Technology Offer

Ref.-No. M0413

Transgenic mouse model for a pruritus-like skin disease

Introduction

All human species experience pruritus in the course of their life time, distinction between acute itch, which is of a limited time period ranging and chronic pruritus, which lasts for greater than 6 weeks. Due to the poorly understood pathophysiology, the development of effective treatment modalities for pruritus has proven to be particularly difficult. At present, there is no universally accepted, well established therapy regime for pruritus-like skin disease and pruritus therapy varies depending on the underlying etiology.

Because of the lack of an appropriated animal model, pruritus research is often practiced with cell culture systems. However, since development and forwarding of pruritus depend on many different types of cells as e.g. neurons, mast cells or lymphocytes, cell cultures are only partly suitable to disclose processes and signaling involved in pruritus-like skin disease. There exists a need for a new model to study development and treatment of pruritus-like skin diseases for analyzing the molecular and cellular mechanisms underlying the development of itch. Such a model should be useful to design new medicaments for treatment of patients suffering from pruritus and to test the efficacy of such therapeutics in order to improve their healthy situation. The model should be applicable for a simple evaluation in order to predict the responsiveness of a human patient to said medicament and to adjust the treatment regimen.

The Mouse Model

4-1BB transgenic mice show a uniform transgenic overexpression of 4-1BB in basal keratinocytes under control of a keratin 14 (K14) promoter. Beginning at the age of three months, 4-1BB tg mice exhibit hallmarks of human pruritus and develop a pruritus-like skin disease characterized by inflammatory skin lesions at the ears, snout, and neck and an increased scratch behavior. Immunohistology of the lesional skin revealed characteristic hallmarks of human pruritus such as epidermal hyperplasia, irregular acanthosis, fibrosis, collagenosis, and the infiltration of lymphocytes like T cells, mast cells, and eosinophils into the dermis. It could be proven that patients suffering from prurigo or diabetic prurigo exhibit an increased expression level of 4-1BB and 4-1BBL in the lesional skin as compared to a healthy human subject.

Thus, the transgenic animal model overexpressing 4-1BB in basal keratinocytes we provide seems to be well suited for analyzing the molecular and cellular mechanisms underlying the development of pruritus and for evaluating the efficacy of novel therapeutics in treatment of pruritus-like skin diseases.

For further detailed information please contact:

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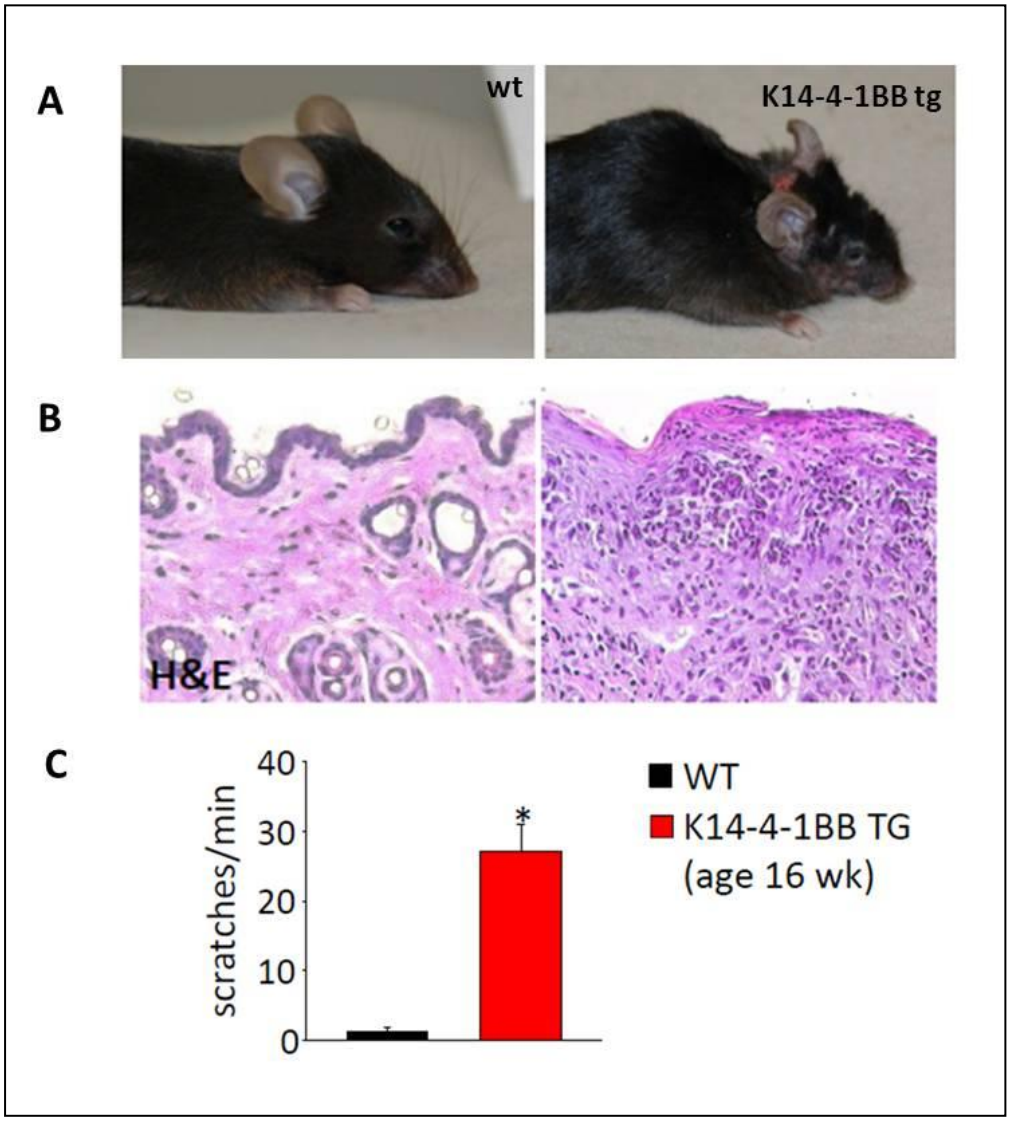

Figure 1: K14-4-1BB transgenic mice develop pruritus-like skin lesions and show increased scratch behavior. (A) Typical skin pathology of wild type and K14-5-1BB transgenic mice at the age of 16 weeks. (B) Hematoxylin and Eosin (H&E) staining of lesional skin from wild type and transgenic mice. (C) Scratching behavior of wild type and K14-4-1BB transgenic mice at the age of 16 weeks, assessed by counting the scratches per minute from n = 10 mice each group over a time frame of 3 x 60 min. *, $p < 0.05$ versus wild type (wt).

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