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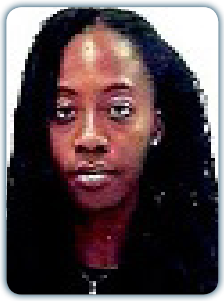

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Molecular imaging biosensors for precise therapeutic interventions in regenerative medicine

Precision medicine aims to provide personalized treatment plans tailored to the specific needs of individual patients. With the growing need for more personalized therapeutic regimens in regenerative medicine, we will demonstrate the importance of cellular imaging biosensors to noninvasively visualize, characterize, and quantify the effective delivery, biodistribution, survival, and engraftment of transplanted stem cells in vivo. The applicability of a novel dual-contrast magnetic resonance imaging (MRI) technique to noninvasively image transplanted stem cells will be discussed. This dual-contrast MRI technique involves two different classes of MRI contrast agents, possessing different diffusion coefficients: high-molecular-weight superparamagnetic iron oxide nanoparticles (SPIONs; T2/T2* contrast agents, with low diffusion coefficients) and low-molecular-weight gadolinium chelates (T1 contrast agents, with high diffusion coefficients). Human mesenchymal stem cells were dual labelled with SPIONs and a gadolinium-based chelate (GdDTPA). The viability, proliferation rate, and differentiation potential of the labelled stem cells were then evaluated. The feasibility of this MRI technique to distinguish between live and dead stem cells was next evaluated using MRI phantoms. We next evaluated the efficiency of this technique to image transplanted stem cells in vivo in both immune-competent and immune-deficient mice, following the induction of radiation-induced brain injury in the mice. All MRI results were validated with bioluminescence imaging. In immune-deficient mice where the transplanted stem cells survived, and both contrast agents were in close proximity, the T2/T2* contrast from the SPIONs predominated and the T1 contrast from the gadolinium chelates was quenched. This T2/T2* MRI contrast was used to track stem cell delivery and stem cell migration. In immune-competent mice where the stem cell died following transplantation, a diffused positive (T1) MRI contrast was generated in the vicinity of the dead cells and served as an imaging marker for cell death (Figure 1). Ultimately, this technique could be used to manage and personalize stem cell therapies in regenerative medicine.

Biography

Ethel J Ngen has expertise in targeted drug delivery systems and bioresponsive molecular sensors for applications in regenerative medicine. She is currently a research faculty member at the Johns Hopkins University School of Medicine, Department of Radiology and Radiological Sciences. Her research focuses on developing cellular and molecular imaging strategies and drug delivery systems for applications in regenerative medicine and in oncology. A major component of her research focuses on developing molecular imaging biosensors for tracking cell-based therapies. Prior to joining the faculty at Johns Hopkins University, she received her PhD in Organic/Medicinal Chemistry from the South Dakota State University's Department of Chemistry and Biochemistry, where her PhD research focused on developing targeted drug delivery systems for applications in Oncology. She then pursued Post-doctoral training in cellular and molecular imaging, at the Johns Hopkins University School of Medicine Department of Radiology and Radiological Sciences, before joining the faculty. Her research interests include targeted and activable drug delivery systems; biosensors and biomaterials for cell based therapies.

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