and perhaps find other clock-controlled behaviors as well, says Rob Jackson of Tufts University College of Medicine in Boston. Indeed, even though it is not yet certain that PDF really is the clock's output signal, the flurry of speculation about its possible roles has begun. **–MARCIA BARINAGA**

HUMAN GENETICS

mtDNA Shows Signs of Paternal Influence

Women have struggled to gain equality in society, but biologists have long thought that females wield absolute power in a sphere far from the public eye: in the mitochondria, cellular organelles whose DNA is thought to pass intact from mother to child with no paternal influence. On page 2524, however, a study by

Mighty mitochondria. Human sperm mitochondria (yellow line) can gain entry to eggs.

Philip Awadalla of the University of Edinburgh and Adam Eyre-Walker and John Maynard Smith of the University of Sussex in Brighton, U.K., finds signs of mixing between maternal and paternal mitochondrial DNA (mtDNA) in humans and chimpanzees. Because biologists have used mtDNA as a tool to trace human ancestry and relationships, the finding has implications for everything from the identification of bodies to the existence of a "mitochondrial Eve" 200,000 years ago.

The study "is pretty compelling and I can't think of good alternative explanations," says Richard Hudson, a population geneticist at the University of Chicago. Anthropologists agree that if the study holds up, it could trigger a major shake-up in their field. "There is a cottage industry of making gene trees in anthropology and then interpreting them," says Henry Harpending, an anthropologist at the University of Utah, Salt Lake City. "This paper will invalidate most of that."

Yet not everyone is ready to grant a role to fathers in mtDNA inheritance just yet. Hudson and others caution that the new result "changes our view dramatically enough that we have to continue to think of other ways to explain it." Fathers contributing mtDNA to their offspring "implies several different novel and important biological phenomena that no one's ever seen before," such as contact between maternal and paternal mtDNA, adds Neil Risch, a human geneticist at Stanford University School of Medicine.

Researchers have assumed that mtDNA passes only through the mother, in part because experiments have shown that eggs destroy sperm after fertilization, and that mitochondrial traits, including a variety of inherited disorders, seem to come only from mothers. But some mtDNA sequences didn't fit neatly into a tree of maternal descent (*Science*, 5 March, p. 1435), so the scientists decided to look for signs of mixing between paternal and maternal mtDNA.

Such mixing—the usual fate of DNA in the cell nucleus—is called recombination, and it takes place when a piece of a DNA strand from one parent crosses over and pairs up with a strand from the other parent. The process generates a novel DNA molecule with features donated by each parent.

To probe whether recombination occurs in the mitochondrial genome, the team analyzed DNA variations. DNA in different individuals varies at many positions, so each new mutation arises on a distinctive genetic background. Unless the DNA can reshuffle itself, the new mutation will stick with the variations already on the same chromosome as it is passed on. But recombination, which mixes up pieces of the DNA, should gradually destroy such nonrandom linkages between DNA variations. The farther apart two sites lie on the chromosomes, the faster recombination can eliminate the linkage. Thus, if recombination is operating, specific variations are less likely to be found together if they are far apart on the chromosome than if they are neighbors.

Using mtDNA from humans and chimpanzees, the researchers tallied how often specific mutations at different sites tended to occur together; they also noted the distance between the mutation sites. In four out of five human data sets and one chimp set, nonrandom mutations at distant sites were less likely to be linked than nearby mutations—implying recombination between maternal and paternal DNA, says Eyre-Walker.

Such recombination could be a blow for researchers who have used mtDNA to trace human evolutionary history and migrations. They have assumed that the mtDNA descends only through the mother, so they could draw a single evolutionary tree of maternal descent—all the way back to an African "mitochondrial Eve," for example. But "with recombination there is no single tree," notes Harpending. Instead, different parts of the molecule have different histories. Thus, "there's not one woman to whom we can trace our mitochondria," says Eyre-Walker.

What's more, over time, recombination mixes up genomes so that they become more homogeneous. That "makes even distantly related people look more similar to each other," says Eyre-Walker, and causes past events to seem more recent than they really are. Our last common female ancestor, for example, would be older than the mtDNA implies. But not every mtDNA study would be invalidated by recombination, Eyre-Walker notes. "The major impact will be on the timing of those events and our basic understanding of mtDNA evolution," he says.

Even so, many researchers aren't ready to accept these data as ironclad evidence of recombination. Other genetic processes might create a similar pattern, says evolutionary biologist Rebecca Cann of the University of Hawaii, Manoa. Some researchers have proposed models in which one mutation is more likely to occur close to another. "It's not yet clear whether there aren't explanations other than recombination," agrees Vincent Macaulay, a mathematical geneticist at the University of Oxford.

Skeptics and supporters alike note that how recombination could be happening remains a mystery. Recombination requires physical contact between egg and sperm mtDNA, for example, and it's not clear when or how these molecules touch. In any case, it's possible to square previous observations of mtDNA inheritance with "a little bit of paternal leakage," adds Jody Hey, an evolutionary geneticist at Rutgers University in Piscataway, New Jersey. Just how much leakage might take place is a critical question in practical as well as research uses of mtDNA, such as identifying human remains. "If the sequences are identical, the chances are very good that that's the woman's son or daughter," says Eyre-Walker. "If you get a one-base-pair mismatch, do you say 'This is not your child?' "

–EVELYN STRAUSS

PLANETARY SCIENCE

Galileo Catches Lava Fountain on Io

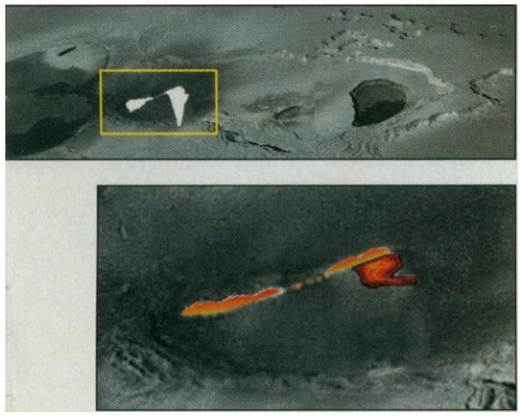
SAN FRANCISCO—Astronomers are galvanized by a new image of what may be a curtain of lava spewing above a volcano on Jupiter's moon Io. The picture, snapped by the Galileo spacecraft during its daredevil dive past Io on Thanksgiving and released last week at a meeting of the American Geophysical Union, also reveals a complex, jagged cliff arcing near the volcano—further evidence of the moon's geologic turmoil.

Planetary scientists have long known that Io is the most volcanically active body in the solar system, thanks to constant gravitational tugs from Jupiter and its other moons that churn Io's interior. Galileo had previously revealed surface flows within vast volcanic

CREDIT: PETER SUTOVSKY

wounds called calderas. The Galileo team hoped they also might find ribbons of fire called "lava fountains," similar to those that spurt skyward from long, narrow gashes in the Kilauea volcano on Hawaii. However, Galileo's camera hadn't yet pointed in the right place at the right time to see one.

That changed during a moment of "dumb luck" on 25 November as Galileo passed within 300 kilometers of Io, says Galileo team member Laszlo Keszthelyi of the University of Arizona, Tucson. The camera was aimed near Io's north pole at a nondescript volcanic



Curtain of fire. Heat from what may be a "lava fountain" on Io blinded Galileo's detector; the inset shows how the 25-kilometer-long fountain may have looked.

feature that the team now calls Tvashtar, after an Indian sun god. Heat flowing from a 25-kilometer-long stripe within Tvashtar's caldera was so intense that it blinded part of the camera's electronic detector and created a white blotch. However, details of parts of the blotch—especially its wavy top edge and a linear section in the middle—convinced Keszthelyi and his colleagues that they were seeing a curtain of lava at least 1.5 kilometers high. Key support for that scenario came from NASA's Infrared Telescope Facility on Mauna Kea, Hawaii, which happened to detect the Tvashtar hot spot from Earth just 3 hours later. According to planetary scientist John Spencer of Lowell Observatory in Flagstaff, Arizona, Tvashtar was so close to Io's horizon at the time that the telescope would not have seen the hot material unless it was jetting above the surface.

Still, the lava fountain scenario is "pretty speculative," says planetary scientist Gerald Schubert of the University of California, Los Angeles. "Because of the bleeding problem [in the image], it's very uncertain exactly what they're seeing," he says. But Spencer and his colleagues think they may be able to dispel those doubts by determining the three-dimensional shape of the hot spot from earlier observations of Io on the same day, when the view was more direct. **–ROBERT IRION**

CREDITS: (LEFT TO RIGHT) GALILEO SSI TEAM; WAKAYAMA *ET AL.*, *PNAS* **96** (26), 14987 (1999)

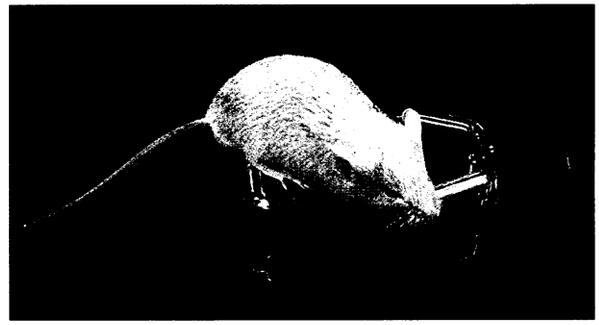
CLONING

Mice Cloned From Cultured Stem Cells

In an experiment that links the hot-button fields of stem cells and cloning, scientists announced this week that they have cloned mice from embryonic stem (ES) cells kept in culture. These cells are capable of developing into any type of tissue but ordinarily can't grow into a complete organism on their own. The technique is still inefficient, but if researchers can improve it, it could provide an easier way to create genetically modified mice.

Although sheep, goats, cows, and mice have all been cloned, in most cases the genetic material came from cells that had not spent much time in culture. In contrast, researchers report in the current *Proceedings of the National Academy of Sciences* that they produced live-born mice from two ES cell lines that had each gone through more than 30 cell divisions in the lab. Although cells in culture are easy to work with, they often accumulate mutations. Those mutations can impede embryonic development, so scientists weren't sure whether long-cultured cell lines would be candidates for cloning.

In the hands of reproductive biologist Teruhiko Wakayama, who created the clones in the laboratory of Ryuzo Yanagimachi of the University of Hawaii, Honolulu, the cultured cells seemed to work as well as cells from a living animal. In collaboration with Peter Mombaerts of The Rockefeller University in New York City, the researchers extracted a nucleus from an ES cell and transferred it into a mouse egg that lacked a nucleus. Like all cloning, the procedure was hit or miss, however. In the team's most successful experiment, it took more than 1000 cloning attempts to obtain 13 mice that survived to adulthood, notes developmental biologist Davor Solter of the Max Planck Institute for Immunobiology in Freiburg, Germany.



Father and son. Hooper the mouse was cloned from the E14 embryonic stem cell line.

If scientists could boost the technique's efficiency and use it to go directly from a genetically manipulated cell to a live animal, "that would be fantastic," says embryologist Brigid Hogan of Vanderbilt University in Nashville, Tennessee. Cloning mice from ES cells could streamline the rather cumbersome procedure used today to produce tens of thousands of so-called knockout mice a year.

Typically, scientists modify genes in an ES cell and then insert the cell into an already-developing embryo, producing a chimeric mouse that has descendents of the ES cell in most of its tissues, including the reproductive organs. When the chimeras mate with normal mice, some of their offspring carry the mutation in all their cells. Those mice are then bred to create knockout mice. If scientists could clone mice directly from particular cells, they could create knockouts in one generation instead of three, Mombaerts says.

But at the moment, cloning mice is far too difficult to rival the traditional procedure, several mouse researchers say; although other labs have tried, no one else has reported cloning a mouse. "Whether [cloning] is going to be a better way of generating mice than chimeras remains an open question," says mouse geneticist Allan Bradley of Baylor College of Medicine in Houston, Texas. "I don't think we're going to drop everything overnight and start trying to clone ES cells." Indeed, Yanagimachi's team reports that they tried to clone mice from ES cells modified to contain a specific mutation, but they produced only one cloned knockout mouse that died soon after birth.

The new work does suggest that in some respects cloning may be easier technically than researchers had thought. Earlier reports seemed to suggest that successful cloning requires starting with cells at the resting phase of the cell cycle; Dolly the sheep was cloned from a so-called "quiescent," starved cell, and other cloning experiments have used cells in the resting phase. But ES cells don't survive long if they are starved, and they divide rapidly, so it is tough to catch one at the resting stage, says Mombaerts. The team found that cell stage didn't seem to matter: They produced live-born mice from cells in several stages of the cell cycle, including some that presumably had just finished replicating their DNA and were about to divide.

The next crucial step is to standardize the procedure. Mombaerts says he and Wakayama, who has recently moved to Rockefeller University, hope to do their part: They're planning a detailed guide on "how to clone a mouse"—a book that may make many researchers' lives a lot easier. **–GRETCHEN VOGEL**