

Gene makes fetal skin become watertight

While growing in a fluid-filled womb, safe from most infectious microbes, a fetus has little need for a protective coating. Yet the outside world is a far drier and more dangerous place. About a month before it's due, a human baby prepares for its new environs by transforming its skin into a watertight barrier that also keeps out bacteria and viruses.

By disabling a single mouse gene, scientists have now created a strain of mice unable to develop such a life-preserving skin barrier. Study of the animals, which die less than a day after birth from shock brought on by rapid dehydration, should help investigators identify other genes that play a role in barrier formation.

The mutant mice may also point the way toward drugs to help human infants born months before this crucial shield takes effect. These premature babies face a high risk of infection and dangerous weight loss due to dehydration.

"If you could pharmacologically intervene and accelerate [skin-barrier formation], you could improve survival," says dermatologist Dennis Roop of Baylor College of Medicine in Houston.

Scientists compare the skin barrier to bricks and mortar. The bricks, nearly indestructible aggregates of protein, collectively form a scaffold called the cornified envelope. Cells in the uppermost layer of skin create this envelope as they die.

Lipids, which are fatty molecules, then provide the mortar that fills the spaces in the scaffold.

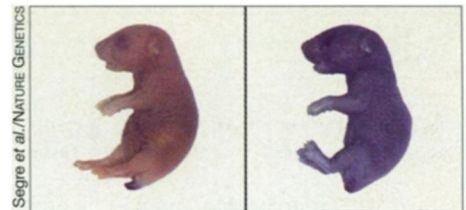
The gene for a protein called Klf4 appears to serve as a switch that turns on barrier formation, Julia A. Segre, Christoph Bauer, and Elaine Fuchs, all of the Howard Hughes Medical Institute at the University of Chicago, report in the August NATURE GENETICS. Klf4 belongs to a family of DNA-binding proteins, each of which regulates a different set of genes.

Investigators knew that the gene for Klf4 is extremely active in maturing skin cells, but they didn't know the protein's exact function. The Chicago team addressed that issue by creating mice that have a mutation in the Klf4 gene.

The resulting newborns looked normal, but all died within 15 hours of birth. The researchers observed that the pups failed to feed, but that didn't explain their early deaths because newborn mice can survive for a full day without feeding.

Suspicious that the mutant mice had a defective skin barrier, the researchers dipped the animals and normal newborn pups in a blue dye. The dye barely stained the normal mice but suffused the newborns lacking Klf4, a sign that the skin barrier was absent in those rodents.

By measuring the skin's ability to conduct an electrical current, which increases



A blue dye barely stains a normal newborn mouse (left) but penetrates into a mutant pup with an ineffective skin barrier (right).

es with the amount of water in the tissue, Segre and her colleagues showed that the mutant mice were losing significant amounts of water through their skin. In people, a similarly dramatic loss of water would lead to kidney shutdown, shock, and ultimately death.

Beginning their search for genes regulated by Klf4, the investigators have already found three that encode proteins of the cornified envelope. In the mutant mice, these genes are abnormally active, leading to the formation of a distorted envelope.

The investigators now hope to use the rodents to identify drugs that can trigger skin-barrier formation in fetuses and newborns. Today, physicians have few options. They can prescribe potentially harmful growth-stimulating hormones to women they suspect will deliver prematurely or, after a baby is born early, place the infant in a humidified incubator and slather its skin with Vaseline. —J. Travis

Kansas cuts evolution from curriculum

In a dramatic revision of science education in the state, the Kansas Board of Education voted 6-4 last Wednesday to remove almost all mention of evolution from its required curriculum. If the decision stands, one of science's central concepts will be cut from state assessment tests at all grade levels. It will become optional for teachers to cover the origins and history of life on Earth, as well as principles that require Earth to be older than creationists believe. These would include theories of the Big Bang, geologic time, and plate tectonics.

Although other states, including Nebraska, New Mexico, Alabama, and Arizona, have taken steps to curtail the teaching of evolution in recent years, none has gone as far as Kansas, says Molleen Matsumura of the National Center for Science Education in El Cerrito, Calif.

"These are some of the most thorough changes we've seen, across multiple curriculum areas," Matsumura says. Although a 27-member science committee wrote a draft curriculum containing evolution, the Kansas board established the new policy when it removed "pages and pages of material" that the committee had recommended for

statewide science tests, she adds.

According to Tom F. Willis of the Creation Science Association for Mid-America in Cleveland, Mo., which helped the board change the curriculum, because evolution cannot be reproduced in a laboratory, it should not be taught "as though it is the only theory believed by sane individuals." He adds, "I absolutely feel that [the new curriculum] would improve science and would improve the honesty with which it is taught."

"We are talking about a complete misunderstanding of how the sciences are integrated," University of California, Berkeley paleontologist Kevin Padian says of the board's action. "It's so absurd to pretend that you can rope off one part of science—especially one such as evolution, which is the central organizing theory of biology—and think that it won't have ramifications."

Many scientists fear that without being required to teach evolution, teachers may bow to local pressures to skip it, leaving students ill prepared for college. "In a lot of small, rural Kansas towns, the science teacher is the most trained person there, so it's just that one person against an entire community, sometimes," says Brad

Williamson, a high school biology teacher in Olathe, Kan.

The new curriculum may be short-lived, however. Four of the board members who voted against evolution will be up for reelection in November. Many scientists hope that voters will oust the four and elect a new board to restore evolution to the curriculum.

"There's a great outrage in the state right now," says biologist Helen M. Alexander of the University of Kansas in Lawrence. "The governor came out against [the new curriculum]. The presidents of the universities came out against it. In the long run, I would be surprised if it stayed." Even so, she says, if teachers skirt the subject of evolution, "the net effect is that children won't be exposed to it, and the decision will have long-term effects on science education."

Following the decision, the American Geophysical Union called for scientists to become more involved in their local school districts. Matsumura agrees that scientists are often best equipped to fight efforts to pull evolution out of the classroom. She says, "People talk about the truth winning out in the end, but truth does not win all by itself. It wins with committed exponents." —S. Carpenter