Project Details	
Project Code	MRCIIAR26Br Dowsey
Title	Artificial intelligence to identify antifungal susceptibility in the clinical diagnostic laboratory
Research Theme	IIAR
Project Type	Wet lab
Summary	Fungal infections have become a major and growing global health crisis, causing an estimated 3.8 million deaths each year particularly among immunocompromised populations. The problem is compounded by the rise of drug-resistant fungal strains and the lack of effective diagnostics. Working with clinical experts in the NHS and abroad, you will adapt data science models and lead development of new deep learning approaches to diagnose critical fungal infections such as azole-resistant Aspergillus fumigatus and echinocandin-resistant Candida glabrata using mass spectrometry techniques available to the diagnostic microbiology lab.
Description	Fungal infections have become a major and growing global health crisis, causing an estimated 3.8 million deaths each year—surpassing the toll of diseases like tuberculosis and malaria. These infections disproportionately affect vulnerable populations and people with weakened immune systems, including those with HIV/AIDS, cystic fibrosis, cancer patients, and organ transplant recipients. The problem is compounded by the rise of drug-resistant fungal strains and the lack of effective diagnostics and treatments, especially in low- and middle-income countries. Climate change and global travel are also contributing to the emergence and spread of new, more drug-resistant fungal pathogens. Addressing this neglected threat requires urgent investment in research, improved diagnostics, wider access to antifungal medicines, and global collaboration to reduce the burden of fungal diseases. The antimicrobial management of patients with systemic infections is considered time critical, and in an era of increasing antimicrobial resistance, the accurate and rapid identification of the agent of infection and its susceptibility to antimicrobial drugs is essential to successful clinical resolution. However, for fungi, susceptibility test results, either by microbroth dilution or by E-test, can take up to 3 days to turn around from microbiological culture. Recent research has demonstrated direct gene sequencing approaches to clinical diagnostics based on marker gene mutations involved in specific antifungal resistance mechanisms, but fungal strain heterogeneity currently limits the sensitivity of these relatively costly approaches. Proteomic approaches with mass spectrometry, and particularly MALDI-ToF mass spectrometry already in routine use in clinical laboratories for species identification, potentially offers an inexpensive route to predicting antifungal resistance based on ribosomal and metabolic protein signatures. In the last few years there has been significant progress in machine learning approaches for mass spectrometry based antibiotic susceptibility testing of bacteria, but relatively little for clinical mycology. The goal of this studentship is to harness our expertise in data science and artificial intelligence approaches for interpreting mass spectrometry data (https://bit.ly/3jM69yS) to develop in-silico susceptibility predictors for clinically-important fungal pathogens. To achieve this, the student will be embedded within the UKHSA National Mycology Reference

	Laboratory in Bristol, with access to their processes, procedures and comprehensive archive of samples, genetic and MALDI-ToF data for patient care and surveillance. From this exemplar, classification studies will be selected and the student will initially apply our current spectral deconvolution methodology used for bacteria to score new fungal isolates from clinical samples based on a library of historic acquisitions linked to antifungal susceptibility test results. The student will then compare these results to novel artificial intelligence methodology based on representative learning approaches that in a data-driven way jointly learn to differentiate diverse phylogenetic signal from consistent signal from resistance mechanisms. The student will also explore how sample preparation and acquisition parameters can be modified to optimise the model, in a data-driven way. In addition, there will be an opportunity to visit LMIC collaborators at the University of Cape Town to adapt and tune models to key local applications such as azole-resistant Aspergillus fumigatus in cystic fibrosis patients. The project is suitable for a students who come from a variety of academic backgrounds, and the supervisory team is experienced in interdisciplinary working. The project will be tailored to the student: we will consider those with a mathematical/computational background open to learning skills in bioinformatics and laboratory work, or those with a biological/biomedical background who desire skills in basic programming, data science and machine learning. The student will be supported to determine the weight they wish to give to each strand during the PhD, and potentially also the target organisms and resistance mechanisms, where their reading and interaction with clinicians suggest the most clinically valuable avenues. For example, the PhD could either have a larger focus on (i) artificial intelligence methodology for modelling strain and resistance specific signals; or (ii) optimisation of sample preparation and mass spectrometry acquisition to maximise distinguishing signals, or (iii) evaluation of how the approaches can be translated within LMIC scenarios.
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