Using three types of stains, Sowa’s work shows that injured spinal discs of rabbits become more damaged (we see less staining and fewer cells) when treated with glucosamine (4A–C) than when they are left alone (3A–C). For comparison, the discs of healthy rabbits not treated with glucosamine (1A–C) and healthy glucosamine-treated rabbits (2A–C) are shown.
One of the most common questions that patients with back problems ask Gwendolyn Sowa, an MD/PhD associate professor of physical medicine and rehabilitation at the University of Pittsburgh, is a simple one: “Should I take glucosamine?”

An estimated 5 million U.S. adults take this supplement, many to alleviate back pain. But there is little research to suggest that it actually works. To get some solid answers, Sowa has been putting glucosamine to the test. She doesn’t know yet how the supplement works in humans. But if the results are similar to what she’s seen in rabbits, people with lower back pain might be better off without it.

Sowa’s investigation into the issue began in 2008, when she and her colleagues exposed cells isolated from the spinal discs of rabbits to glucosamine. They found that the compound reduced markers of inflammation in the cells, and that it also seemed to interfere with the cells’ ability to produce matrix proteins important for supporting the structural integrity of spinal discs.

“It was surprising. No one had ever seen this negative effect on matrix proteins,” Sowa explains. “We thought that we really needed to confirm this finding to make sure it wasn’t an artifact of our in vitro system.”

To do so, Sowa and her colleagues used a live rabbit model of disc degeneration associated with lower back pain in older people. Then, Sowa and her colleagues fed the affected rabbits, as well as a group of healthy rabbits, daily over-the-counter glucosamine, in doses comparable to the amount that people typically take. The team periodically evaluated the rabbits’ spinal discs using magnetic resonance imaging (MRI), histological studies, and gene expression assays.

Twenty weeks later, “My resident came back with the first set of results, and I was convinced that she’d switched the ID numbers on the animals.”

Twenty weeks later, “My resident came back with the first set of results, and I was convinced that she’d switched the ID numbers on the animals,” says Sowa.

“On every outcome measure we looked at, we saw this . . . negative effect.”

Among other things, the glucosamine appeared to interfere with the production of matrix proteins—and to erode the central gelatinous protective layer found in the center of the discs.

Sowa and her team also noticed that glucosamine reduced inflammation in the disc. Because inflammation is closely tied to the sensation of pain, the finding could explain why people with lower back pain feel better after they take glucosamine. But if “people are taking it and causing damage to their discs, then that’s a bad thing,” she says.

Sowa stresses that her findings, published online in January in Spine, are still preliminary:

“I’ve had people say, ‘Do I stop taking glucosamine?’ and I say, ‘I don’t know, because you’re not a rabbit.’ It’s hard to say how much of this is clinically relevant.”

To understand whether this effect is present in humans, Sowa intends to study the mechanism of how glucosamine causes these negative effects on matrix. “Understanding the molecules affected by glucosamine will allow us to answer questions regarding the long-term effects on humans. It will give us the tools to study the immediate response to this compound. Disc degeneration is a chronic process, so it could otherwise take decades to determine the effects in humans,” Sowa says.

Sowa’s work reminds us that just because many supplements and alternative remedies are “natural” does not mean they are intrinsically safe.

“We don’t know the risks of many supplements, so patients assume there aren’t any,” she says. But “not knowing the risks does not equate with not having any risks.”
Lymphoma Breakthrough May Have Broader Significance

By Ben Korman

The Lucases thought they were lymphoma researchers.

So did David Perlmutter, chair of the Department of Pediatrics for the University of Pittsburgh and physician-in-chief and scientific director of Children's Hospital of Pittsburgh of UPMC, when he recruited them from the University of Michigan in late 2012. After all, Linda McAllister-Lucas, MD/PhD chief of service in hematology/oncology and associate professor of pediatrics at Pitt, and Peter Lucas, MD/PhD associate professor of pathology and pediatrics at Pitt, had already done seminal work on the genetic triggers behind MALT lymphoma—a form of cancer that typically proliferates along mucosal surfaces like the stomach. (MALT stands for mucosa-associ-ated lymphoid tissue.)

A little over a year later, it’s clear that the lab/life partners’ work reaches far beyond the disease they’ve studied for well over a decade. Since their move to the John G. Rangos Sr. Research Center at Children’s, the two have been applying their insights to several other forms of cancer, as well.

The couple first began studying MALT lymphoma in 1999. They noticed that two subsets of the disease are defined by two distinct chromosomal translocations. (Translocations, which pair up segments of genes in the wrong places, are common in lymphomas.) They found that these mismatched couplings give rise to aberrantly expressed versions of the proteins BCL10 and MALT1. When expressed correctly, these proteins play a vital role in the function of lymphocytes (white blood cells).

“But if [BCL10 and MALT1 are] targeted by chromosomal translocation,” says McAllister-Lucas, “that can contribute to the development of a cancer.”

And so began the team’s foray into how these triggers fit into a larger picture.

In a 2011 Science paper, the couple characterized a third translocation unique to MALT lymphoma: Part of the API2 gene links to part of the MALT1 one, creating a fusion protein that “normally shouldn’t even exist in the cell,” says Lucas. This new protein attracts an enzyme called NIK. But once NIK is attached to the fusion, MALT1 chops NIK in two.

You might think splitting NIK in two would make it weaker. But when MALT1 cuts NIK, it also slices off an important regulatory portion, sending NIK into a renegade mode and allowing it to act unchecked. Cells, then, are likely to rapidly proliferate, potentially into cancer.

Because NIK functions as a kinase—a kind of enzyme that can alter neighboring proteins—it can influence the life and death of cells. Kinase activity, along with API2-MALT1’s NIK-cutting aptitude, is considered potentially “druggable” by the pharmaceutical industry. “There are laboratories that are working on early stage drugs to target MALT1,” says Lucas.

Since their own “translocation” from Michigan, the team has been examining the roles these proteins play when they are not in lymphocytes.

BCL10 and MALT1, it turns out, are present in nearly every cell in our bodies. And even when these genes are expressed normally, they can be stimulated to control cell behavior.

It seems that BCL10 and MALT1 may also play roles in the development of certain breast cancers, hepatocellular carcinoma, and osteosarcoma. The Lucas lab is in the early stages of investigating the role of BCL10 and MALT1 in these cancers. It’s an unexpected shift, but a welcome one—like their move to Pittsburgh.

“We actually never intended to leave Michigan,” says McAllister-Lucas.

“But over the years,” adds Lucas, “we became aware of good departments of pediatrics at various places and good departments of pathology in other places. It’s unusual to find really strong departments in both of those areas in the same place like you have at Pitt.”
To heal by implanting something inside a person that is not of the person, like a metal pin, for example, is a feat of biomedical engineering—but it comes with risks, including infection and inflammation. And after the procedure, the implanted metal either becomes part of the person forever or has to be removed later in yet another procedure, which carries its own risks, as well as costs.

But now on the horizon, says a group of Pitt scientists, is the next generation of these devices—metal implants that will do their job and then perform a vanishing act. Biodegradable plastics, such as those widely used in sutures and more recently in cardiac stents, actually aid the healing process. Up next, many expect: biodegradable metals that can do the same, says William Wagner, who is director of the Pitt/UPMC McGowan Institute for Regenerative Medicine and PhD professor of surgery in Pitt’s School of Medicine and of bioengineering and chemical engineering in its Swanson School of Engineering.

The McGowan Institute brings together scientists, engineers, and clinical faculty. In 2008, with $18.5 million in funding from the National Science Foundation, McGowan joined a consortium of institutions, led by the North Carolina Agricultural and Technical State University, to develop biodegradable metal implants for surgical use in orthopaedic, cardiac, and reconstructive procedures. The NSF Engineering Research Center for Revolutionizing Metallic Biomaterials (ERC-RMB), as it’s known, is producing biodegradable metals designed to promote healing while degrading. It’s also supporting research on novel coatings, alloys, and miniaturized sensing systems so that physicians can monitor and control the degradation process.

Across the ERC-RMB team, researchers have developed several device prototypes, including bone-fracture plates and surgical screws. A Pitt crew, for example, has been working with scientists at the University of Cincinnati to develop a stent that will stabilize the arm veins of patients requiring kidney dialysis.

“The field of medical implants has moved to looking at ways to get the body to heal itself,” says Wagner.