What is needed now, Paroda says, is a greater commitment from international agencies and the developing nations themselves to explore the potential of these crops. Experience in India and elsewhere has shown that most farmers are receptive to the idea of growing new plants if it can be shown that they will yield a profit, he says.

Plants as Cleanup Artists

In advanced nations, plants are valued largely as food, but in developing countries they serve more varied roles, often acting as the main source of food, fiber, fuel, and medicine. Now, several research groups have shown that plants can aid environmental cleanup, too—most recently by capturing heavy metals from groundwater and locking them in their tissues.

One hint of plants' cleanup abilities came a few years ago from Monash University in Victoria, Australia. Australian plant scientist Douglas R. Laing, who is in the process of moving from the International Center for Tropical Agriculture in Cali, Colombia, to become director of the Commonwealth Agricultural Bureau in Wallingford, England, reported that some colleagues at Monash conducted field experiments, using Australian swamp plants growing in a shallow, gravel-filled ditch, to filter suspended, finely divided organic matter from contaminated water supplies. "This is a fancy way of saying they used plants to take sewage out of the rural, local water supplies," he says. More recently, the Australians discovered that the plants were even more versatile as cleanup artists: They could also absorb a large proportion of the water's heavy metals.

Other researchers have tried to improve on this ability by genetic engineering. R. Keith Downey of the Agriculture Canada Research Station in Saskatoon, noted that a colleague at the University of Calgary, molecular biologist Lashitew Gedamu, has genetically engineered oilseed rape (*Brassica napus*), tobacco, and alfalfa, inserting a human gene for metallothionein, which chelates metals. He is now testing how various promoters may put this sequestering system into high gear to guide the metals into nonedible portions of plants. Gedamu's long-term goal is to use such transformed plants to trap metals and help clean the polluted areas around Canada's many mines.

But won't these metal-contaminated plants create a cleanup problem of their own? Laing suggests that if they are good enough at socking away precious metals along with the posionous ones, they may be burned to reclaim, for example, gold and platinum. In any case, he says, it is far easier to dispose of heavy metals once they are trapped in plants rather than when they are floating free in the water system.

–Anne Simon Moffat

Chemistry Pitches Its Big Tent At Washington Gathering

When the American Chemical Society (ACS) held its 204th national meeting in Washington, D.C., last week, traditional, benchtop chemistry was all but eclipsed by the myriad of other disciplines–materials science, environmental research, and pharmacology, to name a few–that were gathered under the banner of chemistry. Several of the most intriguing sessions focused on a hot biomedical topic: cancer prevention and treatment.

Radioactive Antibodies Start Hitting Home

Since the early 1960s, doctors have routinely injected radioactive isotopes into patients in order to scan organs for disease. Some researchers also tried from time to time to develop isotopes for therapy, the idea being to destroy diseased tissue with the isotopes' radiation. But most such approaches have come up short, in part because of the difficulty of getting high doses of isotopes to home in specifically enough on diseased tissue. At a session of the ACS meeting last week, though, several researchers reported encouraging results in their effort to create the clinical equivalent of laser-guided missiles: isotopes attached to monoclonal antibodies that home in on aggressive cancers and deliver their cell-killing payloads.

The concept, known as radioimmunotherapy, isn't new—a team at Memorial-Sloan Kettering first attached iodine to rat antibodies in the 1950s. But for years radiopharmaceutical companies essentially ignored this work and concentrated on developing medical isotopes for diagnostic procedures. Attention began to shift toward therapy in the early 1980s, says Leonard Mausner, a nuclear chemist at Brookhaven National Laboratory. That was when new, nonradioactive techniques such as ultrasound began offering sharp competition in the diagnostic field, leaving isotope mavens to hunt for novel applications. And sure enough, new research showed how to attach isotopes to a variety of monoclonal antibodies.

That research is already paying off, National Institutes of Health (NIH) inorganic and nuclear chemist Otto A. Gansow told meeting attendees. Two years ago, Gansow and Thomas A. Waldmann, chief of the metabolism branch at NIH, began clinical tests of targeted isotopes in patients with adult T-cell leukemia an agressive cancer. The chemists attach yttrium-90, an isotope with a 64-hour halflife, to a monoclonal antibody designed by Waldmann that homes in on the interleukin-2 receptor of T cells. The yttrium-90 molecules shed beta particles that kill the T cells but spare other cells outside an 8 millimeter radius, reducing the damage to healthy tissue.

Gansow now reports that 10 of the 14 patients treated with the yttrium-antibody combination experienced at least a 95% reduction in tumor cells and eight went into partial or complete remission; five are still alive, and three appear to be completely free of cancer. "It's really lovely experimental work," says oncologist Steven Rosenberg of the National Cancer Institute. But Gansow warns that the technique needs refining; the isotopes sometimes detach from the antibodies before they reach their targets. "If your chemistry isn't perfect, the yttrium goes to the bone," he says. What's more, because the yttrium isn't as potent a weapon as some other isotopes, the NIH team, along with Johns Hopkins pharmacologist Mette Strand, envisions replacing it with bismuth-212, an isotope that emits both beta and alpha particles, which pack a greater therapeutic punch.

Besides tinkering with the weapon, researchers are toying with the antibody guidance system to get new anticancer weapons. Researchers at Newark-based Immunomedics Inc., in collaboration with the nuclear medicine group at Oak Ridge National Laboratory, are developing isotope-linked monoclonal antibodies targeted to a specific cancer antigen on colorectal cancers. The researchers recently began testing the efficacy of their system, based on rhenium-188, in monkeys. In addition, they've injected small doses of the antibody-rhenium conjugate into four patients with colorectal cancer. The doses weren't large enough to provide therapeutic benefit, but Gary L. Griffiths, director of chemistry at Immunomedics, points out that his team "hasn't seen any adverse effects yet."

Just how hopeful is this work? Robert E. Henkin, director of nuclear medicine at Loyola University of Chicago, warns that "therapeutic labeled antibodies are a few years away from becoming a common radiological tool." One potential stumbling block: Approving this sort of drug might prove to be a daunting task for the Food and Drug Administration (FDA), says Henkin, because "no one group at the FDA has experts on both antibodies and radioactivity." An FDA offi-

cial confirmed that while one FDA center handles applications for new radiopharmaceuticals, another handles monoclonal antibodies—including those linked to isotopes. Scientists counting on fast approval for their antibody-isotope conjugates had better hope that the FDA comes up with some bureaucratic conjugating to match.

–Richard Stone

Wresting Anticancer Secrets From Garlic and Soy Sauce

FRANCISCO ONTAÑON/THE IMAGE BANK

It's not news that eating certain foods helps prevent cancer; the big question is why? Now researchers believe they are closing in on some answers. Epidemiological studies have long shown, for instance, that people who eat plenty of cruciferous vegetables—cabbage, cauliflower, broccoli, and brussels sprouts—are much less likely to develop colon cancer than those who, like George Bush, disdain them. Since such studies say nothing about the how and why of the foods' anticancer properties, however, they give scientists few options beyond urging people to change their eating habits.

But over the past few years a band of chemists, biochemists, and molecular biologists has started to map out the specific compounds in foods that give them their anticancer properties, and they are beginning to discover how these chemicals disrupt the molecular pathways that lead to cancer. As described in a series of sessions at the meeting, the recent work could lead to cancer prevention programs for high-risk populations and even to the creation of designer foods rich in anticancer chemicals.

So what is the magic ingredient in broccoli? There are actually a variety of them, says Bandaru Reddy, a biochemist at the American Health Foundation in Valhalla, New York. He and his colleague Chinthalapally Rao have concentrated on one group of organosulfur compounds from broccoli and its cousins and shown that they can inhibit colon cancer in rats. In one test, they fed experimental and control rats the same diet except for one ingredient: anethole trithione, a chemical isolated from cruciferous vegetables. At 7 weeks old, all of the animals were dosed with a carcinogen that produces colon tumors very similar to those that develop in humans. A year later, the treated rats had developed only half as many tumors as the nontreated ones. "The implications of this research may be quite profound," Reddy says, noting that colon cancer is the second leading cause of cancer deaths in the United States. Ultimately, he predicts, these or other food-derived chemicals may be prescribed for human patients who have already developed a colon tumor, in order to prevent the formation of secondary tumors.

Fung-Lung Chung, another American Health Foundation chemist, has set his sights on food-derived compounds that could battle an even deadlier killer: lung cancer. Just which cigarette smoke ingredient to combat isn't obvious, Chung notes; the smoke has so many different carcinogens that researchers still don't know which bear most of the blame for lung cancer. But one favorite villain is a chemical called NNK. This nitrosamine compound, which is created in tobacco by the curing process, causes lung cancer in every species in which it has been tested, says the foundation's Stephen Hecht, and the tumor-producing dosage in rodents is about equivalent to the exposure a human gets from decades of heavy smoking. Researchers don't think NNK tells the whole story in humans. Nevertheless, NNK-induced lung cancer in mice and rats is the best available model for human lung cancer, and Chung decided to look for compounds that would protect lab animals from NNK's ravages.

Once again, cruciferous vegetables provided the raw material—a class of compounds called isothiocyanates. These chemicals, Chung found, slow down the body's metabolism of NNK and other nitrosamines into secondary compounds that trigger mutations leading to cancer. In tests on rats and mice, Chung showed that one member of the family, phenethyl isothiocyanate, is particularly effective in inhibiting lung cancer brought on by exposure to NNK.

Where does all this leave people, like President Bush, who won't eat their broccoli? Fortunately, there are plenty of other foods in which researchers are discovering anticancer compounds. Chemicals that inhibit lung tumors have been found, for instance, in citrus fruits (D-limonene), in tea (epigallocatechin gallate), in garlic (diallyl sulfide) and even in licorice (glycyrrhetinic acid). And Reddy and Rao found that garlic's diallyl disulfide also matched the broccoli compounds in suppressing colon cancer in rats.

If garlic isn't your favorite condiment, soy sauce turns out to have similar anticancer virtues. That's a bit of a turnaround—a decade ago, Japanese researchers suspected that fermented soy sauce, the type common in Japan, might be responsible for the very high rate of stomach cancer there. Nothing could be further from the truth, says Michael Pariza, a food researcher at the University of Wisconsin, Madison. Pariza discovered that soy sauce actually inhibits stomach cancer in mice, and recently he has isolated an ingredient that appears to be responsible. It is called HEMF (for 4-hydroxy-2-ethyl-5-methyl-3(2H)-furanone) and it is, Pariza says, what gives soy sauce its distinctive flavor. "If you taste HEMF, it tastes just like soy sauce."

Just a tiny portion of pure HEMF—25 parts per million of the mouse's diet—was enough to reduce the number of stomach tumors by 75%, Pariza says. (There's no word on whether the mice preferred the soy sauce-flavored food to the ordinary lab chow.) Since the mice were given HEMF after they were exposed to a carcinogen, Pariza suspects that the HEMF was acting to slow tumor promotion instead of to block tumor initiation. If so, HEMF could be effective against a range of tumors: Although tumor initiation is likely to follow different pathways for each carcinogen, promotion is likely to follow a similar path for a variety of carcinogens.

The identification of HEMF and other cancer-fighting compounds may eventually open the way to breeding or genetically engineering food crops that would let you eat healthy while eating whatever you like. Broccoli's cancer-fighting prowess, for example, could be packaged in something more palatable, like strawberries. But the food-derived cancer compounds are likely to make their first appearance as new drugs.

For instance, oltipraz, a synthetic compound that belongs to yet another family of cancer-fighting chemicals found in cruciferous vegetables, is now undergoing Phase I clinical studies in the United States. Thomas Kensler of Johns Hopkins University in Baltimore says that oltipraz has already proved to be extremely effective in preventing liver cancers in rats exposed to aflatoxins, carcinogenic contaminants often found in the food supplies of Third World countries.

A dramatic example of aflatoxins' ravages comes from Qidong City, in China. A recent study there found that two out of every three people in Qidong showed signs of aflatoxin exposure. At the same time, about 60 out of every 100,000 people die from liver cancer each year—the highest rate of liver cancer in China, and many times higher than rates in Western countries. If oltipraz passes its clinical trials, Kensler suggests that Qidong City would be a natural place to start applying the medical lessons being gleaned from anticancer foods. And it would probably be a lot easier to convince the people there to take a tiny pill each day than to start plowing through platefuls of broccoli.

–Robert Pool