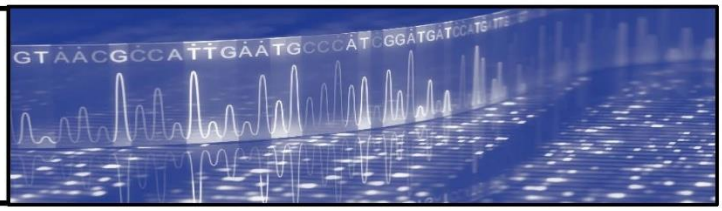
Yale Center for
Biomedical Data Science



CBDS Seminar Series

"Predicting drug response and synergy using deep learning models of human cancer"

Trey Ideker, PhD
UC San Diego, Professor of Medicine
UC San Diego, Adjunct Professor of Bioengineering & Computer Science
Director, Cancer Cell Map Initiative
Director, National Resource for Network Biology
Director, San Diego Center for Systems Biology

Zoom: https://yale.zoom.us/j/92975828553

Most drugs entering clinical trials fail, often related to an incomplete understanding of the mechanisms governing drug response. Machine learning techniques hold immense promise for better drug response predictions, but most have not reached clinical practice due to their lack of interpretability and their focus on monotherapies. To address these challenges I will describe development of DrugCell, an interpretable deep learning model of human cancer cells trained on the responses of thousands of tumor cell lines to thousands of approved or exploratory therapeutic agents. The structure of the model is built from a knowledgebase of molecular pathways important for cancer, which can be drawn from literature or formulated directly from integration of data from genomics, proteomics and imaging. Based on this structure, alterations to the tumor genome induce states on specific pathways, which combine with drug structure to yield a predicted response to therapy. The key pathways in capturing a drug response lead directly to design of synergistic drug combinations, which we validate systematically by combinatorial CRISPR, drug-drug screening in vitro, and patient-derived xenografts. We also explore a recently developed technique, few-shot machine learning, for training versatile neural network models in cell lines that can be tuned to new contexts using few additional samples. The models quickly adapt when switching among different tissue types and in moving to clinical contexts, including patient-derived xenografts and clinical samples. These results begin to outline a blueprint for constructing interpretable AI systems for predictive medicine.

Wednesday, February 3, 2021
4 p.m. to 5 p.m. Seminar

If you would like to receive email notification of future seminars please email cbds@yale.edu

Trey Ideker, Ph.D. is a Professor in the Departments of Medicine, Bioengineering and Computer Science at UC San Diego, and Director or co-Director of three NIH-supported research centers: the NCI Cancer Cell Map Initiative, the NIGMS San Diego Center for Systems Biology, and the NIGMS National Resource for Network Biology. Dr. Ideker received Bachelor's and Master's degrees from MIT in Electrical Engineering and Computer Science and his Ph.D. from the University of Washington in Molecular Biology under the supervision of Dr. Leroy Hood.

Dr. Ideker's research is led by the vision that given the right experimentation and analysis, it will be possible to automatically assemble maps of pathways just as we now assemble maps of genomes. During graduate work, he developed a general iterative framework for how biological systems can be systematically perturbed, interrogated and modeled. This framework laid the foundation for many studies in the discipline of Systems Biology. He demonstrated that biological networks could be integrated with gene expression to systematically map pathways and aligned, like sequences, to reveal conserved and divergent functions. He showed that the best biomarkers of disease are typically not single proteins but aggregates of proteins in networks.

Dr. Ideker has founded influential bioinformatic tools including Cytoscape, a popular network analysis platform which has been cited >12,000 times. Ideker serves on the Editorial Boards for Cell, Cell Reports, Nature Scientific Data, EMBO Molecular Systems Biology, and PLoS Computational Biology and is a Fellow of AAAS and AIMBE.

He was named one of the Top 10 Innovators of 2006 by Technology Review magazine and was the recipient of the 2009 Overton Prize from the International Society for Computational Biology. His work has been featured in news outlets such as The Scientist, San Diego Union-Tribune, Forbes magazine, NPR, and The New York Times.

About the Ideker Lab

The long-term objective of the Ideker Laboratory is to create artificially intelligent models of cancer and other diseases for translation of patient data to precision diagnosis and treatment. We seek to advance this goal by addressing fundamental questions in systems biology and bioinformatics, including: What are the genetic and molecular networks that promote cancer, and how can we best chart these? How do we use knowledge of these networks in intelligent systems for translation of genotype to phenotype?