

Methylated PP2A stabilizes Gcn4 to enable a methionine-induced anabolic program

Metabolites can directly act as 'growth signals' for cells, as is often the case in cancers. In earlier work from laboratory had reported that the amino acid, methionine, and acts as one such growth signal. Scientists at DBT's Institute of Stem Cell Science and Regenerative Medicine (DBT-inStem), Bengaluru, showed that methionine activated a major transcription factor, Gcn4/ATF4, which controls gene expression and metabolic programs that help cells grow. However, the mechanism by which Gcn4 was activated was unknown. This gap in understanding is bridged in recent study, which elucidates the mechanism of Gcn4 activation.

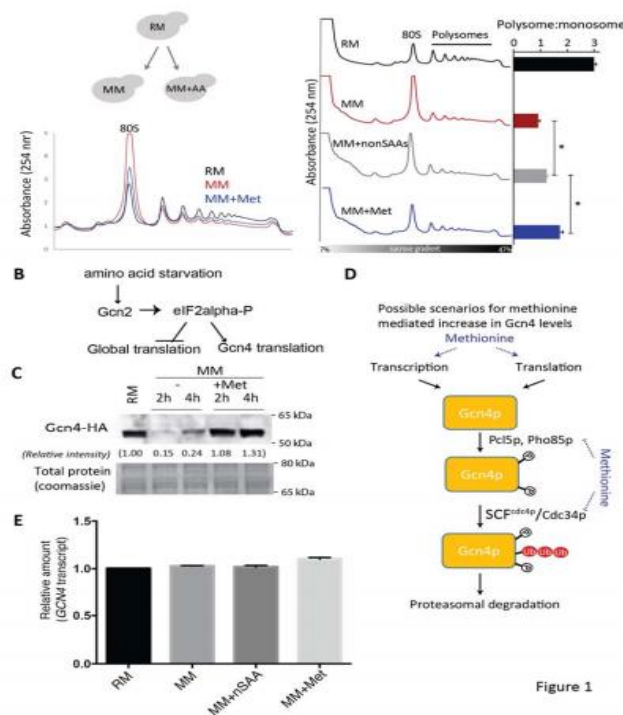


Figure 1

In this study, the team showed that methionine prevents the Gcn4 protein from being degraded/removed by cells. This is brought about by (methionine-dependent) methylation of the regulatory protein (PP2A), which removes another modification (a phosphorylation) on Gcn4. By doing so, Gcn4 becomes stable and protected from being removed by cells. Since many tumours are addicted to methionine, this study provides one mechanism as to how such dependence may be brought about. This work has been published recently in the *Journal of Biological Chemistry* titled 'Methylated PP2A stabilizes Gcn4 to enable a methionine-induced anabolic program'.

The investigator is an Assistant Investigator at Regulation of Cell Fate (RCF) theme, inStem and his research interests are focused on nutrient sensing and metabolic regulation of cell fate transitions. He is also an Intermediate Fellow of Wellcome Trust/DBT India Alliance.

Link:<https://www.biorxiv.org/content/10.1101/2020.05.05.079020v1#:~:text=This%20methylation%20of%20PP2A%20shifts,Gcn4%2Ddependent%20anabolic%20program%20collapses>

Contact details:

Dr. Amrita Tripathy,

E-mail: tripathya@instem.res.in