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Search for hits and early leads from soil bacteria to combat infectious diseases

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Abstract

Introduction: Natural products are the source of a large fraction of the current pharmaceutics available against human disease. However, the discovery of novel compounds with new mechanisms of action is becoming increasingly challenging. We focused our work on soil-dwelling Myxobacteria from highly diverse samples, which are more and more recognized as an important natural product source.

Methodology: Our discovery pipeline combines traditional whole cell-based activity screens with state-of-the-art analytical techniques and a comprehensive dereplication process. Having identified an antimicrobial compound we aim at elucidating its target, MOA and MOR in diverse microbiological screens and by applying 'omic' technologies.

Results: Two case studies of currently investigated compound classes will be highlighted. Cystobactamids are novel topoisomerase inhibitors that display very pronounced activity on Gram-positive and Gram-negative bacteria. Telomycins from *Streptomyces canus* bind to cardiolipin and our studies revealed other putative cellular targets.

Conclusion: We were able to isolate several new natural products with potent and selective activity against clinically relevant pathogens. Interestingly, underlying MOAs often differ from those of already described antimicrobial agents.

Key words: myxobacteria; streptomyces; natural products.

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