MS7-P6 Structural analysis of human polo-like kinase 1 polo box domain in complex with peptide inhibitors

Hye-Yeon Kim[1], Woo Cheol Lee[2], Ravichandran N Murugan[1], Mija Ahn[1], Jeong Kyu Bang[1]

1. Protein Structure Group, Korea Basic Science Institute, Ochang, Chungbuk 28119, South Korea
2. Department of Bio-Analytical Science, University of Science and Technology, Daejeon 34133, South Korea.

email: hyeyeon@kbsi.re.kr

Human polo-like kinase 1 (Plk1) is a serine/threonine-protein kinase 13(STPK13), which is overexpressed in human tumor cells. Plk1 consists of N-terminal kinase domain and C-terminal two polo-box domains. Polo-box domain (PBD) interacts with phosphoserine/phosphothreonine (pS/pT)-containing motif and is critical for tumorigenesis. Based on the crystal structure of hPlk1-PBD and PLHSpT, we designed a series of PLHSpT-derived peptide analogues to improve the binding affinity. To examine the interaction mode between hPlk1-PBD and peptide inhibitors in detail, hPlk-PBD protein was purified and crystallized with peptide analogues. Here, we report the crystal structures of hPlk1-PBD in complex with several peptide inhibitors.

Keywords: polo-like kinase 1

MS7-P7 Structural studies of the virulence factor peptidoglycan-associated lipoprotein from a Gram-negative pathogen

Eun-Hee Kim[1], Kwon Joo Yeo[1], Woo Cheol Lee[1], Eunha Hwang[1], Saeyoung Lee[2], In-Geol Choi[2], Hye-Yeon Kim[1,3]

1. Protein Structure Group, Korea Basic Science Institute, Ochang, Chungbuk 28119, South Korea
2. College of Life Sciences and Biotechnology, Korea University, Seoul 02841, South Korea
3. Department of Bio-Analytical Science, University of Science and Technology, Daejeon 34133, South Korea

email: keh@kbsi.re.kr

Acinetobacter baumannii is a multi-drug resistant Gram-negative pathogen that causes hospital-acquired infection of immunocompromised patients. Peptidoglycan-associated lipoprotein (Pal) of Gram-negative bacteria is one component of the Tol-Pal system, which plays an important role in the integrity of the outer membrane and it is found in the outer membrane vesicle used to deliver virulence effectors into host cells. *A. baumannii* Pal (AbPal) is composed of an N-terminal motif that is required for delivery and anchoring to the outer membrane and a C-terminal OmpA-like domain. OmpA-like domains interact noncovalently with peptidoglycan via a unique bacterial amino acid, *meso*-diaminopimelic acid (*meso*-DAP).

Incorporation of a D-amino acid moiety in the peptidoglycan structure has been suspected to be a method which bacteria can evade the host immune system. Specific binding to D-amino acid by this domain is of particular interest in terms of pathogenicity{Walsh, 1989 #31}{Walsh, 1989 #31}. However, the enantiomeric specificity of OmpA-like domains for the interaction with peptidoglycan has not been studied.

Here, we report molecular basis for the interaction with *meso*-DAP of peptidoglycan by OmpA-like domain of AbPal using X-ray crystallography, NMR spectroscopy, isothermal titration calorimetry (ITC), and site-directed mutagenesis. We performed the NMR backbone assignment of AbPal and firstly solved the crystal structure of AbPal in complex with *meso*-DAP or *LL*-DAP to evaluate a key determinant region for the stereospecific interaction with peptidoglycan. Our findings provide a foundation for the development of antibacterial agents that disrupt stability of cell wall of Gram-negative pathogen.

Keywords: peptidoglycan-associated lipoprotein, X-ray crystallography, NMR spectroscopy, ITC