ALTERNATIVE MEDICINE

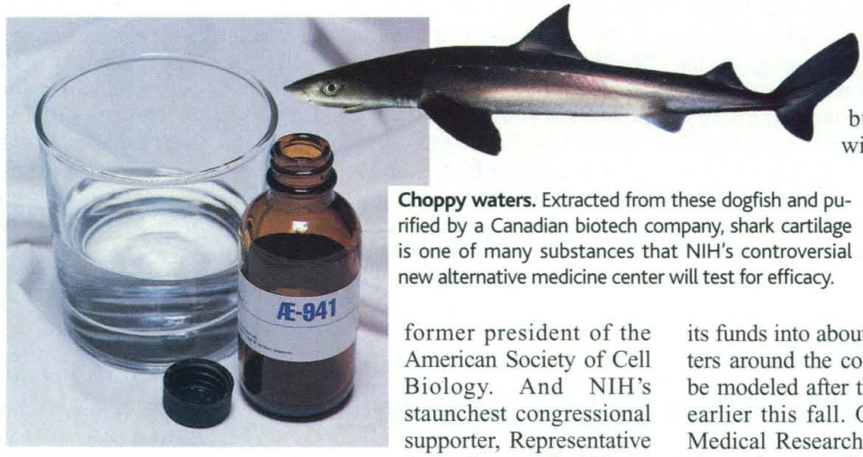
Beefed-Up NIH Center Probes Unconventional Therapies

To the consternation of some, Congress has given a controversial program to test alternative treatments an elevated status and a bigger budget

A team of scientists at the National Cancer Institute (NCI) is busy drawing up plans for a $2.5 million clinical trial next year to test the effectiveness of a controversial anticancer compound that is already being used by thousands of patients. Many researchers and physicians say the substance, derived from shark cartilage, is not worthy of serious study. But company officials point to promising lab results as reason enough to use it in a clinical trial of up to 800 lung cancer patients. And they are joined by politicians and supporters of alternative medicine, who believe its popularity demands attention from the government's leading biomedical research institution, the National Institutes of Health (NIH).

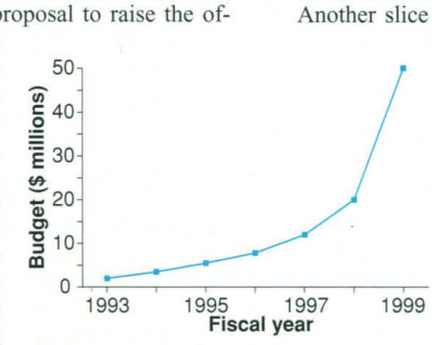
When Congress bestowed a $2 billion increase on NIH earlier this fall, it included $50 million for research on alternative medicine—and ordered NIH to upgrade its Office of Alternative Medicine (OAM) to a full-fledged center. The 6-year-old office, whose budget had risen steadily to $20 million in the fiscal year just ended, will no longer be an appendage of the office of NIH Director Harold Varmus. Instead, renamed the National Center for Complementary and Alternative Medicine (NCCAM), it now enjoys an autonomy similar to that of NIH's 18 existing institutes and centers. The new center, which is co-sponsoring the shark cartilage trial with NCI, presents NIH with a delicate challenge: How should a bastion of conventional science credibly test unconventional therapies frequently dismissed by scientists as bogus?

For Varmus, the answer is simple: The center will be held to the same high standards as are the rest of the institutes. "This is going to be done the way we do science in every area," he says. But some critics question whether the public will accept even the most rigorous research if it exposes popular remedies as useless. "There have been a gazillion studies showing that astrology doesn't predict anything at all, and people still use astrology," says Ursula Goodenough, a Washington University, St. Louis, biologist and a former president of the American Society of Cell Biology. And NIH's staunchest congressional supporter, Representative John Porter (R–IL)—a backer of NCCAM—warns that the agency's reputation could suffer if it dismisses such therapies without a careful analysis. "I don't think it would be good to have a stream of negative messages" about the value of such treatments that were not based on sound science, says Porter, who chairs the subcommittee that handles NIH's budget. To a public that's supportive of such therapies, says Porter, it would "seem like a conspiracy [against alternative medicine]."



Choppy waters. Extracted from these dogfish and purified by a Canadian biotech company, shark cartilage is one of many substances that NIH's controversial new alternative medicine center will test for efficacy.

Advocates like Porter see the center playing an important public health role: A recent study in the *Journal of the American Medical Association*, they note, found that 42% of Americans used alternative medical therapies in 1997. Senator Tom Harkin (D–IA), who drew up the proposal to raise the office's stature, says alternative therapies offer cost-effective approaches to managing and preventing complex chronic illnesses such as diabetes. Harkin—a devotee of alternative therapies who believes that bee pollen cured his allergies—was joined by a bevy of other members of Congress, including Senator Arlen Specter (R–PA) and Porter, in voting to raise the budget and status of alternative medicine in NIH. All cite the widespread use of unconventional therapies, which are often marketed as dietary supplements not subject to the same rigorous testing and regulation as are medications cleared by the Food and Drug Administration (FDA). NIH, says Porter, has resisted venturing into alternative medicine, despite the fact that millions use it to manage their health.



Rapid growth. Congress has smiled on funding for alternative medicine at NIH.

NIH no longer has any choice. NCCAM now has the budget and the authority to fund studies of alternative therapies in a big way. The largest slice of the center's expanded budget—about a third—will be spent on grants to individuals that have gone through peer review by panels formed by the center itself. NCCAM is also expected to channel 20% of its funds into about a dozen specialized centers around the country; most of these will be modeled after three large centers funded earlier this fall. One, at the Minneapolis Medical Research Foundation, is studying alternative remedies for addictions; another, at the University of Michigan, Ann Arbor, is focusing on cardiology; and a third, at the University of Arizona, Tucson, is working toward new treatments in pediatrics. Each of these entities received about $1 million in the first installment of a 3-year award.

NCCAM officials are now seeking proposals for about eight more centers to conduct toxicity trials of alternative therapies for diseases such as asthma, cancer, AIDS, and neurological disorders and strokes. Possible treatments run the gamut from homeopathy to energy healing to music therapy. Even so, some things are off-limits: Officials say they don't have the money to fund studies to isolate the active ingredient in any of the herbal medicines being tested.

Another slice of the $50 million is expected to go toward large-scale clinical trials conducted in cooperation with other NIH institutes. These include the shark cartilage trial, one of the largest ever conducted of an alternative therapy. It will test a substance made by Æterna Laboratories, a Quebec biotech company that also markets

CREDITS: (TOP LEFT TO BOTTOM) BERNARD DUFOUR, ÆTERNA; D. B. FLEETHAM/OXFORD SCIENTIFIC FILMS; SOURCE: NIH

cosmetics and food supplements. Marc Rivière, Æterna's vice president of clinical affairs, says that laboratory studies showed the substance (which the firm calls Neovostat) blocked blood-vessel development, suggesting it would block tumor growth, and that in small-scale human studies, those receiving a higher dose of Neovostat experienced less tumor progression and weight loss than did those taking lower doses. The trial will combine cartilage treatment or a placebo with a standard regimen of chemotherapy and/or radiation.

Although Neovostat is considered a drug and thus must be approved by the FDA, more than a dozen other versions of shark cartilage labeled as dietary supplements are exempt from FDA scrutiny and available in supermarkets and health food stores.

Other expansive trials include a study co-sponsored by the National Institute of Mental Health and NCCAM to determine the effectiveness of St. John's Wort in curbing depression, as well as another NCI/NCCAM trial examining the effects of a complex nutritional regimen on pancreatic cancer. "We're concerned about the wide use of these remedies," says Varmus. "The NIH has a public health responsibility" to determine which substances might work and which ones are potentially toxic.

Although the center's scientific mission is clear, the need for a higher profile is open to debate. "We could have done this through the existing office," says Varmus. But in a floor speech advocating creation of the center, Harkin complained that the office had no control over its grants process and that alternative medicine specialists were conspicuously absent from the peer-review panels passing judgment on alternative medicine studies.

Now that the center is a fait accompli, Varmus hopes to put it on a solid scientific footing. His first move will be to appoint a new director. OAM's chief, Wayne Jonas, who has been criticized for a dearth of results during his tenure, stepped down this month after 3 years to return to family practice at the nearby Uniformed Services University of the Health Sciences. Varmus says he's looking for a "serious scientist" to lead the center—one with strong credentials in clinical trials and experience with alternative medicine. Jonas and other NIH officials say that any center-funded study must use randomized trials with placebos whenever possible. Center officials pledge that will happen, but outside critics say that OAM's record should have been thoroughly reviewed before Congress spent more money on alternative medicine and elevated its status. They contend that the office, in an effort to distribute funds broadly, conducted small trials that lacked placebo groups. "Clearly the political push for expanding [the office] into a center didn't want to wait for any critical review," says Nobel prize–winning biologist Paul Berg of the Stanford University School of Medicine.

Nevertheless, Berg and Goodenough both say they would support rigorous clinical trials of treatments such as acupuncture, homeopathy, and herbal therapies. As Varmus puts it: "I think there's a lot to learn; there's probably a lot to debunk."

–JENNIFER COUZIN

BIOTECHNOLOGY

Toting Up the Early Harvest Of Transgenic Plants

Many plants sporting foreign genes are winning big and others show promise, but some efforts to develop new plants are lagging

In the early 1980s, after centuries of improving their crop plants and domestic animals the old-fashioned way—by breeding in desirable traits—agricultural scientists took a big step. They decided to circumvent the uncertain, and often lengthy, standard breeding process by using the tools of modern molecular biology to introduce genes into plants and animals for the traits they wanted. Some 15 years after the first such gene transfers, 700 researchers and policy-makers from 30 countries attended the Second Agricultural Biotechnology International Conference, held last summer in Saskatoon, Canada, to assess the fruits of their past labors and look ahead.

Although researchers have had some success in genetically modifying animals, especially in producing sheep or cows that make medically valuable human proteins (see sidebar), most progress so far has been with plants. For example, several major crop plants, including corn, oilseed canola, soybean, and cotton, have been engineered with genes that make them resistant to insect pests or to the herbicide glyphosate, so that the weedkiller doesn't threaten the crop.

Such transgenic plants have met opposition in many European countries because of fears that they may be unsafe for the consumer, damage the environment, or lead to further, costly surpluses (*Science*, 7 August, p. 768). But they are winning acceptance in other countries, including the United States, Argentina, China, and Canada. During this past growing season, at least 30 million hectares worldwide were planted with the modified crops. As a result, more than one-half of the world soybean harvest and about one-third of the corn harvest now comes from plants engineered with genes for herbicide or disease resistance. These commodities find their way into hundreds of foods, such as breakfast cereals, cooking oils, corn syrup, soft drinks, and candies.

Bumper crop? Gene transfer may make sweet potatoes, shown here in Uganda, a better protein source.

CREDIT: C. S. PRAKASH

"The speed of commercialization of agribiotech applications has taken many by surprise," says Anatole Krattiger, executive director of the International Service for the Acquisition of Agribiotech Applications in Ithaca, New York. He adds that for industrialized nations, agbiotech can increase the efficiency of producing existing crops by reducing the need for pesticide applications and other costly treatments; in developing, food-short nations, it can increase yields, essentially without the cost of additional inputs, such as pesticides. And a few genetically modified plants that promise entirely new products—including some that make ingestible vaccines for human diseases and at least one, sweet potato, with an improved protein content—are moving through the pipeline.

But not all efforts to genetically engineer plants are going smoothly. Researchers are running into trouble in their efforts to transform conventional crops into factories for high-value novel products, such as a "natural" cotton/polyester blend grown by cotton plants, or for substances traditionally supplied by synthetic chem-