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Use of dual-mode cellular imaging in cancer vaccine development

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Further clinical optimization of the dose, route, vaccine composition, and use of immunoadjuvants could greatly benefit from clinical imaging approaches that can interrogate the biological fate of cells repeatedly and non-invasively without the need for obtaining biopsies. By pre-labeling DCs with superparamagnetic iron oxide nanoparticles as an MRI contrast agent, it is not only possible to follow their migration to nearby lymph nodes, but also to verify if the injections have been performed accurately. Surprisingly, in our first clinical DC MRI cell tracking study, we showed that the target lymph node was routinely misinjected in 50% of stage IV melanoma patients.

A different kind of cancer vaccine developed at our institute is GVAX, which consists of lethally irradiated tumor cells engineered to secrete GM-CSF. By pre-labeling GVAX with SPIO, we developed "magnetovaccination" as a novel MRI technique to monitor serially over time DC antigen capture and subsequent homing to draining lymph nodes. Using magnetoGVAX and MRI for serially monitoring the afferent arm of the immune response (DCs), and bioluminescent imaging (BLI) for monitoring the efferent arm (T cells), we applied dual-mode imaging to better understand the time course of antigen capture, lymph node delivery, and clonal T cell expansion. Depending on the timing of administration, toll-like-receptor (TLR) agonists either reduced or enhanced antigen capture and delivery to the lymph nodes. The lack of antigen delivery to lymph nodes was consistent with the lack of T cell BLI signal in the lymph nodes. In those cases, a massive extranodal T cell proliferation occurred in the liver and spleen. Our studies show how dual-mode imaging can be used to evaluate and optimize combinatorial cancer vaccines.

Biography:

Dr. Jeff W. M. Bulte is a Professor in the Johns Hopkins Departments of Radiology, Oncology, Biomedical Engineering, and Chemical & Biomolecular Engineering. He serves as the Director of Cellular Imaging at the Johns Hopkins Institute for Cell Engineering. He specializes in molecular and cellular imaging.

Dr. Bulte has pioneered methods to label cells magnetically, making them visible by magnetic resonance imaging (MRI). His team is developing MRI cell tracking techniques, reporter genes and immunoprotective semi-permeable microcapsules detectable by MRI, computed tomography, ultrasound, and bioluminescent imaging.

Dr. Bulte received his undergraduate degree in biology and masters in medical biology from the Free University of Amsterdam in The Netherlands. He earned his Ph.D. in medicine summa cum laude from the University of Groningen in the Netherlands in 1991. He subsequently spent 10 years with the National Institutes of Health, first as a postdoctoral fellow and then a staff scientist in the Laboratory of Diagnostic Radiology Research. Dr. Bulte joined the Johns Hopkins faculty as an Assistant Professor in 2001, became an Associate Professor in 2002, and a Professor in 2006.