For a WEB EXTRA interview with José Conejo-Garcia, see dartmed.dartmouth.edu/fall08/html/disc_pilar_we.php.

Put this finding on a PILAR

Researchers in the lab of José Conejo-Garcia, M.D., Ph.D., have found a receptor on T cells that helps to regulate the immune system's response to antigens. The discovery of the receptor, which they named PILAR (proliferation-induced lymphocyte-associated receptor), may have important implications for the development of cancer immunotherapies and the treatment of autoimmune diseases.

T cells play a crucial role in adaptive immunity, but they have to be activated by other cells to become effective. The first step in that process comes when a T cell recognizes an antigen presented by a cell called, logically enough, an antigen-presenting cell (APC). But to ensure that T cells do not respond when they shouldn't—say, when the antigen is produced by the host—it takes a second signal to get the T cell to mount a full defense. If the antigen does, indeed, represent a threat, the APC should express molecules called costimulators, which provide the second signal—the alarm that tells the T cell to proliferate and respond. If costimulators are not present, the T cell should either die or become ineffective.

Antigen: What's interesting about PILAR is that it acts as a costimulator despite being expressed on T cells, not on APCs. Conejo-Garcia calls this discovery "a new paradigm." He found that when some T cells recognize an antigen, they produce PILAR. Once expressed, PILAR can provide the costimulatory signal to a nearby T cell by interacting with another molecule, CD161, activating that T cell. If the neighboring T cell does not express CD161, PILAR causes it to express genes that lead to apoptosis, or cell death.

Conejo-Garcia is curious about the possibilities that the new paradigm, published in the journal *Blood*, offers for treating cancerous tumors. T cells have the ability to fight off tumors, but only if they recognize tumor cells as a threat. Because tumor cells are similar to regular host cells, APCs often do not provide the costimulatory signal that activates T cells. Conejo-Garcia found that the type of T cells that are most effective against ovarian cancer express PILAR—but usually not CD161. It's possible, he believes, that those T cells could be manipulated to express CD161, thus making them more likely to become activated by their interactions with other T cells that express PILAR.

Conejo-Garcia calls PILAR's mechanism "a new paradigm."

Target: "Our most interesting direction," Conejo-Garcia says, is investigating how PILAR might affect autoimmunity. A number of autoimmune diseases are caused when helper T cells, which often express PILAR, secrete inflammatory cytokines. So he hypothesizes that by looking for PILAR in inflamed areas, it might be possible to identify—and then target—those cells. Working with other researchers, Conejo-Garcia is now investigating that and other prospects raised by PILAR. As with many findings, it seems that it will take some time to figure out all the discovery's implications. AMOS ESTY

For a WEB EXTRA with video of the HazBot in action, see dartmed.dartmouth.edu/fall08/html/disc_hazbot_we.php.

Jurmain, at left with the HazBot and above with its control mechanism, was an undergraduate when he began work on the device with DMS's Joe Rosen.

The little robot that could

Emergency responders, suited up in protective gear, cautiously approach a building that's been badly damaged by an explosion. They need to clean up the hazardous materials inside, but the structure is too unstable for anyone to enter. Then along comes HazBot—a suitcase-sized army tank with a seven-foot-long extendable arm. The little robot zips up to the building, opens the door, climbs over debris, maneuvers around obstacles, collects samples of hazardous materials, identifies them, and even begins the clean-up operation.

Some day there may be a robot that is smart enough to handle all that. In fact, in war zones, robots already neutralize roadside bombs, examine suspicious vehicles, find snipers, evaluate danger zones, and even sample and collect hazardous materials. But they can't yet operate independently. They are all remotely controlled, or teleoperated, by humans. Trouble is, it takes a while for humans to learn to master the controls. And that can be a problem in emergency situations when trained operators are not on hand.

Device: So Dartmouth researchers, led by DMS plastic surgeon Joseph Rosen, M.D., and undergraduate Jacob Jurmain, set out to design a hazmat robot that would be easy to operate. They built their HazBot prototype out of existing components—the PackBot Explosive Ordinance Disposal manipulator robot, made by iRobot Corporation, and Mantis, a control device made by Mimic Technologies. Then they modified and integrated the device's software to come up with a system easy enough for anyone to master.

The control mechanism is a thimble-sized device. "You just grab [it] and move it around," says Jurmain, now a graduate student at Dartmouth's Thayer School of Engineering. "You immediately get the hang of it." And the robot mimics every move the operator makes.

Further work is needed to make the system more rugged, say the researchers, who reported on their work in the *American Journal of Disaster Medicine*. One day, HazBot may help in all kinds of dangerous situations—from investigating methamphetamine labs to helping patients in infectious disease outbreaks. LAURA STEPHENSON CARTER