

TURNBULL Clare EOI 2022 - ICR

Project title: Massive germline exome sequencing to identify novel breast cancer susceptibility genes.

Project Summary:

Genomic analyses in breast cancer have been highly productive with >45% of the heritable risk explained by high- and intermediate-penetrance genes identified via linkage/candidate gene sequencing and >250 common variants identified by GWAS. Many of these genes are tested for in the clinic and studies are underway examining risk-stratified breast-cancer screening based using polygenic risk scores comprising GWAS-identified SNPs. At the ICR we hold the largest series of hereditary breast-ovarian cancer samples in the world, which were used for the first breast cancer GWAS analyses and the experiments by which BRCA2, ATM, CHEK2, PALB2 and RAD51D were identified as cancer susceptibility genes. We have now initiated exome sequencing of this entire series (>20,000 probands plus familial samples), offering unprecedented opportunity for identification of additional breast cancer susceptibility genes with accordant high impact outputs.

The appointed clinical fellow will lead on bioinformatics and statistical analyses of the case control exome data, focusing on a range of gene discovery analyses spanning breast cancer subtypes and genetic inheritance models. Whilst experience in programming, statistical and/or data-processing would be an advantage, the fellow will be fully trained in the relevant methods, be supported by 3 experienced bioinformaticians and will sit with 4 other data-focused clinical fellows/PhD students. The team is focused not only on gene discovery experiments but also on characterisation of risk and variant pathogenicity, and has a large program of work partnering with Public Health England in linkage of NHS genomic data with cancer registry data.

There would be multitudinous opportunities for involvement in national clinical-facing activities led by Turnbull (Clinical Geneticist), including the monthly national NHS lab CanVIG-UK (Cancer Variant Interpretation Group-UK) MDT and/or clinical guidance development as part of the CGG-CanGene-UK national clinical cancer genetics MDT. The fellowship would reside in the ICR/Imperial Joint Cancer Epidemiology and Prevention Research Unit (CEPRU)

Supervisory Team:

- Prof Clare Turnbull, Genetics and Epidemiology, Institute of Cancer Research
- Dr. Kostas Tsilidis, Department of Epidemiology and School of Public Health, Imperial College London
- Professor Marc Gunter, Imperial College Department of Epidemiology and Public Health, and International Agency for Research on Cancer (IARC), France. Expertise in genetic epidemiology of breast cancer susceptibility.

Clinical Specialities: Clinical Genetics, surgical/medical/clinical Oncology, pathology or Public Health.