

## Stem cells of a feather flock together

Hair stem cells have been studied extensively in recent years; however, less is known about feather stem cells, which evolved independently 155–255 million years ago. Interestingly, common precursor cells generate different feather morphologies. Chuong and colleagues mapped the activities of stem cells in feather follicles during growth and molting phases. Slow-cycling long-term label-retaining cells (LRCs), transient amplifying cells, and differentiating keratinocytes were identified in the feather follicles, as they are in hair follicles. LRCs that appeared in the collar bulge niche were able to migrate and become incorporated keratinocytes upon transplantation. Additionally, several similarities with the hair follicle were observed, including localized proximal growth zones, essential dermal papillae for cyclic regeneration, and known signaling pathways. These findings support the idea that LRCs and transient amplifying cells populate different niches depending on their microenvironment and that the bulge stem cells are critical for maintaining and regenerating episodically renewing organs such as feathers. (*Nature* 438:1026–9, 2005)

## PF antibodies cop a plea

Skin blistering in patients with pemphigus foliaceus (PF) results from the generation of immunoglobulins (IgG) against the desmosomal cadherin family members, especially desmoglein 1 (Dsg1). These antibodies may block cell adhesion via direct steric hindrance or by activation of additional cellular mechanisms. Drenckhahn and colleagues addressed this quandary by using laser tweezers and atomic force microscopy to explore the cellular dissociation at the single-molecule level. Although treatment with IgG from PF patients disrupted cell association, treatment of the cells with the antibodies did not prevent the interaction with Dsg1-coated beads. In addition, the anti-Dsg1 antibodies did not preclude interaction between Dsg1 molecules in a cell-free system. Taken together, these results strongly suggest that autoantibodies do not directly block the interaction between keratinocytes, suggesting that activating signaling pathways may cause pathology. (*J Clin Invest* 115:3157–65, 2005)

## Using the “omics” to understand disease

Typical linkage analysis to associate genes with complex diseases has definite limitations. The literature is filled with so-called “omics” data (genomics, transcriptomics, proteomics, and metabolomics) just waiting to be used for complex-disease research. Recently, Zhou and colleagues proposed a systems biology approach to identify genes involved in the development of diseases. This approach uses multiple data

sets to construct a genetic network of candidate genes through mathematical equations. Differentially regulated genes can then be identified through examination of normal and abnormal samples. Moreover, perturbations of the network using RNA interference empirically probe the predicted genetic network. The authors used this approach to uncover affected genes in systemic sclerosis and were ultimately able to identify six differentially expressed genes and ten genes involved in transforming growth factor- $\beta$  signaling. This systems method promises a more comprehensive means of investigating the etiology of complex diseases. (*FEBS Lett* 579:5325–32, 2005)

## Plants need sun protection too

Although exposure to UVB in sunlight is essential for photosynthesis, plants must protect themselves from harmful rays that can cause DNA damage and generate reactive oxygen species. At non-damaging levels, UVB exposure promotes expression of a wide range of genes essential for absorbing the light, mending oxidative stress, and repairing DNA damage. Typical photoreceptors and signaling molecules are not used in this response. In a recent study by Jenkins and colleagues, a genetic screen in *Arabidopsis* identified UV RESISTANCE LOCUS 8 (UVR8), which responds specifically to UVB exposure and effectively regulates the expression of a range of genes (at least 72) involved in UVB protection. In particular, UVR8, a chromatin-associated protein, controls the expression of *HY5* (ELONGATED HYPOCOTYL 5), which is a key effector of this signaling pathway and is clearly required for plant survival during UVB radiation. Thus, a new plant UVB-specific signaling pathway has been identified that coordinates the protective gene expression program. (*Proc Natl Acad Sci USA* 102:18225–30, 2005)

## In through the sweat glands

Recessive mutations in a gene encoding a transmembrane conductance regulator (*Cftr*) cause cystic fibrosis (CF). Gene therapy efforts have focused on combating the characteristic abnormal airway secretions, chronic infection, and inflammation in the lungs. Typically, gene therapy vectors are studied in cultured cells and animal models; however, *Cftr* knockout mice do not display the pulmonary pathology of human CF patients. Recently, Hu and colleagues demonstrated helper-dependent adenoviral vector transduction to human sweat glands. *Cftr* was delivered to and expressed in the target epithelial cells in the lumen of sweat glands. Disperse treatment to disrupt the basement membranes improved the delivery and expression, suggesting that this membrane is an important barrier to transduction. Translation of this finding to clinical settings would be exciting, as the more convenient and safe sweat gland transduction may be achieved by microperfusion. This delivery method may allow testing of particular gene therapies on individual patients before administration of vectors to affected organs. (*Gene Ther* 12:1752–60, 2005)