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AMVAD adjuvant for mucosal vaccines (L-11561)

Highlights

Many microbial pathogens invade their mammalian hosts through the mucosal surfaces of the respiratory, gastrointestinal and urogenital tracts. The majority of approved vaccines are administered systemically, and fail to elicit effective mucosal immunity. There is thus a demand for safe, effective, non-replicating mucosal adjuvants and vaccines capable of preventing respiratory infections such as tuberculosis, streptococcal pneumonia, and influenza, as well as sexually transmitted infections such as HIV and genital *Chlamydia*.

The NRC has developed a novel archaeal polar lipid mucosal vaccine adjuvant and delivery (AMVAD) platform capable of generating mucosal and systemic immune responses against a wide range of pathogens that infect mucosal surfaces or use them to gain entry to the body.

Technology transfer

- A commercial exploitation licence for the technology
- Development of this technology through a joint collaboration

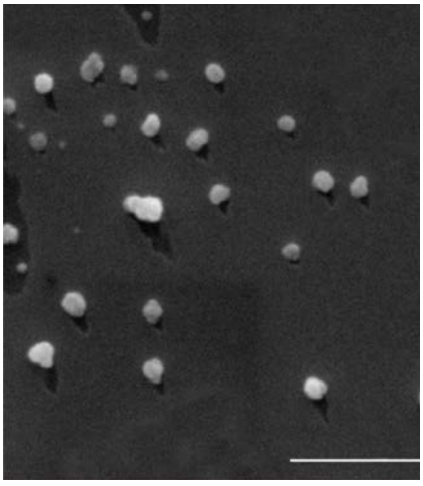
Market applications

- Vaccines against bacterial and viral pathogens affecting the respiratory system, such as tuberculosis, streptococcal pneumonia, and influenza
- Vaccines against sexually-transmitted infections, such as HIV and genital *Chlamydia*

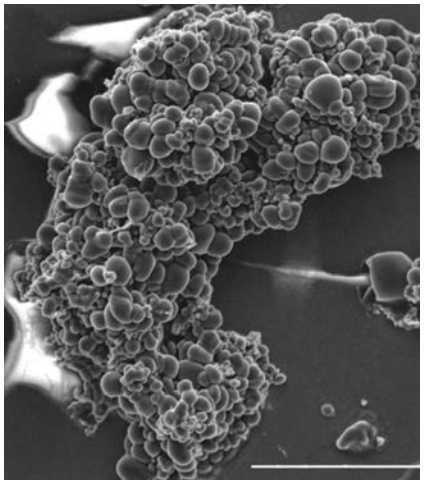
How it works

Immunity at the mucosal surface is desired to prevent pathogens from infecting the surface and/or disseminating to other organs to cause systemic disease. The few mucosal vaccines currently on the market are all based on the use of live-attenuated or whole-killed pathogen cells. Although these vaccines are efficacious, there are lingering concerns regarding potential reversion to virulence, overall safety in immunocompromised populations, and the possible inclusion of toxic cell components such as endotoxins. Vaccines based

Archaeosomes



AMVAD



Comparison of small, individual, spherical archaeosomes vs. AMVAD's larger spherical structures aggregated into clumps ("bunch of grapes") as a result of interaction with cations.

on acellular or subunit antigens would be safer, but such antigens are generally poorly immunogenic on their own.

To address these concerns, the NRC has developed AMVAD, a self-adjuvanting platform capable of stimulating mucosal immunity against a wide range of pathogens. AMVAD vaccines are formulated by adding multivalent cations to a suspension of antigens and archaeosomes (liposomes made from archaeal polar lipids). The interaction with the cations transforms the small, individual spherical archaeosomes into larger spherical structures that aggregates into clumps ("bunch of grapes"). When presented to the mucosal surface, this "bunch of grapes" elicits mucosal and systemic immune responses, whereas the antigen-archaeosomes that have not interacted with cations do not generate mucosal responses.

Strong, sustained and memory-boostable antigen-specific IgA antibody responses at local (nasal, respiratory) and distal (gastrointestinal, vaginal) sites were elicited in mice, upon intranasal administration of antigens formulated with AMVAD. Robust, antigen-specific systemic antibody (serum IgG1 and IgG2a) and CD8+ cytotoxic T lymphocyte (CTL) responses were also generated. Intranasal administration of experimental vaccines adjuvanted with the AMVAD system have shown protective efficacies in the murine model of respiratory tularemia using *Francisella tularensis* live vaccine strain (LVS), and in the genital Chlamydia infection model using *Chlamydia muridarum*.

Benefits

- Mucosal (e.g. nasal) or systemic (e.g. subcutaneous) vaccine administration
- Self-adjuvanting delivery platform
- Strong, sustained mucosal and systemic immune responses (humoral, CTL)
- Memory-boostable immune responses
- Low antigen/adjuvant dose
- Good preclinical safety profile (no toxicity or anti-lipid antibodies)
- Excellent stability, significant formulary/storage advantages: < 5% antigen release in 12 months at 5°C
- Proof-of-concept in murine models of respiratory tularemia and genital *Chlamydia*

Patents

NRC file 11561: Patents granted in Europe, pending in the United States, Canada and India.

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