Researchers find key player in immune system regulation

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Studies led by Dartmouth Medical School researchers have revealed a crucial link in how the immune system works. In a study published online on August 20 in the journal *Nature*, the researchers found that mast cells, known for their role in allergy reactions such as watery eyes and runny noses, are connected to the activity of regulatory T cells, which suppress immune responses. The researchers say theirs is the first study to find that mast cells mediate immune system suppression.

"Our finding is a complete surprise. We were studying transplant tolerance and what's required to protect a graft from rejection," says Randolph Noelle, professor of microbiology and immunology at Dartmouth Medical School. "When we went looking to see what genes were responsible in a successful graft, we found high levels of mast cell gene products, which made the connection between regulatory T cells and mast cell recruitment. The fact that mast cells may be instrumental in orchestrating regulatory T cell tolerance was new, unanticipated, and surprising."

In their study, the researchers determined that mast cells are crucial for sustaining immune suppression in transplanted skin on mice, which means longer acceptance or tolerance of the transplant. Mice that were mast cell deficient rejected the skin graft. Furthermore, the researchers found that IL-9, a protein already known for playing a role in mast cell activation and recruitment, was discovered to be produced by regulatory T cells. As such, the other key discovery in this study was that Il-9 appears to be an essential ingredient in the success of transplanted skin.

"Because of this study, mast cells are now the new cellular target in understanding immune suppression," says Noelle, who is co-director of the Immunotherapy Program of the Norris Cotton Cancer Center at Dartmouth-Hitchcock Medical Center. "We now have a whole new set of cellular, and eventually molecular, interactions to study."

According to Noelle, the findings might also impact some cancer treatments as mast cells are known to promote growth in some tumors. Future research might look into suppressing mast cells to boost the immune system, which could lead to tumor rejection.

"It is only because of the extremely high quality of the graduate students in Dartmouth's Molecular and Cell Biology Program and the hard work of post-docs and colleagues that this new paradigm of cellular interactions in immunology was discovered," says Noelle.

Collaborating researchers on this study include Li-Fan Lu, Evan Lind, David Gondek, Kathy Bennett, Michael Gleeson, Karina Pino-Lagos, and Zachary Scott, all at Dartmouth; Anthony Coyle and Jennifer Reed at MedImmune in Gaithersburg, Md.; Jacques Van Snick at the Ludwig Institute for Cancer Research at the University of Louvain in Brussels, Belgium; and Terry Strom and Xin Zheng at Beth Israel Deaconess Medical Center in Boston, Mass.

Source: Dartmouth Medical School