Developmental biologist Larry Zipursky of the University of California, Los Angeles, describes the work as "a beautiful set of results." And he and other researchers say this picture, in which cell division simply provides a large pool of undifferentiated cells that can then be "recruited" to develop into cells with specialized roles, may prove to be a general paradigm for development in multicellular creatures. "In a lot of systems in which cell division is followed by cell type determination, similar mechanisms may be operating," says Kevin Moses, a developmental geneticist at the University of Southern California.

Hariharan and de Nooij had long been intrigued by the fact that all but the first five photoreceptor cells in the ommatidium acquire their fates after the second of two waves of mitosis that sweep over the fruit fly eye. "The only way we could ask what role this mitotic division has in programming specialized states," Hariharan says, "was to stop it." To accomplish this feat, de Nooij and Hariharan targeted expression of a human mitosis-inhibiting protein called p21 to cells poised to undergo the second mitotic wave.

When the researchers abolished the wave in this way, they found that those cells that hadn't already differentiated to produce the first five photoreceptor cells went on to differentiate normally, producing the additional photoreceptors and other cells of the ommatidia. The eyes ended up with a clumpy, disordered appearance, however, because they simply didn't have enough of the building blocks needed to complete many of the 800 ommatidia.

Because the work rules out the possibility that the second mitotic wave is necessary for subsequent cell differentiation in the eye, de Nooij and Hariharan's experiment "enormously simplifies how we can think about cell fate determination in the eye," says Donald Ready, a developmental biologist at Purdue University. "It appears as though it is simply the local environment that communicates to the cell what it should become."

Tracking down those local influences is the goal of ongoing research in many laboratories. But the transgenic flies may also offer clues to another puzzle: the genes that regulate cell division in the fruit fly eye. Geneticists can now screen the transgenic *p21* flies for mutations that make their gnarled eyes either better or worse. Genes found to blunt or amplify *p21*'s effects are likely to be promoters or inhibitors of the cell cycle, Hariharan explains. Combined with the demonstration that some *Drosophila* eye cells acquire their fates independently of mitosis, the work could help solve an old mystery about young organs.

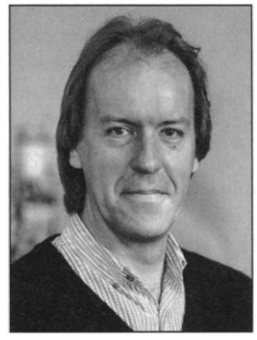
–Wade Roush

AIDS RESEARCH

New Clues Found to How Some People Live With HIV

Nearly 15 years ago, before it was possible to screen for the AIDS virus, an infected gay man donated blood in Sydney, Australia. In the next 3 years, no fewer than seven people received transfusions of products containing his HIV-contaminated blood—seemingly a tragedy in the making. But as more than a decade passed, the expected tragedy failed to materialize. Neither the donor himself nor any of the transfusion recipients appear to have been harmed by this HIV.

Now investigators have uncovered a possible explanation for this anomaly that may shed light on a long-standing AIDS mystery—why a few "long-term nonprogessors" (LTNPs) can live normally with HIV while most infected people sicken and die. It may also bolster an unpopular strategy for developing an AIDS vaccine that might altogether prevent a lethal HIV infection.



Harmless HIV? Nicholas Deacon finds a defective virus in some LTNPs.

On page 988, a research team from three Australian institutions reports results suggesting that the members of the Sydney group have not developed the immunodeficiencies of AIDS because they were infected with a particularly weak strain of the virus. Specifically, the team, led by molecular biologist Nicholas Deacon of the Macfarlane Burnet Centre for Medical Research in Victoria, Australia, found that the virus is missing parts of the *nef* gene, which has been shown in other studies to be needed for full-scale viral replication.

This is not the first time that a defective *nef* gene has been linked to an LTNP. In the 26 January issue of the *New England Journal of Medicine* (*NEJM*), Ronald Desrosiers of the New England Regional Primate Research Center and colleagues reported a similar finding in HIV isolated from a hemophiliac LTNP. But, says Desrosiers, the number of cases in the Sydney Bloodbank cohort makes it "more significant and more dramatic."

Indeed, Anthony Fauci, head of the National Institute of Allergy and Infectious Diseases (NIAID), says the Sydney cohort provides a unique opportunity for studying nonprogression. "It's a very important experiment of nature," says Fauci, whose own lab is also studying LTNPs. "It nails down the concept that one of the reasons people might be [LTNPs] is due to defective virus." He cautions, however, that a defect in the virus is "certainly" not the only explanation. His group and others have found that immunologic factors, such as the presence of strong antibodies that can neutralize the virus and potent killer cells that can clear infected cells, appear to account for other cases of nonprogression.

Deacon and his colleagues came to their conclusion after sequencing HIV isolates from four of the eight Australians. (Two of the recipients had died of non–AIDS-related diseases, and the researchers have not been able to isolate HIV from the other two.) All four had large deletions of the *nef* gene, as well as defects in other genetic elements that may have crippled the virus. But the researchers are particularly interested in the *nef* defect as a possible cause of nonprogression because of previous animal studies.

Work done by the Desrosiers group and others, for example, suggests that Nef, the protein produced by the *nef* gene, signals HIV-infected cells to make more copies of the virus. The lack of an intact *nef* may therefore account for the fact that members of the Sydney cohort have low HIV concentrations in their blood. And in 1991, Desrosiers and co-workers reported in *Cell* that deleting *nef* from SIV, HIV's simian cousin, effectively disarms that lethal virus. "What our study adds is that the same applies for HIV in humans as applies to SIV in macaques," Deacon says.

Still unclear, however, is how common *nef* gene defects are in LTNPs. Virologist David Ho, director of the Aaron Diamond AIDS Research Center, says the Deacon team's paper clearly shows that *nef* deletions can weaken HIV, but "it's not the usual explanation for LTNPs." Indeed, Ho and coworkers reported, also in the 26 January *NEJM*, that they found no evidence of gross *nef* defects in any of 10 LTNPs studied.

But even if *nef* defects aren't a major cause of nonprogression, there's another reason the Australian results may be important: They might influence AIDS vaccine development. Three years ago, Desrosiers showed that in addition to being nonpathogenic, *nef*-deleted SIV is a powerful vaccine, protecting monkeys from subsequent infection with deadly SIV. He suggested then that it

might be possible to produce a human vaccine from a similarly modified HIV.

From the get-go, however, that suggestion met with controversy as researchers raised a bevy of safety concerns—including the possibility that the weakened virus might trigger the development of cancer. And any such approach to vaccine-making appeared doomed last year when studies by Ruth Ruprecht of the Dana-Farber Cancer Institute in Boston showed that SIV lacking *nef* and two other key genetic elements could still cause disease in infant monkeys (*Science*, 18 November 1994, p. 1154). Presumably, the animals' immune systems were too immature to combat even that virus.

But Desrosiers, who believes it is possible to engineer a safe attenuated vaccine by deleting several genes, hopes the Sydney Bloodbank cohort will open minds again. "I think it's going to refocus attention on the live attenuated vaccine," he says. Deacon agrees. "It's not necessarily saying OK, go out and make a vaccine strain out of one of these viruses," says Deacon. But, he says, "I'm sure that there are populations where the live attenuated is on balance the best immediate hope."

NIAID's Fauci acknowledges this point but is holding out for something safer. "We may ultimately have to go for a live, attenuated vaccine," says Fauci, "but there are many reasons [for] concerns about that approach."

–Jon Cohen

PALEOANTHROPOLOGY

Asian Anthropoids Strike Back

The dawn of the higher primates may just have gotten a bit earlier—and perhaps even moved to another continent. For the past year or so, several tiny primates have been battling for the distinction of being the oldest known anthropoid, the group of higher primates that includes humans as well as apes and monkeys. The African contenders, led by a small 37-million-year-old anthropoid called *Catopithecus*, had a lock on the title for several years, but last year a tiny challenger called *Eosimias* appeared in China. Still, *Catopithecus* appeared to be holding its own, in part because the *Eosimias* fossils were so fragmentary (*Science*, 30 June, pp. 1851 and 1885).

But at the annual meeting of the Society of Vertebrate Paleontology, held last week in Pittsburgh, *Eosimias* partisans revealed dramatic new finds that they say establish their animal as one of the earliest higher primates. "*Eosimias* is a member of the missing 'phantom lineage' of ancestral anthropoids," said K. Christopher Beard of the Carnegie Museum of Natural History as he showed slides of a remarkably complete fossil jaw. "It's a basal anthropoid."

If Beard is right, the new finds have major implications for the hotly contested issue of how and where higher primates evolved. *Eosimias*, newly dated to roughly 40 million years ago, could edge out *Catopithecus* as the first undisputed anthropoid and also raises the possibility that Asia was the birthplace of higher primates. In addition, the fossils offer new evidence concerning the thorny question of how to draw the primate family tree.

Various camps of researchers have argued that anthropoids are closely related to particular groups of primates—the tarsiers, for example, or a group of extinct primates called the omomyids. *Catopithecus* discoverer Elwyn Simons of Duke University, for his part, nominated another extinct group, the adapids, as the likely ancestor of anthropoids. And Beard maintains that the new *Eosimias* fossils show that anthropoids themselves are an ancient branch of the primate family tree, with roots extending deep into the past.

Given the diverse views of anthropoid origins, it's perhaps not surprising that early reports of *Eosimias* were greeted with skepticism. Last year, Beard and Qi Tao of the Institute of Vertebrate Paleontology and Paleoanthropology (IVPP) in Beijing named their fragmentary fossils *Eosimias*, or dawn monkey—and sparked a shower of criticism from those who felt the material was too incomplete to deserve the name. But last spring, Beard returned to localities along central China's Yellow River. There, he and colleague Tong Yongsheng of the IVPP found a remarkable new specimen of *Eosimias* that preserves both sides of the lower jaw and almost every tooth, including the often-lost incisors and canines.

PHOTOS BY K. C. BEARD

Small beginnings. At right is a reconstruction of what *Eosimias*, which weighed about 100 grams, looked like. The fossil jaw is at left.

Speaking to an intent audience of several hundred at the Pittsburgh meeting, Beard reeled off a list of features possessed by the new fossil that link *Eosimias* to anthropoids. Among them: The incisors are vertical, the second lower incisor is larger than the first, the premolars are obliquely oriented, and the angle of the back of the jawbone is rounded. Because *Eosimias* looks nothing like an adapid, Beard argued that adapids should be relegated to a distant branch of the primate family tree. Although *Eosimias* has more in common with omomyids and tarsiers, Beard says these groups are at least one step away from anthropoids.

Many researchers, including some of the skeptics, say that the new finds add weight to Beard's arguments. "I still have problems with some of his interpretations, but we've got to take this seriously now," says Duke paleoanthropologist Richard Kay, who has been reluctant to consider *Eosimias* a higher primate. "It seems that *Eosimias* is close to anthropoids." Kay remains skeptical, however, about Beard's proposed primate family tree; he continues to see a close kinship between anthropoids and tarsiers.

Other scientists remain wary of conferring anthropoid status on *Eosimias*. "Every single feature Beard uses to link *Eosimias* and anthropoids can be found alone or even in combination in other ancient primates that aren't anthropoids," says Tab Rasmussen of Washington University in St. Louis, the lone member of the adapid camp who attended the meeting. He also points out that there's a third, less well-established candidate for the first anthropoid, *Algeripithecus*, which may be older than both *Eosimias* and *Catopithecus*, but is known only from very fragmentary fossils. *Algeripithecus* resembles the other African finds—but not the Chinese ones, implying that *Eosimias* was a side branch. "I think Chris has found a fascinating new group—but they aren't anthropoids," says Rasmussen.

Despite the new finds, it's still too soon to classify the Chinese fossils, sums up omomyid expert Blythe Williams of Duke. She notes that although *Eosimias*'s incisors and canines are indeed similar to those of anthropoids, the molars resemble those of more primitive primates. "It's a beautiful specimen, but I don't think we have the evidence yet to say what it is," she says.

The real clincher, all agree, would be a skull. But time may be running out on the search. The Chinese government plans to dam the Yellow River—which will drown many of the *Eosimias* localities—by 1997. So Beard and colleagues will be out searching for one more year, hoping to find a definitive fossil to at last silence the skeptics.

–Elizabeth Culotta