Discovery of novel bioactive compounds through epigenetic engineering and systematic microbial co-cultures

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The majority of drugs used in medicine are small molecules of natural or synthetic origin. One of the strongest drivers for the discovery of bioactive compounds for medicinal use was activity screening of compounds derived from natural sources such as plants and microbes. Taking this approach, nature's chemical diversity has been exploited successfully over the last decades and brought up the most useful and important medical drugs, such as antibiotics (derived from bacteria and fungi), anti-cholesterol, anti-cancer drugs or anti-inflammatory substances. The annotation of microbial genomes revealed that many more genes are present than metabolites known for each sequenced species. Thus generally, microbes do not activate the genes under laboratory conditions and thus underlying biosynthetic pathways potentially producing novel, so far not yet identified products remain inactive. Only under the very diverse and probably competitive conditions of growth in natural habitats these genes might be expressed and the corresponding products might be produced to serve as defense or signaling compound.

The goal of the research platform "BiMM-Bioactive Microbial Metabolites" (www.bimm-research.at) is to identify new active substances from fungi and bacteria. This platform offers high-throughput equipment and provides know-how and scientific expertise to run high content screens for the identification and characterization of novel bioactive metabolites. To obtain bioactive metabolites a library of fungal and bacterial strains were exposed during combinatorial growth (i.e. fungi and bacteria co-culture) in different growth conditions or in the presence of compounds that interfere with epigenetic regulation of fungal gene clusters. We will report on the successful upscaling, preparation and identification of bioactive and novel substances induced by fungal and bacterial co culture