New method targets sites for gene therapy

With federal agencies on the brink of approving the first U.S. injections of therapeutic genes into humans, researchers have begun devising strategies to direct these genes to the specific body tissues that need them. A new report suggests that tiny balloons threaded into blood vessels may help gene therapists perform site-specific gene insertions.

The first human gene-therapy experiments likely to gain government approval involve injections of genetically engineered cells that can do their job while circulating freely throughout the body, or can find their own way to their intended destinations (SN: 6/16/90, p.380). But in the future, says Gary Nabel of the University of Michigan Medical Center in Ann Arbor, physicians will want to constrain certain gene-altered cells within smaller areas so they secrete their therapeutic compounds only where needed.

In previous research, Nabel and others implanted genetically engineered cells into targeted blood vessels in pigs and dogs (SN: 6/17/89, p.373). But that procedure was rife with hassles, he says. The cells had to come from a compatible donor, and it took about five weeks to engineer them in the laboratory. Now, Nabel's team has a better method.

With co-workers Elizabeth G. Nabel and Gregory Plautz, Nabel has adapted a common medical procedure used by cardiologists to open clogged blood vessels. The technique, called balloon angioplasty, normally involves threading a catheter containing a tiny, uninflated balloon into a constricted vessel, then briefly inflating the balloon to compress accumulating deposits against the vessel walls.

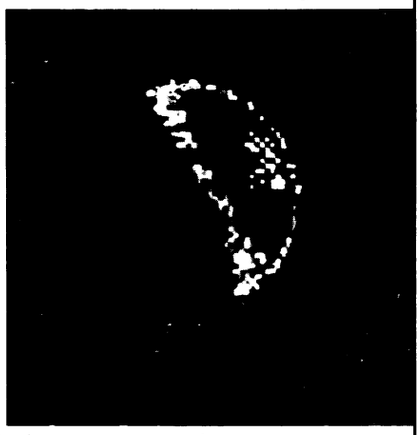
The researchers used a customized catheter with two balloons. Working with pigs, they inflated both balloons, leaving the stretch of vessel between the balloons temporarily isolated. Into that space they injected several thousand copies of the desired gene – in this case, one that is nontherapeutic but easily traced. Within minutes, the genes – which the researchers had packaged in either viral "shuttles" or fatty globules called liposomes – made their way into cells lining that length of blood vessel. The genes remained active in those cells for up to 21 weeks and settled nowhere else in the body, the team reports in the Sept. 14 SCIENCE.

"The idea is a very clever one. It's an exciting advance," says W. French Anderson of the National Heart, Lung and Blood Institute, who is awaiting final permission to perform the nation's first human gene-therapy experiments. "The question is going to be: Can you get sufficient gene activity in that site?" He says it remains unclear whether the relatively small number of gene-altered cells in a few centimeters of vessel can deliver enough of a therapeutic effect.

Nabel thinks the technique may prove useful for delivering small, constant supplies of a drug to specific locations. For example, he says, stretches of blood vessels prone to clogging by recurrent blood clots could be engineered to secrete clot-busting drugs. Or vessels supplying blood to tumors could be engineered to secrete cancer-fighting compounds such as tumor necrosis factor, he says. – *R. Weiss*

Reflected glory: Moon shines in X-rays

Nearly three decades after their initial attempt, astronomers have obtained the first X-ray image of the moon. The crescent outline of the first-quarter moon – glimpsed through one of two telescopes aboard ROSAT, the German-British research satellite launched by NASA on June 1 – glows brightly as it reflects X-rays striking its surface from the sun's corona. The dark side of the moon blocks diffuse X-ray background radiation, visible in this 1,000-second exposure as white dots in the surrounding sky area. The X-ray background, believed to come from distant sources, shows a uniform distribution.



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ROSAT scientist Ken Pounds, of the University of Leicester in England, says X-ray images of the solar system may one day become commonplace as astronomers begin "prospecting" – detailing the chemical components of planets and asteroids by bouncing X-ray beams off their surfaces and analyzing the reflected radiation with space-borne detectors. This lunar image, released late last month, is one of the first produced by ROSAT as the craft maps sources throughout the universe that emit X-rays and extreme ultraviolet radiation – wavelengths that cannot penetrate Earth's atmosphere.

Astronomers first tried to capture the moon's X-ray image in 1962 with a rocket-borne instrument. ROSAT's sky survey began July 30 and is expected to continue through January 1991; the satellite will then focus on individual targets for the remainder of its seven- to 10-year mission. □

Salty superconductor champ

Take a long-named compound known conveniently as ET, combine it with another ingredient and crystallize them. Squeeze the shiny black crystals with 300 atmospheres of pressure while chilling them to temperatures colder than the dark side of Pluto. The result? A new record-breaking organic superconductor.

In the Sept. 5 INORGANIC CHEMISTRY, 16 researchers from two national laboratories and North Carolina State University in Raleigh report the discovery of an organic salt that loses all resistance to carrying electrical current when placed under pressure and cooled to 12.8 kelvins (−437°F) or less. The squeeze-play prevents an unwanted structural transition that would compete with the superconducting transition.

The best of the ceramic-oxide superconductors enters a resistance-free state at a relatively cozy 125 kelvins under normal pressure. But chemist Jack M. Williams of Argonne (Ill.) National Laboratory, who led the ET project, notes that the transition temperatures of new organic superconductors have been rising faster proportionally than those of the ceramic versions. "There's every reason to believe that the organics can have as a high a transition temperature [as the ceramics], or even higher," he says.

Salt crystals are made of matched components that donate and accept electrons. In the record-breaking salt, layers of a chlorine- and copper-containing complex accept electrons from alternating layers of ET, otherwise known as bis(ethylenedithio)tetrathiafulvalene.

Williams' team laid claim to the previous organic superconducting record last July with a structurally similar ET salt in which a bromine complex, rather than a chlorine complex, serves as the electron acceptor. It superconducts under normal pressure at 11.6 kelvins. University of Tokyo researchers had previously reported making a related salt with a transition temperature of 11.4 kelvins.

Researchers continue to mix and match different donors and accepters in the push for higher transition temperatures. Because the resulting salts typically have about one-seventh the density of ceramic superconductors, they would be well suited for use in spacecraft and other devices requiring lightweight materials, Williams says. – *I. Amato*