EuroSciCon

EuroSciCon conference on

Protein, Proteomics and Computational Biology

December 06-07, 2018
Amsterdam, Netherlands

Abhishek Basu et al., Biochem Mol biol J Volume:4
DOI: 10.21767/2471-8084-C5-020

DECIPHERING THE STRUCTURAL BASIS OF TRANSLOCATOR-CHAPERONE INTERACTION OF TYPE III SECRETION SYSTEM-A KEY TO DRUG DESIGN AGAINST PATHOGENIC *YERSINIA ENTEROCOLITICA*

Abhishek Basu[1], Debjani Mandal[1], Manali Biswas[1], Indranil Saha[2] and Shamsuzzaman Ahmed[2]

[1]Department of Molecular Biology and Biotechnology, Sripat Singh College, University of Kalyani, India
[2]Department of Chemistry, Sripat Singh College, University of Kalyani, India

Yersinia enterocolitica is an opportunistic pathogen which causes enteric diseases like gastroenteritis and mesenteric adenitis in immune-compromised individuals. The gastrointestinal phase of *Y. enterocolitica* infection is mediated by *Yersinia* secretion apparatus - *Yersinia* secretion protein (Ysa-Ysp) Type III Secretion System (T3SS). Enhanced virulence of *Y. enterocolitica* Biovar 1B is attributed to the activation of Ysa-Ysp T3SS, which is further regulated by the formation of functional injectisome. YspB and YspC are hydrophobic translocator proteins which are responsible for the formation of functional translocon at the tip of the needle complex. These translocators are sequestered in the bacterial cytoplasm by their cognate chaperone SycB. SycB plays the dual role of a class II chaperone and a regulator of Ysa-Ysp T3SS. Homology model of SycB depicts a structure with a concave core formed by tetratricopeptide repeats (TPRs) and a flexible N-terminal helix. Deletion mutants of SycB showed that the N-terminal helix of SycB is responsible for its dimerization, which is further corroborated by molecular docking analysis. The dimeric state of SycB dissociates during the interaction with YspC due to steric hindrance. It forms a 1:1 heterodimeric YspC-SycB complex as confirmed by size-exclusion chromatography, chemical cross-linking and molecular docking studies. FRET analysis indicated that the tyrosine residues present in first two TPRs of SycB is responsible for its interaction with YspC. Deletion mutants of SycB possessing the first two TPR regions interacted with YspC, as depicted by the YspC-SycB interaction model. YspC is a unique minor translocator protein having monomeric form with high stability and rigid tertiary structure unlike any other translocator proteins. It shows structural alteration in the complex form with SycB as shown by spectroscopic data and proteolytic digestion. YspC has a Y-shaped three dimensional structure and SycB completely localizes within the fork formed by the two arms of Y-shaped YspC. Like other major translocator proteins YspB possesses a highly helical structure and transmembrane helices required for its translocation through the narrow conduit of the needle and its insertion within the host cell plasma membrane. Being a translocator protein it has to interact with chaperones and other translocators, which is evident from the existence of intramolecular coiled-coil regions in YspB structure. The YspB model depicted a star-shaped structure with alpha helices interspersed by random coil regions. The inner concave core of SycB forms the interface of interaction with YspB. This interaction is polar or ionic in nature and mediated by the first two TPRs of SycB. Therefore, simultaneous binding of YspB and YspC to SycB is not possible due to the common interaction domains. ConSurf analysis predicted that the evolutionarily conserved residues are mostly present in the regions of YspB involved in interaction with SycB. Exposure of translocator proteins to the extra-cellular milieu makes them potential drug targets. Therefore, elucidation of the three dimensional structure of translocators would enable us to determine precise antigenic epitopes for drug targeting. Structural analysis and understanding the mechanism of interaction between translocators and chaperones would be beneficial in designing peptide drugs to deregulate the Ysa-Ysp T3SS and attenuate the virulence of *Yersinia enterocolitica*.

EuroSciCon

December 06-07, 2018
Amsterdam, Netherlands

EuroSciCon conference on

Protein, Proteomics and Computational Biology

Abhishek Basu et al., Biochem Mol biol J Volume:4
DOI: 10.21767/2471-8084-C5-020

Biography

Abhishek Basu completed his PhD at the age of 29 years from the Structural Biology and Bioinformatics division of CSIR-Indian Institute of Chemical Biology. He was the recipient of prestigious CSIR-NET Fellowship during the course of his research. He also qualified GATE with 99.8 percentile. At present, Dr. Basu is working as the Head of Molecular Biology and Biotechnology department in SS College, under University of Kalyani. He is continuing his research in the DBT-BOOST sponsored laboratory of the same department. Dr. Basu has published 16 research articles in reputed international journals and he is the author of two book chapters. Besides having a master degree in Biophysics and Molecular Biology and a PhD in Biochemistry, Dr. Basu also possesses an MBA degree in Financial Management.

abasu4@rediffmail.com