Expression of *p65, DD3* and *c-erbB2* genes in prostate cancer*

E. Balcerczak[1], M. Mirowski[1**], A. Sasor[2], R. Wierzbicki[1]

[1]*Department of Pharmaceutical Biochemistry, Molecular Biology Laboratory, 90-151 Lodz, Poland, e-mail: mirowski@ich.pharm.am.lodz.pl;* [2]*Department of Pathomorphology; Central Teaching Hospital of the Military Medical University in Warsaw, Poland*

Received September 23, 2002

The expression of *p65*, *DD3* and *c-erbB2* genes was analyzed in 39 histologically verified human prostate cancers. The expression of *p65* and *DD3* genes was observed in significant percentage in well- and moderately-differentiated tumors. Both genes expression was lower in poorly differentiated tumors. On the contrary, *c-erbB2* gene expression increased with advanced histological grading and reached the highest percentage in poorly-differentiated cancers. In the all investigated groups straight dependence between *p65* and *DD3* genes expression occurred. Opposite dependence was noticed in expression of *p65*/*DD3* and *c-erbB2* genes.

Key words: p65, DD3, c-erbB2, PCR, RT-PCR, prostate cancer.

Prostate cancer is the second leading cause of cancer deaths in male population [16]. Therefore, there is need to develop sensitive and specific tests for its detection and also for accurate determination of the degree of malignancy. A number of prostate-specific markers are known, including prostate-specific membrane antigen [8], prostate stem cell antigen [17], and prostate-specific antigen [21]. The most useful method for screening and monitoring prostate cancer disease till now is prostatic acid phosphatase and prostate-specific antigen (PSA) estimation [3]. PSA serves as an indicator of metastatic involvement and as a good parameter for following the response to surgery and therapy. Both of these proteins are secreted to the serum and may serve as markers of the disease. However, on the basis of these markers is difficult to get straight answer about cancer development. An evaluation of additional markers may be helpful for routine diagnosis. To such markers belongs *c-erbB2* oncogene, which is known as a poor prognostic factor, *DD3* a newly described prostate-specific gene and also *p65* gene investigated by us.

c-erbB2 is homologous with the gene of epidermal growth factor receptor and codes of membrane receptor protein. Expression and amplification of *c-erbB2* are connected with more aggressive disease in many human cancers. The clinical importance of *c-erbB2* became apparent with the recognition of gene amplification and overexpression of the encoding protein in breast cancer patients, which are associated with poor prognosis. The same dependence was found in prostate cancers. Immunohistochemical study showed expression of protein *c-ErbB2* in benign prostate hyperplasia and in prostatic adenocarcinoma [24]. Oncogene *c-erbB2* is also amplified and/or overexpressed in both benign and malignant prostate tissue [5]. Overexpression/amplification of this oncogene in prostate cancer is associated with large tumor volume [20], high tumor grade and distant metastases [18].

DD3 gene is specifically and highly expressed in prostate cancer, none or very low expression was found in normal prostate tissue or in patients with benign prostate hyperplasia. Expression of this gene was not observed in any other normal human tissue and in some investigated tumors of breast, cervix, endometrium, ovary and testis. The role of this gene is unclear. *DD3* is expressed as a spliced and polyadenylated RNA molecule what suggests that it could be a pseudogene [2]. Verhaegh et al [23] identified the promoter elements that are responsible for the prostate cancer specific expression of *DD3*. It was shown that the high mo-

*The work was supported by the grant 502-13-844 from the Medical University of Lodz, Poland and by the L'Oreal and UNESCO fellowship "For women in science" for Mrs. Ewa Balcerczak.

**Author to whom correspondence should be sent.