Medical Xpress

A new mechanism protecting the liver from dangerous inflammation

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Life-threatening liver inflammation can be caused by excess alcohol, fatty foods, toxins, as well as viral, bacterial, and parasite infections. A study published on May 28th in *PLOS Pathogens* reports that a specific immune cell type in the liver can dampen the immune response, reduce inflammation, and protect against liver damage.

Alain Beschin, from the Vrije Universiteit Brussel, Belgium, and colleagues studied the immune response to trypanosome parasites in mice, where they frequently cause liver inflammation and failure. They focused on the role of monocytes, immune cells that normally pass along the blood vessels and in response to a local infection move quickly into the affected organ and contribute to the localized immune defense there.

Monocytes come in two different "flavors", those positive for a specific cell surface marker, or Ly6C-positive monocytes, and those lacking the Ly6C marker, or Ly6C-negative monocytes. What the researchers found was that, after they infected mice with trypanosomes (which accumulate in the liver), initially mostly Ly6C-positive monocytes and subsequently also Ly6C-negative monocytes subset moved into the liver. However, whereas the Ly6C-positive subset promoted inflammation through release of the pro-inflammatory factor TNF and initiated wide-spread liver injury, the Ly6C-negative monocyte subset suppressed inflammation and prevented progression of liver disease.

The researchers went on to show that the Ly6C-negative monocytes protected the liver in two distinct ways. On one hand, they released a

molecule called IL-10 which dampens the immune response, and on the other they made direct contact with the inflammation-promoting Ly6C-positive monocytes, which induced a change in these cells, forcing them to differentiate into so-called macrophages (a related immune cell) and turn on anti-inflammatory genes.

Regarding possible therapeutic implications, the researchers suggest that "augmenting Ly6C-negative monocyte accumulation or functionality may represent a useful intervention strategy complementing anti-infective medication in conditions of liver injury due to chronic infections."

More information: Morias Y, Abels C, Laoui D, Van Overmeire E, Guilliams M, Schouppe E, et al. (2015) Ly6CMonocytes Regulate Parasite-Induced Liver Inflammation by Inducing the Differentiation of Pathogenic Ly6C+ Monocytes into Macrophages. *PLoS Pathog* 11(5): e1004873. DOI: 10.1371/journal.ppat.1004873

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