

**CIHR STAGE  
International Speaker  
Seminar Series:  
Dr. Gil McVean**

**Friday June 7  
12 – 1pm**

**Robert B. Salter Auditorium**  
Peter Gilgan Centre for  
Research and Learning  
686 Bay Street  
Toronto, Ontario M5G 0A4



# Mapping the structure of genetic risk for common disease in the UK Biobank

**Dr. Gil McVean**

Professor of Statistical Genetics, University of Oxford  
Director, Big Data Institute, University of Oxford

Genetic risk factors frequently affect multiple common human diseases, providing insight into shared pathophysiological pathways and opportunities for therapeutic development. However, systematic identification of genetic profiles of disease risk is limited by the availability of both comprehensive clinical data on population-scale cohorts and the lack of suitable statistical methodology that can handle the scale of and differential power inherent in multi-phenotype data. We have developed a disease-agnostic approach to cluster genetic risk profiles for 3,025 genome-wide independent loci across 19,155 ICD-10 diagnostic codes from 320,644 participants in the UK Biobank, representing a large and heterogeneous population. We identify several hundred distinct disease association profiles and use multiple approaches to link clusters to underlying biological pathways. We show how clusters can decompose the variance and covariance in risk for disease, thereby identifying underlying biological processes and their impact. We demonstrate the use of clusters in defining disease relationships and informing therapeutic strategies.

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