Alexey Novikov et al., J Vaccines Vaccin 2017, 8:3(Suppl)
DOI: 10.4172/2157-7560-C1-058

LPS/endotoxins molecular diversity impacting vaccines and adjuvants activities and toxicity

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Endotoxins are major antigens of the Gram negative bacterial membrane. Their use in vaccines is known for years, both for their antigenic properties and for their immuno modulator capacities used in vaccine adjuvants. Endotoxins are mixtures of lipopolysaccharides (LPS), made of a lipidic moiety, "lipid A" anchored in the membrane, to which an oligosaccharide core is substituted, in Smooth-type bacteria, by a long chain of repetitive oligosaccharide units, extending outside of the membrane. This high-specific chain named O-chain, is unique for a given bacterium, thus characteristic of each serotype of a given species, and efficiently used as an antigen for vaccines or for bacterial detection tests. As for the glycol-phospho-lipid lipid A region, it is responsible for most of the toxic and beneficial properties of LPS. All endotoxins are LPS, but all LPS are not toxic. Different biochemical methods have been described for detoxifying LPS molecules. The most efficient and recognized one is the lipid A glycophosphate release under mild acid conditions. This leads to mono-phosphoryl-lipid A (MPLA) production. This process, when completed by de-O-acylation, results in the well-known MPL© adjuvant commercialized by GSK and used in a new vaccines generation. During more than forty years, researchers working now at LPS-BioSciences have established tens of lipid A structures from different bacterial species. Our structure to activity studies has shown that each structural element can have a drastic impact on LPS biological activities. We have also described a number of naturally non-toxic LPS structures. We will show how heterogeneous and variable lipid A structures can be due to culture conditions, strains, etc., with a major impact on their biological activities. The methods used for LPS extraction and structural characterization are thus crucial for understanding the structure to activity relationships and mastering their activities for a safe use.

Biography

Alexey Novikov is working as the Head of R&D at LPS-BioSciences Company, a start-up created in 2011 by Martine Caroff. He also has 10 years of experience in academic research in the field of bacterial lipopolysaccharides. He has done his Master's in physical properties of endotoxins, their extraction methods and their structural characterization by mass spectrometry. He is the author of 50 papers published in reputed journals. He has his expertise in Physics, Chemistry and Biochemistry.

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