

THE ROLE OF MOLECULAR BIOLOGY IN DETECTION AND MONITORING OF PROSTATE CANCER

Zummerová A.¹, Böhmer D.², Fillo J.³, Danihel L.⁴, Repiská V.²

¹Department of Pathology and Forensic medicine, Health Care Surveillance Authority, Bratislava, Slovakia

²Institute of Medical Biology, Genetics and Clinical Genetics, Faculty of Medicine, Comenius University, Bratislava, Slovakia

³Department of Urology, Faculty Hospital, Bratislava, Slovakia

⁴Department of Pathology, Faculty of Medicine, Comenius University, Bratislava, Slovakia

Summary

The study of molecular markers in various types of human carcinomas, as well as in carcinoma of prostate, is focused on genes responsible for the formation of carcinoma. Mutation, amplification or other changes in these genes or in their protein products are being examined and compared with traditional prognostic markers. These genes can be characterized as oncogenes, tumor suppressor genes or genes for other significant cell functions. However, studies are often limited by heterogeneity and multifocality of tumors, especially in prostate cancer. In this review, we offer a survey of some of the most frequent diagnostic and prognostic parameters of molecular biology research in relation to prostate cancer.

Key Words: prostate cancer – molecular biology – molecular markers

Súhrn

Úloha molekulárnej biológie pri diagnostike a monitoringu karcinómu prostaty

Štúdium molekulových markerov v rôznych neopláziách ako aj pri karcinóme prostaty je založené na analýze génov, ktoré sa spolupodieľajú na vzniku karcinómu. Boli sledované mutácie, amplifikácie a iné zmeny týchto génov alebo ich produktov, ktoré sú porovnávané s tradičnými prognostickými markermi. Tieto gény možno označiť ako onkogény, tumor supresorové gény alebo gény s inými významnými bunkovými funkciami. Štúdie karcinómu prostaty sú často limitované heterogenitou tohto nádoru. V predloženej práci predkladáme prehľad niektorých najčastejších diagnostických a prognostických molekulovo biologických markerov vyšetrovaných v súvislosti s karcinómom prostaty.

Kľúčové slová: karcinóm prostaty – molekulárna biológia – molekulárne markery

Čes.-slov. Patol., 46, 2010, No. 4, p. 95–97

Prostate cancer has become one of the most frequently diagnosed tumors in men and is one of the leading causes of death in men over the age 50 (3). In most cases, it is represented by acinar (conventional) adenocarcinoma (11). Prostatic adenocarcinoma is a heterogenous group of neoplasms with a broad spectrum of pathologic and molecular characteristics and clinical behaviors (15). Standardly used diagnostic and prognostic parameters of prostate cancer have too many limitations and seem to be insufficient in the prediction of the behavior of this disease in many cases. The tendencies to impose molecular-genetic methods grow more and more stronger (18). The target of the molecular biology research is to find more persuasive markers of biological character of prostate gland carcinoma in individual patients that would be essential for the follow-up determination of adequate strategy and aggressivity of the treatment. The purpose of this article is to review some novel molecular agents that play a role in the diagnosis and monitoring of prostate cancer.

PSA/PSM EXPRESSING CELLS AND THE RT-PCR REACTION

The serum biomarkers – prostatic acid phosphatase and especially prostate-specific antigen (PSA), which is

a glycoprotein, have both been widely used for diagnosis and clinical monitoring of patients with prostate cancer (8). However, they are not accurate enough to predict occult invasion or metastatic disease, which are diagnosed at the time of radical surgery in almost half of the patients believed to have localized disease. Detection of circulating PSA-positive malignant cells by amplification of PSA mRNA has opened new expectations and proved to be useful to identify cancer cells in lymph nodes. To better identify early extra-prostatic spread of cancer, blood samples of patients with clinically localized or locally advanced disease are being assessed (4, 19). Reverse Transcriptase – Polymerase Chain Reaction (RT-PCR) was introduced to improve the limit of PSA mRNA detection (7). Besides, prostate-specific membrane antigen (PSM), an integral transmembrane glycoprotein, is another promising prostate-specific marker, and RT-PCR reaction is used not only to detect PSA- but also PSM-expressing cells in peripheral circulation (14).

The circulating tumor cells in patients with prostatic carcinoma are originally epithelial prostatic cells that are characterized by very specific expression of genes for prostate specific antigen (PSA) and for prostate-specific membrane antigen (PSM) (2). Normal immunological reaction of human organism does not anticipate the survival of normal, non-malignant prostatic cells in blood and their presence in circulation is regarded as one of the first steps in the cascade of metastasing process (6). Circulating