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Gene expression in the endocannabinoid system in the endometrium of women with and without endometriosis

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Purpose – Endometriosis is a significant health issue for women. It causes debilitating pain symptoms and infertility impacting the social participation and mental health. The endocannabinoid system (ECS) has been recognised as a potential molecular therapeutic target for endometriosis. The objective of this study was to investigate the effects of genetic variants on the gene expression of the endocannabinoid system.

Methods – Endometrial tissue samples were collected and RNA isolated. Genome-wide gene expression datasets were generated using RNA-seq technology. Expression quantitative trait loci (eQTL) analysis was performed based on the association between RNA-seq counts and genotype data.

Results – 40 of the 70 ECS genes examined were expressed in >90% of the samples. We identified 2 eQTLs that passed Bonferroni correction for multiple testing on chromosome 1 near FABP3, an intracellular endocannabinoid transporter. Furthermore, there was an additional 1,114 FDR significant eQTLs for additional 12 ECS genes. 9 genes encode synthesising enzymes (3 isoforms of PLC, 3 isoforms of PLA2, GDE 1 and 4, and ABHD4) and 3 genes encode catabolising enzymes (NAAA, ABHD12, ALOX5).

Conclusion – FABPs were the first protein identified as intracellular carriers that deliver endocannabinoids to catabolising enzyme for inactivation. These genotypes which significantly affect FABP3 gene expression present a potential for establishing disease subtypes for personalised cannabinoid-based treatment and biomarker development. In addition, genotype effect on expression of NAAA is a particular interest. NAAA is one of the main catabolising enzyme for palmitoylethanolamide (PEA) which has been shown to improve pain and quality of life among women with endometriosis. Genotyping may play a role in predicting treatment response with PEA.