Specific detection of HER-2 positive tumors in mice using superparamagnetic relaxometry (SPMR)

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Superparamagnetic Relaxometry (SPMR) is a non-invasive technique that utilizes superconducting quantum interference device (SQUID) detectors to localize and quantify the magnetization of superparamagnetic iron oxide (Fe_3O_4) nanoparticles (NPs) specifically bound to cancerous tumors. In an SPMR measurement, polyethylene glycol (PEG) coated NPs are functionalized with a tumor-targeting monoclonal antibody and injected intravenously. NPs that reach and bind to the target tissue are measured by the MRX™ instrument, while unbound nanoparticles, such as those freely circulating in the bloodstream, are not detected.

Here, we demonstrate the use of SPMR for specific detection of HER2 positive tumors in mice using long-circulating anti-HER2 antibody conjugated PrecisionMRX® NPs in vitro and in vivo. The stability and biofunctionality of conjugated nanoparticles were measured by dynamic light scattering, gel electrophoresis, and ELISA. Specific binding of the nanoparticles was defined by the ability of the native HER2 antibody to competitively block the binding of the anti-HER2 conjugated NPs to HER2 positive cells in vitro and in vivo. Nude mice with xenograft BT474 tumors were intravenously injected with anti-HER2 NPs at a dose of 20 mg/kg of body mass, while 'competition' mice were injected with native anti-HER2 up to 24 hours prior to injection of anti-HER2 NPs. Mice were measured individually on the MRX™ instrument over 4-hours. At 4 hours, blood, tumor, and organs were harvested and analyzed for SPMR signals and anti-HER2 content.

SPMR measurements of mice injected with anti-HER2 NPs were detected in the tumor and liver (the site of NP elimination), as illustrated in Fig. 1. Conversely, in mice dosed with native antibody prior to anti-HER2 NP injection, only the tumor signal was reduced. These results suggest targeted delivery of conjugated NPs to HER2 positive tumors and the utility of SPMR for the sensitive and specific detection of cancer in vivo.

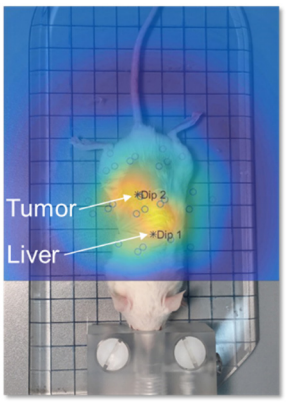

Figure 1. MRX dipole map showing the locations of a BT474 tumor and the liver following injection of anti-HER2 NPs.

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