Aptamer-Facilitated Prostate Cancer Treatment and Detection

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Prostate cancer is the second leading cause of cancer death in American men. In 2015, it is estimated there will be 220,800 new cases of prostate cancer and 27,540 deaths from prostate cancer. [1] Like most cancers, treatment for this disease is limited. A common practice for a patient who receives an initial diagnosis for prostate cancer is to have the patient go through endocrine therapy. However, this approach is typically a short-term fix as many patients develop metastatic castration-resistant prostate cancer (mCRPC); mCRPC has a mean survival time of only 30 months following the diagnosis. [2] Patients who are not cured with endocrine therapy are usually administered chemotherapy options and/or drugs targeting the androgen receptor (AR). Drugs such as abiraterone and enzalutamide prolong survival rates but are not curative, with median duration of efficacy around 6-12 months. [2]

For therapeutic and diagnostic purposes, an increasingly recognized marker of prostate cancer is prostate-specific membrane antigen (PSMA). PSMA is a glycosylated type-II membrane protein which is primarily expressed in prostatic epithelial cells. Although PSMA can be present on normal cells, its expression of the transmembrane isoform is greatly upregulated in prostate specific cancer cells. This leads to interesting avenues in terms of theranostics, diagnostics, and therapeutic interests.

Initial results from targeting PSMA with aptamers are positive. PSMA is an intriguing target due to not only being a good marker but also due to growing evidence which shows that it has a role in facilitating the growth of prostate cancer. The very nature of cancer makes it difficult to find biomarkers that are present among large subsets of patients. Veraptus will continue exploring this target to verify the efficacy of Veraptus aptamers. A multifaceted approach of treating prostate cancer is being played out in in vivo experiments. The advantages of VISTA can also be harnessed in fighting prostate cancer. Drug-loaded aptamers and VISTA techniques will be utilized in the targeting of prostate cancer. Initial experiments indicate that aptamers binding to PSMA can also facilitate the slowing or regression of prostate cancer. This is exciting news since it allows for multiple strategies to fight prostate cancer.

In addition to targeting PSMA, Veraptus is employing cell-SELEX in order to target prostate cancer stem cells (CSCs). CSCs have been observed in acute and chronic myeloid leukemia, as well as in various solid tumors, including those of the breast, brain, lungs, and prostate gland. [3] Cancer stem cells are believed to be the root of cancer cells and provide good targets for aptamers due to an aptamer's ability to recognize different cell lines.

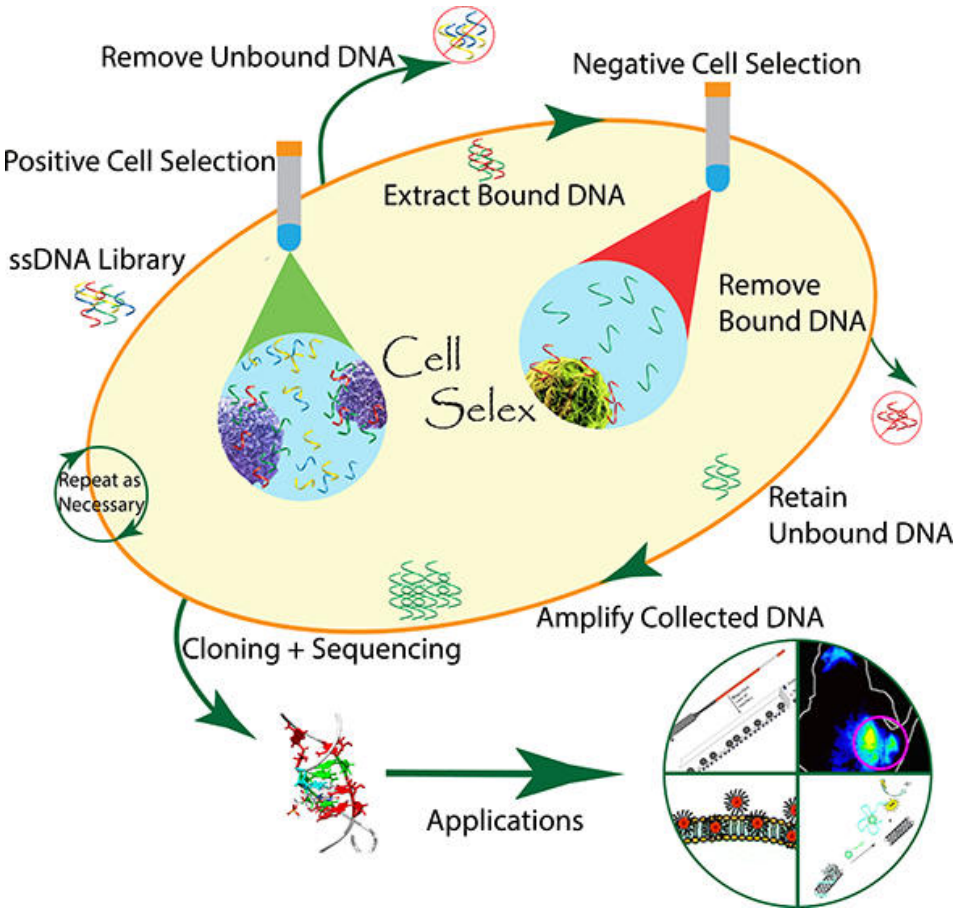

Figure 1: Cell-Selex Process (W. Tan, M. J. Donovan and J. Jiang, Chem. Rev., 2013, 113, 2842-2862)

There is currently no cure for prostate cancer. Veraptus intends to find a cure. With growing theranostic abilities relating to prostate cancer, accurate monitoring of PSMA levels as well as ablation of the growth of PSMA positively overexpressed cells is critical. Many different variables need to be addressed throughout multiple stages of metastasis, as well as regression. This means highly specific aptamers must be employed. The specificity of Veraptus aptamers towards PSMA positive cells gives our researchers a much-needed powerful tool.

References

1. Prostate Cancer Prevention. National Cancer Institute. http://www.cancer.gov
2. Cereda, V. F. (2014). Expert Opin Investig Drugs, 23: 469-487.
3. G. Gu, J. Yuan, M. Wills, S. Kasper, Cancer Res. 2007, 67, 4807 – 4815.