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Radioactive and gastrin releasing peptide receptor specific gold nanoparticles in molecular imaging and therapy of cancer

The most recent study involving 77,000 North American men has shown that regular prostate specific antigen (PSA) screening did not save a significant number of lives over 10 years. Development of cancer receptor specific gold nanoparticles will allow efficient targeting/optimum retention within tumors and thus provide synergistic advantages in oncology as it relates to molecular imaging and therapy of prostate cancer. Bombesin (BBN) peptides have demonstrated high affinity toward Gastrin Releasing Peptide (GRP) receptors in vivo that are over expressed in prostate, breast, and small cell lung carcinoma. We have synthesized a library of GRP receptor-avid nanoplatfroms by conjugating gold nanoparticles (AuNPs) with Bombesin (BBN) peptides. Cellular interactions and binding affinities (IC₅₀) of AuNP-BBN conjugates toward GRP receptors on human prostate cancer cells have been investigated in detail. In vivo studies using AuNP-BBN and its radiolabeled analog 198AuNP-BBN, exhibiting high binding affinity (IC₅₀ in microgram/nano/pico molar ranges), have provided unequivocal evidence that AuNP-BBN constructs are GRP receptor specific showing accumulation with high selectivity in GRP receptor rich pancreatic acine in normal mice and also in tumors in prostate tumor bearing SCID mice. The selective uptake of AuNP-BBN peptide analogs have demonstrated realistic clinical potential in molecular imaging via X ray CT techniques as the contrast numbers in prostate tumor sites are several fold higher as compared to the pretreatment groups ($\Delta HU = 150$ units). On the therapeutic front, recent results on therapeutic efficacy and clinical translation efforts of GA-198AuNP (NBI-29)—a glyco protein matrix-conjugated radioactive gold nanoparticulate therapeutic agent will be discussed. Intratumoral administration of a single dose of β -emitting GA-198AuNP (70 Gy) resulted in clinically significant tumor regression and effective control in the growth of prostate tumors over 60 days and the overall reduction in tumor volume reached an unprecedented 82%. This presentation will include: (a) details on clinical utility of AuNP-BBN as a tumor specific molecular imaging agent for X ray CT imaging of prostate and other GRP receptor positive cancers; (b) details on clinical translation efforts of GA-198AuNP (NBI-29) with early Phase I clinical trial results involving therapeutic efficacy in treating prostate tumor bearing dogs. The overall oncological implications on how GA-198AuNP and cancer specific peptide conjugated gold nanoparticles will provide significant benefits to prostate tu, pancreatic, and breast tumor patient community will be discussed.

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