

Researchers Isolate, Synthesize Growth Factor

A research team's 15-year search for an elusive brain chemical has ended in apparent success. The researchers report that they have isolated and chemically analyzed a molecule they believe is identical to growth hormone releasing factor (GRF), a substance responsible for regulating many of the body's growth and metabolic processes. The researchers also managed to reproduce the molecule synthetically, raising the possibility that manufactured copies might soon be made available for a wide array of applications in medical research and therapy. The team conducted the work at the Salk Institute for Biological Studies in La Jolla, Calif., and was led by Roger Guillemin, who shared the 1977 Nobel Prize for Physiology or Medicine.

Although GRF is normally produced by the brain's hypothalamus region, the researchers derived the newly reported molecule from a rare human pancreatic tumor. Certain tumors are known to produce hormones and other natural substances in unlikely parts of the body. "What can certainly be said is that the molecule we have now characterized has all the attributes expected from the long sought hypothalamic releasing factor," the researchers write in the Nov. 5 SCIENCE, where the findings were announced.

Scientists have long been aware that a chemical messenger from the hypothalamus stimulates the release of growth hormone from the pituitary gland. But the releasing factor, dubbed GRF, resisted study because it was normally present in only vanishingly small quantities. On several occasions various groups claimed to have isolated GRF, "but have never been able to establish its structure," says Nicholas Ling, a member of the Salk Institute team.

Guillemin and colleagues began their own quest for the structure in 1968, but the decisive step did not take place until two years ago. French physicians provided Guillemin with samples of a pancreatic tumor, removed from a patient, that was producing relatively large amounts of GRF. (Scientists think such abnormal production results from a breakdown of genetic controls in the tumor.) Guillemin and co-workers proceeded to extract and analyze the human pancreatic GRF, or "hpGRF." They have successfully identified its precise chemical structure—a short peptide of 44 amino acids—and have constructed replicas using an automated peptide synthesizer.

If synthetic hpGRF acts on the human pituitary the way natural hypothalamic GRF does, it could prove to be an invaluable pharmaceutical compound. Growth hormone (GH) has been implicated in a huge range of physiologic functions. And scien-

tists have speculated that GRF, by correcting imbalances in growth hormone production, might be used to treat such GH-related disorders as pituitary dwarfism. Other possible applications that have been mentioned include speeding healing of wounds and burns, controlling gastrointestinal bleeding and even stimulating the growth of beef cattle.

Though growth hormone itself has been mass-produced by genetically engineered bacteria and has shown promise as a pharmaceutical agent in clinical trials, GRF may offer some advantages, according to Ling. GRF is a much smaller, possibly more stable, molecule than GH and might be manufactured at a lower cost, he says. Because GRF is small, scientists may also be able to produce large quantities through chemical, rather than bacterial, synthesis. This might permit structural modification of the peptide to yield analogs with different physiological effects or greater potency.

But many scientists are cautious in assessing hpGRF's potential value. Dorothy

Krieger, director of endocrinology at Mount Sinai Hospital in New York, points out that "while there is some evidence that fragments of growth hormone are involved in wound and burn healing, it remains to be proven whether healing could be promoted by increasing the amount of circulating growth hormone." She adds that "before GRF could be used to treat pituitary dwarfism, it will have to be determined which cases are due to hypothalamic, rather than pituitary, dysfunction." GRF would be unable to trigger the release of growth hormone from a defective pituitary.

Perhaps the biggest question to be answered is whether the tumor-derived hpGRF is truly identical to the natural hypothalamic peptide. The effects of hpGRF on laboratory rats are virtually indistinguishable from those of rat hypothalamic GRF, according to Ling. But conclusive evidence won't come until researchers obtain sufficient hypothalamic GRF to analyze chemically—"and that may prove very difficult," he says. —R. Pollie

Aluminum linked with dialysis dementia

Aluminum, once thought to be a harmless environmental element, has been implicated during the past few years in two different types of dementia (mental deterioration) diseases—senile dementia and parkinsonism-dementia. And now it is being linked to a third dementia as well, that due to kidney dialysis, A. M. Davison and colleagues at St. James's University Hospital in Leeds, England, report in the Oct. 9 LANCET.

In part, Davison and his team have confirmed what other investigators reported between 1976 and 1978—that dialysis dementia, which afflicts a surprisingly large number of kidney dialysis patients, seems to be due to aluminum in the water that helps comprise the dialysate (fluid) used to cleanse their blood. But Davison and his colleagues have gone further than previous researchers in that they have also shown that removing aluminum from the dialysate appears to lessen or even prevent dialysis dementia.

From 1968 to 1978, they studied 108 patients receiving kidney dialysis in the hospital and 150 receiving kidney dialysis at home. Of the total, 18 developed dialysis dementia, all of whom had been getting dialysis at home. Analysis of the 18 patients' domestic water supplies revealed that all had a high concentration of aluminum—greater than 80 $\mu\text{g/l}$ (micrograms per liter). In contrast, those patients on hospital dialysis were being exposed to dialysate with deionized water, which con-

tains virtually no aluminum.

After 1978, the researchers removed the high levels of aluminum from the domestic water of nine of the 150 home dialysis patients who had been dialyzed at home for one to four years and who had not yet succumbed to dementia. They wanted to see whether aluminum removal could prevent the development of dementia. They got mixed results. While aluminum removal appeared in varying degrees to benefit six of the nine patients—four developed no dementia at all, and two developed a mild dementia from which they are slowly recovering—it did not prevent two other patients from getting dementia and dying from complications related to it. (The remaining patient died from a kidney transplant complication unrelated to dialysis dementia.) In a second, more favorable, experiment, however, the researchers removed the high levels of aluminum from the water supplies of 24 other patients before they started home dialysis. The preventive measure seemed to work: none of the patients has developed dialysis dementia.

Thus aluminum appears to be causally related to dialysis dementia, Davison and his team conclude.

Arnold R. Brody of the National Institute of Environmental Health Science in Research Triangle Park, N.C., one of the scientists who linked aluminum to senile dementia (SN: 4/19/80, p. 246), says that the research by Davison and his team sub-

stantiates the case that aluminum can cause dementia diseases. Clarence J. Gibbs Jr. of the National Institute of Neurological and Communicative Disorders and Stroke in Bethesda, Md., one of the investigators to link aluminum to parkinsonism-dementia (SN: 9/11/82, p. 166), finds the data reported by Davison and his colleagues "kind of sketchy." But both agree that more research has to be done before aluminum can truly be said to cause dementia diseases. For instance, as Brody points out, no one has yet attempted to see whether aluminum damages nerve cells in the brain, and if so, how. "This is an area that is really fertile," he says. Also yet to be answered is whether areas rich in aluminum produce an excess of senile dementia, as they have already been shown to do for dialysis dementia and parkinsonism-dementia.

—J.A. Treichel

Making solar cells in the sunlight



Set in what was once a cornfield near Frederick, Md., a new factory is getting ready to use sunlight to manufacture solar cells. Dedicated last week and billed as the world's first "solar breeder," the facility built by the Solarex Corp. is due to go into full production next year. An array of 224,640 solar cells, mounted on a steeply pitched roof facing south, provides the 200 kilowatts of power necessary to meet all the plant's needs, including electricity for production equipment for making solar cells, lighting, air conditioning and even typewriters. A bank of 480 special lead-acid batteries stores the energy generated by the roof array and provides power for rainy days. The \$6 million demonstration project is the first solar cell-powered factory totally independent of a utility, company officials say.

Although it would be cheaper to buy electricity from a utility, admits Joseph Lindmayer, Solarex president, the plant is a model for future factories in remote areas like mountaintops or deserts where power is not readily available. The company is prepared to sell the concept of solar-powered factories because the factories could produce any kind of product and are economic now in many parts of the world. Lindmayer says, "In most cases, we will provide an industrial shell, like a prefabricated building with its own power supply attached." □

U.S. export controls snag spacecraft filters

As Comet Halley sails into view (SN: 10/30/82, p. 277), the European Space Agency is racing to ready a rendezvous spacecraft for launch in July 1985. Last month, however, preparations for one of the spacecraft's 10 instruments hit a snag when U.S. Customs delayed the shipment of a set of optical filters from a U.S. company to the Max Planck Institute for Aeronomy in West Germany. The three-week delay ended last week when the Department of Commerce finally decided that high-technology export controls were not being violated.

The action is the latest in a string of incidents reflecting the Reagan administration's clampdown on the flow of certain scientific information and sophisticated technology out of the United States (SN: 3/20/82, p. 204; 4/3/82, p. 229; 9/4/82, p. 149). Customs officials concede that delaying the filters was part of a general "tightening up" aimed at catching illegal high-technology exports that could end up in Soviet-bloc countries.

W. Alan Delamere of Ball Aerospace Systems Division in Boulder, Colo., part of the international team building the multi-color camera for which the filters are needed, told SCIENCE NEWS, "The delay is significant . . . and it's going to hurt for the next three months."

Delamere adds, "But that's the side you can see; that's tangible. The intangible is the total manhours that have been spent in overcoming a difficulty like this, readjusting planning, time talking on the phone. It really becomes a terrible inefficiency if you've got people that are fully occupied."

The fuss centers on a set of 13 glass filters mounted in a fiberglass wheel, 50 millimeters in diameter and 2 mm thick, manufactured by Omega Optical, Inc., in Brattleboro, Vt. Robert Johnson, Omega Optical president, says his company was chosen to produce the filter wheel because it could do the entire operation quickly while meeting stringent specifications. The \$75,000 contract calls for a prototype wheel, five flight wheels plus backups and five ground observation sets.

Johnson says the prototype wheel left the plant on Oct. 8. "On the 12th we were notified that Customs in Boston was holding the package for a decision on whether it was possibly a military project," he says. The action came as a surprise. "We've been exporting optical interference filters worldwide for over 10 years and have never required an export license," Johnson says.

Edward Goggin, assistant regional commissioner for U.S. Customs, says this particular shipment was new to the inspectors at Logan International Airport in Boston. "We did not know whether or not it needed a license," Goggin explains. Customs referred the matter to the Commerce Department for a ruling.

For Johnson the following weeks were a

frustrating time. In a telephone interview before the matter was resolved late last week, Johnson told SCIENCE NEWS, "The most disheartening thing is that we are having a very difficult time communicating with anybody in adequate authority to release the package. We've made well over 100 phone calls and just get shifted from person to person."

When the Commerce decision that released the package finally came, the ruling also specified that future shipments would not be automatically released. "They want to have the technical data on those shipments for examination prior to authorizing their export," says Johnson. "It appears that we are essentially doing what you would have to do to get an export license."

Johnson says that the project is now behind schedule. The first flightworthy filter wheel, originally due on Dec. 1, requires six weeks of work after the company hears from the institute whether any modifications to the prototype filter wheel are necessary. "Everybody seems to be really understanding about the problem but very nervous about the time lost," Johnson says. "We're pretty well set now. I'm hoping that before we're ready to ship again we can resolve any questions so that there isn't a holdup."

Delamere has studied the high-technology export regulations carefully. He notes that the regulations contain a "catchall" that can be interpreted to mean that anything to do with a spacecraft needs an export license. "You could interpret that a screw that's used on a spacecraft is subject to export license," he says. The problem is deciding at what point an export license is applicable. "My interpretation is that it's really applicable only when you put together a complete system that is unique in some manner," says Delamere. "The safe thing to do is, when in doubt, apply for an export license, and apply for it a long time before you ever need it."

Goggin says, "We're just tightening up on procedures. As companies become more familiar with what our requirements are, and we become more familiar with what the Department of Commerce's requirements are, things will run much smoother. It's a kind of learning process, both for us and for the companies."

William Brunk, acting chief of the National Aeronautics and Space Administration's planetary science branch, says the bulk of U.S. involvement in the European mission to Comet Halley is to provide expertise in particular fields and certain types of instrumentation. However, European scientists are finding that the United States is the best, and sometimes only, source of components they need for the spacecraft. Johnson worries that the Europeans will be much more cautious in the future about dealing with U.S. companies.

—I. Peterson