The role of RIPP proteins in plant pathogenic fungi

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Project description:

Recently a small secreted toxin called Ustiloxin has been characterised from Aspergillus sp. It is the first Ribosomally synthesised Post-translationally modified Protein (RiPP) of its class in fungi, where a small peptide sequence (present in multiple tandem copies) is excised from a larger peptide then cyclised and extensively modified, indeed the modifications make it impossible to distinguish such products from NRPS-derived natural products, the only other fungal RiPPs to date are the amatoxins from Amanita sp (fly agaric, deathcap & etc), fungi famous for having wide ranging biological activities.

The Wheat-pathogenic fungus Zymoseptoria tritici has a similar gene cluster to ustiloxin within its genome, and RNAseq data shows abundant expression during the biotrophic growth stages, peaking at the transition to necrotrophic growth of this major wheat pathogen. This is the sort of expression profile that might be expected from an effector molecule, perhaps being used to minimise host-defence reactions during early stages of infection. Other studies have also shown this locus to be variable between isolates, suggesting that it is under diversifying selection as might be expected if involved in host-pathogen interactions where the hostplant is undergoing frequent genetic change (due to the activity of plant breeders). The gene for the core protein is embedded in a co-expressed gene cluster with genes for various tailoring functions also present so that the chemical structure of the final mature compound cannot be readily predicted – other than its core peptide sequence and a likely cyclisation event involving an internal tyrosine residue.

The project will aim to identify the final mature metabolite made by the fungus, to characterise its role (if any) during disease and to then seek to explore the wider implications of this class of metabolite in various host-pathogen interactions.

The project will involve genomic and genetic analysis of Z. tritici and related fungi, using gene disruption techniques to explore the role of the gene cluster in disease in these fungi. It will also involve heterologous expression of the genes as a synthetic biology approach to explore the biosynthetic pathway for this compound, coupled with analytical chemistry to determine the structure and conformation of the metabolites.