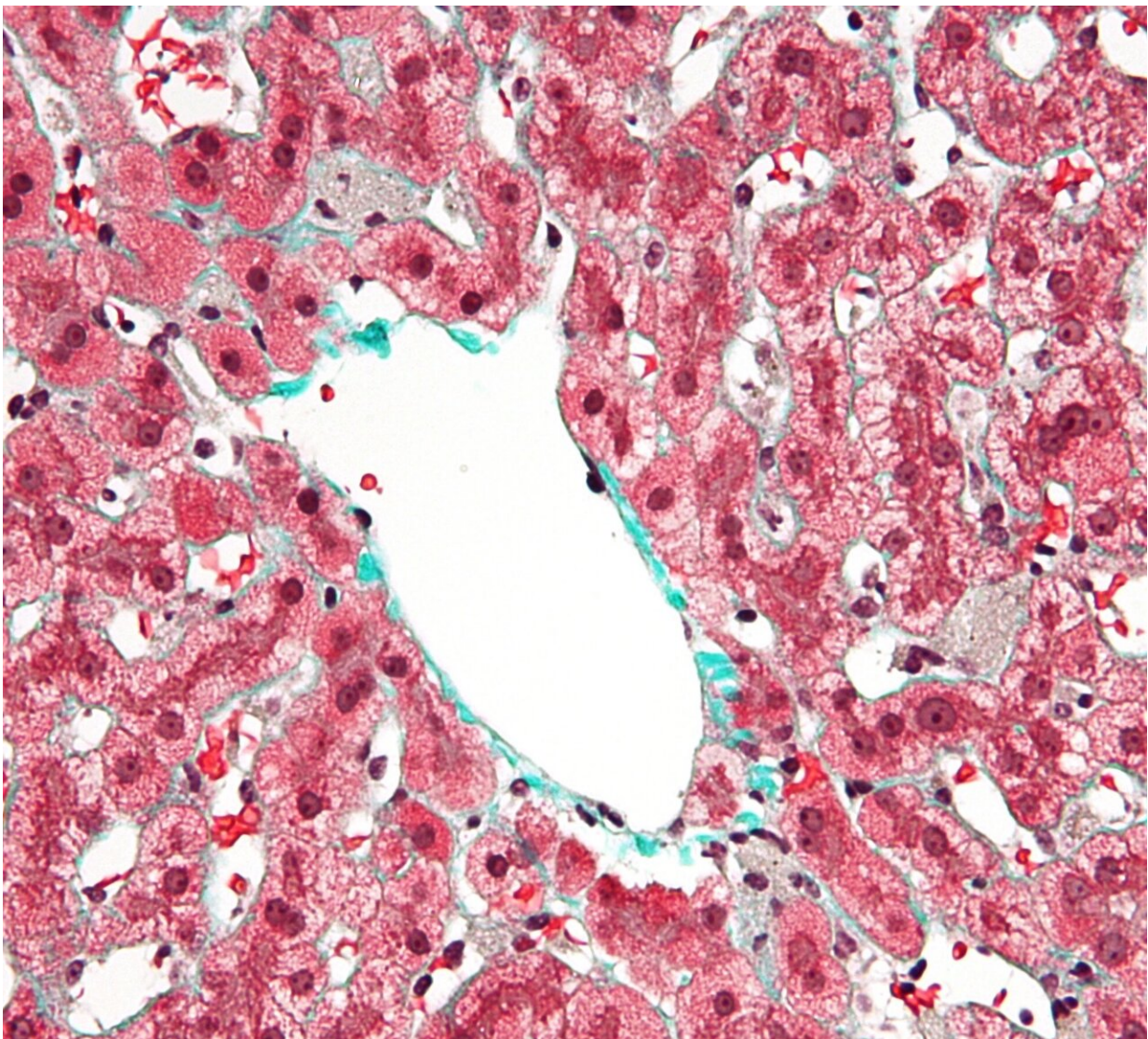


Research team discovers new mechanism in the liver that helps prevent invasive fungal infections

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An expert in intravital microscopy, Meiqing Shi, University of Maryland, is making breakthroughs in invasive fungal infections. In *Nature Communications*, Shi has discovered a pathway by which liver macrophages capture fungi before dissemination to target organs like the brain. This not only provides an explanation as to why individuals with liver disease have enhanced risk of fungal infection, but also points to therapeutic options to prevent these infections, which kill 1.5 million people annually. Credit: Nephron [CC BY-SA 3.0 (creativecommons.org/licenses/by-sa/3.0)]

As a world-renowned expert using intravital microscopy to observe fungal infection progression in live samples, Meiqing Shi, associate professor with the University of Maryland Department of Veterinary Medicine, continues to make new breakthroughs in the field. In his latest paper published in *Nature Communications*, Shi and his lab have discovered a new pathway by which liver macrophages called Kupffer cells (KCs) capture potentially fatal fungi in the bloodstream before dissemination to target organs like the brain or kidney. This mechanism not only provides an explanation as to why individuals with liver disease tend to have enhanced risk of contracting fungal infections, but it also points to therapeutic options that could be used in the future to prevent fungal dissemination and invasive fungal infections, which kill 1.5 million people worldwide each year.

"Under intravital microscopy, we can directly see how the KCs catch fungi in real time," says Shi. "This is a protective mechanism that is working once the fungus becomes invasive, or gets into the bloodstream, to prevent it from spreading. Stopping the [dissemination](#) process throughout the body is so important, because once you get dissemination, you get the disease. These findings suggest therapeutic strategies for preventing dissemination, and this could be applied across many types of [fungal infections](#), since they work in similar ways."

Fungal infections affect 1.2 billion people globally each year. In the current paper, Shi specifically examined two types of fungi - *Cryptococcus neoformans* and *Candida albicans*. Both of these fungi, if disseminated to their target organs (the brain for *Cryptococcus* and the kidney for *Candida*), are fatal infections that are very difficult to treat once contracted. *Cryptococcus*, for example, is the main cause of meningitis. Each year, more than a million people are infected and contract meningitis, and 60% of those who are infected will die from the disease.

"*Cryptococcus* and *Candida* are fungi that are actually everywhere," says Shi. "People with healthy immune systems can usually control the fungi after [infection](#), but once it gets into the bloodstream, either one of these fungi can get into the target organs and become fatal. For *Cryptococcus*, this is especially a problem for those with impaired immune systems, like HIV patients or organ transplant patients. Patients with [liver disease](#) are also more prone to *Cryptococcus* infection, and no one understood why before."

This new discovery that KCs or liver macrophages are responsible for catching free [fungi](#) in the bloodstream to prevent further dissemination helps explain this phenomenon, since if the liver is impaired as it is in patients with liver disease, it would stand to reason that this [protective mechanism](#) would also be impaired.

"This finding is very interesting and very unusual, because in the field of fungal infections, nobody focuses on the liver," says Shi. "Researchers tend to look at the target organs like the brain or kidney. The liver is not a target organ, but it tries to clean out the fungus in the bloodstream. As the whole body is connected, this paper gives a more whole system approach to how fungal dissemination interacts in the entire body."

With this whole body approach in mind, the discovery of this

mechanism has implications not just for those with liver [disease](#), but for the treatment of fungal infections as a whole by targeting this mechanism, preventing fungal dissemination, and treating invasive fungal infections.

The paper, entitled "Fungal dissemination is limited by [liver](#) macrophage filtration of the blood," is published in *Nature Communications*.

More information: "Fungal dissemination is limited by liver macrophage filtration of the blood," *Nature Communications* (2019).
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