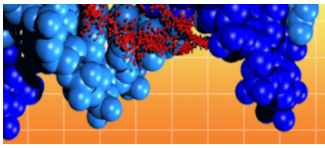

CENTER FOR BIOINFORMATICS & COMPUTATIONAL BIOLOGY

BIOINFORMATICS 2015 FALL SEMINAR SERIES

Hosted by: Department of Computer and Information Sciences,
Department of Electrical and Computer Engineering &
Center for Bioinformatics and Computational Biology
http://bioinformatics.udel.edu/Seminars/Current

MONDAY, November 2, 2015
3:30pm
DBI Room 102

Screening of NSD1 Inhibitors for Pediatric Acute Myeloid Leukemia Based on Compound Selectivity and Binding Affinity

Melanie Salinas

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ABSTRACT: The high attrition rate of screening chemical libraries for lead compounds calls for novel methodologies to identify compounds with a suitable activity profile to test in high-throughput screens. Integrating computational methods in the screening of chemical libraries can guide the search for potential inhibitors of the NSD1 protein, which is implicated in an aggressive form of pediatric acute myeloid leukemia. The Broad Institute reported a confirmatory bioassay for the screening of the highly related protein, NSD2, which is associated with prostate cancer and multiple myeloma. The PubChem Compound and BioAssay databases were utilized to determine the promiscuity of each compound reported as active. Virtual screening was then performed using the AutoDock Vina and NN Score to predict the compounds' binding affinity to the SAM binding pocket of the NSD1 protein. A total of 26 compounds were mined from the 390 active compounds from the reference bioassay. This work suggests a systematic way of screening chemical libraries for lead compounds based on compound selectivity and predicted binding affinity.

Data-Driven *In silico* Screening of Small molecule inhibitors for NSD1 protein

Qingliang (Leon) Li, Ph.D.

Department of Biochemistry; Georgetown University

ABSTRACT: BigData has created great opportunities and challenges for biomedical research including drug discovery. How to take advantages of the large-scale biological data available in both public and private sectors becomes a critically important question in front of researchers. From the point of view of an academic researcher, it is the best time ever to be part of drug discovery adventure, since it used to be a privilege of big pharmas. In the present work, we incorporated large scale bioassay data from public domain, PubChem and in house proprietary High Throughput Screening (HTS) data into the campaign of *in-silico* screening of small molecule inhibitors for NSD1 protein. By combining both structure based (Molecular Docking) and ligand-based (Pharmacophore and 3D Shape) strategies, we were able to achieve a short list of 534 promising inhibitor candidates from 68,000 chemical compounds of ChemBridge library. The strategy can be adapted to other biological targets for small-molecule drug/chemical probe discovery.