Herbert Levine (Rice University, Center for Theoretical Biological Physics)

General Lecture: Phenotypic plasticity and Tumor progression

EMT, the epithelial-mesenchymal transition, has been invoked as the underlying causes of cell motility during the metastatic cascade. This popular approach has however led to several problems. EMT is connected to many other physiological changes and conversely EMT seems at least partially dispensable for motility. Also, EMT must apparently be reversed to allow for metastatic lesion growth. Here we identify EMT as a type of trans-differentiation and create mechanistic models of the circuitry underlying this switch. Our models range from very simple constructs involving only a few of the most critical transcription factors and microRNA regulators up to intermediate scale networks. This approach leads to the prediction of new partial E/M states that are more likely to be drug-resistant and tumor-initiating than either of the fully differentiated E or M phenotypes. Our model naturally predicts the importance of small clusters as a route to metastasis. W e discuss tests of these ideas in cell lines and uses of these ideas in explaining in vivo data.

Specialized Lecture: Towards an understanding of the tumor microenvironment

Progression of cancer involves not just the malignant cells per se, but also a whole slew of supporting cells and supporting biomaterials that collectively determine the environment in which the cancer cells grow and/or migrate. Here I will sketch a number of different research avenues that will hopefully begin to yield insights into some of these players. Topics to be covered include ECM mechanics, fibroblast patterns, tumor-associated macrophages and the interaction of tumors with T-cells.

Projects

- Incorporate cancer cells into a recent model of macrophage polarization switching (reference: Bistability of the cytokine-immune cell network in a cancer microevironment X Li, H Levine Convergent Science Physical Oncology 3 (2), 024002)
- Simulate the motion of firbroblasts around an expanding tumor mass (reference: On the mechanism of long-range alignment order of fibroblasts Xuefei Li, Rajesh Balagam, Ting-Fang He, Peter P. Lee, Oleg A. Igoshin, Herbert Levine bioRxiv 119669; doi: https://doi.org/10.1101/119669)