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Using Indium-111 labeled radiopharmaceuticals to target the BB2 receptor on human prostate cancer cells

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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. Our laboratory have been involved, for over a decade, in synthesizing Bombesin analogues that target the BB2 receptor for the purpose of developing radiopharmaceuticals for diagnostic and/or therapeutic treatment of cancer. Radiopharmaceuticals based on Bombesin are typically composed of a chelator, isotope, linking group and targeting vector [See Bifunctional Conjugate Design [figure below]]. Previous studies by our group and others have shown that variations in linking groups 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 this study, we seek to determine the pharmacokinetic benefits achieved in altering the linking group using aliphatic and aromatic linking groups. In-vitro analysis of the radiopharmaceuticals studied found that the Bombesin derivative with the aliphatic linking group demonstrated a slightly higher affinity for the BB2 receptor compared to the Bombesin analogs containing aromatic linking groups. In vivo pharmacokinetic and imaging studies were performed using pre-clinical models of prostate cancer. The tumor uptake of the Bombesin derivatives with the aromatic linking groups were found to be significantly higher compared to that of the Bombesin derivative with the aliphatic linking group. In contrast, the aromatic Bombesin analogs also exhibited higher amounts of undesirable accumulation in the kidneys and other non-target tissues. In conclusion, we found that the aliphatic compounds were more appropriate for diagnostic imaging of prostate cancer due to the reduced non-target retention. The Bombesin analogs with aromatic linking groups showed potential for use as therapeutic agents for prostate cancer treatment.

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