pendent on IL-3 for survival[3]. What is the nature of the receptors expressed by pDC_2 that are involved in the interaction with different viruses, and what is the role of ILT3, which may inhibit DC functions? What are the effects mediated by virus on pDC_2 function, differentiation and maturation? Can, for example, persistent viruses like CMV or HIV escape immune surveillance by subverting pDC_2 function and/or maturation? Do pDC_2 secrete any other principal cytokines? And finally, what is the function of pDC_2 in the context of tumor immunity? Do tumor cells block IFN-α release by pDC_2 to escape immune surveillance, or could the type 2 T-helper cell responses induced by mature DC_2 be favoring tumor growth? Finding answers to all these questions will open new exciting research avenues that will increase our understanding of the development and maintenance of protective immunity.

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Downless is a tumor necrosis factor-like receptor

First described by Darwin in 1875 as a condition affecting the 'toothless men of Sind'—members of a Hindu kindred from the Hyderabad region of India—hypohidrotic ectodermal dysplasia (HED) is characterized by abnormal development of the teeth, hair and sweat glands.

Three mouse lines, Tabby (*Ta*), Crinkled (*cr*) and Downless (*dl*), show the same phenotype as HED, and Overbeek and colleagues have now cloned the *dl* gene using a classic positional cloning approach, as described in the August issue of *Nature Genetics*.

They report that the *dl* expression pattern changes from being uniform in the basal cells of the epidermis to being restricted to placodes during follicular morphogenesis.

The figure shows *in situ* hybridization of *dl* on an Ove951 mouse embryo at day 15. Epidermal placodes begin to form on the trunk by day 14, and distinct waves of new follicle formation occur until a few days after birth. Placodes are clearly visible as scattered, regularly spaced dots. The low level of expression in the surrounding cells suggests that a complex form of inductive and inhibitory signals is responsible for epithelial patterning.

Based on sequence similarities, the protein encoded at the *dl* locus is thought to encode a tumor necrosis factor-like transmembrane receptor. In fact, Tabby cDNA has been cloned recently, and sequence analysis shows it has homology to the tumor necrosis factor family, indicating that the product of *Ta* could be a *dl* ligand. Moreover the human homolog of *Ta* has been found mutated in the X-linked form of HED. A new signaling pathway responsible for cell induction and hair follicle cell fate seems to emerge.

In the same issue of *Nature Genetics*, Monreal *et al.* report the identification of *dl* human homolog mutations in three HED families. So now the race is on to clone Crinkled.

Beatrice Renault

Amyloid-β vaccine for Alzheimer Disease

Amyloid beta (Aβ) peptide, a 40-42 amino acid protein cleaved from the amyloid precursor protein (APP), is a main constituent of the amyloid plaques found in the brains of Alzheimer Disease (AD) patients. Much debate has revolved around the question of whether Aβ is part of the biochemical process that causes the loss of function associated with AD or whether it is simply a by-product of the disease pathology.

In the July 8 issue of Nature, Shenk *et al.* report new a tool that may be useful in answering this critical question. They describe the immunization with $Aβ_{42}$ of PDAPP mice (a transgenic strain that overexpresses the mutant human APP) and show that this "AD vaccine" prevents and even reverses Aβ plaque formation and other typical AD-like neuropathologies.

In an accompanying News and Views, Peter St. George-Hyslop points out that this mouse vaccine system can now be used to test whether depletion of amyloid plaques is accompanied by a reduction in the behavioral and neurophysiological symptoms of AD. Perhaps of even more interest to many biomedical researchers is the question of whether this $Aβ_{42}$ immunization approach is feasible in humans.

Kristine Novak