Integrating Network and Pathway Information for Drug Repurposing in Diffuse Large B Cell Lymphoma

Her, Yuchan (School: Coral Reef Senior High School)

Diffuse large B-cell lymphoma (DLBCL) is the most common aggressive non-Hodgkin lymphoma. Standard R-CHOP chemotherapy leaves many patients with relapsed or refractory disease, and salvage procedures or CAR T-cell therapies are toxic, expensive, and available only at specialized centers. Drug repurposing could provide more accessible options, but no systematic way exists to prioritize DLBCL candidates using molecular data. This project developed a computational, network- and pathway-based pipeline to repurpose existing drugs for DLBCL using public transcriptomes and drug–target databases. Bulk RNA-seq data from DLBCL cohorts were compared to GTEx spleen controls with DESeq2 to identify differentially expressed genes and dysregulated pathways. These genes were combined with curated gene–disease associations and projected onto a protein–protein interaction network, where the DIAMOnD algorithm expanded them into a DLBCL disease module. I then found that this module is significantly more connected than random gene sets, indicating a coherent disease neighborhood in the interactome. Next, I mapped 87 approved drugs to their protein targets, computed network proximity and diffusion scores to the DLBCL module, and integrated these with module targeting, expression patterns, clinical evidence, and safety to rank candidates. Known or investigational lymphoma drugs showed more favorable proximity scores than other drugs, supporting the relevance of the network metric. The final shortlist contained one approved lymphoma therapy and four non-DLBCL-approved drugs with acceptable safety profiles. This study demonstrates that a network-medicine pipeline can both rediscover existing lymphoma treatments and systematically highlight repurposing candidates for future testing in DLBCL.

Awards Won: