The Association of American Medical Colleges reported that DMS's Department of Microbiology and Immunology ranks 6th out of 126 medical schools in research income per faculty member.

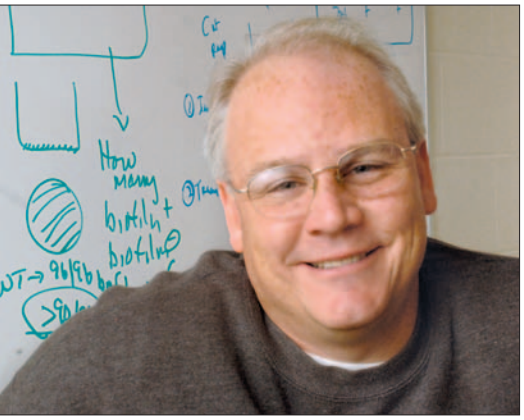
"Dramatic" finding from a casual chat

It's not often that a casual chat leads to a research project with important implications. But at DMS, at least one study began that way.

Microbiologist George O'Toole, Ph.D., explains that the project—on biofilm infections associated with catheters—grew out of a conversation between Robert Shanks, Ph.D., a postdoctoral fellow in microbiology, and DHMC nephrologist Martha Graber, M.D. And *that* conversation was stimulated by a chat Graber had had with ophthalmologist Michael Zegans, M.D., about biofilm-related eye infections. As Graber listened, she wondered if some of the *Staphylococcus aureus* infections she was seeing in the dialysis unit might be biofilm related. Biofilms, which are bacteria in communities rather than in free-swimming or planktonic form, are more resistant to antibiotics.

Later, Graber had lunch with Shanks and other biofilm researchers. And *that* led to a collaboration with O'Toole, Shanks, and others to investigate whether heparin, an anticoagulant commonly used in dialysis procedures, has an impact on the ability of *S. aureus* to form biofilms.

"The answer to that question is most definitely yes," O'Toole says. The finding that heparin stimulates the formation of bacterial biofilms was reported in the journal *Infection and Immunity* in 2005. A follow-up study published this year in *Nephrology Dialysis Transplantation* reported that sodium citrate—an anticoagulant used widely in Europe, but not in the U.S., to prevent clotting in catheters between uses—can inhibit biofilm formation.



JON GILBERT FOX

George O'Toole's lab studies biofilm formation.

Patients with failing kidneys must undergo dialysis several times a week. They are connected to a machine via a catheter placed in a large neck vein or via a fistula, a surgically created connection between an artery and vein in the arm. The machine removes, purifies, and returns blood to the patient. Fistulas are less likely to become infected but cannot be used until the surgery site heals.

There are 400,000 vascular catheter infections a year in the U.S., caused mostly by *S. aureus*. "Bugs get in through the hole where the blood goes," Graber says. "It's the Achilles' heel of catheters."

And so is heparin. Although it's effective at preventing clotting in catheters, it can leave patients vulnerable to hard-to-treat biofilm infections.

Staph: In order for biofilms to form, "you need cells attaching to a surface and cells attaching to each other," O'Toole explains. "Heparin seems to stimulate the ability of staph to bind to itself."

Shanks, who is now on the faculty at the University of Pittsburgh, is studying the mechanism by which heparin does this. And at DMS, O'Toole's lab is investigating how sodium citrate works and is testing alternatives. Sodium citrate is not widely used in dialysis in the U.S. because of fear of accidental infusion of highly concentrated forms. DHMC uses heparin.

The heparin-biofilm association was unknown until the Dartmouth papers. "This was such a clear finding—it was so dramatic," says Graber. "I was incredibly surprised." LAURA STEPHENSON CARTER

Fat chance

One could say that breast cancer cells are addicted to fat—or, rather, to a protein called S14 that allows the cells to manufacture their own fat. "This makes sense, as fat is a crucial fuel for breast cancers," explains William Kinlaw, M.D., an associate professor of medicine at Dartmouth. He recently published three papers revealing potential for S14 as a new anticancer target. "We're now working to examine this idea rigorously in cancer-prone mice engineered to lack S14 in the mammary gland," adds Kinlaw, "and to find areas on the S14 protein that might be suitable for attack with a drug."

Brain teaser

Exposure to nonylphenol—a prevalent environmental pollutant derived from herbicides, pesticides, polystyrene plastics, and paints—may harm a developing brain, a team of Dartmouth researchers recently reported. "Our results suggest that this environmental estrogen, if present at elevated levels, . . . may have deleterious effects on neuronal differentiation," wrote Leslie Henderson, Ph.D., et al. in the journal *Endocrinology*. "Because nonylphenol bioaccumulates, our results may be broadly applicable to a wide range of . . . terrestrial species that are higher in the food chain," not just the aquatic organisms they studied.