



Mitchell - Genetics of Cardiometabolic Health in the Amish (Amish)

Updated 10/7/2022

[Introductory slides from the June 4, 2015 Steering Committee/EAP meeting \(requires log-in\).](#) [1]

The Amish Complex Genetic Disease Research Program

The Amish Complex Disease Research Program includes a set of large community-based studies focused largely on cardiometabolic health carried out in the Old Order Amish (OOA) community of Lancaster, Pennsylvania ([Amish Complex Genetic Disease Research Program | University of Maryland School of Medicine \(umaryland.edu\)](#) [2]). The OOA population of Lancaster County, PA immigrated to the Colonies from Western Europe in the early 1700's. There are now over 30,000 OOA individuals in the Lancaster area, nearly all of whom can trace their ancestry back 12-14 generations to approximately 700 founders. Investigators at the University of Maryland School of Medicine have been studying the genetic determinants of cardiometabolic health in this population since 1993. To date, over 7,000 Amish adults have participated in one or more of our studies.

Due to their ancestral history, the OOA are enriched for rare exonic variants that arose in the population from a single founder (or small number of founders) and propagated through genetic drift. Many of these variants have large effect sizes and identifying them can lead to new biological insights about health and disease. The parent study for this WGS project provides one (of multiple) examples. In our parent study, we identified through a genome-wide association analysis a haplotype that was highly enriched in the OOA that is associated with very high LDL-cholesterol levels. At the present time, the identity of the causative SNP - and even the implicated gene - is not known because the associated haplotype contains numerous genes, none of which are obvious lipid candidate genes. A major goal of the WGS that will be obtained through the NHLBI TOPMed Consortium will be to identify functional variants that underlie some of the large effect associations observed in this unique population.

Source URL (modified on 10/07/2022 - 2:48pm):<https://topmed.nhlbi.nih.gov/group/amish>

Links

[1] https://topmed.nhlbi.nih.gov/system/files/meetings/mitchell_Amish_NHLBI_TOPMed_20150604.pdf [2]

<https://www.medschool.umaryland.edu/endocrinology/Amish-Research-Program/Amish-Complex-Genetic-Disease-Research-Program/>