Stavros S. Niarchos Associate Professor in Pediatric Cardiology. “We were lucky to have the tools—molecular biology, microarrays, characterization of the proteins on the surface of the cells, the known enzymes that participate.”

Lyden has high hopes that today’s analytic tools and the insights they reveal will transform the prognosis for patients with advanced cancer. Ninety percent of cancer fatalities owe to metastasis, says Lyden—yet oncologists don’t know enough about the process in humans to short-circuit it. “Even though standard treatment of surgery and chemotherapy has improved survival, there are too many deaths and too many side effects,” says Lyden, who treats children with brain tumors at Memorial Sloan-Kettering Cancer Center. “We need selective therapies and targets.” Chemotherapy works by killing any rapidly dividing cell, he notes, from cancer to hair to the lining of the digestive tract. That means there’s a lot of collateral damage associated with current treatment options. “The better approach is to understand all of the steps in metastatic disease,” he says. “If we understand what’s going on in metastatic tissue, and if it’s specific to metastatic tissue, then we should target that rather than anything that’s a dividing cell.”

Already, Lyden and his collaborators have documented the role of growth factors secreted by the tumor in preparing the way for metastasis, described how stem cells in bone marrow establish the vascular supply for distant lesions, and detailed the influence of inflammation on the pre-metastatic niche using mouse models. In April 2009, Nature Reviews Cancer published “The Metastatic Niche: Adapting the Foreign Soil” by Lyden and Bethan Psaila, a research associate in the Department of Hematology at London’s Imperial College School of Medicine, who completed a Fulbright fellowship in his lab. “There’s a balance of the cancer and the host,” says Psaila. “Targeting the cancer cells alone isn’t enough. You also need to target the normal cells, the normal microenvironment, because they play a role. It’s obvious that you need to design treatments that attack cancer cells, but it’s less obvious that the body is playing a role as well.”

Perhaps, the researchers say, the team’s most important insight boils down to a matter of timing. “The tumor cells are released early on, circulating even when you have a small, localized tumor,” says Rosandra Kaplan, Weill Cornell’s Charles, Lillian, and Betty Neuwirth Clinical Scholar in Pediatric Oncology and an assistant professor of pediatrics who did a fellowship in Lyden’s lab and continues to collaborate with him. “The circulating cells make a welcoming committee. They’re changing the landscape and changing the microenvironment.” In their current work using human tissue samples, Lyden and Kaplan have focused on further exploring the biochemical processes under way at prospective metastatic sites at the earliest stages of a primary tumor’s development. Says Kaplan: “David challenges people to think differently.”

— Sharon Tregaskis

In Practice

Studying physicians on the front lines

As debate rages over health-care reform, many opponents of the Obama Administration’s plan have repeated a common refrain: a system of national health care “will put a bureaucrat between you and your doctor.” Regardless of where one stands on the proposals currently battling their way through Congress, a study by Weill Cornell researchers has found that one thing’s for sure: there’s plenty of red tape already—though not necessarily from government bureaucrats.

In a national survey of physician practices, Lawrence Casalino, MD, PhD, and colleagues reported that, on average, doctors spend the equivalent of nearly three work weeks a year on administrative tasks required by private health insurance companies—and the figure is even higher (more than four weeks) for primary care physicians in small practices. The study, whose results were published in Health Affairs in May, also found that nurses spend more than twenty-three weeks per physician per year on such tasks—which include prior authorization, pharmaceutical formularies, claims, billing, and
Talk of the Gown

One of the most common reasons for a lapse in reporting results, he says, is the practice of telling patients to assume that “no news is good news.” He was motivated to undertake the study after it happened in his own household: his wife had gone for a routine Pap smear, and when the nurse practitioner looked at her record, he says, she “went white.” The previous year, Casalino explains, his wife had had a uterine ultrasound, but the troubling results—which might have indicated endometrial cancer—had never been reported to her. “After all the stories she had heard from me over the years, my own wife assumed no news was good news,” Casalino says. “These mistakes are widespread.” (Luckily, she proved to be cancer-free.)

Having served as a family physician in a nine-doctor group practice in California from 1980 to 2000, Casalino is devoted to improving medicine by focusing on its front lines. Physicians, he says, are the “final common pathway” for health care. “Not to say that nurses and other staff are not important,” he says, “but things don’t happen unless physicians order them. The cost and quality of health care depend heavily on what physicians do. Understanding more about how physicians practice is fundamental to understanding medical care in the U.S.”

Casalino admits that studying physician practices is logistically challenging. “It’s devilishly hard to get data,” he says, because unlike hospitals or health plans, there’s no national census of medical practices. “When we started doing this in the early Nineties, not many people were studying them, for that reason: no one knows who they are or what physicians are in them.” Now, he says, “more people are getting into the field of studying physician practices—but it still isn’t studied as much as it ought to be in relation to its importance.”

— Beth Saulnier

Blood Ready

Getting closer to a cure for an ‘orphan’ disease

A
fter sickle-cell anemia, beta-thalassemia major—known as Cooley’s anemia—is the world’s most common inherited disease. The World Health Organization estimates that between 50,000 and 100,000 children are born with it each year; an estimated 60 million to 80 million people carry the beta-thalassemia trait, which is especially prevalent in Mediterranean countries, North Africa, and Asia. In the U.S., the number of Cooley’s patients is estimated to be between 1,000 and 1,500. While it is a small population, they’re among the largest consumers of red blood cells in the nation. A 2007 study in the American Journal of Hematology estimates that Cooley’s anemia can cost as much as $75,000 per patient per year in the U.S. Weill Cornell treats 100 to 200 Cooley’s patients annually.

Stefano Rivella, as a PhD student of genetics at Italy’s University of Pavia, worked on the Human Genome Project and human genetic disorders. Later, as a postdoc at Memorial Sloan-Kettering Cancer Center, he focused on beta-thalassemia, using mouse models to study the disorder. At Weill Cornell, Rivella and his collaborators have further characterized these mouse models that have mutations in the beta globulin gene responsible for the mutations in red blood cells that cause Cooley’s anemia. The finding, published in the journal Blood in 2008, is one step toward a cure; preclinical trials show promise for new therapies for patients with splenomegaly (an enlarged spleen), a frequent symptom.

One of the obstacles to research on Cooley’s anemia is its status as a so-called “orphan” disease. Although the Centers for