You are cordially invited to a Computational Genomics Seminar

Binyamin A. Knisbacher, PhD

Head of Cancer Genomics and Immunogenomics lab, Goodman Faculty of Life Sciences, Bar-Ilan University

*"Multiomic data from 1148 chronic lymphocytic leukemia patients delineates their molecular map and its impact on outcome"*

Wednesday September 7 at 11:15

School of Computer Science, Check Point Building, Room 420

**Abstract:** Recent advances in cancer characterization have consistently revealed marked heterogeneity, impeding the completion of integrated molecular and clinical maps for each malignancy. Chronic lymphocytic leukemia (CLL) is a B cell neoplasm with highly variable natural history, which is conventionally categorized into two subtypes distinguished by the extent of somatic mutations in the heavy chain variable region of immunoglobulin genes (IGHV). Previously, two independent studies analyzed genetic data from ~500 CLL patients. To provide a more complete bioclinical understanding of CLL, we devised the ‘CLL-map’ project - an international endeavor to harmonize and analyze genomic, transcriptomic, and epigenomic data from 1148 patients ([Knisbacher et al, Nature Genetics,](https://www.nature.com/articles/s41588-022-01140-w%22%20%5Ct%20%22_blank)*[in press](https://www.nature.com/articles/s41588-022-01140-w%22%20%5Ct%20%22_blank)*).

Doubling the cohort size and integrating with new multiomic data facilitated novel discovery. The greater statistical power enabled identification of 202 candidate genetic drivers of CLL (including 109 novel ones) and refined the characterization of IGHV subtypes, which revealed distinct genomic landscapes and leukemogenic trajectories. Using ~600 CLL RNA-seqs, we discovered new gene expression subtypes that further subcategorized this neoplasm and proved to be independent prognostic factors. We devised a machine learning classifier for these RNA expression subtypes and show their relevance to independent cohorts.

Integrative analysis using all molecular features shows that clinical outcomes are associated with a combination of genetic, epigenetic, and gene expression features, further advancing our prognostic paradigm for CLL. Overall, this work reveals fresh insights into CLL oncogenesis and prognostication and advances us towards improved precision medicine for CLL patients. In the current post-TCGA era, our findings motivate the initiation of cancer multiomics projects at larger scale for additional tumor types.

Host: Prof. Ron Shamir, School of Computer Science, TAU