Nanoparticles Make Cancer Cells Visible

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Wouldn't it be nice if we could detect tumors and their metastases as easily as we find broken bones with X-rays? A team of scientists headed by S. Bhatia in Boston has been working on this problem. They have found a way to make a tumor-specific protease visible by using Fe_3O_4 nanoparticles and magnetic resonance imaging (MRI).

Organic tissue is mostly made of water and fat, substances that contain many protons (positively charged hydrogen ions or hydrogen nuclei). These have an intrinsic angular momentum, known as spin, and thus a magnetic moment. In a magnetic field, they line up and rotate with a certain frequency that is proportional to the strength of the external field. If electromagnetic waves with the same frequency (resonance) are beamed in, they disturb the orientation of the protons in the external material field.

When the electromagnetic wave is switched off, the protons flip back to their original position, which causes them to give off an electromagnetic signal of their own. This can be detected and gives information about the proton density and the chemical environment in the region being studied. These data allow for the computation of a 3D image that depicts the different tissues in the body.

How can this be used to detect mutated cells with the best possible resolution and high confidence? The Boston researchers used nanoparticles of Fe_3O_4 whose magnetic properties change when they aggregate into large multimeric complexes.

Two biomolecules that bind to each other with high affinity, biotin and neutravidin, act as a “glue” to hold the Fe_3O_4 particles together. Half of the nanoparticles are coated with biotin, the other half with neutravidin. Long polyethylene glycol (PEG) chains are coupled to these biomolecules in order to keep the particles from interacting with each other. The anchor for the PEG chains is a peptide that contains a segment that can be cleaved by a tumor-specific enzyme, matrix metalloproteinase-2 (MMP-2).

MMP-2 is mostly found in the immediate area around growing tumor cells, meaning that the PEG chains are only cleaved from the Fe_3O_4 nanoparticles when they are near a tumor. This then allows the biotin–neutrovidin glue to do its job—the Fe_3O_4 particles aggregate and the tumor becomes visible in the MRI image.

Reference: Proteolytic Actuation of Nanoparticle Self-Assembly, *Angewandte Chemie International Edition* 2006, 45, No. 19, 3161–3165, doi: 10.1002/anie.200600259

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