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Magnetic localization of drug-loaded nanoparticles for tumor therapy: Pre-clinical validation

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Abstract

Breast cancer is the second leading cause of cancer death in women with estimated 2013 incidence of new cases of invasive breast cancer at >230,000 and deaths at ~40,000. Many patients will undergo systemic, multi-drug chemotherapy, including those with locally advanced breast cancer (LABC), or those who fail hormonal modulation and other forms of targeted therapy. Treatment-related adverse events may be experienced by up to 90% of these patients. Thus, demand is growing for targeting methods that enhance therapeutic efficacy while concurrently minimizing associated toxicities. Our proposed nanobiotechnology platform employs an external Magnetic Localization Unit (MLU) to generate focused magnetic field gradients covering the tumor volumes of either superficial orvisceral tumors, to amplify extravasation**,** via the EPR effect**,** of magnetically responsive nanoparticles (MNP) carrying a drug payload. MNP-paclitaxel (MNP-TXL) prodrug constructs, based on bioreversible linkages, demonstrated significant anti-tumor efficacy in a human LABC xenograft model, validating the bioreversible linker chemistry; over 40% of treated mice remain cured and have survived for over a year. In pilot toxicology studies, MNP constructs and MNP-TXL prodrug constructs displayed minimal toxicity against 32 different types of normal tissues, including clearance organs. Vizimag^{tm} 2D software visualizations of magnetic field gradients generated by a proprietary MLU comprised of small permanent magnet arrays indicate that sufficiently-powered magnetic field gradients can be generated to meet varying tumor characteristics of size, area, and depth, for both superficial and deep-seated visceral tumors. Thus, essential pre-clinical validation has been achieved for this magnetic nanovector approach for tumor-specific localization of therapeutics.

Biography

Jim Klostergaard, Ph.D., joined the University of Texas, MD Anderson Cancer Center in Houston, TX over 30 years ago and currently is Professor in the Department of Molecular and Cellular Oncology and has twice served as chair of the Faculty Senate. His doctoral training was at the Roswell Park Cancer Institute, one of three original Comprehensive Cancer Centers designated in the National Cancer Act of 1971. His post-doctoral training was accomplished at the University of California, Irvine. His current interests are in targeted therapeutics and magnetic drug delivery, and he has more than 110 publications in peer-reviewed journals.