Contribution ID: **22** Type: **not specified**

Genetic Instability –from matrix rigidity effects to physics of tumor elimination by eng'd macrophages

Wednesday 18 September 2024 14:25 (35 minutes)

Cancer always exhibits genetic changes, but solid tumors show more changes and greater variance than liquid cancers and soft tumors. To visualize chromosome loss at single cell resolution, a novel fluorescence 'ChReporter'method was developed and enables tracking of heritable losses in colonies. Systems studied thusfar range from in vivo tumors to spheroids in gels of controlled stiffness and single cell confinement. ChReporter loss following interphase nuclear rupture is compared to mitotic perturbations, particularly in strong confinement relevant to solid tissues and tumors. The mean and variance of changes conform to the seminal theory of Luria & Delbruck for genetic evolution.
Chromosome number changes often associate with poor prognosis in solid tumor types, and for melanoma therapy with Tcell checkpoint blockade also fails. Using poorly immunogenic mouse melanoma, we pharmacologically induce chromosome losses & gains, and find it skews macrophages towards an anti-cancer phenotype. We measure the cohesiveness of the tumors, and upon macrophage addition, cooperativity of low entropy macrophage clusters is revealed in tumor elimination. Success benefits from disrupting the tumor's Macrophage checkpoint and yields durable cures with anti-cancer antibodies.

Presenter: DISCHER, Dennis (University of Pennsylvania)