Infectious Disease

The Lisa Morici Lab: 3 Areas of Research

The emergence of multidrug resistant organisms represents the single greatest threat to our ability to successfully combat infectious diseases. In addition, the potential for deliberate misuse of biological organisms that are highly virulent or drug resistant has ushered the need for novel medical countermeasures against these "select agents." To address these public health burdens, the lab of **Lisa Morici** focuses on three main areas of research:

Novel vaccine platforms against intracellular bacteria

Vaccine platforms that are effective against intracellular bacterial pathogens remain a high priority. In addition to the global impact of intracellular bacterial infections on public health, the alarming increase in multidrug resistant strains, such as *Mycobacterium tuberculosis*, and the potential threat of biological attack with select agents, such as *B. pseudomallei* (*Bps) and B. mallei*, highlight the urgent need for safe and effective vaccines against this collective group of pathogens. A vaccine that can elicit a range of immune responses, including antibody, helper $CD4^+$ and cytotoxic $CD8^+$ T cells is especially desirable for bacteria that establish intracellular infection. We were the first to demonstrate that immunization with naturally-derived outer membrane vesicles (OMVs) could provide protection against an aerosolized, intracellular bacterium, *Bps*. Furthermore, our OMV vaccine provides superior protection to any other *Bps* vaccine candidate tested thus far. OMVs are constitutively shed by Gram-negative bacteria and are often enriched with numerous virulence factors and Toll-like receptor agonists, which make them ideal multi-antigen vaccine candidates. We are currently evaluating the OMV vaccine platform against other intracellular bacteria, including *Salmonella*, and working to understand the mechanisms of its immunogenicity and protection.

Naturally-derived antimicrobials to treat multidrug resistant organisms

By 2050, it is estimated that 10 million people globally will die each year from multidrug-resistant organisms (MDROs), surpassing all other major causes of death. Some bacteria, such as *Acinetobacter baumannii*, possess such broad spectrum antibiotic resistance that few available drugs remain to treat infections with these MDROs.

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Naturally-derived antimicrobials… (cont'd)

Infection of acute and chronic wounds, such as diabetic ulcers, pressure wounds, and burns, impairs wound healing and leads to further morbidity and mortality. MDROs are also particularly problematic to the military and frequently infect the type of complex wounds seen from combat. It is therefore imperative to develop novel therapeutics that can circumvent the antimicrobial resistance mechanisms of these pathogens. To address this need, our group has developed a novel antimicrobial platform utilizing bacterial membrane vesicles that are designed to specifically degrade the bacterial cell wall, arguably the bacteria's most important line of defense. We have shown that MVs containing cell wall-degrading enzymes display potent antimicrobial activity against *Escherichia coli*, methicillin-resistant *Staphylococcus aureus*, multidrug-resistant *A. baumannii*, and *Pseudomonas aeruginosa.* MVs also exhibit potent activity against bacterial biofilms. We are currently examining the therapeutic potential of MVs in treating wound infections caused by MDROs.

In vitro and in vivo models of infection

In order to assess the safety and efficacy of medical countermeasures against infectious pathogens, it is essential to establish and validate both *in vitro* and *in vivo* models of infection that closely mimic human disease. The Morici lab, in collaboration with other investigators in the Divisions of Aerobiology, Surgery, and Biochemistry, has developed numerous models to evaluate disease pathogenesis, immune responses, and wound healing and repair in response to infection with bacteria such as *Pseudomonas aeruginosa*, *Burkholderia mallei* and *B. pseudomallei*, *Staphylococcus aureus*, and *Salmonella typhimurium*. These models can be used to evaluate prophylactic therapeutics and vaccines, as well as post-exposure therapies to treat infection.

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