Stages d'été
Centre de recherche Azrieli
du CHU Sainte-Justine

Un été ensoleillé
avec prévision de science

15 – Optimization of a Trans-Ancestry Polygenic Risk Score for Type 1 Diabetes

Accepted Academic Levels (in progress):
☐ College ☒ Bachelor's ☒ First-cycle PhD ☒ Master's

Research Team

Despoina Manousaki, M.D,Ph.D
Endocrinologue pédiatre, CHU Sainte Justine
Clinicienne-chercheuse, Centre de Recherche du CHU Sainte-Justine, Montréal, Canada
Professeure agrégée de clinique, Départements de pédiatrie et de biochimie et médecine moléculaire, Université de Montréal, Canada
https://manousakilab.wordpress.com

Research Project Description

Type 1 Diabetes (T1D) is a chronic autoimmune disease characterized by the destruction of insulin-producing beta cells in the pancreas, leading to lifelong insulin dependence. Genetic predisposition contributes to about 50 % of T1D risk. The strongest genetic signals are located within the Human Leukocyte Antigen (*HLA*) class I and II genes, although non-*HLA* loci have also been identified through genome-wide association studies (GWAS).

Polygenic risk scores (PRS) quantify an individual's genetic susceptibility to a disease by aggregating the effects of many risk-associated variants. Importantly, PRS can identify individuals at the highest genetic risk of developing T1D, before clinical symptoms appear. enabling early monitoring and potential preventive interventions. However, most

PRS are based on European-ancestry data, limiting their accuracy in other populations and emphasizing the need for their trans-ancestry optimization.

Our laboratory recently developed and validated a Trans-Ancestry Polygenic Risk Score (TA-PS) for T1D, incorporating multi-ancestry non-*HLA* variants, *HLA* variants derived from Europeans, and *HLA* interactions. The TA-PS demonstrated higher predictive performance compared to ancestry-specific PRS across European and non-European ancestries.

Recently, a cross-ancestry optimized *HLA*-focused PRS (T1D GRShla) significantly improved the prediction of T1D across diverse populations. Using over 41,000 samples from multiple ancestry studies, this score identified conditionally independent *HLA* SNPs and *HLA* alleles associated with T1D.

Since *HLA*-based scores alone cannot fully capture the polygenic nature of T1D, integrating both trans-ancestry optimized *HLA* and non-*HLA* components into a single score is essential. Our project therefore aims to combine our TA-PS with T1D GRShla into a new, optimized version of TA-PS and test its performance in an independent, Montreal-based T1D case-control cohort, as well as in the British UK Biobank.

Role of the candidate during the internship

During the internship, the candidate will contribute to the optimization of a trans-ancestry polygenic risk score (TA-PS) for Type 1 Diabetes. Their work will involve integrating recently developed cross-ancestry *HLA*-focused PRS components with existing TA-PS models and optimizing model architecture through recalibration and statistical refinement. The candidate will assist in analyzing multi-ancestry genomic data, performing model validation across diverse cohorts, including the Montreal-based and UK Biobank datasets, and assessing predictive performance using metrics such as AUROC. Through this work, the intern will gain hands-on experience in genomic data analysis, genetic epidemiology and statistical modeling.

Academic Programs

Students enrolled in one of the following academic programs, or in a related field, are invited to apply:

- Bioinformatics program at University of Montreal, Quantitative Life Sciences (QLS) program at McGill University

Required Skills and Expertise

The candidate should have a background in bioinformatics, and statistical modeling, with programming skills in R or Python and experience analyzing genomic data.

Centre de recherche Azrieli
CHU Sainte-Justine
Le centre hospitalier universitaire mère-enfant
Université de Montréal

https://event.fourwaves.com/fr/stagerecherchechusj2026

Internship Details

Schedule

☒ Full-time (35 hrs/week)
☐ Part-time

Duration (approximative)

☒ 4 months
☐ 3 months
☐ 2 months
☐ 1 months

Funding

Funding will vary depending on the type of internship:

- Internship recognized by the academic institution: A minimum stipend of CAD **$550 per week** (based on a 35-hour schedule) will be provided from the supervisor's research funds or in combination with other funding sources.
- Internship outside the academic curriculum: An hourly wage ranging from **CAD $16.10 to $18.72** will be provided from the supervisor's research funds.

Keywords

Type 1 Diabetes (T1D), Polygenic Risk Score (PRS), Multi-ancestry analysis

Address

Centre de recherche Azrieli du CHU Sainte-Justine
3175 Chemin de la Côte-Sainte-Catherine
Montréal, Qc, H3T 1C5
Canada