Dr. Ori Hassin

Will lecture about:

**Different hotspot p53 mutants exert distinct phenotypes and predict outcome of colorectal cancer patients**

Sporadic CRC is characterized by high prevalence of TP53 hotspot missense mutations. In particular, over 20 percent of all TP53-mutated CRC tumors carry missense mutations at p53 amino acid position 175 (structural mutants) or 273 (DNA contact mutants). By combining in vitro CRC cell line models and human CRC data mining, we identified a distinct transcriptional signature orchestrated by p53R273H, implicating activation of oncogenic signaling pathways and predicting worse patient outcome. Concordantly, p53R273H selectively promotes rapid CRC cell spreading, migration and invasion in vitro and metastasis in vivo. Thus, different TP53 missense mutations contribute differently to cancer progression. Moreover, p53R273 mutations possess distinct gain-of-function activities in CRC, which bear on disease course and possibly on patient management strategy.