The Morici Lab: Pathogen/Host Interactions and Vaccinology

The emergence of multi-drug 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 counter-measures against these "select agents." To address these public health bur-dens, the lab of Lisa Morici focuses on four main areas of research.

Vaccine Platforms Against Intracellular Bacteria

Vaccine platforms that are effective against intracellular bacteria are a high priority for development. In addition to the global impact of these infections on public health, the increase in multidrug resistant strains, like Mycobacterium tuberculosis, and the potential threat of biological attack with select agents, (*i.e. B. pseudomallei* (*Bps*.) and *B. mallei*) highlight the need for safe and effective vaccines against this group of pathogens. A vaccine that can elicit a range of immune responses, including anti-body, helper CD4+ and cytotoxic CD8+ T cells is especially desirable for intracellular bacteria. The Morici Lab was the first to demonstrate that immunization with naturally-derived outer membrane vesicles (OMVs) could provide protection against an aerosolized, intracellular bacterium Bps. OMVs are shed by Gram-negative bacteria and are often enriched with virulence factors and Toll-like receptor agonists, making them ideal multi-antigen vaccine candidates. The lab is evaluating the OMV vaccine platform against other intracellular bacteria, including *Salmonella*.

Novel Adjuvants to Increase Vaccine Efficacy

The antigenic potential of OMVs has been known for some time, but their adjuvanticity and ability to drive cellular immune responses to co-delivered antigens has not been well-studied. The Morici Lab is studying the adjuvanticity of OMVs, and their data indicates that OMVs are extremely potent adjuvants, outperforming even licensed vaccine formulations in their ability to drive dendritic cell (DC) activation and to elicit both Th1 and Th17 CD4 T cell responses.

Infectious Disease

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Novel Adjuvants… (cont'd)

Importantly, the OMV adjuvant is derived from a bacterial strain that has a naturally-attenuated lipid A, which eliminates toxicity while preserving the full adjuvanticity of OMVs through Toll-like receptor (TLR) 4-dependent and –independent path-ways. OMVs can be admixed with peptides, subunits, or whole inactivated strains to promote humoral and cellular immunity against a wide range of microbial pathogens.

Naturally-Derived Antimicrobials to Treat Multidrug Resistant Organisms

By 2050, it is estimated that 10 million people per year globally will die 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. It is therefore imperative to develop novel therapeutics that can circumvent the resistance mechanisms of these pathogens. The Morici Lab has shown that bacterial-derived outer membrane vesicles OMVs possess potent antimicrobial activity against ESKAPE (*Escherichia coli*, methicillin-resistant *Staphylococcus aureus*, multidrug-resistant *A. baumannii*, and *Pseudomonas aeruginosa*) pathogens. OMVs also exhibit potent activity against bacterial biofilms. The lab is currently defining the therapeutic potential of OMVs and their products in treating biofilms and 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 Mori-ci lab, in collaboration with other investigators across different departments at Tulane, has developed numerous models to evaluate disease pathogenesis, immune responses, and wound healing/repair in response to infection with bacteria such as *Pseudomonas aeruginosa*, *Burkholderia mallei* and *B. pseudomallei*, and *Staphylococcus aureus*. These models can be used to evaluate prophylactic therapeutics and vaccines, as well as post-exposure therapies to treat infection.

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