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How metastatic cancer survives in the subarachnoid space

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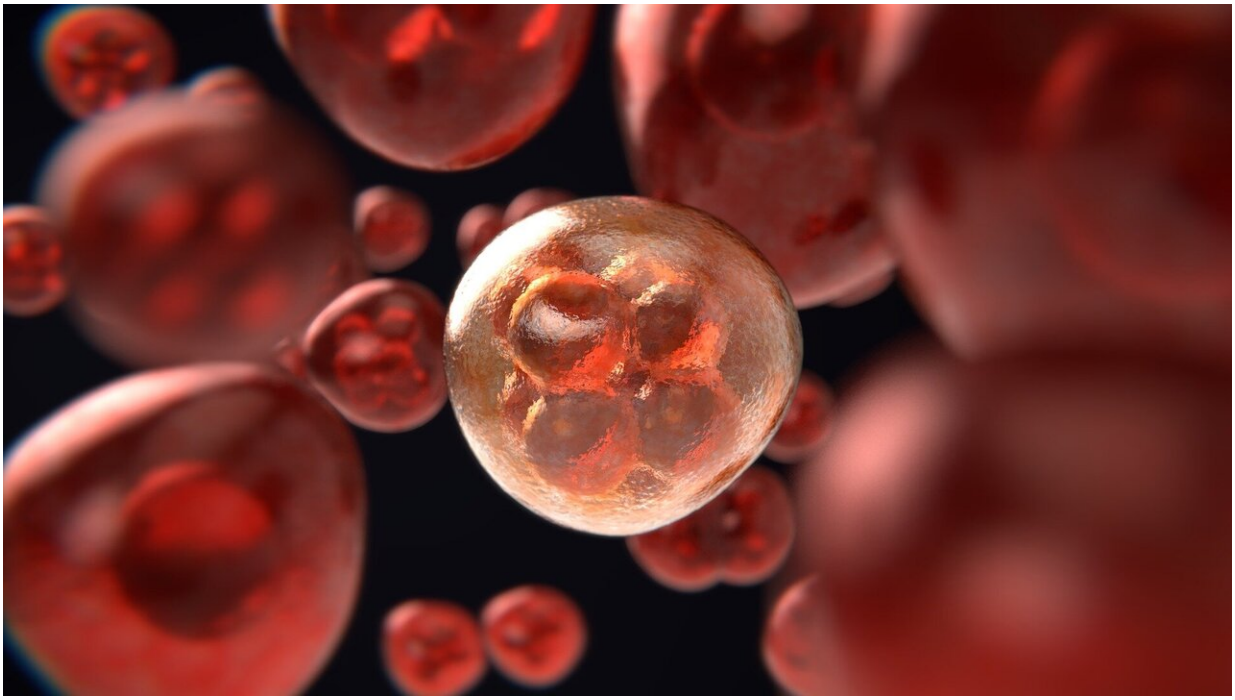

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A team of researchers working at Memorial Sloan Kettering Cancer Center in New York has discovered how metastatic cancer is able to survive in the hostile subarachnoid space. In their paper published in the journal *Science*, the group describes RNA sequencing studies they conducted with patients with leptomeningeal metastases (LS)—a type of cancer involving membranes of the spinal cord and brain—and what

they learned about it. Livia Garzia and Michael Taylor with McGill University and the Hospital for Sick Children in Toronto have published a Perspective piece in the same journal issue outlining the work by the team in New York.

Because of its importance and extreme sensitivity, the central nervous system has extra protections against foreign invaders. One of them is the brain-blood barrier—a semipermeable border of endothelial cells that blocks solutes from entering. Another is the host of macrophages that exist in the spinal fluid that seek out and destroy possible invaders. One of the mysteries in cancer research is how some types of cancer can exist in such a hostile environment. In this new effort, the researchers focused on one specific kind of cancer in the central nervous system—LS. Their main goal was to find out why certain types of cancer can not only appear in the subarachnoid space (the isolated part of the central nervous system that is filled with cerebrospinal fluid), but also survive and metastasize.

To learn more, the researchers collected spinal fluid samples from five patients with LM. They then conducted single-cell RNA sequencing on the samples. They discovered that the cancer cells have a high-affinity iron collection system that allowed them to use iron found in the spinal fluid. They note that there is very little iron in spinal fluid, which makes it a precious commodity—it is necessary for DNA synthesis and cell metabolism. Grabbing and using the iron allowed the cancer cells to outperform the macrophages, which gave them the upper hand. The net result, the researchers note, is that iron capture allows cancer cells not only to survive, but to flourish.

More information: Cancer cells deploy lipocalin-2 to collect limiting iron in leptomeningeal metastasis, *Science* (2020). 10.1126/science.aaz2193