Synthesis of BODIPY-based fluorescent analogues of the molecular adjuvants Sulfavants

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The sea represents a huge source of biologically active compounds characterized by a wide structural variety and a great potential for therapeutic uses.[1] During the ongoing exploration of the immunomodulatory potential of marine natural products, the work of recent years has been focused on the identification of novel chemical candidates able to stimulate dendritic cells (DCs), a specific type of antigen-presenting cells (APCs) that operate as master regulators for the adaptive immune response.

Inspired by the natural immunomodulators α-6'-sulfoquinovosyldiacylglycerols (α-SQDGs), a synthetic sulfolipid, named Sulfavant A, has been described as the progenitor of a novel class of molecular adjuvants able to stimulate an unconventional maturation of human dendritic cells (hDCs) via the Triggering Receptor Expressed on Myeloid cells-2 (TREM2).[2] Crucial step for the pharmacological development is the elucidation of the biological mechanism and sub-cellular localization of the cellular targets. For this reason, in this communication, the synthesis of fluorescent analogues (**1-3**) of Sulfavant A, bearing the 4,4-difluoro-1,3,7-tetramethyl-4-bora-3a,4a-diaza-*s*-indacene moiety (Me_3-BODIPY), is provided (**Figure 1**).[3]

The fluorescent probe **1**, showing unaltered *in vitro* activity compared to that of Sulfavant A, has been used for both live cell imaging experiment in presence of hDCs and biodistribution studies in Zebrafish animal model, while the other two fluorescent derivatives (**2-3**) were prepared to investigate emission wavelengths closer to the IR region, in order to overcome the overlapping problem with basic natural fluorescence.[4] The development of a general synthetic strategy for the preparation of fluorescent analogues of this new family of immunomodulators and their *in vitro* and *in vivo* applications open the way for more in-depth studies on the interaction with cellular targets and biological behaviour.

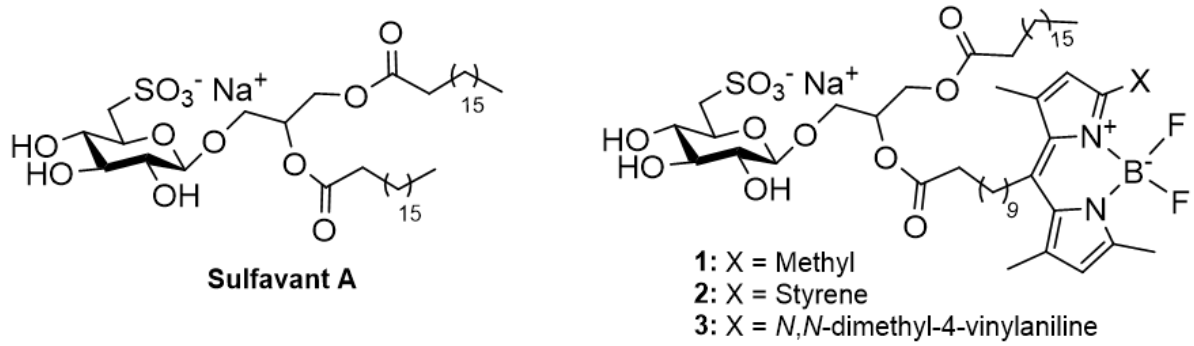

Figure 1: Sulfavant A and its fluorescent analogues.

Bibliographic references:

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