ing the notion that these "garbage disposal" pathways may be important in organ formation, says the study's lead author, developmental biologist and pediatric cardiologist Deepak Srivastava of the University of Texas Southwestern Medical Center at Dallas.

"This is a major breakthrough," says developmental biologist Paul Krieg of the University of Texas, Austin. "It opens up a whole new area of research in heart development, because it links a clinical syndrome to a new and exciting pathway in cell biology." Others are more cautious, arguing that it's still possible that other genes also contribute. "This is beautiful work," says Christine Seidman, a cardiologist and geneticist at Harvard Medical School. "But I think it's not yet possible to attach the DiGeorge syndrome to a single gene."

Researchers already knew that in 90% of DiGeorge patients, chromosome 22 is missing a large chunk of DNA—about 3 megabases. This presumably causes the syndrome by eliminating one or more crucial genes, and human geneticists have been trying to pin them down. Srivastava, however, plucked out the key gene not through clinical studies but through basic research—in mice. He and colleagues were studying a transcription factor called dHAND, which turns on an array of genes crucial to the development of the mouse heart. Notes Krieg, "This is a nice example of how basic research can yield clinical answers."

As the heart takes shape, so-called cardiac neural crest cells migrate from the neural fold (the spinal cord precursor) into specific niches in various tissues. These neural crest cells form the connection between the heart chambers and nearby vessels (see figure)—which are precisely the regions affected in DiGeorge syndrome.

In mice lacking the gene for dHAND, these cells did not develop properly. The researchers picked out a dozen genes normally activated by dHAND by looking for messenger RNAs found in normal mice but absent when dHAND was shut down. One corresponded to a gene called *Ufd1* (for ubiquitin fusion degradation), which was infamous for being one of 25 or so genes known to lie within the DiGeorge deletion site.

The link between *Ufd1* and the syndrome tightened when they studied the distribution of its protein product in mouse tissues. "*Ufd1* showed up in virtually all tissues that were affected by the DiGeorge syndrome," says Srivastava, including structures that give rise to the thymus and facial bones. Srivastava then turned to humans and found that of 182 DiGeorge patients, all were missing the gene for *UFD1*. The team also came across one patient who had all the classic symptoms, yet, like 10% of all DiGeorge patients, had no apparent genomic deletion. But after more detailed analysis, the team found a minideletion affecting only two genes, *UFD1* and a cell cycle control gene called *CDC45*. Although he admits that *CDC45* cannot be formally ruled out, Srivastava says that "together this indicates that *UFD1* is the cause for the 22q11 deletion phenotype."

Not quite, cautions cardiologist Seigo Izumo of the Beth Israel Deaconess Medical Center in Boston. "*UFD1* is the most attractive candidate," he says, but "it could still be a combined effect of *UFD1* and *CDC45*." Indeed, the DiGeorge syndrome is probably a game of several players, comments Beverly Emanuel, a human geneticist at the University of Pennsylvania in Philadelphia. "It's clear that *UFD1* contributes, but this is not the complete answer," she says. She notes that there are patients who have genetic disruptions at the suspect region, but seem to have an intact *UFD1* gene. "They need to be explained. Clearly there are other things going on at this locus," she says.

Srivastava, however, is already seeking the proteins that *Ufd1* normally helps degrade. Their untimely accumulation when one copy of the gene is missing might somehow cause the developmental problems, he suggests. And Izumo thinks the discovery may even eventually brighten the outlook for afflicted infants, many of whom must currently undergo open heart surgery. "New studies may eventually lead to a better treatment and perhaps even preventive interventions" for those whose hearts need a little help to be made whole.

–MICHAEL HAGMANN

CREDITS: WILLIAM MCCOY/RAINBOW/PNI

VIROLOGY

Virus Suspect Identified In Elephant Deaths

When Kumari, the first elephant ever born at the Smithsonian Institution's National Zoological Park in Washington, D.C., was just months old, the youthful pachyderm would frolic for adoring crowds, splashing in the pool or playing with the pumpkins she got on Halloween. But the good times didn't last for Kumari: On a sunny spring day in 1995, after a 5-day bout with a mysterious illness, the 16-month-old Asian elephant lay down and died. At the time, zoo scientists had no idea what had killed the 1000-pound youngster.

But now, on page 1171, a team led by Laura Richman and Gary Hayward of Johns Hopkins School of Medicine in Baltimore and the National Zoo's Richard Montali reports that it has found the killer—a novel herpesvirus distantly related to the virus that causes cold sores in humans. The new virus has killed at least seven other juvenile Asian elephants at zoos.

Exactly how Kumari became infected with the virus is unclear, but it may have been transmitted to her or her mother by an African

ScienceScope

Everglades Summit A trio of prominent ecologists will serenade Interior Secretary Bruce Babbitt in Washington, D.C., next week with concerns about a controversial $8 billion plan to restore Florida's Everglades ecosystem. The 22 February gathering in Washington was arranged after six scientists—including Stuart Pimm of the University of Tennessee, Knoxville, Peter Raven of the Missouri Botanical Garden in St. Louis, and Gordon Orians of the University of Washington, Seattle—wrote Babbitt last month, complaining of the plan's "deep, systematic" scientific failings. They called for a review by an independent body such as the National Academy of Sciences.

That would take too long, say Interior officials, who hope to submit a blueprint to Congress later this year. Instead, officials have suggested a faster, internal study that examines the concerns, which have made headlines in Florida. The letter "obviously touched a raw nerve," says Pimm. Now, he and his colleagues are waiting to see how the department responds to such external stimuli.

Healthy Ties Canada wants to create a "virtual" Canadian Institutes of Health Research. Unveiled this week as part of the government's 1999–2000 budget proposal, the institutes are expected to replace the Medical Research Council (MRC) as Canada's primary mechanism for funding biomedical research at academic centers.

The new structure—conceived by MRC President Henry Friesen as part of a bid to increase federal support for health research (*Science*, 8 May 1998, p. 821)—will also involve an electronic network linking scientists in particular fields. But the research will continue to be carried out at universities around the country, and the new institutes are not expected to have their own labs.

Details of the plan will be worked out over the next year. One unknown is funding. Proponents want $325 million a year on top of the MRC's current budget of $163 million, but it remains to be seen whether Parliament will be so generous.

elephant also kept at the National Zoo. Richman, Hayward, Montali, and their colleagues have found that the same virus that killed the Asian elephants is carried by African elephants. In these animals, however, the virus apparently causes only relatively innocuous skin or genital warts. The researchers also suspect that Asian elephants harbor a virus that is fatal to their African cousins.

By raising the possibility of fatal crossover infections, the work could influence how the world's zoos take care of their elephants, which can no longer be imported from the wild because most populations are dwindling there. "This has tremendous implications for whether or not [zoos] mix these two species," says Michael Hutchins, director of conservation and science for the American Zoo and Aquarium Association, which oversees a species survival plan for the endangered animals.

The first clues to the cause of Kumari's death came in a postmortem conducted by veterinary pathologists Montali and Richman, who was then at the National Zoo. Their initial exam revealed that Kumari had suffered extensive internal bleeding—a finding that, along with other necropsy findings, "didn't add up to anything we were aware of in elephants," Montali says. The next day, however, while examining slides of Kumari's tissues under the microscope, they spotted a telltale sign of a virus infection: amorphous inclusion bodies in the nuclei of cells from her blood vessel linings. Further examination under an electron microscope revealed dark, round particles with the expected diameter, about 90 nanometers, of a herpesvirus.

The group followed this lead by hunting for herpesvirus genes in Kumari's infected cells with the polymerase chain reaction (PCR), a sensitive DNA amplification technique. The PCR allowed them to pull out the gene encoding an enzyme, called terminase, that helps to assemble the herpesvirus particle, thus confirming that Kumari had suffered a herpesvirus infection. "Of course, we're thinking [Kumari's] can't be the only case that ever occurred," Richman says. And indeed, a review of a century's worth of elephant studbook records uncovered 26 suspicious deaths at zoos throughout North America. After collecting preserved tissue from more than 20 long-dead elephants, Richman found that the damaged tissues of seven Asian elephants carried the same viral terminase gene as Kumari, indicating that they had succumbed to the same infection.

To find out where the virus came from, the researchers scrutinized herpesviruses obtained from skin and genital warts of several otherwise healthy African elephants. The viral terminase sequence turned out to match exactly that from the dead Asian elephants—strong evidence that both species were infected by the same virus, Richman says. She suspects that the virus causes only skin and genital sores in African elephants, but becomes lethal when it infects Asian elephants who were not previously exposed.

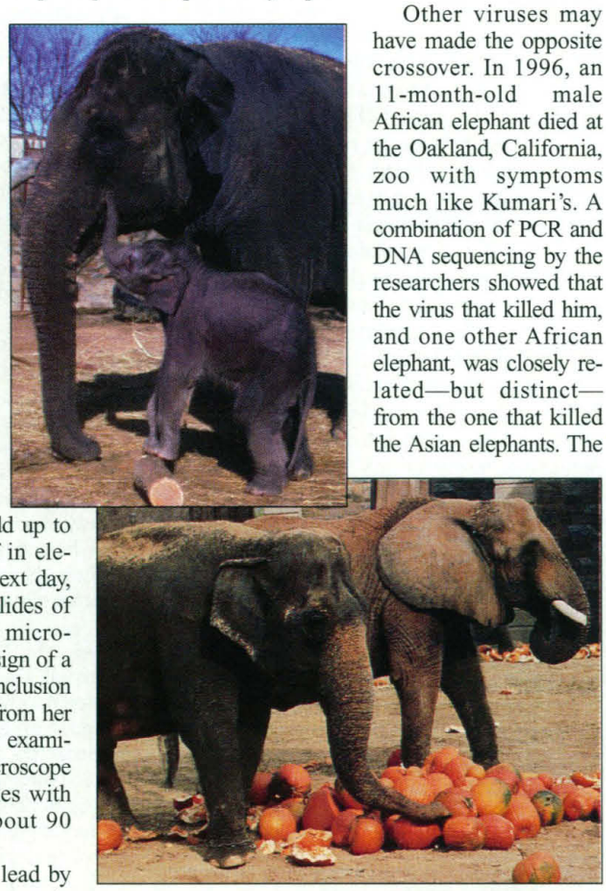
Other viruses may have made the opposite crossover. In 1996, an 11-month-old male African elephant died at the Oakland, California, zoo with symptoms much like Kumari's. A combination of PCR and DNA sequencing by the researchers showed that the virus that killed him, and one other African elephant, was closely related—but distinct—from the one that killed the Asian elephants. The team suspects that the virus that killed the African elephants originated as a mild strain in Asian elephants, although they haven't shown that directly.

If cross-transmission of the herpesviruses does turn out to be causing the fatal infections, developing vaccines could be one solution. Until then, however, zoo keepers may have to consider keeping Asian and African elephants separated to prevent the lethal disease—a difficult task, Richman says, because some zoos don't have the space or the facilities and would have to build new barns.

But at least there's hope of treating the new disease, now that it has been recognized. Montali, Dennis Schmitt of Southwest Missouri State University, and other team members managed to save an infected female Asian calf in 1997 at the Springfield, Missouri, zoo, by giving her the antiherpes drug famciclovir, in elephant-sized doses.

–DAN FERBER

Dan Ferber is a writer in Urbana, Illinois.



Medical mystery. Did mingling of Asian and African elephants (*shown above*) lead to the fatal infection of Kumari (*top*, with her mother)?

CREDITS: J. COHEN/SMITHSONIAN NATIONAL ZOO

BIOENGINEERING

Preliminary Data Touch Off Genetic Food Fight

The controversy in Britain over genetically modified food reached a new high on 12 February, when preliminary data from experiments on potatoes made headlines for the second time in 6 months. The latest media frenzy was touched off when 21 European and American scientists released a memorandum in support of Arpad Pusztai, a protein biochemist who was suspended last year by the Rowett Research Institute in Aberdeen, Scotland, after he appeared on a TV show and sounded an alarm about potatoes altered to resist pests (*Science*, 21 August 1998, p. 1124). After reviewing the case, the scientists said Pusztai's statements were correct and demanded that the Rowett Institute exonerate him.

Their action immediately prompted members of the British House of Commons to urge a moratorium on genetically modified food and triggered allegations that the government or the biotech industry had a hand in suppressing the data. "This raises questions about the extent to which the biotech industry seeks to permeate every level of government," says Labour MP (Member of Parliament) Alan Simpson.

The Rowett affair erupted on 10 August 1998, when Pusztai appeared on Granada's TV show *World in Action* and declared that transgenic potatoes had stunted growth and suppressed immunity in rats that had eaten them for 110 days. The potatoes contained a gene encoding a lectin, a plant protein that can deter insect pests. The world press immediately besieged Pusztai's institute, which initially supported the claim; Rowett chairman and European Parliament member James Provan urged European Union (EU) President Jacques Santer and British Health Secretary Frank Dobson to require more rigorous testing of transgenic food. Just 2 days later, however, the institute's director, Philip James, said Pusztai's data turned out to be "a total muddle"; the disconcerting conclusions, James said, were based on experiments with nontransgenic potatoes spiked with a lectin. The institute apologized for spreading "misleading information," suspended Pusztai, and turned