

1 SUMMARY

The breast cancer affects over one million women all over the world every year. [Approximately](#) 60 – 80 % of these tumours are declared as hormone sensitive, which means they are able to respond on a stimulation of estrogens that work as cocancerogens. The breast cancer incidence increases according to an age, a majority of new cases is detected during the postmenopausal period when the ovaries ceased to be functional. In postmenopausal patients the local estrogen production becomes a considerable stimulating growth factor of tumours.

In this thesis we have brought together a review of enzymes participating on the intratumoral biosynthesis of estrogens or estradiol. The enzymes responsible for the local synthesis include predominantly the aromatase, 17 β -hydroxysteroid dehydrogenases and steroid sulphatase. We have specified by each type of the enzymes its biochemistry, biological characteristics and also its engagement in a breast cancerogenesis as well as their advantage as a pharmacological target.

We have also placed pieces of information about members of the AKR1C subfamily. Professor Wsól from the department of biochemistry sciences of our faculty focuses on their study (a participation on a biodegradation of carbonyl groups xenobiotics). AKR1C3 (also called 17 β -hydroxysteroid dehydrogenase type 5) is able catalyse synthesis of estradiol directly in a breast cancer, inactivates anticancer drug doxorubicin and causes its less antitumor activity as well. This group of enzymes is not a major topic of a Czech clinical literature and we would consider appropriate to extend those experiments on a bioptic sample of a carcinoma tissue of patients.

We have devoted couple paragraphs of this thesis to survey the laboratory possibilities of the estradiol detection in a breast cancer tissue regarding to methods used in a routine practice. Nowadays the immunohistochemical determination of concentration of hormone receptor in a bioptic carcinoma tissue is common use. The determination of an intratumoral level of estradiol could be helpful for such patients who have an indecisive concentration of a hormone receptor. The physician could receive from this scan the additional information that could help him in a decision about a suitable therapy. Moreover, in case of the positive samples – it could be followed the determination of enzymes which are responsible for this increased level of estradiol. Therefore it could be used for deciding about the specific inhibitors in the treatment.

