Human exome-chip meta-analysis identifies novel genetic loci associated with smoking behaviour

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Smoking is a major risk factor for many diseases, including common respiratory disorders such as chronic obstructive pulmonary disease. Previous GWASs have been successful in identifying 13 common SNPs associated with smoking behaviour. Meta-analysing summary data from up to 33 cohorts, we have carried out an association study between the SNPs found on the exome-chip (n ≈250k SNPs), which predominantly assays rare putatively functional variants, and four traits: Smoking Initiation (n≈80k), Smoking Cessation (n≈41.5k), Cigarettes Per Day (n≈26.5k) and Pack Years (n≈33k).

In addition to identifying previously reported signals with regards to smoking behaviour, we have identified SNPs in 5 novel regions, including a rare variant on chromosome 16 (MAF=0.01%). The previously identified SNPs fall within *CHRNA5* (rs16969968, missense), *CHRNA3* (rs938682, intronic) and *IREB2* (rs13180, synonymous) – which are all located at the 15q25 locus. We are currently initiating follow-up studies; and if replicated, the novel loci identified in this study will facilitate understanding the genetic aetiology of smoking behaviour and may lead to identification of drug targets of potential relevance to smoking cessation.