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NRC Institute for Biological Sciences

Mycobacterial Lipids for Use in Vaccine Delivery Liposomes with an Adjuvant Effect

The Business Opportunity

Pediatric vaccines have historically dominated this field that has remained steady for many years. However, with the advent of adult vaccines such as those against influenza and hepatitis, the field is again seeing a resurgence. Cancer vaccines will also become a major player with the current uptake of the human papilloma virus vaccine already expected to account for 20 % of vaccine revenues by 2012. Key challenge for vaccine development remains in the quest for novel non-toxic, potent adjuvants that can appropriately drive immune responses against difficult to control emerging and re-emerging pathogens. The burgeoning knowledge that pathogen specific molecular patterns interact with key pathogen specific receptors on immune cells and can drive the development of potent innate and adaptive immune responses has led to the quest for novel immunomodulators and adjuvants.

The Technology

Historically, human vaccines have consisted of live attenuated or killed viral or bacterial pathogens. Patient acceptance and safety is a concern, based on possible side-reactions of complex and ill-defined vaccines, and the possibility for reversion to virulence. A more current approach is to use defined, highly purified antigens. Side-reactions are minimized, but the efficacy of these subunit vaccines is generally poor because of a loss in immunogenicity when the antigen is purified. A further difficulty is efficient targeting of both the antigen and adjuvant to antigen-presenting cells. Further, the lack of efficacy may be explained by an inappropriate immune response, because protection may require that humoral, cell-mediated or cytotoxic T cell (CTL) responses predominate depending on the pathogen in question. The use of Alum as an adjuvant (approved for human use) is based on forming a complex with antigen to give a depot effect, resulting in only a Th2 response, and not CTL. Further, local reactions may occur at the injection site with aluminum-based adjuvants such as Alum.

Mycobacterium spp. are often associated with pathogenesis and are best known as causative agents for tuberculosis, leprosy, and as opportunistic pathogens. The ability of the immune system to respond to mycobacterial cells, or their components, has been an area of keen interest for decades because of the pathogenicity associated with this genus.

NRC-IBS technology relates to the use of polar lipids from the human vaccine strain of *Mycobacterium bovis* BCG, and other *Mycobacteria* with similar unique lipids, to prepare liposomes that adjuvant an

immune response to an associated antigen. Total polar lipids of BCG are used to form liposomes to activate antigen-presenting cells by engaging specific Toll like receptors. The invention more specifically relates to vaccine development by providing a stable vehicle for antigen delivery to antigen-presenting cells using immunostimulatory, polar BCG glycerolipids, resulting in enhancement of immune responses.

Patent Position

Patents Pending – NRC File 11305

Key Publications

Sprott GD, Dicaire CJ, Gurnani K, Sad S, Krishnan L. *Activation of dendritic cells by liposomes prepared from phosphatidylinositol mannosides from Mycobacterium bovis bacillus Calmette-Guerin and adjuvant activity in vivo*. Infect Immun. 2004 Sep;72(9):5235-46.

The Market

The world vaccine market is projected to see a growth of 16 % by 2012, with US \$ 30 billion revenue. Adult vaccines are expected to account for >20 % of the market share by 2012.

Technology Transfer Possibilities

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

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