Poster Presentation

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Structural basis for hydroxymethylcytosine recognition by the SRA domain of UHRF2

N. Yang[1], T. Zhou[1], J. Xiong[2], M. Wang[1], J. Wong[3], B. Zhu[2], R. Xu[1]

[1]Institute of Biophysics, Chinese Academy of Sciences, Beijing, China, [2]National Institute of Biological Sciences, Beijing, China, [3]East China Normal University, Shanghai, China

Methylated cytosine of CpG dinucleotides in vertebrates may be oxidized by Tet proteins, a process that can lead to DNA demethylation. The predominant oxidation product, 5-hydroxymethylcytosine (5hmC), has been implicated in embryogenesis, cell differentiation and human diseases. Recently, the SRA domain of UHRF2 (UHRF2-SRA) has been reported to specifically recognize 5hmC, but how UHRF2 recognizes this modification is unclear. Here we report the structure of UHRF2-SRA in complex with a 5hmC-containing DNA. The structure reveals that the conformation of a phenylalanine allows the formation of an optimal 5hmC-binding pocket, and a hydrogen bond between the hydroxyl group of 5hmC and UHRF2-SRA is critical for their preferential binding. Further structural and biochemical analyses unveiled the role of SRA domains as a versatile reader of modified DNA, and the knowledge should facilitate further understanding of the biological function of UHRF2, and the comprehension of DNA hydroxymethylation in general.

Keywords: DNA hydroxymethylation, SRA domain, 5hmC recognition