analyzed to directly infer the majority of cellular components in GO and their hierarchical relationships. Our 'data-driven gene ontology' recognizes many potential cellular components suggested by data but not present in the literature-curated GO. This approach

raises the possibility that, given appropriate tools, gene ontologies might evolve over time with each new high-throughput experiment that is published. It enables a philosophical shift in bioinformatic analysis, from a regime in which GO is viewed as gold standard to one in which it is the major result. GO is the closest thing to a whole-cell model that we as biologists have—knowing how to inform this model with systematic data is a key next step. Our data-driven ontology is accessible at http://nexontology.org/.

a. Dutkowski J, et al. A gene ontology inferred from molecular networks. *Nature Biotechnology.* 2013 Jan;31(1):38-45. PMCID: PMC3654867
b. Kramer M, Dutkowski J, Yu M, Bafna V, Ideker T. Inferring gene ontologies from pairwise similarity data. *Bioinformatics* 30(12):i34-42 (2014). PMCID: PMC4058954
c. Carvunis AR, Ideker T. Siri of the cell: what biology could learn from the iPhone. *Cell*. 2014 Apr 24;157(3):534-8. PMCID: PMC4154484
d. Yu M, et al. Translation of Genotype to Phenotype by a Hierarchy of Cell Subsystems. *Cell Systems.* 24;2(2):77-88 (2016) PMCID: PMC4772745

5. **Differential network biology.** My laboratory performed early work showing that protein-protein, transcriptional, and genetic network maps can change dramatically across conditions and species. Despite the great success of network mapping for elucidating molecular mechanism, networks were typically examined under a single static (usually standard laboratory) condition. Biological networks, however, are highly dynamic entities that continuously respond to a host of environmental and genetic changes. We developed a new approach, termed differential interaction mapping, for measuring the quantitative differences in genetic interaction resulting from a shift in conditions. Using this approach, we found widespread differences between damaging and non-damaging conditions and, remarkably, more interactions unique to each condition than in common. Since publication of our initial work, differential networks have been used repeatedly as a new type of interaction landscape for mapping cellular responses to stimuli. Very recently, we have mapped a large differential genetic network connecting tumor suppressor genes and drug targets.

a. Kelley BP, et al. Conserved pathways within bacteria and yeast as revealed by global protein network alignment. *Proc Natl Acad Sci U S A. 2003 Sep 30;100(20):11394-9*. PMCID: PMC208768
b. Suthram S, et al. The Plasmodium protein network diverges from those of other eukaryotes. *Nature*. 2005 Nov 3;438(7064):108-12. PMCID: PMC2830740
c. Workman CT, et al. A Systems Approach to Mapping DNA Damage Response Pathways. *Science*. 2006 May 19;312(5776):1054-9. PMCID: PMC2811083
d. Bandyopadhyay S, et al. Rewiring of genetic networks in response to DNA damage. *Science*. 2010 Dec 3;330(6009):1385-9. PMCID: PMC3006187

D. Ongoing Support

9 R01 HG009979-14 Ideker (PI); Bader (Co-I) 09/01/2017 - 06/30/2021
NIH / NHGRI
Cytoscape: A modeling platform for biomolecular networks
Cytoscape is an Open Source bioinformatics software environment for biological network analysis and modeling. This award funds continued development and maintenance of the existing functionality of Cytoscape as well as a pipeline for identification of network modules through integration with gene expression data and through evolutionary comparison. Ideker collaborates in this work with Co-I Gary Bader's lab at University of Toronto.

5 R01 GM084279-04 Ideker; Krogan (Multiple Co-Is) 08/01/2008 – 02/28/2018
NIH / NIGMS
Comparative physical and genetic interaction mapping in yeasts
This grant funds work to generate high-density physical interaction maps (protein-DNA, protein-protein) and genetic interaction maps (synthetic lethals and epistasis) in the model organism *Schizosaccharomyces pombe*. These network data are providing a major resource for evolutionary comparison to existing interaction maps of *Saccharomyces cerevisiae*. This proposal is jointly directed by Drs. Ideker and Krogan, at UCSF.

5 P41 GM103504-06 (prev. RR031228) Ideker (PI); (Multiple Co-Is) 09/13/2010-04/30/2020
NIH / NIGMS
National Resource for Network Biology (NRNB)

The National Resource for Network Biology is a Biomedical Technology Resource Center (BTRC) previously funded by NCRR and now funded by NIGMS. The aim of this resource is to provide a freely available, open-source suite of software technology that broadly enables network-based visualization, analysis, and biomedical discovery for NIH-funded researchers. This software is enabling researchers to assemble large-scale biological data into models of networks and pathways and to use these networks to better understand how biological systems operate under normal conditions and how they fail in disease.

5 P50 GM085764-06 Ideker (PI) 09/18/2010-05/31/2019
NIH / NIGMS
San Diego Center For Systems Biology: From Maps to Models
The San Diego Center for Systems Biology is a cross cutting initiative directed by Trey Ideker and involving investigators from UCSD, Salk, Scripps, and the Sanford/Burnham Institute. Ideker is leading a genetic interaction-mapping project on stress responses in yeast, and he is also running the Bioinformatics Core, which provides broad bioinformatics support to dozens of Center investigators.

U24 CA184427 Ideker (PI) 05/01/2014 – 04/30/2022
NIH/NCI
NDEx – The Network Data Exchange A Network Commons for Biologists
The Network Data Exchange (NDEx) is a collaborative web resource that captures knowledge of the structure and function of molecular networks giving rise to cancer. This system will be comprised of (1) a freely available, open-source server platform and (2) a public website built on that platform. Cancer researchers will use NDEx to access, share, and publish biological knowledge in multiple network formats.

1 UL1TR001442-01 Firestein (PI); Ideker (Faculty) 08/13/2015 – 03/31/2020
NIH / NCATS
UC San Diego Clinical and Translational Research Institute
The CTRI provides infrastructure support and educational opportunities related to clinical and translational research at UC San Diego and its affiliated institutions.

1 OT3TR002026-01 Huang (PI) Ideker (Project Leader) 09/22/2016 – 08/31/2018
NIH/NCATS
Biomedical Data Translator Technical Feasibility Assessment and Architecture Design
The goal is to design and prototype the Deep Translate strategy for biomedical data translation.

1U54CA209891-01A1 Krogan (PI); Ideker (PI) (MPI) 05/11/2017 – 04/30/2022
NIH
The Cancer Cell Map Initiative, a National Research Center for Cancer Systems Biology
The goals is to actively engage in the design of new methods for classifying head and neck tumors and for building cancer-specific ontologies.

R01 ES014811 Ideker (PI); Sobol (Co-I) 09/26/2005 – 08/31/2022
NIH / NIEHS
A systems approach to mapping the DNA damage response
The goal of this proposal is to elucidate the eukaryotic DNA damage response through an integrated experimental / computational approach leading to in-silico models of signaling and regulatory networks. These studies are performed in collaboration with the laboratory of Co-I Robert Sobol at University of Alabama.

Completed Support

4 R01 GM070743-13 Ideker (PI); Bader (Co-I) 06/01/2004 - 08/30/2017
NIH / NIGMS
Cytoscape: A modeling platform for biomolecular networks
Cytoscape is an Open Source bioinformatics software environment for biological network analysis and modeling. This award funds continued development and maintenance of the existing functionality of Cytoscape as well as a pipeline for identification of network modules through integration with gene expression data and through evolutionary comparison. Ideker collaborates in this work with Co-I Gary Bader's lab at University of Toronto.