Biomedical Informatics Grand Rounds
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Computational methods for studying the 3D organization of the human genome

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Bio: Ferhat Ay received his B.S. degrees in Computer Engineering and Mathematics both from Middle East Technical University (METU), Turkey in 2007 and his Ph.D. in Computer Science at the University of Florida in 2011. He subsequently joined the Department of Genome Sciences at the University of Washington as a Computing Innovation Fellow awarded by Computing Research Association and National Science Foundation (NSF). He was a Research Assistant Professor in the Department of Preventive Medicine-Health and Biomedical Informatics at Northwestern University in 2015 before establishing his lab at the La Jolla Institute for Allergy and Immunology (LJI) in 2016. He is currently the Institute Leadership Associate Professor of Computational Biology at LJI, an adjunct faculty at the UC San Diego School of Medicine, and an affiliate faculty of the UCSD Bioinformatics Ph.D. Program. His primary research areas are bioinformatics, computational biology, epigenomics, and regulatory genomics. His lab works on understanding the relationship between three-dimensional genome architecture and gene regulation in the context of different diseases including cancer, malaria, and immune-mediated diseases. He is a recipient of an R35 MIRA grant from the National Institutes of Health (NIH) and serves as an Associate Editor of PLoS Computational Biology.

Abstract: The field of regulatory genomics has recently witnessed significantly increased interest in the three-dimensional structure of DNA in the nucleus, catalyzed by the development of chromosome conformation capture techniques (e.g., Hi-C, HiChIP) that profile genomic proximities on a genome-wide scale. Systematic analysis of these proximities is particularly important to identify targets of disease-associated genetic variants, more than 90% of which reside in non-coding regions with unknown gene targets. Our lab works on developing computational methods to understand the role of human genetic variation in gene regulation through various epigenetic mechanisms, and in particular, through chromatin structure. I will talk about our work in developing computational methods (FitHiC, FitHiChIP, Mustache) for the analysis of Hi-C and HiChIP data in order to determine functional loops between regulatory elements in our DNA. I will then present the results of our recently published work (Chandra et al. Nature Genetics 2020), in which we profile such loops in primary human immune cell types and revisit the functional roles of GWAS SNPs in immune-mediated diseases. Our results highlight the problems with "the nearest gene" approach for mapping GWAS hits or enhancers to target genes and the importance of combining high resolution, high throughput experiments with novel computational techniques to achieve an accurate mapping of target genes.

Educational Objects: Upon completion, participants should be able to:

- Understand the importance of three-dimensional folding of DNA in impacting cellular function.
- Learn about the latest experimental approach that profile genome 3D structure using sequencing.
- Understand the computational challenges in the analysis of such high-throughput experimental data.
- Learn how the development of new computational methods enable discoveries in human genetics and immunology.

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