Pertussis remains an important disease with annual worldwide estimates conservatively approaching 16 million cases and 200,000 deaths. Although most cases of pertussis are prevented by vaccination, neither vaccination, nor natural infection generates life-long immunity. Furthermore, it has recently been discovered that the duration of immunity derived from vaccination with the acellular pertussis vaccines (introduced ~15 years ago) is much shorter than expected, creating a looming public health concern and underscoring the need for new vaccines or approaches. Surprisingly, there are many gaps in our knowledge regarding B. pertussis pathogenesis and the mechanisms that limit the generation of long-term immunity.

Our research focuses on the ability of B. pertussis to dampen the effects of the complement system and to modify the lipid A portion of its lipopolysaccharide to modulate immune responses. We are currently dissecting the mechanisms that account for the different responses to minor variations in B. pertussis lipid A both in human and mouse cells and in so doing, are addressing how human TLR4-MD-2 (the lipid A receptor) recognizes B. pertussis lipid A. Indeed, variation in lipid A has significant consequences for TLR4 activation and we propose that host-specific immunity to a particular Gram-negative bacterial pathogen is, at least in part, mediated by very subtle tuning of one the earliest interactions at the host-pathogen interface.