COMPUTATIONAL BIOLOGY WEBINAR @ IMSc

SHAPESHIFTERS IN CANCER: HOW DO TUMOR CELLS SWITCH AMONG DIFFERENT PHENOTYPES TO DRIVE AGGRESSIVE BEHAVIOR?

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THURSDAY, 1 OCTOBER 2020, 4 PM IST

Metastasis (the spread of cancer cells from one organ to another) and therapy resistance cause above 90% of all cancer-related deaths. Despite extensive ongoing efforts in cancer genomics, no unique genetic or mutational signature has emerged for metastasis. However, a hallmark that has been observed in metastasis is adaptability or phenotypic plasticity – the ability of a cell to reversibly switch among different phenotypes in response to various internal or external stimuli. Phenotypic plasticity has also been recently implicated in enabling the emergence of resistance for many cancers across multiple therapies. However, a mechanistic understanding of these processes from a dynamical systems perspective remains incomplete. This talk will describe how mechanism-based mathematical models for phenotypic plasticity can enable our improved understanding of cellular decision-making at individual and population levels from these perspectives:

a) Multistability (how many cell states exist en route?)

b) Reversibility/irreversibility (do cells come across a 'tipping point' at specific time and/or dose of inducers beyond which they do not revert?)

c) Hysteresis (do transitioning cells follow same/different paths?)

d) Cell-cell communication (how do cells affect tendency of their neighbors to exhibit plasticity?)

Collectively, our work highlights how an iterative crosstalk between mathematical modeling and experiments can both generate novel insights into the emergent nonlinear dynamics of cellular transitions and uncover previously unknown accelerators of metastasis and therapy resistance.

GOOGLE MEET LINK:

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