Technology Offer

Ref.-No. M23/11

TTP/MRP14 double knock out mouse as a model for psoriasis and inflammatory intestinal diseases

Introduction

Psoriasis is a chronic skin disease that affects about 2 % of the population. In humans psoriasis appears especially on the scalp, trunk, ears and genitalia and the skin over bony prominences, like knees and elbows. The exact cause of psoriasis is not known and so far there is no therapy to cure psoriasis. Chronic intestinal inflammatory diseases such as Crohn's disease und ulcerative colitis are characterized by mucosal lesion, stricture formations, abdominal pain and weight loss. To develop new therapies for the treatment of psoriasis, psoriatic arthritis, psoriasis-like symptoms and inflammatory diseases of the bowel, preferably therapies with less side effects and lower costs, there is a need to better understand the mechanisms underlying these diseases. Cell models and in particular animal models are extremely valuable tools therefore. So far there is no animal model reflecting all hallmarks of human psoriasis, including skin, arthritic and enteric phenotypes. Moreover there is no animal models that reflect suitably both phenotypes of psoriasis and phenotypes of inflammatory diseases of the bowel and therefore would be suitable for the investigation of the relationship between psoriasis and inflammatory diseases of the bowel.

In sum, there is a need to provide new means and methods that help to diagnose and/or treat patients suffering from psoriasis, psoriasis arthritis and inflammatory intestinal diseases.

The Mouse Model

We could show for the first time that transgenic animals deficient in the expression of the proteins Tristetraprolin (TTP) and myeloid-related protein-14 (MRP14; S100A9) develop severe psoriasis-like phenotypes and can therefore be used as an animal model for psoriasis and diseases associated with psoriasis. The model overcomes the problems of the prior art by providing an improved model for psoriasis and diseases associated with psoriasis. Unlike the prior art the model of the present invention reflects all major histological characteristics of human psoriasis, mimics psoriatic arthritis and exhibits alterations of the intestine characteristic for patients suffering from psoriasis and/or inflammatory diseases of the bowel. The model is therefore i.a. useful for studying the immunopathogenesis of psoriasis, psoriatic arthritis, psoriasis-like diseases and/or inflammatory diseases of the bowel and for evaluating therapeutic agents for ameliorating or preventing said diseases. Moreover the model disclosed herein is useful for studying the correlation between psoriasis and inflammatory diseases of the bowel.

For further detailed information please contact:

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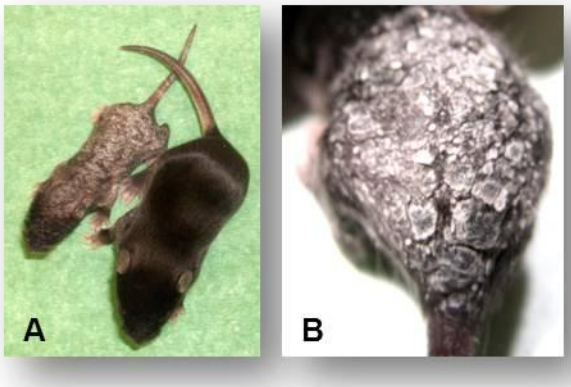

Figure 1: TTP-/- x MRP14-/- (A) and control (B) mouse at day 11. The TTP-/- x MRP14-/- mouse exhibits a highly rigid shell-like skin with widespread scaling and it´s growth is retarded.

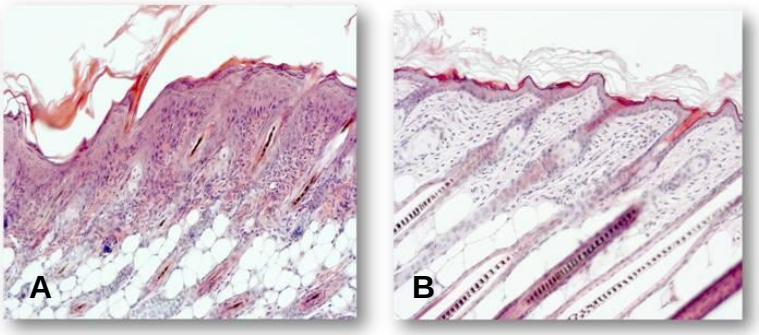

Figure 2: Inflammation in the skin of TTP-/- x MRP-/- mice (day 9) (A) and control (B). Mice were stained with haematoxylin/eosin (H&E). TTP-/- x MRP-/- mice revealed a markedly thickened epidermis with loss of the granular layer, pronounced hyperkeratosis, focal parakeratosis and increased cellularity in the dermis.

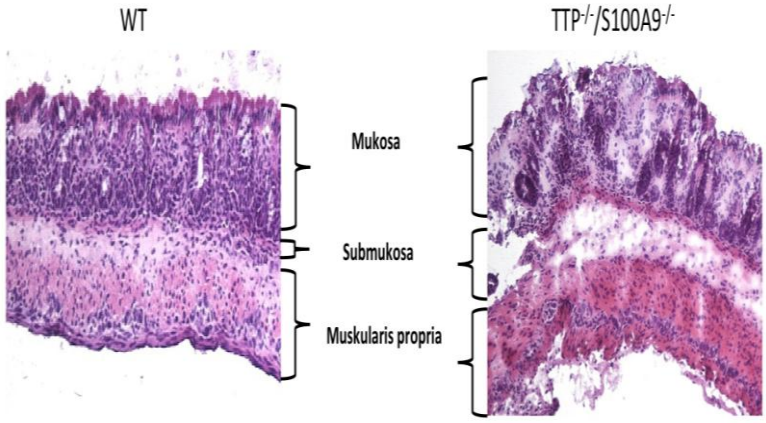

Figure 3: Hematoxilin/Eosin (H&E) staining of colon sections from TTP-/- x MRP14-/- and WT mice. TTP-/- x MRP14-/- mice showed a strong effected epithelial layer with ulcerations and loss of the colon crypt structure. The muscularis propria in the enlarged submocosa and mucosa was infiltrated with inflammatory cells . There were also edematous distensions. This shows that the loss of MRP14 leads not only to a severe psoriatic phenotype but also to an inflammatory intestinal disease.

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