Profound immune system discovery opens door to halting destruction of lupus

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A researcher funded by the Lupus Research Institute (LRI) has discovered an entirely new and powerful molecular switch that controls the inflammatory response of the immune system. The major finding, reported in the December 14th issue of the journal Cell, means that new methods can now be pursued to shut down uncontrolled inflammation, restore immune system regulation, and treat chronic autoimmune disorders such as lupus.

In autoimmunity, the immune system designed to fend off outside invaders mistakenly mounts an out-of-control destructive inflammatory attack against the body's own tissues and organs. "We have found an essential switch that controls immune inflammation,' said LRI award recipient, Greg Lemke, PhD, professor of Molecular Neurobiology at the Salk Institute.

The breakthrough was supported at a critical juncture by the LRI, the nation's only organization solely dedicated to funding novel and innovative science to prevent, treat, and cure lupus. "Without the LRI, this project would have stopped—and a fundamental discovery in immunology would not have happened," Dr. Lemke said.

Major Implications

In this study, Dr. Lemke builds upon findings that he and his team previously reported, when he noticed that mice genetically engineered to

be born without a tiny family of three receptors—TAM receptor tyrosine kinases—developed an autoimmune illness similar to lupus in humans.

In the Cell article, Dr. Lemke now illustrates how these "TAM" receptors, under normal circumstances, are so critical in stopping the immune system from mounting an out-of-control inflammatory response against invading viruses and bacteria. When chemical messengers (cytokines) prompt immune cells to attack, he explains, they also activate TAM receptors, which then alert the cells to no longer react to the cytokines. This keeps the immune system orderly as well as relatively tranquil.

But in people with lupus and certain other autoimmune illnesses, the TAM signalling network may be seriously compromised. The switch to inhibit inflammation on this network may be absent—thereby resulting in immune system pandemonium.

People with lupus tend to have low levels of a blood factor (proteins S) that TAM receptors require to carry out their job. Giving modified versions of protein S, or its related TAM activator Gas6, to people with lupus may represent a means of halting the immune system destruction of precious organs and tissues. "This is definitely something we intend to investigate," Dr. Lemke said.

Winning Strategy

Dr. Lemke is one of 85 recipients of $300,000, 3-year grants given by the LRI since 2000 to explore brilliant but untested novel hypotheses as to why and how lupus occurs, and what can be done to prevent and stop the illness.

Founded by families and shaped by scientists, the Institute has had

remarkable success in breathing life in to ideas such as Dr. Lemke's that would otherwise not have obtained funding. LRI recipients span the nation—they are at 51 academic medical centers in 20 states—and work in such diverse disciplines as immunology, genetics, cardiology, nephrology, dermatology, and neurology.

"This strategy of funding only novel scientific ideas in lupus has more than demonstrated its power," said William E. Paul, MD, chief of the Laboratory of Immunology at the National Institute of Allergy and Infectious Disease-National Institutes of Health and chair of the LRI's Scientific Advisory Board. "Through its annual support, the LRI strengthens the lupus research landscape and moves novel concepts forward to secure large-scale federal funding."

Already, LRI-funded scientists have turned the Institute's $9 million investment from 2001 to 2004 into a record $30 million in new grant funding from the National Institutes of Health (NIH) and other sources. Dr. Lemke's research program provides an example of this leveraging: as a result of the success of his LRI-funded work, he very recently obtained NIH funding to sustain and extend the program.

Source: Lupus Research Institute