

At the Heart of Blood Pressure Control

In the regulation of blood pressure, the heart may contribute more than just its pumping force. Its auricles produce a hormone that might coordinate the various organs that together control a person's sodium excretion, fluid volume and blood pressure. Scientists at four institutions and one biotechnology company now report that they have isolated from heart tissue the gene encoding this recently discovered hormone. They are employing the gene to produce material for use in developing new treatments for congestive heart and kidney failure and for hypertension and related disorders.

The search for a heart hormone, called auriculin or atrial natriuretic (salt-excretion) factor, began with the observation that an extract of auricular (also called atrial) tissue when injected into a rat's veins triggers its kidneys to increase sodium and fluid excretion. The active material more recently was shown to be a mixture of different-sized peptides, which are derived from a common precursor. All these peptides share a sequence of about 20 amino acids.

The mixture of peptides recently has been found to have an additional physiological effect that may also contribute to blood pressure regulation. It relaxes the smooth muscle of vascular tissue, thus dilating blood vessels.

In the June 21 NATURE, U.S. and Japanese scientists report isolation of the genes for the precursors of the rat and human atrial natriuretic factors. The rat precursor is 152 amino acids long and contains the sequences for all the active peptides characterized so far. It also has a sequence resembling those that in precursors of other hormones act as signals to the cell to package the material for secretion, report two teams of scientists. One group includes investigators at Cornell University Medical College in New York and California Biotechnology Inc. in Mountain View, Calif. The other group is at Vanderbilt University School of Medicine in Nashville, Tenn.

The gene for the precursor of human atrial natriuretic factor is remarkably similar to that of rat. It has a similar signal sequence and includes the sequence of the only human atrial natriuretic peptide so far sequenced, report Japanese scientists at the Suntory Institute for Biomedical Research in Osaka and Miyazaki Medical College in Miyazaki.

The human peptide differs from the rat peptide by only one amino acid. However, there are some further variations between the rat and human genes. One of these differences suggests that cells of the two species have somewhat different mechanisms for converting the precursor into

active products, suggest G. A. Sagnella and G. A. MacGregor of Charing Cross Hospital Medical School in London in a commentary accompanying the research reports in NATURE.

Many questions remain about the action of these hormones. How do they relax vascular smooth muscle? How do they increase sodium excretion? What role do these activities play in regulation of blood pressure? The analyses of the amino acid sequence of the atrial natriuretic peptides and of the genes that encode them are expected to provide tools for investigating

their physiological roles. For example, methods are needed to detect trace concentrations of these hormones in circulating blood. The ability to synthesize the peptides is expected soon to allow scientists to make specific antibodies, labeled with radioactivity, to serve as sensitive detectors.

Auriculin's discovery offers great potential for the treatment of hypertension, says John H. Laragh of Cornell. Current treatments, which affect a single element in blood pressure regulation, often have undesirable side effects. —J. A. Miller

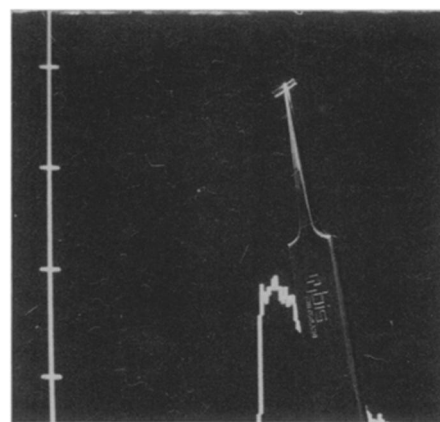
New solid-state vibrational laser

Cornell University physicists have demonstrated the first of what may turn out to be a new class of lasers. These solid-state devices emit a coherent beam of infrared radiation as embedded vibrating molecules attempt to dissipate the energy that had set them in motion. The fact that the device lases at all surprised its developers, Timothy Gosnell and Robert Tkach, because it had been assumed that molecules in a solid would transfer all of their vibrational energy kinetically, as heat—not radiated light.

When energy is pumped into a resonating material, the material becomes excited and jumps to a higher energy state. Before it can return to its preferred "ground" state, the affected material must first shed the extra energy. And in materials that lase, some of the dissipated energy is emitted as photons of light. In solids, it is electrons that have traditionally been excited. In some gas lasers, whole molecules are excited into vibrating energetically. The new Cornell device is the first to operate through the stimulation of whole molecules in a solid.

In this laser, cyanide molecules are embedded into a crystal of pure potassium-bromide salt at levels of between one part in 10 and one in 10⁴. To create the laser cavity, a thin layer of gold is evaporated onto one end of the crystal, forming a mirror to reflect any emitted photons back into the crystal. Opposite it is a semi-transparent mirror of germanium. To lase, the crystal is cooled to less than 4 kelvins (−269°C), then pumped with energy using a 4.8 micron (infrared) laser. This stimulates the cyanide molecules, making them vibrate vigorously. Emitted photons bounce between the mirrors, stimulating the production of even more light. Eventually some portion of that light flux leaks through the germanium mirror creating a laser beam having a 4.9 micron wavelength.

According to Albert Sievers, who directed the experiments, his laboratory



New laser's efficiency means it can be small: This one is 8 millimeters by 1 mm.

stumbled onto this lasing accidentally. In a telephone interview from his Ithaca, N.Y., laboratory, Sievers explained, "We were putting in radiation that was coincident with the first vibrational mode that you can excite [cyanide to] from the ground state. But we found radiation came out at a whole bunch of other frequencies corresponding to lots of vibrational overtones—frequencies that have to do with higher excited states of the molecule." Said Sievers, "That these other internal vibrations had much more output than the frequency that we were at" suggested the system might be capable of lasing.

Sievers and colleagues are now attempting to find out whether this is the first of a new class of lasers or just a "fluke" associated with cyanide. Experiments are also underway to find out why the vibrating molecules don't heat the solid.

The new laser is potentially tunable to other infrared wavelengths. Aside from its intriguing physics, it may make possible efficient lasing at previously unattainable frequencies. Among its disadvantages: You have to use a laser to make this laser. Sievers' lab is also looking for ways around that. —J. Raloff