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Blood-filtering organs fight infections that enter through the skin

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New information about how and where the innate immune system fights off viral infections that enter through the skin could lead to better treatments for viruses like Zika, dengue and measles, according to Penn State College of Medicine researchers. The innate immune system is the body's first line of defense, providing broad protection as opposed to the specific immune system which targets the specific threat.

One role of the innate immune system is to quickly block the spread of infection. It was once believed that white blood cells, called macrophages, destroy viruses at the site of an infection, like a mosquito bite. Viruses that escape this checkpoint drain through lymph vessels to local lymph nodes, where it was assumed macrophages finished the job of the innate immune system before specialized adaptive immunity kicked in.

Researchers led by Christopher C. Norbury, professor of microbiology and immunology, recently found that some viruses get past the local lymph node, enter the blood and are fought off at a third checkpoint: organs that filter the blood.

Working in mice, Norbury's team used several methods to deplete different types of innate immune cells—collectively known as myeloid cells—at the three checkpoints before infecting the rodents with poxvirus. They found that depletion of macrophages in the liver and spleen had the biggest effect on allowing the virus to continue to spread through the body.

"If you have a deficit in immunity in those organs, it's actually much worse than if you have a deficit in the local lymph node," Norbury said. "This means even something as small as a pin prick in the skin still involves a response in your entire body."

Among the strengths of the study: Instead of using just one method to deplete macrophages, the researchers used nine distinct methods to deplete different myeloid cells in various locations, allowing them to pinpoint the most important cell type and its primary location of action. The researchers used a technique that closely mimics natural infection.

Results were published in *PLOS Pathogens*.

Future studies could focus on boosting the response of liver and spleen macrophages in people with ongoing viral infections, Norbury said. The findings could also be used to identify populations that are at risk for particular infections.

"Future research should look at if susceptible people had profiles of biomarkers in blood that correlate with a lack of function of these cells," Norbury said. "For instance, if you've got hepatitis B infection, then you're going to have impaired macrophage function in the liver, which is going to impair the ability of those cells to go on and respond to other viruses.

"Going in and boosting those things—it's not absolutely clear how you would do that right now. But the fact that we've identified that these cells are playing the systemic role means that maybe people will turn their attention to these cells now."

Provided by Pennsylvania State University