Unstructured regions of large enzymatic complexes control the availability of metabolites with signaling functions

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Video Byte

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Abstract

The molecular mechanisms behind diseases and malignancies were once considered to follow a basic paradigm. Cells use a network of protein-protein interactions to detect environmental changes, signal the nucleus, and then trigger a response through changes in gene expression. Recent evidence, however, suggests the products of protein breakdown, rather than the proteins alone, could play an important role. A new review from the Kastritis Laboratory outlines how the fatty acid metabolites acetyl-CoA, α-ketoglutarate, and palmitic acid, in particular help orchestrate cell signaling and communication. These metabolites are regulated by large enzymatic complexes, or “metabolons”; acetyl-CoA by the pyruvate dehydrogenase complex, α-ketoglutarate by the 2-oxoglutarate dehydrogenase complex and palmitic acid by fatty acid synthase. Despite their apparent rigidity and organization, these complexes hide a considerable amount of disorder which is critical for facilitating substrate accessibility, enhancing protein-protein interactions, and increasing overall reaction speed. Understanding how protein metabolites interact with these unstructured regions of large enzymatic complexes could offer new and vital clues to how disease unfolds in the body.