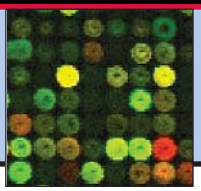
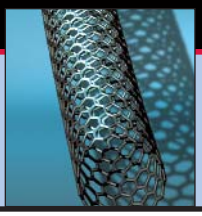








virus in cell culture and plans to slog through *all* drugs currently approved for *any* condition by the Food and Drug Administration, says Army virologist Peter Jahrling. If an approved drug works against SARS, it could be available much faster than a new one. CDC and other labs are comparing the virus's genome sequence to those of other coronaviruses—which can infect a range of avian and mammalian species—to determine its likely origin.

For network scientists, Stöhr has tried to orchestrate the fair distribution of a key commodity: scientific credit. He initially proposed that they submit three papers to *NEJM*: one produced by three groups in Hong Kong, one co-authored by German researchers and CDC, and one by groups that found the metapneumovirus. That plan fell apart when CDC, which had been invited by *NEJM* to write a paper, decided it preferred to go it alone. Fortunately, *NEJM* editors said they would consider publishing all four. Drosten has teamed with colleagues across Germany as well as Osterhaus and a group from the Pasteur Institute in Paris to describe the methods they used to track the coronavirus. "It appears there's enough flesh on the bones for everybody," says Osterhaus.

Meanwhile, Stöhr is also compiling a paper for *The Lancet* chronicling the current collaboration. He concedes to being slightly taken aback last week when, after each lab had submitted 250 words about its own role, Gerberding stole some of the network's thunder in an *NEJM* editorial that was posted online 2 April. But his hope is that the example set by the SARS network will long outlast any debate over who came first.

–MARTIN ENSERINK AND GRETCHEN VOGEL

NUCLEAR TRANSFER

# Misguided Chromosomes Foil Primate Cloning

While governments around the world debate how to prevent human reproductive cloning, it seems that nature has put a few hurdles of its own in the way. On page 297, a team reports that in rhesus monkeys, cloning robs an embryo of key proteins that allow a cell to divvy up chromosomes and divide properly. Unpublished data from this and other groups suggest that the same problem may also thwart attempts to clone humans.

There are potential ways around the newfound obstacle, but for now, groups that made controversial claims that they would use the techniques that produced Dolly the sheep to create human babies are unlikely to succeed.

It is almost as if someone "drew a sharp line between old-world primates—including people—and other animals, saying, 'I'll let you clone cattle, mice, sheep, even rabbits and cats, but monkeys and humans require something more,' " says Gerald Schatten of the University of Pittsburgh School of Medicine, a leader of the rhesus monkey study.

Schatten and his colleagues have tried hundreds of times to clone monkeys, only to fail. Indeed, although several groups have attempted it, no one has yet produced a monkey through somatic cell nuclear transfer, the process by which a nucleus from one cell is extracted and injected into an egg whose own nucleus has been removed. "The failure to clone any primate has so far been startling," says Rudolf Jaenisch of the Massachusetts Institute of Technology in Cambridge, who studies cloning in mice.

The scientists had suspected for several years that something was disturbing cell division in cloned embryos. The embryos seemed normal at their earliest stages, but none developed into a pregnancy when implanted. When the researchers looked more closely, they realized why: Many of the cells in a given embryo had the wrong number of chromosomes. Some had just a few, whereas others had twice as many as they should. Although embryos can survive for a few cell divisions with such defects, soon the developmental program becomes hopelessly derailed.

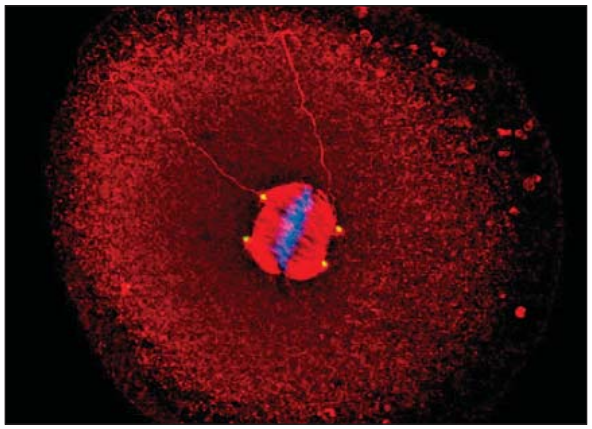
To find out what was interfering with proper cell division, the team fluorescently labeled the cell-division machinery. The cells' mitotic spindles, which guide chromosomes to the right place during cell division, were completely disorganized. And two proteins that help organize the spindles, called NuMA and HSET, were missing.

A look at unfertilized rhesus oocytes explained why. The team found that the spindle proteins are concentrated near the chromosomes of unfertilized egg cells—the same chromosomes that are removed during the first step of nuclear transfer. In most other mammals, Schatten says, the proteins are scattered throughout the egg, and removing the egg's chromosomes seems to leave enough of the key proteins behind for cell division to proceed.

The work "explains why no one has yet succeed in achieving normally developing embryos from human nuclear transfer," says Roger Pedersen of the University of Cambridge, U.K., who attempted human nuclear transfer experiments at his previous laboratory at the University of California, San Francisco. "Primate eggs are biologically different." Schatten says preliminary data suggest the proteins are also concentrated near the nuclear material in unfertilized human eggs.

A cloning lab might surmount the hurdle, says Schatten, by reversing the order of the traditional nuclear transfer procedure: First add an extra nucleus, then activate cell division, and finally remove the egg's DNA. The find "will make people think differently about the optimum sequence of nuclear transfer procedures," says Ian Wilmut of the Roslin Institute in Midlothian, Scotland, a leader of the team that cloned Dolly.

Even if scientists could overcome the obstacles, however, another study suggests that ▶



**Missing in action.** In human embryos, as in this egg fertilized by two sperm (red lines), proteins from egg and sperm combine (yellow) to guide cell division. Embryos formed by nuclear transfer lack these proteins.

CREDIT: G. SCHATTEN/UNIVERSITY OF PITTSBURGH SCHOOL OF MEDICINE

further developmental problems threaten clones of all species. Jaenisch and his colleagues report in the 15 April issue of *Development* that genes important to early development frequently fail to turn on in mouse embryos cloned from adult cells. That failure helps explain the low survival rate of such embryos, Jaenisch says. But he notes that the team's work—which examined the expression of just 11 genes—is only the tip of the iceberg. In other experiments, the researchers have found that even apparently healthy cloned mice show abnormal levels of gene expression. "There may be no normal clones," Jaenisch says.

Although revising the nuclear transfer procedure might help solve the cell-division problem, it is harder to imagine a solution for the faulty gene regulation that Jaenisch and his colleagues see. "We're looking at a more fundamental problem," he says.

The biological roadblocks would seem to be good news for those worried about the ethical implications of human cloning, says Schatten. "This reinforces the fact that the charlatans who claim to have cloned humans have never understood enough cell or developmental biology" to succeed, he says. The debate will go on, but nature already seems to have imposed its own limits on cloning.

–GRETCHEN VOGEL

GENE EVOLUTION

# Cannibalism and Prion Disease May Have Been Rampant in Ancient Humans

Some call it the laughing disease; others, kuru. This neurodegenerative disorder is universally fatal and 40 years ago killed almost 10% of a small New Guinea tribe called the Fore. Now molecular biologists propose that similar epidemics plagued prehistoric humans. Both then and more recently, kuru, a prion disease, was transmitted through cannibalism, Simon Mead and John Collinge of University College London and their colleagues claim in a report online in *Science* this week (www.sciencemag.org/cgi/content/abstract/1083320). They base their conclusions on the worldwide distribution of variants of the prion gene.

The work lends support to the idea that ancient people once regularly munched on their peers. This conclusion will be controversial, says John Hardy, a geneticist at the National Institute on Aging in Bethesda, Maryland. Nonetheless, "I think [Collinge and colleagues] might be right."

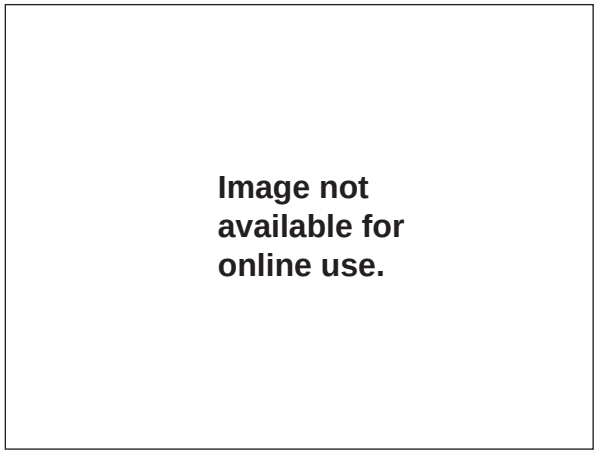
Until 50 years ago, the Fore reportedly had a tradition of eating the dead. In the 1960s, Carleton Gajdusek of the National Institute of Neurological Diseases and Stroke in Bethesda demonstrated that kuru was an infectious disease: Once cannibalism was banned, kuru disappeared.

Gajdusek blamed a slow-growing virus for the disease, but now the prime suspect in kuru is a malformed miniature protein called a prion. Contorted prions cause other, native prions to misfold, clump together, and kill brain cells. A similar process is believed to cause Creutzfeldt-Jakob disease (CJD) in humans and scrapie in sheep. Although some prion diseases occur spontaneously, in many cases, humans or other animals contract them by eating infected tissue.

A decade ago, Collinge showed that people carrying two identical copies of the gene for the prion protein are more susceptible to developing CJD than people who carry two unmatched gene variants. Although the variants create proteins that differ by only one amino acid, the mismatch somehow protects people against the disease.

To understand the history of the prion gene, Collinge's team looked at DNA from the Fore and also from 1000 people representing other groups around the world. All ethnic groups examined carried two versions of the prion gene.

The variants' widespread existence suggests that they have been conserved throughout human history, the team claims. Based on additional comparisons across cultures and with chimp DNA, the ▶




CREDITS: (TOP TO BOTTOM) P. BAGLA; WHO

**Deadly epidemic.** Prehistoric people may have succumbed to the prion disease that killed this man from a New Guinea tribe.

## ScienceScope

### India, WHO Attack Polio

**NEW DELHI**—Calling India "the number one priority for stopping the transmission of polio," WHO Director-General Gro Harlem Brundtland this week traveled to the north Indian state of Uttar Pradesh to launch a final assault on the disease. With 55 new cases already this year, Brundtland says that "Uttar Pradesh is the epicenter" of a global battle to eradicate polio by 2005.

India joins Nigeria, Egypt, Pakistan, Afghanistan, Niger, and Somalia as the only countries with indigenous wild polio, and last year it was home to five of every six new cases. Uttar Pradesh was also the source of outbreaks in two other Indian provinces, and this winter a Lebanese youth who never left his village was paralyzed by a virus traced back to India.

WHO officials say the latest epidemic is the result of fewer vaccination campaigns than planned and a failure to achieve blanket coverage during home visits. This year officials hope to reach every child under 5 in six campaigns. Although Brundtland says that "we have the tools and the strategies to finish this job," WHO remains $275 million short of what it estimates is needed to eradicate the disease.

–PALLAVA BAGLA

### Fast Flux, R.I.P.

**PORTLAND, OREGON**—After displaying more lives than a cat, the Fast Flux Test Facility, a nuclear research reactor in Hanford, Washington, has finally run out of luck. A federal appeals court in San Francisco last week denied a local group's bid to keep the Department of Energy reactor on standby for possible conversion to a for-profit producer of medical radioactive isotopes.

The research reactor went online in 1980 but was shut down just 12 years later because of high operating costs. The government has since spent about $35 million a year to keep the reactor idle while searching for possible new missions, such as producing tritium for nuclear weapons and radioisotopes for spacecraft batteries. Those hopes came to an end this week, as workers began draining molten sodium coolant from the reactor's core. Once drained, the reactor "would be extremely hard to restart," says Michael Turner of Fluor Hanford, the company doing the work. The shutdown could take 10 years and cost more than $600 million.

–ROBERT F. SERVICE