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Single particle cryo-EM unveils multiple states in PdxR mechanism of transcriptional regulation

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Pyridoxal 5′-phosphate (PLP) is an enzyme cofactor required in a large number of metabolic processes, and its amount needs to be finely tuned in response to cell requirements.
A bacterial transcription factor of the MocR family, PdxR, plays a fundamental role in the regulation of the *de novo* biosynthesis of PLP in many bacteria, acting as either an activator of the PLP synthase complex or as an autorepressor, depending on PLP availability [1-4].
The biochemical and DNA-binding properties of PdxR, and the organization of its target regulon have been widely studied in the probiotic bacterium *Bacillus clausii* [4]. Nevertheless, a comprehensive understanding of the molecular mechanism underlying its function has been hindered by the absence of structural information.
In this study, X-ray crystallography and cryo-EM have been employed to gain structural insights into the DNA recognition and regulatory activity of PdxR.
Our cryo-EM structures of holo-PdxR in complex with its target DNA revealed the presence of multiple conformational states representing different snapshots within the overall dynamics of the PdxR-DNA complex formation.
Binding assays performed on PdxR mutants and altered DNA fragments at either the intrinsic curvature or the cognate binding sites pointed out that the specificity of the PdxR-DNA interaction is the result of a complex interplay between sequence and shape readout.
The investigation of the structure and dynamics of PdxR-DNA complex represents a fundamental step to clarify the mechanism governing the DNA-binding mode and the transcriptional regulation of MocRs transcription factors.

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