Encapsulation of Gli-inhibitors blocks tumor invasion into the bone.

Joseph P. Vanderburgh, Shellese A. Cannonier, Kristin A. Kwakwa, Alyssa R. Merkel, Thomas A. Werfel, Craig L. Duvall, Scott A. Guelcher, and Julie A. Sterling

1Department of Cancer Biology, Vanderbilt University; 2Vanderbilt Center for Bone Biology, Vanderbilt University Medical Center; 3Department of Chemical and Biomolecular Engineering, Vanderbilt University; 4Department of Veterans Affairs, Tennessee Valley Healthcare System; Division of Clinical Pharmacology, Department of Medicine, Vanderbilt University Medical Center; 5Department of Biomedical Engineering, Vanderbilt University

Nashville, TN, USA

BACKGROUND

- Tumors including breast, prostate, lung, and oral cancer can establish in bone and disrupt normal bone remodeling.
- Our group and others have shown that Gli2, a Hedgehog signaling transcription factor regulates parathyroid hormone related protein expression and bone destruction.
- Genetic inhibition of Gli2 dramatically reduces tumor induced bone disease.
- Hedgehog inhibitors have not been successful in most tumor in bone, since they often do not express Hedgehog receptors.
- The available Gli inhibitors (including GANT58) are hydrophobic and challenging to deliver in vivo.

HYPOTHESIS

Encapsulation of Gli inhibitors will facilitate delivery of these agents to tumors in bone will help reduce tumor induced bone disease.

RESULTS

Experimental Design:

- Intratibial injection of 2.5 x 10^6 MDA-MB-231 GFP cells or PBS.
- ≤10 mg/kg of GANT58-NPs in 10μl administered intravenously.

Figure 4: GANT58-NP biodistribution. A. In vivo imaging shows the GANT58-NPs in circulation after injection and its gradual clearance through the liver and kidneys. B. Ex vivo imaging shows a preferential localization of the NPs at the tumor site in bone (left) compared to non-tumor bone (right). Images were taken with the Pearl® Impulse system and are representative.

CONCLUSIONS

Microencapsulation of GANT58 microparticles (GANT58-MPs) was fabricated using an oil-in-water single emulsion technique. GANT58-MPs averaged 4.2 μm in diameter and exhibited ROS-dependent release characteristics in vitro.

PARTICLE FABRICATION

- Microparticles: GANT58 microparticles (GANT58-MPs) were fabricated using an oil-in-water single emulsion technique. GANT58-MPs averaged 4.2 μm in diameter and exhibited ROS-dependent release characteristics in vitro.
- Nanoparticles: The GANT58 nanoparticles (GANT58-NPs) were made using an oil-in-water solvent evaporation method. Reactive oxygen species (ROS) trigger particle disassembly and drug release.

FUNDING

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