

Discovery of long-lived macrophages in the intestine

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Macrophages are not just the vacuum cleaners of the immune system. They also support other cells. These long-lived macrophages in the intestines of mice (in green) make contact with the nerve cells of the gastrointestinal tract (in red). The macrophages provide growth factors for the nerve cells. The nerve cells die off without the macrophages. Credit: © TARGID - KU Leuven

Macrophages are specialised immune cells that destroy bacteria and other harmful organisms. Scientists at KU Leuven, Belgium, have come to the surprising conclusion that some macrophages in the intestines of mice can survive for quite some time. Most importantly, these long-lived macrophages are vital for the survival of the nerve cells of the gastrointestinal tract. This sheds new light on neurodegenerative conditions of the intestine, but also of the brain.

In the immune system, macrophages play the role of Pac-Man: They are white blood cells that clean up foreign substances by engulfing them. Apart from this, macrophages themselves provide vital growth factors and support many tissues in the body, allowing them to function and develop properly. As such, these specialised immune cells are soldier and nourisher at the same time. Their

proper functioning is immensely important in the <u>intestine</u>, as they have to differentiate between harmful bacteria, harmless bacteria and nutritional components.

Scientists assumed that macrophages in the intestine live for about three weeks at most in both mice and humans before being replaced by new cells. A KU Leuven study now shows that this is not entirely true, explains Professor Guy Boeckxstaens. "We've discovered a small percentage of long-lived macrophages in mice. We marked certain macrophages and found that they still functioned after at least eight months. They can be found in very specific places in the intestine, particularly in close contact with nerve cells and blood vessels."

Additionally, the small group of long-lived macrophages play a very important role in the gastrointestinal tract, adds Ph.D. student Sebastiaan De Schepper. "If the long-lived macrophages don't do their job properly, after only a few days, the mice suffer from digestive problems. This leads to constipation or even the complete degeneration of the nervous system in the stomach and intestine." The discovery that longlived macrophages do, indeed, exist in the intestine and that they are crucial for the normal functioning of the intestine is therefore immensely important.

These new insights offer promising opportunities for further research, concludes Boeckxstaens: "Next, we want to study the role of long-lived macrophages in human diseases where nerve cells of the intestine are affected, for instance in obese and diabetic patients with abnormal gastrointestinal function. Moreover, the results can also be meaningful for brain research. In the brain, we have microglia, similar long-lived <u>macrophages</u> that play an important role in neurological conditions such as Alzheimer's and Parkinson's disease. Scientists currently believe that <u>nerve cells</u> in these patients die off because microglia do not provide sufficient care. Maybe one day, research of the intestine can



offer us a better understanding of these brain conditions."

More information: Sebastiaan De Schepper et al, Self-Maintaining Gut Macrophages Are Essential for Intestinal Homeostasis, *Cell* (2018). <u>DOI:</u> <u>10.1016/j.cell.2018.07.048</u>

Provided by KU Leuven

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