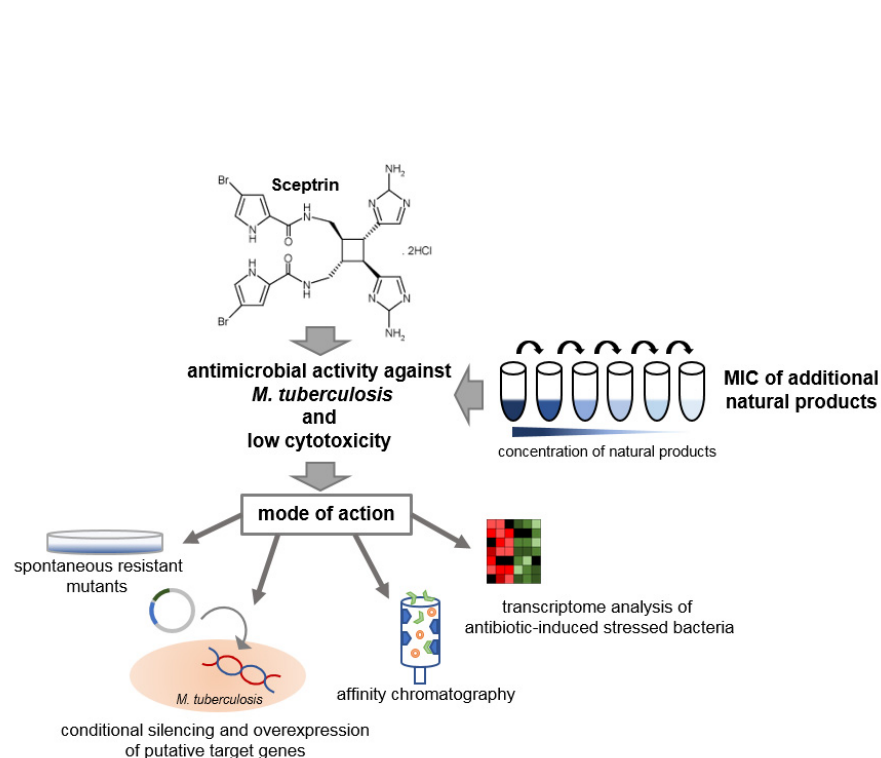


Functional characterization of the antimicrobial activity of sceptrin and other natural compounds in *Mycobacterium tuberculosis* and nosocomial pathogens



Mult-drug resistance in infectious diseases such as those caused by *Mycobacterium tuberculosis* or nosocomial bacterial pathogens such as *Staphylococcus aureus* is a major limitation for antimicrobial chemotherapy. In this doctorate project, the known antimycobacterial activity of the Sponge-derived molecule Sceptrin will be studied at the molecular level. Additionally, further natural sourced molecules (provided by the group of Prof. Peter Proksch) will be tested for their antimicrobial activity against *Mycobacterium tuberculosis* as well as various Gram-positive and -negative bacterial pathogens including *Staphylococcus aureus* and *Acinetobacter baumannii* in order to identify several more interesting hit structures. Promising candidates exhibiting sufficient antimicrobial activity but only low general cytotoxicity against human cells will subsequently be studied regarding their mode-of-action, molecular targets and resistance mechanisms. These functional characterizations comprise, among other analyses, the isolation and molecular-genetical characterization of spontaneous resistant mutants, transcriptome and proteome profiling of sublethally stressed cells, conditional silencing or overexpression of putative target genes, as well as customized biochemical experiments to corroborate hypothesized targets and mechanisms.

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