17 β -estradiol reverses apelin-inducing ovarian cancer cell proliferation

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INTRODUCTION

Apelin:

- ✓ bioactive adipocytokine that is highly expressed by various tissues in the human body with serum concentration $1,31 \pm 0,12$ ng/ml
- ✓ apelin and its receptor (APLNR) are expressed by ovarian tumor cell lines and acts as a mitogenic factor in these cells (Hoffmann et al., 2017)
- ✓ apelin by binding to its receptor, share the same signaling pathways with 17 β -estradiol (E2) and insulin-like growth factor 1 (IGF-1) such as ERK1/2.

Moreover, alterations in the secretion of adipokines affect cell proliferation, apoptosis, tumor invasion and angiogenesis.

Thus, we investigated whether apelin can interact with E2 or IGF-1 and regulate ovarian cancer progression.

RESULTS

Fig. 1. Effects of apelin (2 ng/ml) on expression of estrogen receptor α (ESR1), estrogen receptor β (ESR2) and G-protein coupled estrogen receptor 1 (GPER1) in OVCAR-3 cells. Expression of ESR1, ESR2 and GPER1 after exposure to the apelin for 24 h. RQ, relative quantity; C, control (untreated cells).

Fig. 2. Effects of apelin (2 ng/ml) in combination with the 17 β -estradiol (E2) or insulin-like growth factor 1 (IGF-1) on OVCAR-3 cell proliferation at 48 h. C, control (untreated cells). Statistically significant differences are indicated by * $p < 0.05$, *** $p < 0.001$ (compared with control untreated cells).

Fig. 3. Effects of ERK1/2 inhibition on apelin- and E2-induced changes in cell proliferation in OVCAR-3 cells. The cells were pretreated for 2 hours with the ERK1/2 inhibitor PD098059 (5 μ M) and then exposed to the apelin (2 ng/ml), E2 (1 nM), or both for a further 48 hours (in the presence of the inhibitor). C, control (untreated cells). Statistically significant differences are indicated by * $p < 0.05$, ** $p < 0.01$ (compared with control untreated cells).

Methods

- Cell line: human ovarian serous carcinoma cell line OVCAR-3 (ATCC)
- Cell proliferation: CellTiter-Glo Luminescent Cell Viability Assay reagent (Promega)
- qPCR: TaqMan Gene Expression Cells-to-CT (Applied Biosystems)
- Statistical analysis: one-way ANOVA followed by Tukey's test ($P < 0.05$), (GraphPad Software)

CONCLUSION

Taken together, our results suggest that ERK1/2 signaling pathway is involved in apelin and E2 regulated ovarian cancer cell proliferation. We also showed that antagonistic effect of apelin and E2 together is not mediated by ERK1/2 pathway and further studies are needed.

Hoffmann M, Fiedor E, Ptak A. Bisphenol A and its derivatives tetrabromobisphenol A and tetrachlorobisphenol A induce apelin expression and secretion in ovarian cancer cells through a peroxisome proliferator-activated receptor gamma-dependent mechanism. *Toxicol Lett.* 2017, 269:15-22.