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New immunostimulatory synthetic compounds for the Treatment of Leishmaniasis and Tuberculosis

Focus Indications

- Tuberculosis
- Leishmaniasis

Project Key Words

- Immune response
- Synthetic immunostimulator
- Intracellular Infections
- Leishmaniasis
- Tuberculosis

Development Status

- POC
- *In vitro* tests on human NKT cells
- *In vivo* tests on mice
- Compound administration studies ongoing

Patent Procedure Status

- PCT Patent Application filed

Chances for Cooperation

- R&D Cooperation
- Licensing
- Patent Sale

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Innovation and Customer Benefit

Inadequate immune response leads to an insufficient elimination of pathogens in intracellular infective diseases.
Current treatment options involve the supportive stimulation of the immune system by administering immune activators like αGalCer. Experience has shown that treatment with αGalCer can lead to undesirable side effects due to an unspecific induction of cytokines.

The present treatment alternative describes novel immunostimulatory compounds based on active glycolipid molecules -*Eh*LPPG analogues- isolated from *Entamoeba histolytica*. These synthetic immune activators are characterized by:

- Efficient stimulation of the immune response
- Reliable induction of favourable cytokines
- Better performance and less side effects than current treatment options

Possible Indications

To date the novel synthetic activators have been successfully tested with regard to their anti-infective activity *in vivo* in mice (ongoing) and *in vitro* with murine and human macrophages.

Therapeutical indications are intracellular infections such as:

- Tuberculosis: latent and active forms, as combination with antituberculosis therapy
- Leishmaniasis: cutaneous and visceral

The current treatment options are insufficient due to long, systemic treatment durations, toxic side effects and high treatment costs. Moreover, they bear the risk of the induction of resistances.

Leishmaniasis: >2 million new cases/year
Tuberculosis: >9 million new cases/year

New well-tolerated and effective compounds are needed which are able to activate or re-stimulate the otherwise insufficient immune response in patients.

Technical Description

Synthetic *Eh*LPPG derivatives answer the need for good availability and purity in an actually complex extraction process.

The stimulation activity of *Eh*LPPG is linked to its active Phosphatidylinositol (PI) anchor. As stimulators of the immune system, they are a valuable tool to fight resistance problems of current treatments.

Our invention covers different synthetic PI anchor analogues and derivatives.
*Eh*LPPG activates the immune response through a cascade reaction involving the stimulation of infected antigen presenting cells (APCs) and Natural Killer T (NKT) cells.

The application of EhLPPG analogues allows an increased expression of IL-12p35, IL1ß and NOS2 in infected and treated APCs and a favourable cytokine profile in NKT cells (IFNγ; IL-4) and lead to a reliable anti-infective effect. Furthermore unlike in αGalCer treatments, the production of TNFα and IL-17 is minimized and the putative related side effects will be reduced.

Tests on compound administration using nanocarriers are ongoing.

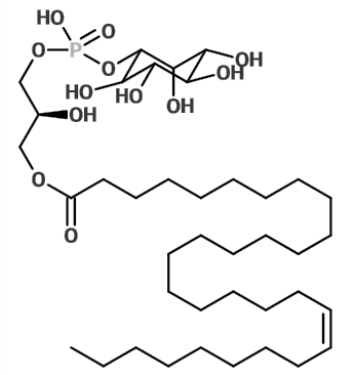

Fig 1. Molecular structure of an *Eh*LPPG analogue (C30-*Eh*Pla-*cis*)

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