CENTER FOR RNA BIOMEDICINE

RNA Innovation Seminar
Monday, October 1st at 3:00pm
ABC Seminar rooms, Biomedical Research Science Building (BSRB), 109 Zina Pitcher

Li Guan, PhD candidate in the Program in Biomedical Sciences (PIBS) program with Bioinformatics track. She is working with Dr.Laura Scott and Dr.Michael Boehnke. She received her Bachelor of Medicine degree from Peking University Health Science Center in China. Her interest in understanding the impact of genetics on human health stemmed from the project studying the associations of 8 genetic variants with Nonalcoholic fatty liver disease in her undergraduate study. Her current research focuses on the identification of genetic variants that affect gene expression levels in human skeletal muscle and adipose tissues, with the goal of understanding the genetic regulation in human tissues and exploring the underlying mechanism through which a genetic variant may influence traits and disease.

"Human skeletal muscle eQTL meta-analysis reveals long-range genetic regulations"

Abstract:
Genome-wide association studies (GWAS) have identified loci associated with a wide range of complex human traits and diseases, however, the mechanistic underpinning of these genetic associations remain elusive. GWAS SNVs (single nucleotide variants) may influence traits and disease through their modulation of gene expression. SNVs that affect RNA expression levels are called expression quantitative trait loci (eQTL). To date, most studies have focused on proximal eQTLs, which influence expression of nearby genes (≤1Mb from gene TSS to variant); fewer studies have examined distant eQTLs, which influence expression of distant genes (>1Mb from gene TSS to variant). Our goal is to identify genes that are regulated by distant variants, and then to identify gene(s) proximal to the variant that may influence the expression levels of these distant genes. We performed RNA-Seq of human skeletal muscle biopsies from 301 FUSION (Finland-United States Investigation of NIDDM Genetics) study participants and used existing RNA-Seq data from 491 GTEx (Genotype-Tissue Expression project) donors. First, within each study, we tested for associations between SNVs (7.28M SNVs in FUSION, 9.51M in GTEx) and all expressed genes ≤ 1 Mb away and protein-coding/lincRNA genes > 1 Mb away. We meta-analyzed all SNV-gene pairs at distance ≤ 1Mb and 352M SNV-gene pairs at distance > 1Mb with p-values<0.05 in either FUSION or GTEx. For SNV-gene pairs at distance > 1Mb, we identified 107 genes whose expression level were significantly affected by SNVs at false discovery rate (FDR) ≤ 0.05 (p≤1.23×10-10) out of 23357 genes. Within the 107 genes, 79 were regulated by SNVs on the same chromosomes (all within 10Mb, suggesting potential regulation from the same haplotype) and 28 were regulated by SNVs on different chromosomes. We used a series of Mendelian randomization and mediation techniques to identify proximal genes that may influence the expression levels of distant genes. These findings will help increase our understanding of the long-range regulation of gene expression by genetic variation in human skeletal muscle.