**A DMS team analyzed 200 randomly chosen press releases put out by 20 academic medical centers and concluded that they often overstate research findings and fail to acknowledge study limitations.**

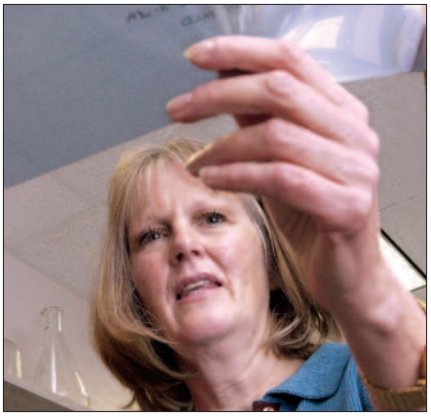
# Protein shows promise in reversing plaque

If only "atherosclerosis" weren't such a tongue-twister. The disease kills more Americans than cancer but has nowhere near the frightening ring for most people as the word "cancer." Atherosclerosis involves a buildup within the arteries of fatty deposits called plaque. The arterial wall compensates for the blockage in the blood flow by expanding around the plaque deposits. As a result, atherosclerosis is a "silent" disease until the deposits overwhelm this compensatory mechanism.

A heart attack or stroke caused by a blockage may be the first sign of the disease. By then, irreversible damage has often occurred. Treatment options include lifestyle changes (such as diet, exercise, and smoking cessation), medication, and surgery. There may one day be another option on that list.

**The protein reduced cholesterol in plaque deposits by 49%.**

**Fat:** In a paper published in *Circulation Research*, DMS's Mary Jo Mulligan-Kehoe, Ph.D., and colleagues revealed a possible new way to reduce plaque. The team administered a protein molecule called rPAI-$1_{23}$ to mice that had been fed a high-fat diet to foster the creation of plaque deposits. The protein inhibited angiogenesis —the growth of new blood vessels—in the plaque-filled arteries, affecting the plaque's growth and stability. Of particular note was the fact that the protein also reduced the cholesterol in plaque deposits by an impressive 49%. The authors hailed this as "a dramatic effect."



JON GILBERT FOX

**Mulligan-Kehoe studied plaque deposits in mice.**

**Protein:** Mulligan-Kehoe explains that rPAI-$1_{23}$ is a truncated form of a parent protein called PAI-1, whose role in angiogenesis remains controversial. "In everything you read about atherosclerosis relative to PAI-1," she says, "they cannot put a handle on whether it's pro- or anti-angiogenic"—that is, whether it promotes or inhibits the formation of blood vessels. And, she adds, "they've looked at it in plaques and they can't tell you whether it's protective or causes plaque progression."

So Mulligan-Kehoe, with funds from two NIH grants plus Philips Imaging, set out to identify the functions of PAI-1. The researchers started by cutting away certain regions of the protein. They found that truncated forms were pro-angiogenic if they contained a certain domain, such as rPAI-$Hep_{23}$. But when that domain was removed, the truncated protein became anti-angiogenic, such as rPAI-$1_{23}$.

In addition, using samples of plaque obtained from DHMC patients, Mulligan-Kehoe has shown the presence of both native and truncated PAI-1 in some patients, suggesting that truncated forms of the protein are physiologically relevant.

**Lab:** The finding that different forms of PAI-1 can be pro- or anti-angiogenic may have application to other diseases as well. Mulligan-Kehoe's lab is also looking at how rPAI-$Hep_{23}$ can improve blood circulation in patients with diabetes.

But as excited as she is about the therapeutic potential of rPAI-$1_{23}$, Mulligan-Kehoe is eager to continue using it as a tool to study PAI-1. "I just love the science," she says. TINA TING-LAN CHANG

## Rural complications

For people with HIV, depression is a serious complication. "HIV-infected patients with depression experience poorer physical and social well-being and greater bodily pain," wrote DMS's Timothy Lahey, M.D., et al. in the journal *BMC Infectious Diseases*. HIV patients with depression are less likely to follow treatment regimens strictly, and they have lower CD4 counts. Lahey found that this problem is worse in rural areas, where people with HIV are more likely to suffer from depression than are those in cities—possibly, he concluded, due to a lack of social support systems.

## A smoking gun

It's great when an actor lights up the silver screen, but not so great when one lights up *on* the silver screen. That's because, according to research from Dartmouth's Hood Center for Children and Families, smoking in movies encourages adolescents to become smokers themselves. After tracking the film-watching habits and smoking behaviors of about 2,000 adolescents over seven years, the researchers concluded that about a third of those who took up smoking wouldn't have done so if not for repeated exposure to smoking in movies. "The implications of this finding are highly significant for prevention," they wrote in *Pediatrics*.