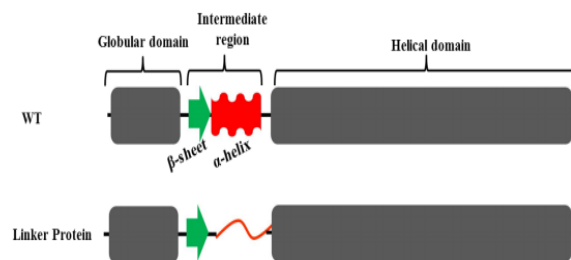


Scientists at NII found that α -helix of the intermediate region in hGBP-1 acts as a coupler for enhanced GMP formation

Scientists at DBT's National Institute of Immunology (NII), New Delhi found that substitution of the helix with a flexible peptide sequence in the full-length hGBP-1 (termed as linker protein) showed a drastic decrease in GMP formation. Unlike wild-type, the linker protein is not capable of undergoing substrate-induced oligomerization, suggesting the importance of the helix in oligomerization during the GTP hydrolysis.



Furthermore, they examined the effect of interactions between this helix and the $\alpha 2$ -helix of the globular domain in GMP formation through mutational studies. A single residue mutation (L118G) in the $\alpha 2$ -helix showed a significantly reduced GMP formation, indicating that the interactions of the α -helix with the $\alpha 2$ -helix are essential for enhanced GMP production. It was proposed that these interactions may help in the oligomerization-assisted proper positioning of the catalytic machinery for efficient second phosphate cleavage. Thus, the helix of the intermediate region may act as a 'coupler' or 'relay arm', which transmits conformational changes between the two domains during oligomerization, thereby regulating GMP formation. These findings thus provide a better understanding into the regulation of GMP formation in a large GTPase hGBP-1.

The interferon-gamma inducible large GTPase human guanylate binding protein-1 (hGBP-1) plays key role in anti-pathogenic and anti-proliferative functions. The hGBP-1 protein hydrolyzes GTP to GMP through successive phosphate cleavages, which makes it functionally distinct from other known GTPases. The enhanced GMP formation of this enzyme is associated with biological functions. It is a 592-residues long protein consisting of the two domains, an N-terminal globular- and a C-terminal helical domain, which are linked by an intermediate region

comprising a β -sheet and an α -helix. The role of the helix in the intermediate region of the full-length protein in GMP formation was not clearly understood.

Link: <https://pubmed.ncbi.nlm.nih.gov/31954926/>

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