Mandigo A.C., Tomlins S.A., Kelly W.K., Knudsen K.E. 2021. Relevance of pRB Loss in Human Malignancies. Clin. Cancer Res. V. 28. P. 255.

McNair C., Xu K., Mandigo A.C., Benelli M., Leiby B., Rodrigues D., Lindberg J., Gronberg H., Crespo M., De Laere B., Dirix L., Visakorpi T., Li F., Feng F.Y., de Bono J., Demichelis F., Rubin M.A., Brown M., Knudsen K.E.. 2018. Differential impact of RB status on E2F1 reprogramming in human cancer. J. Clin. Invest. V. 128. P. 341.

Piunti A., Shilatifard A. 2016. Epigenetic balance of gene expression by Polycomb and COMPASS families. Science. V. 352. P. aad9780.

Polager S., Kalma Y., Berkovich E., Ginsberg D. 2002. E2Fs upregulate expression of genes involved in DNA replication, DNA repair and mitosis. Oncogene. V. 21. P. 437.

Popov B., Petrov N., Ryabov V., Evsyukov I. 2020. p130 And pRb in the maintenance of transient quiescence of mesenchymal stem cells. Stem Cells Int. https://doi.org/10.1155/2020/8883436

Reynolds M.R., Lane A.N., Robertson B., Kemp S., Liu Y., Hill B.G., Dean D.C., Clem B.F. 2014. Control of glutamine metabolism by the tumor suppressor Rb. Oncogene. V. 33. P. 556.

Sage J. 2012. The retinoblastoma tumor suppressor and stem cell biology. Genes Dev. V. 26. P. 1409.

Sharma A., Yeow W.S., Ertel A., Coleman I., Clegg N., Thangavel C., Morrissey C., Zhang X., Comstock C.E., Witkiewicz A.K., Gomella L., Knudsen E.S., Nelson P.S., Knudsen K.E. 2010. The retinoblastoma tumor suppressor controls androgen signaling and human prostate cancer progression. J. Clin. Invest. V. 120. P. 4478.

Siegel R.L., Miller K.D., Fuchs H.E., Jemal A. 2021. Cancer Statistics, 2021. CA Cancer J. Clin. V. 71. P. 7.

Sherr C.J. 1996. Cancer cell cycles. Science. V. 274. P. 1672.

Varambally S., Dhanasekaran S.M., Zhou M., Barrette T.R., Kumar-Sinha C., Sanda M.G., Ghosh D., Pienta K.J., Sewalt R.G., Otte A.P., Rubin M.A., Chinnaiyan A.M. 2002. The polycomb group protein EZH2 is involved in progression of prostate cancer. Nature. V. 419. P. 624.

Vélez-Cruz R., Manickavinayaham S., Biswas A.K., Clary R.W., Premkumar T., Cole F., Johnson D.G. 2016. RB localizes to DNA double-strand breaks and promotes DNA end resection and homologous recombination through the recruitment of BRG1. Genes Dev. V. 30. P. 2500.

Viatour P., Sage J. 2011. Newly identified aspects of tumor suppression by RB. Dis. Model Mech. V. 4. P. 581.

Vlachostergios P.J., Puca L., Beltran H. 2017. Emerging variants of castration-resistant prostate cancer. Curr. Oncol. Rep. V. 19. P. 32.

Wang C.Y., Xu Z.B., Wang J.P., Jiao Y., Zhang B. 2017. Rb deficiency accelerates progression of carcinoma of the urinary bladder in vivo and in vitro through inhibiting autophagy and apoptosis. Int. J Oncol. V. 50. P. 1221.

Weinberg R.A. 1995. The retinoblastoma protein and cell cycle control. Cell. V. 81. P. 323.

Xu Y., Chen S.Y., Ross K.N., Balk S.P. 2006. Androgens induce prostate cancer cell proliferation through mammalian target of rapamycin activation and post-transcriptional increases in cyclin D proteins. Cancer Res. V. 66. P. 7783.

Role of the Tumor Suppressor *RB* in Development of Localized and Castration-Resistant Prostate Cancer

V. M. Ryabov[a], M. A. Voskresenskiy[b], and B. V. Popov[a, *]

[a] *Institute of Cytology of the Russian Academy of Sciences, St. Petersburg, 194064 Russia*

[b] *Second City Hospital, Ministry of Health of the Russian Federation, St. Petersburg, 194354 Russia*

**e-mail: borisvp478@gmail.com*

Prostate cancer (PC) currently occupies leading positions in morbidity and mortality among all oncogenic diseases of men in west countries. PC occurs in the form of adenocarcinoma (localized PC), which may exist uncertainly long time in dormant non-life-threatening patient form or transform into an aggressive cancer that is insensitive to androgen deprivation therapy, castration-resistant prostate cancer (CRPC), with metastasis and a rapidly fatal outcome. PC arises from the epithelium of the prostate gland, the formation and functioning of which occurs under action of androgens. Androgens, mainly dihydrotestosterone, induce the androgen receptor signaling pathway and regulate the growth and division of the prostate epithelium under normal conditions and in the cells of localized PC. Androgen deprivation therapy, such as androgen receptor inhibitors, blocks the development of localized PC within 1.5–2 years, but then loses its effectiveness that inevitably leads to transition of the disease into an aggressive and lethal CRPC. Inactivation of the tumor suppressor *RB* due to mutations, gene loss or post-translational modification of its product results in the development of cancer of any tissue specificity. However, assessment of the status of *RB* and its product shows that *RB* gene is altered in less than 1% of patients with localized PC, but its loss occurs in 17–33% of patients with CRPC. This review of the literature considers the role of the pRb–E2F1 signaling pathway in the pathogenesis of localized and castration-resistant PC.

Keywords: tumor suppressor *RB*, *RB* product (pRb), methyltransferase Ezh2, signal pathway pRb–E2F1–Ezh2, androgen receptor (AR), androgen-deprivation therapy, localized prostate cancer (PC), castration-resistant prostate cancer (CRPC), neuroendocrine prostate cancer (NEPC)