

Streszczenie w języku angielskim

The continuous advancement in scientific knowledge regarding the molecular basis of cancers, including prostate cancer, has led to the increasingly widespread use of targeted therapies in treating oncology patients, resulting in improved survival rates for these patients. Current research on the biology of prostate cancer has confirmed the significant impact of disruptions in gene repair mechanisms, such as mismatch repair (MMR) and double-strand break repair (DSBR), on patient prognosis and the selection of proposed therapies, including targeted therapies.

These findings have already been applied in clinical practice, with the FDA approving PARP inhibitors like olaparib and rucaparib, as well as the checkpoint inhibitor pembrolizumab, for treating specific cases of prostate cancer. The aim of this project was to determine the relationship between the expression levels of selected proteins in the MMR and DSBR pathways—MDC1, TP53BP1, MLH1, MSH2, MSH6, and PMS2—and the progression of prostate cancer.

In one study, we used immunohistochemical analyses to compare the expression of these proteins in primary prostate cancer tissues without lymph node metastases, primary tumors with lymph node metastases, and metastatic prostate cancer tissues in lymph nodes. We demonstrated that the expression of MLH1 and TP53BP1 proteins significantly differed among these tissues. Prostate cancer with lymph node metastases is characterized by low expression of TP53BP1 and MLH1 proteins. Metastatic prostate cancer in lymph nodes exhibits lower TP53BP1 protein expression than primary tumors. In another study, we focused on analyzing the expression of MDC1, TP53BP1, MLH1, and MSH2 proteins in relation to the histological malignancy of prostate cancer and its intratumoral heterogeneity. Our analysis revealed that the expression levels of MSH2, MDC1, and MLH1 proteins significantly varied with the degree of histological malignancy, as determined by Gleason score. The results of our analysis showed that the expression levels of MSH2, MDC1, and MLH1 proteins significantly differed depending on the histological grade of malignancy determined by Gleason score.

Our findings indicate that as Gleason score increases, the nuclear and cytoplasmic expression of MSH2 protein increases. Additionally, Gleason pattern negatively correlates with nuclear expression of MSH2 protein. As Gleason score increases, the cytoplasmic expression of MDC1

protein decreases. Gleason pattern positively correlates with the cytoplasmic expression of MLH1 protein.

Our findings suggest not only the potential use of MMR and DSB repair pathways or specific proteins as biomarkers but also as targets for potential targeted therapies. Moreover, these results align with current research on prostate cancer, emphasizing the heterogeneity of the disease and supporting the theory of cancer immunoediting. The data collected from global literature on the impact of DNA repair mechanisms, particularly MMR and DSB repair, on the development of prostate cancer, highlighted in our review article, underscore their usefulness and potential application in future studies aimed at improving the diagnosis and treatment of prostate cancer patients.

The collected literature data on the impact of DNA repair mechanisms open the way for further research, which may lead to the development of new biomarkers and therapeutic strategies for prostate cancer.