

Novel Th1-polarizing alfa-galcer analogs useful as adjuvant or adjuvant therapy

- **Novel class of superior Th1 polarizing glycolipids valuable as vaccine adjuvant or adjuvant therapy in oncology**
- **Effective modulation of the CD1d-TCR complex on iNKT cells**
- **In vivo proof-of-concept in B16 melanoma mouse model inhibiting metastasis**
- **Drug-able chemical profile ready for upscaling.**
- **Availability of evaluation batches**

Introduction

Invariant natural killer T cells (iNKT) are a unique subset of peripheral blood cells that play a pivotal role in the activation of the adaptive immune system through the rapid release of Th1 and Th2 cytokines. This cytokine release is initiated by the interaction of the T cell receptors (TCR) of iNKT cells with a MHC class I-like molecule (CD1d) on antigen-presenting cells (e.g. dendritic cells) complexed with self- and foreign lipids and glycolipids.

The prototypical antigen for iNKT cells is α -galactosyl ceramide (aGalCer or KRN7000), a synthetic analog of glycolipids originally isolated from a sponge. This compound has sparked drug discovery efforts to identify analogs capable of skewing the adaptive immune response in a Th1 or Th2 direction ("polarisation"). Potent Th1 polarizing GalCer analogs have a therapeutic potential as a vaccine adjuvant (bacterial, viral or tumor vaccines) or in cancer therapy (adjuvant therapy).

Technology

The groups of Prof. Serge Van Calenbergh (medicinal chemistry) and Prof. Dirk Elewaut (UGent Hospital, molecular immunology) have extensive experience in the development of innovative aGalCer analogs with a clinical focus. Recently, they identified a novel class of aGalCer analogs with a superior Th1-skewing profile.

Advantages

- extremely strong production of IL-12 and IFN- γ in two different application models (injected solubly and when loaded onto bone marrow dendritic cells)
- less IL-4 production compared to aGalCer
- in vivo proof of concept in BL6-B16 melanoma mouse model (lung metastasis inhibition)
- UGent glycolipids have a drug-able profile and have been optimized for easy synthesis. Availability of SAR data for rational design strategies
- Patent protected (priority year) with a broad claim scope anticipating chemical optimization processes and a broad range of immune-modulatory applications.

Partnership

We are actively seeking partners to develop or co-develop the UGent GalCer molecules to therapeutic applications in the vaccine or oncology field. Evaluation batches are available for in-house evaluation. University and regional innovation funds allow for risk sharing collaboration models.

Intellectual property

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Keywords

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