

Preface

Type I interferon (IFN) signaling has long been recognized as a critical component of innate immune defense to viral pathogens. It is now established that bacteria too are able to activate this pathway. Typically bacteria activate type I IFN signaling through TLR-dependent mechanisms, through recognition of LPS in Gram negative organisms or via TLRs and cytosolic receptors that respond to nucleic acids and messaging molecules that are either endocytosed or secreted directly into the eukaryotic cells. The consequences of type I IFN signaling on host outcome can be either protective or damaging, depending on the organism.

The signaling behind the type I interferons is a rapidly progressing field. Initial activation of type I IFNs was limited to the innate receptors that had been identified such as LPS via TLR4 or nucleic acids through TLR3 and TLR9. Recent work has uncovered several cytosolic receptors that are able to recognize different microbial products, such as nucleic acids, cell wall components, and signaling molecules. In many cases these different receptors ultimately converge on shared adapter proteins, kinases, or transcription factors that lead to the production of type I IFNs. The activation of type I IFNs through their cognate receptors and JAK/STAT signaling leads to the production of hundreds of gene products that are likely unique to each pathogen.

The activation of type I IFNs differs between each microbial pathogen and also within some species. In many cases activation of the pathway is a passive process, whereby cell wall components such as LPS or peptidoglycan are exposed to receptors or nucleic acids are sensed during cellular destruction. Bacteria also activate type I IFNs by actively assaulting host cells. In these instances toxins or bacterial secretion machinery is designed to lyse or inject effector proteins that alter host machinery allowing microbial patterns to be sensed.

The consequence of this activation also varies by organism. In *Legionella pneumophila* type I IFNs play a positive role, restricting replication of bacteria inside macrophages. This is also the case for some *Chlamydia* species; however, in vivo results have shown the opposite result with reduced bacterial burden in mice unable to respond to type I IFNs. Type I IFNs are detrimental in the context of chronic *M. tuberculosis* infection, while type I IFNs appear to play a negative role in response

to several bacteria including streptococci, *Salmonella*, and *Staphylococcus aureus*. In the case of *S. aureus*, different strains signal the production of type I IFNs through different receptors. The activation of similar and divergent pathways within the same species as well as other different species of bacteria makes for interesting comparisons. This book provides an overview of how type I IFNs are activated and the role they play in several important bacterial pathogens, highlighting how the immune response can influence the outcome to infection.

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