Abstract

Ovarian cancer is the most common cause of death from gynecological malignancy. Taxanes and platinum derivatives are most used therapeutics for its treatment. Development of multi drug resistance to chemotherapy represents a serious complication of the treatment. Therefore, new chemotherapeutic and therapeutic targets are investigated, which could help to overcome tumor cell resistance.

The main objectives of the thesis were to study: i) the efficiency of new derivatives of conventional taxanes in vitro with the aim to determine the potentially most effective taxane derivatives in resistant tumor ovarian cells and, ii) the gene expression profile of the Notch signaling pathway, as a possible therapeutic target for the treatment of ovarian cancer. Specifically, the thesis focused on the relationship between levels of Notch signaling gene expression in patients with ovarian carcinoma and their prognosis, progression and survival.

This thesis revealed that Stony Brook Taxanes – „SB-T“; SB-T-121402, SB-T-121605, and SB-T-121606 derivatives are very effective in NCI/ADR-RES tumor carcinoma cells resistant to conventional taxane – paclitaxel, and should be further studied in more advanced models, e.g. in vivo patient derived xenografts.

In a study of the importance of the Notch signaling pathway in ovarian cancer patients, a gene expression of the major representatives of the Notch signaling pathway and its target genes were monitored by real-time polymerase chain reaction. Significant changes in this pathway were observed in tumor compared to control ovarian tissues. In addition, the relationship between expression levels of seven genes with the most aggressive ovarian cancer HGSC subtype and the association of NOTCH3 gene expression with the survival of ovarian cancer patients were found.

In conclusion, new taxane derivatives are very effective in resistant tumor cells and could play an important role in the treatment of ovarian carcinoma, where resistance is a serious problem for successful treatment. The Notch signaling pathway appears to be a potential prognostic biomarker and therapeutic target that could help in individualized ovarian cancer therapy.

„(In Czech)“

Key words: taxanes, ovarian cancer, Notch signaling pathway