Clinical trial seeks to cure advanced Crohn's disease using bone marrow transplant

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Researchers at Fred Hutchinson Cancer Research Center have opened a clinical trial to test the theory that giving a patient a new immune system can cure severe cases of Crohn's disease, a chronic inflammatory condition of the gastrointestinal tract.

Funded by an infrastructure grant from The Eli and Edythe Broad Foundation, the initial goal of the Crohn's Allogeneic Transplant Study (CATS) is to treat a small number of patients with treatment-resistant Crohn's disease by transplanting matched bone marrow cells from a sibling or unrelated donor. Such a bone marrow transplant replaces a diseased or abnormal immune system with a healthy one.

The idea of swapping out the immune system is based on evidence that Crohn's is related to an abnormal immune response to intestinal bacteria and a loss of immune tolerance. There is strong evidence that genetic abnormalities in the immune regulatory system are linked to the disease, according to CATS principal investigator George McDonald, M.D., a transplant researcher and gastroenterologist in the Hutchinson Center's Clinical Research Division.

Although the CATS clinical trial represents a new direction for bone marrow transplantation, the procedure has precedent. The Hutchinson Center, which pioneered bone marrow and hematopoietic cell transplantation to treat blood cancers, has used allogeneic transplants to cure patients who suffered from both leukemia and Crohn's, with subsequent disappearance of the signs and symptoms of Crohn's. Similar

experiences have been reported from studies done in Germany.

While autologous stem cell transplants – in which the patient's own hematopoietic cells are removed and then returned after high-dose chemotherapy is given to suppress the immune system – have been used to treat Crohn's patients, the benefits have not always been permanent, probably because the risk genes for Crohn's are still present. "Autologous transplantation following chemotherapy beats the disease down but the Crohn's tends to come back," McDonald said.

More information about CATS can be found on the website www.cats-fhcrc.org, which includes a patient-eligibility questionnaire. In general, patients must be 18 to 60 years of age and have failed all existing conventional treatments but be healthy enough to undergo a bone marrow transplant. A matched donor of bone marrow must be found from either a sibling or an unrelated person who has volunteered to donate marrow. Private insurance must cover the cost of the transplant and related medical expenses.

Crohn's disease is usually discovered in adolescents and young adults but can occur from early childhood to older age. The incidence of Crohn's disease varies in different parts of the world with rates of four to nine persons per 100,000 people in North America. According to the Crohn's and Colitis Foundation of America, a leading advocacy organization, Crohn's may affect more than 700,000 Americans. Of those affected by Crohn's, about 10 percent suffer from the most severe form for which no treatment is completely effective.

Symptoms of Crohn's may include pain, fever, diarrhea and weight loss. Substantial progress has been made in medical treatment of Crohn's disease over the last 15 years. However, even with the best immunosuppressive therapy, less than half of patients with moderate to severe Crohn's achieve long-term relief. When patients stop taking their

medicines, their intestinal inflammation returns. Some severe infections have been seen in patients who took prolonged courses of medicines that suppress the immune system.

"The burden of this disease lays heavily on those who don't respond to any therapy," McDonald said.

The CATS investigator team includes transplant physicians, gastroenterologists, pathologists and nurses from the Hutchinson Center, University of Washington, Seattle Children's and the Benaroya Research Institute. The bone marrow transplant procedures will be conducted at the Seattle Cancer Care Alliance, the University of Washington Medical Center, and Seattle Children's Hospital.

Provided by Fred Hutchinson Cancer Research Center