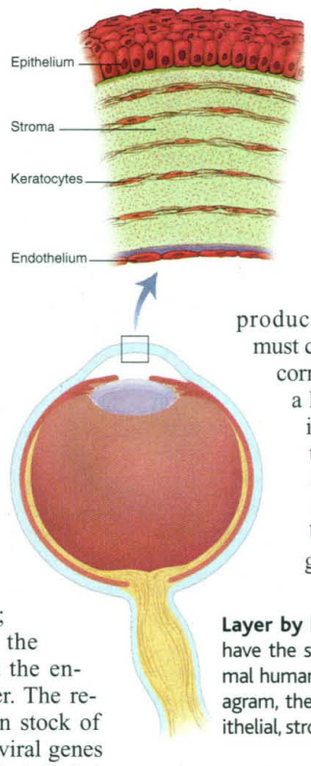
Tennessee College of Medicine in Memphis, and their colleagues report that they have used lines of cultured human cornea cells to fashion the first working equivalent of a human cornea. Although the engineered cornea is far from ready for use in human transplants, it should come in handy for research, experts say. And for toxicologists, the artificial tissue is a sight for sore eyes, potentially offering a new way to conduct safety tests and thus reduce the use of animals. "I think it's beautifully done work," says ophthalmologist and surgeon Stephen Foster of the Massachusetts Eye and Ear Infirmary in Boston.

The researchers originally made the corneas because they wanted to understand what sometimes causes corneas to fail to heal properly after laser eye surgery. But the few human corneas they could get from the eye bank were often old or diseased. "The eye-bank corneas didn't work out, so we decided to build our own," Griffith says.

Corneas contain three types of cells: the epithelial cells that form the outer layer; the keratocytes that populate the middle, or stromal, layer; and the endothelial cells of the inner layer. The researchers first created their own stock of all three cell types by inserting viral genes that enabled the cells to grow indefinitely in the lab. Then, before assembling them into corneal tissue, they tested the cells to make sure they retained the traits of healthy corneal cells and did not have any telltale signs of cancer, such as the ability to grow in a Jell-O–like medium called soft agar.

To construct the artificial corneas, the researchers first grew a thin layer of endothelial cells in a culture dish, covered that with a mixture of keratocytes and support proteins, and then layered epithelial cells on top. After letting the cornea mature for 2 weeks with its epithelial cells sitting at an air–culture media interface, just as in a real cornea moistened by tears, the researchers found they had a transparent tissue that behaved much like a human cornea. For example, a mild detergent activated the same set of wound-healing genes as it does in human corneas.

The engineered corneas also clouded up in response to irritating detergents to about the same extent as human and rabbit corneas, says study co-author Rosemarie Osborne, a toxicologist at Procter & Gamble in Cincinnati, Ohio. The company, which has been dogged by animal-rights activists, co-sponsored the study as part of a long-term effort to devise new ways to test the toxicity of its consumer products without having to use animals. Here they hoped to find a reliable replacement for the Draize test, which measures how irritated the corneas of rabbits become following chemical exposure.



Layer by layer. The artificial corneas have the same three cell layers as normal human corneas. As shown in the diagram, these are, from the top, the epithelial, stromal, and endothelial layers.

The engineered corneas are "a significant advance" along that road, says Alan Goldberg of the Center for Alternatives to Animal Testing at The Johns Hopkins University School of Public Health. But he adds, "It's not yet an alternative to the Draize test." Researchers must first learn to mass-produce the corneas, and they must confirm that the engineered corneas respond the same way a human eye does. As a step in that direction, the Procter & Gamble group has teamed up with another household-products giant, Unilever, and a nonprofit group called the Institute for In Vitro Sciences in Gaithersburg, Maryland, to examine, among other things, how the engineered corneas respond to known ocular toxins.

For transplant surgeons, the corneas are clearly not ready for prime time. Even though the cells the researchers used did not have any of the telltale signs of cancer, they might still become cancerous later on. Before using them for human transplants, researchers would have to dispel that concern, among others, including that the engineered corneas don't provoke an immune response and that they remain transparent over the long haul. The corneas have "some potential" for use as transplants, Foster says, but "I think it's a long way off."

In the meantime, the engineered tissue could prove a boon to laboratory research on the cornea. "The work is exciting," says corneal surgeon Terrence O'Brien of The Wilmer Eye Institute at Johns Hopkins School of Medicine. "It could be used as a model system to … answer a lot of fundamental questions." **–DAN FERBER**

Dan Ferber is a writer in Urbana, Illinois.

CREDITS: (LEFT TO RIGHT) ILLUSTRATION BY CARIN CAIN; BRANDON D. COLE/CORBIS

ScienceScope

Over the Top Despite a wobbly economy, Japan appears likely to top an ambitious goal to spend 17 trillion yen (U.S. $166 billion) on science and technology over 5 years. But Japanese officials aren't resting on their laurels: They are already working on a new 5-year plan that will address some of the problems created by expanding the country's scientific infrastructure.

The 17-trillion goal flowed from a 1995 law intended to boost the nation's publicly funded research efforts. This week the Diet is expected to approve yet another supplemental spending package, bringing total spending for 1996 to 1999 to 13.9 trillion yen. Officials are also putting the finishing touches on an R&D science-related budget for 2000 of 3.5 trillion yen that would boost the 5-year total to about 17.4 trillion yen.

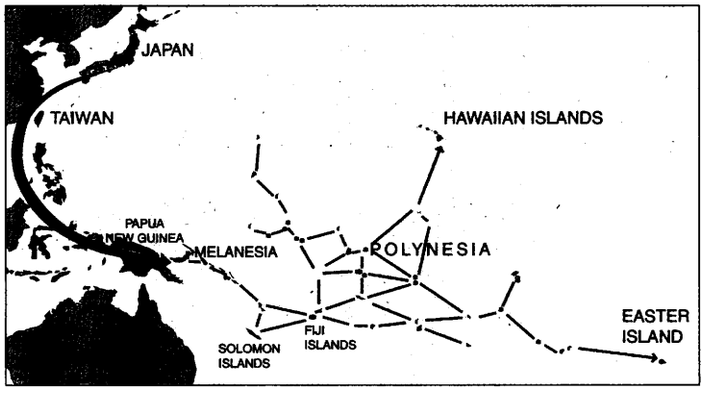
"A lot of good things have come out of this [spending]," including a dramatic expansion of competitive grant programs and the introduction of postdoctoral positions and other schemes to boost the careers of young scientists, says Hiroyuki Yoshikawa, president of the Science Council of Japan, the nation's most influential scientific group. "But new problems have emerged," he adds, noting that there is insufficient lab space and a dearth of positions for those completing postdoctoral fellowships. Yoshikawa says he hopes to address both issues in the next 5-year plan, which begins 1 April 2001.

Salmon Summit? Conservation groups are anxiously waiting to see if President Bill Clinton takes them up on their call for a special review of the science behind federal plans to save endangered Pacific salmon. American Rivers and 16 other groups wrote to Clinton last month urging him to organize a "summit to address serious errors in the science now being employed by the National Marine Fisheries Service (NMFS)," the U.S. agency charged with saving dozens of declining runs in the Pacific Northwest. The groups charge that the agency's analyses underestimate the risk of extinction and downplay the benefits of a controversial proposal to remove four dams that block the Snake River (*Science*, 23 April, p. 574).

Judging by the noises coming from NMFS, a summit is unlikely: Ongoing regulatory studies, set to be finalized late next year, have "already provided for significant peer review," says one NMFS biologist.

nal of Physical Anthropology, "adds important new primary genetic data" and is "strongly consistent with" a rapid intrusion, sometimes called the "express train" model, says Patrick Kirch, an archaeologist at the University of California, Berkeley. "This is important work," adds geneticist Rebecca Cann of the University of Hawaii, Manoa. "We have the history of evolution in our bodies. If we decipher that, we have an independent and useful record of human history."

Still, not everyone is convinced the patterns are so simple. Although he praises the accumulation of data, archaeologist John Terrell of The Field Museum in Chicago says he's mystified "that people try to reduce 45,000 years of prehistory down to a story as simple as two peoples [Melanesians and Southeast Asians] and two migrations. It's a lot more interesting, complicated, and significant than that."



Cruising the Pacific. New data suggest that ancestral Polynesians came from Southeast Asia and swept rapidly through Melanesia.

D. Andrew Merriwether of the University of Michigan, Ann Arbor, chose to examine Melanesian DNA and language more closely because, he says, "the islands are a critical crossroads to explain where everyone in the Pacific passed through or came from." The languages spoken reflect that complexity: Some Melanesians speak Austronesian languages, as do all Polynesians, but other Melanesians speak non-Austronesian languages, dozens of which can be heard on the island of Bougainville alone.

Merriwether and Jonathan Friedlaender of Temple University in Philadelphia, Pennsylvania, opened up lab freezers in the United States and Melanesia and resurrected blood samples taken from Melanesian islanders in the 1960s and '70s. They extracted mitochondrial DNA (mtDNA) from the blood and searched its nucleotide bases for a genetic signature shared by all Polynesian and many Southeast Asian people—a nine–base pair deletion that was presumably part of the genetic heritage the Polynesian forebears carried eastward.

The researchers found that throughout Melanesia, the nine–base pair deletion is most common near the coast and absent in remote, hilly areas. And it is present in all Austronesian speakers, but only in some non-Austronesian–speaking groups. This pattern fits the idea of a rapid, relatively recent migration of ancestral Austronesian speakers through the area, Merriwether says. As the newcomers arrived on the already-inhabited islands, they settled along the coasts, introducing their languages and their genes. But these seafarers were slow to penetrate into the rugged, volcanic interior.

Merriwether and Friedlaender found more evidence for a recent, rapid migration through Melanesia when they examined the sequence of some 500 bases in a hypervariable region of mtDNA known as the d-loop. The number of nucleotide differences in the d-loop sequences of any two individuals in a population provides evidence for how much time has passed since a small population began expanding—the more differences, the longer ago the population began to grow. Polynesians share a nearly identical d-loop sequence, varying by perhaps one nucleotide base. The same is true for Melanesians who have the nine–base pair deletion, indicating that both Polynesians and Melanesians who carry the deletion are recent descendants of the same small population. On the other hand, Melanesians who lacked the deletion had an average of seven to nine d-loop differences, evidence of a much older population that remained on Melanesia while the ancestors of Polynesians cruised the Pacific.

Other researchers approve of combining genetic and linguistic data, but even some geneticists say that the results don't rule out other scenarios of settlement. Henry Harpending, a population geneticist at the University of Utah, Salt Lake City, says, "It's a lot of data that doesn't … consider other explanations such as migration from South America or genetic drift," in which some genetic variation, lost by random chance in small populations, led to apparent genetic similarities today. More convincing would be data from "around 100 genetic loci," he adds.

As the Polynesian picture becomes clearer, researchers are probing other ques-

SOURCE: (LEFT) D.A. MERRIWETHER; (RIGHT) DIANA WALKER/GAMMA LIAISON

ScienceScope

Converted Energy Secretary Bill Richardson has gotten religion on science. He pledged last week to create a "vigorous plan" to recruit and retain scientists at the Department of Energy's (DOE's) national laboratories, and promised to make science and technology a more central concern next year on Capitol Hill.

Richardson has had relatively little to say about science since he took over DOE in 1998. But at a 1 December briefing for Washington science writers, he said he wants to boost funding for the new neutron source planned for Oak Ridge National Laboratory in Tennessee and for fusion, a program that has received little attention from DOE chiefs in the past decade.

Richardson also plans a recruiting drive to address department fears that the espionage scandal and resulting furor—including threats to submit more than 1000 scientists to polygraph testing—are scaring away talented young researchers. He is considering a package that would include increasing pay rates and freeing up slots via early retirement. Better salaries could help stem a mini–brain drain from the labs: "We're losing people to the private sector," he says. Late last week, Richardson also said he would grant waivers to some foreign scientists from sensitive nations barred from doing certain kinds of research at DOE labs.

Polio Push Two of the world's richest men have joined the crusade to rid the world of polio by the end of next year. The Bill and Melinda Gates Foundation, a charity founded by Microsoft CEO Bill Gates, will put $50 million into the campaign, while the United Nations Foundation, which administers the 1997 $1 billion gift of CNN founder Ted Turner to the UN, has pledged another $28 million. The money will be used to strengthen vaccine delivery efforts in countries like Angola and India, where the disease is still a scourge, and to boost polio surveillance. "This is wonderful," says Bruce Aylward, coordinator of the World Health Organization's polio eradication initiative. "Having big players like Turner and Gates involved really raises the profile of the campaign."

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