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Marine-inspired synthetic glycolipids as new immunomodulatory substances in the treatment of cancer and neurodegenerative diseases

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Glycolipids are primary metabolites present in all living organisms and characterized by interesting biological properties. In recent years, glycoglycerolipids and ceramides have attracted particular interest as either agonists of cellular receptors, e.g. Toll-Like Receptors (TLRs) and MHC-related glycoproteins of the CD1 family, or chemical entities for the development of anti-tumoral and immunological drugs.
In the last years, we have focused our study on the immunological properties of sulfoglycolipids, that have wide distribution in terrestrial and marine photosynthetic organisms. This communication summarizes our work about the synthetic preparation and development of this family of molecules and their analogs as novel immunomodulators. In this regard a representative example was a sulfoquinovosyl diacylglycerol named β-SQDG18 (Sulfavant) 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 against melanoma. Sulfavant induces maturation of DC with expression of MHC II molecules and upregulation of costimulatory proteins (CD83, CD86). Mice immunized with OVA associated to Sulfavant (1:500) produced a titer of anti-OVA Ig comparable to traditional adjuvants. In an experimental model of melanoma, vaccination of C57BL/6 mice by Sulfavant-adjuvanted hgp10 peptide elicited a protective response with reduction of tumour growth and increase of survival. The study of the mechanism of action of this molecule highlighted new cellular processes at the basis of the regulation and modulation of the immune response and which favor the rapid achievement of cellular homeostatic conditions following perturbative events.

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