Novel Predicted B-Cell Epitopes of PSMA for Development of Prostate Cancer Vaccine

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Abstract

Prostate cancer is one of the most common cancers around the world. Vaccines are a new hope for prevention of this cancer. In the case of prostate cancer, PSMA is considered as a target for vaccine development. Here, the initial data from the computational analysis of this specific antigen of the prostate membrane to find potential B-cell epitopes are described using a new bioinformatic tools. Based on the results, 673RHVIYAPSSHNKYAGE25 is the peptide with best binding affinity. These data may be useful for the effective vaccines development.

Keywords Prostate cancer · B-cell · Epitope · PSMA

Introduction

Prostate is a small gland located below the men's bladder and helps sperm production. Testosterone hormones regulate the function of the prostate gland (Gathirua-Mwangi and Zhang 2014). Prostate cancer is the most common cancer among men; about one in six man (16%) (Jemal et al. 2005). Prostate cancer in the populations of Africa and Asia has the highest and lowest incidence rates, respectively (Steinberg et al. 1990). Researchers believe that the incidence of prostate cancer is related to hormonal factors. For example, the conversion of testosterone to dihydrotestosterone is known as an important factor in the progression of this disease (Parsons et al. 2005). Development of prostate cancer is associated with several factors including age, diet, heredity, race

and the environment factor (Karan et al. 2008). The most important factor in developing prostate cancer among these factors is the rise in age (De Marzo 2008). The most common symptoms of prostate cancer are frequent and difficult urination, impotence in the urination, intermittent and poorly flowed urine, blood in the urine and seminal outflow with pain are main symptoms (Arrighi et al. 1990).

Prostate surgery, radiotherapy, chemotherapy, and hormone therapy are routine treatments for this cancer (Stamey et al. 1993). Prostate cancer has poor prognosis and in the advanced stages the chance of treatment highly decreased (Voeks et al. 2002). Therefore, finding the more effective treatment for coping with this disease is very important (McNeel and Malkovsky 2005).

Immunological approaches have introduced new insights to treatment and prevention of this disease. Recombinant vaccine is one of this approaches. In this method, cancerous antigens or tissue that was targeted by T cells or B cells are used in the design of recombinant vaccines. (Hurwitz et al. 2003).

Prostatic membrane antigen (PSMA) is important antigen in prostate cancer and expression of it significantly increased (Jacobson 2007). PSMA has molecular weight about 100 kDa and belong to membrane glycoprotein family (Zeng et al. 2005). Although this antigen express highly in prostate cancer tissue, its expression is limited in other tissues (Silver et al. 1997). For this reasons, PSMA

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Table 1 Predicted B-cells epitope

Rank	Sequence	Start position	Score
1	RHVIYAPSSHNKYAGE	673	0.96
1	LNGAGDPLTPGYANE	246	0.96
2	DSSIEGNYTLRVDCAP	438	0.95
3	HSVYETYELVEKFYDP	538	0.92
4	PGIYDALFDIESKVDP	691	0.91
4	GWFIKSSNEATSITPK	25	0.91
5	IASGRARYTKNWETNK	515	0.90
5	TQKVKMHIHSTNEVTR	324	0.90
5	IVIARYGKVFRGNKVK	185	0.90

is appropriate target for the development of cancer vaccine to prevent prostate cancer (Olson et al. 2007).

Based on many advances in bioinformatics, it has become a new alternative to the development of vaccines (Brusic et al. 2005). By increasing the amount of available information in the genome databases, vaccine specialists use epitope mapping tools to display vaccine candidates. New databases have been launched to facilitate epitope prediction (De Groot 2006).

The main objective of this study is to investigate the potential B cell epitope of PSMA antigen by using a new bioinformatics tools.

Materials and Methods

The complete sequence of PSMA antigen (Entry: A4UU13) retrieved from the UniProt Knowledgebase (UniProtKB) in FASTA format. ABCpred Prediction Server was used to find potential B-cell epitopes (<https://crdd.osdd.net/raghava/abcpred/>). The ABCpred server provide a powerful tool for prediction of B cell epitope(s) in an antigen sequence by using an artificial neural network. ABCpred is the first server developed based on a neural network based technique (a machine-based technique) using fixed-length patterns (Saha and Raghava 2006).

Results

The ABCpred server predict approximately 81 epitope peptides. The peptides with the first 9 best orders of predicted binding affinities are presented in Table 1.

Discussion

Prostate cancer is the second most common cancer and the sixth cause of cancer-related deaths in men (Ryan et al. 2013). Also, it is the most common cancer in men in developed countries (Drake 2010). Radiotherapy, chemotherapy, prostate surgery, hormonal therapy have been used for the treatment of prostate cancer. Most of these procedures have side effects and, in the case of advanced prostate cancer, these therapies are no longer effective (Tran et al. 2009; Zhou and Zhong 2004).

In recent years designing vaccines against cancers have been noticed. Lack of side effects, easy manufacturing, low cost, and immune system stimulation make vaccines ideal for cancers. PSMA is one of the prominent antigens in prostate cancer that can stimulate the immune system and produce antibodies (Zhu et al. 1999). PSMA expression in normal prostate tissue is less than prostate cancer (Olson et al. 2007). PSMA expression is restricted to the prostate secretory epithelium (Chang et al. 1999). Based on research, recombinant immunogen peptide that stimulates B-cell might have applications in the prevention of PSMA overexpressing prostate cancer (Dakappagari et al. 2000). Overexpression of PSMA in prostate cancer and its membranous nature have made this antigen as an effective candidate for the prevention and treatment of prostate cancer. Studies showed that PSMA based vaccine had no side effect in patients (Olson et al. 2007).

Although using PSMA antigen for vaccine had their beneficial but designing a multi-epitope vaccine will improve the efficiency of vaccine. Selecting appropriate epitopes with highest antigenicity for B cells is key point to develop of this kind of vaccines.

In this study, a new bioinformatic tool was used to predict potential B-cell epitopes. The determined peptides should be useful for further vaccine development because they can reduce the time and minimize the total number of required tests to find the possible proper epitopes.

Conclusion

A computational method was used to determine the potential B-cell epitopes of PSMA. According to this work, 673RHVIYAPSSHNKYAGE25 is the peptide with the best binding affinity. The results are only predictions and further confirmation is required. The peptide synthesis in the laboratory and the in vivo experimental study to test the efficacy are the next steps in the prostate cancer vaccine development.

Compliance with Ethical Standards

Conflict of interest All authors declare that they have no conflict of interest.

Ethical Approval This article does not contain any studies with human participants or animals performed by any of the authors.

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