Clinical Snippets

Lowell Goldsmith, UNC-CH, Chapel Hill, NC USA

THE FARMER’S WIFE

In the nursery rhyme the farmer’s wife runs after mice with a carving knife and alters a mouse’s phenotype. In the twenty-first century she uses homologous recombination to eliminate important molecules from the mouse and its progeny; in the case of Uitto and his co-workers (p. 1237), the molecule is desmoglein 3. This cadherin contributes to the attachment of basal cells to each other in both the epidermis and oral mucosa. The mutation the authors created allowed extracellular portions of the molecule to be present; but not most of the intracellular portion. The defect led to altered shape and eventual disadhesion. Identifying intracellular modulators of adhesion can lead to new concepts for treating epidermal blistering diseases.

THE INSIDE SCOOP ON DESMOGLEINS

Uitto cut it out. Hanakawa (p. 1231) and colleagues instead inserted intracellular portions of desmoglein 1 (Dsg1) and desmoglein 3 (Dsg3) into an epidermal cell line (HaCaT), allowing these molecules to interact with their normal Dsg targets. Dsg1 inhibited keratin insertion into cell-contact sites and disrupted desmosomes; Dsg3 did not. We should expect continued emphasis on the role of the intracellular functioning of adhesion molecules.

JUMP OVER THE CANDLESTICK

One model of dermatomyositis (DM) is that light damages cells and releases antigens that lead to an immune response. One of the stages is the clearing of dead, apoptotic cells, and this clearance involves a protein which binds the sugar mannose; MBL (mannose-binding lectin) is the focus of this project by Werth and colleagues. The regulatory portion of this protein (its “promoter”) has several genetic variants. Two variant alleles were associated with DM and not with lupus erythematosus. These variants were associated with low levels of MBL and hence could be hypothesized to allow apoptotic cells to persist, have antigens more available for stimulating the immune system and begin or perpetuate the allergic reaction. Twenty percent of normals have the variants and studies of other disorders such as polymorphous light eruptions might be interesting (p. 1394).

THIS LITTLE PIGGY WENT TO LABORATORY

Translating knowledge from molecular and cellular studies to the intact organism and eventually into new therapies for people is the challenge for many investigators. The regulation of transcription (message RNA synthesis) is commonly the final pathway in producing new proteins or decreasing the production of already synthesized proteins. As Dr. Lin and her collaborators demonstrate, a cornucopia of agents including natural extracts from traditional Chinese medicine (8-methoxy psoralen are able to affect a key transcription factor MITF, microphthalmia associated transcription factor), both in melanocyte culture and on the skin of Yucatan swine (p. 1330). New agents for altering melanocyte function in the clinic are always needed. This may be a pathway for developing such agents.

BAA, BAA, BLACK SHEEP

Luxurious hair in the proper body location is the goal of many humans. Sheep seem to do it without any effort. Hair research has been enlivened in the past decade by the identification of the major sources of renewing cell populations of stem cells for the follicle. Plucking is used in many animal models of hair growth to stimulate growth, although clinicians tell patients, “Don’t worry – plucking doesn’t cause growth.” The cellular details of these studies by Dr. Kizawa and his associates, including the role of cell death (apoptosis) in the early stages of this process, are described on p. 1310.