DIFFERENT PROFILES OF PROGESTERONE METABOLITES IN ENDOMETRIAL CANCER CELL LINES ISHIKAWA AND HEC 1A


Endometrial cancer (EC) is the sixth most common malignant disorder in women in the world. It is associated with chronic exposure to estrogens and insufficient protection by progesterone (P4). In breast cancer it has already been shown that P4 does not act only in the protective manner, but may also enhance development and growth of cancer. Breast tissue and also endometrial tissue possess a number of P4 metabolizing enzymes that can form two different classes of metabolites, 4-pregnenes and 5?-pregnanes. In breast cancer cell lines Wiebe et al. demonstrated that 5?-pregnanes promote cell proliferation and detachment, while 4-pregnenes have the opposite effect. Additionally, in breast cancer the ratio between 4-pregnenes and 5?-pregnanes is disrupted in favor of 5?-pregnanes (1).

We investigated P4 metabolism in EC cell lines Ishikawa, which originates from a pre-menopausal patient, and HEC 1A, which was establish from a post-menopausal patient. The metabolites formed in these cell lines were identified and quantified with a combined liquid chromatographic/ tandem mass spectrometric method. In Ishikawa P4 was metabolized mainly to 5?-pregnane-3?,20?-diol (28%), 5?-pregnane-3ß,20?-diol (16%) and 4-pregnene-20?-ol-3-one (14%). The ratio between 5?-pregnanes and 4-pregnenes was 3.3. In HEC 1A the main metabolites detected were 4-pregnene-20?-ol-3-one (39%) and 5?-pregnane-20?-ol-3-one (7%). Here, the ratio between 5?-pregnanes and 4-pregnenes was 0.3. Our data thus indicate that pre- and post-menopausal EC differ in P4 metabolism, where more 5?-pregnanes are formed in pre-menopausal EC. To better understand this difference in P4 metabolism the effects of P4 metabolites on cell proliferation are currently studied. We expect our results will clarify the potential role of P4 metabolites in pathophysiology of EC.