**You are cordially invited to a Computational Genomics Seminar**

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*"The evolution of aneuploidy in cancer models: Perils and opportunities"*

Wednesday **January 8** at **11:15**

**Check Point** building, **room 420**, School of Computer Science, TAU

Host: **Prof. Ron Shamir** ([rshamir@tau.ac.il](mailto:rshamir@tau.ac.il)), School of Computer Science

**Abstract:** Aneuploidy, an imbalanced number of chromosomes or chromosome arms, is a distinct feature of cancer. Recent years have seen conceptual, methodological and technical advances in the field of cancer aneuploidy research, but we are just beginning to scratch the surface of the underlying biology, and the potential vulnerabilities of aneuploid cancer cells remain under-explored. Cancer aneuploidy is therefore a biological enigma and a missed opportunity for cancer therapy. Studying aneuploidy in cancer models is necessary in order to functionally dissect the role(s) of aneuploidy in tumorigenesis, and to identify cellular vulnerabilities of aneuploid cancer cells. In order to properly use cancer models in aneuploidy research, we must understand how faithful their aneuploidy landscapes are to those of their tumors-of-origin, and dissect their heterogeneity and stability throughout model propagation. We have recently studied the aneuploidy landscapes of three major cancer models:

1. First, we generated a comprehensive catalogue of aneuploidy in breast cancer mouse models. Mining this novel resource, we found that chromosomal aberrations accumulated late during breast tumorigenesis, and observed marked differences in aneuploidy patterns across mouse mammary tumours initiated with distinct drivers. We then used the mouse data to narrow down the region-of-interest in one of the most recurrent chromosomal changes in human breast cancer (chr1p loss), and identified a gene (*Sfn*) that contributes to the recurrence of this aneuploidy (Ben-David et al. *Nature Communications* 2016).
2. Next, we analyzed tumors from patient-derived xenografts (PDXs) and revealed distinct trajectories of aneuploidy evolution in patients and in mice. Importantly, some recurrent aneuploidies that tended to disappear in PDX models were associated with drug response to anticancer therapies (Ben-David et al. *Nature Genetics* 2017).
3. Finally, we analyzed cancer cell lines and characterized how their genomic evolution altered their transcriptional programs and drug response. This work exposed associations between recurrent chromosomal changes and drug response, and yielded a novel genetically-matched system to study cancer aneuploidy *in vitro* (Ben-David et al. *Nature* 2018).

In this talk, I will discuss emerging themes from these studies, and describe unpublished ongoing follow-up studies, focusing on: a) the selection pressures that shape cancer aneuploidy landscapes; b) strategies to identify cellular vulnerabilities associated with recurrent aneuploidies; and 3) the relevance of genomic evolution of cancer models to cancer aneuploidy research.