Magnetic Resonance Imaging and Spectroscopy – Based Evaluation of Biotherapeutics

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Magnetic resonance imaging and spectroscopy (MRI/S) offer non-invasive but detailed insights into various aspects of biopharmaceutical drug development and applications. This work leverages ultra-high field MRI/S to study efficacy, biodistribution and molecular behavior of emerging biotherapeutics, focusing on extracellular vesicles (EV) and monoclonal antibodies (mAb). The central hypothesis is that advanced MRI/S techniques can reveal subtle, yet critical insights on changes at the cellular and molecular levels, influencing therapeutic performance in biologically challenging environments.

The therapeutic potential of extracellular vesicles derived from 3D aggregated hMSC was investigated in rodent models of transient middle cerebral artery occlusion. Longitudinal imaging using ultra-high field ^{23}Na MRI was employed to monitor tissue sodium levels as a marker for cell viability, while ^{1}H T_2-weighted and diffusion-weighted imaging were used to assess cellular swelling and cytotoxic edema. MRS was used to monitor metabolic recovery. Biodistributions of EV were tracked using superparamagnetic iron oxide nanoparticles. Female animals demonstrated improved recovery across most metrics compared to male animals.

To facilitate EV labeling while preserving therapeutic integrity, a novel glucose-coated iron oxide nanoparticle was developed that leverages the GLUT-1 transporters to achieve passive uptake without the need for membrane disruption. The labeling efficiency was evaluated using *in vitro, in vivo* and *ex vivo* MRI. Successful uptake of contrast agent was confirmed along with *in vivo* detection within 4 h of treatment administration.

As another biotherapeutic, mAb remain one of the most widely used pharmaceutical platforms, particularly in oncology and immunology. However, their stability and structural integrity can be compromised during manufacturing, storage and administration due to exposure to hydrophobic interfaces. such as air-water or oil-water boundaries. To investigate potential changes, localized diffusion-weighted and T_2-weighted MRS protocols were developed and implemented to evaluate mAb alterations at oil-water interfaces. These measurements provide insights into molecular mobility, relaxation dynamics and conformational stability. The resulting data can inform formulation strategies and improve handling protocols to preserve therapeutic efficacy throughout the product lifecycle.

In total, this work demonstrates how advanced MRI and MRS techniques can be employed to characterize biotherapeutics across multiple biological scales. By integrating high-field imaging with molecular spectroscopy, unique noninvasive metrics that are sensitive to cellular recovery, protein integrity and therapeutic delivery were evaluated.