September 6th, 2018

OPENING SESSION

Dissecting the Molecular Mechanisms of Complex Diseases Through a Pathway and Network Oriented Analysis of - omics Data

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This seminar was part of the BioInfo4Women series.

Abstract
The tremendous boost in the next generation sequencing technologies and in the "omics" technologies makes it possible to look for the coordinated behavior among different levels of biochemical activity. In contrast to isolated molecules, network and pathway oriented analyses are thought to better capture pathological perturbations and hence, better explain predisposition to disease. Especially in complex diseases, which are intrinsicly multifactorial, there are no strong associations for a single factor. In this regard, we have recently proposed a new methodology to analyze the -omics data in a

network related context to identify pathways that are involved in disease development mechanisms. In this seminar, I will introduce our approach and talk on its applications on different Genome-wide Association Study (GWAS) datasets and –omics datasets. I will also present how this approach can help us to identify disease-associated pathway markers across different populations and discuss how these pathway markers can help us to understand individual disease development mechanisms in terms of the determination of individual targets for treatments, and hence bridging the gap between the -omics data and personalized medicine.

Briefly, PANOGA (Pathway and Network-Oriented GWAS Analysis) combines nominally significant evidence of genetic association with current knowledge of biochemical pathways, protein–protein interaction networks, and functional information of selected single nucleotide polymorphisms (SNP). With its multifactorial basis, we have shown on four complex diseases that PANOGA has a good potential to decipher the combination of biological processes underlying disease. Then via comparing GWASs of two different populations, we have shown that the few SNPs that are identified in GWAS and their associated genes are mostly targeting the same pathway combinations, and these biological pathways show higher conservation across populations. If the combination of these pathways does not function properly, a specific disease may develop.

Although PANOGA is originally developed to identify disease- associated pathways via further analyzing GWAS data, later it is shown to work well on different -omics datasets including transcriptomics, proteomics, and epigenomics studies. Using different –omics datasets, our group is currently working on the development of methodologies to extend this approach to individual level to identify specific modifications occurring on the genes within these identified pathways. Dissecting the individual disease development mechanisms will provide a valuable insight for discovering individualized therapy targets

and will pave the way towards personalized medicine applications. This approach would enable biomedical researchers to identify affected pathways and function-altering factors within these pathways. For diagnostic purposes, the identification of the disease-related pathways is also instrumental in the determination of biomarkers at different levels (e.g., SNPs, gene expression levels, protein levels in serum, miRNA levels, metabolite concentration).

Short bio

Burcu Bakir-Gungor received her B.Sc. degree in Biological Sciences and Bioengineering from Sabanci University; her M.Sc. degree in Bioinformatics from Georgia Institute of Technology; and her PhD degree from Georgia Institute of Technology/Sabanci University. She worked at the Bioinformatics Research Center, Medical College of Wisconsin, from 2007-2009. From 2009 to 2011, she worked at the Department of Computer Engineering, Bahcesehir University. Then, she worked as an Assistant Professor at the Department of Genetics and Bioinformatics, at the same university. From 2012 to 2013, she was part of the Advanced Genomics and Bioinformatics Research Center, UEKAE, BILGEM, TUBITAK. Now, she works as an Assistant Professor at the Department of Computer Engineering at Abdullah Gul University. She is the recipient of “Best Paper” award at the 4th EvoBIO Conference; and a member of the advisory board of the Turkish Genome Project. She is the reviewer of several prestigious international journals including Bioinformatics, Machine Learning, Journal of Computational Biology; and she is the Technical Program Committee member of UBMK and HIBIT conferences. Her research interests include bioinformatics,

computational genomics, network and pathway oriented analysis of genome-wide association studies and next-generation sequencing datasets; and applications of machine learning, data mining and pattern recognition in bioinformatics.