Nanoparticles 'hitchhike' on immune cells to catch cancer metastasis early

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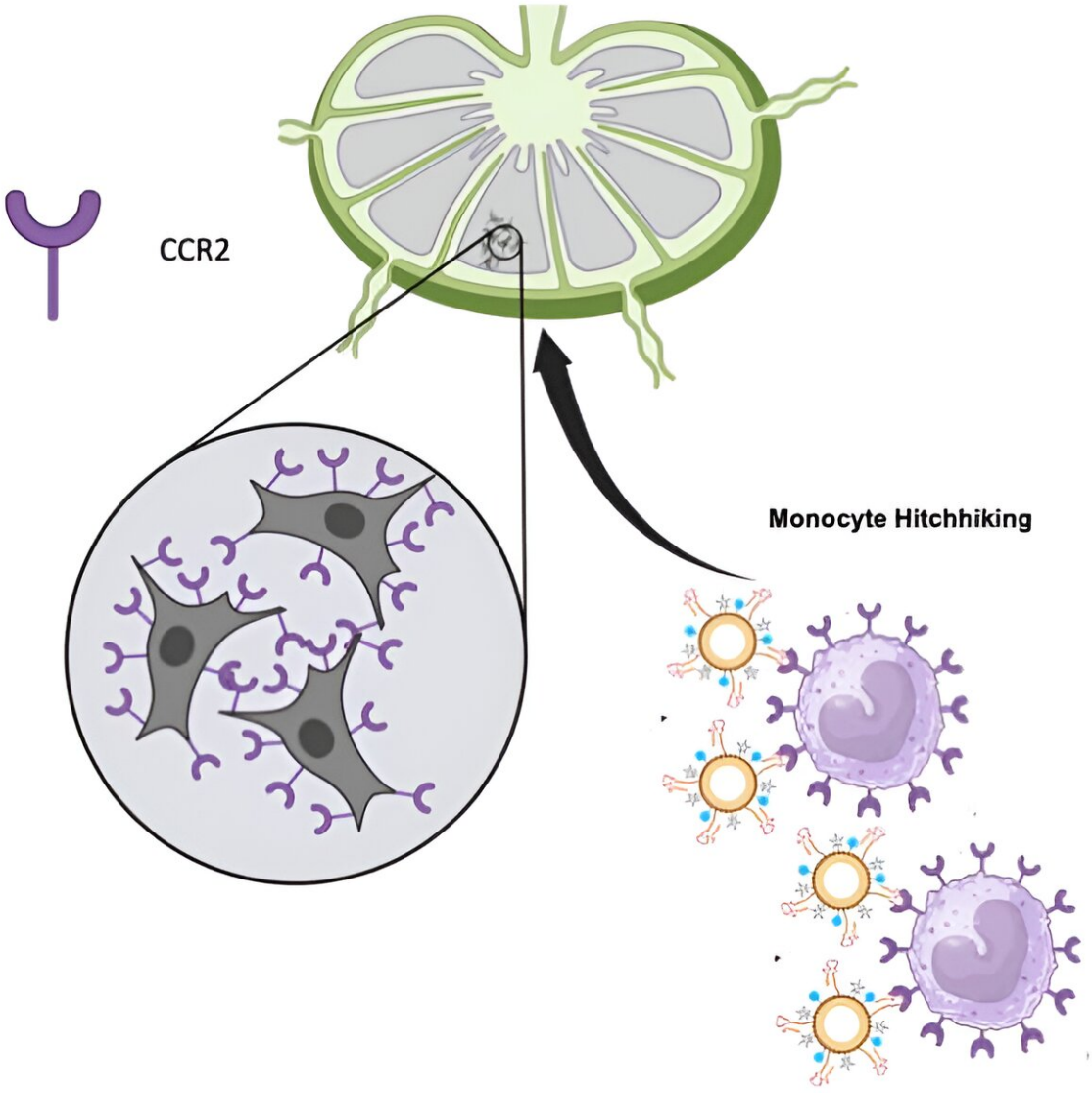

The Chung Lab has developed a nanoparticle that can hitchhike on immune cells and travel to the lymph nodes. Credit: Chung Lab

Lymph nodes are the canaries in the coal mine of our immune system—firing into gear at the first indication of illness, then sending immune cells where they're needed in the body to fight infection and disease.

For the nearly 20 million patients around the world diagnosed with cancer each year, the lymph nodes are an invaluable early indicator of whether their cancer has metastasized—when cancer cells begin to spread to another organ. Catching metastasis as early as possible means that the patient can be administered the necessary chemotherapy and immune therapies that will vastly improve their prognosis.

Researchers at USC's Alfred E. Mann Department of Biomedical Engineering have developed a new nanoparticle that can "hitch a ride" on immune cells, or monocytes. Because of its tiny size, the particle can tag along directly into lymph nodes and help metastasis show up on MRIs where it would otherwise be too hard to detect. The results could lead to more advanced contrast agents that can be injected into patients to improve MRI cancer screenings of the lymph nodes.

The work has been published in *ACS Nano* and was led by Dr. Karl Jacob Jr. and Karl Jacob III Early-Career Chair Eun Ji Chung, and Noah Trac, a Ph.D. student in the Chung Lab.

While lymph nodes are an essential factor in cancer detection, screening them via biopsy is painful and invasive, and can lead to unwanted side effects like infection, lymphedema and thrombosis. Imaging tools such as MRI detection are non-invasive. Still, they also have significant

shortcomings when it comes to screening lymph nodes,

"MRIs will look at the lymph node's size, but that does not have a great connection and correlation to the fact that it is metastatic," Chung said. "Even if you have a cold, your lymph nodes will start inflaming."

"The major issue with current MRI techniques is not that they don't detect the immune cells," Trac said. "A major issue with current contrast agents is that there is no cancer-targeting mechanism, so most lymph nodes are lit up equally, regardless of whether or not there is cancer."

To address this challenge, Chung, Trac and their co-authors developed a nanoparticle that targets a receptor present on both tumor cells and immune cell monocytes—cells that travel to the lymph nodes and are increasingly prevalent under disease conditions.

"The idea behind this nanoparticle is to try and direct the delivery of the gadolinium contrast agent to lymph nodes that have cancer, so that they show up brighter on the MRI than healthy lymph nodes," Trac said.

The diagnostic tool would also offer strong clinical value for doctors to not only catch first-time metastasis during an initial cancer diagnosis, but it will also allow clinicians to keep track of cancer recurrence.

"Just say a primary tumor has been removed, but perhaps they didn't get all of it, or the cancer comes back and it's metastatic for the second time. Recurrent metastasis is much harder to detect and can lead to worse outcomes for the patient," Chung said.

Hitching a ride to light up cancer

The nanoparticles work by targeting a protein expressed by cancer cells, known as C–C chemokine receptor 2 (CCR2). The particles "hitchhike"

onto the immune cell monocytes that the body produces that also express this same receptor in response to the cancer. The monocytes then give the particles a free ride into the lymph nodes, where the particles can effectively highlight the metastatic cancer cells and enable clearer detection via MRI.

"The reason why this mechanism works, in addition to the targeting elements, is because our particle size is also very unique, and it can reach the lymph nodes," Chung said. "We found there's a size cut-off and our particle type is able to pass into the lymph nodes and target cancer cells that have gotten there, along with the monocytes that express this receptor."

The process offers game-changing benefits for the early detection of cancer metastasis in the lymph nodes. While previously, metastasis could only be assessed by an increase in lymph node size; the new Chung Lab particles could lead to MRI contrast agents that can highlight metastatic cells in lymph nodes that may otherwise appear normal. In experiments using a mouse model, the team demonstrated that the particles increased the signal detected by MRI by up to 50%.

"The particles are amplifying the signal, and we can see that at points where the lymph nodes haven't yet changed in size, and the metastasis is very early. We're providing this benefit where, clinically, you wouldn't be able to see metastasis at all," Chung said.

The next step for the research team is to get their work closer to clinical applications for MRI contrast agents. The work has been submitted to the Nanoparticle Characterization Laboratory at the National Institutes of Health, where a third party will assess and validate the work to enable it to move closer to human trials.

More information: Noah Trac et al, MRI Detection of Lymph Node

Metastasis through Molecular Targeting of C–C Chemokine Receptor Type 2 and Monocyte Hitchhiking, *ACS Nano* (2024). DOI: 10.1021/acsnano.3c09201