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The Role of Oxysterols as Selective Oestrogen Receptor Modulators (SERMs) at Promoting Tumour Growth in Adrenocortical Carcinoma.

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Abstract

Adrenocortical carcinoma (ACC) is an aggressive and rare endocrine malignancy with very limited treatment options at present. Besides, its recurrence rate is high and can occur following a short period. ACC is a steroidogenic cancer which produces steroid hormones, that all share cholesterol as a key building unit. Thus, cholesterol active metabolites (oxysterols) could potentially interfere with these steroid pathways and produce different cellular modifications through different receptors including ERs. In ER+ breast cancer cells, oxysterols (i.e. 27Hydroxy Cholesterol) promote cell proliferation through oestrogen receptor alpha ERα. Therefore, we hypothesized that oxysterols as selective oestrogen receptor modulators (SERMs) could act similarly via ERs in ACC cells (H295R) and promote cell growth. In this study, H295R cells were treated for 24-h with (27HC) at various doses (0, 10, 20, 40, 80 uM) alone or combined with hydroxyl-tamoxifen (10uM OHT) or/ and 10nM 17-β estradiol (E2) in order to investigate the proliferative effect. The same treatment scheme was applied on MCF7 breast cancer cells. The principle experimental technique was crystal violet staining in which cells growth was measured via spectrophotometer at 550nm.

The findings showed that 27HC plays a role in stimulating cell division on H295R cells. However, this effect is being further enhanced in the presence of other agents: E2 and OHT. As for the MCF7 control cells, the outcomes were correlated to a previous work that 27HC stimulates cell proliferation and OHT inhibits tumour formation. Overall, 27HC showed an expected effect, whereas, OHT unexpectedly induced cell density. Therefore, further work should consider the unexpected stimulatory effect of OHT and its mechanistic pathway, prior to suggesting it as an anti-estrogenic drug in ACC setting.

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