Article

6 **Structural basis for cAMP-mediated allosteric control of the catabolite activator protein.**

Popovych N, Tzeng SR, ..., Ebright RH, Kalodimos CG
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Evaluations

Evaluated by Peter Artymiuk

After almost thirty years, this paper fills in the vital missing piece in the cAMP receptor protein (CRP) jigsaw -- the structure of CRP in its apo form. This reveals the nature of the allosteric transition that switches CRP between its DNA-binding "on" and its weakly binding "off" states.

CRP, also known as CAP (catabolite activator protein), is an archetypal bacterial transcription factor, which regulates hundreds of genes in E. coli, and it is the most studied of the huge CRP/FNR family of prokaryotic transcription factors. CRP was one of the first DNA-binding protein structures to be solved, first in the absence of DNA {1} and later complexed with DNA {2}. Both these existing structures have cAMP bound and thus correspond to the DNA-binding "on" state of the protein. What has been missing is a structure of CRP in its "off" state, which would reveal the nature of the allosteric transition that regulates CRP/DNA binding. Using advanced NMR methodology, Popovych et al. show that, in the absence of cAMP, the ends of the CRP dimerization helices adopt a coil structure; as a result, the C-terminal DNA-binding domains rotate by approximately 60 degrees and are no longer correctly positioned to bind DNA. Thus, at last, a simple but elegant switch mechanism is revealed.

References: {1} McKay and Steitz, Nature 1981, 290:744-9 [PMID:6261152]. {2} Schultz et al. Science 1991, 253:1001-7 [PMID:1653449].

Competing interests: None declared

Cite this evaluation

Evaluated by:
Peter Artymiuk
University of Sheffield, UK
Structural Biology
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Rating 6
Recommended

Classification Key: Changes Clinical Practice | Novel Drug Target | Technique | Clinical Trial | Review

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