Superparamagnetic relaxometry (SPMR) for sensitive detection of HER-2 positive tumors in mice

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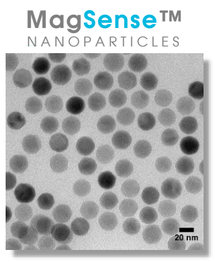
Introduction

- The MagSense™ platform consists of superconducting quantum interference devices (SQUIDs) to detect tumor targeted MagSense™ nanoparticles (MSNPs) that are specifically bound to cancer cells.
- The detection relies on SQUIDs high sensitivity to magnetic field produced by the superparamagnetic relaxation (SPMR) of the NPs.

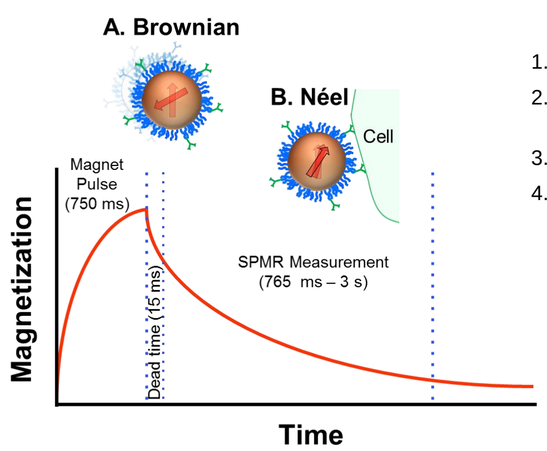


Conceptual MagSense™ clinical instrument

Objectives

- Imagion Biosystems, Inc. is developing the MagSense™ platform for the sensitive and specific detection of HER2-positive breast cancer.
- Preclinical studies will generate validation data for the first clinical trial, wherein the MagSense-anti-HER2 platform will be used to accurately HER2-positive breast cancer

The SPMR Measurement



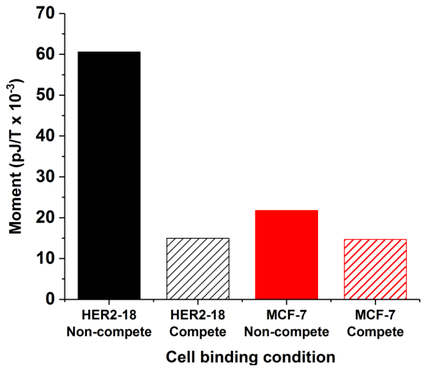
1. Inject anti-HER2 MSNPs
2. Small magnetizing pulse is applied
3. Field turned off
4. MSNPs relax to their equilibrium states.
   - **Brownian** motion of unbound MSNPs (fast and **undetectable)**
   - **Néel** relaxation of MSNPs bound to cells (slow and **detectable**)

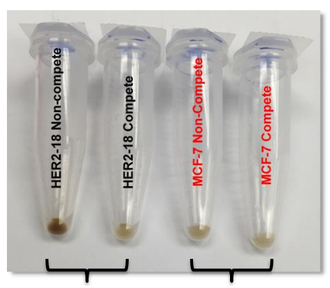
SPMR only detects nanoparticles bound to cells/tissues

Characterization of MSNPs

Analytical Test	Method
Particle Size	Small angle X-ray scattering (SAXS)
Hydrodynamic size	Dynamic light scattering (DLS)
Anti-HER2 Content	Direct ELISA
Specificity	Competition ELISA
Specificity	SPMR, digital photography
Stealth	Zeta potential, agarose gel electrophoresis

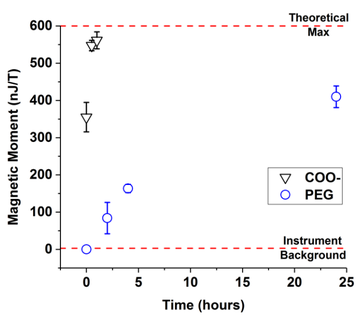
In Vitro Pharmacology



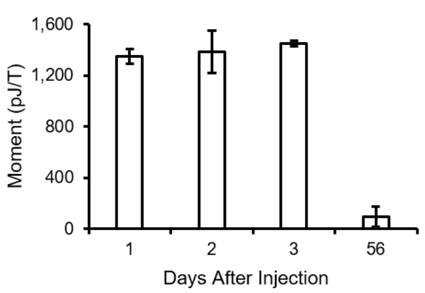


- Competitive binding of anti-HER2 MSNPs can be correlated to the HER2 cell expression

In Vivo Pharmacology

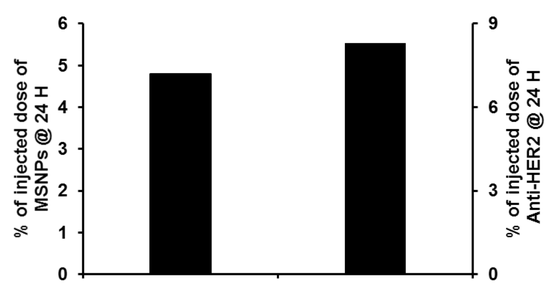


- PEGylation significantly increases the circulation time of MSNPs

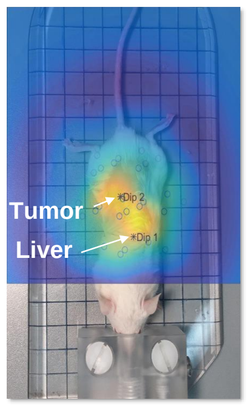


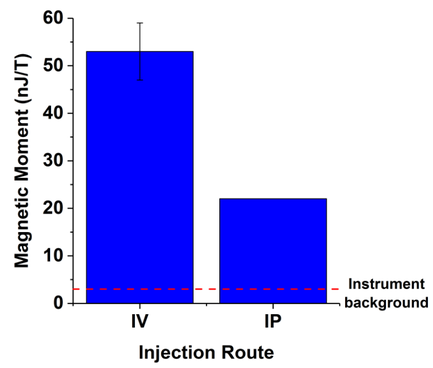
- PEGylated MSNPs degrade by 8 weeks post injection

Anti-HER2 MSNPs remain stable in circulation



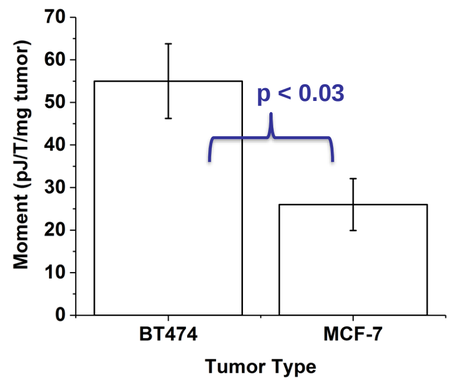
In Vivo Diagnosis





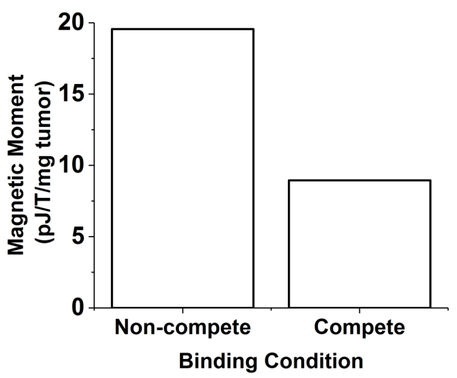
- 4% MSNP delivery to tumor

In vivo specificity



- SPMR signal corresponds with HER2 expression in vivo

In vivo competition



- ~50% competition of anti-HER2 MSNPs by native anti-HER2

Conclusions and Future Work

- Developed anti-HER2 conjugated, PEGylated MSNPs that specifically bind to HER2 expressing breast cancer cells in vitro and in vivo and degrade within 8 weeks
- Future work is focused on clinical translation of the MagSense™ anti-HER2 platform for detection of breast cancer metastases in the lymph nodes.

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