

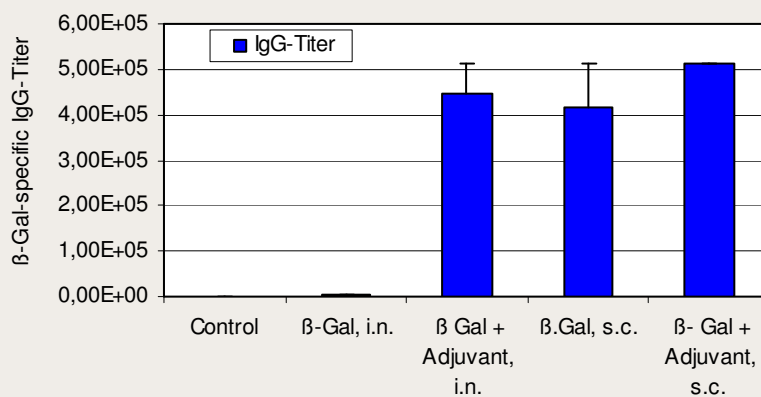
Technology Offer

Four highly potent adjuvants for mucosally administrable vaccines

The Challenge

Mucosal delivery of vaccines allows concerted combat of diseases caused by pathogens that either invade through, or cause disease at mucosal surfaces. A novel vaccination approach is to combine systemic response and local mucosal immune response in order to induce specific protection in distant mucosal sites. Easy application of vaccines as e.g. a nasal spray or nebuliser for inhalation increases patient acceptance and convenience of administration. In developing countries ease of use and low costs of these vaccines are important prerequisites for mass vaccinations. Moreover, injections are a potential risk for infections and disease transmission e.g. HIV, especially in developing countries. In addition many new mucosal vaccine candidates do not elicit sufficiently strong immune responses.

The vaccination through mucosal membranes requires potent adjuvants in order to enhance the immunogenicity of the vaccine antigen, to decrease the rate of its degradation and to target the vaccine to the site of immune function. There are only very few adjuvants such as Alum that are approved for the use in humans. Thus the demand for new adjuvants is high and still unmet. Scientists of the Helmholtz Centre for Infection Research (HZI) recently found out about the applicability of a variety of substances as potent adjuvants for mucosal vaccination.



Humoral responses stimulated following vaccination using a representative adjuvant. Mice were immunised by intranasal (i.n.) and subcutaneous (s.c.) routes with either β -galactosidase (30 μ g) alone or β -galactosidase mixed with the adjuvant

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The Technologies

This portfolio of highly potent novel adjuvants presents the advantage of being applicable for mucosal vaccination. These known substances are associated with the special ability of increasing significantly the immune response.

02-00158 c-diGMP - Cyclic diGMP is a key regulator in the bacterial metabolism. In eukaryotic organisms c-diGMP serves as a signalling molecule.

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The presence of this bacterial signalling cue seems to simulate an upcoming infection and therefore provokes a corresponding reaction of the immune system. Increased stability, increased tolerance and decelerated renal excretion is achieved by the linkage of c-diGMP to PEG (Polyethylenglycol). A European patent application was filed in 2005 (EP05024266.8). An international application (PCT) was filed in 2006.

02-00159 PQS-Hydroxyquinolon – 2-Heptyl-3-hydroxy-4quinolon (PQS) is a bacterial messenger molecule, that mainly plays a role in bacterial communication. The family of quinolones are used for various therapeutic purposes (e.g. antibiotics). Fluoroquinolones are known to activate the cellular immune response through the stimulation of cytokine secretion. The bacterial messenger molecule PQS-Hydroxyquinolon as well seems to provoke an immune reaction by the simulation of a bacterial infection. Linkage of PQS-Hydroxyquinolon to PEG mediates the above described favourable pharmacological effect. A European patent application was filed in 2005 (EP05024266.8). An international application (PCT) was filed in 2006.

02-00160 α -GalCerMPEG – α -Galactosylceramid is a membrane lipid that originally derives from the marine sponge *Agelas mauritianus*. Bound to MPEG the solubility of α -GalCer is improved. α -GalCerMPEG interacts with CD1d on antigen presenting cells which communicates the linkage between NK-cells or iNKT-cells and the antigen presenting cells at the very beginning of the induced immune response (before the specific immune reaction is initiated). Also in this case linkage to PEG improves the pharmacological properties of the molecule. A European patent application was filed in 2005 (EP05022771.9). An international application (PCT) was filed in 2006.

02-00183 Glycolipide Mal-1,3-C14 and Mel-1,3-C14 – these artificially synthesised glycolipids provoke a strong immune response in combination with an antigen. They consist of a unit maltose or melibiose that represents the polar part of the molecule. The unpolar tail of the molecule consists of two glycerine bound fatty acids. The natural counterpart of this glycolipids is a component of biological membranes. There is strong evidence that these molecules can be used as adjuvants for subcutaneous and mucosal vaccination. A European patent application was filed in 2006 (EP06018723.4). An international application (PCT) will follow in 2007.

Commercial Opportunity

- dramatic increase of elicited humoral and cellular immune response
- cost effective synthetic production
- low toxicity

Further Reading

The bacterial second messenger cyclic diGMP exhibits potent adjuvant properties. Ebensen, T., Schulze, K., Riese, P., Link, C., Morr, M., Guzmán, C. (2006), doi:10.1016/j.vaccine.2006.10.033

Patent Situation

All novel adjuvants are protected by pending European and International Patent applications, respectively.