ABSTRACT

The human gastro-intestinal (GI) tract is colonized by approximately 1014 bacterial cells that belong to about 400 different species and co-exist with host cells. However, introduction of pathogens such as enterohemorrhagic E. coli (EHEC) disturbs this homeostasis and rapidly leads to colonization and infection. A characteristic feature of the GI tract is the abundance of signaling molecules, both of prokaryotic and eukaryotic origin, present in the lumen. Both pathogenic and non pathogenic bacteria secrete various quorum sensing and metabolic signals such as AI-2, AI-3, and indole. Similarly, host hormones like norepinephrine and dopamine are also synthesized in the GI tract by the enteric nervous system. The close proximity of bacteria and the host cells, as well as the abundance of the signals they secrete, has led to a new signal-centric paradigm where the different GI tract signals are considered to be important mediators of homeostasis and infections through intra-kingdom (i.e., recognition of bacterial signals by other bacteria) and/or inter-kingdom (i.e., recognition of host signals by bacteria and vice-versa) signaling and communication.

Our central hypothesis is that inter-kingdom signaling between bacteria and host cells, as well as intra-kingdom signaling between different bacterial species, are key determinants of pathogen colonization of the GI tract. Using EHEC as the model pathogen, we are investigating the role of signaling interactions in three distinct stages of infection in the GI tract: (1) initial sensing and migration of EHEC towards epithelial cell surfaces, (2) spatial organization and localization of EHEC during colonization, and (3) interaction with host cell inflammatory signaling. In this talk, I will discuss some of our recent results on elucidating the role of signals in bacterial chemotaxis and on recognition of bacterial signals by host cells. Our results provide the basis of an inter-kingdom signaling framework and illustrate the potential for using inter-kingdom signaling to develop synthetic signaling systems.