Poster Presentation

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Distinct DNA-binding feature of the peroxide response regulator from group A streptococcus

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Group A streptococcus (GAS) is a significant human pathogen, renowned for its rapidly and highly desctructive ability to infect a wide variety of tissues. Clinical manifestation of GAS infection ranges from mild pharyngitis to severe life-threating disease such as necrotizing fasciitis. Unlike other gram-positive bacteria, GAS does not produce catalase, but has an ability to resist killing by reactive oxygen species through unknown novel mechanisms. Our previous studies have discovered that the peroxide response regulator (PerR) is crucial for GAS to cope with oxidative stress and it directly regulates the expression of an iron-binding protein Dpr [1,2]. PerR is a member of Fur (ferric uptake regulator) family which is known to be dimeric, metal-binding regulators. Currently, no structural information is available to understand how the similar structures of the Fur family regulators recognize divergent DNA sequences. To study how PerR interacts with dpr promoter DNA, we have conducted a series of mutagenesis, biochemical and structural studies by combining protein crystallography and small-angle X-ray scattering (SAXS). We have determined the PerR crystal structure to 1.6 Å resolution and identified the DNA-binding residues, which suggest PerR binds to the dpr promoter through a winged-helix motif. By performing SAXS studies, we confirmed that the PerR crystal structure reflects its conformation in solution. Furthermore, SAXS analysis allowed us to resolve the molecular architecture of PerR-DNA complex, in which two 30 bp DNA fragments wrap around two PerR homodimers by interacting with the adjacent positively-charged winged-helix motifs. Our results have revealed the PerR-DNA interaction model and illustrated the DNA-binding mode of PerR that is distinct from all other regulators in Fur family [3].

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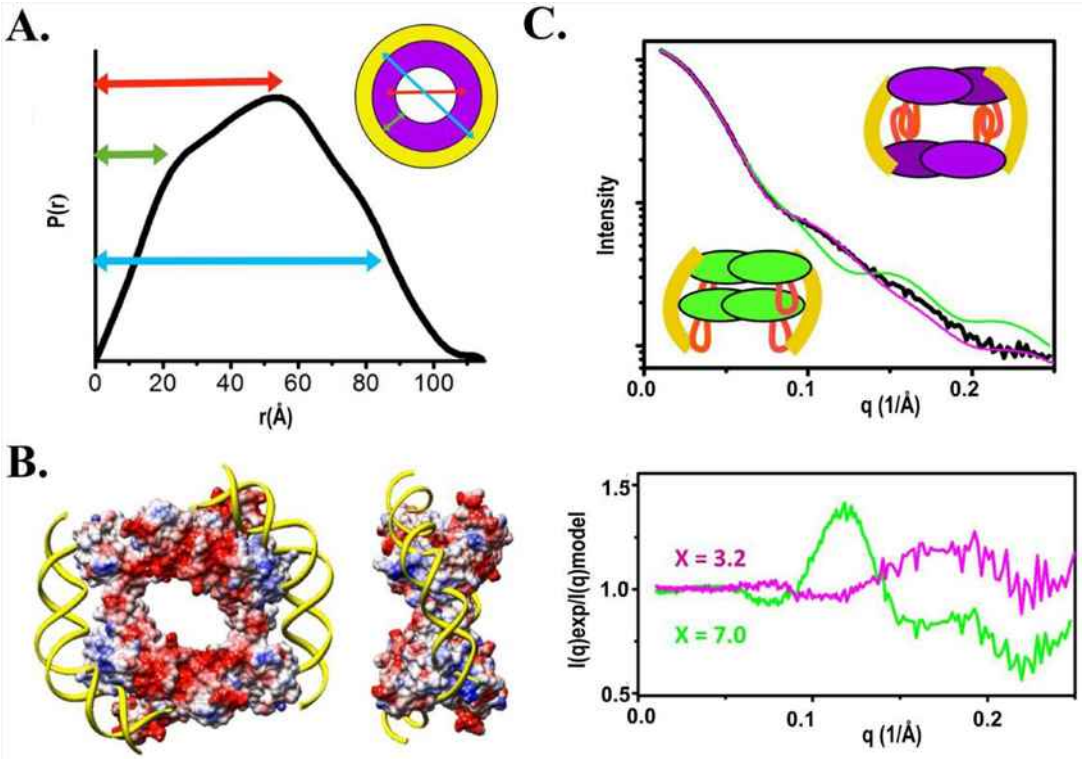

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