Dr. Joyce DeLeo, the chair of Pharmacology and Toxicology, was recently quoted in *Nature Biotechnology* about progress in studying glial cells; she's worked in the field since the 1980s.

Vioxx shows some long-term cardiac effects

In 2000, John Baron, M.D., had high hopes for Vioxx, and he wasn't alone. The drug was helping to ease the pain of millions of patients worldwide, without causing the gastrointestinal problems associated with aspirin. When Merck, Vioxx's manufacturer, asked Baron to help lead a clinical trial testing the drug's effectiveness for colon-cancer prevention, he was excited. "Here were drugs almost without side effects, so it seemed, and with potential cancer-protective properties," he recalls thinking. "But, well, that's not what happened."

In the study—the Adenomatous Polyp Prevention on Vioxx (APPROVe) trial—the drug did, indeed, show signs of protecting patients from adenomas, benign growths that can progress to cancer. Unfortunately, it also doubled the risk of cardiovascular problems, such as heart attacks and strokes. When this became clear, in September 2004, the trial's safety and data monitoring committee let Baron know; he informed Merck, and within a week Vioxx was off the market.

Trial: Over the next few years, Baron and his collaborators analyzed the data from the trial and wrote two papers on the drug's apparent cardiovascular risks and chemopreventive effects. In a third paper, recently published in the *Lancet*, Baron discussed a follow-up effort intended to discover if the heightened risk of cardiovascular problems continued even after patients stopped taking Vioxx.

Risks: The APPROVe subjects were contacted and asked if they'd had a heart attack or stroke in the year after going off Vioxx. The results were broadly similar to those of the earlier studies, though the overall relative risks were somewhat smaller. Baron says that the number of people in the study and the number who suffered death or disease were too low to draw definitive conclusions. The risk in the year after going off Vioxx "was not statistically significant but was elevated," he says. "Probably . . . there is an increased risk but . . . the study was too small to see it conclusively."

Baron says that he is "marginally confident" about the conclusion.

Baron's analysis also revealed that preexisting cardiovascular risk factors—such as hypertension, smoking, or being overweight—seemed to raise the cardiovascular risk from taking Vioxx. Baron says that he is "marginally confident" about the conclusion but cautions that he can't be certain of this link.

Questions have been raised recently about when Merck first knew about the risks of Vioxx. According to the *New York Times*, lawsuits against the firm have stated that "scientists at Merck were worried about Vioxx's potential cardiovascular risks as early as 1997." Still, for a time, the drug appeared to have real benefits.

Baron, who has stayed out of the legal turmoil that followed the revelations of 2004, says it can be difficult to come to definitive conclusions about the risks and benefits of a treatment. "You have to weigh the merits of one kind of endpoint against the harms of another," he says. "And that's not easy." AMOS ESTY

JON GILBERT FOX

Baron has written several papers about Vioxx.

Pressure point

Albuterol, an asthma medication, may contribute to acid-reflux attacks, according to a DMS study. The study, published in *Digestive Diseases and Sciences*, found that repeated use of albuterol may reduce pressure in the lower esophageal sphincter (LES). The LES normally prevents stomach acids and enzymes from entering the esophagus, so decreased LES pressure may "raise the possibility that gastroesophageal reflux may occur after bronchodilator therapy," wrote Brian Lacy, M.D., et al., suggesting that changes in LES pressure could be the link between asthma and gastroesophageal reflux disease.

Infective idea

A common ingredient in cosmetics, foods, and drugs—an emulsifier called polysorbate 80 (PS80)—inhibits the colonization of bacteria on a variety of surfaces, a DMS team recently found. About 80% of health-care-associated infections are caused by bacteria in the form of biofilms—the very structure that PS80 breaks down. "Potential clinical applications of the antibiofilm effect of PS80 or derivatives include the treatment of medical prosthetic devices, such as artificial joints and intraocular lenses, prior to implantation," wrote Michael Zegans, M.D., and his coauthors in *Antimicrobial Agents and Chemotherapy*. ■