OXFORD INTERDISCIPLINARY BIOSCIENCE
Doctoral Training Partnership

Industrial CASE Studentship Advertisement 2022-23

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Project Title:	Improving molecular pharming with pathogen-derived effectors

Brief description of project:

The transient expression of proteins in plants offers unprecedented opportunities for the fast, safe, cheap and flexible production of vaccines, therapeutic antibodies and research proteins. Many proteins can be expressed *in planta* within days upon infiltrating leaves of the tobacco relative *Nicotiana benthamiana* (*Nb*) with *Agrobacterium tumefaciens* (agroinfiltration) carrying genes-of-interest on a transfer-DNA. Several companies use the agroinfiltration platform to produce vaccines (MedicaGo, Canada), antibodies (iBio, USA) and research proteins (LES, UK). However, although transiently expressed GFP can reach 50% of the total protein content, most recombinant proteins accumulate to a much lower level for various reasons, including immune responses induced by agroinfiltration, mRNA degradation (silencing), and by bottlenecks in protein folding, secretion, post-translational modifications and protein stability.

The PROJECT AIM is to overcome these bottlenecks by identifying novel pathogen-derived effector proteins that boost recombinant protein expression levels. Plant pathogens secrete hundreds of proteins that modify the host to suppress immunity and alter protein expression levels. During this project, we will screen >200 effectors for boosting recombinant protein expression by co-expressing them with our triple reporter system, consisting of bacterial luciferase (LUX, to monitor Agrobacterium); cytoplasmic GFP (cGFP, to monitor gene expression), and secreted RFP (sRFP, to monitor the secretory pathway). These effectors are from a pathogenic bacterium (*Pseudomonas syringae)*, fungus (*Botrytis cinerea)* and oomycete (*Phytophtora infestans*), which all carry effectors that manipulate *N. benthamiana* effectively. Effectors that boost the expression of the reporters will be tested on boosting expression levels of pharmaceutical proteins, such as covid-neutralising antibodies and vaccines. During the internship at Leaf Expression Systems (LES, the industrial partner of this project), these effectors will be tested to ensure they are beneficial to production in a

commercial environment. Finally, we will characterise the mechanism(s) by which the selected effectors boost recombinant protein levels through a broad range of well-established assays.

Attributes of suitable applicants:

We seek an enthusiastic student who is not afraid of large scale experiments and interested in both molecular pharming and plant-pathogen interactions. Experience in protein biochemistry and molecular biology are helpful but not essential.

How to apply:

Applicants should first contact the lead supervisor to discuss whether their research interests are a suitable fit for the project, then apply online via this webpage Interdisciplinary Bioscience (BBSRC Doctoral Training Partnership) | University of Oxford. Please note that we are implementing measures to limit implicit bias in the application process and taking positive action to support students from groups that are under-represented in bioscience. Applicants therefore need to follow the instructions available on the following webpage when preparing an application: Pilot assessment procedure: MPLS doctoral training courses | University of Oxford.

Funding notes:

This project is funded for four years by the Biotechnology and Biological Sciences Research Council UKRI-BBSRC. UKRI-BBSRC eligibility criteria apply (https://www.ukri.org/files/funding/ukri-training-grant-terms-and-conditions-guidance-pdf/). Successful students will receive a stipend of no less than the standard UKRI stipend rate, currently set at £15,609 per year.

This project is supported through the Oxford Interdisciplinary Bioscience Doctoral Training Partnership (DTP) studentship programme. The student recruited to this project will join a cohort of students enrolled in the DTP's interdisciplinary training programme, and will participate in the training and networking opportunities available through the DTP. For further details, please visit www.biodtp.ox.ac.uk. The DTP and its associated partner organisations aim to create a community that is innovative, inclusive and collaborative, in which everyone feels valued, respected, and supported, and we encourage applications from a diverse range of qualified applicants.