new HSD17beta1 inhibitors in Cancer Therapy

Development status

Preclinical trials

IP protection status

PCT/CZ2017/050022

Partnering strategy

Collaboration, licensing

Institution

The Institute of Organic Chemistry and Biochemistry of CAS

Challenge

17βHSD1 is an enzyme that has been known to play a pivotal role in tissue specific estradiol (E2) synthesis for more than fifty years. E2 is a very potent hormone, which regulates the expression of a variety of genes by binding to estrogen receptors (ER) and thus it plays a crucial role in the physiological as well as pathological proliferation and differentiation of the target cell. 17βHSD1 affects breast cancer cell proteome and modulates expression of several genes at both mRNA and protein levels. Furthermore, it is associated with an increased risk of cell migration and cancer relapse. Therefore regulation of 17βHSD1 should be considered as potential novel endocrine therapy or 17βHSD1 expression as an independent prognostic marker in breast cancer patients.

Description

We have successfully developed highly potent and specific non-estrogenic inhibitors of 17βHSDs. We have recently shown the efficacy of these compounds in in vitro and in vivo testing of E1 to E2 conversion after application of lead compounds. SAFETY - NOVELTY No toxic effect up to 2mg/kg Low estrogenisity of lead compound EP449 Experiments on T47D cells show inhibition of HSD17b1 (accumulation of E1 in HPLC MS/MS detectable) proof of concept experiment in eggs has been successful - with reduced tumor size and number of metastases, in comparison to Tamoxifen (standard care)

Commercial opportunity

We are looking for out-licensing partners or partners to co-develop the project further