**EGFR as potential new molecular target in the medical treatment of Adrenocortical Cancer**

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**BACKGROUND**

Adrenocortical cancer (ACC) is a rare and aggressive malignancy. Currently the main therapeutic option is surgery, but due to difficult and delayed diagnosis and to the onset of metastases, medical therapy is often tried. ACC treatment is mainly represented by Mitotane alone or in association with chemotherapy, with variable results. Understanding the molecular mechanisms that regulate ACC proliferation could be useful to identify new therapeutic options.

**AIM**

The aim of our study is to verify whether EGF pathway could represent a target for Sunitinib in human ACC cells. For this purpose we used 2 human adrenocortical carcinoma cell lines (SW13 and NCI-H295 cells) and human adrenal tumor primary cultures.

**METHODS**

As an in-vitro model we use 2 ACC cell lines, NCI-H295 and SW-13, and human primary cultures. We evaluate cell viability by ATPLite assay. Protein expression was evaluated by western blot and Surefire assay. By a Caspase 3/7 assay we determined apoptosis.

**CONCLUSION**

We investigated in both cell lines the expression of EGF family members, which are more expressed in SW13 cells as compared to NCI-H295 cells. Moreover, we investigated the intracellular signal transduction pathway of EGF in ACC cells. Our results show that in SW13 cells Sunitinib inhibited EGF phosphorylation on tyrosine 1068, and counteracted EGF-induced phosphorylation of ERK1/2. In SW13 Sunitinib increased the expression of SAPK/JNK leading to caspase 3/7 activation. In NCI-H295 Sunitinib did not reduce EGF phosphorylation, but inhibited PI3K/mTOR/AKT pathway.

**Conclusion**: EGF may be important in regulating EGFR expressing ACC cell proliferation.

In conclusion our data suggest that EGF pathway could represent a new molecular target in drug design for treatment of ACC that display enhanced EGFR expression.