Best of Mizzou Research

Today's research is big news. Some of the headlines are timely: "Coronavirus Identified as SARS Culprit." Some are controversial: "Is Cloning Part of the Divine Plan?" Others show research as big business: "Biotech Companies Race to Unravel Genetics Riddles." But whatever the topic, the heart of research is solving problems and creating knowledge to help people live healthier, longer, richer and more productive lives.

Mizzou's researchers are no different. In this story, a handful of researchers from across campus explain their work: A statistician helps physicians and other researchers arrive at answers with the least disruption to patients' lives; an agronomist builds drought-resistant soybean plants to help ensure a strong food supply; an engineer helps the Army search safely for land mines.

Much research takes place at the level of cells, genes and molecules. But no matter how small and technical their work becomes, researchers keep the big picture in mind as they make discoveries.

Getting Better Answers

Ask **Nancy Flournoy** if it's difficult being a pioneering female researcher in the vastly male field of statistics, and she offers a telling analytical response: "It's always hard to start something new. You might imagine that it would be more difficult as a female, but it's hard to see what the additional factor of being female would add."

Flournoy laughs. Mixed variables such as these — being a female and a pioneer — present just the type of statistical conundrum she could solve with her groundbreaking statistical models. Flournoy, who came to MU to lead the Department of Statistics in 2002, has addressed social science issues, including those concerning gender and career advancement.

For now, researchers apply Flournoy's work primarily to health sciences. Her "adaptive sequential designs" allow for midstream changes in experiments to help researchers get better answers faster. For instance, if researchers find during a study that a certain radiation treatment for a cancer isn't working, Flournoy's algorithms allow them to discard it and continue the experiment. That flexibility didn't exist in traditional study designs, and it can save time, money and human suffering. Some older studies took so long to complete that the treatment became obsolete. "What you have then is a very precise answer to the wrong question," she says.

Flournoy got the idea for adaptive sequential designs while working on drug trials for bone marrow transplant patients. "I became disenchanted because the statistical tools for deciding whether treatment A is better than treatment B were very wasteful of human lives," she says. She used her statistical designs as part of the interdisciplinary team that pioneered bone marrow transplantation. Her work provided the first empirical support for the theory that transplanted bone marrow would mount a fight against a patient's leukemia cells.

These aren't the only milestones in Flournoy's career. She devised interdisciplinary research models for the National Science Foundation in the 1980s, she helped establish new standards for statistical models and risk-assessment techniques for the Environmental Protection Agency in the 1990s, and she now advises government agencies on alternative methods for toxicology.

"What we've really seen since the 1980s is an evolution of departments becoming involved with each other and, returning to their roots, getting their problems from the real world," she says. "Statistics as a field grows because you're trying to solve problems that come out of the real world."

STORIES BY SETH ASHLEY

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Faster

PHOTO BY ROB HILL

In the hands of Nancy Flournoy, statistics is one of the helping professions. She pioneered algorithms that allow researchers to alter experiments midstream if they discover that a medical treatment isn't working.

Something in the Air

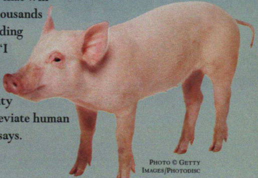
In response to the tragic events of Sept. 11, 2001, **Sudarshan Loyalka** and several other MU professors and alumni pooled their considerable expertise to help out. They wrote chapters and combined them into a book called *Science and Technology of Terrorism and Counterterrorism*. A Curators' Professor of nuclear engineering, Loyalka provided expertise on nuclear terrorism and aerosol mechanics. Understanding the tools of terrorism is a key to making the world a safer place, but Loyalka also wants nations to work together to build a sustainable peace: "We need to make sure everyone in the world has a stake in the world's future."

With funding from the National Science Foundation, the Department of Energy, the Environmental Protection Agency and the Nuclear Regulatory Commission, Loyalka seeks to understand how tiny particles move and spread in the air. "The scope of applications is vast, from human respiration to global warming," he says. Particle movement is indeed a global issue, especially when the particles are dangerous. "Wind storms in the Sahara can put particles in the U.S.," Loyalka says. "They can travel all over the globe."

Man's New Best Friend?

More than 82,000 Americans are awaiting organ transplants right now. Thousands will die before appropriate donors are found. Some scientists believe that xenotransplantation, the process of transplanting an organ from one species into another, may help people get the organs they need. **Randy Prather** works to reduce the barriers to making xenotransplantations successful.

Using a process called nuclear transfer, Prather and his team created a litter of cloned pigs born without the molecules that cause the human body to immediately reject a transplanted foreign organ. "Because bacteria have the same molecule on their cell surface, we've already developed antibodies to it," Prather says. Antibodies attack the cells of the foreign organ, thinking they're just harmful bacteria. Prather's pigs may provide organs that will one day save thousands of lives by avoiding that problem. "I think we have such tremendous opportunity before us to alleviate human suffering," he says.



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BEST of MIZZOU

Research that Feeds the World

Photo by Rob Hill

Henry Nguyen applies the fruits of the genetics revolution to soybeans. By engineering plants that resist drought, he helps feed a hungry world.

Henry Nguyen is a farmer's best friend. As a researcher in molecular genetics and soybean biotechnology, Nguyen (pronounced "win") works to improve crop yields by making plants more resistant to environmental stresses such as drought. Losses of hundreds of millions of dollars can occur when rain doesn't come at the right time. But some plants handle the stress of drought better than others. "It's like humans," Nguyen says. "Some of us cope with stress better, and some collapse very quickly!" As the world's population continues to grow and the demand for food increases, Nguyen's genetically modified crops may be our best hope for fighting starvation and malnourishment.

Delegates to the World Food Summit in 1996 called for a second "Green Revolution" to help bring food security to the world's projected 2025 population of 8 billion. The first Green Revolution, which doubled and tripled crop yields through the use of improved irrigation and crossbreeding, came just in time in the 1960s and has helped keep food supply ahead of rising demand for the past 30 years. But as the global population continues to climb, so must the food supply.

Nguyen works to understand the molecular basis of plant responses to drought and hot weather. As a researcher in the Department of Agronomy's Plant Sciences Unit, Nguyen works with the Center for Soybean Genomics and Biotechnology and coordinates the Plant Root Genomics Consortium, which is funded by a $4.5 million grant from the National Science Foundation. The researchers also receive funding from the Missouri Soybean Association. During the next four years, the consortium hopes to unravel genetic mechanisms and develop molecular strategies for improving drought tolerance.

"By the end of the process, we need to understand the genetics of drought tolerance," Nguyen says. "We can actually look at the DNA of maize or soybeans and figure out whether a particular plant will carry the desirable genes or not." The desirable genes help the plants survive through periods of water deficit. "The idea is, we take something that already has a number of good characteristics and build an additional genetic system to equip it to do well under drought conditions."

"Drought is an important state, national and global issue," Nguyen says. "That's why it is crucial that we learn more about the molecular basis of drought tolerance." Developing tougher crops will help keep farming profitable and feed the mouths of tomorrow.

The Tiniest Tank

Peter Pfeifer says history has taught us that putting hydrogen in leaky vessels, which caused the Hindenburg and Challenger explosions, is not the best idea. Even with today's safe containment systems, hydrogen-powered cars of the future would have to accommodate more gas tanks than passengers.

Photo © Alamy

That's where Pfeifer comes in. Since 1996, the professor of physics has been working to develop a compact, low-pressure storage system for methane gas, from which hydrogen gas is easily made. By shooting X-rays through carbon, Pfeifer and his team discovered "nanopores," the molecular equivalent of a suburb's endless cul-de-sacs. The tremendous surface area of the porous carbon means lots of good storage space for the tiny methane molecules, and the narrow cul-de-sacs tightly pack the molecules. Coming soon to a fuel-cell car near you!

Growing the Bottom Line

Since 1950, the National Science Foundation (NSF) has made it possible for researchers across the country to expand our understanding of basic science. "The NSF is the driving force for basic research in the nation," says **Doug Randall**, MU professor of biochemistry and recent presidential appointee to the NSF governing board. "Basic science is the economic driving force for the nation," he says. "The return on the dollar is phenomenal."

Randall has received NSF funding since 1974 for his research on plant metabolism and the interaction of cellular processes. As a founding researcher in MU's interdisciplinary plant group, Randall seeks to understand how plants regulate metabolism to improve their use for food production and possibly to produce a form of biodegradable plastic. "This will be the century for biology," he says.

Photo © Getty Images/Photodisc

Stop the Swelling

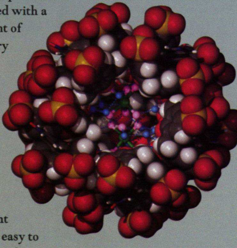
About 40 percent of breast cancer survivors experience a condition called lymphedema, a painful swelling of the limbs that occurs following surgery. "Any time lymph nodes are removed, there is a lymphedema risk," says **Jane Armer**, associate professor at the Sinclair School of Nursing and a researcher at the Ellis Fischel Cancer Center. The condition can be painful and debilitating, but there are also psychological effects. "It's something that's a constant reminder of the cancer every day," Armer says.

With her research, Armer seeks to understand the constellation of factors that cause the condition. "We hope some day we'll have an intervention to prevent swelling," she says. "We need to know when the risk is the greatest so we know when to intervene." A $1.6 million grant from the National Institutes of Health helps fund her five-year study.

A ZIP Code for Drugs

Jerry Atwood has lots of good analogies for explaining how his nanocapsules may revolutionize drug-delivery systems within the human body. Conventional systems are comparable to looking for a stranger in a crowded room; without knowing what the person looks like, you have to approach everyone in the room. Similarly, most drugs can't recognize their target sites, so they approach every site in the body and thereby cause side effects.

The allergy drug Claritin, for example, can't specifically recognize histamine receptors, so the bloodstream gets flooded with a million times the amount of the drug that's necessary to treat allergies. Atwood's nanocapsules may change that by sending drugs only where they need to go. "It's like putting a ZIP code on the outside," says the Curators' Professor of chemistry. "Once you have the right code on the outside, it's easy to get the letter where it needs to go."



The Art of Science

Linda Randall may be the only faculty researcher whose ice buckets match the walls of her lab. She designed the renovation plans for Stephens Hall, where her labs are, and added a touch of elegance more commonly found in art museums. "Things should be beautiful," she says.

In fact, Randall feels that art is often the best method for demonstrating the beauty of biology. Most people have difficulty understanding Randall's groundbreaking research in protein export, the process that allows amino acid chains to pass through cell membranes. So, when asked to give a lecture at Washington State University in 1990, she told her staff of researchers, "We're going to dance protein export!" They went along with what they thought was a joke until they found themselves on stage.

In addition to her forays into dance and design, Randall holds MU's Wurdack Chair in Biochemical Sciences and was elected to the National Academy of Sciences in 1997. Her work in understanding how proteins fold within bacteria cells helps to combat diseases such as Alzheimer's and diabetes.

PHOTO BY ROB HILL

With an eye for beauty and a mind for science, Linda Randall teaches and researches protein export, a process that allows amino acids to pass through cell membranes.

Magic Bullets for

For more than two decades, labs in the basement of the Truman Veterans Hospital have been buzzing with researchers in MU's Radiopharmaceutical Science Institute (RSI), which develops radioactive molecules that target cancer cells from inside the body. It's a welcome alternative to traditional external radiation therapy, which wreaks havoc on both good and bad cells. "This is really where nuclear medicine is going," says **Wynn Volkert**, director of the RSI and Curators' Professor of radiology. "We hope to be able to replace some of the external beam therapy."

Radiopharmaceuticals kill cancer cells without harming healthy cells. The specially designed radioactive molecules target receptors that are unique to different types of tissue. For example, a molecule designed to target bone does not bind to the surrounding muscle tissue. That's how the bone-cancer drug Quadramet, developed at MU in the 1980s, works. The molecules are also attracted to areas with rapid cell division — cancer's calling card.

When cancer spreads, a condition called metastasis, it becomes difficult to target the disease from outside the body. "If someone has metastatic disease, with external beam therapy, you may not know where all these cells are," Volkert says. "So the potential power would be to inject your radioactive drug to spread throughout the body, and if you've got the right homing technology, no matter where the cells are, it'll pick them up. It's the magic bullet hypothesis."

For about eight years, RSI investigators have been working with a molecular model based on a design by researcher Timothy Hoffman. "We showed the potential value of it pretty quickly," Volkert says. Already they are using the model to develop drugs to treat breast, prostate and pancreatic cancers, and they're working to target other human cancers including melanoma, lymphoma and colon cancers. Their current funding — which comes from the National Institutes of Health, the American Cancer Society, the Veterans Administration and the departments of Energy and Defense — allows the researchers to develop basic techniques and strategies for treating cancer before licensing their work out to drug companies that may be interested only in short-term results.

But the chief benefit of the institute may be the development of a cross-disciplinary approach to cancer research. "The nice thing about the institute is, we formed it to help facilitate interactions between our faculty and faculty outside the institute as well," Volkert says. "It's a group that's capable of starting from fundamental processes and concepts and moving all the way up into human patients."

Killing Cancer

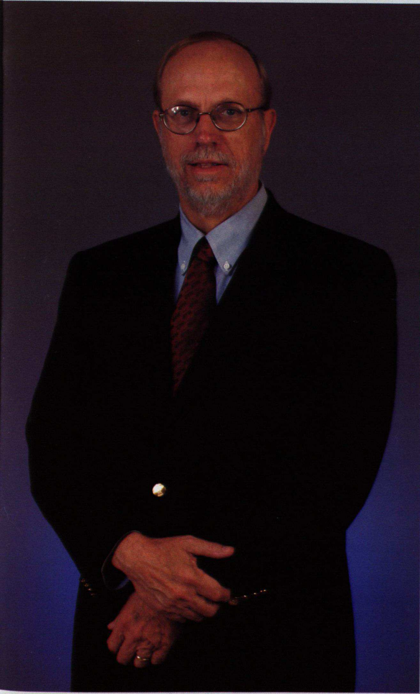
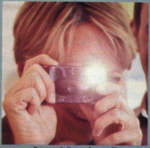


PHOTO BY ROB HILL

Wynn Volkert develops radiopharmaceuticals, which kill cancer cells without harming healthy cells as traditional radiation therapy can.

A Finger on Pulse Power

As an electrical engineer, **Bill Nunnally** likes to solve practical problems. Unlike many university researchers, Nunnally is a generalist with a broad expertise in a host of applications, from developing optical communication tools and helping the Army search for land mines to improving techniques for de-icing airplanes and building communications sensors for Predator reconnaissance drones. "As an engineering professor, there are two philosophies," Nunnally says. "I believe in being a broad-based person rather than being the world's greatest specialist in a really narrow area."



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One of Nunnally's focus areas is pulse power, a way of delivering increased power in a short period of time. Like a camera flash, pulse power uses capacitors to store energy over a period of time and then release it in an instant. Nunnally has worked with universities and national laboratories to improve pulse-power technology. "We're just trying to do things better, faster and more efficiently," he says.

Programmed for Health

Dividing his time between research, patient care, hospital administration, fund raising and program development, **Charles Caldwell** gets to wear many hats. Part of Caldwell's mission as director of programs at Ellis Fischel Cancer Center is to acquire the National Cancer Institute's (NCI) coveted comprehensive cancer center designation. With 15 NCI grants totaling more than $30 million, the center has come a long way in the past few years. "We started a planning process to beef up the cancer programs," Caldwell says. "I think what we're seeing now is the payoff from those efforts of two or three years ago."

For his part, Caldwell studies lymphomas and leukemia, and he examines the process of gene regulation called DNA methylation, which helps tumors form. Reversing abnormal methylation may help treat cancer, and blocking it may wipe out cancer altogether. "We're hoping to move this back further to actually prevent cancer before it ever forms," Caldwell says. ✱