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Wellcome Trust’s Mainstreaming Cancer Genetics Programme

Summary of research
Cancer, variant interpretation, genomic medicine

Application Lay Summary:

1a: Clinical testing of cancer predisposition genes is becoming routine. It is important to ensure accuracy in interpretation of identified variants. The sample size of UK Biobank enables us to generate improved estimates of frequencies of variants in cancer predisposition genes in the UK population. Using this information, we can better evaluate which variants are most likely to be causally-related with cancer (since variants that are more common in the population are less likely to be linked with disease). This information will greatly facilitate our ongoing strategies to develop and evaluate informatics tools and resources for rapid, robust clinical variant interpretation.

1b: A key aim of UK Biobank is “improving the prevention, diagnosis and treatment of a wide range of serious and life-threatening illnesses”. In this research, we will be studying variants in cancer predisposition genes. By improving understanding of the underlying genetic contribution to disease, the proposed research will have direct clinical utility to inform patients and relatives
of the genetic nature of their disease. In turn, this can improve the prevention, diagnosis and treatment of disease.

1c: We will calculate the frequency of variants in cancer predisposition genes in the Biobank general population. With this information, we can formally categorise common variants as non-pathogenic. Additionally, we can improve stratification of less common variants by comparing the frequencies between the Biobank general population, Biobank individuals who have had cancer, and data from other sources, including national and international databases and our own extensive cancer data.

1d: We request genome-wide genotyping data on the full cohort. We will set-up and undertake analyses on the first available set of ~150,000 individuals and then we will analyse the full series when it is available.