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„The influence of calcitriol and its analogues on the inflammation accompanying the development of murine mammary gland carcinoma"

The main aim of this reseach was to evaluate the influence of calcitriol and its analogues (PRI-2191, PRI-2205) on the growth and metastasis of mouse mammary gland carcinoma, through the indirect impact on the immune system of the host in young and postmenopausal mouse model.

Conducted *in vivo* studies revealed, that the applied vitamin D derivatives do not influence primary 4T1 tumors, but stimulate metastatic process in lungs mainly in young mice. Moreover obtained results indicate the immunosuppressive activity of calcitriol and its analogues, which is demonstrated by the increase in the percentage of Treg cells and the level of TGF-β in splenocytes, as well as IL-10 in tumor tissue, mainly in the model of young mice. In response to calcitriol and/or its analogues there is also a disturbed balance of Th1/Th2 cytokine pattern in spleen and the predominance of type Th2 inflammatory response. In addition, elevated gene expression of *Spp1* encoding osteopontin, correlates with the activity of Th17 lymphocytes in the lymph nodes of young animals. Induced iTh17 cells derived from the spleens are stimulated by calcitriol and its analogues together with the increased expression of the VDR receptor. Consequently, this leads to increased metastatic potential of 4T1 cells in young mice. In the postmenopausal model, no similar effect of tested compounds was observed, which may indicate that aging influences the type of the inflammatory response in the pathological conditions, and the age-related differences in the functioning of the immune system affects the tumor microenvironment.

In the light of the obtained results, further research is necessary to fully understand the immunomodulatory mechanism of calcitriol, depending on age and hormonal status, as well as to determine the safety of this potential treatment in invasive breast cancer patients.