

Preliminary results from genome-wide meta-analysis of survival time in idiopathic pulmonary fibrosis

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Introduction: Idiopathic pulmonary fibrosis (IPF) is a rare lung disease of unknown cause, with few effective treatments available and poor prognosis (median survival time of 3 years). Genome-wide studies have identified variants associated with susceptibility to IPF. Although the effects of those variants on survival time have been investigated, no study has investigated survival time genome-wide for IPF. We set out to identify novel signals of association with IPF survival time and to replicate previous reports that variants in *MUC5B* that are associated with increased susceptibility to IPF, are paradoxically associated with an increase in survival time.

Methods: We performed genome-wide analyses investigating survival time in a UK IPF study and a USA IPF study and meta-analysed the results. Survival analyses were performed on variants with minor allele frequency (MAF)>0.5% in both studies using a Cox Proportional Hazards model. Independent variants meeting meta-analysis $P<5\times 10^{-6}$ and $P<0.05$ in each of the separate studies (with consistent direction of effect estimate between studies), are being investigated further in an independent replication dataset.

Results: A total of 963 individuals and 7,730,466 variants were included in the final meta-analysis with maximum follow-up of 16.5 years. A total of 79 independent signals (11 with MAF>5%) reached the criteria described above. Consistent with previous reports, the allele in rs35705950 in *MUC5B* that is associated with increased susceptibility to IPF, shows some association with increased survival time (HR=0.73, 95% CI: [0.61, 0.87], $P=5.08\times 10^{-4}$).

Conclusions: This details the first analysis to investigate survival time genome-wide in IPF.