
Emerging MRI-based approaches for in-vivo cell tracking of cellular therapeutics and inflammation

Eric Ahrens*¹

¹UC San Diego (UCSD) – États-Unis

Résumé

My research focuses on adapting magnetic resonance imaging (MRI) to visualize cellular and molecular processes in vivo. My research has been on two inter-related tracks. The first track leverages molecular genetics to develop reporters that impart exogenous MRI contrast to tissue in a cell-specific or event-related manner. We have developed first-generation MRI reporters by using transgenic and vector technologies to express reporter genes coding for novel iron-binding proteins in the ferritin family. Following transgene expression in situ, the ferritin shells sequester physiologically available iron, and bio-mineralization in the ferritin core renders the complex paramagnetic, which produces MRI contrast. My laboratory has designed recombinant ferritin molecules and performed detailed characterizations of their structure, function, and toxicity. A multitude of applications exist for these reporters, including labeling stem cells for long-term tracking and imaging transgene expression. In a second parallel track, my laboratory has developed a new field of cell tracking called ‘in vivo cytometry.’ In this platform technology, cell populations of interest are labeled, tracked, and quantified in vivo. Cells are initially labeled in culture using novel perfluorocarbon (PFC) nanoemulsions. Following transfer to the subject, cells are tracked in vivo using fluorine-19 (19F) MRI. The fluorine inside the cells yields cell-specific images. Images are readily quantified to measure apparent cell numbers at sites of accumulation. We and others have demonstrated that in vivo cytometry can track a wide variety of cell types including stem cells, dendritic cells (DCs), T cells, and tumor cells. Importantly, we have demonstrated that in vivo cytometry is clinically feasible. Moreover, my lab is working on next generation PFC agents and imaging methods that will yield a 5-10 fold sensitivity increase. We have also devised novel PFC nanoemulsions that are designed for intravenous injection and target inflammatory leukocytes in vivo. Following injection, nanoemulsion droplets are predominantly taken up by monocytes and macrophages. Since these in situ labeled cells participate in inflammatory events in the body, the result is 19F accumulation at inflammatory loci. The 19F MRI signal can be quantified in inflammation hot-spots, and this signal is linearly proportional to the macrophage burden. We have used these facile agents to follow inflammation with high sensitivity and specificity in a wide range of animal models. To push the field of cellular-molecular MRI forward, my lab takes an integrated approach that applies principles of chemistry, biology, medicine, nuclear spin physics, and image processing.

*Intervenant