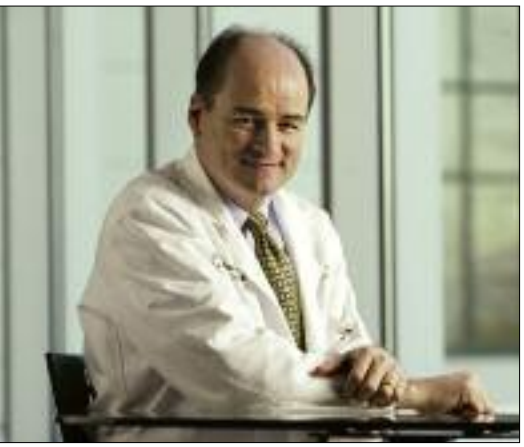
DMS's Department of Genetics, according to data from the Association of American Medical Colleges, ranks in the top 10% nationwide in terms of grant funding per faculty member.

A new ally against multiple myeloma

Kenneth Meehan, M.D., has taken on a formidable adversary. His foe is multiple myeloma, an incurable cancer of the blood. To improve the survival of patients with the disease, he is trying to take advantage of one of the strongest weapons patients have against cancer—their own immune systems. In a recent DHMC clinical trial, Meehan combined immunotherapy—stimulating the immune system to fight a disease—with standard treatments for multiple myeloma.

Stem: A typical treatment regimen for multiple myeloma begins with high doses of chemotherapy. Such doses destroy not only the cancer cells but also patients' bone marrow—where all blood cells, including those that make up the immune system, are made. That requires giving patients an autologous stem-cell transplant. "In a sense, we have to rescue them by giving them their own cells back," says Meehan, who heads DHMC's Bone Marrow Transplant Program. Hematopoietic stem cells, cells that can give rise to all the different types of blood cells, are isolated from patients before they're given the chemo regimen. After the treatment, the patients get back their own stem cells, which then repopulate the bone marrow.



MARK WASHBURN

Meehan has joined forces with the immune system.

Yet even after the chemo and the transplant, multiple myeloma recurs in most cases. That indicates, says Meehan, "that after the transplant something more is needed." Even if only a few cancer cells survive the chemo, they will continue to divide and patients will eventually relapse. So Meehan decided to try stimulating patients' own immune systems to kill any remaining cancer cells.

He gave patients in the trial Interleukin-2 (IL-2) and granulocyte macrophage colony stimulating factor (GM-CSF) right after the transplant. These substances, produced naturally in the body, increase the production of immune cells. Meehan hoped this would accelerate the post-treatment recovery of the immune system. Other studies have found that patients whose immune systems recover more quickly after a transplant show better overall survival.

Trial: The purpose of the Phase I/II trial was to assess the safety of the treatment, to determine the optimal dosages, and to determine if the treatments elicit a response in the immune system. The results, published in the journal *Bone Marrow Transplantation*, show that IL-2 and GM-CSF were well tolerated and elevated levels of cytotoxic T cells—immune cells thought to be important in killing cancer cells. In addition, blood from participating patients was able to kill myeloma cells grown in the lab.

Meehan hopes the immune response will lead to longer survival. The trial has laid the groundwork for future clinical trials, in which he plans to use more types of immunotherapy, including some that are even more specific for the tumor cells. He also hopes to use the concept to gain insight into the exact mechanism by which immune cells kill tumor cells—maybe unleashing a powerful warrior that's been there all along. KRISTEN GARNER

Watery worry

Arsenic—at levels commonly found in contaminated wells in the United States—can interfere with numerous important biological pathways. Molecular epidemiologist Angeline Andrew, Ph.D., and other Dartmouth investigators observed in mice that arsenic altered signaling pathways important in angiogenesis, lipid metabolism, oxygen transport, apoptosis, the cell cycle, and immune responses. Publishing in *Toxicological Sciences*, Andrew and her colleagues expect that their research "will help guide investigations into mechanisms of arsenic's health effects and clarify the threshold for biologic effects and potential disease risk."

Complex matters

A team of DMS biochemists recently took some of the mystery out of how organelle membranes merge within a cell. Membrane merging is essential for moving and sorting proteins and has been known to include a protein complex called SNAREs, as well as the Rab family of proteins. By detailing how SNAREs and Rabs interact to drive membrane mergers and to protect organelles from lysis, the paper earned principal investigator William Wickner, M.D., and his coauthors "feature article" placement in the August 21 *Proceedings of the National Academy of Sciences*. ■