

Prof. Benjamin Aroeti

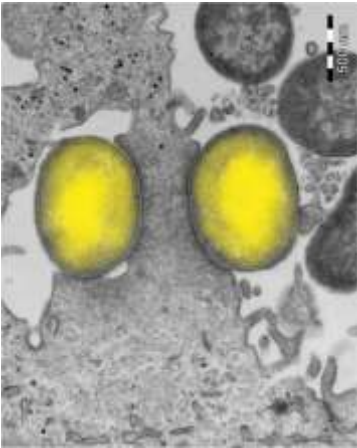
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Research theme: The study of the molecular mechanisms by which enteric bacterial pathogens assault epithelial cells and how the host cells defend themselves



Our research group is focused on studying the molecular mechanisms underlying host-pathogen interactions, with special emphasis on how enteric bacterial pathogens elicit epithelial host cell infection.

Since its discovery in 1945, enteropathogenic *E. coli* (EPEC) has been viewed as an important human pathogen. The microbe, which is considered to adopt an extracellular life style, colonizes the epithelium of the small intestine, and causes acute children's diarrhea and gastroenteritis. One most prominent feature of EPEC infection is the induction of localized attachment and effacement (A/E) lesions in the epithelial brush border and the formation of actin-rich pedestal-like structures at bacterial host contact sites (see image; bacteria are artificially stained in yellow). Another well characterized hallmark of EPEC infection is the perturbation of the tight-junctions barrier functions. EPEC, and its close relatives, enterohemorrhagic *E. coli* (EHEC) and *citrobacter rodentium*, subvert numerous host cell signaling pathways, cytoskeletal elements and membranous organelles through injecting via the type III secretion system ~ 21 protein effectors from the bacterial cytoplasm into the host. The mechanisms by which these protein effectors hijack the host has been studied rigorously. However, their mechanism of action is still not well understood. A major challenge in our lab is to study these mechanisms. Upon contacting the host cell surface, EPEC generates a specialized plasma membrane domain, through which it manipulates host signaling and other processes. Another aim of our studies is explore how EPEC constructs this domain and what is its function in pathogenesis. Epithelial cells are highly polarized cells. EPEC infection seems to cause epithelial depolarization and the breakdown of epithelial barrier functions. How EPEC manipulates polarized membrane traffic machineries to break cell asymmetry (polarity), and how this contributes to EPEC pathogenesis is of major interest to our lab.

We use a variety of methodologies to address these research questions, ranging from classic biochemical and imaging techniques, to advanced proteomics and bioimaging analyses. Our research also integrates basic with translational science to study in-depth the molecular basis of the EPEC-epithelial host cell interface and how this leads to a disease state. We think that only through such an interdisciplinary and integrative approach one can achieve a better understanding of the basic principles underlying host cell biology. Our philosophy foresees pathogens as the best cell biologists in the planet. They have co-evolved with their hosts over billions of years, and therefore have optimally adapted themselves to their hosts. Therefore, they can be elegantly harnessed to help us gain better insights into the basic principles underlying the host cellular organization and functions in health and disease states. We hope that studying cell biology through microbial pathogens will lead us to develop better therapeutic platforms to combat severe diseases of the human intestines, such as diarrheal diseases. Finally, bacterial infections have been associated with inflammatory bowel diseases (IBDs), such as the Crohn's disease. Hence, our studies on *E. coli* infections may lead to better understanding of IBDs, as well as define a potentially broadly applicable context for designing novel interventions to block these devastating human diseases.