



Project on Antibacterial Antibiotic Discovery and Development

Most of the antibiotics currently in medical use are produced by bacteria and fungi. We have access to various unique collections of microbial isolates with high antibiotic production potential and possess wide experience in isolation and targeted screening of unique microbes. We offer projects on novel antibiotic discovery and development.

BACKGROUND

The emergence and rise of multidrug resistant bacteria represents an eminent threat to public health. As there are fewer or no effective antibiotics available for treating bacterial infections, the discovery and development of novel antibiotics is urgently needed. Termination of antibiotic discovery programs by Big Pharma over the last 2 decades was due, among other reasons, to frequent re-discovery of already known compounds. Recent studies by Prof. Zotchev's lab strongly suggest that new environmental niches and isolation methods can yield unique microbial strains producing new bioactive secondary metabolites. New bacteria and fungi are being isolated and characterized in Zotchev Lab from medicinal plants and their rhizospheres, marine sediments, sponges and bryozoans. In addition, Zotchev Lab has, via co-operation agreements, access to unique microbial collections in China and Ethiopia.

ANTIBAC PROJECT SYNOPSIS

The AntiBac project on novel antibiotic discovery is designed to consist of two phases. The first phase would start with collection (or acquisition) of unique environmental samples, their chemical analyses, 16S/18S amplicon sequencing and bioinformatics-based assessment, and design of isolation methods. This will be followed by isolation and phylogenetic analysis of microbial strains, followed by the development of cultivation methods designed to ensure secondary metabolite production. Extracts from microbial cultures will be analyzed in bioassays targeting Gram-negative (1st priority) and Gram-positive bacteria. Active compounds will be identified using bioactivity-guided fractionation and high-resolution HPLC-MS analysis.

Potentially novel compounds will be subjected to NMR for structure elucidation and their MIC values on a selection of bacterial strains determined. If confirmed novel, and effective *in vitro*, selected compounds will have to be produced in larger quantities in order to allow more comprehensive testing of drug-like properties.

The second phase of the project will comprise optimization of novel antibiotic production and purification methods. The latter may include genome sequencing of the producer organism and identification of the antibiotic biosynthesis genes to allow me-

tabolic engineering toward enhanced production. The genomic data will be combined with metabolomics and transcriptomics (RNAseq) that will guide the engineering efforts. In parallel, optimization of production media and conditions, the use of various elicitors of secondary metabolism (e.g. co-culturing with other microorganisms, histone deacetylase inhibitors etc). Downstream processes to ensure isolation of pure compounds needed for animal testing will also be optimized.

OUR OFFER

We offer to develop such a project with interested industrial partners, taking into consideration their particular requirements for a novel antibiotic and thus adjusting the discovery/development strategy accordingly.

EXPERTS

Prof. Dr. Sergey B. Zotchev

DEVELOPMENT STATUS

TRL 1-2

KEYWORDS

- Novel antibiotics
- Antibacterial
- Antifungal
- Bioactive compounds
- Unique microbial collection

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