Understanding Tumor Heterogeneity and Plasticity
Through the Lens of Cancer Stem Cell Model and Mathematical Modeling

Tumor heterogeneity and plasticity provide a driving force for tumor progression and metastasis as well as treatment response. Tumor heterogeneity can be explained by the same mechanisms that govern the developmental programs of an organism and share many of the properties observed in cellular differentiation and physiological processes including stem cell biology and epithelial-mesenchymal transition (EMT). In this seminar series, I will talk about biological basis of tumor heterogeneity from the perspectives of three spatial levels: tissue, cell, and molecule. Tumor heterogeneity is often viewed at tissue level, which is determined by cellular heterogeneity and ultimately determined by gene regulatory networks consisting of genome sequences, transcription factors, signaling molecules, and epigenetic information. The sources of tumor heterogeneity include intrinsic developmental programs, tumor microenvironment, and stochastic processes. I will describe gene regulatory network and mathematical modeling and discuss how mathematical modeling can help understand the sources of heterogeneity as well as the initiation and dynamics of cellular states and epigenetic memory. I will describe differential equations and quasi-potential as a mathematic tool to quantify Waddington's epigenetic landscape and predict trajectory of cancer cell evolution and treatment response.

1) Cancer stem cell model and evolutionary dynamics
2) Gene regulatory network (GRN) and differential equation model
3) Waddington's epigenetic landscape quantified with quasi-potential
4) Network motifs and dynamics of cellular states
5) Sources of tumor heterogeneity: deterministic vs stochastic effects
6) Drug-tolerant persister (DTP) and cancer dynamics