# ATP-Driven Allosteric Regulation of 14-3-3: Positive Modulation of ATP Hydrolysis and Negative Regulation of Peptide Binding.

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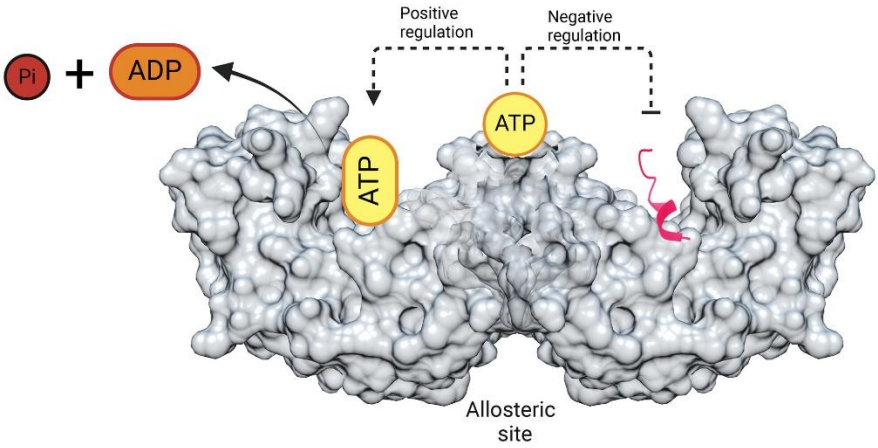
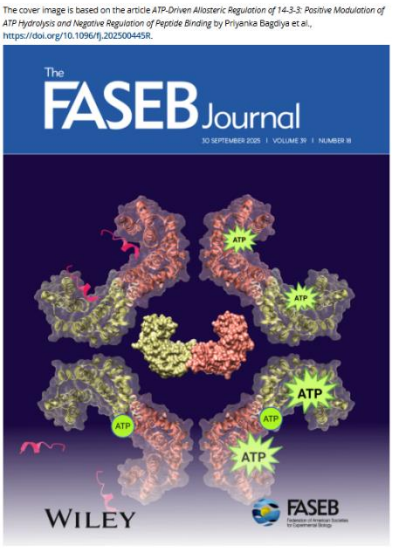
## Graphical Abstract

This graphical abstract illustrates dual allosteric modulation by ATP. ATP binding at allosteric site activates the enzyme and hydrolyzes the ATP at catalytic site to ADP and iP. On contrary, ATP binding at allosteric site exhibits the inhibition to the natural ligand peptide of 14-3-3.




Most 14-3-3 protein types (except one called sigma) can bind to and break down ATP (a molecule cells use for energy), but scientists didn't know how or why. This study confirms that 14-3-3 proteins have two ATP binding sites - one where they usually bind other proteins, and one at the spot where two 14-3-3 proteins join together (the dimer interface).

Using computer predictions and lab techniques, the researchers found two key amino acids (E131 and E180) that help break down ATP. They showed that this ATP breakdown is a natural feature of 14-3-3 proteins, and changing these amino acids significantly decreases this activity confirming their role in catalysis.

Importantly, the two-part (dimer) structure of 14-3-3 is necessary for ATP breakdown. ATP binding at the dimer interface turns on ATPase activity (breaking down ATP), but also blocks 14-3-3 from interacting with a specific peptide derived from ExoS protein of the infectious bacteria, *Pseudomonas* involved in disease.

This is the first study to reveal that ATP can control how 14-3-3 proteins behave, including preventing them from binding to selective ligands — a potentially important discovery for disease research.