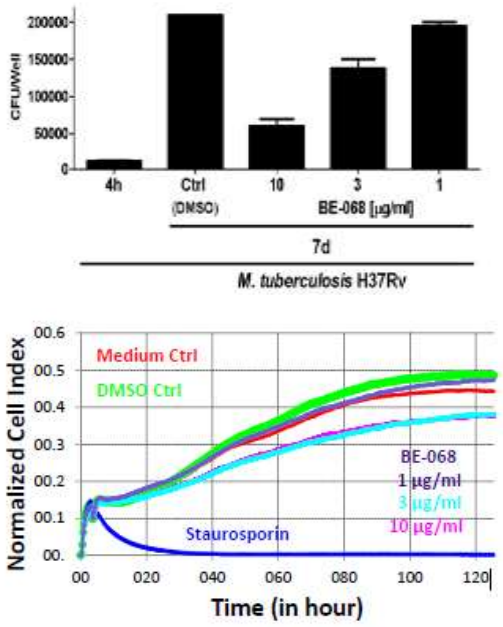
Novel Anti-Tuberculosis

Novel *Mycobacterium tuberculosis* thioredoxin reductase inhibitors with antimycobacterial activity in infected macrophages

Invention

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. 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.



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)

Commercial Opportunities

The technology is offered for licensing and further therapeutic development.

Current Status

The researcher are preparing the further development towards mice studies to confirm *in vivo* efficacy, as well as ADME Tox studies. In case of interest we are pleased to inform you about the patent status.

Relevant Publications

Koch, O., *et al.* (2013) Identification of M. tuberculosis thioredoxin reductase inhibitors based on high-throughput docking using constraints *J. Med. Chem.* 56(12): 4849-59.

An invention of the TU Dortmund University.

Competitive Advantages

- 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

Technology Readiness Level

1 2 3 4 5 6 7 8

Technology validated in lab

Industries

- Pharmaceutical Industry

Ref. No.

4941

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