

NOVEL ANTI-TUBERCULOSIS COMPOUNDS

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HINTERGRUND

The resurgence of tuberculosis, caused primarily by Mycobacterium tuberculosis (Mtb), and the appearance of multi-drug and extensively drug resistant Mtb strains strengthen the need for new drugs with alternative modes of action.

LÖSUNG

The interaction between the mycobacterial thioredoxin reductase (TrxR) and its substrate thioredoxin (Trx) is a promising new drug target for the treatment of tuberculosis, since Mtb lacks the common glutathione system and the mycobacterial TrxR shows a substantial difference in sequence, mechanism and structure to human TrxRs. It was shown that TrxR is essential for thiol redox homeostasis and genetic inactivation in vivo eradicates Mtb during acute and chronic mouse infections (Lin et al., PLoS Pathog. 2016).

In order to further improve the bioactivity of promising compounds, researchers of the TU Dortmund University have focused on optimizing the physico-chemical properties that are important for permeability, since M. tuberculosis shows an unusual thick and impermeable cell wall.

The researcher are preparing the further development towards mice studies to confirm in vivo efficacy, as well as ADME-Tox studies.

PROvendis GmbH
Prof. Dr. Frank Entschladen
+49.208 94105-20
fe@provendis.info
www.provendis.info

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CATEGORIES
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Compounds with improved physicochemical properties with regard to increased permeability and bioactivity were designed. The most promising compound (BE-068) was also tested on infected human macrophages and showed a clear dose-dependent activity on mycobacterial growth (upper graph), without affecting macrophage viability (lower graph).

VORTEILE

- Novel class of compounds that inhibit a novel target with potential to overcome resistance problems of M. tuberculosis to other drugs
- Viability of infected macrophages is not affected
- Increased bioactivity by optimized permeability through the cell wall of M. tuberculosis

SERVICE

The technology is offered for licensing and further therapeutic development. In case of interest we are pleased to inform you about the patent status.

PUBLIKATIONEN & VERWEISE