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Aptamers as the Next Generation of Ovarian Cancer Detection

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Introduction

Ovarian cancer is one of the seven most common types of cancer in women, and it is the most lethal gynaecological tumour due to the difficulty of early detection. Aptamers are useful tools for improving tumour diagnosis by recognising specific molecules produced by tumours. Aptamers and their potential targets in ovarian cancer cells were studied using in silico methods. The Cell-SELEX method was used to select specific aptamers from Caov-3 and OvCar-3 cells. The five most common aptamers from the previous round of selection were computationally modelled. Proteomic data for the Caov-3 and OvCar-3 cell lines were used to identify potential targets for those aptamers in cells. Overexpressed proteins in each cell were classified based on their three-dimensional model, cell location, and function.

Description

Ovarian cancer is the seventh most common type of cancer in women, as well as the one with the worst prognosis. It is the most lethal and the third most common gynecological tumor, trailing only cervical and uterine tumours in terms of incidence. Although the prevalence of this type of cancer is not particularly high, its lethality is quite high. Ovarian cancer, for example, is three times more lethal than breast cancer. This high mortality rate can be attributed to three major factors: silent and asymptomatic tumour growth, late onset of symptoms, and a lack of proper population screening, which frequently results in the diagnosis of advanced stage disease [1].

Some cell surface markers may increase, decrease, and undergo modifications in tumour cells, or new markers may appear. These molecular differences can distinguish healthy cells from tumour cells. In this regard, the use of aptamers represents a promising approach that could improve tumour diagnosis specificity. Aptamers are small, single-stranded synthetic oligonucleotides that bind to a molecular target with high specificity, making them excellent candidates for diagnostic tests and therapy. Aptamers are chosen in vitro through a process known as "Systematic Evolution of Ligands through Exponential Enrichment," which can result in the recognition of a wide range of target molecules, from small structures to macromolecules.

Despite the benefits described above, the Cell-SELEX method does not provide information about the aptamer target in the cell. As a result, we used in silico methods to discover information about potential tumour targets. Computational tools that predict the three-dimensional structures of nucleic acids and target proteins could be useful for molecular docking simulations. A bioinformatics methodology for aptamer-target complex validation was proposed in three stages, beginning with the prediction and modelling of the aptamer nucleic acid structure and progressing to molecular docking between the aptamer and the potential protein target in an attempt to reproduce the experimental aptamer-protein interactions. However, building three-dimensional models of DNA aptamers remains difficult, owing to a lack of algorithms for three-dimensional modelling of DNA.

Ovarian cancer is the most dangerous gynaecological tumour. The high lethality rate associated with ovarian tumours is directly related to the cancer's late diagnosis. There are currently no methods with high sensitivity and specificity for detecting early epithelial ovarian cancer. Aptamers are thus an important tool for improving the specificity of ovarian cancer diagnosis, particularly because they are molecules capable of binding to a target with high specificity. Aptamers could also be investigated for use in imaging exams or the detection of tumour biomarkers. The current study identified an aptamer capable of specifically recognising ovarian tumour samples. Furthermore, the three-dimensional structure and stability of this aptamer were determined using computational methods.

We aimed to improve the selection of aptamers with potential use in the clinical diagnosis of ovarian cancer by combining computational tools, favouring the identification of more stable aptamers and their respective targets. The discovery of specific aptamers, including those with the potential to detect metastasis, can help to close gaps in clinical practise for ovarian cancer diagnosis. As there are currently no methods with reliable sensitivity and specificity for the early diagnosis of epithelial ovarian cancer, aptamers represent an important tool for improving specificity for the diagnosis, leading to more accurate and faster disease detection and, as a result, an increase in patient life expectancy [2-5].

Conclusion

All of the free energy values obtained for each analysed aptamer sequence's secondary structure were negative, indicating that these structural conformations are spontaneous. As previously stated, free energy values in aptamers can vary depending on their sequence and thermodynamic profile. While aptamers can be selected against a wide range of structural targets, surface protein targets are more appealing because they allow for more structural and functional studies. By identifying the most promising targets for interaction with aptamers, the extracellular region of selected proteins for the two cells of interest in the study was characterised. The topology of membrane proteins allows us to determine the orientation of the C and N terminals in the protein. Furthermore, bioinformatic computational methodologies such as docking and molecular dynamics have been proposed as alternatives to SELEX, the traditional method for selecting aptamers for a specific protein. The development of new methodologies that contribute to the selection of the best protein-aptamer complex identification is especially important for aptamers chosen using Cell-SELEX methodology because the aptamer target in the cell is unknown in this case.

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Conflict of Interest

There are no conflicts of interest by author.

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