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Funding Source: NSF-REU/NIH Program in Radiochemistry

Targeting the BB2 receptor on human prostate cancer cells using Indium-111 labeled radiopharmaceutical

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The BB2 receptor, belonging to the Bombesin receptor family, has been shown to be highly over expressed in a variety of cancer cell lines, including human prostate cancer. Over expression of the BB2 receptor offers an appealing target for the design of targeted radiopharmaceuticals. The Hoffman laboratory and others have been involved, for over a decade, in synthesizing Bombesin analogues that target the BB2 receptor for the purpose of developing a viable radiopharmaceutical for diagnostic or therapeutic treatment of cancer. Radiopharmaceuticals based on Bombesin analogues are typically composed of a targeting vector, radioisotope, chelator and linking group [See Bifunctional Conjugate Design figure below]. Previous studies have shown that variations in linking groups may affect the retention time of the bifunctional conjugate in prostate cancer (PC-3) cells. Higher retention time allows for more efficacious therapeutic benefits and enhanced diagnostic imaging capabilities. In the work presented, we designed and synthesized a 111In-Bombesin analogue with a phenyl linker group in order to determine if the phenyl linker group would provide higher retention times in prostate cancer. In-vitro analysis of the radiopharmaceutical was performed using PC-3 cells to determine the affinity of the new compound for the BB2 receptor to be 1.09 nM. In-vivo studies of the radiopharmaceutical were also conducted by injection of the radiopharmaceutical into CF-1 (“normal”) mice, as well as SCID (Severe Combined Immunodeficient) mice bearing 2-3 week old PC-3 tumors. Experimental results on SCID mice revealed uptakes of 6.36, 3.34, 2.42 and 1.69 % Injected Dose of radiopharmaceutical per gram of tumor tissue at 0.25, 1, 4 and 24 hours, respectively. Imaging using Micro-SPECT (Single-Photon Emission Computed Tomography) was performed to track the dispersion of the radiopharmaceutical throughout the mouse model and confirmed the targeted uptake of the radiopharmaceutical.