Application Number / Title: 21146 - Genome-wide association study for cervical intraepithelial neoplasia and cervical cancer.

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Keywords provided by the Applicant PI to describe the research project: Cancer, cervix, dysplasia, GWAS, CIN.

Application Lay Summary:

1a: Cervical cancer develops after HPV (human papilloma virus)-infection through detectable cervical intraepithelial neoplasias (CIN) that can be treated before their progression into invasive disease and thus prevent the cancer. Most women, however, clear the HPV infection within few months and only a fraction of women infected with HPV develop a CIN or an invasive cancer. Using Northern Finland Birth Cohort 1966 we identified ten novel SNPs (p<5x10E-8) associated with increased risk of CIN or cervical cancer. To significantly increase the sample size, and to replicate the initial findings, we are applying relevant data from UK Biobank.

1b: Identifying novel mutations predisposing to cervical cancer would improve the understanding of the genetic susceptibility to cervical cancer and potentially enable new strategies to diagnose and even prevent the disease.

1c: We aim to perform a nested case-cohort GWAS (genome wide association study) for cervical intraepithelial neoplasia (CIN) and cervical cancer. Women with GWAS data in the cohort with diagnosed CIN or cervical cancer will serve as cases and all other women with GWAS data and without CIN or cervical cancer diagnosis as controls. Group members have vast experience in the field of genetic epidemiology and GWASs and the analyses will be performed at Imperial College London, School of Public Health, using the Imperial College’s High Performance Computing facilities.

1d: UK Biobank has over 700 cervical cancers and over 5700 Ca in situ (CIN3) cases (Data fields 40006 & 40013). We apply to include all women in the UK Biobank cohort with GWAS data in our study cohort. Based on initial power calculations,
including all approximately 6,400 cases with only 1:4 control ratio, would already give 80% statistical power with alpha of 1E-8 to detect single SNP Or of 1.4 at minor allele frequency (MAF) of 5%, OR of 1.3 at MAF 10% and OR of 1.2 at MAF of 15%.