How do novel membrane-bound antifungal drug targets control fungal diseases of crops?

Supervisory team:
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Host institution: University of Bath

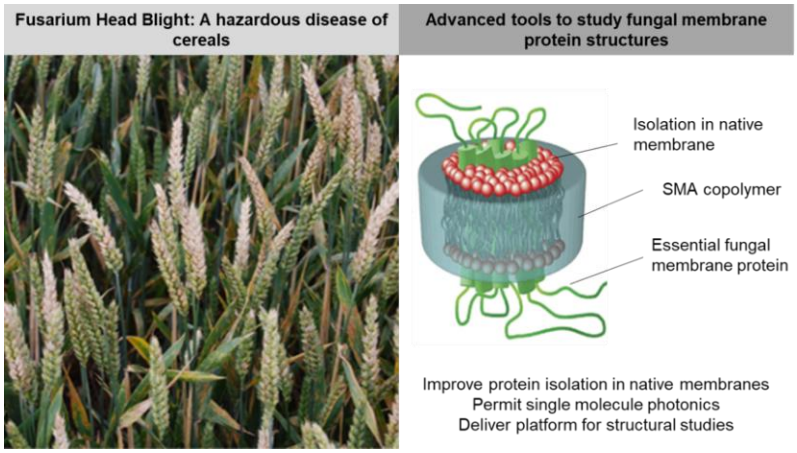
Project description:

WHY ARE FUNGAL DISEASES A THREAT? Increasingly fungal pathogens are destroying and contaminating our crops with harmful toxins. New fungicides are needed to ensure sustainable disease control and our future food security. Fusarium Head Blight (FHB) is the most damaging floral disease of cereals worldwide and a serious health hazard, for which there is no effective control.

ARE FUNGAL MEMBRANE PROTEINS A TARGET FOR CONTROL? Fungal membrane proteins are key cellular components and signalling molecules, with many being essential for life and/or disease (Brown, Nature Microbiology doi:10.1038/s41564-018-0127-5). This includes Fusarium receptors and transporters required for FHB and toxin contamination of wheat (Dilks, Plos Pathogens doi:10.1371/journal.ppat.1007666). But we do not have effective tools to study fungal proteins in their native membrane environment. This impedes our understanding of their functions and their development as novel fungicide targets.

HOW DO FUNGI SENSE THEIR HOST TO PROMOTE DISEASE? Here, we will combine technological advances in nanotechnology, biophysics and gene editing study how fungal membrane proteins sense their host plant environment and promote disease. We will use of styrene maleic acid lipid particles (SMALPs) to isolate Fusarium proteins in their native membranes (doi:10.1021/acs.biomac.7b01539; doi:10.1007/s12274-014-0560-6). Subsequently, we will use single-molecule photonics to study their structures, interactions and functions at an unprecedented scale (doi:/10.1038/s41467-020-15822-8; doi:10.1126/sciadv.1603044). Insights into these dynamic protein structures and functions will then be validated by fungal gene editing and the importance to FHB and toxin contamination on wheat confirmed.

WHAT IMPACT WILL THIS HAVE? This research will deliver a cutting-edge platform to study fungal membrane proteins, with 'transferable' applications to many pathogens, opening fungal membrane proteins as new avenues for fungicide discovery. This FHB study will serve as a proof-of-principle, by advancing our fundamental understanding of why Fusarium membrane proteins are essential for disease, while providing tools to develop novel approaches to inhibit their function and combat FHB.



HOW WILL WE SUPPORT THE STUDENT? Collectively, we offer the student advanced cross-disciplinary training in plant pathology, nanotechnology and structural biology, applying molecular, biochemical and biophysical approaches. The expert supervisory Bath and Exeter teams have a proven track record in funding and publishing high-quality science. The student will join their vibrant Infection & Immunity (Bath) and the interdisciplinary community of the Living Systems Institute (Exeter) and associated postgraduate support communities. They will benefit from spending significant time at both institution and gain expert mentoring from the diverse supervisory team throughout, enhancing their career development opportunities.