In This Issue . . .

Gina Kolata

Growing Hair Follicles in Culture

For years, says Stuart Yuspa of the National Cancer Institute, his group has been trying to develop a cell culture system for hair follicles. Now, at last, they have succeeded and they are starting to use their system to study carcinogenesis and differentiation. He and George Rogers, Nadine Martinet, Peter Steinert, Peter Wynn, Dennis Roop, Anne Kilkenny, and David Morgan report on their culture method in this issue.

Yuspa explains that the group undertook the hair culturing project for two reasons. First, he says, the work was done in the cancer research laboratory and hence the interest in models of carcinogenesis. The mouse skin cell tumors are thought to resemble tumors of epithelial cells in humans, and hair follicles are likely to play an important role in the genesis of these mouse tumors. For example, the hair follicle releases enzymes that activate and deactivate chemical carcinogens, and when hair follicles are in a resting state, the mouse skin is most susceptible to chemical carcinogenesis. In addition, says Yuspa, "it is possible that one class of tumors arises from hair follicle cells."

The second reason why the investigators wanted a hair follicle culture system was to study the regulation of normal differentiation. Hair follicles go through repeated cycles of growth, which means that researchers studying these follicles can investigate the entire complex process of differentiation. "There is just nothing else I know that does that after embryogenesis," says Yuspa. But what controls these differentiation cycles "is totally unknown," he adds.

The culture system that Yuspa and his colleagues developed is one in which isolated hair follicles are grown in a collagen matrix. So far, the researchers have used this culture system to establish that the growing follicles release collagen-degrading enzymes—a finding that may explain how follicles expand into the dermis. They also demonstrated that since the cultured hair follicles retain their biologic function, the investigators can graft the follicles back onto mouse skin and the skin grows hair. But, says Yuspa, "we still lack clear-cut evidence that the follicles are making all the hair proteins." Nonetheless, Yuspa is greatly encouraged by his group's success in developing the follicle culture system. "We are excited," Yuspa says. "We think it's an advance in the field."

Blistering in Epidermolysis Bullosa

Blistering in epidermolysis bullosa may be due to the effects of prostaglandins, according to a group at the Efamol Research Institute in Nova Scotia and at the Rockefeller University. Their results, reported in this issue, are by no means a complete explanation of the disease but may offer new clues to its pathogenesis.

The work, which was done by Stephen Cunnane, who is now at the University of Toronto, E. Trevor Kent and Kelly R. McAdoo of the Efamol Research Institute, and Dorothea Cladwell, Andrew Lin, and Martin Carter of the Rockefeller University, began when Cunnane saw EB patients on a television show. "The condition of their skin reminded me of an essential fatty acid deficiency," he says. When people are deficient in linoleic acid and alpha-linolenic acid, they develop blisters and scabs that resemble those of EB. They also tend to have growth retardation and alopecia, which are typical of EB as well. So Cunnane asked his colleagues whether children with EB might have diets deficient in these essential fatty acids.

Kent located a child with EB who lived in Nova Scotia and the research team asked the parents if they could examine the child. They also asked the parents to keep a record of what the boy ate. The results, says Cunnane, were intriguing. Because children with EB have blisters inside their mouths, they have trouble eating. The child that the Nova Scotia researchers studied "seemed to survive on jello and ice cream," Cunnane remarks.

So the investigators suspected a fatty acid deficiency or a zinc deficiency, which also can produce EB-like symptoms. In collaboration with the researchers at Rockefeller University, they compared plasma and erythrocyte fatty acid profiles of children with EB with those of normal controls. They found that the children with EB had normal fatty acid and zinc profiles, although, says Cunnane, "where they get their fatty acids from, I don't know." But they did find that the children with EB had elevated levels of arachidonic acid in the plasma and erythrocytes. Arachidonic acid is synthesized from linoleic acid and one of the major metabolic products of arachidonic acid is prostaglandins. It is known that when prostaglandins are injected under the skin, the skin blisters. Moreover, the blisters look like the blisters of EB.

When EB cells are grown in culture, they produce large quantities of prostaglandins. It is possible that patients with EB, who have high levels of arachidonic acid in their plasma and red blood cells, use this arachidonic acid to synthesize prostaglandins in the skin which in turn cause blistering. In support of this hypothesis, the researchers at the Efamol Institute and the Rockefeller University report that children with EB who are being treated with diphenylhydantoin have lower levels of arachidonic acid in their plasma and erythrocytes and also have less blistering. Of course, Cunnane notes, the story is still unfinished. "We can't determine why there should be an increase in arachidonic acid and in prostaglandins in EB patients," he says.

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