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Summary of research

Key words: Asthma, severe, GWAS, Idiopathic Pulmonary Fibrosis

Application Lay Summary:

1a: This study aims to use Genome Wide Association (GWA) to investigate the genetic basis of severe asthma and Idiopathic Pulmonary Fibrosis (IPF) using patients we recruited from the UK. The approach is to see if genetic changes are found in patients more or less frequently than in people without disease. Both analyses require non-disease control data available in UK Biobank.

Aims:

i) *To identify genetic variants associated with severe asthma.

ii) To identify genetic variants associated with IPF.

*UK Biobank have kindly made data enabling recruitment of mild and severe asthma patients from UK Biobank extending the preliminary application.

1b: A key aim of UK Biobank is “improving the prevention, diagnosis and treatment of a wide range of serious and life-threatening illnesses”. By further defining the genetic basis of asthma and IPF in the proposed study there is potential to gain novel insight into disease mechanisms with scope to contribute to each of these specific aims, e.g. early diagnosis and identification of new

therapeutic targets.

1c: We (lead Ian Sayers) have recruited 2,857 severe asthma and 750 IPF (lead Gisli Jenkins) patients from the UK and are measuring 825,928 genetic changes. Using UK Biobank we will identify subjects without asthma, IPF or other respiratory disease that have these same data. This will enable us to use statistics to identify disease associated genetic variation. We also aim to identify mild and severe asthma subjects from UK Biobank in order to i) compare our severe subjects to UK Biobank mild asthma subjects and ii) provide a replication cohort for the severe asthma-control analyses.

1d: We request access to genotyping data from the entire cohort (anticipated late 2015). To initiate the project we have requested access to available genetic data now (150,000) meeting control, mild or severe asthma definition. We envisage; 105,000/150,000 subjects will meet control criteria. This number will decrease when selected for normal lung function but will provide adequate control subjects (case 1:4 control subjects). We envisage ~18,000/150,000 subjects will have asthma, 1,800 with severe disease. Access to the entire dataset will facilitate identification of additional asthma cases for the replication phase.