Novel regulatory process for T cells may help explain immune system diseases

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A newly identified regulatory process affecting the biology of immune system T cells should give scientists new approaches to explore the causes of autoimmunity and immune deficiency diseases.

In findings posted online ahead of publication in Proceedings of the National Academy of Sciences (*PNAS*), scientists at Cincinnati Children's Hospital Medical Center report a novel process of coordinated cellular communications vital to the maintenance of T cells. If the process breaks down, T cells proliferate rapidly and die off. This could disrupt the immune system's normal defensive functions.

"This study involves an important mechanistic finding affecting the molecular regulation of T cell biology that will have implications in our future understanding of immunodeficiency and autoimmunity," said Yi Zheng, Ph.D., co-investigator on the study and director of Experimental Hematology/Cancer Biology at Cincinnati Children's.

T cells – named such because they originate in the thymus – are a type of white blood cell vital to the body's immune system and its defense against pathogens and disease.

Scientists entered the current study knowing from earlier research that normal T cell biology involves carefully coordinated signaling between what are known as T cell receptors and a gene/protein called interluken-7 receptor (IL-7Ra). IL-7Ra is vital to the formation of white blood cells called lymphocytes, which include T cells. Unknown before

this study, however, were the detailed mechanisms that regulate this coordination.

In a variety of test tube experiments and experiments involving mice, researchers determined the cell division control protein Cdc42 is essential to coordinating a signaling network of genes/proteins and enzymes that control normal T cell biology. The disruption caused by loss of Cdc42 included restricted signaling by IL-7Ra, an initial hyper-proliferation of T cells and their rapid loss through programmed cell death. When the researchers were able to reconstitute Cdc42 in their experiments, T cell biology became more normalized, they report.

Provided by Cincinnati Children's Hospital Medical Center