New role for protein molecule that inhibits response of immune-system cells

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Researchers at the University of Pennsylvania have identified a new role for a protein molecule that inhibits the response of immune-system cells to inflammatory signals associated with many human diseases.

An international group of scientists, with lead researchers in Penn's School of Veterinary Medicine and School of Medicine, has shown the unique ability of a protein subunit called IL-27p28 to bind with a key cell receptor (gp130), effectively preventing it from transmitting signals necessary for triggering an immune response. Regulating the production of the molecule could lead to new, targeted interventions for cancer, asthma, lupus, multiple sclerosis, arthritis and other diseases.

"Lots of pharmaceutical companies are focused on possible targets upstream or downstream of this key receptor," said Christopher Hunter, professor and chair of pathobiology in Penn Vet. "Here, we've discovered a natural molecule that limits signaling through that receptor. There's already genetic data out there saying this protein is important in human medicine. We agree with that, but maybe it works a different way than we thought before. Then, having this information means that this natural molecule provides a new way to manage different types of inflammatory diseases."

Cytokines are important molecules that can promote or limit inflammation and are key contributors to the development of cancer and autoimmune diseases such as lupus, asthma, arthritis, multiple sclerosis, inflammatory bowel disease and Crohn's disease. Previous research has sought to better understand how cytokines like IL-27 interact with their receptor complexes to develop new approaches for managing inflammation.

The Penn findings were surprising to the researchers because they showed that, alone. the p28 component of IL-27 was able to inhibit a receptor used by many immune cells, and the findings suggest that it may be useful therapeutically. These find ings highlight the combinatorial biology of this family of cytokines and raise questions about whether other subunits in this family have other unappreciated biological activities. Additional studies are needed to address the potential targets of IL-27p28 and whether IL-27p28 can be used as a therapeutic agent for the treatment of inflammatory conditions and malignancies that work through the gp130 receptor.

More information: The findings appear in this week's *Nature Immunology*.

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