Detection of the ovarian cancer biomarker in body fluids using nucleic acid aptamers as diagnostic probes

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Abstract Text:

Introduction

Ovarian cancer is the deadliest gynecological cancer. The majority of the patients are diagnosed in advanced stages, with a 5-year survival ranging from 15 to 40 %. Currently, there are no easy early-stage and screening methods available, so late diagnosis remains a main factor contributing to poor prognosis. Recently, small synthetic nucleic acids, called aptamers, have emerged as potential diagnostic tools to detect cancer biomarkers. Here, we present high-affinity DNA aptamer probes for the detection of ovarian cancer biomarker in body fluids and its implication in diagnostics.

Material and Methods

Human Epididymis protein 4 (HE4) is a protein overexpressed in ovarian cancer and a valuable clinical biomarker. As a single blood biomarker, HE4 has the highest specificity and sensitivity in detecting ovarian cancer. The anti-HE4 DNA aptamers for diagnostic applications are selected from a random, highly diverse DNA library using High-Fidelity Systematic Evolution of Ligands by EXponential enrichment (Hi-Fi SELEX), a method based on digital droplet Polymerase Chain Reaction (ddPCR), which ensures amplification of rare specific sequences. The sequences that are able to recognize HE4 are identified by Next-Generation Sequencing followed by bioinformatics.

Results and Discussions

Bioinformatics analysis on selected DNA sequences allowed the identification of anti-HE4 aptamer sequences that specifically target biomarker HE4. The characterization between candidate DNA probes and HE4 in body fluids is still undergoing, with the aim to evaluate

binding affinity and specificity in blood and urine. To further investigate the diagnostic potential of these aptamers, the most potent anti-HE4 probe is used for the development of the Enzyme-Linked OligoNucleotide Assay (ELONA) for the detection of HE4 in surrogate samples of healthy individuals, low malignant potential ovarian masses, early stage (I/II) and late-stage (III/IV) ovarian cancer. ELONA offers a sensitive approach for detecting very low levels of HE4 in body fluids.

Conclusion

This prospective method can be used to detect HE4 in patient samples such as standard blood or non-invasive urine samples. Due to high-affinity and specificity, the identified anti-HE4 aptamer can offer cheap alternative to conventional antibodies in diagnostic tests. Therefore, it can be utilized as molecular probe in the various diagnostic methods, biosensors or point-of-care devices, and could be an additional tool towards reducing the high mortality of ovarian cancer.