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**Industry-linked 4 year PhD studentship in**

**Molecular Cell Biology (fully funded)**

Centre for Biomedical Sciences

Royal Holloway University of London

Laboratory of Prof Robin SB Williams

**Harnessing the power of cannabinoids as medicinal treatments**

Phytocannabinoids represent a group of over 100 secondary metabolites derived from the Cannabis flower. Medicinal properties of these compounds was initially recognised by traditional Indian healers around 1000 years BC, relating to the treatment of various ailments including tetanus, diarrhoea, tuberculosis and epilepsy. These compounds are still being used in medicine today, where cannabis-based products have recently been shown to be effective in the treatment of chronic pain, multiple sclerosis, epilepsy, and nausea and vomiting, with potential in the treatment of Alzheimer’s disease and cancer. In the last decade, research in this area has focused on the medicinal effects of a range of non-psychotropic cannabinoids, such as cannabidiol (CBD), which has been validated through clinical trials for the treatment of two severe epilepsies. Despite a range of cellular mechanism proposed for specific cannabinoids, our understanding of how they function as medicines in these various roles remains to be defined.

Our research, based in the model system *Dictyostelium discoideum,* has been instrumental in identifying the molecular mechanisms of action of numerous drugs and naturally occurring medicines1-8. This organism enables a range of innovative research approaches to identify the cellular and molecular mechanism of action of medicines9, which we have successfully translated to mammalian or human pre-clinical models4-8. In some fields, our research has had significantly changed our understanding of the mechanisms of widely used treatments10 and the introduction of new therapeutic approaches for disease treatment based upon these discoveries11. In relation to this project, we have used *Dictyostelium* to identify a role for CBD in regulating the folate one carbon cycle relating to epilepsy treatment8, and in reducing mTORC1 activity relating to multiple sclerosis treatment2. We have also identified several potential novel mechanisms of cannabinoids which may underlie effects in other medicinal roles. These studies have thus validated our approach to investigate cannabinoids in the treatment of multiple diseases.

This project will initially be based in *Dictyostelium* to identify and characterize molecular effects of cannabinoids in disease treatment, in collaboration with an industrial partner. The research will involve a range of disciplines including molecular cell biology, biochemistry, metabolomics, pharmacology and neuroscience, and will ultimately include the translation of discoveries to relevant pre-clinical models. Appropriate research training will be given as necessary.

This will be an extremely competitive program, and we are looking for outstanding Masters Graduates or undergraduate students that have finished their degree, with experience in molecular or cell biology research, to join our vibrant research team.

The project will provide a standard RCUK PhD stipend for 4 years. Please note that successful applicants must have appropriate UK/EU residence eligibility. EU student must start in or before January 2022.

 **Closing Date: 6 Sept 2021**

**For further enquiries, please email Prof Robin SB Williams (****robin.williams@rhul.ac.uk****)**

**References**

1. Warren EC, Dooves S, Lugara E, et al. Decanoic acid inhibits mTORC1 activity independent of glucose and insulin signaling. *Proc Natl Acad Sci U S A* 2020; **117**(38): 23617-25.

2. Damstra-Oddy JL, Warren EC, Perry CJ, et al. Phytocannabinoid-dependent mTORC1 regulation is dependent upon inositol polyphosphate multikinase activity. *Br J Pharmacol* 2021; **178**(5): 1149-63.

3. Waheed A, Ludtmann MH, Pakes N, et al. Naringenin inhibits the growth of Dictyostelium and MDCK-derived cysts in a TRPP2 (polycystin-2)-dependent manner. *Br J Pharmacol* 2014; **171**(10): 2659-70.

4. Chang P, Orabi B, Deranieh RM, et al. The antiepileptic drug valproic acid and other medium-chain fatty acids acutely reduce phosphoinositide levels independently of inositol in Dictyostelium. *Dis Model Mech* 2012; **5**(1): 115-24.

5. Chang P, Terbach N, Plant N, Chen PE, Walker MC, Williams RS. Seizure control by ketogenic diet-associated medium chain fatty acids. *Neuropharmacology* 2013; **69**: 105-14.

6. Chang P, Zuckermann AM, Williams S, et al. Seizure control by derivatives of medium chain fatty acids associated with the ketogenic diet show novel branching-point structure for enhanced potency. *J Pharmacol Exp Ther* 2015; **352**(1): 43-52.

7. Kelly E, Sharma D, Wilkinson CJ, Williams RSB. Diacylglycerol kinase (DGKA) regulates the effect of the epilepsy and bipolar disorder treatment valproic acid in Dictyostelium discoideum. *Dis Model Mech* 2018; **11**(9).

8. Perry CJ, Finch P, Muller-Taubenberger A, et al. A new mechanism for cannabidiol in regulating the one-carbon cycle and methionine levels in Dictyostelium and in mammalian epilepsy models. *Br J Pharmacol* 2020; **177**(4): 912-28.

9. Schaf J, Damstra-Oddy J, Williams RSB. Dictyostelium discoideum as a pharmacological model system to study the mechanisms of medicinal drugs and natural products. *Int J Dev Biol* 2019; **63**(8-9-10): 541-50.

10. Augustin K, Khabbush A, Williams S, et al. Mechanisms of action for the medium-chain triglyceride ketogenic diet in neurological and metabolic disorders. *Lancet Neurol* 2018; **17**(1): 84-93.

11. Schoeler NE, Orford M, Vivekananda U, et al. K.Vita: a feasibility study of a blend of medium chain triglycerides to manage drug-resistant epilepsy *Brain Communications* 2021; [doi.org/10.1093/braincomms/fcab160](https://doi.org/10.1093/braincomms/fcab160).