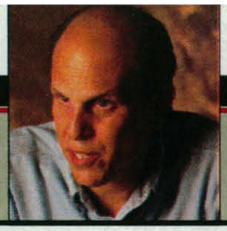
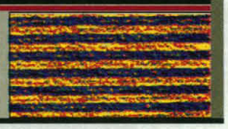




ing. "You don't want to wait 10 years."

Fultz also takes strong exception to Prince and Andrus's statement that preventing disease in the chimp model is not a relevant criterion for judging vaccines. Says Fultz, "That's one of the stupidest statements I've ever heard." Letvin, too, dismisses the contention. Focusing only on chronic infection might lead researchers to overlook a useful vaccine, he argues. "If we have a vaccine that can make people live decades longer, we need to know that," says Letvin.

The next step in this debate could be a meeting to hash out these issues. Alan Schultz, who oversees AIDS vaccine research at NIAID, says he will do his "public servant best" to organize one. **–JON COHEN**

SCIENTIFIC MISCONDUCT

Baylor Saga Comes To an End

Molecular physiologist Kimon Angelides last week ended a long, costly battle against his former employer, Baylor College of Medicine, which had found him guilty of fabricating data, stripped him of tenure, and evicted him from his lab. On 10 February, Angelides settled a civil suit filed against Baylor and 14 individuals at the university, just hours after a federal appeals board had released a report backing Baylor's findings that Angelides had "committed scientific misconduct." Angelides has agreed to accept the appeals board's decision and will receive no payment, although Baylor will pay his attorneys $500,000.

"We're quite pleased with the result," says Baylor lead trial counsel Gerard G. Pecht of the Houston-based firm Fulbright & Jaworski LLP, who says those sued "have been totally vindicated." The settlement also may bring a measure of relief to officials at other universities, who have worried about being sued simply for following the federal government's requirements to investigate misconduct allegations (*Science*, 12 February, p. 913). "This kind of suit shouldn't have gotten to this point at all, in our view," says Allan Shipp of the Association of American Medical Colleges (AAMC).

The saga began in 1992, when a Baylor department chief questioned data in Angelides's grant applications for research on the transmission of nerve impulses through sodium channels. After a 2-year investigation, a Baylor panel found that Angelides had falsified and fabricated figures in five journal articles and five grant applications. In 1997, the Office of Research Integrity (ORI) of the Department of Health and Human Services (HHS) concurred with Baylor's findings and barred Angelides from receiving federal grants for 5 years.

Angelides, who claimed that other scientists in his lab were the ones who had falsified data, appealed the ORI ruling. He also sued Baylor, its president, the seven panelists who examined his case, two former members of his lab, and four others for slander and denial of due process.

A jury had listened to more than a week's worth of plaintiff's testimony when the HHS appeals board released its 171-page report on 10 February. The board, which conducted its own investigation, found that Angelides's "accusations against other researchers were unsubstantiated." The evidence, the board concluded, showed "not honest error, not disputes in interpretation of data, not preliminary results that later proved overly optimistic, not even carelessness, but rather intentional and conscious fraud."

According to Angelides's attorney, James Pianelli of McGehee and Pianelli LLP in Houston, "the timing of the [appeals board report] influenced our decision to settle the litigation." Under the 10 February agreement, Angelides accepts the appeals decision and ORI debarment and will neither appeal nor criticize the decision publicly, will not claim "he has been exonerated or vindicated," and dismisses all claims against the defendants.

The appeals board's validation of Baylor's findings "certainly says that the system is working properly," says Barbara Mishkin, a Washington, D.C.–based attorney who specializes in scientific misconduct. But while Baylor came out ahead, the Angelides case may still discourage universities from pursuing misconduct cases—and scientists from serving on review panels, experts say. "It's not reasonable for people to make this very difficult, painful decision and expose their personal assets to risk," says C. K. Gunsalus, associate vice chancellor for academic affairs at the University of Illinois.

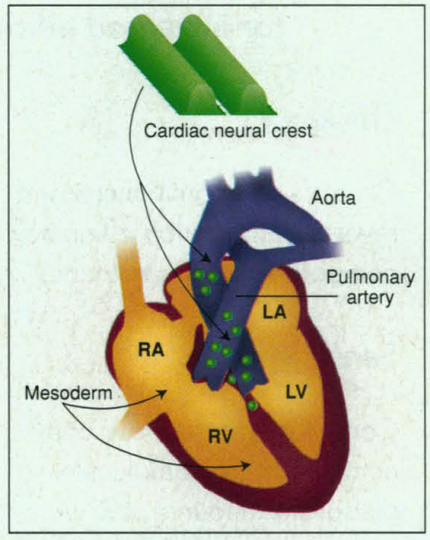
The case may yet leave a positive legacy for researchers. In response to the Angelides affair, the AAMC and ORI have argued that universities and faculty who conduct proper scientific misconduct investigations should be shielded legally from lawsuits. At least, argues Pecht, any civil action should be delayed until the case has been through appeal at HHS. ORI acting director Chris Pascal says HHS "is considering whether additional legal protections are needed in this area," via legislation or regulation. "Otherwise," says Pecht, "the inclination may be for some institutions to sweep the problem under the rug."

–JOCELYN KAISER

HUMAN GENETICS

A Gene That Scrambles Your Heart

Building the perfect heart is hard. Each year about 30,000 babies are born with one of the more than 30 different types of congenital heart defects (CHDs), making these the most common of all human birth defects. Despite much searching, until now the genes behind only three rare disorders had been found. But on page 1158, researchers identify a gene that appears to be key to a widespread form of CHD associated with DiGeorge syndrome, which is second only to Down syndrome in causing malformations of the heart.



The heart of the problem. Parts of the heart's outflow tract and its vessels are derived from neural crest cells (green), which rely on the *Ufd1* gene.

The findings may finally end a frantic hunt for the DiGeorge gene, which when damaged or missing prevents a proper connection between the outflow of the heart and the main blood vessels and also causes malformations in the facial bones and thymus gland. Surprisingly, the gene encodes a component of the cell's protein degradation machinery, support-

SOURCE: SRIVASTAVA *ET AL.*, *NATURE MEDICINE*, 12, 10, P. 1069 (OCTOBER 1996)

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

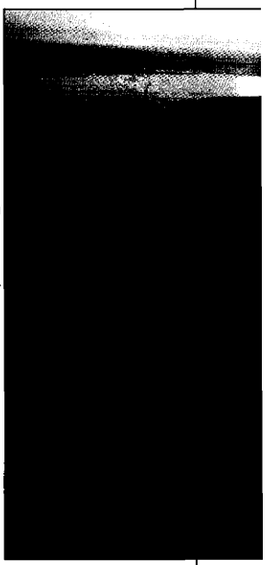
When Kumari, the first elephant ever born at the Smithsonian Institution's National Zoological Park in Washington, D.C., was just months old, the youthful pachyderm would frolic for adoring crowds, splashing in the pool or playing with the pumpkins she got on Halloween. But the good times didn't last 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.