# Structural Studies of the Stress Response Regulator PerR from *Streptococcus pyogenes* by Small-angle X-ray Scattering

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The objective of this project is to understand the molecular mechanism by which PerR regulates the expression of Dpr, a stress response protein, for *Streptococcus pyogenes* to survive in an aerobic environment and to maintain its pathogenicity. *S. pyogenes* is a Gram-positive human pathogen that causes life-threatening diseases such as necrotizing fasciitis and toxic shock syndrome. *S. pyogenes* does not produce catalase, an oxidoreductase that, in other Gram-positive bacterial species, repairs damage to the bacteria when grown in an aerobic environment. Instead, *S. pyogenes* depends upon an iron-binding protein, Dpr, to confer the resistance to multiple stresses. The expression of Dpr is induced when the concentrations of iron, zinc, nickel, and hydrogen peroxide increase.

PerR binds to the promoter region of *dpr*, thereby negatively regulates Dpr expression. Increased concentrations of iron and hydrogen peroxide decrease PerR binding to promoter DNA. This observation suggests that the regulation of Dpr by environmental signals is mediated by PerR directly. It was proposed that PerR may undergo conformational change upon the binding of iron or others stress signals and that this conformational change leads to the loss of its DNA-binding ability, therefore released from *dpr* promoter. To test this hypothesis, we combined the techniques of both protein crystallography and small-angle X-ray scattering for studying the structural conformations of PerR.

To delineate the conformational change of PerR protein in solution, we intend to obtain the low-resolution structures of both active and inactive PerR protein in solution by small-angle X-ray scattering (SAXS). We prepared the iron-free PerR protein, PerR-DNA complex as well the PerR protein treated with 80 mM hydrogen peroxide for SAXS studies. Because of the difficulty in obtaining the soluble iron-bound PerR protein, we treated PerR with hydrogen peroxide and demonstrated that this treatment also abolished the PerR DNA-binding ability. The SAXS data collection was carried out at beamline 23A1 with various concentrations of each sample ranged ~1-5 mg/ml and each exposed for 30 s, 100 s, and 300 s, respectively. The representative scattering curves are shown in Fig. 1. The analysis of the data is in progress now.

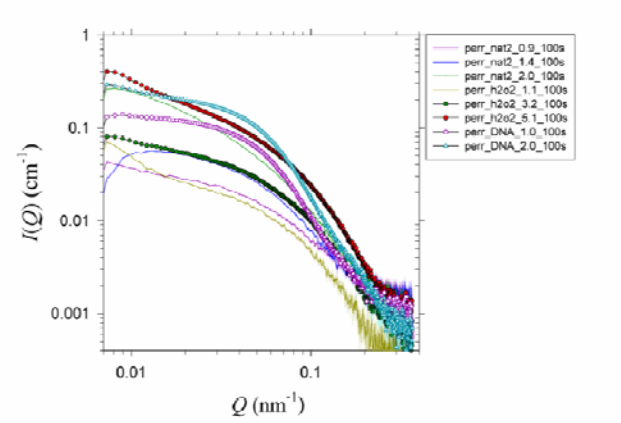


**Fig. 1:** SAXS scattering curves of PerR, PerR treated with hydrogen peroxide and PerR-DNA complex.