Bacterial Vaccine Technology

Outer membrane vesicles (OMVs)

Introduction

A novel approach for bacterial vaccines is the use of Outer Membrane Vesicles. Intravacc has a strong focus and expertise in development of outer membrane vesicle vaccines and uses this as a platform technology for various bacterial vaccines.

Candidates for vaccine development

The strongest asset of OMV vaccines is the native conformation of protective antigens. Genetic engineering techniques can be used to achieve the required antigenic composition, the adjuvating properties of the bacterial lipopolysaccharides and hence the type of immune response. Gram-negative bacteria naturally release vesicles from the outer membrane: outer membrane vesicles (OMVs). OMVs are spherical particles (±20-200 nm) that harbour many bacterial antigens which play a role in establishing the infection and survival of the bacterium within the human host.

Benefits:

- Immunogenic properties
- Self-adjuvanticity
- Ability to be taken up by mammalian cells
- Possibilities to influence properties by genetic engineering.

Homologous or heterologous approach

At Intravacc we use two approaches to develop OMV vaccines: homologous and heterologous. Homologous OMV vaccines are in general the best choice if multiple antigens of the pathogen are needed to induce protective immunity. However, not all bacteria are suited for OMV generation. This may be due to the inability to cultivate these bacteria under laboratory conditions or may be impractical if a bacterium is classified as a BSL-3 or BSL-4 organism. In these cases heterologous OMV vaccines are generated.

Homologous approach

An example of a homologous approach is our own candidate vaccine against *Neisseria meningitidis* which has been based on 9 PorA proteins (NonaMen). To achieve broad protection against different circulation serotypes of Neisseria, multiple porA genes from different *Neisseria meningitidis* strains have been placed into the bacterium using genetic engineering. In this way each OMV harbors 3 distinct PorA proteins. Three separate OMV are then mixed to achieve a single vaccine with 9 PorA proteins.

Heterologous approach

On our platform for heterologous OMV vaccines multiple foreign antigens can be expressed in a bacterium that is easily cultivated and purified and gives high OMV yields.

Genetic engineering

Genetic engineering is used to improve the characteristics of bacterial vaccines, like for example enhancement of vesicle formation or reduction of lipopolysaccharides (LPS) related toxicity without affecting the intrinsic adjuvant properties of the target OMVs.
Our processes are preferentially detergent free, which keeps the highly immunogenic lipoproteins attached to the OMVs. Genetic engineering techniques are also used to achieve the required composition of virulence factors and the type of immune response.

Production process

The robust production process is designed to be scalable, achieve high yields and is compatible with GMP requirements. With the equipment in place we can produce batches of approximately 50,000 doses per run which is sufficient for phase 1 and phase 2 clinical trials.

Our key assets in R&D on bacterial vaccine technology are:

- Optimization of bacterial cultivation conditions and selection of chemically defined media free of animal components
- Dedicated genetic engineering to minimize LPS toxicity and optimize antigen composition
- State of the art analytical methods to characterize vaccines
- Design and coordination of pre-clinical, toxicological and clinical trials
- Process models for scale-up and scale-down
- Multi-reactor and downstream systems at laboratory scale for Design of Experiment approach
- Capability and expertise to perform activities under GMP
- Providing strategies for selection of model processes for new vaccine candidates.

Partnering opportunity

Patented LPS modifications and production processes make our OMV technology uniquely detergent free and allow the incorporation of lipoprotein in OMV vaccines. With our skills, infrastructure and equipment, Intravacc is your perfect partner for the development and production of Outer Membrane Vesicle vaccines. Either via homologous or heterologous techniques we can design:

- OMVs using our existing methods and processes
- Completely new OMV designs and processes.

Intravacc

Intravacc is a renowned, not-for-profit R&D organization. With our unique capabilities and infrastructure, we are able to optimize vaccines, vaccine processes and vaccine technologies. Our aim is to increase equality in access to vaccines throughout the world in order to contribute to public health. We achieve this by transferring our knowledge and technologies to public and private partners worldwide and through collaborative R&D. A team of 150 professionals is at your disposal at Science Park Bilthoven in The Netherlands.

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Factsheet OMVs

Left: Schematic representation of OMV release.
Right: Immunofluorescent photo of Neisseria meningitidis