Growth Factor Signaling and Metabolic Homeostasis in Single Cells

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12 - 1 PM
Tong Auditorium (1003 Engineering Centers)

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As single-cell technologies expand, it is becoming clear that many cellular signaling events are very dynamic, necessitating a time-lapse approach to capture rapid kinetics within the cell. I will present our work on using live-cell imaging with genetically encoded reporters to approach two long-standing questions in the regulation of cell growth in humans. This work centers on two kinases – ERK and AMPK – that play key roles in homeostasis of healthy tissues and which are currently being targeted by cancer therapies.

The first question is how the dynamics of ERK activity encode information from extracellular stimuli, allowing different growth factor receptors to activate distinct gene expression programs using the same intermediate signaling pathways. Mutations in this pathway, and candidate therapies targeting these mutations, exert unique effects on ERK kinetics, making it essential to decode the cellular “language” of ERK activity dynamics.

The second question is how cellular energetics are maintained and balanced despite continuing fluctuations in both the supply of nutrients and the demand created by anabolic processes required for cell growth. We find that the interlinked AMPK, Akt, and ERK pathways undergo surprisingly dynamic fluctuations in response to metabolic stresses, suggesting new models for how cellular homeostasis is maintained on the scale of minutes by coordination of catabolic and anabolic processes.