Biomedicine

Carol Ezzell reports from Keystone, Colo., at a Keystone Symposium on tissue engineering

Cartilage grafts grown in lab dishes

Replacements for joint cartilage ground down during athletics or inflamed by arthritis may one day come in sheets of living cells grown in the laboratory.

A team led by orthopedic researcher Daniel Grande of North Shore University Hospital/Cornell University Medical Center in Manhasset, N.Y., has cultured sheets of cartilage-secreting cells called chondrocytes in quantities large enough for use in resurfacing the injured knee joints of rabbits and dogs. If these animal trials succeed, Grande and his colleagues at Advanced Tissue Sciences, Inc., a La Jolla, Calif.-based biotechnology company, plan to test the grafts in humans.

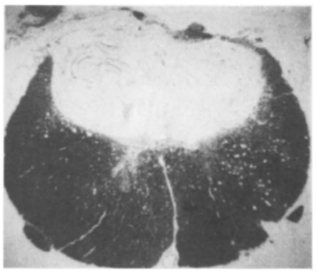
The grafts consist of chondrocytes seeded on a matrix of dissolvable suture material. Grande's team grew the grafts in a tissue culture system, developed by Advanced Tissue Sciences, that maintains the proper oxygen level and physical stress for cartilage formation.

Because transplanted chondrocytes are poorly recognized by a recipient's immune system, Ron Cohen, Advanced Tissue Sciences' vice president for medical affairs, expects the grafts to provide a universal source for replacing cartilage in a wide variety of patients, regardless of tissue type. He predicts that the recipients' bodies will eventually substitute their own chondrocytes for the foreign ones.

Several other research groups have cultured chondrocytes in the laboratory, but Cohen says the resulting cartilage proved too weak to bear the weight of large animals. He asserts that the new technology should yield stronger cartilage.

Paving the way for spinal cord repair

By laying down bridges of Schwann cells — cells that normally coat nerves — researchers have coaxed severed nerve fibers in the spinal cords of adult rats to heal and grow toward each other. Although the researchers cannot determine yet whether the therapy alleviates the rats' partial paralysis, they hope the finding will lead to new ways of treating spinal cord injuries.



Paino

Two transplanted rolls of Schwann cells wrapped in collagen rest in the injured cleft of a rat's spinal cord (darker material at bottom). The Schwann cells show up as dark spirals in this cross-section of the rolls (lighter material at top).

Developmental neurobiologist Mary Bartlett Bunge of The Miami (Fla.) Project to Cure Paralysis and Carlos L. Paino of the Hospital Ramon y Cajal in Madrid grew thin layers of Schwann cells in culture dishes coated with collagen, a connective tissue. When they rolled the Schwann cell-collagen sheets up like carpets and transplanted them into the spinal cords of 20 injured rats, they found that the rolls bridged the ends of the severed nerve fibers of all 20 rats.

The new cord tissue contained 20,000 regenerating nerve fibers, Bunge and Paino found. Moreover, the new tissue developed its own blood supply, and some of the budding nerves acquired coatings of myelin, the insulating substance secreted by Schwann cells.

Preliminary results of the experiment appeared in the November 1991 EXPERIMENTAL NEUROLOGY.

Next, Bunge plans to test whether the Schwann-cell transplants can improve the ability of injured rats to move their hind legs. She hopes that such transplants may one day restore at least some motor function to humans with damaged, but not completely severed, spinal cords.

Chemistry

Janet Raloff reports from San Francisco at the American Chemical Society's spring meeting

Nickel: Plants gotta have it

The Agricultural Research Service (ARS) this month designated nickel an essential micronutrient for all higher plants. This is the first time in 38 years that an element has won such a distinction.

Until recently, physiologists had few clues to the metal's vital role, says plant nutritionist Ross M. Welch. Indeed, his team at the ARS Plant, Soil and Nutrition Laboratory in Ithaca, N.Y., found that viable seeds carry enough nickel to sustain a plant throughout life. Establishing nickel's function therefore required studying second- and third-generation progeny of plants fed no nickel.

What caused anyone to look? Australian researchers had shown that the enzyme urease requires nickel in order to function. Present in most plants, urease breaks down urea, liberating the nitrogen present in this end product of protein decomposition. Welch's group decided to investigate whether plants fed nitrogen sources other than urea still need urease.

In 1983, the Ithaca researchers showed that legumes do need urease; four years later, they found that cereal grains do too. The cereal finding was somewhat surprising, Welch says, because plant physiologists had never seen urea — or active urease — in grains. The reason, it now turns out, is that their urease worked so quickly that urea never had a chance to accumulate.

The ARS team has since demonstrated nickel's vital role in other plants and has identified functions beyond the liberation of nitrogen. For instance, says Welch, "we showed that nickel is required for iron absorption in plants."

In order to germinate, seeds need nickel concentrations of somewhere between 10 and 100 parts per billion, Welch says. Plants grown without additional nickel will gradually dilute this initial store to a level that becomes critical at about the time they mature and begin reproductive growth, the ARS scientists find.

Engineering whiter bites

For cost and longevity, it's hard to beat the silver-amalgam fillings that glitter through the smiles of baby boomers and their parents. But over the past two decades, dentists have tended to fill gum-line and other very visible cavities with tooth-colored composites made from ceramic particles embedded in an organic polymer known as BIS-GMA (for bisphenol-A, glycidyl dimethacrylate).

Most dentists have resisted using the more aesthetically pleasing composites for grinding surfaces — initially because the BIS-GMA materials did not hold up as well to wear. Even now, the presence of saliva on the tooth being filled reduces the composites' ability to adhere — and therefore to last — as long as silver-amalgam fillings.

Researchers at the University of North Carolina School of Dentistry in Chapel Hill and Virginia Tech's Center on High-Performance Polymeric Adhesives and Composites in Blacksburg are collaborating to make the composites less sensitive to saliva. Normally, BIS-GMA carries some hydroxyl (OH) subgroups that cause portions of the molecule to attract water. The researchers began by substituting methyl (CH_3) groups — which shun water — for the OH groups, explains UNC materials scientist Duane F. Taylor. In another version, they've started with the methyl-substituted molecule and incorporated some fluorine. "Fluorine makes Teflon water repellent," Taylor says. "We thought that by adding fluorine groups . . . we could also increase this molecule's water repellency."

Though both strategies worked, versions still on the drawing board may prove even better, he says. When will volunteers get to chew on the new composites? Perhaps within a year, Taylor suggests.