Novel chemistry amplifies ability of nanoparticles to detect rare cells

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One of the most promising characteristics of nanoparticles as diagnostic agents is the ability to attach to the nanoparticles surface any of a wide variety of targeting molecules that can increase the distinction between malignant and healthy cells, making it easier to spot small numbers of diseased cells within a sea of healthy cells. However, the development of such targeted nanoparticles has been hampered by the need to optimize the chemical methods used to link the targeting molecule to the nanoparticle for each unique combination of the two.

Now, a team of investigators at the Massachusetts General Hospital and Harvard Medical School has developed a chemical methodology that can be used to attach virtually any antibody to a nanoparticle without the need to optimize the reaction conditions. This team, led by Ralph Weissleder, who is a co-principal investigator of the MIT-Harvard Center of Cancer Nanotechnology Excellence, published their findings in the journal *Nature Nanotechnology*.

Using a nanoparticle that is both magnetic and fluorescent and three different monoclonal antibodies known to target tumor-associated surface molecules, Dr. Weissleder and his collaborators applied what they call "bioorthogonal chemistry" to create nanoparticles that bind strongly to the targeted tumor types. They showed that binding took place with the proper cells using a novel miniaturized magnetic resonance detector system developed by the Weissleder team for use in point-of-care applications.

The investigators then compared the binding ability of their targeted nanoparticles with those prepared using one of the now-standard approaches for linking antibodies to nanoparticles. The new process created nanoparticles that stuck to their targeted cells with 10 to 15 times the avidity of those nanoparticles prepared with standard methods. In addition to improving the sensitivity of tumor cell detection using targeted nanoparticles, this new chemistry could also improve strategies for developing targeted drug delivery applications.

This work, which was supported in part by the National Cancer Institute, is detailed in a paper titled, "Bioorthogonal chemistry amplifies nanoparticle binding and enhances sensitivity of cell detection." An abstract of this paper is available at the journal's Web site.

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