THE GIS
SPEAKER SERIES

Genome Institute of Singapore
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Wrestling a disease locus to the ground: Defining the mechanism of CD40 in human autoimmunity

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Walbert Professor of Medicine and Professor Biomedical Informatics
Harvard Medical School

Host: Shyam PRABHAKAR

Tuesday 28 April 2026
11.00am – 12.00pm

GIS L2 – Seminar Room
60 Biopolis Street, Genome, Singapore 138672

About The Speaker

Dr. Soumya Raychaudhuri is the Timothy P. and Keli B. Walbert Professor of Medicine in the Field of Rheumatology at Harvard Medical School and an Institute Member at the Broad Institute. He serves as the Director of the Center for Data Sciences and an Associate Physician at Brigham and Women's Hospital. Dr. Raychaudhuri holds a Ph.D. in Biomedical Informatics and an M.D. from Stanford University.

His research program integrates computational biology, human genetics, and clinical rheumatology to identify the genetic basis of immune-mediated diseases. His laboratory has made significant contributions to discovering pathogenic loci in rheumatoid arthritis, type 1 diabetes, and tuberculosis. A pioneer in single-cell genomics, his group developed widely used algorithms like Harmony and Symphony to define disease-associated cell states. Dr. Raychaudhuri has authored over 240 peer-reviewed publications and is a Fellow of the American Association for the Advancement of Science. In addition to his research, he is a dedicated mentor to graduate students and maintains an active clinical practice in rheumatology

About The Seminar

Translating statistical associations from GWAS into biological mechanisms remains a formidable challenge. For example, we and others have established the CD40 locus as a major risk factor for autoimmune conditions like rheumatoid arthritis and multiple sclerosis.

In this talk, I describe multidisciplinary strategies to define disease mechanisms, specifically using dynamic eQTL mapping in single cells. By modeling genetic effects across continuous cell-state trajectories, we capture regulatory signals that emerge only during specific stages of immune activation. We apply this to autoimmune loci, and immune cell states – including the CD40 locus.

We apply our novel CRAFT-seq platform, which enables us to link the effects of base-pair resolution CRISPR edits to simultaneous single-cell transcriptomic and surface-protein outputs. Our data reveal a protective SNP that disrupts a Kozak sequence, selectively reducing CD40 protein levels without altering mRNA expression. This reduction raises the threshold for B cell activation and triggers significant trans-regulatory effects that are most prominent in activated naive B cells. In this specific context, the SNP suppresses gene modules essential for downstream signaling. These findings demonstrate how subtle non-coding variation scales into systemic disease. They provide a blueprint for how non-coding variants can be used to define disease mechanisms.