

ENDOMETRIOSIS – LINKAGE, POSITIONAL CLONING AND GENOME WIDE ASSOCIATION

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Endometriosis is a complex disease which affects up to 10% of women in their reproductive years. Common symptoms include severe dysmenorrhea and pelvic pain. The disease is associated with subfertility and some malignancies. Genetic and environmental factors both influence endometriosis. The aim of our studies is to identify genetic variation contributing to endometriosis and define pathways leading to disease. We recruited a large cohort of affected sister pair (ASP) families where two sisters have had surgically confirmed disease and conducted a 10 cM genome scan. The results of the linkage analysis identified one chromosomal region with significant linkage and one region of suggestive linkage. The regions implicated by these studies are generally of the order of 20–30 cM and include several hundred genes. Locating the gene or genes contributing to disease within the region is a challenging task. The best approach to the problem is association studies using a high density of SNP markers. The recent development of human SNP maps and high throughput SNP genotyping platforms makes this task easier. We have developed high throughput SNP typing at QIMR using the Sequenom MassARRAY platform. The method allows multiple SNP assays to be genotyped on the same sample in a single experiment. Throughput and genotyping costs depend critically on this level of multiplexing and we routinely genotype 6–8 SNPs in a single assay. We are using bioinformatics and functional approaches to develop a priority list of genes to screen early in the project. SNP markers in these genes are being genotyped using the MassARRAY platform to search for genes contributing to endometriosis. In the future, genome wide association studies with our families may locate additional genes contributing to endometriosis.