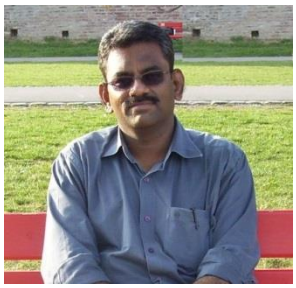
Listeria Monocytogenes High Temperature Requirement A (HtrA) Protease and Its Interaction with Extracellular Matrix Molecules



Karthe Ponnuraj

Centre of Advanced Study in Crystallography and Biophysics, University of Madras, Guindy Campus, Chennai 600025, India
Email: pkarthe@hotmail.com; karthe@unom.ac.in

Abstract

High temperature requirement A (HtrA) is a widely expressed serine protease and chaperone in bacteria. It was also identified as a secreted virulence factor in many pathogenic bacteria, including *Listeria monocytogenes*. Recently, it was discovered that *Helicobacter pylori* and *Campylobacter jejuni* HtrAs can directly cleave the human cell-adhesion molecule E-cadherin, which facilitates bacterial transmigration. HtrAs also interact with extracellular matrix (ECM) molecules; however, only a limited number of studies have been conducted in this regard. In the present study, the protease and ECM binding properties of HtrA from *L. monocytogenes* (*Lm*HtrA) were studied using native *Lm*HtrA, catalytically inactive *Lm*HtrA (S343A), and *Lm*HtrA lacking the PDZ domain (ΔPDZ) to gain insights into HtrA–ECM molecule interaction. Different ECM molecules, such as fibronectin, fibronectin fragment, fibrinogen, plasminogen, laminin, mucin, and collagen were used to study the binding affinity of *Lm*HtrA. The results show that (1) cleavage of fibrinogen, fibronectin, plasminogen, and casein by native *Lm*HtrA is in a time and temperature dependent manner, (2) interaction of *Lm*HtrA with various host proteins was found in the micromolar to the nanomolar range, (3) when compared with native *Lm*HtrA, no drastic reduction in the binding affinity toward the host molecules in the absence of the PDZ domain and (4) the PDZ domain plays a significant role in the substrate cleavage as native *Lm*HtrA cleaves all tested substrates whereas *Lm*HtrA$_{1\text{-}394}$ΔPDZ cleaves only certain substrates. The proteolysis of various ECM molecules by *Lm*HtrA possibly highlights the role of HtrA in *L. monocytogenes* pathogenesis involving ECM degradation. Hence, the findings of this study provide valuable new insights into the function of *L. monocytogenes* HtrA.