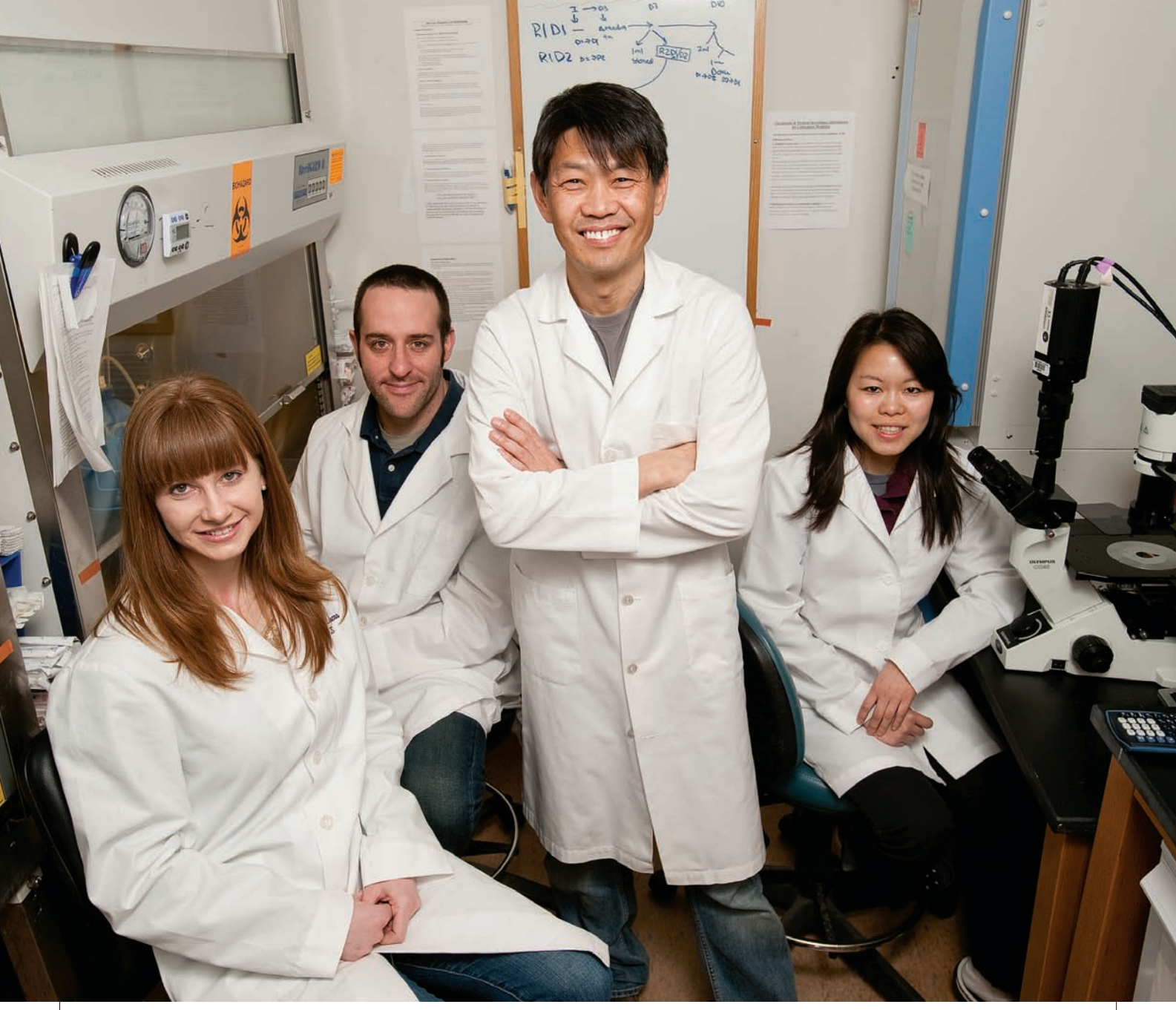

HIV/AIDS

A New Front Opens

Discovery of how HIV gains a foothold in the body points to a fresh way forward in the effort to stop the virus.

By Kathleen McGarvey

FOR MORE THAN 15 YEARS, BAEK KIM, A PROfessor of microbiology and immunology, has been fascinated by HIV's ability to hide in the body. How can the virus take cover in a cell—the macrophage—whose very job it is to kill foreign cells?

New research by Kim and Raymond Schinazi, director of the Laboratory of Biochemical Pharmacology at Emory University's Center for AIDS Research, has uncovered HIV's novel mechanism for survival in a class of cells that typically provide the first line of immunological defense.

▲ **HIDE & SEEK: With doctoral students Amanda Lucas, Edward Kennedy, and Laura Nguyen, Kim hopes to understand the molecular trickery that allows HIV to hide in cells that normally fight off invaders.**

Their research, published in the *Journal of Biological Chemistry,* indicates that HIV is able to exploit the unusual molecular makeup of macrophages to gain an often-overlooked foothold in the immune system.

The breakthrough may open up a new front in the battle against HIV, which infects more than 30 million people worldwide. Kim's and Schinazi's finding may provide the basis for an unexpected tactic for stopping the virus, perhaps before HIV infection can take hold.

"If we have a drug that blocks HIV repli-

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cating in the macrophage, then we can use it as a preventive medication," says Kim.

When HIV first enters the body—at least in cases of sexual transmission—it infects macrophages, white blood cells that Kim calls the "first defenders of our system."

Normally, HIV uses dNTP—deoxynucleoside triphosphate, the building blocks for making the viral genetic machinery—to replicate, but those molecules are scarce in macrophages. Instead they contain high levels of the closely related molecule rNTP—and HIV adapts to exploit that resource within the defensive cells, Kim and Schinazi found.

"This is a surprise," Kim says. "The virus just wants to finish replicating, and it will utilize any resource it can to do so."

When the team blocked the ability of the virus to interact with rNTP, HIV's ability to replicate in macrophages was slashed by more than 90 percent.

"HIV replicates in the macrophage for months, for years—and then evolves to move on to T cells," another form of immune cell, Kim says.

The 20 drugs currently used to combat HIV go after the infection when it's already in the T cells. These are drugs "made to help already sick people, not to prevent infection," Kim says.

With this new information about how HIV operates, it may be possible to "create a microbicide to stop the virus or limit its activity much earlier."

Kim and his colleagues are already pursuing that possibility.

There are some plant species—such as some wild mushrooms—that possess chemical compounds that protect them from viral replication using rNTP. One such substance, cordycepin, is an experimental compound derived from wild mushrooms that's being tested as anticancer drug. Kim's team is working with a pharmaceutical company to develop similar compounds that may stop HIV.

So far, they're "very primitive" chemical compounds, Kim says, but he's hoping they'll lead to others that are more effective and less toxic.

By looking to other species that have developed such protections, he adds, it may be possible for researchers to find a way "to defend against HIV." ®

Additional reporting by Tom Rickey, associate director of research communications at the Medical Center.

CITATIONS

Research Roundup

OLDER DRIVERS STEER SCIENTISTS TOWARD ANSWERS

It can be difficult for older drivers to see other vehicles and pedestrians—not because they can't perceive the moving objects but because they have a heightened awareness of the background against which they move. Duje Tadin, an assistant professor of brain and cognitive sciences, and colleagues have isolated the cause of this phenomenon—a discovery that may not only help train elderly people to be better drivers, but may also help psychiatrists understand abnormal brain processes in conditions like depression and schizophrenia. In healthy young people, a brain region called the middle temporal visual area, or MT, actively suppresses often irrelevant background motion so they can concentrate on the more important motions of smaller objects in the foreground. Tadin and colleagues found—in research published in the *Journal of Neuroscience*—that an improperly functioning MT may be the cause behind heightened perception of background motion in older adults.

RESEARCHERS PINPOINT DEADLY BRAIN TUMOR'S ORIGIN

Scientists have identified the type of cell that's at the origin of brain tumors known as oligodendrogliomas, which are a type of glioma—a category that defines the most common type of malignant brain tumor. In a paper published in the journal *Cancer Cell*, investigators found that the tumor originates and spreads through cells known as glial progenitor cells—often referred to as "daughter" cells of stem cells. The work comes at a time when many researchers are investigating the role that stem cells gone awry play in causing cancer. For scientists trying to create new ways to treat brain tumors, knowing whether stems cells or progenitor cells are part of the process is crucial. Steven Goldman, a professor of neurology, was part of the study team.

UNZIPPING MRSA AND DISCOVERING A VACCINE ROUTE

Orthopaedic scientists are a step closer to developing a vaccine to prevent life-threatening methicillin-resistant staphylococcus aureus (MRSA) infections following bone and joint surgery. Known as a "superbug" because of its antibiotic resistance, MRSA causes nearly half a million hospitalizations and 19,000 deaths a year in the United States. Most research has targeted the surface of the bacteria, but a team of Rochester scientists has discovered an antibody that reaches beyond the microbe's surface and can stop the MRSA bacteria from growing, at least in mice and cell cultures. The team—led by Edward Schwarz, a professor of orthopaedics and associate director of the Center for Musculoskeletal Research—presented its findings at the annual meeting of the Orthopaedic Research Society.

FIRST NATIONAL STUDY SHOWS HELICOPTERS BRING BENEFITS

Severely injured patients transported by helicopter from an accident scene are more likely to survive than those brought to trauma centers by ground ambulance, according to a new study published in *The Journal of Trauma: Injury, Infection, and Critical Care*. The study is the first to examine the role of helicopter transport on a national level and includes the largest number of helicopter-transport patients in a single analysis. Mark Gestring, an associate professor of acute care surgery and the director of the Kessler Trauma Center, is lead author of the study.

TINY PARTICLES, AND THE DNA TIES THAT BIND THEM

A team of researchers at Rochester, Scripps Research Institute, and MIT have used DNA as a tool to guide the precise positioning of tiny particles just one-millionth of a centimeter across. The resulting structure—a diamond-like lattice composed of gold nanoparticles and viral particles, woven together and held in place by strands of DNA—marks a remarkable step in scientists' ability to combine an assortment of materials to create infinitesimal devices. Sung Yong Park, a research assistant professor of biostatistics and computational biology, is coauthor of the study, which was published in *Nature Materials*.