New evidence for epigenetic inheritance

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Mouse Finding Violates Laws of Heredity

DNA has long been considered the sole arbiter of heredity. New research seems to show, however, that its lesser known cousin, RNA−−previously thought only to facilitate the creation of proteins as dictated by the genetic code−−may itself pass traits down through the generations. Fifty years ago, researchers observed that the factors controlling the amount of purple coloring in certain corn kernels deviated from the accepted laws of genetics. Genetic variants that should have been bred out could sometimes exert their empurpling effect in subsequent generations. Dubbed paramutation, the phenomenon remained unexplained.

In experiments with mutant mice, Minoo Rassoulzadegan of Inserm in France and his colleagues observed a similar phenomenon. A mutation in the Kit gene is known to produce white patches of fur on the toes and tails of brown mice. The researchers bred together mice that each carried one normal copy of the gene and one aberrant copy−−that is, they were heterozygous. Mice that inherit two normal copies of the gene should not exhibit this coloring. But oddly enough, the team found that a large percentage of the resulting mice in their study that inherited only normal copies of the gene from their heterozygous parents did in fact have the white spots.

Searching for an explanation, the scientists found that the mutant mice bore unusually low levels of regular RNA interspersed with unusually large versions of the messenger molecule. Further, they noticed that this RNA found its way into mouse sperm. And when they injected the RNA into developing embryos it produced the telltale patches in nearly 50 percent of the offspring, who in turn passed the trait along to their offspring. Control mice occasionally exhibited white spots as well, though they rarely passed the trait to subsequent generations.

The exact mechanism by which RNA transmits the spotting trait to progeny in the absence of the gene that causes spotting in the parent remains mysterious. But the finding does challenge the existing understanding of

genetics, and it may have implications for humans. In a commentary accompanying the report, Paul Soloway of Cornell University remarks: "A particularly intriguing possibility is that such RNAs regulate other non−genetic modes of inheritance, such as metabolic or behavioral imprinting."

The research and commentary appear in today's Nature. −−David Biello

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