

Fungal potentiators of Neuronal differentiation

Project ID: 3521

Supervisory team

Main supervisor: Dr Tim Craig (University of the West of England (UWE))

Second supervisor: Dr Maria Niklison Chirou (University of Bath)

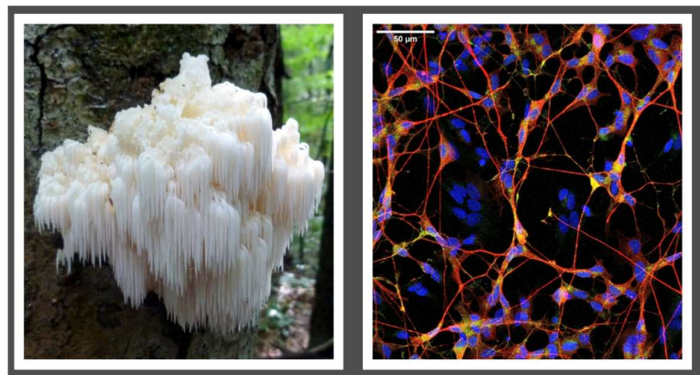
Non-academic (CASE) supervisor: Tom Baxter (The Bristol Fungarium)

Other supervisors: Dr Katherine Williams (University of the West of England (UWE)) & Dr Lucy Crompton (University of the West of England (UWE))

Host institution: University of the West of England (UWE)

CASE partner: The Bristol Fungarium

Project description: Use of medicinal mushrooms is increasingly popular in the alternative health and nutraceutical sector. Several studies have reported neurological benefits of medicinal mushroom extracts and their components, including cognitive enhancement, reduced neuroinflammation, neuroprotection and improved sleep. However, despite this growing interest, there has been little systematic investigation of the biological activity of many of these compounds, or of the cellular signalling pathways and biological processes that they influence.



This project is a collaboration between the University of the West of England and the Bristol Fungarium. We will investigate the biological activity and mechanisms of action of potentially bioactive compounds from medicinal fungi, focusing initially on *Hericium erinaceus* (Lion's Mane) and *Ganoderma lucidum* (Reishi). These fungi produce a diverse range of compounds, including erinacines, hericenones, ergosterols and ganoderic acids, providing an exciting and relatively unexplored source of biologically active molecules. Our preliminary research has identified that *H. erinaceus* extracts enhance neurite outgrowth in a cellular model of neuronal differentiation, with additional evidence suggesting increased synapse formation. Using HPLC, we have identified two potentially bioactive compounds within the extract, and application of the isolated compounds at equivalent concentrations reproduces these effects. This provides an exciting opportunity to investigate how fungal natural products influence fundamental cellular processes involved in neuronal differentiation and maturation. Working in collaboration with the Bristol Fungarium, the project will combine fungal biotechnology, natural-product chemistry, molecular biology and cellular neuroscience. You will investigate how *H. erinaceus* compounds influence intracellular signalling, neuronal differentiation, synapse formation, neurotransmitter release and receptor trafficking using Western blotting, cell biology, confocal microscopy and functional assays. The project will subsequently investigate *G. lucidum* and identify compounds responsible for any neuronal effects. The project will also explore whether these compounds can protect neurons from cellular stress and influence processes relevant to neurodegenerative disease, including amyloid-beta production/oligomerisation and α -synuclein aggregation. Experiments will progress from SH-SY5Y cells (for initial studies) to hiPSC-derived neurones. Continued on next page....

The collaboration with the Bristol Fungarium will provide an additional biotechnology component, investigating how fungal growth and extraction conditions can be optimised to increase production of compounds of interest, supported by HPLC analysis. This is form the basis of the placement component of the PhD project. This interdisciplinary project offers training across fungal biotechnology, natural-product discovery, analytical chemistry and molecular and cellular neuroscience, while addressing fundamental questions about how bioactive compounds influence neuronal function and healthy ageing.

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.