Editorial: Proteases of the prokaryotic cell envelope

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Editorial on the Research Topic

Proteases of the prokaryotic cell envelope

Proteolysis plays a fundamental role in cell physiology and is exerted by enzymes (proteases or peptidases) that cleave or degrade protein or peptide substrates. Proteases localized in the context on the prokaryotic cell envelope are implicated in cell signaling, regulation of gene expression, protein quality control, protein export and membrane anchoring, biogenesis/remodeling of the cell wall and surface structures, antibiotic resistance mechanisms among other key cellular processes. These membrane proteases belong to various protease families, show different catalytic mechanism, and can have their active site at/outside the membrane surface in an aqueous environment (cytoplasm, periplasm, extracellular medium) or embedded within the lipid bilayer (Wolfe, 2009; Dalbey et al., 2012). The first group includes signal peptidases (SP), site-1-proteases (S1P), HtpX and AAA+ proteases FtsH and the archaeal type-LonB. The second group, denoted as Intramembrane Cleaving Proteases (ICliPs or IMPs) is represented by the rhomboid family, site-2 proteases (S2P), GxGD-aspartyl proteases (presenilin and eukaryal signal peptide peptidase SPP), and Rce1-type glutamyl proteases (Sun et al., 2016).

The goal of this Research Topic was to advance knowledge and stimulate/promote discussion on different aspects of the biology of the proteolytic systems that occur in the context of the cell envelope of prokaryotes.

Compared to other proteases, there is a much bigger gap in research for those that occur in the prokaryotic cell envelope. First, while many of the membrane protease families are conserved in the three domains of life (e.g., the Rhomboid family) they have been studied mainly in eukaryotes and to a more limited extent in prokaryotes. Second, our current knowledge on the archaeal protease biology (function, targets) is comparatively much limited. Obvious open questions are how these proteases recognize substrates and whether this involves mechanisms/motifs unique to prokaryotes. Concerning protease function and targets, there is a dire need for more studies covering a broad range of prokaryotes to adequately inform about range as well as conservation of targets and functions, in particular those important for biomedicine and biotechnology.
The original research articles and mini-review in this Issue describe work that address current research gap by extending our understanding of the substrate recognition mechanisms, diversity, and biological function of proteases localized in the cell envelope of various prokaryotic organism. These articles exemplify how modern analytical tools such as proteomics have facilitated the identification of potential targets and contribute to unraveling the biological function of membrane proteases in bacteria and in some archaea.

Site-2- Proteases (S2P) participate in Regulated Intramembrane Proteolysis (RIP) in various organisms. In E. coli, S2P protease RseP regulates an extracytoplasmic stress response through a mechanism that involves the sequential cleavage of the membrane-spanning anti-σ factor (anti-σF) RseA first by the SIP protease DegS, which cleaves RseA periplasmic domain, and then by RseP, allowing the release of σF and subsequent gene activation. The periplasmic PDZ domains of RseP act as a filter to exclude the intact substrate RseA from the active site of RseP. In his work, Miyake et al. provide insights on the substrate recognition mechanism of RseP protease. They showed that an amphiphilic segment of RseP downstream the PDZ domains and located in the periplasmic surface of the membrane (helix H1), directly interacts with the DegP-cleaved form of RseA, facilitating its discrimination by the PDZ-domains of RseP. The authors propose that H1 is important for the proteolytic function of RseP as it relates to the PDZ-mediated discrimination of its substrate and contributes to its proper positioning and cleavage.

The cell wall is critical for bacterial survival. Its main component is the peptidoglycan, a highly cross-linked heteropolymeter of glycans and short peptide chains. This structure is modified/remodeled by the action of peptidoglycan hydrolases, which are very diverse in specificity and structure. Autolysins are implicated in cell wall metabolism during bacterial growth, division and elongation while bacteriocins provide insights on the substrate recognition mechanisms, diversity, and biological function of proteases localized in the cell envelope of various prokaryotic organism. These articles exemplify how modern analytical tools such as proteomics have facilitated the identification of potential targets and contribute to unraveling the biological function of membrane proteases in bacteria and in some archaea.

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Author contributions

RD and AP have both contributed to the Editorial and approved the submitted version.

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