DNA aptamers targeting a GBM cell line which mediated siRNA delivery

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Glioblastoma multiforme (GBM) is the most aggressive brain tumor in adults and remains incurable despite multimodal intensive treatments. One of the most commonly mutated proteins in GBM is epidermal growth factor receptor variant III (EGFRvIII), which has been linked to radiation and chemotherapeutic resistance, and enhanced tumorigenic behavior. Its inhibition can interfere with growth of GBM so a few drugs including monoclonal antibodies and tyrosine kinase inhibitors currently are used in clinic. However, some of these drugs resulted in toxicity and acquired resistance, it’s extremely urgent to develop novel drug targeting EGFRvIII with low toxicity and high specificity. DNA aptamers may be a good alternative solution. After several rounds of selection with an approach named cell systematic evolution of ligands by exponential enrichment (Cell-SELEX), aptamers specifically bound to EGFRvIII-overexpressing U87MG cells (U87Δ) were selected. A biotin-avidin ELISA method was used to measure the binding affinity. Selected aptamers were able to distinguish the U87Δ cell line from other cell line and with an equilibrium dissociation constant (Kd) in the nanomolar to picomolar range. One of these aptamers specifically bound to EGFRvIII protein with high affinity as that of EGFR antibody, and could localize in the cell nucleus. In the siRNA transfection experiment, DNA aptamer mediated siRNA delivery with the same efficiency compared with lipofectamine2000. These cell-based aptamers are promising molecular probes for the diagnosis and treatment of GBM. Aptamers can recognize the membrane protein of target cells and be endocytosed, so they may be effective vehicles for drugs or siRNA delivery.

Biography

Yan Tan has completed her M.D. at the age of 26 years from Southern Medical University of neurobiology and worked at Shenzhen Institutes of Advance Technology as a research assistant.

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