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Scientists discover the specific types of macrophages that affect Crohn's disease severity

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For those coping with Crohn's disease, a new research report published in the *Journal of Leukocyte Biology* offers hope for the development of new and more effective drugs. In the report, scientists show for the first time, precisely what type of immune cells are involved in driving the inflammation process in the disease. With this knowledge, new compounds can be identified which reduce the activity of these cells or lessen their inflammatory effects.

"By increasing the knowledge on the different macrophage subsets in the intestine and their blood counterparts, we hope to contribute to the discovery of more specific targets in Crohn's disease, increasing the efficiency of new treatments," said Olof Grip, M.D., Ph.D., a researcher involved in the work from the Department of Clinical Sciences Malmö, at Lund University in Malmö, Sweden.

To make this discovery, scientists studied blood and intestinal biopsy samples from healthy individuals and from people with Crohn's disease. They compared the proportions and specific characteristics of the cells between the two. The blood monocytes were classified into three different subsets, classical, intermediate and non-classical monocytes, and the intestinal macrophages into CD14hiHLA-DRdim, CD14hiHLA-Dbright and CD14loHLA-DRint. Researchers then purified these three subsets from the blood using advanced fluorescence-activated cell sorting techniques. Several functional properties of the purified cells

were investigated by analyzing components that have been shown to be important in disease such as release of pro-inflammatory cytokines, matrix metalloproteinases and the ability of the monocytes to migrate toward CCL2. In people with Crohn's disease the specific subset of CD14hiHLA-DRdim macrophages is increased while the resident macrophage population is unaltered. These CD14hiHLA-DRdim macrophages are most likely derived from recruited classical blood monocytes, which are the most pro-inflammatory. This suggests that the CD14hiHLA-DRdim macrophages are driving the inflammation seen in Crohn's disease, exacerbating the inflammation and leading to tissue destruction.

"This work provides new leads for drugs and therapeutic targets for Crohn's disease and possibly other conditions that involve runaway inflammation," said John Wherry, Ph.D., Deputy Editor of the *Journal of Leukocyte Biology*. "Most of our therapies for intestine inflammatory diseases like Crohn's involve non-specific immunosuppression that have variable efficacy and many side effects. These new studies suggest that targeting specific cell types could increase the ability to specifically treat disease, reduce unwanted side effects, and hopefully, help people lead healthier lives."

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