University of Leicester

PhD Project Template

Please complete all fields and email to pgr3i@le.ac.uk

Project Title	Characterisation of novel fungal allergens involved in the pathogenesis of asthma
Supervisors (2 Max) Include email addresses	Dr Catherine Pashley chp5@leicester.ac.uk
	Professor David Cousins dc282@leicester.ac.uk
Funding Status	Self-Funded Students Only
Application Deadline date	Ongoing
Project Description (max 700 words)	Asthma is a common global disease causing considerable morbidity and significant avoidable mortality. Allergy to thermotolerant, airway colonising, filamentous fungi such as *Aspergillus fumigatus* is associated with severe asthma and lung damage, particularly fixed airflow obstruction and bronchiectasis (1,2). However not all asthmatics who are sensitised to *A. fumigatus* develop these complications of asthma for reasons that are not clear. *A. fumigatus* is found in the normal airway and it is possible, as cross reactivity between fungi is common, that allergy to *A. fumigatus* is a surrogate for another fungal species with a more direct pathogenic role. We have used high throughput sequencing (HTS) to characterise the fungal airway microbiome, revealing fungi which could be involved in asthma pathogenesis. Little is known about the allergens produced by these fungi. We hypothesise that the risk of lung damage from fungal airway colonisation in asthma is related to the precise allergenic proteins to which a person is IgE sensitised. We therefore aim to characterise the allergens derived from fungi identified through our HTS analysis as being potentially involved in asthma pathogenesis. Specific objectives include: 1) Development of techniques to detect novel fungal allergens. 2) Full characterisation of allergens from fungal species of interest identified by culture and HTS. 3) Production of recombinant forms of the allergens and development of an ELISA to detect specific IgE against them. 4) Determination of the frequency of sensitisation to the allergens in asthma. 5) Correlation of the presence of specific IgE to these allergens with relevant clinical outcomes. Research plan

	This project will focus on fungi identified from our HTS work as being of potential importance in asthma pathogenesis. You will study a number of these fungi; identifying IgE binding proteins using western blotting and developing techniques to fully characterise these allergens. This will involve the use of patient serum derived IgE bound to magnetic beads to immunoprecipitate IgE binding proteins from specific fungi. These proteins will be characterised by mass spectrometry. Recombinant proteins will be obtained by standard cDNA cloning techniques and their identity as allergens confirmed using western blotting. ELISAs will be developed to help determine their clinical relevance. Using the ELISAs you will determine the percentage of asthmatics IgE sensitised to these allergens and relate sensitisation to clinical outcomes, in particular, lung function and bronchiectasis. You will learn a wide range of techniques in the disciplines of protein biochemistry, molecular biology and mycology.
References	1.) Fairs, A., J. Agbetile, B. Hargadon, M. Bourne, W.R. Monteiro, C.E. Brightling, P. Bradding, R.H. Green, K. Mutalithas, D. Desai, I.D. Pavord, A.J. Wardlaw, and C.H. Pashley. 2010. IgE sensitization to *Aspergillus fumigatus* is associated with reduced lung function in asthma. *Am. J. Respir. Crit. Care Med.* 182:1362-1368. 2.) Woolnough, K.F., M. Richardson, C. Newby, M. Craner, M. Bourne, W. Monteiro, S. Siddiqui, P. Bradding, C.H. Pashley, and A.J. Wardlaw. 2017. The relationship between biomarkers of fungal allergy and lung damage in asthma. *Clin Exp Allergy* 47:48-56
Funding Information	This is a self-funded project.
Link to online Application web page	https://www2.le.ac.uk/research-degrees/phd/applyphd
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