Development of a fungal platform for the expression of high-valuable natural products

Supervisory team:
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Host institution: University of Bristol, Swansea University
Submit applications for this project to University of Bristol

Project description:
The current antimicrobial resistance crisis is one of the biggest threats impacting health and agriculture and we urgently need to discover new bioactive molecules to target human infections, invertebrate pests for livestock, and fungal crop diseases. Fungi are an incredible source of bioactive compounds such as penicillin, lovastatin and ciclosporin. Recent advances in bioinformatics and sequencing revealed that fungal genomes encode many biosynthetic gene clusters that could synthesize many new compounds, but they are usually inactive under laboratory conditions. Heterologous expression is a successful technique that enables the production of these cryptic bioactive compounds in a host strain. Aspergillus oryzae NSAR1 has been used successfully as a host to express several biosynthetic gene clusters, but improvement of this system is essential in order to deliver a high-throughput expression platform which will accelerate the discovery of new molecules with improved titers. In this multidisciplinary project, microbiological, bioinformatic and chemical techniques will be used to discover new natural products.

The project has two main objectives, one will develop and upgrade the heterologous expression toolkit, which will consist of improving the expression vectors, building a library of tunable promoters, optimizing fermentation and high-throughput compatibility with robots. The second objective will focus on expressing promising gene clusters from two fungal strains that showed good biological activity against a range of plant pathogens. During this project several techniques will be undertaken, these include: microorganism fermentation, genetic manipulation, natural product purification through preparative HPLC, LC-MS/MS for metabolite profiling and dereplication, structural elucidation with MS and NMR techniques, antimicrobial activity assays, including MIC determination and bioinformatics analysis. The research project will be undertaken in the Biosciences Department at Swansea University and in the School of Chemistry at the University of Bristol.

Our aim as the SWBio DTP is to support students from a range of backgrounds and circumstances. Where needed, we will work with you to take into consideration reasonable project adaptations (for example to support caring responsibilities, disabilities, other significant personal circumstances) as well as flexible working and part-time study requests, to enable greater access to a PhD. All our supervisors support us with this aim, so please feel comfortable in discussing further with the listed PhD project supervisor to see what is feasible.