Boolean Networks Reveal Opposing Roles of SLC22A5 and SLC22A15 in Inflammatory Bowel Disease

Rohan Subramanian[1], Sanjay Nigam[2], Debashis Sahoo[2,3]

[1]Department of Computer Science, Harvey Mudd College [2]Department of Pediatrics, University of California San Diego [3]Department of Computer Science, University of California San Diego

Inflammatory bowel disease (IBD) is a chronic autoimmune condition that affects the normal function of the gut. SLC22A5 and SLC22A15, both members of the SLC22 family of solute carriers, contribute to cellular uptake and clearance of various substrates, crucial for maintaining cellular homeostasis and metabolic functions. Additionally, mutations or dysregulation in these genes have been linked to metabolic disorders and may play roles in the pathogenesis of IBD. Identification of therapeutic targets for IBD has been limited by heterogenous disease phenotypes and variable response rates.

Network-based analyses can capture complex genetic interactions that characterize disease states and identify drug targets. We leveraged large-scale transcriptomic data and Boolean implication networks, a scalable computational approach capable of capturing asymmetric relationships and nonlinear interactions between genes, to build a model of IBD that reveals critical insights into the disease continuum and therapeutic opportunities. Our computational platform Boolean Network Explorer (BoNE) enables analysis of this network, focusing on paths or clusters important to IBD progression.

Using BoNE, we found that SLC22A5 and SLC22A15 occupy opposite sides of the disease spectrum: SLC22A5 is downregulated in IBD and associated with healthy states, while SLC22A15 is upregulated in IBD. These opposing roles suggest cell type-specific expression patterns and highlight unique opportunities for drug targeting. Agonists for SLC22A5 and antagonists for SLC22A15 may be useful in IBD therapeutics, paving the way for novel targeted molecular therapies. Future validation in experimental and clinical models will assess the therapeutic potential of these findings.