



At last count, DMS had received more than \$32 million in research funding through the American Recovery and Reinvestment Act, advancing research (and securing jobs).

Allergies may affect skin graft rejection

Could an allergic reaction complicate a skin graft? Graduate student Victor de Vries asked himself that question when he started working in a DMS immunology lab, and he recently reported the results of his investigation.

The lab, led by Randolph Noelle, Ph.D., uses mice to study how the body accepts or rejects skin grafts and transplanted organs. For a skin graft to be successful, the immune system has to be suppressed. Otherwise, it will attack the graft as if it were any other foreign object.

Mast: Just prior to de Vries's arrival in the lab, Noelle's team had discovered that mast cells, a type of immune cell, are required for skin graft tolerance. (For more on that study, see dartmed.dartmouth.edu/w06/d01.) That finding was surprising, de Vries says, because mast cells are best known for their ability to activate the immune system in response to allergens. When mast cells encounter an allergen, they release molecules that cause inflammation—a process called degranulation. But this previous discovery indicated that mast cells were required for suppressing the immune system in response to a skin graft, leading de Vries to ask what would happen if the cells reverted to their proinflammatory ways.

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In a study published in the *American Journal of Transplantation*, de Vries and colleagues simulated an allergic response in mice that had been given skin grafts. When the researchers forced mast cells in a skin graft to degranulate, the graft was rejected within 15 days.

Allergen: Furthermore, where the allergen entered the body didn't matter, indicating that if an allergen arrives through the airway—as happens with hay fever in humans—it could cause rejection of an organ transplant. In a control group of mice that were given grafts but no allergens, it took about 70 days for tolerance to start to break down.

Noelle says the paper shows “for the first time that allergy can disrupt the delicate balance of tolerance in the immune system.” Though the study was in mice, “usually the general principles that mice teach you are true in humans.”

In another experiment, the researchers found that cromolyn, an allergy drug that stabilizes mast cells, stopped the grafts from being rejected, even if degranulation had already occurred. In fact, the use of cromolyn resulted in grafts lasting for more than 120 days. Cromolyn has been used in humans to treat allergies for more than 30 years. So, two immunologists pointed out in an editorial that accompanied the Dartmouth paper, “it should be straightforward to test whether it could improve the success of organ transplantation in humans.”

Triggering: The study has implications for cancer therapy, too, says de Vries. Many tumors have an increased number of mast cells, so triggering degranulation around a tumor might help the body's immune system to fight it off. Immune tolerance may be crucial for successful grafts and transplants, but no one wants a tumor sticking around.

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Noelle's lab studies immune system activation.

Primary numbers

A popular health-care reform idea is to pay doctors based on how well they care for patients rather than the number of procedures they perform. But most primary-care physicians don't see enough patients “to produce statistically reliable performance measurements on common quality and cost measures,” according to a paper in the *Journal of the American Medical Association* by researchers at Dartmouth and the Centers for Medicare and Medicaid. Few primary-care practices are big enough to reliably measure performance in blood-sugar testing, for example. “Novel measurement approaches appear to be needed,” the authors wrote.



Sick of smoke

Smoking can make one more susceptible to infectious diseases, such as influenza and pneumonia. Exactly how it does that was the focus of a recent study conducted at DMS. In cell cultures of human airways, the researchers found that cigarette smoke thwarts the body's own innate antimicrobial properties. “Cigarette smoke is a complex mixture and has many biological activities,” they wrote in the *Open Immunology Journal*. “Additional studies are needed to better understand the effects of this and other environmental pollutants on functions of the innate immune system.” ■

