CRUK Cambridge Centre MRes rotation project

Rotation Project Title	**Using data from large scale international collaborative studies to understand the associations of genetic/lifestyle/hormonal risk modifying factors by breast cancer tumour subtypes in BRCA1 and BRCA2 mutation carriers.**
Head of Laboratory (PI) Name	Antonis Antoniou
Second supervisor if applicable	
Programme	Quantitative Breast Gynae
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Laboratory Location	Strangeways Research Laboratory, Department of Public Health and Primary Care

Project Outline	**Aims and objectives** Genetic testing and assessment for *BRCA1*and *BRCA2*, is widely available and has become an integral part of the genetic oncologic and gynaecologic practice and is used to inform women's treatment or clinical management options. Studies have identified several common genetic variants (SNPs) which modify breast and ovarian cancer risks for BRCA1 and BRCA2 mutation carriers. In addition, evidence suggests that mutation location and mutation characteristics and other hormonal/lifestyle factors also influence cancer risks for BRCA1/2 mutation carriers. Combining data on other genetic variants and hormonal/lifestyle factors can improve our ability to estimate individualised cancer risks for mutation carriers and will allow for informed choices about the type and timing of cancer risk management. The specific aims of this project will be: • To assess whether common genetic variants or lifestyle/hormonal risk factors are associated with the risk of specific breast cancer subtypes in BRCA1 and BRCA2 mutation, in particular whether they are associated with the risks of oestrogen receptor positive or oestrogen receptor negative breast cancer. • To investigate the implications for predicting future cancer risks for BRCA1 and BRCA2 mutation carriers.
Experimental plan	Analyses will be based on data available at the Centre for Cancer Genetic Epidemiology and include data from large international Consortia (Consortium of Investigators of Modifiers of BRCA1/2: >55,000 samples; International BRCA1/2 Carrier Cohort Study: ~10,000 mutation carriers) and data from the UK national study study EMBRACE.
Main Techniques	• Statistical genetics, epidemiology, genetic epidemiology, biostatistics • Genome-wide association studies, cohort studies, survival analysis • Statistical software/programming: R, STATA

Key References	Modifiers of breast and ovarian cancer risks for BRCA1 and BRCA2 mutation carriers. Milne RL, Antoniou AC. Endocr Relat Cancer. 2016 Risks of Breast, Ovarian, and Contralateral Breast Cancer for BRCA1 and BRCA2 Mutation Carriers. Kuchenbaecker et al JAMA 2017 Evaluation of Polygenic Risk Scores for Breast and Ovarian Cancer Risk Prediction in BRCA1 and BRCA2 Mutation Carriers. Kuchenbaecker KB JNCI 2017