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A Cholecystokinin B Receptor-Specific Aptamer Does Not Activate Receptor Signaling

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ABSTRACT

Targeted nanoparticles which deliver effective doses of chemotherapeutic drugs directly to pancreatic tumors could improve treatment efficacy without the toxicities associated with systemic drug administration. One protein on tumor cells that can be targeted by nanoparticles is a G-protein coupled cell surface receptor, the cholecystokinin B receptor (CCKBR). Previously, we had shown that attaching the CCKBR ligand gastrin to the surface of nanoparticles can enhance their up-take by tumors. The drawback of using gastrin is that it can also activate the receptor, causing tumor cell growth. This study shows that a DNA aptamer that binds to the CCKBR and enhances nanoparticle up-take by tumors does not activate this receptor.

PANC-1 cells, a cultured human pancreatic cancer cell line, were treated for 24 h with CCKBR aptamer 1153. Cell lysates were run on Bis-Tris gels, transferred to membranes, blocked in 5% BSA and incubated overnight with primary antibodies, including antibodies directly against phosphorylated-Akt (Ser473), total Akt, and beta-actin, a protein loading control. Although the CCKBR aptamer 1153 is internalized by pancreatic cancer cells in a receptor-mediated fashion, it does not stimulate cell proliferation. Because of this, we anticipate that it will not activate CCKBR signaling. If aptamer 1153 does not activate downstream receptor signaling, our future work will test whether the aptamer could be used to specifically direct drug-containing nanoparticles to tumors, making chemotherapy treatments for pancreatic cancer patients more effective with fewer off-target effects and toxicity.

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