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Research points the way for custom cures of intractable diseases

Human stem cells carrying leukemia are found to replicate consistently in mice blood, potentially leading to novel approaches for 'bespoke' disease treatments.

Your doctor discovers that you have the early stages of a potentially terminal illness, say a particularly intractable form of adult-onset leukemia. As per the long-standing plan, your clone is deliberately given the disease, and while you head off to the tennis courts, the doctors use your 'other' to determine the best therapy. In a few weeks or so, you return to the hospital and begin the proven treatment for your specific illness, leaving after several visits completely disease-free - perhaps with your clone for a nice set of doubles.

It is not a reality yet. At *this* moment in time, rodents are being substituted for human clones. As part of a multi-institution global research project coordinated from the RIKEN Research for Allergy and Immunology in Yokohama, cancer specialists are attempting similar approaches using specially bred laboratory mice they inject with diseased human blood stem cells cultivated in a lab dish. The early evidence is that this novel approach to 'custom cures' may work.

The results of the cooperative study are being published this week in *Nature Biotechnology*. Twelve separate research facilities and hospitals cooperated in the study, including Kyushu University in Japan, the Jackson Laboratory in Bar Harbor, Maine, and two research facilities at Harvard University.

While inducing the growth of human leukocytes in the bone marrow of lab animals has been done before, this is the first reported instance in which human stem cells infested with acute myelogenous leukemia (AML) cells have been cultured and grown in a lab dish, then found on injection to aggressively and consistently develop in the peripheral blood cells of test animal recipients. The researchers expressed the belief that such 'sleeper' cancer cells in the peripheral blood cells may be why leukemia can return following apparently successful cancer treatment. Human AML was maintained cumulatively *in vivo* from the human donor in a series of mouse recipients for over one

year, demonstrating the long-term self-renewal capacity of leukemic stem cells.

The presence of circulating peripheral-blood AML cells, in addition to better reproducing primary AML disease *in vivo*, allows the examination of a specific patient's AML cells over multiple time points in a single lab mouse. In this way, the mice can serve as an ideal vehicle for studying the mechanism of the disease and are potentially the best means to counter it. As is often the case for patients with AML, in lab mice the effect of a single round of treatment by a standard cancer-fighting drug can be transient, followed by a return of the disease in just a few weeks.

The ultimate significance of the study is the suggestion that instead of patients being subjected to a battery of chemotherapy or radiation treatments to cure or arrest their disease, the less onerous alternative could be a few weeks of lab research on their specific diseased cells that are reproduced in a lab dish then custom-cured in lab mice. Ultimately, the single, most effective course of treatment would be selected from the laboratory results. Then it becomes the patient's turn to be cured.

Original work:

F. Ishikawa, S. Yoshida, Y. Saito, et al., Chemotherapy-resistant human AML stem cells home to and engraft within the bone-marrow endosteal region. *Nature Biotechnology*, Oct. 21, 2007

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