

'Personalized immune' mouse offers new tool for studying autoimmune diseases

March 14 2012

Columbia University Medical Center (CUMC) scientists have developed a way to recreate an individual's immune system in a mouse. The "personalized immune mouse" offers researchers an unprecedented tool for individualized analysis of abnormalities that contribute to type 1 diabetes and other autoimmune diseases, starting at the onset of disease. The findings were published today in the online edition of *Science Translational Medicine*.

The <u>mouse model</u> could also have clinical applications, such as predicting how a particular patient might respond to existing drugs or immunotherapies, reports senior author Megan Sykes, Michael J. Friedlander Professor of Medicine and Professor of <u>Microbiology</u> & Immunology and Surgical Sciences (in Surgery) at CUMC. Dr. Sykes is also Director for the Columbia Center for Translational Immunology. In addition, the model might prove useful for developing individualized immunotherapies for fighting infection or cancer or for lessening a patient's rejection of transplanted tissue.

Researchers have been searching for new ways to tease apart the various factors that contribute to autoimmune disease. "While large-scale studies of human populations have provided important clues to the genetic basis of immune diseases, they have offered little information about the specific role the genes play," says Dr. Sykes. "It's difficult to isolate these mechanisms when looking at groups of patients who have had disease for different lengths of time or have been receiving different treatments. And the fact that they already have the disease makes it



difficult to distinguish what underlies and propagates the autoimmune process."

Several research groups have attempted to create a personalized immune mouse. However, each model has had significant limitations, such as an inability to generate the full complement of <u>immune cells</u> and incompatibilities between tissues used to recreate the human <u>immune system</u>, leading to graft-versus-host disease.

Dr. Sykes' model, in contrast, is able to recreate a robust and diverse human immune system, including T cells, B cells, and myeloid cells (which generate a variety of immune cells), free of immune incompatibilities.

The model is made by transplanting human bone marrow stem cells (also known as CD34+ cells), along with a small amount (approximately 1 cubic mm) of HLA-matched immature thymus tissue, into an immunodeficient mouse. (The HLA, or human leukocyte antigen, system mediates interactions among various immune cells.) The thymus tissue is implanted into the mouse's kidney capsule, a thin membrane that envelops the kidney and serves as an incubator. Within six to eight weeks, the transplanted thymus tissue is seeded by circulating human CD34+ cells (which are infused into the mouse's bloodstream), and begins generating human immune cells from the CD34+ cells.

A key to the model's success was the team's discovery that freezing and thawing the transplanted thymus tissue, as well as administering antibodies against CD2 (a glycoprotein that mediates T cell development and activation), depletes mature T cells from the tissue graft. This prevents rejection of the human CD34+ <u>cells</u> and graft-versus-host disease, while preserving function of the thymus tissue.

Dr. Sykes intends to use the personalized immune mouse to study type 1



diabetes. "We hope to find out what is fundamentally different about patients' immune systems, compared with those of healthy individuals, before any disease develops," she says.

The studies should also reveal more about the genetics of type 1 diabetes. "A number of HLA-associated genes have been linked to type 1 diabetes," she explains. "About a third of the population has one of more of these genes. But a much smaller percentage of the population actually develops the disease. What this means is, the HLA genes are necessary, but not sufficient, to cause type 1 diabetes. Using the personalized immune mouse, we expect to learn more about the role that non-HLA genes play in the disease."

More information: Dr. Sykes' paper is entitled, "A model for personalized in vivo analysis of human immune responsiveness."

Provided by Columbia University Medical Center

Citation: 'Personalized immune' mouse offers new tool for studying autoimmune diseases (2012, March 14) retrieved 3 May 2024 from <u>https://medicalxpress.com/news/2012-03-personalized-immune-mouse-tool-autoimmune.html</u>

This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.