ATP-cone: evolutionary mobile, structurally conserved domain with different regulatory functions

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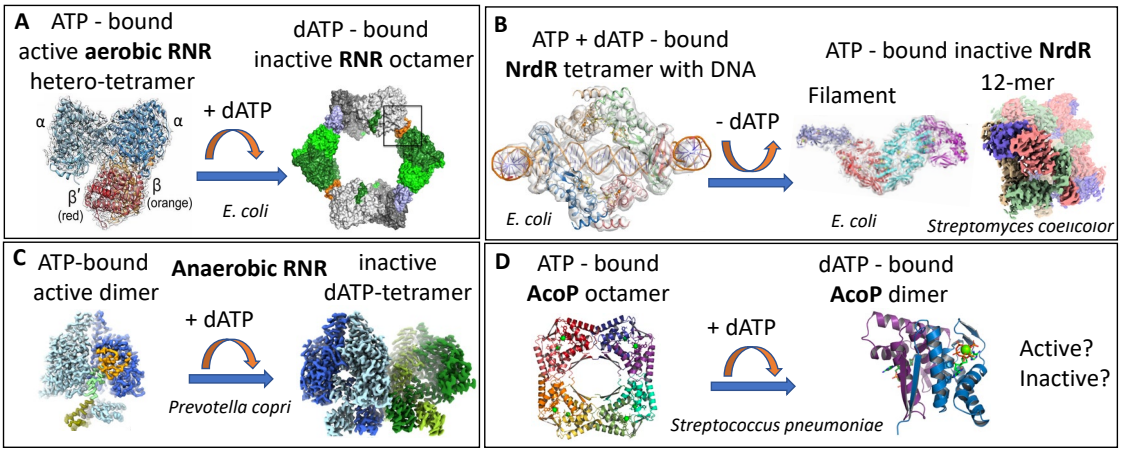
The ATP-cone (Aravind, 2000) is an evolutionary mobile structurally conserved domain of ~100 amino acids found in the majority of ribonucleotide reductases (RNRs), in the RNR-specific transcriptional repressor NrdR, and in a few 2-phosphoglycerate kinases. In RNRs, the ATP-cone allosterically regulates enzyme activity by acting as a master switch (Hofer 2012; Rozman Grinberg 2018; Bimai 2024). In NrdR, the ATP-cone regulates the binding of the repressor to DNA via a zinc-ribbon domain (Rozman Grinberg 2022). The ATP-cone binds one or two adenosine ribo- or deoxyribonucleotides, and depending on mode of binding it promotes formation of different oligomeric complexes via self-interactions or via interaction with core protein domains.

We present crystal and cryoEM structures of a variety of ATP-cone proteins:

- aerobic RNRs in which ATP-cones regulate activity by preventing radical transfer to the active site,
- an anaerobic RNR in which the ATP-cone regulates activity by preventing substrate binding,
- two different NrdRs in their DNA-bound and unbound forms, demonstrating their flexibility to adapt to the promoter binding conformation.

We also present structures of an enigmatic protein named AcoP that is abundant in a few bacterial genera. AcoP is comprised exclusively of the ATP-cone, forming octamers in its ATP-bound form and dimers in its dATP-bound form. The mechanism of action of AcoP is unknown, but its conservation suggests an important biological function.
Our results demonstrate the great variety of ways in which the ATP-cone domain acts as a regulatory module in different systems.



Aravind L. et al. (2000); J Mol Microbiol Biotechnol 2: 191-194. Hofer A. et al. (2012) Crit Rev Biochem Mol Biol 47: 50-63. Rozman Grinberg I. et al. (2018) eLife 7:e31529. Bimaï O. et al. (2023) eLife 12:RP89292; Rozman Grinberg I. et al. (2022) Nat Commun.13(1):2700.