

# The Science of Sticking|Together

*In collaboration with faculty and students throughout Ohio University, Professor of Chemical and Biomolecular Engineering Doug Goetz and colleagues are investigating cell adhesion and initiating a multidisciplinary master's program in biomedical engineering*

**W**hen bacteria invade, your white blood cells snap to attention. These microscopic Marines rush to the defense, attach themselves to and storm through blood vessel walls, then stream through the tissues to the point of attack.

Usually, it's good when white blood cells rank up, but sometimes they jump the gun. When white blood cells rally without an infection to fight, they can cause pathological inflammation such as arthritis, heart disease, Crohn's disease, and colitis, to name a few.

"This phenomenon is the basis for my entire lab," said Doug Goetz, professor of chemical and biomolecular engineering. Since before he joined the Russ College in 1999, Goetz has applied his studies of white blood cell adhesion to investigate the fundamental dynamics underlying such inflammatory diseases. His efforts have attracted funds from the American Heart Association, the National Science

Foundation, the National Institutes of Health, and the Whitaker Foundation.

Goetz's work involves cross-disciplinary collaboration among engineering, the Colleges of Osteopathic Medicine and Arts and Sciences, the Edison Biotechnology Institute, and local companies such as Diagnostic Hybrids. The alliances yield valuable health research and help to lay the foundation for the University's new biomedical engineering master's program, which Goetz directs.

While pathological inflammation can occur throughout the human body, two of Goetz's current projects focus on the cardiovascular system. Goetz, with colleagues from the College of Osteopathic Medicine and the Department of Physics and Astronomy, tackles inflammation of the aorta and lungs, laying groundwork for future targeted drug-delivery and possible preventions for heart disease.

Assistant Professor of Physics **David Tees**, chemical and biomolecular engineering Ph.D. candidate **Prithu Sunudd**, Professor of Chemical and Biomolecular Engineering **Doug Goetz**, and 2007 Russ Prize Recipient **Yuan-Cheng "Bert" Fung** watch how white blood cells travel through capillaries – the body's smallest blood vessels – in the lung.



Rick Fatica

## Beginning with the Basics

Imagine your blood vessels as an elaborate system of biomechanical highway tunnels. Blood cells and platelets zoom past in a constant traffic flow. For white blood cells to fight infections in your body, they must leave the traffic flow along the tunnel walls, roll a bit, and finally come to a stop before they can exit the tunnel to hunt for bacteria.

“If you have an infection in your left hand, the white blood cells accumulate in your left hand,” Goetz said. “How do they know how to do that? The (blood) vessel wall releases chemicals that tell the white blood cells to come and the number of proteins on the vessel wall increases, making it ‘stickier,’” he added.

In the case of pathological inflammation, Goetz explained, vessel walls get “sticky” when they shouldn’t. To treat these inflammations, scientists have begun to engineer drug carriers that mimic how white blood cells adhere to those sticky vessel walls.

“The field of white blood cell adhesion relates very closely to drug delivery research,” Goetz said. He explained that scientists like his collaborator Justin Hanes at Johns Hopkins University make spherical porous particles that are filled with medicine and “targeted” to specific areas. These drug carriers, made from biodegradable polymers, imitate the white blood cell’s mechanism for rolling, tumbling, and sticking to vessel walls.

Such drug delivery research attempts to selectively target diseased tissue and spare the rest of the body from the stress of tough treatments such as chemotherapy or, in the case of pathological inflammation, steroid-based medications.

While Goetz and other researchers in his lab are not actively trying to get a drug delivery vehicle on the market themselves (“You would need millions of dollars to actually create a new drug,” Goetz said), they do inform drug design by testing the underlying biophysical principles.

## Matters of the Heart

“This might be how you die someday,” Goetz said as he outlined his research on atherosclerosis on a dry-erase board. Blunt or not, with heart disease ranking as the number one cause of death in the United States, it’s a pretty sound bet.

When fat sticks to the walls of blood vessels, white blood cells come along, eat the fats, then die there, causing pathological inflammation and contributing to the plaque build up that leads to heart attacks.

Goetz and Ramino Malgor, assistant professor of pathology in the College of



Professor of Chemical and Biomolecular Engineering **Doug Goetz** talks with chemical and biomolecular engineering Ph.D. candidate **China Malakondaiah Kummitha** in the lab.

Osteopathic Medicine, have discovered the existence of an additional, and potentially critical, protein in hardened arteries. The protein, called wnt5a, is normally found in embryos, and helps to coordinate the growth and movement of embryonic cells.

They also found evidence that wnt5a interacts with something called “toll-like receptors,” which activate the innate immune response. Interestingly, toll-like receptors have been implicated in pathological inflammations like atherosclerosis.

Goetz and Malgor are now trying to understand the relationship between wnt5a and toll-like receptors and the role wnt5a plays in the development of heart disease. Their research lays groundwork for the development of novel therapeutics for atherosclerosis.

## “Breath” of Knowledge

“Doug and I were brainstorming, and I got this idea,” said David Tees, assistant professor of physics. Tees suggested they use micropipettes, tiny cylindrical glass instruments about the size of capillaries—the smallest blood vessels in the body—to study cell adhesion.

Researchers and students in Tees’ lab went to work, sucking white blood cells into micropipettes to simulate blood flow through the capillaries. Because capillaries are so small, a large fraction of the white blood cells are lodged in the intricate maze of these tiny vessels inside your lungs.

“It’s not a perfect model,” Tees said of his micropipettes. “But we can use it to find the underlying parameters (of white blood cell adhesion in capillaries) with our research.” The model could some day be used to test drug treatments for inflammation, as it

could determine whether the treatments block or enhance cell adhesion in capillaries. Tees, who recently received a prestigious NSF CAREER grant—a grant that Goetz also won—to continue this research, credits many of his professional moves to the success of his collaborations with Goetz.

“Doug is my closest collaborator,” Tees said. “He’s a great colleague to work with, and to have collaboration between physics and engineering is really considered a figure of merit around here.”

## Sticking with It

This spirit of collaboration among engineering, physics, and medicine has inspired a new master’s program in biomedical engineering, which started this fall.

A few years back, Russ College Dean Dennis Irwin charged Goetz with expanding biomedical engineering opportunities for students. He contacted some colleagues to help develop a program, which eventually evolved into the master’s offering.

According to Goetz, the level of synergetic expertise in the life sciences, medicine, and engineering made the decision to launch this program obvious.

“People have really begun to recognize the impact and benefits you get when people in the life sciences and engineering team up,” Goetz said. “The collaborative value of biomedical engineering is really growing on the national level, both in academia and in industry.”

With the many established and growing biomedical collaborations between engineering, the life sciences at Ohio University, the biotech industry, and the medical community, the new biomedical engineering program should snap perfectly into place. 🧪