

## Abstract S-114: The Medium-Chain Free Fatty Acid Receptor GPR84 in Endometriosis Associated Pain

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**INTRODUCTION:** The G-protein coupled receptor GPR84 binds and becomes activated by saturated medium-chain free fatty acids, is expressed on pro-inflammatory macrophages and pharmacological inhibition leads to reduction of inflammatory markers. **METHODS:** First, we study GPR84 expression and medium-chain free fatty acids levels in eutopic endometrium and endometriotic lesions. Furthermore, we study the effect of GPR84 agonists and antagonist in various in vitro inflammatory models on cytokine secretion. Finally, we characterized the link between GPR84 and inflammatory pain in experimental models including an endometrial explant and an in vivo CFA inflammatory pain model. **RESULTS:** Our results indicate that GPR84 is expressed in endometriotic lesions and that the endogenous agonists, the medium-chain free fatty acids, are more abundant in lesions than in eutopic endometrium. Furthermore, the receptor is induced by pro-inflammatory stimuli such as LPS and IFN $\gamma$  and regulates production of inflammatory mediators such as TNF $\alpha$  and IL-6 in peripheral blood monocytes. Inhibition of GPR84 with the antagonist CMPD139 reduces pro-inflammatory cytokines and growth factors in inflammatory macrophage and endometrial tissue slice assays. Pharmacological GPR84 inhibition in an in vivo inflammatory pain model leads to significant reduction of pain scores. **CONCLUSION:** GPR84 is a pro-inflammatory receptor and inhibition reduces cytokine levels and pain score in inflammatory in vitro and in vivo models suggesting therapeutic benefit of modulating GPR84 ligand binding in inflammatory conditions such as endometriosis.