DESIGN PRINCIPLES AND FUNCTIONAL RESILIENCE OF MUTUALLY REPRESSING NETWORK MOTIFS INVOLVED IN CELLULAR DECISION-MAKING

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Abstract: Elucidating the design principles of regulatory networks driving cellular decision-making has important implications in understanding cell differentiation and guiding the design of synthetic circuits. A well-studied network motif involved in cellular decision-making is a toggle switch-a set of two opposing transcription factors A and B, each of which is a master regulator of a specific cell fate and can inhibit the activity of the other. A toggle switch can lead to two possible states-(high A, low B) and (low A, high B)-and drives the 'either-or' choice between these two cell fates for a common progenitor cell. However, the principles of coupled toggle switches, and the behavior of such network motifs when embedded in larger networks, remains unclear. Here, we investigate the dynamics of three

master regulators A, B and C inhibiting each other, thus forming three-coupled toggle switches to form a toggle triad, and its implications in CD4+ T-cell differentiation into Th1, Th2, Th17 and hybrid phenotypes. These observations offer insights into design principles of biological networks containing these network motifs, as well as help devise optimal strategies for integrating these motifs into larger synthetic networks.

Short Biography： Dr. Mohit Kumar Jolly leads the Cancer Systems Biology laboratory at Indian Institute of Science. He earned his Bachelors' and Masters from IIT Kanpur and PhD from Rice University, all in Bioengineering. He has made important contributions to decoding the emergent dynamics of cellular plasticity in cancer metastasis, through mathematical modeling of underlying regulatory networks. He won the 2016 iBiology Young Scientist Seminar Series – a coveted award for communicating one's research to a diverse audience. Currently, his lab develops mechanism-based and data-based models to decode the mechanisms and implications of non-genetic heterogeneity in metastasis and drug resistance, working in close collaboration with cancer biologists and clinicians. He serves as co-Chair of Mathematical Oncology subgroup at the Society for Mathematical Biology (SMB) and Secretary of International Epithelial-Mesenchymal Transition Association (TEMTIA).