Tata Institute of Fundamental Research
Survey No. 36/P, Gopanpally Village, Serilingampally, Ranga Reddy Dist., Hyderabad – 500 046

Webinar

Metabolic basis of cellular specialization in microbial systems

Sriram Varahan

inStem, Bengaluru

A common strategy employed by microorganisms to adapt to fluctuating nutrient environments is the formation of complex communities that exhibit functional specialization (biofilms). Previous studies in the field have characterized the gene regulatory networks and signalling pathways that control microbial community development in response to nutrient limitation. However, we lack a precise understanding of how conserved metabolic events orchestrate cellular decision making in the context of microbial community development and how metabolic processes can drive the evolution of cooperation and specialization in these communities. Recently, my postdoctoral work identified metabolic constraints that control cell fate decisions resulting in functional specialization and division of labour in clonal yeast communities in response to glucose limitation. A novel concept that emerged from this study was that threshold levels of certain metabolites (trehalose, in this case) can result in the emergence and maintenance of multiple cell states even in clonal communities growing in the same environment. I also found that the metabolic plasticity of certain metabolites like aspartate allow the cells in the community to use them either as a carbon source or a nitrogen source depending on their metabolic requirement. This in turn allows the cells to deferentially budget for these resources and use them for distinct processes which in turn is critical for the emergence and maintenance of distinct cell states. Finally, I showed that specialized sub-populations of cells in these communities exhibit cooperative division of labour wherein the gluconeogenic sub-population of cells produce the resource (trehalose) needed for the emergence and maintenance of the glycolytic sub-population of cells. Each cell state confers distinct advantages to the community (gluconeogenic cells are resistant to environmental stresses while glycolytic cells enables the colony to efficiently expand and forage) and both are important for collective growth and survival of the community.

My long term research interest is to understand how conserved metabolic events regulate cellular specialization in microorganisms in response to changing nutrient availability which in turn is critical for their ability to form communities and cause infections in a host. I will employ simple fungal models (Saccharomyces cerevisiae), as well as pathogenic fungi (primarily Cryptococcus neoformans), to understand how metabolism regulates cell fate decisions at a community level in response to nutrient limitation, and how this influences fungal pathogenesis.

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4:00 PM