Structural Studies on Novel Streptococcal Virulence Factors

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Streptococcus pyogenes (*S. pyogenes*) is responsible for a variety of illnesses ranging from mild sore throat to life-threatening toxic shock syndrome. The strain most strongly associated with highly invasive infections is *S. pyogenes* M protein serotype 1 (M1).

We have identified a number of putative genes from the *S. pyogenes* M1 genome which possess various sequence motifs that are often present in bacterial toxins. Three of the proteins encoded by these genes have been expressed, purified and crystallized with the aim of determining their structures by X-ray crystallography.

The protein encoded by gene *spy1492*, Spy1492, contains the GDSL-like lipase motif which is commonly found in lipolytic enzymes including some bacterial toxins such as hemolysin. Its lipolytic activity was detected in biochemical assays. Multiwavelength anomalous diffraction (MAD) data to 3.0 Å resolution have been collected from crystals of the SeMet-substituted protein and are being used for the structure determination.

We have also purified and crystallized a sortase protein, encoded by the gene *spy0129*, together with its putative substrate surface protein, Spy0128. Sortases are responsible for the covalent attachment of specific proteins to the Gram-positive bacterial cell wall. Spy0128 contains a sortase-mediated cell wall anchoring motif specific for the sortase Spy0129. We present progress in the molecular structure determination of Spy0129 and its substrate protein Spy0128.

Keywords: bacterial toxins, x-ray crystallography, structure of proteins