



You have only to wish it and you can have a world without hunger, disease, cancer, and toil—anything you wish, wish anything and it can be done.  
**Albert Szent-Gyorgyi, American biochemist, 1970**

### AGRICULTURE & FARMING

## A Less Polluting Pig

There's good news in the fight against farm pollution, say researchers in the Department of Molecular Biology and Genetics at the University of Guelph in Ontario, Canada. In August, John Phillips, Cecil Forsberg, and Serguei Golovan announced a new kind of pig that makes better use of phosphorus, a nutrient that in high concentrations can deplete oxygen levels in waters downstream. Phosphorus runoff from livestock farms has been blamed for killing aquatic life and creating algae blooms in lakes and rivers. By identifying a gene that promotes recovery of phosphorus in a pig's digestive tract, Phillips and his colleagues say they have devised a pig that pollutes less.

Genetic engineering in foods has become common in the past few years. Initial widespread breakthroughs came with pest-resistant grains. Since then, scientists have explored genetic modification of milk cows, fish, and other animals for improved food production. With the enviropig (as the Guelph researchers have dubbed their porker), genetic engineering is being used to fight in a new environmental arena: reduced pollution production.

For Phillips, a professor of molecular biology and genetics, phosphorus waste was an obvious focus for swine research. Farmers like to use hog manure as fertilizer because it is rich in nutrients, but because pigs cannot completely digest the phosphorus in their diet, their manure contains much higher

concentrations of phosphorus than of other nutrients. When runoff carries the manure downstream, the excess phosphorus fuels extremely high algae growth. "It's not just a local problem, it's an international problem," Phillips says.

To reduce the phosphorus concentrations in hog manure, the researchers looked for an enzyme that could break down the element in the digestive tract. They found a phytase enzyme in a strain of *Escherichia coli* bacteria (although *E. coli* is found in the intestinal tract, it appears too late in the digestive process to handle phosphorus). The phytase could survive the chemical rigors of digestion and proved very active in acidic conditions; that meant it could break down the phosphorus in feed grain in a pig's stomach before it reached the intestine. The researchers then spliced the enzyme with a genetic "directional trigger" from mice that would target the enzyme to the salivary glands. The fused gene (or transgene) was tested first in mice to make sure the phytase appeared only in the salivary glands and would not otherwise affect an animal's health. The transgene was then introduced into pig embryos. DNA and enzyme analysis confirmed that the piglets carried the gene and that their saliva contained the phytase. The pigs, now several months old, appear healthy and normal, according to Phillips. The Guelph scientists are confident that the salivary phytase will be passed to successive generations.

Other efforts to reduce phosphorus runoff from livestock farms have sought to

decrease the amount of phosphorus in feed grains. Victor Raboy, a plant geneticist with the U.S. Department of Agriculture (USDA) Agricultural Research Service in Aberdeen, Idaho, developed and tested low-phytic-acid corn and found that by making phosphorus easier to absorb, the amount that ends up in hog manure is reduced. Vincent Varel, a microbiologist at the USDA's Roman L. Hruska U.S. Meat Animal Research Center in Clay Center, Nebraska, says that the corn feed (being released commercially in cooperation with Pioneer Hi-Bred International) may be more versatile than the enviropig because the corn can be fed to any pig as well as to poultry.

Varel notes another benefit of nutritional approaches over genetic solutions: the public's discomfort with genetically modified (GM) products. Most European countries require labels to specify GM ingredients. In Europe, public suspicion over the health effects of GM products is running high and was heightened by a trade flap between the United States and the European Union last June in which the European Union imposed a ban on imports of hormone-treated beef and other GM foods from the United States. Varel says the issue "could be a negative factor in selling enviropig products."

Critics say that the enviropig marks only a stopgap solution to farm pollution. Jane Rissler, a plant pathologist and senior staff scientist with the Union of Concerned Scientists, a nonprofit organization based in Washington, DC, says, "The solution to the hog production [waste] problem is not to genetically engineer pigs but to return to a more sustainable form of farming." According to Rissler, today's large hog "factories" will likely merely use the enviropig to boost hog densities at their facilities, packing more hogs into the same size facility while still complying with total phosphorus runoff limits. What's more, the effect on the hogs' long-term health is still unclear. Phillips points out, however, that enviropigs will also be useful on low-density hog farms and in less developed countries, where inadequate phosphorus in pigs' diet limits their growth.

Farmers will have to wait several years to compare enviropigs with low-phytic-acid feed. Phillips says that farmers won't be able to get enviropigs from breeders for three years or so, and it's too early to say how much they will cost. —David A. Taylor



**Cleaner pooping porkers.** Transgenic pigs have been engineered to produce less phosphorus, a component of hazardous runoff.

## MOLECULAR BIOLOGY

## Protein Protection from the Sun

New information reported by researchers at the University of Texas Southwestern Medical Center in Dallas could eventually help scientists develop better ways to protect against and treat the adverse effects of too much sunlight. In a paper published in the June 1999 issue of *Molecular Cell*, the researchers demonstrated that the interaction between a protein called Rad23 and a protein complex known as the 26S proteasome is important for the ability of yeast cells to repair DNA damage caused by ultraviolet (UV) light. Human cells contain very similar proteins, so this finding may lead to insights into how human skin responds to UV exposure.

The study built on earlier work by researchers from the Robert Wood Johnson Medical School in Piscataway, New Jersey, published in the 12 February 1998 issue of *Nature*, that first demonstrated a physical interaction between Rad23 and the 26S proteasome. The 26S proteasome is a large, two-part complex involved in the degradation of many different cellular proteins: the 19S regulatory complex is thought to bind to damaged proteins, unfold their twisted lengths, and thread them into the barrel-shaped 20S structure, where they are degraded by protease enzymes.

The site of interaction between the 26S proteasome and Rad23 appears to be Rad23's ubiquitin (Ub)-like domain, a section of the protein that physically resembles true Ub, a small protein that connects to other proteins and targets them to be degraded by the 26S proteasome. (This does not seem to be the case for the Ub-like domain of Rad23, however; its function is still not understood.) Other, earlier research had shown that yeast missing the Rad23 protein or its Ub-like domain were more sensitive to UV radiation. With the *Molecular Cell* study, the Texas scientists were able to show that the physical interaction between Rad23's Ub-like domain and

the 26S proteasome is necessary for optimal DNA repair to take place.

To investigate the relationship between Rad23 and the 26S proteasome, the researchers prepared yeast extracts that had either the Rad23 full-length protein, no Rad23 at all, or a Rad23 from which the Ub-like domain had been deleted. Yeast with the full-length Rad23 were found to repair UV damage very well. Those without the Rad23 protein displayed almost no repair activity. Those with the truncated version of the protein—in other words, those in which a Rad23–proteasome interaction would be impaired—were in the middle, with damage being repaired half as well as with the full-length protein.

Next, the scientists looked at whether the 26S proteasome is important for DNA repair *in vitro*. To explore the role of the 19S regulatory complex, they added to the yeast extract an antibody to inhibit one of the complex's subunits and examined the consequences for DNA repair. Addition of this antibody was found to inhibit 50% of

repair activity. Antibodies against unrelated proteins had no effect on repair activity, indicating that the 26S proteasome does have a role in DNA repair. Eventually, the Texas team's findings may lead to innovations in the prevention and treatment of skin cancer.

Coauthor Steven

J. Russell says the 26S proteasome is already being investigated as a drug target for wasting diseases such as AIDS and cancer in which the complex is overactive, degrading proteins too quickly. Proteasome inhibitors are also being investigated as protectants against inflammation, which may be useful in conditions such as arthritis and sepsis. Russell says, "A couple of recent papers suggest that drugs already in use may work in part by inhibiting the proteasome in addition to their known mechanism."

Russell continues, "Our ultimate goal is to understand exactly how the proteasome is involved in DNA repair. We need to work out the details, but the implication is that we have a novel mechanism of proteasome action and a novel facet of the DNA repair process." —Susan M. Booker



**Sun spot.** The site of interaction between a protein and a proteasome is yielding clues to the repair of DNA damage from UV light.

## Pinpointing Asthma

Researchers at the U.S. Department of Energy's Lawrence Berkeley National Laboratory in Berkeley, California, have uncovered two genes that influence an individual's susceptibility to asthma using a novel way to determine if specific genes are linked to diseases. The two asthma-related interleukin genes, *IL4* and *IL13*, are located in the chromosome 5 region of the human genome. Study scientists believe that finding a way to limit the activity of these genes will reduce the probability of asthma attacks.

In the study, published in the 1 October 1999 issue of *Nature Genetics*, the researchers divided a several-million-base-pair region of chromosome 5 into large chunks and then introduced these pieces separately into the genomes of mice. The scientists then matched the physical characteristics of the mice with the same characteristics exhibited by human asthma sufferers to pinpoint *IL4* and *IL13* as susceptibility genes.

## Ending River Blindness

A World Health Organization (WHO) program to eradicate onchocerciasis, or river blindness, has proven hugely successful. River blindness affects millions of people in West Africa.

According to the WHO, the program has so far saved 100,000 people from the immediate risk of contracting the disease and has prevented the potential infection of 12 million children. Also due to these efforts, over one million people infected with river blindness have been successfully treated.

## Regulating Medical Recycling

On 1 November 1999 the U.S. Food and Drug Administration (FDA) announced proposals for new rules regarding the reuse of disposable medical devices including surgical clamps, cardiac catheters, and angioplasty balloons.



Critics allege this growing practice, adopted by some hospitals as a cost-cutting measure, poses health risks. The hospitals and companies that resterilize the items counter that the manufacturers of the items label them as disposable only to increase sales.

The FDA has been brought into the debate by Congress to determine which of the devices can be safely reused and how many times, and to classify disposable medical devices using these determinations. Under the proposed regulations, hospitals would have to register with the FDA if they choose to reuse these devices.

## ENVIRONMENTAL MEDICINE

## Vitamin E vs. PCBs

Studies by scientists at the University of Kentucky in Lexington indicate that vitamin E appears to be an effective protectant against damage resulting from exposure to polychlorinated biphenyls (PCBs), toxic chemicals whose manufacture has been banned in the United States since 1977.

Although out of use for nearly 30 years, PCBs still remain the object of intense research interest because of their widespread presence and persistence in the environment. Produced as insulating fluids for electrical equipment and formerly released by industries such as paper mills and electronic equipment factories, PCBs are still found in soils and the sediments of rivers such as the Hudson in New York and the Fox in Wisconsin. The chemicals are also found in the atmosphere, drifting thousands of miles from warm climates and precipitating out into the Arctic region. PCBs are labeled as a probable human carcinogen by the U.S. Environmental Protection Agency and have also been shown to affect learning in both animals and humans. They are absorbed through the skin and can also be part of a meal if a person eats fish that have been swimming in contaminated water. David Carpenter, a professor of environmental health and toxicology at the

State University of New York at Albany, notes that everyone carries around some PCBs in their blood and fat tissue.

The Kentucky group, which includes Bernhard Hennig, a professor of toxicology and nutrition, and Larry Robertson, a pro-



**E is for effective.** New research shows that vitamin E can protect against damage from PCBs.

fessor of toxicology, has found that PCBs generate oxidative stress, the creation of tissue-damaging free radicals, in endothelial cells. Endothelial cells line blood vessels, and free radicals cause them to become inflamed, one of the early developments leading to atherosclerosis.

The group reported in the August 1995 issue of the *Journal of Biochemical and Molecular Toxicology* that damage occurred when cells in culture were exposed to PCBs for only 24 hours. In the December 1999 issue of *Toxicological Sciences*, they report that the damage can be blocked if the cultured cells are simultaneously exposed to vitamin E.

Hennig says the most recent results have a

clear and immediate message: "Some outreach programs might suggest that people who are at risk [for PCB exposure] take supplements of antioxidants to make them less susceptible to PCB-mediated toxicity," he says, noting that workers who clean up PCB-contaminated sites are one such high-risk group. He endorses the recommendation with no hesitation, even after such a preliminary experiment, because even large doses of vitamin E have not been shown to be harmful.

"[The Kentucky group's] work is really significant in showing that a major environmental contaminant alters the inflammatory system," says Bruce Hammock, a professor of entomology and head of the Superfund Basic Research Program at the University of California at Davis. "[This] is a very interesting finding that has not been demonstrated in most other systems," notes Carpenter, who adds that its newness enhances the knowledge of the impact of PCBs. "It's important because we're finding that PCBs affect organ systems that have not been previously demonstrated to have been altered. Once one finds these effects on different cell types, the question is how are they mediated," he says. Because vitamin E is known to counter the effects of free radicals, the fact that it can block damage helps firm up the idea that the damage is caused by PCB induction of free radicals, thus opening a new window onto the impact of PCBs on the body. —Harvey Black

## ENDOCRINE DISRUPTORS

## NRC: Not Enough Data

A committee of experts convened by the National Research Council (NRC) at the request of the U.S. Environmental Protection Agency, the Department of the Interior, and the Centers for Disease Control and Prevention has concluded that there is insufficient research, and therefore insufficient evidence, to say whether particular environmental contaminants known as endocrine disruptors, or hormonally active agents (HAAs), may be dangerous to humans and wildlife. A 4 August 1999 report released by the NRC titled *Hormonally Active Agents in the Environment* says it is clear that exposure to HAAs—chemicals that interfere with normal hormonal functions such as behavior, growth, and metabolism—can affect wildlife and human health, but uncertainties lie in not completely understanding their causal mechanisms. In its report, the committee addressed potential harm for developmental, reproductive, neurological, and immune systems. "The field is rife with uncertainty," said committee chairman Ernst Knobil, a professor of biology at the University of Texas Medical School in Houston, in an article in the 4 August 1999 issue of *The New York Times*.

The NRC report states that 70,000 industrial chemicals in use cannot be tested for endocrine-disrupting activity because the necessary tests do not even exist. "Determining what these exposures actually are is therefore of primary importance," says Knobil. The NRC report recommends improved monitoring of the development of

HAAs, studies to determine exposure pathways and background concentrations of HAAs in humans, and initiation of long-term studies of HAA exposures.

The committee concluded that the lack of evidence could not be taken as an indication that HAA exposure is completely risk-free. Although the report clearly states this consensus, it also addresses the disagreements among committee members. "Differences among committee members could be divided among two perspectives on the weight-of-evidence approach," says the report. Some members placed more weight on experimental evidence than others. Members were also divided on the use of the precautionary principle—the idea that in the face of uncertainty the most cautious approach is the best. "The absence of information can't be used to say these chemicals are safe," says committee member Frederick vom Saal, a professor of biology at the University of Missouri in Columbia.

Committee members agreed that wildlife and human populations should continue to be studied for effects including defects in development, declines in fertility, increased incidences of various cancers, and possible population declines in wildlife species.

"Determining the risk of environmental HAAs to humans and wildlife is difficult because exposure to these agents has not been routinely monitored," says the report. "We need to focus our research on the embryo, from conception to birth," adds Theo Colborn, a senior conservation scientist at the World Wildlife Fund. "When studying the research results, once the embryos have reached a reproductive age we are almost a generation late." —Lindsey A. Greene



## Chemical Guide

When the people of Midland, Michigan, heard in November 1998 that toxic dust had been spilled repeatedly at The Dow Chemical Company's plant there, concern and confusion followed. While the chemical giant kept largely silent, rumors spread about the chemicals contained in the dust and what effect they might have on humans and the environment. Some environmentalists accused Dow of trying to hide or understate its pollution problems.

In the year that followed, Dow changed its stance, allowing environmentalists to take a firsthand look at many of its Midland processes and suggest ways to cut toxic emissions. The result of that cooperative effort has been a 43% reduction in the chemicals released into the air and water by the Midland plant—waste reductions that are saving Dow over \$5 million a year.

Such incidents have caused many within the chemical industry to conclude that transparency is often a better policy than secrecy. The Chemical Manufacturers Association (CMA), the trade group that represents over 90% of this country's chemical manufacturing capacity, is now urging all its members to give the public a window into their processes by utilizing the Internet.

In August 1999, the CMA launched its Chemical Guide Web site at <http://www.chemicalguide.com/> as a place where the public can turn for basic health, safety, and environmental information about chemical manufacturing facilities in their towns. The Web site is part of the CMA's Responsible Care program. More information about the CMA and Responsible Care is found on the Chemical Guide home page.

The Plant Locator link is the entrance into the heart of the Chemical Guide site. On this page, visitors can search for a facility either by company name and address or by clicking on the interactive maps found under the Search by Map link. A search for manufacturing facilities in Midland, for example, yields a link to information on the Dow plant there. Following the link for any of the individual facilities listed on the CMA site brings visitors to a basic description of what that plant manufactures. Contact information for some plant employees is also frequently provided here.

Links found on each facility's page take visitors to information on the health, safety, and environmental programs at that plant. The Performance link leads to a page about the facility's record for reducing emissions, while the Public Safety link leads to descriptions of the facility's emergency response and risk management plans. At the bottom of the Plant Locator page, clicking on the small world map takes visitors to a similar search page for facilities outside the United States.

"The primary audience for Chemical Guide is people living in [chemical] plant communities," says Jim Solyst, leader of the CMA's Information Management and Right-to-Know Team. To increase communication between these people and their chemical industry neighbors, Chemical Guide provides the Getting Involved page. This page provides a form for making suggestions to the CMA and offers links to local groups that have organized to address concerns about plants in their communities.

Eventually, the CMA plans to list all of the approximately 1,000 manufacturing facilities of its 191 member companies on the site. Currently, however, only a quarter of these facilities are listed and information is incomplete for many of them. Also, while the site is a good place to access basic, nontechnical information about the safety of chemical manufacturing facilities, few specifics are provided. For example, while the Performance page for each facility describes that plant's progress in reducing total emissions, details concerning what chemicals are being released and what their health effects may be are often missing. For now, people searching for this type of information will probably want to check other data sources as well, such as the U.S. Environmental Protection Agency's Toxic Releases Query Form Web site, located at [http://www.epa.gov/enviro/html/tris/tris\\_query.html](http://www.epa.gov/enviro/html/tris/tris_query.html).

—Christopher G. Reuther



## Tighter Release Regs

On 1 January 2000, U.S. Environmental Protection Agency regulations went into effect that change reporting requirements for companies that use at least 100 pounds a year of any of 27 persistent bioaccumulative toxicants including dioxin. Because these toxicants bioaccumulate rather than break down once they enter the environment, even very small releases of them could eventually lead to serious negative effects on human and environmental health.

Critics charge that such reports may unnecessarily alarm the public because they do not require reporting of the toxicity of the substances released, just the amount.

## Gas Stoves May Increase Asthma Attacks

Studies by researchers at the University of California at San Francisco have determined that frequent use of gas cooking stoves by asthma



sufferers increases their chances of serious asthma attacks.

Focusing on the asthma-related emergency room visits of more than 500 adult asthma patients, the research team found that those who used a gas cooking stove seven or more times per week had double the rate of such visits compared to those who used this type of stove less frequently or not at all.

The researchers theorize that the increase in asthma attacks may be due to nitrogen dioxide released by the gas stoves while they are in use.

## Friendly Fire

Focusing on the 700 million bullets fired annually at its 3,000 firing ranges nationwide, the U.S. Army's environmental research headquarters at the Picatinny Arsenal in New Jersey has developed a two-step plan to reduce the amount of lead found in firing range soils.

The RangeSafe program uses a new remediation method in which soil is floated in columns of water, allowing the lead to sink and be captured. Lead-absorbing plants are used to remove the remaining lead from the soil. The plants are then processed to remove the lead for use in batteries.

To prevent more lead from accumulating in the soil at the firing ranges, the second part of the Army's plan involves the development of a "green bullet" made of the inert metal tungsten. An Army spokesman says these new technologies are part of the Army's Range 21 initiative to improve the environmental quality of its training and testing sites.