

# Biological Therapy of Prostate Cancer

*Vakhtang Shoshiashvili, Vili Pachkoria*

National Center of Oncology, Tbilisi, Georgia;  
Department of Topographical Anatomy of Tbilisi State Medical University, Georgia

## **Abstract**

Biological therapy strategies of prostate cancer are based on antigenic structure of malignant cells and contribute correction of immune reaction and enhancement of immunogenicity of malignant cells. There are used as specific as non-specific methods of immune therapy such as: cytokine therapy, vaccine therapy, gene therapy, treatment with dendrite cells and their combinations together with other traditional methods. Mainly, the subjects for clinical studies are patients with disseminated androgen-undefended prostate cancer. The obtained data allows us to make hopeful prognosis.

**Keywords:** *prostate, cancer, PSA, PSMA, PSCA, Her2/neu, MUC1, interleukins, antigenic vaccines, gene therapy, monoclonal antibodies*

**D**uring the last decade, intensive elaboration of new bio-therapy strategies in oncology (among them - of prostate cancer) is the result of advanced development of basic biology [17]. Prostate cancer is considered as widely spread endocrine tumor. In men population of North America, prostate cancer occupies the first place due to its spreading, while due to the mortalities, caused by malignant tumors - it gets the second place [13].

For biotherapy of prostate cancer as specific as well as non-specific methods are applied [7]. Approximately 500 exceptional promoters and antigens [11,16], have been found by studying of genetic information of normal prostate and prostate cancer, could be used as the targets of specific biotherapy. Only some among them, that have been used at clinics so far, are the followings: PSA, PSMA, PSCA, Her 2/neu, MUC1) [4,6,8,12,19].

At the first sight the plurality of cancer antigens would cause development of adequate immunity against cancer, but really it doesn't happen so. On the hand it is caused by weak immunogenicity of antigens and on the other hand - by immune suppression induced by the above-mentioned antigen [10]. For correction of immune reaction, induced by tumor, it should be used non-specific immune-therapy (cytokine therapy or cytokine gene therapy). At present, for treatment of prostate

cancer there are conducted clinical studies by using of interleukins, TNF- $\alpha$ , IFN- $\alpha$ , G-CSF, GM-CSF and their regulating genes [3,14,15] and the first clinical results are already reached which is expressed by PSA level reduction [14, 20].

For specific biotherapy antigenic vaccines of viral and non-viral nature and gene therapy on monoclonal bodies are applied [7].

Dendrite cells have been applied for vaccine-therapy [19]. Antigens' presentation at immune system is the function of these cells, promoting proper immune-reaction development.

During the exposition with proper antigens, dendrite cells in vivo gain the ability of antigen's presentation. Creation of dendrite-cellular vaccines is based on this feature. First clinical results for prostate cancer treatment have already been taken by using of such vaccines [8,18]. It should be emphasized that this method of treatment is expensive and work full enough (needs distinguishment of dendrite cells by leucopoiesis, their exposition with carcinoma antigens and afterwards their re-infusion).

Application of synthetic vaccines for treatment of cancer has been proved to be easier, clinically.

To increase their immunogenicity tumor antigens are connecting to the immunogenic proteins covalently, while for strengthening of immune reaction have been used immune adjuvant [19]. Peptic vaccine focused on MUC1 mucin has been created by this way, where antigen is connected to the keyhole lymph hemocianine and saponini QS-21 is used as immunologic adjuvant. By application of this vaccine at prostate cancer has been reached enhancement of specific antibodies titer of IgG1 and IgM classes and reduction of PSA [19].

Gene therapy is the most intensively developing strategy of biotherapy. It is based on genic transfer existed in human cells promoting desirable effect for cancer treatment. This method could be used as ex vivo as well as in vivo [2,13].

Viral or synthetic vectors carry out Gene transfer. Viral vectors carry genetic information into cells. There are used as DNA as RNA viral vectors (retro-viruses) [2,5].

Strategies of gene therapy are as follows: cytoreductive, cytolytic, proapoptotic and corrective ones. The aim of corrective therapy is the prevention of cancer progress in phenotypically normal cells.

Application of corrective therapy gives the possibility to regress or reverse transformed cells into non-neoplastic cells [13].

During the cytoreductive gene therapy induction of autoimmune antitumoral reaction is observed. For this

reason can be used genetic influence to course the expression of cytokines by tumoral cells. In comparison with the tumoral cytokinotherapy this therapeutical method proved to be less toxic [18].

Polyvalent tumoral vaccination is considered as very perspective method, targets of which are several antigens simultaneously [9].

Cytolytic - proapoptotic strategies cover enzymo-promedicamentous gene therapy by using cytolytic, oncologic viruses. Increasing proapoptotic activity can be reached as by p53 independent as well as by depended ways [11,15,17].

Choosing treatment strategy it should be foreseen resistance and heterogeneity of tumoral cells.

Therefore, there are elaborated combinations of treatment methods for example - combination of gene and radiotherapy [1].

At prostate cancer among the other treatment strategies should be emphasized application of antisensory oligoribonucleotids contributing neutralization of protooncogenes and factors for inhibition of angiogenesis [7,14].

Biotherapy is the modern tendency in treatment process.

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## **Биологическая терапия карциномы предстательной железы**

*Вахтанг Шошиашвили, Вили Пачкория*

Национальный центр онкологии, Тбилиси, Грузия

Кафедра топографической анатомии Тбилисского государственного медицинского университета, Грузия

### **Р Е З Ю М Е**

Биотерапевтическая стратегия лечения карциномы предстательной железы основана на антигенной структуре клеток и направлена на коррекцию иммуносупрессии и повышение иммуногенности опухолевых клеток. Применялись специфические и неспецифические методы: цитокинотерапия, вакцилотерапия, генотерапия, лечение дендритическими клетками, а также комбинация традиционных методов лечения. В основном субъектами лечения являлись больные с диссеминированным андрогеннезависимым раком простаты. Полученные данные дают основание для оптимизма в лечении рака предстательной железы.

**Ключевые слова:** *рак, простата, PSA, PSMA, PSCA, Her2/neu, MUC1, интерлейкины, антигенная вакцина, генная терапия, моноклональные антитела*