BRIGHAM AND WOMEN'S HOSPITAL

HARVARD MEDICAL SCHOOL

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Channing Network Science Seminar
Nov 20, 2015, 11am @ 5th floor large conference room

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Widespread Interactome Network Perturbations in Human Genetic Disorders

Abstract: How disease-associated mutations impair protein activities in the context of biological networks remains mostly undetermined. Although a few renowned alleles are well characterized, functional information is missing for over 100,000 disease-associated variants. Here we functionally profile several thousand missense mutations across a spectrum of Mendelian disorders using various interaction assays. The majority of disease-associated alleles exhibit wild-type chaperone binding profiles, suggesting they preserve protein folding or stability. While common variants from healthy individuals rarely affect interactions, two-thirds of disease-associated alleles perturb protein-protein interactions, with half corresponding to "edgetic" alleles affecting only a subset of interactions while leaving most other interactions unperturbed. With transcription factors, many alleles that leave protein-protein interactions intact affect DNA binding. Different mutations in the same gene leading to different interaction profiles often result in distinct disease phenotypes. Thus disease-associated alleles that perturb distinct protein activities rather than grossly affecting folding and stability are relatively widespread.

Short Bio: Dr. Nidhi Sahni is an expert in network biology, and has years of experience in functional proteomics and disease biology. Dr. Sahni will soon move to MD Anderson Cancer Institute, and lead her lab in the area of cancer network medicine. Dr. Sahni worked as a research fellow at the Center for Cancer Systems Biology (CCSB) at Harvard Medical School and Dana-Farber Cancer Institute. Her research was focused on protein interaction networks and perturbation profiling in human disease. Dr. Sahni received her doctoral degree from the University of Iowa, where she published 13 high-impact papers in just 3.5 years. As a postdoc fellow at Harvard Medical School, Dr. Sahni continued to be highly productive with multiple publications in leading journals in the field. She has made many seminal discoveries to reveal complex molecular interaction networks and how perturbation of these signaling networks leads to human disease. Her works have been widely cited, with over 600 citations from scientists around the world, including highlights in Nature as one of the most important breakthroughs in science. Dr. Sahni serves as a guest editor and reviewer for academic journals. Dr. Sahni has received numerous awards, and has been invited to present platform talks and posters in numerous academic institutions and conferences.

Hosted by Yang-Yu Liu