LUXEMBOURG INSTITUTE OF HEALTH
RESEARCH DEDICATED TO LIFE

UNIVERSITÉ DU LUXEMBOURG

LECTURE SERIES & WORKSHOPS

TRANSLATIONAL BIOINFORMATICS AND SYSTEMS BIOMEDICINE

18 PhD DAYS

OCT. 2018
Thursday

LECTURE*
UniLU *Belval Campus*
Maison du Savoir
2, av. de l'Université
Room: Auditorium 3.530

11.30am - 12.30pm

8 9 10 11 12 1 2 3

*Please register by sending a mail to florence.henry@lih.lu

SPEAKER
Prof Boris KHOLODENKO

Professor of Systems Biology, Deputy Director of Systems Biology Ireland (SBI), Conway Institute Member, University College Dublin, Ireland
Professor Adjunct of Pharmacology, Department of Pharmacology, Yale University School of Medicine, New Haven, USA

HOST:
LIH

RESPONSIBLE SCIENTIST:
Feng He
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GETTING INSIGHTS INTO CELL BIOLOGY BY NETWORK RECONSTRUCTION AND MODELLING

ABSTRACT

Omics technologies have generated large inventories of genes, transcripts, proteins, and metabolites. The challenge is to find out how they work together to regulate cellular responses to external and internal cues. Computational models provide insight into the intricate relationships between stimuli and cellular responses. I first overview a suite of physics-based methods, known as Modular Response Analysis, which infer both direct causative connections and their strengths in cellular signaling and gene networks from perturbation data (https://www.ncbi.nlm.nih.gov/pubmed/12242336). Further, I show that drug resistance resulting from dimerization of kinases (such as, BRAF/CRAF, JAK2, etc) can be explained by allosteric inhibitor effects and the emergence of different drug affinities between free kinase monomers versus dimers (https://www.ncbi.nlm.nih.gov/pubmed/26344764). Finally, I overview an exciting and counter-intuitive discovery made using a new type of mathematical modelling, which combines aspects of protein structure, post-translational modifications, thermodynamics, and dynamic reaction mechanisms (https://www.ncbi.nlm.nih.gov/pubmed/30007540). We used model predictions to block oncogenic RAS signalling in metastatic melanoma cells. RAS is mutated in 30% of all human cancers, and RAS mutated cancers are clinically considered to be undruggable and resistant to current treatments. Our approach identified non-intuitive drug combinations that synergise to block critical RAS effector pathways.

Website: http://www.ucd.ie/sbi/
https://people.ucd.ie/search/Kholodenko

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