

## MS08-P07 | CRYSTAL STRUCTURES OF STREPTOCOCCUS PYOGENES CAS1 AND CAS2 IN THE TYPE II-A CRISPR-CAS SYSTEM

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Clustered regularly interspaced short palindromic repeats (CRISPRs) and CRISPR-associated (Cas) proteins constitute a microbial adaptive immune system against invading mobile genetic elements such as bacteriophages and plasmids. CRISPR acts as a genetic memory that has an array of invariable 'repeat' sequences interspaced with variable 'spacer' sequences. CRISPR adaptation is achieved by integrating short fragments of the invading foreign nucleic acids into CRISPR array as new 'spacer' sequences. Cas1 and Cas2 are conserved in almost all CRISPR types and form the 'spacer' integrase complex in the CRISPR adaptation process. Here, we report the crystal structures of *Streptococcus pyogenes* Cas1 and Cas2 proteins in the type II-A CRISPR-Cas system. Cas1 reveals a unique structural features distinct from type I Cas1 homologues, including extensive dimerization interface, globular overall structure, and disrupted metal-binding sites for catalysis. Cas2 displays a significant structural difference from *Enterococcus faecalis* Cas2 of the same CRISPR type, suggesting conformational variability in the type II-A Cas2 homologues. We also characterized interactions of Cas1 and Cas2. A single Cas2 dimer interacts with two Cas1 dimers through its C-terminal tails to form a heterohexameric complex. The Cas1-Cas2 complex and Csn2 comprise a larger type II-A CRISPR adaptation module. Furthermore, we demonstrated that the Cas1-Cas2 integrase complex interacts with Cas9 via Csn2. Our results provide structural information for *S. pyogenes* Cas proteins and lay a foundation for a network of molecular interactions among type II-A Cas components involved in the adaptation and interference stages of CRISPR-mediated immunity.