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Structural, Biochemical and Functional characterization of Salmonella BcfH: an unusual Dsb-like fimbrial protein

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Bacteria use folding enzymes to produce functional virulence factors. These foldases include the Dsb family of proteins, which catalyze a key step in the protein-folding pathway, the introduction of disulfide bonds. The Dsb oxidative system, which includes an oxidative DsbA/DsbB pathway and an isomerase DsbC/DsbD pathway, is present in numerous bacterial species. Conventionally, Dsb proteins have specific redox functions with monomeric and dimeric Dsbs exclusively catalyzing thiol oxidation and disulfide isomerization, respectively. This contrasts with the eukaryotic disulfide forming machinery where the modular thioredoxin protein PDI mediates thiol oxidation and disulfide reshuffling. In this study, we identified and structurally and biochemically characterized a novel Dsb-like protein from Salmonella enterica termed BcfH and defined its role in virulence. Encoded by a highly conserved bcf (bovine colonization factor) fimbrial operon, the Dsb-like enzyme BcfH forms a trimeric structure, exceptionally uncommon among the large and evolutionary conserved thioredoxin superfamily. BcfH also displays very unusual catalytic redox centers, including an unwound α-helix holding the redox active site and a trans proline instead of the conserved cis proline active site loop. Remarkably, BcfH displays both thiol oxidase and disulfide isomerase activities contributing to Salmonella fimbrial biogenesis. Typically, oligomerization of bacterial Dsb proteins modulates their redox function, with monomeric and dimeric Dsbs mediating thiol oxidation and disulfide isomerization, respectively. The present study demonstrates a further structural and functional malleability in the thioredoxin-fold protein family. BcfH trimeric architecture and unconventional catalytic sites permit multiple redox functions emulating in bacteria the eukaryotic protein disulfide isomerase dual oxido-reductase activity.

Level of Expertise

Early Career <5 Years

Presenter Gender

Man

Pronouns

He/Him

Which facility did you use for your research

Australian Synchrotron

Students Only - Are you interested in AINSE student funding

Do you wish to take part in the Student Poster Slam

Condition of submission

Yes

Primary author(s) : SUBEDI, Pramod (La Trobe University); PAXMAN, Jason (La Trobe University); Dr WANG, Geqing (La Trobe University); HOR, Lilian (La Trobe University); Dr HONG, Yaoqin (2Centre for Immunology and Infection Control, School of Biomedical Sciences, Queensland University of Technology); Dr D. VERDEROSA, Anthony (Anthony); WHITTEN, Andrew (ANSTO); PANJIKAR, Santosh (Australian Synchrotron); Mr F. SANTOS-MARTIN, Carlos (La Trobe University); MARTIN, Jennifer (University of Queensland); Dr TOTSIKA, Makrina; HERAS, Begoña (LA Trobe University)

Presenter(s) : SUBEDI, Pramod (La Trobe University)

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