Principal Investigator

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Summary of research:

Cardiomyopathy, genetics, diagnosis, genes, variants, population

Application Lay Summary:

1a: Genetic testing is routinely undertaken in the NHS for inherited heart muscle diseases, which affect up to 1 person in 500. Making a genetic diagnosis in an affected individual allows early diagnosis and management of their relatives, who may show no clinical signs of the disorder, but are at risk of disease related complications, including sudden death.

More than 1500 variants in over 30 genes have been reported in individuals with these conditions, but not all are disease causing. The success of genetic testing relies on our ability to distinguish between normal and disease causing variants. Each individual disease-causing variant is presumed to be rare in the general population; however, comparative population data on healthy individuals is not readily available (as most existing studies focus on people with disease). If specific variants are not as rare as expected it is unlikely that they cause disease as previously assumed.

Our aim is to interrogate the Biobank data set to determine the frequency of genetic variants previously detected in heart muscle disease patients. The results of this analysis will improve our ability to interpret the results of genetic testing and thereby increase the clinical utility of testing in these conditions.

1b: This research will advance our understanding of normal and disease causing variation in the most common cardiomyopathy genes; this will significantly enhance our ability to interpret the results of genetic testing for this condition. Ultimately this will improve the diagnosis and treatment of these serious, life threatening conditions.

1c: The focus of our research is the Biobank Axiom Array genotype data; specifically the subset of 1,710 markers which represent variants previously detected in individuals with cardiomyopathy and other markers which lie within

known cardiomyopathy genes. We will interrogate this data to determine the frequency of cardiomyopathy gene variants in the Biobank cohort.

1d: Full cohort.