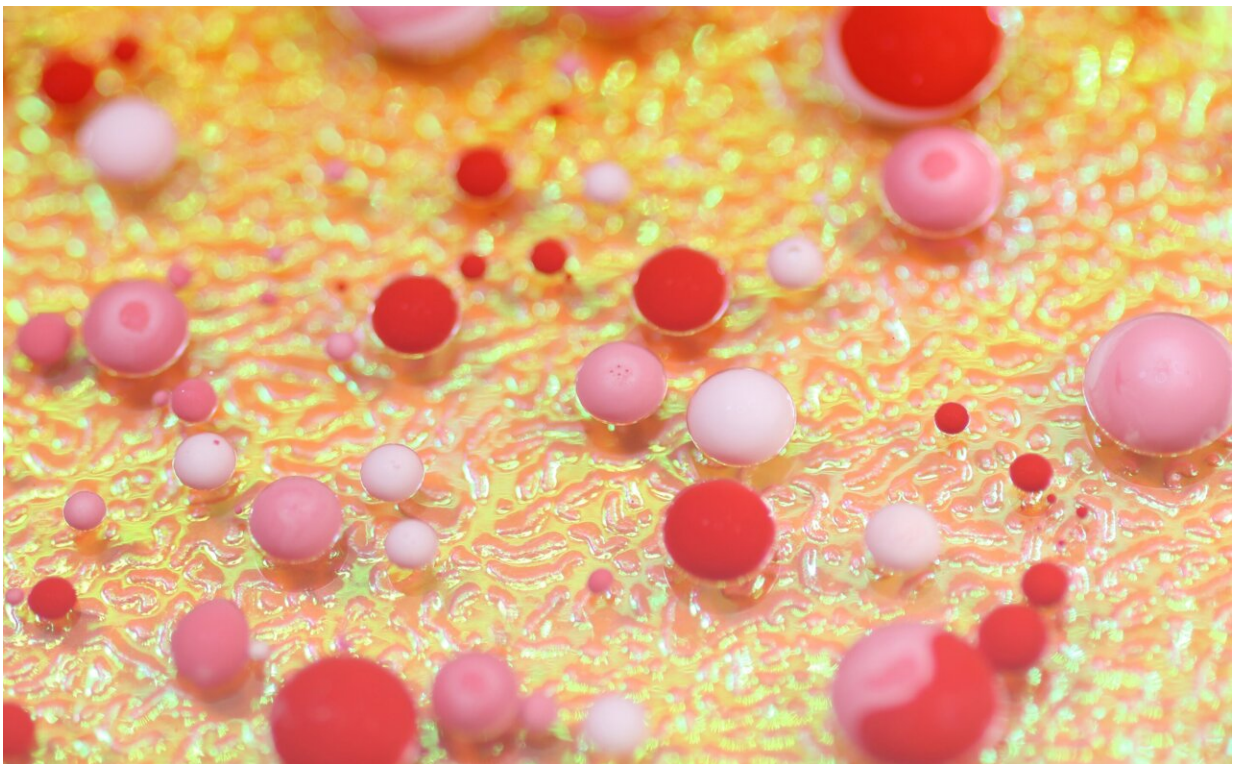


Researchers develop strategy to non-invasively monitor key immune cells in tumors

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A Ludwig Cancer Research study has developed a strategy to non-invasively track immune cells known as macrophages within brain and breast tumors in living mice. Cancers often recruit and reprogram these

tumor-associated macrophages, or TAMs, to support their own growth and confer resistance to therapies. Led by Ludwig Lausanne's Johanna Joyce and Davide Croci and their colleague at the Lausanne University Hospital, Ruud B. van Heeswijk, the study appears in the current issue of *Science Translational Medicine* and is featured on the cover of the journal.

"Macrophage monitoring has the potential to significantly improve the therapeutic management of a variety of cancers," said Joyce. "Brain malignancies, among the deadliest primary cancers and metastases, especially depend on the presence of macrophages and the targeting of these [immune cells](#) may represent a key strategy for their treatment."

The Joyce lab has for several years investigated the critical role played by TAMs and other immune cells in tumors that originate in the brain or metastasize there from elsewhere, such as the breast, lung or skin. She and her colleagues have shown, for example, how drugs that block the action of a factor essential to macrophage growth can reprogram TAMs from a cancer-supporting state to a cancer-killing state. They've discovered how the resident macrophages of the brain, microglia, and those drawn to tumors from the [blood circulation](#)—monocyte-derived macrophages (MDMs)—differentially populate gliomas and brain metastases. Their studies have also demonstrated how TAMs contribute to the recurrence and therapeutic resistance of brain tumors, and identified strategies to address each of these challenges.

The ability to track changes in macrophage numbers and distribution over time could, therefore, do much to improve the management of brain cancer therapy. But this is easier said than done. Currently, the immune landscape of gliomas can only be viewed via biopsy, which—aside from being highly invasive and thus anything but routine—provides just a glimpse of a small segment of a [tumor](#) at a particular point in time.

To non-invasively study TAM populations over time, Joyce and her colleagues exploited a basic function of the immune cells, which is to roam around the body, gobbling up particulate matter. They injected mouse models of gliomas, breast cancer and breast-to-brain metastases with two different types of nanoparticles, both labeled with a fluorine isotope (^{19}F), that each emits a distinctive and discernible signal detectable by [magnetic resonance](#) imaging (MRI)—a standard imaging technology of cancer care. The signals emitted by these nanoparticles are also distinct from the one transmitted by a hydrogen isotope (^1H), which is used to image tissue, including cancerous growths.

The researchers demonstrate that the [nanoparticles](#) accumulate in TAMs, permitting a direct and non-invasive means to ascertain with "multispectral" MR imaging not just the abundance but also the location of the immune cells across the geography of tumors. Their imaging revealed, for example, that the labeled TAMs accumulate around the leaky, malformed blood vessels generated by tumors, a discovery that could have implications for combination therapies under development that seek to normalize tumor vasculature to improve drug delivery.

Radiotherapy is a standard treatment of glioma, and recent research by the Joyce lab has shown that it significantly alters the overall number and types of TAMs after initial irradiation and upon disease recurrence. In the current study, Joyce, Croci, van Heeswijk and colleagues confirmed that while microglia and MDMs are found in roughly equal numbers in untreated gliomas, MDMs tend to take over and cluster together at a distance from microglia in tumors that recur following radiotherapy.

"The imaging revealed previously unknown niches for TAMs in untreated, dormant and recurrent gliomas," says Joyce. "It also captured how the distribution of TAMs differs between gliomas and brain metastases. The imaging approaches developed in this study could, with further development, help clinicians non-invasively identify brain tumor

types, better monitor prognosis and drug resistance and thus improve the therapeutic management of brain tumors."

Moreover, those strategies will provide scientists a window into the changing immune landscapes of tumors, revealing insights critical to the development of new cancer therapies.

More information: Davide Croci et al, Multispectral fluorine-19 MRI enables longitudinal and noninvasive monitoring of tumor-associated macrophages, *Science Translational Medicine* (2022). [DOI: 10.1126/scitranslmed.abo2952](https://doi.org/10.1126/scitranslmed.abo2952)

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