Fungal hosts for production of unusual and unnatural terpene cyclase feedstocks

Supervisory team:
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Project description:

Current methods of crop protection from insects focus largely upon use of insecticides acting as insect toxicants. These can be environmentally harmful and put selective pressures on insect populations leading to resistance. This project instead focuses on using potent natural signalling molecules, semiochemicals, that repel rather than kill pests.

Many semiochemicals are terpenoids, a class of natural products based on a specific natural production pathway in most living things. These complex molecules are formidable challenges for chemical synthesis, but can be produced from simple precursors by enzymes. However, while heterologous expression of terpenoid synthases in *E. coli* is well established and the main precursor (2*E*,6*E*)-farnesyl diphosphate (*E*,*E*-FDP, Figure 1) is readily available, many interesting new compounds require the stereoisomers *Z*,*E*-FDP or *Z*,*Z*-FDP as starting materials. These precursors are rare in nature and sources are limited. This work will develop a natural system for production of these compounds as precursors for new biologically active terpenoids.

This project will place, into a fungal host, genes that encode the enzymes needed to make specific FDP isomers and the synthases that convert these into semiochemicals. Metabolic flux analysis will be used to optimise production, allowing synthesis of potential agrochemicals for testing on far larger scales. Later work will examine the structure and function of the FDP isomer synthases to determine the molecular basis for their selectivity.

In this collaboration between Cardiff Chemistry and the Chemical Ecology group at Rothamsted Research the student will perform a rotation project at each institution during year 1 to prime them for the later research. At Cardiff, they will be introduced to practical molecular and synthetic biology and handling fungal expression systems. At Rothamsted, the student will benefit from internationally acclaimed excellence in targeted metabolite analysis, *i.e.* semiochemical analysis, to gain the theoretical and practical grounding necessary for optimising semiochemical production through metabolic engineering.

This project brings together the fields of synthetic chemistry & biology, targeted secondary metabolite analysis and chemical ecology; hence the student will be immersed in a multidisciplinary environment and acquire scientific skills that will arm them for a future career in academic and industrial bioscience. Regular contact with all collaborators will be maintained throughout and the student will be exposed to top class science from around the world through attendance and presentation at regular seminar programmes at both institutions and at conferences.