BRIGHAM AND WOMEN'S HOSPITAL

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Channing Network Science Seminar
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Marriage of Network Biology and Panomics Yields New Promises for Precision Cancer Medicine

A massive amount of somatic alterations has been cataloged in large-scale genomic projects such as The Cancer Genome Atlas (TCGA) and the International Cancer Genome Consortium (ICGC) projects. The effects of those alterations on the fitness of somatic cells lead to evolutionary adaptations such as increased cell proliferative, angiogenesis, and altered anticancer drug responses. However, the majority of the somatic mutations found in tumor genomes are neutral 'passenger' rather than damaging 'driver' mutations. Now, understanding their biological consequences and prioritizing them for druggable targets are urgently needed. In this talk, I will introduce how we developed and applied network-based approaches to decipher the functional consequences of somatic mutations for development of new precision cancer therapies through integrating panomics data (i.e. genomics, transcriptome, etc.). We found that somatic mutational network-attacking perturbations to hub genes play an important role in tumor emergence and evolution. In addition, we found that mutations of a cancer driver gene tend to uniquely cause cancer genome instability and shape adaptive cancer genome evolution by inducing mutations in other genes using a novel gene gravity model. Based the aforementioned observations, we developed a novel approach, SGDriver, a structural genomics-based method incorporating the somatic missense mutations into protein-ligand binding sites using a Bayes inference statistical framework, to prioritize druggable mutations. We identified dozens of new mutated druggable proteins for development of molecularly targeted cancer therapies. Finally, we briefly introduced how we identified new compounds or old drugs for targeting KRASG12D or p53 wild-type non-small cell lung cancers using drug design and network-based drug repositioning approaches. In summary, we suggested that network is a powerful methodology for development of novel precision cancer medicine by integrating panomics data, which also can be applied for other diseases.

Bio: Dr. Feixiong Cheng is a postdoctoral research associate in the Center for Complex Networks Research (CCNR) at Northeastern University and the Center for Cancer Systems Biology (CCSB) at Dana-Farber Cancer Institute (joint appointment). Dr. Cheng was trained both in computer science and biomedical science. He developed new statistical, network-based algorithms, and integrative genomics framework to address the big biomedicine data (e.g., next-generation sequencing, electronic health records, etc) challenges for genomics and genetics, and precision medicine. His interests span several cutting edge research fields of genomics and genetics, genomic medicine, systems biology, systems pharmacology, pharmacogenetics and pharmacogenomics, translational bioinformatics, computational biology and chemistry, and many more. Dr. Cheng received his Ph.D. degree in systems pharmacology from the East China University of Science and Technology at Shanghai (China) in 2013. He received his B.S. degree in pharmaceutics from Shanxi University of Science and Technology at Xian (China) in 2008. During 2013-2015, Dr. Cheng finished a postdoctoral training in the Department of Biomedical Informatics in the Vanderbilt University Medical Center. Dr. Cheng has over 8 years of network biology, systems biology, systems pharmacology, genetics and genomics, computational biology and chemistry research experiences and has published over 40 peer-reviewed papers in these areas. He is considered an experienced scientist in the application of network biology, bioinformatics, and integrative genetics and genomics analysis in disease genetics and genomics, pharmacogenomics, and precision (cancer) medicine. Dr. Cheng has designed, developed, and co-developed a set of computational tools or databases, such as SGDriver, ccmGDB, NBI, CPI-predictor, ademtSAR, MetaADEDB, KinomeNetworkX, The Catalogue of Cancer Gene, among others. Dr. Cheng has received several awards, including Vanderbilt excellent Postdoc of the Year 2015.

Hosted by Yang-Yu Liu