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Enteric pathogen-host interactions: A proteomic perspective

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The interactions of *Shiga toxin producing Escherichia coli (STEC)* and *Shigella dysenteriae* serotype 1 (SD1) with the intestinal host environment were examined in a gnotobiotic piglet model using proteomic analysis techniques. Both pathogens cause severe diarrhea in humans and occasionally serious systemic disease including hemolytic uremic syndrome which can be fatal. The gnotobiotic piglet model is the most human-like non-primate model to study the pathogenesis of both pathogens. Proteomic analyses for each of the bacteria isolated from the gut of infected animals revealed extensive proteomic adaptations. It was evident that these adaptations were required for both Gram-negative bacterial species to survive in the enteric environment. Major changes were the induction of anaerobic energy metabolism pathways, acid resistance systems, transport and metabolic systems to increase bioavailability of lactose, phosphate, ammonia and NADPH and stress responses to detoxify reactive nitrogen species. SD1 expressed a more diverse arsenal of type III secretion system effectors, apparently to boost the survival within epithelial and/or phagocytic cells. Both pathogens modulated their cell surfaces, likely responding to the infiltration of innate and adaptive immunity associated cells at the site of infection. Such changes included outer membrane proteins and biosynthetic machineries for lipopolysaccharides. There was also evidence for the expression and secretion of antimicrobial proteins into the intestinal lumen in response to colonization with STEC and SD1, such as the islet regenerating factor REG-3γ.

Biography

Rembert Pieper is an Associate Professor at the J. Craig Venter Institute in Rockville, Maryland. His laboratory conducts research in analytical biochemistry with a technology emphasis on proteomics and a pathobiology emphasis on host-pathogen interactions and the discovery of disease biomarkers. Dr. Pieper and his research group are currently involved in several projects integrating proteomics into multi-disciplinary system biology. Investigations integrating sequencing-based microbiome analysis with metaproteomics are ongoing activities. He obtained his Ph.D. degree from the Institute of Applied Chemistry, Technical University of Berlin, Germany (1989-1993). He conducted post-doctoral research in the Department of Chemical Engineering, Stanford University (1994-1996), and the National Cancer Institute (1997-1998). He was a Staff Scientist and Director for Protein Chemistry at Large Scale Biology Corporation (1999-2003), with an emphasis on protein biomarker discovery for non-communicable diseases. He has co-authored 13 patent applications (8 issued patents) and 42 original research or review articles.

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