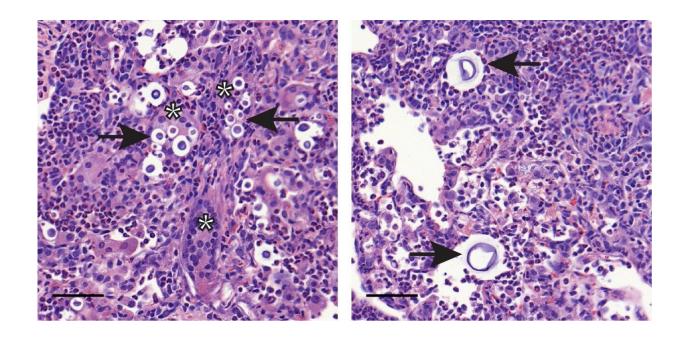


Inflammatory monocytes play contradictory roles in fungal infections

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Cryptococcus neoformans cells (black arrows) are visualized within multinucleated giant cells (white asterisks) in the lungs of wild type mice (left panel). Ablation of monocytes in CCR2-DTR mice (right panel) reduces the number of macrophages and multinucleated giant cells and impedes the proliferation of *C. neoformans* in the lungs. Credit: Heung 2019

Immune cells called inflammatory monocytes are often one of the first responders to infections, but they actually facilitate the progression of *Cryptococcus neoformans* infection in mice, according to a study published March 21 in the open-access journal *PLOS Pathogens* by Lena



Heung and Tobias Hohl of Memorial Sloan Kettering Cancer Center. According to the authors, these disparate results indicate that inflammatory monocytes possess a plasticity of function that can regulate infection outcomes, making them an important target for immunomodulatory therapies against *C. neoformans*.

C. neoformans is a yeast that is prevalent throughout the environment and can result in a fatal infection of the central nervous system when inhaled into the lungs by patients with impaired immune systems. Our understanding of the immune responses that either help clear *C. neoformans* from the lungs or permit development of disease remains limited.

In the new study, Heung and Hohl used a mouse model of lethal *C. neoformans* infection to discover that <u>inflammatory monocytes</u> facilitate the progression of infection rather than clearance. In the absence of inflammatory monocytes, murine survival is improved and there is decreased fungal burden in the lungs and other sites. The results reveal a novel and critical role for inflammatory monocytes in mediating detrimental host outcomes in a model of fatal respiratory infection with *C. neoformans*. These findings contrast with the beneficial functions of inflammatory monocytes described in mouse models of other fungal infections. According to the authors, the results establish a foundation for future work to target the immune response of inflammatory monocytes as a strategy to improve the outcomes of patients who develop *C. neoformans* infections.

More information: Heung LJ, Hohl TM (2019) Inflammatory monocytes are detrimental to the host immune response during acute infection with Cryptococcus neoformans. *PLoS Pathog* 15(3): e1007627. doi.org/10.1371/journal.ppat.1007627



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