


## Presentation Abstract

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**Abstract Title:** Effect of Palmitylethanolamide on Aqueous Humor Outflow

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**Abstract Body:** **Purpose:** To study the effects of palmitoylethanolamide (PEA), a fatty acid ethanolamide and an endogenous cannabinoid, on aqueous humor outflow via the trabecular meshwork pathway. **Methods:** The effects of PEA on aqueous humor outflow via the trabecular meshwork pathway were measured using a porcine anterior segment perfused organ culture model. Different concentrations of PEA were administered to the perfusion medium and the aqueous humor outflow facility was monitored for 5 hours. CB1 antagonist SR141716A and CB2 antagonist SR144528 were used, respectively, to investigate the possible involvement of CB1 and CB2 receptors in the outflow effects induced by PEA. O-1918, a cannabidiol analog that acts as a selective antagonist at the non-CB1/CB2 receptors, was also used to investigate whether non-CB1/CB2 cannabinoid receptors are involved in the PEA-induced outflow effects. PEA induced activation of p42/44 mitogen-activated protein (MAP) kinase was determined by western blot analysis using an anti-phospho p42/44 MAP kinase antibody. **Results:** Administration of PEA caused a concentration-dependent enhancement of aqueous humor outflow facility, with the maximum effect ( $135.6 \pm 7.1$  % of basal outflow facility) achieved at 2 hour after the administration of 30 nM of PEA. Pretreatment with 1  $\mu$ M O-1918 produced a full antagonism on the PEA-induced increase of aqueous humor outflow facility. However, pretreatment with 1 $\mu$ M of SR141716A or 1 $\mu$ M of SR141716A had no effect on PEA-induced enhancement of aqueous humor outflow facility. Treatment of trabecular meshwork cells with PEA for 10 min activated phosphorylation of p42/44 MAP kinase which was blocked by pretreatment with O-1918. Furthermore, PD98059, an inhibitor of the p42/44 MAP kinase pathway, blocked both PEA-induced phosphorylation of p42/44 MAP kinase and enhancement of aqueous humor outflow facility. **Conclusions:** The results from this study demonstrate that PEA increases aqueous humor outflow through the trabecular meshwork pathway, and these effects are mediated by non-CB1/CB2 cannabinoid receptors through activation of p42/44.

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