QUANTITATIVE AND SYSTEMS BIOLOGY COLLOQUIUM:

Functional characterization and therapeutic targeting of gene regulatory elements

Nadav Ahituv

UCSF

Date:

10/2/2025

Time:

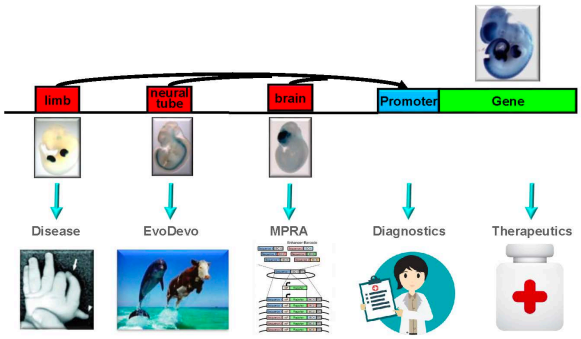
10:30 AM - 11:45 AM

Location:

SSB 130

About the Speaker:

Nadav Ahituv is a Professor in the Department of Bioengineering and Therapeutic Sciences and the Director of the Institute for Human Genetics at the University of California, San Francisco. He received his PhD in human genetics from Tel-Aviv University working on hereditary hearing loss. He then did his postdoc, specializing in functional genomics, in the Lawrence Berkeley National Laboratory and the DOE Joint Genome Institute. His current work is focused on identifying gene regulatory elements and linking nucleotide variation within them to various phenotypes including morphological differences between species, drug response and human disease. His lab was one of the co-developers of massively parallel reporter assays (MPRAs) that allow for high-throughput functional characterization of gene regulatory elements. In addition, he pioneered cis-regulation therapy (CRT), the use of gene regulatory elements as therapeutic targets for haploinsufficient disorders, and adipose modulation transplantation (AMT), a novel cancer cell therapy.



Abstract:

Nucleotide variation in gene regulatory elements is a major determinant of phenotypes including morphological diversity between species, human variation and human disease. Despite continual progress in the cataloging of these elements, little is known about the code and grammatical rules that govern their function. Deciphering the code and their grammatical rules will enable high-resolution mapping of regulatory elements, accurate interpretation of nucleotide variation within them and the design of sequences that can deliver molecules for therapeutic purposes. To this end, we are using massively parallel reporter assays (MPRAs), including capture-C based MPRAs, to simultaneously test the activity of thousands of gene regulatory elements and their target promoter in parallel. Regulatory elements can also serve as therapeutic targets. By targeting regulatory elements via CRISPR activation (CRISPRa), we show that they can be used to rescue a variety of haploinsufficient diseases (having ~50% dosage reduction due to having only one functional allele). In addition, utilizing CRISPRa to engineer adipocytes and adipose organoids to outcompete tumors for nutrients, we show that they can be used as a novel cancer therapy, termed Adipose Manipulation Transplantation (AMT).

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