



Movie characters who smoke, regardless of whether they're "good guys" or "bad guys," influence teens to try smoking, according to a recent study led by DMS's Susanne Tanski, M.D.

## Aiming a knock-out blow at malaria

By knocking out a key gene in the parasite *Toxoplasma gondii*, DMS researchers hope to strike a blow for global health. More than a billion people worldwide may be infected by *Toxoplasma*, which can cause damage to the central nervous system or death in infants and people with compromised immune systems. But the organism has added importance because it's a close relative of several other parasites, including *Plasmodium*, which causes malaria.

**Model:** David Bzik, Ph.D., a professor of microbiology and immunology, and Barbara Fox, a research associate in Bzik's lab, study *Toxoplasma* as a model organism that may help fight malaria and other diseases. In 2002, they created an attenuated, or weakened, strain of *Toxoplasma* that showed great promise as a vaccine. In a normal strain, Bzik says, even a single parasite can kill a mouse. But in the weakened strain, mice could withstand being injected with 10 million parasites. At the same time, the weakened strain prompted an immune response that protected the mice against infection by virulent strains of *Toxoplasma*.

But before the finding could be used, Bzik and Fox had to provide the exact sequence of the strain's genome. "The prob-

lem with the original attenuated strain . . . is that it's not defined genetically," Bzik says. "If you ultimately want to put anything into people, you have to have a genetic definition [of it] . . . and you have to show that it's safe and efficacious."

**Genome:** A peculiar behavior of the parasite frustrated Bzik and Fox's efforts. When *Toxoplasma* encounters foreign DNA, it randomly inserts that DNA into its genome in a process called nonhomologous end-joining (NHEJ), making it hard for scientists to manipulate the organism's DNA and target specific genes.

With their progress stymied, Bzik and Fox looked for a way to disrupt NHEJ. They thought it might be possible to identify—and knock out—a specific gene responsible for allowing *Toxoplasma* to exhibit this behavior. They spent a year trying without success to knock out the gene that produces the protein KU-70, part of the NHEJ pathway in other organisms. Then they tried it with another protein, KU-80, and found that the resulting strain of *Toxoplasma* was much less likely to exhibit NHEJ.

Bzik is excited by the possibilities opened up by the finding. "It's really a major breakthrough," he says. He explains that the immune response prompted by *Toxoplasma* is just what's needed to combat a host of diseases, including malaria, tuberculosis, HIV, and cancer. With the NHEJ problem solved, creating new strains of *Toxoplasma* for use against these diseases will be much easier.

**Host:** Shutting down the NHEJ pathway may also yield other dividends. "By taking a genetic approach to study what the parasite is doing to the host cell, we're actually going to learn a lot about the biology of our cells," Bzik says. "There's so much biological knowledge that can come out of this in the future." AMOS ESTY

**"It's really a major breakthrough," says microbiologist Bzik.**

### Got breast milk?

In some developing countries, as many as one-third of HIV-positive mothers may pass on the virus to their children through breast milk. But intriguing research has found that children are less likely to become HIV-positive if they're fed exclusively breast milk instead of a combination of breast milk and other foods. To discover what protection breast milk might offer, a DMS team examined interactions between breast milk and the virus in test tubes. "Our results indicate that breast milk contains innate factors that potentially inhibit infection with cell-free HIV," they wrote in the *Journal of Acquired Immune Deficiency Syndromes*.



### A dash of cold water

In 2006, the U.S. Environmental Protection Agency lowered the safety standard for the allowable level of arsenic in public drinking water to just 10 parts per billion. But even that level of exposure, reported DMS graduate student Courtney Kozul, affects the expression of genes involved in the immune response in mice. The results of the study, Kozul *et al.* wrote in the journal *Environmental Health Perspectives*, showed that such exposure "can have significant effects on expression profiles in mouse lung and, more important, on the protein levels of many important immune mediators." ■



JON GILBERT FOX



Bzik, left, and Fox manipulated *Toxoplasma's* DNA.