Abstract

Oxysterols are oxidized derivatives of cholesterol that play an important role in the pathogenesis of many diseases, including cancer. They affect processes such as cell proliferation, apoptosis, and cell migration and may also influence the efficacy of some anticancer drugs. Their levels may also be associated with the prognosis of cancer patients. The present thesis summarizes studies that expand the knowledge on the importance of oxysterols in breast cancer at different levels.

In the first study, we analyzed gene expression of key factors of the oxysterol signaling pathway on the prognosis of patients with estrogen receptor (ER)-positive breast cancer. The results of this analysis revealed the association of the expression of some genes with clinico-pathological data of patients, such as tumor stage (according to TNM classification) or the tumor grade. Furthermore, we revealed an association between *ABCG2* gene expression and disease free survival of patients. However, for other genes, the prognostic potential will require validation in a larger cohort of patients.

The second study was designed to determine plasma levels of seven oxysterols in patients with ER-positive breast cancer. This study resulted in an association of the levels of different oxysterols with tumor size or stage. Higher levels of cholestan-3β,5α,6β-triol were then associated with worse prognosis and shorter disease free survival in patients, especially in the tamoxifen-only treated group.

The last study of this thesis was an *in vitro* analysis focused on the effect of 7-ketocholesterol on ER positive and ER negative breast cancer cell lines. In this case, we found that 7-ketocholesterol can influence the efficacy of tamoxifen regarding the ER positivity/negativity of the cell line and also the migratory potential of the studied cell lines regardless of their ER status. Gene expression analysis revealed a different regulation of the *CYP1B1* enzyme, which was then also validated at the protein level.

This thesis thus provides new insights into the prognostic potential of gene expression of the oxysterol pathway or extend the existing knowledge of the relationship between oxysterol levels and e.g. survival of breast cancer patients. It also shows a previously unpublished effect of 7-ketocholesterol, which may have a role in hormonal therapy of breast cancer and is an interesting candidate for our future studies.