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BSSE Seminar

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Design principles of regulatory networks enabling non-genetic heterogeneity in cancer cells

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About the speaker:

Dr. Mohit Kumar Jolly is an Assistant Professor at BSSE (Centre for BioSystems Science and Engineering), Indian Institute of Science. After graduating from Indian Institute of Technology (IIT) Kanpur, he earned his PhD in Bioengineering from Rice University in 2016. His lab focuses on decoding mechanisms and implications of non-genetic heterogeneity in cancer metastasis and therapy resistance, with specific focus on mechanism-based and data-based mathematical modeling in close collaboration with experimental cancer biologists and clinicians. He serves as the Secretary of The Epithelial-Mesenchymal Transition International Association (TEMTIA) and the co-chair of Mathematical Oncology subgroup at the Society for Mathematical Biology (SMB).

Abstract:

Non-genetic heterogeneity has significant implications for development and evolution of organs, organisms, and populations. Recent observations in multiple cancers have unravelled the role of non-genetic heterogeneity in driving metastasis and therapy recalcitrance. However, the origins of such heterogeneity are poorly understood in most cancers. Here, we investigate a regulatory network underlying non-genetic heterogeneity in small cell lung cancer, a devastating disease with no molecular targeted therapy. Discrete and continuous dynamical simulations of this network reveal its multistable behavior that can explain co-existence of four experimentally observed phenotypes. Analysis of the network topology uncovers that multistability emerges from two teams of players that mutually inhibit each other but members of a team activate one another, forming a 'toggle switch' between the two teams. Such ‘teams’ also emerge in networks enabling non-genetic heterogeneity across many cancers, including those in breast cancer and melanoma. Deciphering such topological signatures in cancer-related regulatory networks can unravel their ‘latent’ design principles and offer a rational approach to characterize non-genetic heterogeneity.