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THE HONG KONG UNIVERSITY OF SCIENCE & TECHNOLOGY

Department of Mathematics

SPECIAL COLLOQUIUM

Genetics of Human Longevity: Regional Association Signals and Cross-Cohort Replication

By

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Abstract

Understanding the genetic basis of human longevity remains a fundamental challenge in aging research. Although previous genome-wide association studies (GWAS) have identified a few loci, most prominently *APOE,* their replication has often been inconsistent, and most analyses have relied primarily on single-variant testing. To better understand the genetics of human longevity, we examined genetic determinants of age at death in the UK Biobank (UKB) and conducted independent replication in the All of Us (AoU) cohort. After standard quality control and covariate adjustment, we performed single-variant GWAS and complemented these with the Regional Association Score (RAS) framework to capture cumulative regional effects. To gain functional insight, we carried out transcriptome-wide association studies (TWAS) using RNA sequencing data from Mayo Pilot brain tissue. The UKB discovery and AoU replication analyses revealed robust associations across chromosome 19 encompassing *APOE*, *APOC1*, and *NECTIN2 (PVRL2)*, reaffirming this locus as the major genetic contributor to human lifespan. In addition, suggestive and potentially novel associations, such as those involving *TRIM10* on chromosome 6, highlight new avenues for investigation. Together, these results underscore the enduring importance of the *APOE* region in longevity, demonstrate the value of regional association approaches alongside conventional GWAS, and provide new leads for elucidating the molecular mechanisms of human aging.

This is a joint work with Yiran Jiang and Yue Hu.

Date : 22 December 2025 (Tuesday)
Time : 10:00a.m.-11:00a.m.
Venue : Room 1409 (near lift 25/26)

All Are Welcome!