Novel Selection of Enzymes Loaded in Mesoporous Nanoparticle Carrier Engineered to Selectively Target Cancer Cells Using Aptamer

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Cancer therapies have limitations of selectively delivering cancer-killing agents to cancer cells. After studying apoptosis reactions, I unearthed novel enzymes, Caspase-9 and Cytochrome-C, to induce apoptotic pathways and self-kill cancer cells. Furthermore, I developed a novel delivery system to protect enzymes from biodegradation and target only cancer cells. I started with passively loading the enzymes inside mesoporous silica nanoparticles and sealing surface with cationic lipids. Next, I attached a targeting mechanism to selectively attack cancer cells via fusion of AS1411 aptamer to cationic lipids. This aptamer can selectively target cell surface nucleolin, a marker overexpressed on cell membranes of many cancers including breast cancer. The resulting system called a “protocell” was then delivered to 4t1’s, breast mammary carcinomas, to study effectiveness of targeting and ability to kill cancer cells. Flow-cytometry showed dead cancer cell count increased to ~60% for protocell treatment vs 25% dead cells for control with no treatment, supporting successful cancer cell penetration and kill by protocells. Selective targeting by aptamer was studied by comparing with nanoparticles functionalized with DOTAP which has non-specific binding to cancer cell showing lower kill, supporting that protocell with aptamer was fully interacting with nucleolin makers and taken into cancer cells at a higher rate which was also confirmed by Leica-microscope images. Higher uptake of protocells by cancer cell was observed with higher aptamer dose. Toxicity of silica nanoparticles showed no negative results over the concentration studied. In conclusion, highly selective targeting of cancer cell by the protocells and effectiveness of enzymes in killing the cancer cells is demonstrated.

Awards Won:

Second Award of $2,000