

## GENETICS

Identical animals are found to be not so identical after all; findings suggest genes are not all-powerful

# 64 armadillos threaten a theory

by Barbara J. Culliton



*Williams: Urine and body weight.*

Armadillos come in fours, quadruplet offspring from a single egg, and are endowed with identical genes.

Yet, the quadruplets are often not identical, a fact that calls into question the assumption that genes encased in the nucleus of the cell are the sole determinants of heredity.

In classical theory, inheritance resides only in the genes—the decision-makers that order cells to become blood or bone or armadillo armor—and when genes are identical, so are their owners, whether they are a quartet of armadillos or twin human beings.

The challenge to this theory comes from 64 baby, nine-banded armadillos that deny the identity of genetically identical brothers and raise the possibility that the genes' orders can be modified by the chemical workers assigned to carry them out.

**The challenge** grew out of research that may color the results of decades of scientific experiments which rely on

the genetic similarity of inbred animals. These animals are presumed to be virtually identical because they share a common, limited gene pool, though the identity is not quite that of twins. Inbred animals are so close genetically that one is expected to respond to a drug the same way his cousin does, and pharmacological experiments have been repeated on hundreds of animals as if they were one.

But in 1951, biochemist Roger J. Williams of the University of Texas at Austin observed significant chemical variations in the urine of rats inbred for 101 generations. Pursuing this observation, he found differences up to 60-fold in inbred animals' consumption of alcohol and choice of foods.

The genes were similar, the environment was the same, but the animals were different. Dr. Williams reasoned that factors were at work other than those of classical genetics and environment which he apparently had under

control. He decided to carry his experiment to animals that are in fact genetically identical.

Armadillos, with their habit of always producing four young from a single zygote, were ideal subjects.

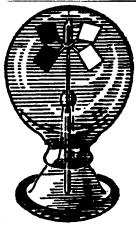
**Dr. Williams**, working with Dr. Eleanor Storrs Burchfield, collected 62 adult female armadillos who produced 249 infants—61 quadruplet sets and one litter with a fifth wheel—of which 16 sets of four were used.

The 64 were sacrificed at birth and tested for 20 parameters including body weight, organ weight (including adrenals, brain, heart, kidney and liver) and levels of various chemicals present in these organs. Each animal was compared to his litter mates.

The ostensibly identical quadruplets showed differences ranging from 2- to 140-fold.

Although the intrauterine environment may be partially responsible for the differences, these variations are too

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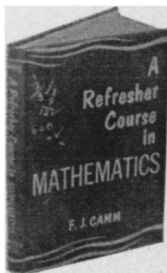
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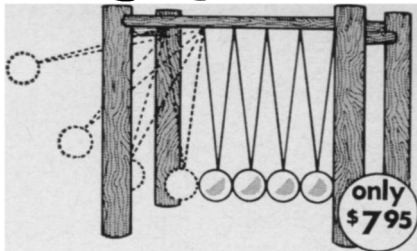
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*Dr. Burchfield: Don't throw out the earlier results, but add the new.*

marked to be attributed to such factors as position in the uterus or the amount of blood supplied to the fetus, Dr. Williams says. The explanation, he believes, can be more accurately attributed to something in the cytoplasm, the fluid surrounding the nucleus of the egg cell from which the animals developed.

The initial single egg that divides into four parts, he explains, is asymmetrical. Information-carrying genes reside on the deoxyribonucleic acid macromolecule within the nucleus of that egg. When it divides, divisions of the double DNA helix carry identical complements of genes to each of the four new cells. But because the egg is not symmetrical, its cytoplasmic components do not disperse equally.

Therefore, each new cell, which will grow into an armadillo, contains identical genes but varying quantities of cytoplasmic components. Those components, Dr. Williams suggests, could affect the genes' ability to express themselves and thereby account for the ultimate differences in the newborns.

The foundation of modern genetics is the Watson-Crick premise that genetic information bound into DNA is the basis of heredity, bearing responsibility for the creation of new differentiated cells and organisms. And DNA, scientists originally thought, existed only within the nucleus of cells. In 1957, Sir Francis Crick wrote, "DNA is always associated with chromosomes [in the nucleus], and not with any other part of the cell."

Since then, scientists working with microbial organisms have found evidence of extra-nuclear DNA as well as evidence of other cytoplasmic components that may play a role in heredity by affecting the action of nuclear DNA. The work on armadillos lends further cre-

dence to this idea and is particularly significant because it involves complex mammalian cells rather than simple microbes.

Locked within each DNA molecule are blueprints for making every kind of cell, but when the molecule issues its instructions, it does so selectively, sometimes ordering construction of liver cells, sometimes blood, sometimes skin.

Something therefore must be controlling this selective process of differentiation, something other than the nuclear DNA itself.

If nuclear DNA were the sole determinant of heredity, in Dr. Williams' view, there would not be an infant armadillo with more liver cells than his supposedly identical brothers. The simplistic answer provided by the Watson-Crick DNA theory, he says, is based on work in single-celled organisms. These make the same kind of cell over and over again and do not offer all the answers for more complicated mammalian genetics.

There are tentative explanations:

**Mitochondria**, energy-producing bodies in the cytoplasm surrounding the nucleus, may influence the expression of nuclear DNA. If, for example, the cytoplasm of some cells contains more mitochondria than others, those cells would have more biochemical energy for making new proteins.

The full story has yet to be written, but scientists now know that mitochondria, as well as nuclei, contain DNA and are able to reproduce themselves quite independently of the nuclear material.

Mitochondrial DNA presumably contains the instructions needed to make at least the structural proteins that hold mitochondria together. It may have other informational capacities. There is preliminary evidence that mitochondria

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can produce RNA, adding another link to the chain of suppositions that all cellular manufacturing activity is not controlled by nuclear DNA.

**Regulator proteins** produced within the cytoplasm of bacteria also affect their DNA expression. These proteins turn genes on and off. Though they have been identified by three Harvard University scientists, their existence was first postulated by two Nobel Prize-winning Frenchmen, Drs. Jacques Monod and Francois Jacob.

At Harvard, Drs. Walter Gilbert, Benno Muller-Hill and Mark Ptashne found two proteins, one large and one small, that can repress, or turn off, certain genes in *E. coli*, the common intestinal bacterium. The repressor proteins, Dr. Ptashne says, bind to strands of DNA and block the expression of certain messages by barring the way when RNA molecules come along to pick up instructions. The extension of bacterial genetics to mammalian systems, however, is a long leap.

**Although every cell** contains the genetic information for making every other kind of cell, scientists estimate that about 85 to 95 percent of that information is locked in, blocked by a repressor, and hence unable to give out more than a few specific types of directions. Intricacies of the system have yet to be unraveled, but the genetic importance of cytoplasm is clear.

While scientists await the unraveling, they weigh the armadillo's serious implications to existing research patterns. Called into question are such research techniques as twin studies and results of experiments based on the assumption that inbred animals are very close to being identical. Dr. Burchfield, now at the Gulf South Research Institute in New Iberia, La., says the results of the armadillo experiments and evidence of extra nuclear factors in inheritance certainly "have a bearing." But it would be an inappropriate jump to discard the results of such studies, because the genes in the nucleus, even if they are not the sole determinants of heredity, certainly exert the dominant influence. Identical twins and highly inbred animals, even if they are not as much alike as they were thought to be, are still much more alike than unrelated animals. The new evidence is just one more thing to be considered.

What about predictions, made by Dr. Marshall W. Nirenberg, one of this year's Nobelists, and others, that within a quarter of a century man will be able to manipulate his genetic constitution, eliminating disease and altering his development by genetic surgery with synthetic genes? Evidence that there are factors besides nuclear DNA appears to complicate even further the future of genetic engineering. ◇



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