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We salute Schering Corporation for their contribution to the Endowment Fund and for their continued support of clinical and investigative dermatology.

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In This Issue . . .

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Homeobox Gene Expression Is Found in Epithelia Destined to Become Skin Appendages

Noveen *et al* (p. 711) find that expression of *Msx-1* and *Msx-2* homeobox genes are early markers for the formation of epithelial appendages. Homeobox genes are transcription factors that contain a conserved DNA sequence called the homeobox. They were first discovered in *Drosophila*, in which mutations resulted in homeotic transformation; that is, one body part was transformed into another, e.g., antenna into leg. The vertebrate homeobox genes are categorized into several classes, including *Hox*, *POU*, *en*, *D11*, and *msh*. During embryogenesis in mouse and chicken, *Msx-1* and *Msx-2* have been found to be expressed in several sites including neural crest, pharyngeal arches, eyes, limb buds, heart, and teeth. The changing expression of homeobox genes in these organs in association with epithelial-mesenchymal interactions suggests that these genes may play a

role in embryonic induction. In addition, the *Msx-1* gene has been shown to play a role in regulating growth and differentiation of cells in culture. In studies of the expression of these two *msh* class homeobox genes during development of embryonic chicken skin, Noveen and his colleagues found that both genes are expressed in early epithelial placodes for skin appendages and in the growing feather bud, but not in the interbud epithelia. The follicular expression of both genes was in the region of continuous cell proliferation, and when feather bud growth was inhibited, the expression of both genes was reduced. The results indicate that the function of *Msx* genes in the formation of epithelial appendages may be twofold: they make epithelial cells competent to become skin appendage cells and they also maintain their potential for growth.

Plakoglobin Binding by Human Desmoglein Requires a Specific Intracytoplasmic Segment

Roh and Stanley (p. 720) report that a highly conserved region in the carboxy terminus of the intracytoplasmic-cadherin-like subdomain in desmogleins is required for the localization of plakoglobin to desmosomes. The major cell adhesion junction in epidermis is the desmosome. The molecules making up the desmosome have been divided into two broad categories, plaque proteins (plakoglobin and desmoplakin) and transmembrane glycoproteins (desmogleins and desmocollins). Desmogleins may be particularly important in epidermal cell adhesion. First, part of the protein crosses the cell membrane, making it available outside the cell to mediate cell adhesion. Second, specific desmogleins have been found to be involved in diseases in which epidermal cells detach from one another, *Dsg 1* in pemphigus foliaceus and *Dsg3* in pemphigus vulgaris. In addition, both desmogleins have been shown to bind plakoglobin, and such

binding may be critical for assembly or stability of desmosomes. To identify the domains of human *Dsg* that are necessary for plakoglobin binding in human keratinocytes, Roh and Stanley constructed expression vectors that contained chimeric cDNAs encoding the extracellular domain of mouse E-cadherin and the intracytoplasmic (IC) domain of human *Dsg3*. They made several constructs, each with more of the *Dsg 3* 1C subdomain deleted, and transfected a keratinocyte line (HaCat cells) with these constructs. Then, using a mouse E-cadherin antibody, they precipitated the chimeric protein. Their data show that although the full complement of desmoglein-specific IC subdomains is not necessary for plakoglobin binding, part of one of these subdomains, the IC-cadherin-like subdomain, is critical. Additionally, they show that this interaction between plakoglobin and *Dsg 3* is direct and does not depend on other cellular factors.