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****Scientists blast their way inside energy units of cells

DALLAS--Using a biological "shotgun," scientists are firing genetic information into the tiny energizer units of animal and plant cells. The method opens future possibilities of controlling some forms of muscle weakness as well as new ways to genetically engineer plants.

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Scientists from The University of Texas Southwestern Medical Center at Dallas, Duke University at Durham, N.C., and Cornell University at Geneva, N.Y., announced the new method in the June 10 issue of the magazine Science.

With the biological/ballistic or "biolistic" gun developed by Dr. John Sanford at Cornell, Dr. Ronald Butow and associates at UT Southwestern and Dr. Stephen Johnston at Duke, have successfully restored a respiratory function in the mitochondria of yeast.

The mitochondria are bacteria-sized units inside animal cells that use oxygen to supply energy to the cell. Shaped like tiny sausages, the mitochondria have their own genetic information in the form of DNA. In fact, it is believed by many scientists that mitochondria are derived from primitive organisms that either invaded or were assimilated by early cells when the use of oxygen from the primitive atmosphere became possible as a source of energy.

"The implications of the new method are profound," declared Butow, who has been working with Dr. Paul Anziano at UT Southwestern. Now it will be possible to alter and "engineer" the mitochondrial genes to discover how they interact with the genes in the cell's nucleus, to probe the evolutionary pathways leading to development of modern animals, including man, and possibly to develop new ways of treating genetic disease, he added.

At the same time, Dr. John Boynton and Dr. Nick Gillham at Duke University have blasted DNA into chloroplasts inside plant cells using the new gun. Chloroplasts control photosynthesis. Butow points out this has broad implications for advances in agricultural research.

In terms of animal cell mitochondria, Butow said "getting the genes out and manipulating them has been easy. But it's not been possible before to reintroduce the altered genes to see what happens. Now it's possible to put them back with the gun.

"The gun," explained Butow, "consists of an object that looks like a pipe bomb mounted on top of a vacuum chamber. Spheres of tungsten one micron (millionth of a meter) in diameter are coated with DNA and suspended in a plastic plug inside the pipe. Then a charge of gunpowder is detonated, causing the plug to hit a plate and spray the tungsten spheres into a target dish much like shotgun pellets."

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Many of the cells were destroyed by the blast, he said, but there were a significant number that were implanted with the DNA.

The success with restoring the oxygen-to-energy function with fired-in DNA may pave the way for intervention in a number of diseases, including muscle weaknesses resulting from faulty energy production.

Butow, a member of the Biochemistry Department faculty at UT Southwestern, has been researching the genetics of yeast mitochrondria for a number of years. Because of two tough membranes, it was previously difficult to introduce genetic material inside a mitochondrion. The yeast--ordinary bakers yeast--has about 40 genes in its mitochrondion and some 5,000 to 10,000 in the cell nucleus. This compares to more than 100,000 genes in the human nucleus.

Scientist-philosopher Lewis Thomas noted in his 1974 book, <u>The Lives Of A</u> <u>Cell</u>, "Actually, the suggestion that chloroplasts and mitochondria might be endosymbionts (cooperative organisms) was made as long ago as 1885 . . ." He also suggested, "There is careful restrained speculation on how they got there in the first place, with a consensus that they were probably engulfed by larger cells more than a billion years ago and have simply stayed there ever since."

With the new gun, Butow hopes to research what he calls novel genes that appear to have primitive functions. And he wants to know more about the interaction between the DNA of the cell's nucleus and the DNA of its mitochondrion.

"That's a delicious problem," he said.

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Note: The University of Texas Southwestern Medical Center at Dallas comprises Southwestern Medical School, Southwestern Graduate School of Biomedical Sciences and Southwestern Allied Health Sciences School.