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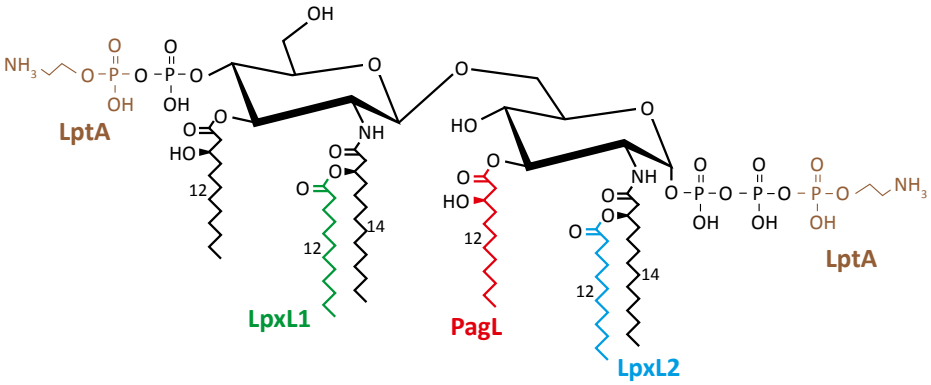
innovating vaccines

Novel LPS adjuvants



Detoxified LPS

Most fully active LPS species are not suitable for use as an adjuvant, due to toxic side effects. For example, *Neisseria meningitidis* contains a very potent hexa-acylated LPS that would be too toxic for therapeutic applications. We used systematic molecular bioengineering of the meningococcal LPS to yield a variety of novel LPS mutant strains with changes in both lipid A acylation and phosphorylation, and thereby differences in immune activation and toxicity as monitored by stimulation of immune cells.

Purification

A novel method for the isolation of LPS from *Neisseria meningitidis* was established that avoids the use of large volumes of toxic phenol for LPS extraction. By this method, LPS can be produced with a high purity (>95%).

Benefits

- The use of this panel of neisserial LPS derivatives is covered by three patents and two patent applications.
- In-house developed LPS purification method available that is phenol free (> 95% purity).
- Detailed compositional determination of the LPS molecular species by mass spectrometry.
- HEK cells expressing TLR4 and MD-2 from different species available, including mouse, chicken, rabbit and human to take species specific effects into account.
- Molecular bioengineering also available for other species, for example also a range of *LPS derivatives from* Bordetella pertussis.

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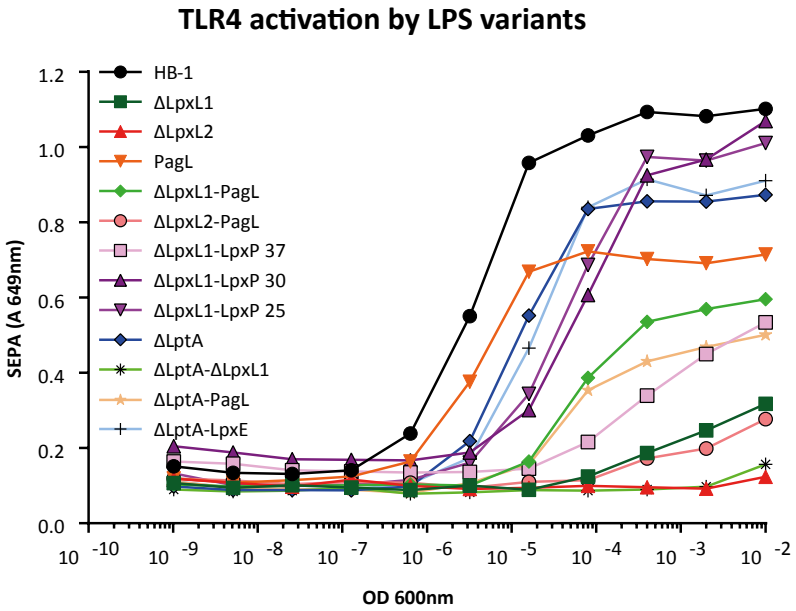

Activity

The biological activity of LPS is largely determined by its interaction with Toll-like receptor 4 (TLR4) and its co-receptor MD-2, which is species-specific. Because animal models are often used for preclinical testing of LPS-containing therapeutics, these modified LPS derivatives were also tested for their activating capacity of TLR4 and MD-2 from different species.

Altogether, these purified LPS derivatives display a broad range of TLR4 activity and differential cytokine inducing properties, which can be exploited for use as an adjuvant in vaccines or for the development of other TLR4-based therapeutics. In addition, they can be used in LPS-containing vaccines such as those based on meningococcal outer membrane vesicles, allowing the fine-tuning of activation of innate immune responses.

Partnering

Intravacc has several detoxified LPS variants available for testing with your antigen of choice. The LPS adjuvant platform technology of Intravacc is open for new collaborations, which can range from out-licensing to large collaborative development, process optimization and cGMP production.

References

- Modulating endotoxin activity by combinatorial bioengineering of meningococcal lipopolysaccharide. A. Zariri, 2016
- Lipopolysaccharide engineering in *Neisseria meningitidis*: structural analysis of different pentaacyl lipid A mutants and comparison of their modified agonist properties. E. Pupo, 2014

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 collaborative R&D. A team of 150 professionals is at your disposal at Utrecht Science Park Bilthoven in The Netherlands

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