Leptin modulates protein expression in endometrial adenocarcinoma cells with distinct localization patterns

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Endometrial cancer, the second most frequently diagnosed malign neoplasm in female genital system after cervical cancer, presents poor survival and association with high body mass index. Leptin, an adipokine elevated in obesity and a key risk factor for endometrial cancer, may modulate tumor progression through angiotensin-converting enzyme 2 (ACE2), a member of renin angiotensin aldosterone system with emerging roles as a potential biomarker in cancer biology [1]. Here, we investigated leptin's effects on ACE2 expression and observed its localization in HEC-1-A endometrial adenocarcinoma cell line (HTB-112). The cells were treated with 100 ng/ml leptin and 24 hours after treatment, ACE2 levels were assessed via immunostaining with ACE2 polyclonal antibody (bs-1004R). Analysis of ACE2 expression in endometrial adenocarcinoma cells revealed that leptin treatment significantly upregulated ACE2 levels compared to untreated controls, as quantified by corrected total cell fluorescence (CTCF) across all cells ($p = 0.0162$) and specifically in non-mitotic cells ($p = 0.0037$). Notably, ACE2 localized predominantly to the nucleus in non-mitotic cells, while exhibiting a cytoplasmic granular pattern in mitotic cells, suggesting cell cycle-dependent distribution [2]. This study provides the first evidence that leptin upregulates ACE2 in endometrial adenocarcinoma, a novel finding that may link obesity-driven mechanisms [3] to tumor behavior. This leptin-ACE2 interaction unveils a previously unrecognized pathway, meriting further exploration of its role in cancer progression.

Keywords: Endometrial Cancer, Leptin, Obesity, ACE2, RAAS

References:

[1] Yang J, Li H, Hu S, Zhou Y. Aging (Albany NY). 2020;12(8):6518-6535. doi:10.18632/aging.103100

[2] Ray I, et al. Cancer Metastasis Rev. 2022;41(1):211-242. DOI: 10.1007/s10555-021-10002-6

[3] Dalamaga M, et al. Curr Obes Rep. 2021;10(3):214-243. DOI: 10.1007/s13679-021-00436-y