Keynote Lecture X

Interaction of *Salmonella* with its Mammalian Host Cell

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The bacterial pathogen *Salmonella enterica* has evolved a very complex functional interphase with its host, the product of the work of co-evolutionary forces operating over millions of years. Central to this interface is the work of a specialized bacterial organelle, the type III secretion system, which delivers a battery of bacterial proteins into the host cell. These proteins have the capacity to modulate a variety of cellular processes ranging from actin cytoskeleton rearrangements and nuclear responses to macropinocytosis and programmed cell death. A theme emerging from structural and functional studies of the *Salmonella*/host interactions is one of mimicry as a strategy to modulate cellular functions. These bacteria utilize proteins that faithfully mimic, structurally and functionally, the activities of host cell protein to modulate a variety of responses. Two bacterial proteins, SopE and SopE2, work as exchange factors for the Rho-family GTPases, Cdc42 and Rac. Remarkably, although through different chemistry, the conformational changes induced by these bacterial proteins in the host GTPases, which result in nucleotide exchange, are virtually identical to those induced by Dbl-like GEFs. In a remarkable Ying and Yang, another bacterial protein, SptP, mimics host GTPase-activating proteins (GAPs) to reverse the bacterial-induced activation of Cdc42 and Rac. In this case, the *Salmonella* protein uses the same chemistry as host GAPs (i.e. insertion of a key arginine) but utilizing different structural context. These and other examples will be discussed to illustrate the power of mimicry as a central strategy to modulate cellular functions by microbial pathogens.

Selected References

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