

IN VITRO AND IN VIVO EVALUATION OF MRI CONTRAST AGENT TARGETING HUMAN PROSTATE CANCER

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Prostate cancer is the most common cancer for men in the US, affecting 1 in 6 men. Noninvasive imaging techniques have played important roles in prostate cancer staging and treatment planning. In particular, diffusion-weighted magnetic resonance imaging (MRI) and MR spectroscopy have shown promise in improving accuracy and specificity for localizing cancer. However, the heterogeneities of prostate cancer and the lack of imaging contrast between cancerous and normal tissues limit the clinical applications of such techniques. Development of novel site-specific imaging agents (i.e. receptor-avid agents) will greatly improve clinical outcome in imaging prostate cancer. This project aims to investigate the imaging efficacy of an MRI contrast agent based on Bombesin (BBN). BBN is known to bind with high affinity to gastrin releasing peptide (GRP) receptors expressed in both primary and metastatic prostate cancers. DOTA-KDOTA- β Ala-BBN[7-14]NH₂ is synthesized *via* solid phase peptide synthesis, followed by metallation with GdCl₃ to form a dual Gd-DOTA BBN[7-14] conjugate. The human prostate cancer cell line, PC-3, is used for the investigation. In vitro studies are performed to determine cell binding affinity and specificity of the conjugate. The MRI relaxivity enhancement is determined in a gel-suspension phantom using inversion-recovery spin-echo pulse sequence on a 7T MRI. In vivo studies are performed using severely compromised immunodeficient mice bearing PC-3 xenografts. 12 mice are used for the experiment, 4 for uptake group, 4 for blocking experiment group, and 4 for Omniscan[®] control imaging group. Samples of harvested tissues are analyzed for gadolinium concentrations using inductively coupled plasma mass spectrometry.