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Live Attenuated Non-Transmissible ("LANT") Vaccines

Overview

Non-typhoidal Salmonella (**"NTS"**) infections are the leading cause of foodborne deaths worldwide, with ~ 80 million (86%) of human NTS infections estimated as foodborne [Majowicz et al, 2010 *Clin Infect Dis*]. Moreover, multiple outbreaks are reported due to contact with infected animals (e.g., poultry, pigs, cattle, and pets). The growing resistance of NTS strains to multiple antibiotics also makes NTS-caused disease difficult to treat [Varma et al, 2005 *J Infect Dis*]. UMB's Center of Vaccine Development and Global Health researchers led by Dr. Sharon Tennant & Dr. Jim Galen are developing a multivalent *Salmonella* vaccine designed to prevent the majority of NTS infections, based on a novel strategy for biocontainment, known as **Live Attenuated Non-Transmissible ("LANT")** technology. Live attenuated vaccines have clear advantages over subunit vaccines, including oral delivery and broad immune stimulation (i.e., serum and secretory IgA intestinal antibodies, and a host of cell-mediated immune responses); however, Dr. Galen's team in particular has shown the need to engineer a live vaccine to produce an optimal balance in its safety and immunogenicity. It's also important to monitor for shedding of live vaccine in a patient's stool, as this could affect close contacts (e.g., immunocompromised), a phenomenon limiting earlier efforts to develop live attenuated *S.* Typhimurium vaccine candidates [Galen et al. 2016 *EcoSal Plus*]. ***Key features of UMB's novel LANT strategy include***: (1) control of live vaccine replication via a structural protein essential for DNA synthesis; (2) replication will cease but cells will not lyse, thus retaining properly folded proteins and protective polysaccharide antigens on outer membrane; and (3) the system may be readily applied to other strains. UMB researchers anticipate the **LANT strategy is adaptable** to ANY bacterium amenable to genetic engineering, and thus it presents a **potential platform** for creating vaccines against several important bacterial diseases.

Inventors
Sharon Tennant
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Description
Live attenuated vaccine to prevent bacterial NTS disease

Field
Vaccine, Salmonella, NTS, AMR

Technology Status
Available for licensing & collaborative research

Patent Status
International Patent Application WO 2020/237246

UMB Docket#
ST-2019-013

References

Galen et al. 2016. EcoSal Plus Nov;7(1):1-17

World Bank 2017 Report on AMR *"A Threat to Our Economic Future"*

Market & Applications

A 2019 CDC report highlighted NTS as one of several "Serious Threats" for antimicrobial resistant (**"AMR"**) infections, and the impact of AMR to the world's population is reinforced by the World Bank's 2017 Report on "*Drug-Resistant Infections: A Threat to Our Economic Future.*" A growing number of public-private initiatives are aimed at promoting AMR solutions (e.g., new drugs and vaccines). Examples of successfully marketed live attenuated vaccines to prevent bacterial disease in endemic countries and travelers include Emergent BioSolutions' VAXCHORA® (cholera) and Vivotif® (*S.* Typhi). While earlier live vaccines against *S.* Typhimurium were not developed further due to unacceptable fecal shedding, UMB's LANT vaccine strategy may be the essential breakthrough that enables such vaccines to advance. ***UMB's LANT Salmonella vaccine has potential for broad use, to prevent NTS disease in infants, the elderly and travelers***.

Stage of Development

Team currently funded to conduct vaccine efficacy studies in animal infection challenge models.

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