Macrophages need two signals to begin healing process

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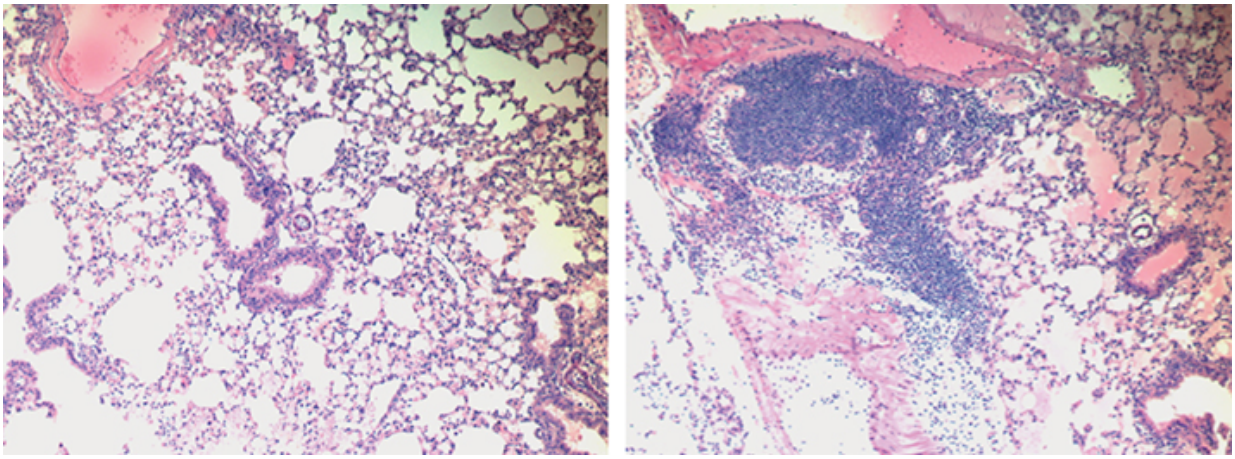

Images of lung sections from control mice (left) or mice lacking sensors for dead cells (right) after infection with the hookworm. Credit: Yale University

In the immune system, macrophages act not only as soldiers responding to invading pathogens but also help rebuild the injured tissue once the infection is defeated. A new study by Yale Medical School researchers published in the journal *Science* show how they accomplish this seemingly unrelated task.

The instructions to macrophages to commence rebuilding were long believed to come from immune system factors called cytokines, which are detected early during infection. But, researchers asked, why would

cytokines such as IL-4/IL-13 be active in wound healing?

"The body does not want to repair an infected wound, so it does not make sense that the cytokines should be sufficient to instruct tissue healing," said Carla V. Rothlin of Yale's Department of Immunobiology and Pharmacology, co-senior author of the paper along with Sourav Ghosh of the Department of Neurology and Pharmacology.

The researchers report that detection of dead cells along with the cytokines are necessary for macrophages to shift into repair mode. "The macrophages have a coincidence detector that triggers their tissue-repair program," Ghosh added.

Understanding this molecular repair mechanism may lead to better treatments of diseases, Rothlin said. "It's not enough to just put out the fire and reduce inflammation; we also need to be able to induce healing in chronic inflammatory diseases such as colitis."

More information: Lidia Bosurgi et al. Macrophage function in tissue repair and remodeling requires IL-4 or IL-13 with apoptotic cells, *Science* (2017). DOI: 10.1126/science.aai8132

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