Discovery of prostate cancer-specific peptides using bacterial viruses

Prostate cancer is the most common cancer and the third leading cause of cancer death among American men. Although chemotherapy has been widely used for prostate cancer treatment, it is not specific to cancer cells. As a result, its efficacy is always hampered because it kills not only cancer cells but also normal cells, leading to severe toxicities. Improving the specificity of chemotherapy to cancer cells has therefore attracted a lot of attention in the last decade.

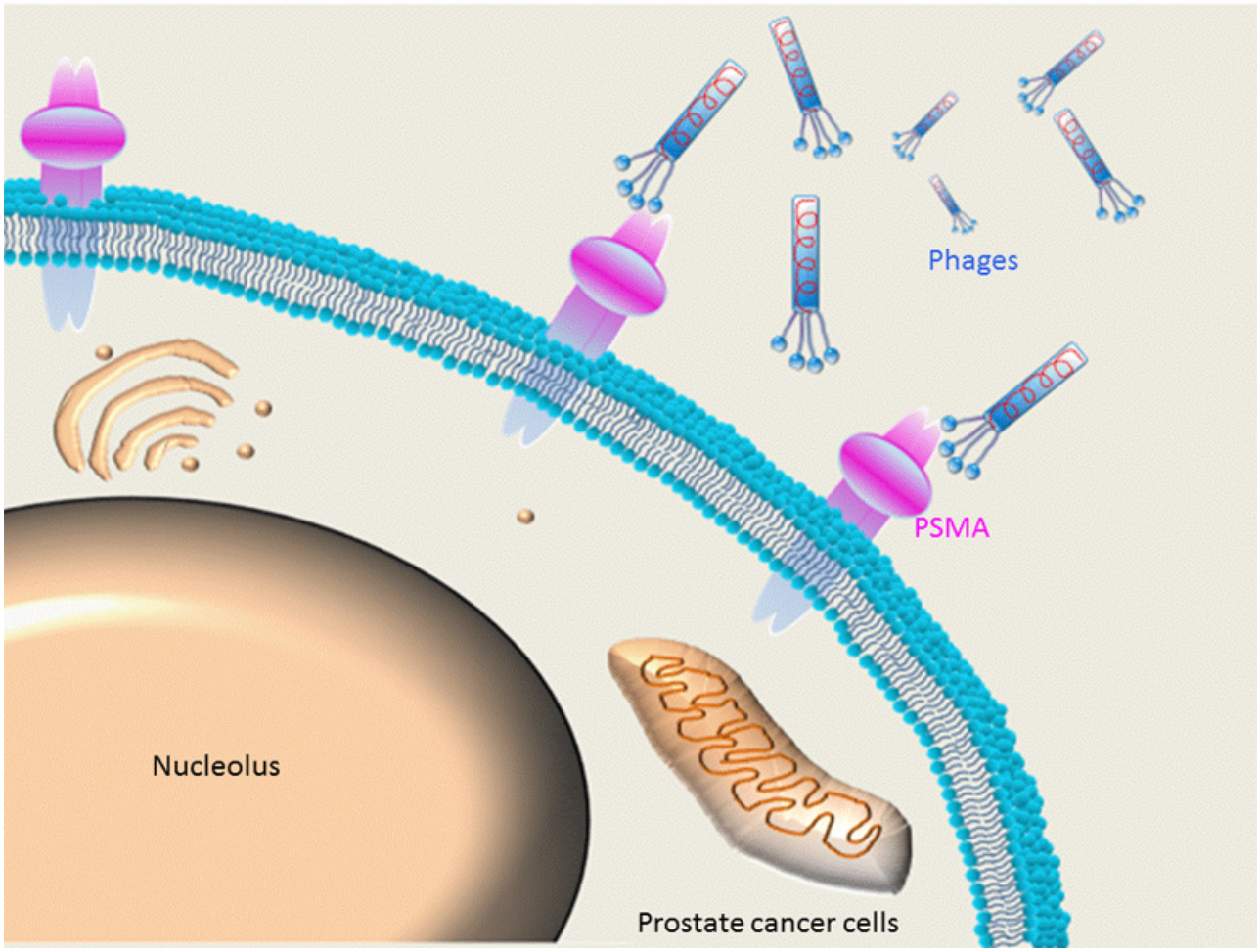

Fig. 1. Binding of phages (a type of bacterial viruses) to PSMA on prostate cancer cells.

Prostate-specific membrane antigen (PSMA) is a protein that is highly expressed in nearly all prostate cancer cells. By contrast, the expression of PSMA in normal tissues is extremely low. Therefore, PSMA is an ideal “marker” on prostate cancer cells that can be utilized for targeted

delivery of chemotherapeutic agents without damaging normal cells. In our study, we used a type of bacterial virus to discover peptides that can specifically bind to PSMA on prostate cancer cells.

The bacterial virus is also called phage display library, which was firstly reported in 1985 and has been widely used to discover peptides for various receptors. The phage display library is constructed by inserting DNA sequence of random peptides into the gene coding for the phage coat protein, and each of the phage will express a unique peptide on its surface. In general, a phage display library may contain billions of different phages.

In our study, a peptide phage display library was incubated with PSMA, and only those phages that have high affinity to PSMA were collected and amplified for the next round affinity selection. After five rounds of affinity selection, we discovered several peptides that can specifically bind to PSMA. The peptides were then incubated with prostate cancer cells and showed high and specific binding. We also injected the peptides to mice implanted with human prostate cancer cells, the peptides also exhibited high accumulation in tumors rather than other tissues. In the future, we will attach the peptides to chemotherapeutic agents to increase their specificity to prostate cancers, thus reducing their toxicity and accordingly increasing efficacy. Moreover, the peptides can be employed as imaging agents to monitor prostate cancer metastasis in the patients.

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