[Researchers Learn How to Turn Cancer Cells into Macrophages](http://blog.fisherbioservices.com/researchers-learn-how-to-turn-cancer-cells-into-macrophages)

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Sometimes we set out in search of one thing, and end up finding something entirely different. This was the case for a group of Stanford scientists who were looking for ways to prevent [cancer cells](http://blog.fisherbioservices.com/amazing-samples-tumor-saving-lives) from dying during experiments, but then discovered that it is possible to force leukemia cells to mature into macrophages.

Published in the March 2015 [Proceedings of the National Academy of Sciences](http://www.pnas.org/content/112/13/4074.abstract), this discovery came as a chance observation in a Stanford University of Medicine laboratory.

**About B-ALL**Precursor B cell acute lymphoblastic leukemia (B-ALL) is characterized by a mutation called the Philadelphia chromosome. In B-ALL, immature B cells are unable to fully differentiate into normal B cells.

Acute lymphocytic leukemia (ALL) is a fast-growing cancer of lymphoblasts. This type of leukemia occurs at a rate of 35 to 40 cases per 1 million people in the United States, according to the [National Cancer Institute](http://www.cancer.gov/types/leukemia/hp/child-all-treatment-pdq#section/all), although the number of ALL cases has risen gradually over the past 25 years.

[ALL is the most common cancer in children](http://blog.fisherbioservices.com/viral-cell-therapies-fighting-cancer), representing about one-quarter of cancer diagnosis in pediatric patients under the age of 15. The risk for developing ALL is highest in children under the age of five, according to the[American Cancer Society](http://www.cancer.org/cancer/leukemia-acutelymphocyticallinadults/detailedguide/leukemia-acute-lymphocytic-key-statistics). The risk declines slowly until the individual reaches their mid-20s, then rises slowly after the age of 50. Though most cases of ALL occur in children, the majority of deaths occur in adults, presenting a mortality rate of about four out of five. Like adult-onset ALL, B-ALL typically presents a poor prognosis.

**Strange Observation in the Lab**
Ravi Majeti, MD, PhD, an assistant professor of medicine and senior author of the paper, and his associates had collected leukemia cells from a patient. They had been trying to keep the cells alive in a culture plate.

“We were throwing everything at them to help them survive,” said Majeti, who is also a member of the Stanford Cancer Institute and the Stanford Institute for Stem Cell Biology and Regenerative Medicine.

The scientists then exposed B-ALL cells to myeloid differentiation-promoting cytokines in vitro and by transient expression of the myeloid transcription factor C/EBPα or PU.1.

The researchers noticed some of the cultured cancer cells began changing in shape and size to look like macrophages. Majeti then remembered an old research paper where scientists forced early B-cell mouse progenitor cells into becoming macrophages by exposing the cells to certain transcription factors.

**What are macrophages?**
Macrophages, discovered by Ilya Mechnikov in 1884, are part of the immune system of vertebrates and are produced by the differentiation of a class of white blood cells known as monocytes. In response to infection, monocytes move into the tissue spaces around the site of infection and proceed to differentiate into dendritic cells and macrophages. Macrophages function mainly by engulfing foreign substances, cellular debris, microbial and cancer cells in a process termed phagocytosis. Key macrophage abilities include:

1. Increasing and decreasing the inflammatory response through modification of the amino acid arginine to either produce nitric oxide (reactive killer molecule) or ornithine (involved in repairing tissues)
2. Stimulating antibody production through antigen presentation on their cell surfaces
3. Production of cytokines to regulate the behavior of other cells as a result of the immune response.

In many ways, B-ALL cells are progenitor cells forced to remain in an immature state that is vulnerable to cancerous mutations. The researchers hope to force these cells into becoming macrophages, which consume apoptotic cells and pathogens. These transformed cells would also produce immune effector molecules that prompt the immune system to assault any remaining cancer cells.

The researchers showed that it was possible to reprogram these cancerous cells, causing the immature cells to change into cells that resemble and function like normal macrophages. Most importantly, the reprogrammed cells can no longer cause cancer in lab mice.

**Next Steps**
The research, supported by the National Institutes of Health (grant U54CA149145), the New York Stem Cell Foundation, the Burroughs Wellcome Fund, the U.S. Department of Defense and the Walter V. and Idun Berry Postdoctoral Fellowship Program, also demonstrates that the reprogramming process may already occur to some degree in B-ALL patients. This means the approach may represent a previously unidentified therapeutic strategy for treating certain types of leukemia or other cancers. Since this form of cancer presents a poor prognosis, finding potential treatment is particularly exciting among medical professionals and patients.

The next step would be to develop a drug that prompts the same reaction. Such a drug could serve as the basis for leukemia therapy. A similar cell therapy focusing on differentiating cells is already in place, one that uses retinoic acid to turn cancer cells into granulocytes to treat acute promyelocytic leukemia. Researchers hope to find more differentiation therapies for cancer.