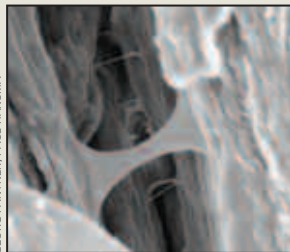


# Bench to Bedside

## Sticky Bones

Bone research dates back many centuries. Galileo, the 16th-century inventor of the telescope, reportedly published some of the first research on bones that explained why elephants need thicker bones than small animals.

Since then, thousands of other scientists have tried to understand the remarkable ability of bone to be both stiff and flexible. For the most part, researchers know that tough protein fibers coated with a thin layer of mineral crystals (mainly calcium and phosphate) make bones stiff.



GEORG FANTNER, PAUL HANSMA

In a surprise finding that may help explain how it can also be flexible, physicist **Paul Hansma** of the University of California, Santa Barbara, has discovered something completely new about bone.

Using a powerful microscope to measure the springiness of a tiny piece of bone sitting in a lab dish, Hansma discovered that a sticky “glue” held the bone together. Hansma thinks that the glue strands stretch like tiny rubber bands to prevent bone cracks.

He now wonders whether the gluey substance may be either missing or defective in some conditions that weaken bone, like osteoporosis.

The finding may also help answer why and how bones weaken with age. Young bones heal fast because they are still growing, but bone mineral density—the most common measure of bone growth—peaks around age 30. Immobilization due to a broken bone in an elderly person can lead to many other associated health problems, like serious infections. Hansma notes that more women die within a year of a hip fracture than after a heart attack.

He plans to continue to study the bone glue and its potential healing properties.—*Alison Davis*

## Forget the Surgery?

Despite the fact that general anesthetics have been used since the 1800s, scientists still do not have a clear picture of how these powerful yet complicated drugs work in the brain. Anesthetics are truly multipurpose medicines: They relieve pain, cause loss of consciousness, and induce amnesia (memory loss).

In relatively rare cases, people undergoing surgery experience some but not all of the intended effects of anesthetic medicines. For example, despite being unable to move, some people are still aware of what is happening and may remember parts of the surgery.

Using rats as a research model, anesthesiologist **Michael Alkire** has uncovered new clues about why this happens. He found that the amygdala—a brain region involved in fear, anxiety, and other emotions—helps anesthetics wipe out memories.

In his lab at the University of California, Irvine, Alkire placed two groups of rats, one mildly anesthetized and the other untreated, in a lighted chamber facing a dark tunnel. If the rats entered the dark area, an environment rodents prefer, he gave them a brief electrical shock. The unanesthetized rats remembered this shock until the next day and quickly learned to stay in the safer, lighted environment.

However, those treated with the anesthetic drug sevoflurane behaved differently. Unable to remember the bad experience, these animals continued to enter the tunnel and receive a shock. Alkire then incapacitated the amygdalas of sevoflurane-treated rats and saw that they could remember, and avoid, the shock.

By pinpointing the amygdala’s role in memory function during anesthesia, the results may help scientists develop ways to prevent awareness during surgery.

—*Kirstie Saltsman*

## Chicken Medicine

Antibodies are the soldiers of our immune system, traveling through blood to defend our bodies against viruses, bacteria, and other germs that can make us sick. Their victory means we stay healthy.



Recognizing the healing power of antibodies, scientists several years ago found a way to make special versions called monoclonal antibodies that zoom in on certain types of unwanted cells.

Just like the antibodies in our body, monoclonal antibodies used as drugs block unhealthy molecular interactions, such as those among cancer cells that form tumors.



Currently, 17 monoclonal antibodies have been approved as drugs for treating cancer, arthritis, multiple sclerosis, and inflammatory bowel disease. Dozens more are on the horizon.

Researchers make these drugs by inserting the genes for antibody proteins into cultured animal cells. But purifying the antibodies from these cells takes a lot of time and money. Now, thanks to an unlikely source—chicken eggs—scientists may have a quicker and cheaper way.

Biologist **Lei Zhu** of Origen Therapeutics in Burlingame, California, inserted into chickens the gene that makes one particular monoclonal antibody. She added extra molecular instructions so that the antibody would only be produced in egg whites.

Extracting the monoclonal antibody from egg whites was simple and provided an abundant supply. What's more, lab tests showed that the chicken-made antibodies were even better at killing cancer cells than were antibodies made with traditional lab methods.

This more efficient approach, made possible by government funding to a small biotechnology company, may lead to less expensive medicine for patients.—*A.D.*

### **Cancer Drug Fights Early Aging Disease**

Most elementary schoolers don't need to worry about wrinkles, brittle bones, stiff joints, and a failing heart. But for some who have a very rare, early aging disorder called progeria, these symptoms begin to appear within a year after birth and usually cause fatal heart attacks and strokes in the teen years.

There is no cure for progeria, which is caused by a genetic error that disfigures the protective covering that envelops a cell's command center, or nucleus. Scientists have suspected that the nucleus becomes misshapen because a molecule called farnesyl sticks to a certain key protein rather than being removed, as happens in healthy cells.

Farnesyl molecules are also found on a protein connected to cancer, and drugs that block farnesyls are currently being tested as treatments for several forms of cancer.

Cell biologist **Susan Michaelis** of the Johns Hopkins University in Baltimore, Maryland, has now discovered that the same drugs, called farnesyl transferase inhibitors, may help treat progeria.

Michaelis added farnesyl transferase inhibitors to lab-grown cells that had the same molecular defect as do the cells of children with progeria. She discovered that the drug treatment returned the nuclei to their normal shape.

Researchers have observed that farnesyl transferase inhibitors appear to be safe and have no toxic side effects in cancer patients who have taken these drugs in clinical trials. While further studies are needed to confirm that Michaelis' approach works as well in people as it does in lab cells, the findings may offer new hope to children with progeria.—*K.S.*

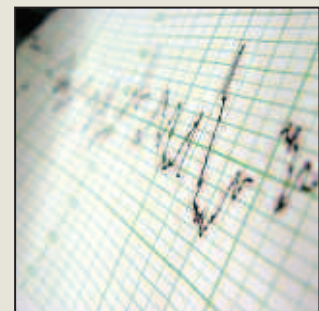
### **Heart Alert**

After leaving the hospital, heart attack patients and those with a type of chest pain called angina are often prescribed medicines called beta-blockers. These drugs slow pulse and lower blood pressure. Beta-blockers can also correct faulty nerve conduction that causes the heart to beat out of rhythm.

Despite their common use, a new experiment shows that beta-blockers may harm people who have a particular genetic profile.

**Howard McLeod** of the Washington University School of Medicine in St. Louis, Missouri, looked very closely at the sequence of two genes known to interact with beta-blockers. The clinical pharmacologist and his team read the sequences in more than 700 patients hospitalized for heart attacks or unstable angina.

They discovered that people who took beta-blockers and who had a particular variation in one of these genes were about three times more likely to die within 3 years as were those who had other versions of the gene or were not taking beta-blockers.



McLeod and his team plan a larger study of 4,500 heart patients across the country to confirm the findings. If further research generates similar results, doctors may want to find out which version of the gene a person has before prescribing beta-blockers.—*A.D.*

These stories describe NIGMS-funded medical research projects. Although only the lead researchers are named, science is a team sport and it is important to realize that many researchers work together to carry out these studies.