11 From Classical Mouse Models of Psoriasis to a Spontaneous Xenograft Model Featuring Use of AGR Mice

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Psoriasis is chronic inflammatory skin disease (Krueger 2002) with a considerable socioeconomic burden. The quality of life of patients suffering from psoriasis is severely impaired (Ashcroft et al. 1999). The pathogenesis of this common disease is still poorly understood. Furthermore, current treatment options are limited, cumbersome, and time-consuming or have considerable side effects. Progress in defining the cause of psoriasis, as well as developing new treatment approaches, is thus urgently needed. Major progress in these areas critically depends on the availability of a relevant animal model of psoriasis (Schon 1999). This chapter briefly reviews current mouse models of psoriasis, and introduces a new xenotransplantation model, the so-called AGR psoriasis mouse model. The basis of any discussion related to this topic begins with the definition of the ideal psoriasis mouse model.
11.1 What Defines the Ideal Psoriasis Mouse Model?

Psoriasis is characterized clinically by persistent thick, reddish plaques, typically covered with silvery scales. These clinical features are explained by the pathogenic hallmarks of psoriasis:
1. Epidermal hyperproliferation
2. Presence of numerous inflammatory cells
3. Increased vascularity

An ideal animal model of psoriasis should reflect these clinical hallmarks, and should also display the typical histomorphological patterns of psoriasis such as acanthosis, papillomatosis, and hyperkeratosis. The overwhelming evidence that T cells play a major role in psoriasis should also be a feature of the ideal mouse model. Finally, psoriasis lesions in such a model should be cleared with known psoriasis drugs. An ultimate goal would be that the pharmacologically validated animal model reflects the clinical response in patients. In the following, we review some of the currently available mouse models, and discuss them according to the proposed criteria of an ideal psoriasis mouse model. A synopsis of the mouse models is given in Table 1.

11.2 Spontaneous Mouse Mutation Models

Certain mutations in mice lead to phenotypes reminiscent of psoriasis with scaling and/or reddening of the skin. Mice homozygous for the asebia locus (ab/ab) display scaling of the skin due to epidermal acanthosis and hyperkeratosis (Arundell et al. 1969). The Flaky skin (fsn) model is an autosomal recessive mouse mutation that causes epidermal hyperplasia and inflammation, starting at 2 weeks of age (Sundberg et al. 1997). These mice have additional pathological features such as lymphadenopathy, mast cell accumulation, elevated serum IgE levels, and autoimmune glomerulonephritis. The chronic proliferative dermatitis (cpd) model displays epidermal hyperproliferation, a mixed inflammatory infiltrate, and enlarged dermal blood vessels. Overall these models seem to be useful to study pathogenic events such as epidermal hyperproliferation, but are limited in their