ROLE OF ECTO-NUCLEOTIDASES IN HUMAN ENDOMETRIAL PATHOLOGIES

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Introduction: Extracellular adenosine concentration in the tissue microenvironment increases during tissue stress conditions such as hypoxia, infection, metabolic stress, tumor transformation, and inflammation. High levels of extracellular adenosine have immunosuppressive and cell proliferation effects. The main source of adenosine is the dephosphorylation of ATP by ecto-nucleotidases. The aim of the present study was to characterize the expression and activity of ecto-nucleotidases in the context of two endometrial pathologies: endometrial cancer and endometriosis.

Material and methods: We analyzed, by means of immunolabeling and *in situ* activity assays, the following human endometrial tissues: 1) endometrial tumors and 2) eutopic endometria, as well as ectopic endometriotic lesions from women with endometriosis. For studies with tumors an *in silico* analysis was also performed. Moreover, endometrial cell lines were used to study the effects of different drugs, such as tamoxifen, known to increase the risk of developing endometrial cancer.

Results: Ecto-nucleotidases showed a differential pattern of expression in pathological conditions when compared with nonpathological endometria. This altered pattern included changes in expression levels and changes in protein localization, mainly a switch between epithelium and stroma. We have identified a novel mode of action of tamoxifen in endometrium that causes an increase in extracellular adenosine concentration.

Conclusions: Dysregulation of ecto-nucleotidase activity in endometrium might be the cause of endometrial pathologies with an inflammatory component such as cancer and endometriosis.

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