

MS05-P115 LATE | STRUCTURAL STUDIES OF THE ATYPICAL SLAMF3 RECEPTOR

Shaikh, Ra'eelah (University of Leicester, Leicester, GBR); Burschowsky, Daniel (University of Leicester, Leicester, GBR)

The signalling lymphocyte activation module family (SLAMF) of type I transmembrane receptors has nine members, expressed broadly on hematopoietic cells. SLAMF3 is also expressed on hepatocytes. Generally, SLAMF receptors have two extracellular Ig-like domains, except for SLAMF3, which has four (D1 to D4). All SLAMF receptors, apart from SLAMF2, homodimerise via their extracellular N-terminal IgV-like domain (D1). On their cytoplasmic region, most SLAMF receptors have multiple immunoreceptor tyrosine-based switch motifs (ITSMs), which act as ligands for the adaptor proteins SAP and EAT-2. SLAMF3 is implicated in systemic lupus erythematosus (SLE), multiple myeloma (MM), hepatocellular carcinoma (HCC) and enhancing hepatitis C virus infection.

Here we present the high-resolution crystal structure of SLAMF3 D1. Similar to other known SLAMF N-terminal IgV-like domains, it comprises a two-layered β -sheet, however it appears to associate more strongly than any previously characterised SLAMF dimers. The interface contains 20 hydrogen bonds and 8 salt bridges, surrounding a hydrophobic patch, compared to the 9 hydrogen bonds and single salt bridge in the SLAMF6 interface and the 17 hydrogen bonds and zero salt bridges in the SLAMF5 interface. The c'' loop of SLAMF3 D1 is truncated. SLAMF3 D2-3 has an atypical distribution of cysteines, which raises the possibility of an interdomain disulphide bond. We have expressed, refolded, crystallised and collected diffraction data of SLAMF3 D2-3, however we have so far been unable to solve the structure by molecular replacement or by sulphur SAD. We suggest that these domains have diverged since the gene duplication event that created them.