# The Hong Kong University of Science and Technology

## Department of Mathematics

# PhD THESIS EXAMINATION

## *Improving Association Mapping and Polygenic Prediction in Trans-ancestry Analysis*

***By***

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***ABSTRACT***

Over the past two decades, genome-wide association studies (GWASs) have successfully advanced our understanding of the genetic basis of complex traits. Despite the fruitful discovery of GWASs, current GWASs were often criticized for their lack of ancestry diversity as most samples are collected from European populations. There is a pressing need to improve association mapping and polygenic prediction in trans-ancestry analysis. To fill the gap of disparities in genetic studies between non-Europeans and Europeans, we propose a statistical method, LOG-TRAM, to leverage the local genetic architecture for trans-ancestry association mapping (TRAM). By using biobank-scale datasets, we showed that LOG-TRAM could greatly improve the statistical power of identifying risk variants in under-represented populations while producing well-calibrated p-values. We applied LOG-TRAM to the GWAS summary statistics of various complex traits/diseases from BioBank Japan, UK Biobank, and Africans. Our method obtained substantial gains in power and achieved effective correction of confounding biases. GWAS-derived polygenic risk scores (PRS) have shown great potential in stratifying patients into different risk groups for individuals of European ancestry. However, PRS becomes less accurate in non-Europeans due to genetic differences across populations. To address this issue, we propose a cross-population and cross-phenotype (XPXP) method for the construction of PRSs in trans-ancestry analysis. By leveraging biobank-scale datasets in European populations and multiple GWASs of genetically correlated phenotypes, we showed that XPXP could substantially improve predictive power in identifying high-risk groups of type 2 diabetes for East Asians.


**Date : 21 July 2022, Thursday**

**Time : 10:30 a.m.**

**Online via ZOOM: ID: 9656130237 (Passcode: hkust)**
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***(Open to all faculty and students)***

**The student's thesis is now being displayed on the reception counter in the General Administration Office (Room 3461).**