Application number/Title: 18870 - Genetics of alcoholic liver cirrhosis

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Keywords provided by the Applicant PI to describe the research project:

Alcoholic, liver, cirrhosis, GWAS, genetics, hepatitis

Application Lay Summary:

1a: Alcoholic liver cirrhosis (ALC) contributes 50% to the liver disease burden with a significant mortality, no specific diagnostic marker or effective therapy. ALC is a major consequence of drinking but only in up to 20% of chronic excessive drinkers, with evidence for a genetic basis that remains unexplored. Our multinational GenomALC Consortium, funded through the US NIH (~£2 million), is investigating the genetic risk factors associated with ALC through GWAS in thousands of chronic excessive drinkers. The UK Biobank can provide independent cohorts of population controls (non-drinkers; drinkers without ALC) and cases (drinkers with ALC) to confirm these associations.

1b: This proposal is consistent with UK Biobank's undertaking of health-related research in the public interest “resource that can support a diverse range of research intended to improve the prevention, diagnosis and treatment of illness and the promotion of health throughout society”.

1c: The GenomALC consortium is prospectively recruiting drinkers with cirrhosis (cases) and without significant liver disease (controls) under well-defined conditions. A significant retrospective cohort from consortium investigators is also available. We will genotype ~5000 samples using SNP-GWAS (Q2 2016). To confirm associations identified through our GWAS, we aim to analyse available phenotype-genotype datasets through UK Biobank. We also have access to datasets from COGA (Collaborative studies on Genetics of Alcoholism), MVP (Million Veterans Program) and Buch et al, Nature Genetics 2015, to identify risk factors that predispose some drinkers to and protective factors that prevent others from developing cirrhosis.

1d: We will need to access the whole UK Biobank cohort in order to identify subsets of suitable cases and controls relevant to this disease.