Development of GRP78-Targeted Peptides for Molecular Imaging and Targeted Radionuclide Therapy

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Technology description

Background

Glucose regulating peptide receptor (GRP78) is a protein that plays a major role in appropriate protein folding and the unfolded protein response. The protein can be found on the surface of the cell when experiencing intracellular and extracellular stresses associated with a tumor microenvironment. GRP78 promotes tumor growth, metastasis, and drug resistance in cancer cells. GRP78’ s expression is emerging as generalizable target for PET imaging and targeted therapy for cancer. Potential cancer applications include metastatic melanoma, breast, and prostate—a combined 544,000 estimated new cases in 2014. Currently, no treatments exist that target GRP78.

Technology Description

This technology uses peptide based ligands to bind to the cell surface of GRP78 for diagnostic imaging or cancer radiation therapy. These ligand molecules bind with high specificity and affinity; they are attractive for targeted molecular imaging due to their rapid blood clearance, low immunogenicity, and ease of chemical synthesis. The researchers have modified the peptide structures to include a chelator —a binding agent that suppresses chemical activity—to be labeled with a radionuclide. A fluorescent molecular functional group can be added to identify and quantify concentration of GRP78. An inexpensive imaging agent lead-203 (^{203} Pb) could be used as a screen for patients that would benefit most from the ^{212} Pb therapy.

In low temperatures, neutral pH, and aqueous conditions, the peptide ligands retained their structure and function. These conditions are optimal for achieving high radiolabeling yields, radiochemical purity, and preparing in vitro cell binding, which is difficult with other imaging agents for GRP78.

Advantages

· Allows for diagnostic imaging and cancer radiation therapy
· Identify and quantify concentration of GRP78
· Patient personalized therapy
· In vitro cell binding

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