MedicalXpress

New clue to lupus: Failed autoimmune suppression mechanism

February 3 2011

Researchers at Dana-Farber Cancer Institute in Cambridge, Mass., in collaboration with Jackson Laboratory scientists, have identified a regulatory defect that drives lupus.

Correcting the defect "may represent an effective therapeutic approach to systemic lupus erythematosus-like autoimmune disease," the researchers state in their research paper, published in the Proceedings of the National Academy of Sciences. The research team was led by Harvey Cantor, M.D., chair of the department of cancer immunology and AIDS at Dana-Farber, in collaboration with the laboratory of Jackson Professor Derry Roopenian, Ph.D.

Autoimmune diseases develop when the immune system, which is supposed to identify and vanquish potentially dangerous infectious agents, instead attacks the individual's own body. Most autoimmune diseases strike specific organs, such as the pancreas in type 1 diabetes. Lupus, however, is a systemic disease in which abnormal antibodies are produced throughout the body, inflaming a variety of tissues and organs, including the skin, heart, lungs, kidneys and brain.

Follicular T helper (TFH) cells fuel B cells to produce antibodies, which can be useful in fighting infections. But in lupus, TFH fuel B cells that produce dangerous antibodies that attack normal tissues (autoantibodies). CD8+ T cells ("killer T cells"), on the other hand, normally attack and destroy only infected cells. Cantor and colleagues discovered that a small, but critically important, population of CD8+ T cells (less than 5

percent), plays a specialized role in protecting from lupus. These so-called CD8+ T regulatory, or Treg, cells are specially equipped to destoy TFH cells, and by doing so, prevent lupus from developing.

Using a mouse model for systemic lupus erythematosus in humans that was originally discovered at 30 years ago by Edwin Murphy at The Jackson Laboratory, the Dana-Farber researchers, working with Roopenian's laboratory, found defects in CD8+ Treg activity.

The new paper, Roopenian explains, is the first to demonstrate the potential breakdown of this suppression mechanism in lupus. "Overcoming this defect," he says, "offers a potential approach prevent lupus."

More information: Kim et al.: Surface phenotype and function of CD8+ T regulatory cells: Defective Ly49+ CD8+ T regulatory cell activity is a hallmark of B6-Yaa autoimmunity. *Proceedings of the National Academy of Sciences*, doi:10.1073/pnas.1018974108

Provided by Jackson Laboratory