Biomedical Informatics Grand Rounds

Wednesday, March 2nd, 2022 3:00 pm – 4:00 pm

Ecology and Evolution of Breast Cancer

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Remote Access
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Bio: Dr. Mehdi Damaghi is the assistant professor at the department of pathology, Renaissance School of Medicine at Stony Brook University. He received his Ph.D. in Cell Biology and Genetic Engineering from Max Planck Institute. The central aim of his research is to use eco-evolutionary principles to understand breast cancer initiation, progression, and invasion. He studies how the tumor microenvironment and metabolism shape selective pressures that play a fundamental role in the evolution of a tumor from initiation to progression and resistance to therapy. He also uses evolutionary principles to discover unique vulnerabilities of breast cancer cells at single cell or whole population level studying genome, epigenome, transcriptome, proteome and metabolome levels. For the same reason, he develops novel imaging techniques and biomarkers as well as unique 3D spheroid and organoid design enabling us to study the eco-evolutionary principle and adaptation mechanism of cancer cells in a physiologically relevant context. These vulnerabilities can be exploited for prognostic, diagnostic, and therapeutic benefit. He applies spatial biology techniques (multiplex IHC and DNA/RNA spatial omics) in combination with mathematical modeling and simulation and machine learning to study selection forces in cancer microenvironment and metabolism such as acidosis, hypoxia, nutrient deprivation, and hormone fluctuations. This will unveil uncharacterized aspects of tumor microenvironment on cancer cells and stroma components such as immune cells and fibroblasts.

Abstract: In early breast carcinogenesis, neoplastic cells grow in multiple layers towards the lumens of ducts, which subjects the periluminal cells to harsh conditions of low oxygen, low pH, and nutrient deprivation. Adaptation to these harsh conditions is a pre-requisite for survival of incipient tumor cells and also responsible for selecting cells with a more aggressive phenotype. Based on the first principle of Darwinian evolution, common phenotypes of cancer cells must have conferred a selective advantage at some point during their evolutionary trajectory.

Adaptations are initially acute and reversible, but eventually Darwinian selection results in cells with hardwired phenotypes. A prominent example of this is aerobic glycolysis, or the Warburg Effect (WE), wherein cells are hard-wired to ferment glucose, even in the presence of oxygen. WE provide an evolutionary advantage which leads to higher fitness of the cancer cells, who have acquired mechanisms of adaptation, such as autophagy and lysosome redistribution.

Notably, a WE is highly correlated with a cancer's metastatic potential and poor outcome. Hence, a major question in carcinogenesis is: "What are the mechanisms by which a harsh microenvironment eventually selects for hard-wired (heritable) phenotypes, such as a WE?". Rather than simply selection of pre-existing phenotypes, we contend that the microenvironment actively induces phenotypic diversity through a systematic set of epigenetic and genetic alterations.

Educational Objects: Upon completion, participants should be able to:

- Evolutionary and Ecological principles governing tumor initiation and progression
- Introducing the physical microenvironment of solid tumors
- Biomarker discovery based on tumor adaptation strategy
- How to translate basic science findings to clinique and propose new treatment strategies

Disclosure Statement: The faculty and planners have no relevant financial relationship with ineligible companies whose primary business is producing, marketing, selling, re-selling, or distributing health care products used by or on patients.

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