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A new marine-derived sulfoglycolipid triggers dendritic cell activation and immune adjuvant response

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Dendritic Cells (DCs) recognize infectious non-self molecules and engage the adaptive immune system thereby initiating long lasting, antigen-specific responses. As such, the ability to activate DCs is considered a key tool to enhance the efficacy and quality of vaccination. Here we report a novel immunomodulatory sulfolipid named β-SQDG18 that prototypes a class of natural-derived glycolipids able to prime human DCs by a TLR2/TLR4-independent mechanism and trigger an efficient immune response *in vivo*. β-SQDG18 induces maturation of DC with the upregulation of MHC II molecules and co-stimulatory proteins (CD83, CD86), as well as pro-inflammatory cytokines (IL-12 and INF-γ). Mice immunized with OVA associated to β-SQDG18 (1:500) produced a titer of anti-OVA Ig comparable to traditional adjuvants. In an experimental model of melanoma, vaccination of C57BL/6 mice with β-SQDG18-adjuvanted hgp10 peptide elicited a protective response with a reduction in tumour growth and increase in survival.

Stimulation of an immune response by using attenuated or inactivated biological agents has been the traditional basis for vaccination against viral and bacterial infections. However, most of the recent vaccines are comprised of highly purified synthetic macromolecules, such as peptides or recombinant DNA produced by genetic engineering technology. These antigens tend to be safer but poorly immunogenic; therefore they need to be combined with agents known as adjuvants that potentiate the immune response mostly by activation of specific accessory cells, named Antigen-Presenting Cells (APCs)[1–6]. Adjuvants are a highly heterogeneous group of compounds with a common property, usually defined as adjuvancy, to enhance the immunogenicity of antigens. Nevertheless, except for the Toll-like receptor (TLR) agonist monophosphoryl lipid A (MPLA, compound 1 in Fig. 1), clinically approved formulations are restricted to aluminium salts and emulsions of lipids (e.g. squalene) in water[7]. Dendritic cells (DCs) are the most efficient APCs[8–14] and are often called 'nature's adjuvant'[15] for their ability to induce activation and specific expansion of $CD4^+$ helper T (Th) and $CD8^+$ cytotoxic T (CTL) lymphocytes determining the functional profile of these cells against bacterial and viral antigens[15]. For these reasons DCs have become the product of choice for the preparation of DC-based vaccines against tumors or infections[16–19].

Here we provide the first evidence of a novel class of molecular adjuvants of marine origin able to stimulate *in vitro* DC maturation and prime *in vivo* specific immune response.

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