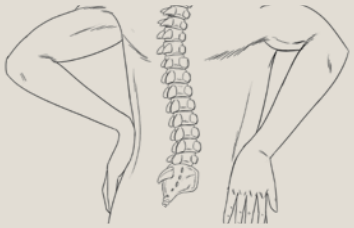
blood cells in the lab. They discovered that the short pieces of siRNA looked like the genome of HIV to the immune cells. "This made sense, since HIV uses RNA for its genome," says Howell. They found that the cells were taking up siRNA and responding as if it were a virus, secreting innate immune factors. "It didn't matter what the sequence of the siRNA was, it was inducing these same protective immune cytokines," she says—namely, a cytokine called interferon-alpha. Howell's group hypothesized that Toll-like receptors, or TLRs, were becoming activated in the immune cells that took up the siRNA, because they knew that some TLRs are specific for small pieces of RNA.

In a recent study published in the journal *AIDS Research and Human Retroviruses*, Howell and her team tested whether the specific TLR that becomes activated by RNA, TLR7, was involved by using a compound called gardiquimod, a drug known to bind to and activate TLR7. What they found was "strange," says Howell: "The cells treated with gardiquimod were almost impossible to infect with HIV." Why? They confirmed that the cells were cranking out interferon-alpha. But even when they blocked production of interferon-alpha, the cells were still resistant to infection, albeit less so. What Howell discovered is that gardiquimod also stops the action of an HIV enzyme called reverse transcriptase, which the virus needs to convert its RNA to DNA, preventing its replication machinery from being inserted into the chromosome of the cell, thus preventing infection.

Now that the researchers have made this discovery, Howell thinks it's possible that eventually gardiquimod or a similar compound might be used as a microbicide. But first she wants to find out exactly how gardiquimod works.

"The discovery part is interesting—that's the sizzle with your steak," she says. But, she adds, what's really important is understanding infection, and figuring out how to prevent it.

LAUREN ARCURI WARE



THE SECRET TO SATISFACTION

Experiencing improvements in function is more important than a decrease in pain for patients with chronic disabling back pain, according to research led by Rowland Hazard, a professor of orthopaedics and of medicine and the director of the functional restoration program at DHMC. The study followed patients enrolled in the functional restoration program. Before beginning the program, patients were asked to record goals to achieve over the next three months. They were later surveyed about their satisfaction with the program and about how fully they felt they had achieved their initial goals. "At least three months after the treatment, functional goal achievement had by far the greatest impact on patient satisfaction," the researchers concluded in *The Spine Journal*.

STUDYING NATURE *AND* NURTURE

THANKS TO A $12-MILLION GRANT FROM THE NATIONAL INSTITUTES OF HEALTH (NIH), the Geisel School of Medicine has established a multidisciplinary center for the study of molecular epidemiology. Over the next five years, the grant, part of the NIH's Institutional Development Award program, will fund research devoted to understanding how environmental exposures interact with genetics to affect human health. The new center is the fourth Center of Biomedical Research Excellence (COBRE) created at Geisel.

"Epidemiology is becoming increasingly valued for its contribution to illuminating the causes, and, in turn, prevention of human disease," says Margaret Karagas, a professor of community and family medicine and the principal investigator on the grant.

The center will have four primary projects. Brock Christensen, an assistant professor of community and family medicine and of pharmacology and toxicology, is investigating the relationship between epigenetic changes and the risk of developing breast cancer.

Diane Gilbert-Diamond, an assistant professor of community and family medicine, is leading an investigation into the relationship between *in utero* vitamin D and immune function in early childhood.

Building on her research in premature babies with cystic fibrosis, Juliette Madan, an assistant professor of pediatrics, is investigating bacterial colonization in pre- and full-term infants and its connection to infection and allergy risk.

Using advanced imaging techniques, Tracy Punshon, a Dartmouth College research assistant professor of biological sciences, will study the transfer of metals from mothers to infants and examine whether the mother's genotype contributes to the risk of transferring metals.

In addition, the creation of a biorepository will allow for the long-term storage and study of specimens, facilitating research by participants in the COBRE and other researchers at the medical school.

EPIDEMIOLOGY IS BECOMING INCREASINGLY VALUED FOR ITS CONTRIBUTION TO ILLUMINATING THE CAUSES OF HUMAN DISEASE.

Karagas is excited about the work being done by these and other researchers. "We have an extraordinarily talented group of early career faculty conducting state-of-the-art epidemiologic research," she says. "We hope this new infrastructure will serve not only the institution, but the region and beyond."

SUSAN GREEN