



## Conference Abstract

# P.29 Involvement of Cannabinoid Receptors in Regulation of MMPs, Cell Proliferation and Apoptosis in Vascular Smooth Muscle Cells

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### Keywords

MMPs VSMC cannabinoid receptors

### ABSTRACT

**Objectives:** Cannabinoid receptors CB1R and CB2R are expressed in the vascular smooth muscle cells (VSMCs) and may contribute to vascular remodeling process (O'Sullivan, 2015). This study aimed to investigate the implication of CB1R and CB2R in the regulation of matrix metalloproteinases MMP2 and MMP9, cell proliferation and apoptosis.

**Methods:** Primary VSMCs of contractile type were derived from rat aorta. Following compounds were studied: the CB1R agonist arachidonyl-2-chloroethylamide (ACEA), the CB1R antagonist/inverse agonist rimonabant, the CB2R agonist JWH133, the CB2R antagonist/inverse agonist AM630. The cells were treated with compounds simultaneously with IL1 $\alpha$  stimulation. MMP2 and MMP9 were analyzed 48h after treatment via gelatin zymography, Western blotting and immunofluorescence. Apoptotic markers FasL, Caspase-3 and TGF $\beta$ 1 were used. This experimental setup was repeated using IncuCyte cell imaging to evaluate cell proliferation and apoptosis.

**Results:** The CB2R agonist JWH133 decreased the activity of proMMP9 ( $p < 0.05$ ), abolished IL1 $\alpha$  -induced up-regulation of proMMP9/MMP9 proteins, and decreased MMP2 activity by tendency (11%). JWH133 also decreased the number of apoptotic cells ( $p < 0.05$ ). Accordingly, CB2R antagonist AM630 did not prevent MMP9 release. CB1R antagonist Rimonabant reduced activity of proMMP9 (35%) and MMP2 (4%) and abolished protein up-regulation of proMMP9/MMP9. CB1R stimulation with ACEA had an ambiguous effect. JWH133 and Rimonabant increased cell proliferation ( $p < 0,05$ ) and decreased expression of apoptosis markers FasL and caspase-3.

**Conclusions:** The CB2R agonist JWH133 and CB1R antagonist Rimonabant prevented release of MMP9 and cell death of VSMCs. Therefore, stimulation of the CB2R or blockade of the CB1R may be favorable by vascular outward remodeling processes.

### REFERENCES

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