IS STICKINESS OF THE UPPER SURFACE OF AN ATTACHED EPITHELIUM IN CULTURE AN INDICATOR OF FUNCTIONAL INSUFFICIENCY?

Dr. Prop (3) wonders if a real discrepancy exists between his own observations (5) and those of DiPasquale and Bell (1) and ours (2). The point at issue is whether the upper surface of an attached epithelium can be used by other cells as a substratum on which to stretch out and move in the normal way. On the basis of our respective observations and the published work of others, both DiPasquale and Bell and we are prepared to suggest that the upper surface of an attached epithelium is generally nonadhesive for other cells. This differentiation is seen as a basic property of functional germinal epithelia. Further differentiation between the two surfaces in terms of absorption, secretion, excitability, ciliation etc. confers the characteristic functional properties of the various epithelia. It appears that many epithelia exhibit a nonadhesive upper surface in culture, and that Dr. Prop has discovered an exception in a hormone-dependent tissue.

Dr. Prop observes a stratification within thick cultures established from mixed cell suspensions from mouse mammary glands; the fibroblastic cells are located on the upper surface of an epithelium attached to the floor of the culture vessel. In the presence of hormones, the fibroblasts retreat from the epithelial surface and collect into "ridges" (Fig. 2 of Visser et al. [5]). The appearance is very similar to that of outgrowth cultures of human embryonic kidney fragments. Dr. Prop's letter has stimulated us to take a further look at these cultures in order to see just how the two cell types interact. We have embedded 6-day cultures in Epon and cut 1-μm sections. Fibroblasts are either under the epithelium or grouped into cables five to six cells thick extending over the epithelium and anchored to the plastic. There is a space between the cables and the epithelium; where a cable anchors to the plastic the epithelium stops. The fibroblasts do not adhere, therefore, to the upper surface of the epithelium. If mammary gland cultured with insulin and prolactin shows the same architecture, and if the figure of Visser et al. is suggestive, then the behavior of fibroblasts is in line with the predictions of DiPasquale and Bell and of ourselves.

The absence of hormone allows the fibroblasts in mammary gland cultures to colonize actively the upper surface of the epithelium; thus, after hormone withdrawal, the fibroblasts in the ridges disperse. Such a rearrangement has not been observed in kidney cultures.

The conclusion that we draw from these observations is that mammary gland cultures conform to the general rule put forward by DiPasquale and Bell and ourselves only in the presence of hormones. Unfortunately, we are not told whether the hormones render the fibroblasts unable to stick to the epithelium, or the epithelium nonadhesive to the fibroblasts. In the light of our own observations, it would be reasonable for us to think in terms of the latter alternative.

In forming our own view of the situation in hormone-less cultures, we note that milk protein production in vitro is induced by hormones (4). This suggests that in the absence of hormones the cultured mammary epithelium is nonfunctional, and that nonadhesivity of the upper surface results from a hormone-dependent membrane change.

Dr. Prop envisages the hormones affecting cell surfaces, but in a quantitative manner "by affecting the equilibrium between the different tendencies for attachment," and he discusses the appropriateness of quantitative measurements of these tendencies and the forces that they generate. We, on the other hand, would stress the possibility that the effects of hormones on the epithelial surface may be highly nonlinear, triggering a yes/no switch.

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