Turning 'cold' tumors 'hot': Guided magnetic hyperthermia for tumor immune stimulation

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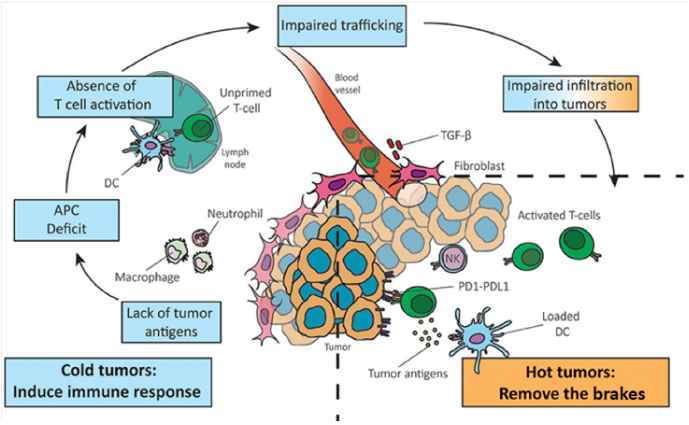
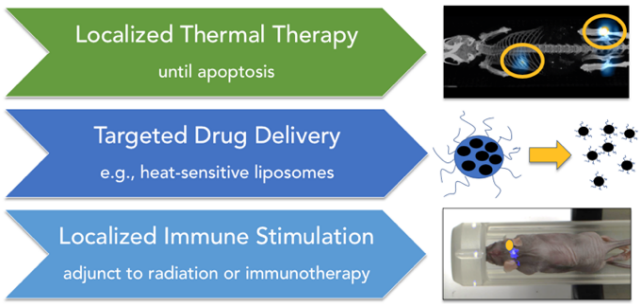
The success of cancer immunotherapy has driven the rapid growth of research into immuno-oncology, which has in turn fueled the need to be able to determine the location of a variety of immune cells in solid tumors and systemically over time. There is a strong association between response to the new checkpoint inhibitor treatments and the immune status of a tumor, and new methods to determine or modify that status are needed.

Magnetic Particle Imaging (MPI) is a novel preclinical molecular imaging technique that can be used to non-invasively track iron-oxide tagged immune (and other) cells in vivo. By combining accurate **quantitation**, specificity, and **depth-independent 3D imaging**, MPI can provide information on macrophage and other cellular biodistributions over time, for weeks or even months.

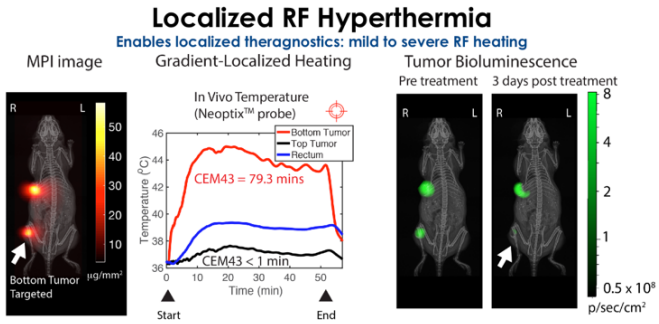
In addition to being an imaging modality, MPI can be used for localized theragnostics and drug delivery. The same or similar nanoparticles that are used for imaging can also be used to generate heat for localized magnetic hyperthermia.



Imaging is used to determine the distribution and amount of iron in a sample, then MPI-based magnetic gradients are used to limit the hyperthermia to only a small, adjustable "field-free region" in the sample. Heating can be severe, until the start of apoptosis, or mild, to promote a localized immune response, which can be beneficial as an adjunct to both radiation and immune therapies, improving radiation therapy efficacy and potentially turning **"cold"** immunologically unresponsive tumors **"hot"**.



The nanoparticles used for both imaging and hyperthermia are superparamagnetic iron-oxide, with considerable differences in imaging sensitivity and resolution and hyperthermia efficiency possible depending on the size, shape and composition of the particles. Unlike many other molecular imaging modalities, resolution for MPI depends strongly on the nanoparticle being imaged, with resolutions from 100um to nearly 2mm being possible with the same imaging system simply using different particles.



In addition, the design and development of heat-sensitive nanoparticles and liposomes for use with mild hyperthermia is an important aspect of MPI development.

MPI is a rapidly growing molecular imaging technique, with applications across many biomedical fields. The non-invasive, 3D tracking of immune cell distributions systemically in vivo, is an important aspect of understanding immune-tumor interactions, and the combination of imaging nanoparticles along with using them for localized mild or severe RF hyperthermia is a powerful addition to the toolkit for oncology research.

References: Zaidi, N; Jaffee, E. J Clin Invest (2018). Sharma, P. et al. Curr Opinion Immunol (2016). Tay Z.W. et al. ACS Nano (2018) https://blog.dana-farber.org/insight/2018/06/enhancing-immunotherapy-race-make-cold-tumors-hot/

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