

Deciphering amino acid starvation responses using yeast

Rajalakshmi Srinivasan, Adhish Walvekar, Ritu Gupta and Sunil Laxman
inStem, Bangalore

Cells respond to different starvations using multiple strategies. This eventually alters gene expressions, which controls the homeostatic response. While global responses to different starvations have fairly universal responses at the level of gene expression, we are trying to dissect unique responses to different amino acids, and also understand how growth is sometimes sustained even during starvation. Hence, we are building a template to understand how eukaryotic cells respond to different types of amino acid starvation. In the current model of responses to amino acid starvation, the accumulation of uncharged tRNAs activates the Gcn2 kinase, which orchestrates global translation downregulation but increased translation of the transcription factor called GCN4. We have shown that the addition of methionine uniquely in the minimal media results in increased growth in *S. cerevisiae* despite other amino acid starvation. Using transcriptome and metabolome analysis we show that methionine switches the cells towards proliferative state by regulating selective metabolic pathways via GCN4. Here, we build a metabolic logic for how this growth is achieved. In addition to this we are also exploring the binding targets of GCN4 under different nutrient conditions in the presence and absence of methionine, i.e. in growth promoting or inhibiting stress conditions. Thus we reveal some of the unexplored connections between methionine and the GCN4.