

SOWING THE SEEDS

SPRAYING CELLS TO REGROW SKIN

BY JOE MIKSCH

PHOTOGRAPHY BY JIM JUDKIS

Jörg Gerlach is a native of Berlin. Before coming to the University of Pittsburgh in 2003, he tooled around his native city on a BMW motorcycle, also native to Germany's capital.

When the MD/PhD arrived in Pennsylvania, he added an American bike—one assembled in York, Pa.—to his fleet: a Harley-Davidson. Gerlach says he's a cautious motorcyclist, one who avoids highways and mostly cruises around Pittsburgh's 88 neighborhoods.

But as Pittsburghers, particularly Steelers fans, know, riding in the city isn't always the safest pursuit—just ask the guy who wears number 7 for the Black and Gold. Gerlach, now a professor of surgery and bioengineering, believes he's found a way to mend damage done by what motorcyclists call "road rash" as well as other injuries, such as burns, that cause skin loss.

At first glance, Gerlach's office at the McGowan Institute for Regenerative Medicine seems to be decorated with an odd kind of modern art: Yellow plastic things that resemble overfed starfish line a glass shelf above his desk. They are bioreactors, he says, three-dimensional breeding grounds for cells. They can, for instance, serve as a temporary liver for a person awaiting a transplant. A dozen patients with acute liver failure already bridged successfully to transplant in clinical trials with the help of the devices. (Gerlach is the chief scientific officer and a trustee of a German company that manufactures and sells the bioreactors). Biogrowth wonders like this are the bread and butter of Gerlach's work.

He disappears into the hallway near his office and comes back with a metal box, which he sets down with a grunt. "This thing is heavy," Gerlach says. The box, about the size of two milk crates, has a hose with a nozzled end on top.

This ordinary-looking box can help people regrow skin. Gerlach describes how the technology works: A patient arrives at a hospital missing a sizable portion of skin. Surgeons take a sample from a healthy piece of skin and isolate skin cells, including skin stem cells, using a method Gerlach and his colleagues developed.

That's where the box comes in—Gerlach calls it a cell-application device. A surgeon loads the stem cells into a sterile syringe, loads the syringe into the nozzle like a cartridge, and sprays the cells through the nozzle directly onto the wound. The device is hefty because of its internal mechanics, which modulate the pressure at which the surgeon expels the cells.

"What we're doing is taking the cells, isolating them, and, in the same procedure on the same day, we're putting the cells onto the wound," Gerlach says. "The progenitor cells can act immediately. The most critical cells are present, and we are using those cells right away from the patient. We just need to take care that we are distributing the cells nicely over the wound." Hence the spray nozzle.

He reports that the procedure has been performed successfully at the Berlin Burn Center, where Gerlach was active before coming to Pittsburgh and which has teamed with McGowan researchers on the skin regeneration project. Pointing at a series of photos, Gerlach recalls patients who've regrown skin over a burned ear or an entire face in a matter of days. Gerlach is part of a six-member group looking for investors so the cell-application device can be manufactured in the United States.

The idea of regrowing skin isn't new, Gerlach says, though his method is. Other doctors harvest skin cells and send them to a company in Boston where they are grown into a sheet of new skin. The lab then sends the sheet of skin back to the hospital to be attached to the wound. The problem with that approach, says Gerlach, is blisters caused by secretions under the new sheet of skin can push the sheet up and damage it.

"This problem can be circumvented by spraying single cells," Gerlach says, allowing them to enter the wound and reproduce right then and there.

The Berlin burn cases have met with success, but Gerlach has improved on the process. He hands over what seems to be a conventional wound dressing, except that one side of it looks like a tangled web of angel hair pasta. The pasta is part of another bioreactor. Tubes extend from each end—one does the work of an artery, the other a vein. Gerlach places another heavy metal box, this one with three pumps, on his desk.

"It's an artificial vascular system," he says of how this machine works with the bioreactor bandage.

"It distributes glucose, sugar, amino acids, antibiotics, electrolytes. It cleans the wound, provides nutrition, and better supports the precious stem cells in the wound until they start to grow and regenerate new skin for the patient."

The Department of Defense is funding animal studies of the wearable bioreactor at the U.S. Army Burn Center in Fort Sam Houston, Texas. The studies start in March and are expected to last a year.

"We have concerns that [the bioreactor] might stick to the wound," Gerlach says, when asked about problems the studies will help address. "We don't know how long is optimal to leave it on the patient. Twenty-four hours? Two weeks?"

He's confident the system will work. It's just a matter of fine-tuning, he says. ■



ABOVE: Bioreactors like these have served as liver surrogates, helping patients in need of transplants survive until a donor liver is found. Such bio-inventions are the bread and butter of Jörg Gerlach's work. LEFT: Gerlach is attempting to help patients regrow skin with this cell-application device.



Patients with Crohn's disease often suffer from a severe narrowing of the small intestine.

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PROTECTION FROM CROHN'S

GENETIC FINDING MAY CONTRIBUTE TO NEW THERAPIES

BY ERICA LLOYD

Crohn's disease has long been part of Anna Stein's family story. Her dad, once a high school football player, was diagnosed at 16 and became too ill with the inflammatory bowel disease (IBD) to graduate with his classmates.

"He was in bed for a few years," says Stein.

Her dad went on to get his GED and become an optometrist in Chicago. But he was often hospitalized for Crohn's flare-ups.

The disease makes it difficult to absorb nutrients and is notorious for causing severe cramps and diarrhea and tunneling intestinal ulcers. (To get a sense for how miserable the disease can be, consider this. For a recent experimental therapy, patients desperate for relief volunteered to ingest eggs of parasitic worms.)

"He was in excruciating pain," says Stein of her father. "He was in pain all the time.

"Having a chronic disease in the family is like having another family member," says Stein. Surgeries to remove sections of her father's bowel as well as kidney stone complications severely restricted his diet. He couldn't digest most vegetables. Whole grains, nuts, and, eventually, fats were off limits, too. He'd try to sneak his forbidden favorites—peanut butter and chocolate—when Stein's mother wasn't looking.

Her father died only three years ago at the age of 82 from an unrelated condition.

"People didn't think he'd live that long, marry, or have children," says Stein.

A few months after her father's death, Stein's then-16-year-old son, Robert, was diagnosed with Crohn's.

Crohn's is an inherited disease, and scientists are just beginning to understand the genetics behind it, notes Richard Duerr, University of Pittsburgh associate professor of medicine and human genetics who runs Pitt's IBD genetics program. Duerr was part of a group of researchers in 2001 who unveiled the first gene linked to Crohn's disease.

"That gene has been widely replicated as a Crohn's disease gene. But it, by itself, doesn't anywhere near explain the genetic risk for Crohn's disease," says Duerr.

Now Duerr and his collaborators have evidence that many people afflicted with Crohn's lack a genetic variant that protects against the disease.

The collaborators make up a U.S./Canadian consortium that includes Pitt's IBD program clinical director and associate professor of medicine, Miguel Regueiro, and M. Michael Barmada, a PhD associate professor in Pitt's Department of Human Genetics. The researchers used 300,000 genetic markers to compare the genomes of several hundred Crohn's patients and healthy controls. Duerr says that the scans yielded many "hits" but that the protective variant was notably absent among cases of people with Crohn's. Its absence was a hundred times more significant than the next most common genetic marker difference found between cases and controls. It was also less common in people with ulcerative colitis.

The protective variant appears to block or alter the effects of a proinflammatory mediator known as IL23. (IL stands for interleukin, a protein released by the immune system.) Research shows the IL23 pathway is a likely culprit in Crohn's as well as other disorders thought to be caused by abnormal operations of the immune system, including rheumatoid arthritis, multiple sclerosis, and psoriasis. "The genetic findings made sense," says Duerr.

When Anna Stein, who now lives in Michigan, read about the links between these diseases in a *New York Times* story about the research, she contacted Duerr. Robert has psoriasis as well as Crohn's. "It was amazing to me. I'd always wondered if there was a connection," she says.

Duerr expects several genes will be linked to Crohn's, yet he is excited about the potential for new therapies that mimic the protective work of the IL23 variant. One recent clinical trial, begun before the consortium released its findings, has already shown promise with a therapy targeting IL23 and another pathway (called IL12).

Robert is in his first year of college. Fortunately, his Crohn's disease history has not resembled his grandfather's. After Robert's initial bouts with the disease, he has been in remission. Yet his mother knows the disease can assert itself again: "I have a fear about that. But I'm also so encouraged by all the advances made." ■

Names were changed in this story to protect patient privacy.



CORBIS

CODE PERSONAL

NEW GRAD PROGRAM INTEGRATES MEDICINE AND COMPUTER SCIENCE

BY SHARON TREGASKIS

More than one-third of all electronic health records systems fail. Like Tolstoy's unhappy families, each unhappy in its own way, the narratives of abandoned systems blame myriad factors—weak interface with existing systems, inattentive tech support, inadequate customization, and other such woes.

Chris Bartos has another theory about why the systems implode so frequently: The opposition of MDs to new roles in the healthcare delivery system.

"An electronic health record changes the work flow of doctors, nurses, and medical secretaries," says Bartos, a nurse with 30 years of experience and a master's degree in information science who worked on the implementation of UPMC's electronic order entry system in the late '80s.

"In some cases, there's tremendous resistance on the part of physicians because [it changes] the way they do their work. My premise is that it's based on issues of personal power and control over work domain." To test her hunch, Bartos will examine individual attitudes and then develop recommendations to enhance system implementation.

Bartos is one of 42 students enrolled in the University of Pittsburgh School of Medicine's new graduate program in biomedical informatics. Thirty core faculty from disciplines including dentistry, biostatistics, genetics, and radiology train the students.

Michael Becich calls the field a "Rosetta stone" for converting raw data into knowledge. Becich, a pathologist and MD/PhD, chairs the Department of Biomedical Informatics, which the school launched this fall.

The field has already changed medicine. Clinicians now benefit from software that flags dangerous drug combinations. Robotic assistants help with diagnosis, treatment, and even patient recovery. In the laboratory, researchers model biological functions, screen chemical compounds, and interpret vast quantities of experimental data with help from computers.

"In biomedical informatics," Becich says, "software, hardware, and telecommunications technologies converge to serve all of medicine—research as well as the clinical practice."

As the field matures, says Becich, clinical care and primary research will converge, with technology bridging the gap. Already, scientists have begun transitioning from publishing only their findings to sharing the raw data that undergird further analysis.

Ultimately, access to extensive data sets will allow researchers to ask increasingly sophisticated—and personalized—questions, says Becich, who studies electronic tissue banking, developing strategies for coding information to accompany tissue samples without compromising patient privacy. Imagine if a scientist studying prostate cancer were able to review not only serum samples or frozen tissue but clinical details about the patient from whom each sample was collected, such as his basic demographics, what stage of the disease he presented with, what treatments he received, even his PSA (prostate specific antigen) numbers over time. Such a study could delve much deeper than one restricted to an analysis of samples independent of patient details.

"We're moving into the era of personalized patient care," says Becich. "The integration of information is the only way to customize treatments."

Geriatrician Steven Handler, a PhD student in the program, has another vision for customized care—this one for frail, older adults. He's creating a system to alert physicians of the potential for adverse reactions in nursing home patients by analyzing medication and lab result combinations.

"It's something that's been done before in hospitals, but never before in the nursing home setting, where there are more beds," he says.

Handler's approach tracks outcomes, alerting clinicians when an individual patient may be at risk. "Say kidney function begins worsening while a patient is receiving a drug," says Handler, who is also an MD. "The system sends an alert to the doctor so he can change the dose or cancel the drug."

Pitt's biomedical informatics program—one of only 13 nationwide—is part of a growing emphasis on graduate science training throughout the medical school, where currently one-third of students plan to earn PhDs.

"There are all kinds of discoveries to be made," says John Horn, the school's associate dean of graduate studies and a professor of neurobiology. "Not just those that inspire the imagination, but those that have huge practical importance for improving human health and treating diseases." ■