2018 Internship Project & Abstract - Peter Gerstenberger

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Correlating Telomere Length with Diseases and Novel Genetic Variants

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Research area: Genetics

Background: Telomeres are the repetitive non-coding short DNA segments that cap chromosome ends and function to protect vital genetic information. Telomere length correlates directly with the proliferative capacity of the parent cell, shortening by approximately 10 base pairs per replication cycle. When telomeres become too short, the DNA damage-response signaling pathway is triggered, causing cellular senescence. Shortened telomeres are associated with many age-related diseases as well as inheritance-related disorders, including type II diabetes and cancer. The goal of this project included two objectives: 1) find new associations between telomere length (TL) and various diseases via a Phenome-Wide Association Study (PheWAS), and 2) discover associations between TL and genetic variants via a Genome-Wide Association Study (GWAS).

Methods: All genetic samples from the Personalized Medicine Research Project (PMRP) Biobank (includes ~20,000 patients) were genotyped to determine the relative average telomere length (raTL) using quantitative PCR, and then compared to each patient's electronic health record, containing codes for 8,989 phenotypic diseases (PheWAS). The telomere data was then correlated with over 8 million genomic single nucleotide polymorphisms (SNPs) to define associations between TL and genetic variants (GWAS).

Results: Preliminary results from the PheWAS show correlations between telomere length and conditions including atherosclerosis, heart disease, obesity, presbyopia, bronchitis, and diabetes. The strongest preliminary association signals in the GWAS were among variants already known to be linked with TL, including the genes RTEL1, TERC, and TERT. This tells us that our initial GWAS analysis was successful, and other discovered associations can be trusted.

Conclusions: We successfully discovered phenotypic diseases and genetic variants associated with telomere length. The remaining data is still in process of being cleaned, adjusted, and associated with the correct health records, but preliminary data is promising. Follow-up studies will be performed to implement a PheWAS of the TL-associated SNPs.