Mom's mitochondria may hold mutation

Scientists discovered in the early 1960s that mitochondria, the power-generating stations inside cells, contain a few genes of their own. Now Emory University scientists in Atlanta have linked a specific defect in mitochondrial DNA to a rare form of blindness. The discovery confirms suspicions that tainted genes in these tiny power packs can indeed cause genetic defects, and suggests a whole new mechanism for inherited diseases.

Several hundred mitochondria exist in the cytoplasm of each cell, their handful of genes distinct and separate from those packed on the chromosomes inside the cell nucleus. Altogether, the mitochondria contain about 0.3 percent of a cell's total DNA. These genes code for proteins vital to the production of adenosine-triphosphate (ATP), the key fuel used by cells. Unlike the DNA in the nucleus, which comes equally from the mother and father, the genes in the mitochondria come only from the mother.

Douglas C. Wallace and his colleagues discovered that people suffering Leber's hereditary optic neuropathy (LHON) have a defect in one mitochondrial gene that codes for a protein involved in the first step of ATP production. This defect results in the amino acid histidine being substituted for the amino acid arginine during the protein's synthesis, Wallace reported this week at the Short Course in Medical and Experimental Mammalian Genetics at the Jackson Laboratory in Bar Harbor, Maine, cosponsored by Johns Hopkins University in Baltimore.

LHON results in optic nerve death and often causes blindness by age 20. Since mitochondria are passed on only by the mother, if she carries the defect, every one of her children will inherit it. Yet only a minority of people who inherit the defective gene go blind, Wallace notes.

"It's clear this mutation, which is a very, very subtle mutation, predisposes you to the problem, but is not sufficient in and of itself to prove you're going to go blind," he says. "So we think there are other factors. Another interesting aspect of these patients is that there is a bias toward males going blind over females. That might be a cultural difference or there might be differential [cell] respiration rates in the sexes." He cites smoking and diet as possible cultural factors.

Wallace and his colleagues found the genetic defect in nine of 11 LHON patients they studied, but failed to detect it in any of 45 controls. He says this could mean that more than one genetic defect predisposes people to the disease or, more likely, that the two people who did not have the protein problem were misdiagnosed as having LHON.

"The exciting thing . . . is that we're now really finding the mutations that can explain this kind of phenomenon, and beginning to understand them at the biochemical level, to be able to develop diagnostic tools," Wallace says.

Researchers suspect several other rare genetic ailments stem from mitochondrial DNA defects. But Wallace suggests some cases of more common diseases also may result from genetic defects in the mitochondria. All cells require ATP to function, but some cells require more of the fuel than others. Evidence suggests different defective genes within the mitochondria will decrease ATP production to differing degrees, so some cells may work quite well with low ATP while others fail, Wallace says.

He speculates that some cases of heart, kidney and central nervous system failure, whose causes are now unknown, may one day prove the result of defective mitochondrial DNA. — *P. Young*

A goodbye wave?

If an extraterrestrial body hit Earth 65 million years ago and precipitated the extinction of the dinosaurs and perhaps half the other living species, chances are three to one it landed in the ocean, unleashing a whopper of a wave. Geologists have identified deposits in Texas that may have been left by such a wave.

Along the Brazos River there are meter-thick beds of coarse-grained sandstones and large chunks of clay that were deposited precisely at the Cretaceous-Tertiary boundary. Only a wave rising 50 to 100 meters above the ocean surface could have created such a layer of uprooted material, report Joanne Bourgeois from the University of Washington and her colleagues in the July 29 SCIENCE. From the pattern of the sediments, the researchers have ruled out storms, mudslides and other possible causes of the deposits. At the end of the Cretaceous, this area of Texas was 75 to 100 meters below the ocean surface.

Since there is almost incontrovertible evidence that one or several comets or meteorites crashed into Earth at the same geologic time as the wave hit Texas, the researchers say it is likely an extraterrestrial body created the tsunami deposits, either by landing in the water or by generating earthquakes or submarine landslides. All of these events can produce tsunamis. Volcanic eruptions — another leading candidate for causing the mass extinctions — also start tsunamis, but the researchers say there is no geologic evidence in Texas for an eruption at that time. The deposits do not explain the extinctions, but these types of deposits in other locations may help in pinpointing the location of ground zero for the impact. □

Protein determines fruit fly physique

Nearly 100 years ago, scientists first published speculation that "a sort of stuff" in young embryos might direct the mysterious process of cell differentiation, development and limb pattern formation as an animal grows from a fertilized egg to adulthood. Now, using a combination of genetic, developmental and molecular biological techniques, West German researchers have provided the first clear evidence that such a stuff exists in extremely young fruit fly embryos and that it organizes the process of differentiation along the fly's longitudinal axis. The research, published in the July 1 CELL, is the latest in a series of groundbreaking papers by Christiane Nüsslein-Volhard and her associates at the Max-Planck-Institut für Entwicklungsbiologie in Tübingen.

"The work has been done absolutely beautifully," says Matthew Scott, a developmental biologist who works with the fruit fly, *Drosophila*, at the University of Colorado in Boulder. "It's one of the nicest studies that's been done in developmental genetics in a long time."

According to the morphogenetic model of development, first proposed in 1897, a biologically active chemical is secreted from one end of an embryo and spreads to other parts in decreasing amounts. The theory says cells can "calculate" where they are in this chemical gradient — and differentiate accordingly — by sensing the local concentration of the chemical.

To date, perhaps the most convincing candidate morphogen is retinoic acid, which plays a major role in limb pattern formation in chick embryos (SN: 6/27/87, p.406). Looking at an even earlier stage of development in *Drosophila* embryos, Nüsslein-Volhard and Wolfgang Driever used labeled antibodies to show that a protein called bicoid diffuses in a steep, head-to-tail gradient within hours after the first cell begins to divide. And by looking at genetic variants of flies that produce different amounts of bicoid, they show that the protein determines the cell differentiation process in a concentration-dependent manner. Specifically, the higher the concentration of bicoid near the head of the embryo, the further various body parts are pushed back toward the tail.

The research shows that cells must have some mechanism for reading the absolute concentration of bicoid, says Welcome Bender, a specialist in *Drosophila* development at Harvard Medical School in Boston. Scientists have yet to discover what that mechanism is, but the protein appears to have a so-called homeobox sequence, which suggests it may act directly on DNA to regulate gene expression. — *R. Weiss*