A trial to see if a tuberculosis vaccine keeps HIV-positive Tanzanians from getting TB found that 94% of the subjects showed an immune response; DMS was a partner in the study.

Pancreatic cancer: Deadly and on the rise

More than 37,000 Americans will be diagnosed with pancreatic cancer in 2007, says the American Cancer Society, and 33,000 of them will die. "No cancer is good," says endocrinologist Murray Korc, M.D., chair of medicine at Dartmouth, "but this is an especially nasty one."

It is also a cancer on the rise. The pancreas, a gland behind the stomach, excretes enzymes that help digest fats, carbohydrates, and proteins; it also secretes insulin. Ten percent of the risk for pancreatic cancer is familial. "But 35 percent is due to cigarette smoking," says Korc. "Eating rich, fatty foods and heavy alcohol use—these are risk factors. Longstanding type 2 diabetes will also lead to more pancreatic cancer down the road."

Hidden: Epithelial cancers, like pancreatic cancer and breast cancer, are very hard to diagnose, says Korc. "The pancreas is a hidden organ. Although the imaging tests are good—you swallow a tube, it takes a picture of the pancreas through the stomach—who should have these studies? When the lesion is small, you don't have any symptoms, so why would you go looking for it?"

By the time it is noticed, a pancreatic tumor is usually too large and aggressive to be cured by surgery. So Korc's team is trying to improve chemotherapy. "It's a complex cancer. It's not easy to figure out. It's like a three-D puzzle with thousands of pieces. In any one person," says Korc, "a pancreatic tumor may have multiple genetic mutations, and there are a plethora of other alterations that let different cells invade, metastasize, and resist chemotherapy. Cells talk to each other, and that conversation may be different in different parts of the tumor."

Korc's lab has focused on these cell-to-cell conversations, or signaling pathways. The work is conducted with human pancreatic cancer cells grown on special substrates, with mouse cells, or with biopsies collected from cancer patients. The researchers have learned how a normal cell begins to overproduce certain growth factors, commandeer the blood supply, and ignore apoptosis, or programmed cell death. And they have found promising ways to block these abnormal signals. "If you can find a way to change the cell so that instead of proliferating it dies," says Korc, "you cure the cancer."

Most recently, the team discovered a way to improve the effectiveness of the drug gemcitabine, which triggers apoptosis; in combination with radiation, it is a standard cancer therapy. "When we screen human pancreatic cancer cell lines, some are sensitive to gemcitabine and some are resistant. But when you add SAHA, suberoylanilide hydroxamic acid, they become sensitive. Taken with gemcitabine, it makes the tumor shrink. Then after it shrinks, you can go in and do surgery.

"The interesting thing about SAHA," adds Korc, whose study was published in *Clinical Cancer Research* in January, "is that it's a relatively nontoxic chemical. It has already been used in clinical trials in human patients suffering from breast cancer, lymphoma, and other kinds of advanced cancer."

NANCY MARIE BROWN

JON GILBERT FOX

Murray Korc studies an "especially nasty" cancer.

Put your right knee in . . .

If you need both knees replaced, should you have them done separately (two operations but easier recovery) or together (harder recovery but one operation)? A recent DMS study in the *Journal of Bone and Joint Surgery* shed light on a factor in the decision. The researchers examined 122,385 Medicare enrollees and found that the adjusted risk of a pulmonary embolism, a blood clot in the lung, is about 80% higher in the three months after a simultaneous procedure than in the three months after a one-knee procedure, which, they wrote, "suggests that the sum of the risks associated with the two operations . . . may equal or exceed the risk of simultaneous total knee replacement."

Mind the gap

Alan Green, M.D., was the lead author of a paper in *Schizophrenia Research* that compared two different medications for patients who experienced a first episode of psychosis. In the double-blind, two-year, multisite trial, 263 patients were randomly assigned to take either olanzapine or haloperidol. Those in the olanzapine group were less likely to stop taking the drug and more likely to experience remission. "The data," wrote the authors, "suggest some clinical benefits for olanzapine," though they added a cautionary note about side effects.