



The Dartmouth Atlas of Health Care has gone global. The British National Health Service just published a compendium of variations in its use and distribution of health-care resources.

Inducing immunity without autoimmunity

ADMS immunologist came up with a surprising explanation for how an antibody is able to stimulate an immune response against cancer without causing an autoimmune reaction.

Finding the delicate balance between triggering the immune system to attack tumors but not allowing it to attack healthy cells has been a major problem for cancer immunologists. When immune cells called CD8 T cells are called to action, they use antigens—proteins on the surface of cells—as a guide to which cells to kill and which to leave alone. Because tumor cells and normal cells share many antigens, killer T cells often leave tumor cells free to grow.

Cells: Scientists knew that using an antibody to stimulate a receptor called GITR that's found on many immune cells could create an immune response against a type of skin cancer in mice, but how that happened was unclear. Mary Jo Turk, Ph.D., was curious about the mechanism. She expected to find that the antibody worked by depleting a type of immune cell called regulatory T cells. They suppress the immune system, keeping CD8 T cells from attacking. Having too many regulatory T cells can lead to problems fighting off

threats such as cancer, but having too few can lead to autoimmune reactions.

Mice: To investigate the mechanism, Turk and her colleagues injected mice with melanoma and treated them with the antibody to stimulate GITR. They then injected the mice with a secondary tumor to see if the combined exposure to the primary tumor and the antibody would provide protection against the secondary tumor. Indeed, the antibody gave strong protection from the secondary tumor without causing an autoimmune reaction. By comparison, when they used a different antibody, one known to deplete the supply of regulatory T cells, they were still able to induce protection against the secondary tumor, but the mice had an autoimmune reaction.

To clarify whether the antibody was working by activating CD8 T cells or by depleting regulatory T cells, they tried a different type of melanoma for the secondary tumor. The antibody did not then provide protection against the secondary tumor—because the CD8 T cells were using the antigens of the primary tumor as a guide to know which cells to attack.

Spot: At first, Turk was so surprised that she had a graduate student repeat the experiment over and over. “We were just dumbfounded,” she says. Finally she was convinced—when GITR on CD8 T cells is stimulated with an antibody, it leads to the growth of killer T cells that will be able to spot antigens specific to tumor cells rather than to shared antigens.

“You get good, long-lived immunity without autoimmunity, and that has been a big challenge in the field,” Turk says.

It's not clear exactly how GITR makes CD8 T cells so much more effective, but her lab is now testing whether anti-GITR will work against a more aggressive form of melanoma.

AMOS ESTY

“We were just dumbfounded,” Turk says of her lab’s early results.

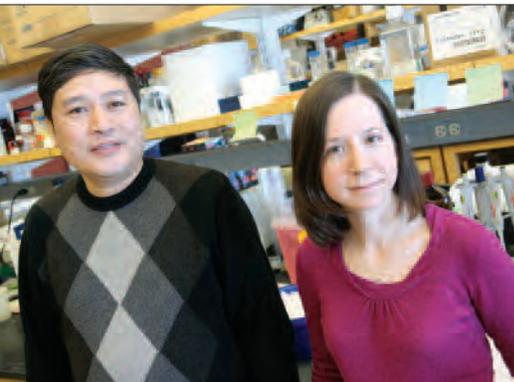
Quality, not quantity

Simply training more physicians might not improve access to health care, found a recent study by DMS's David Goodman, M.D. “Patients living in areas with more physicians per capita had perceptions of their health care that were similar to those of patients in regions with fewer physicians,” Goodman *et al.* wrote in *Health Affairs*. They found no significant differences in the number of visits patients had with their personal physician or in their access to tests or specialists. Instead of focusing on increasing the number of physicians, they wrote that “focusing health policy on improving the quality and organization of care may be more beneficial.”



Appendectomy blues

Appendicitis, though highly treatable, may be more deadly for patients in rural areas, found a recent study led by Dartmouth surgeon Samuel Finlayson, M.D. In 36% of rural patients with appendicitis, the organ had perforated by the time they got medical help, compared to 31% of urban patients, wrote Finlayson and his coauthors in *Annals of Surgery*. Perforations are “associated with increased morbidity, length of hospital stay, and overall health-care costs,” they noted. The urban-rural gap, they concluded, “suggest[s] disparities in timely access to surgical care.” ■



BEROBERY HOLMAN

Mary Jo Turk (right), pictured with her lab manager Peisheng Zhang, studies cancer immunology.