# B6-CAG-LSL-hIL17A-IRES-EGFP

**Strain Name:** B6/JGpt-*Rosa26*$^{em1Cin(CAG\text{-}LSL\text{-}hIL17A\text{-}IRES\text{-}EGFP)}$/Gpt
**Strain type:** Knock-in
**Strain number:** T037029
**Background:** C57BL/6JGpt

## Description

Psoriasis is a disease characterized by increased epidermal thickness (acanthosis), rapid proliferation of keratinocytes, altered keratinocyte differentiation, an abnormal collection of polymorph nuclear leukocytes in the epidermis, and an activated mononuclear cell infiltrate in the underlying dermis [1]. It is a chronic, inflammatory, immune-mediated skin disease, affecting approximately 1~3% of the population worldwide associated with extensive psychological and physical burdens.

A significant amount of both clinical and experimental data have established T helper type 17 (Th17) cells as key players in chronic inflammatory conditions such as psoriasis [2]. IL-17A was first described as a potential mediator in psoriasis after identifying upregulated IL-17A mRNA expression in lesional psoriatic skin [3]. CD4 and CD8 clones derived from psoriasis lesions were also able to produce IL-17A after TCR stimulation. The Th17-supporting cytokine IL-23 was demonstrated to promote the production of IL-17F and tumor necrosis factor-a from primed T lymphocytes [4], and psoriasis-like phenotypes can be artificially induced in mouse skin using intradermal injections of IL-23 [5]. Thus, the important role of the IL-23/IL-17A axis in the pathogenesis of the disease is becoming well established.

We used Cre-loxP approach to generate a mouse strain which could overexpress hIL-17A in keratinocytes when breeding with K14-Cre ((T004833), resulting in a psoriasis-like lesion formation. The ensuing pathogenesis bore many hallmark features of human psoriasis including hyperkeratosis, parakeratosis, epidermal neutrophil accumulation, scaling, erythema and thickening of the skin. The model will be an ideal model to evaluate the effect of psoriasis drugs.

## Strategy

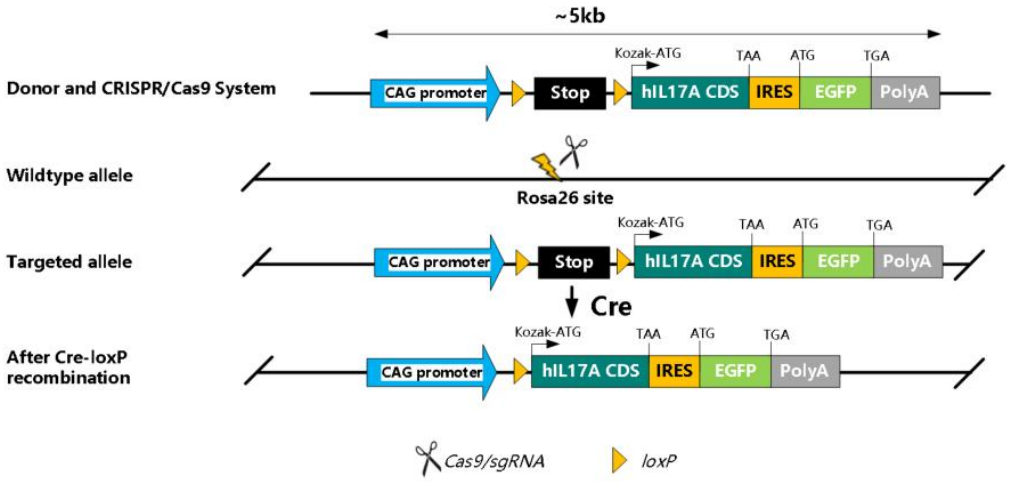


**Fig.1 Schematic diagram of IL17A humanization strategy in B6-CAG-LSL-hIL17A-IRES-EGFP mice.**

## Application

1. Psoriasis model for anti-inflammatory immune drug development and pharmacodynamic evaluation
2. Medical research on IL17A related pathological mechanisms
3. Autoimmune disease research, and antibody drug development

## Supporting data

## 1. Overexpression of hIL17A in keratinocytes

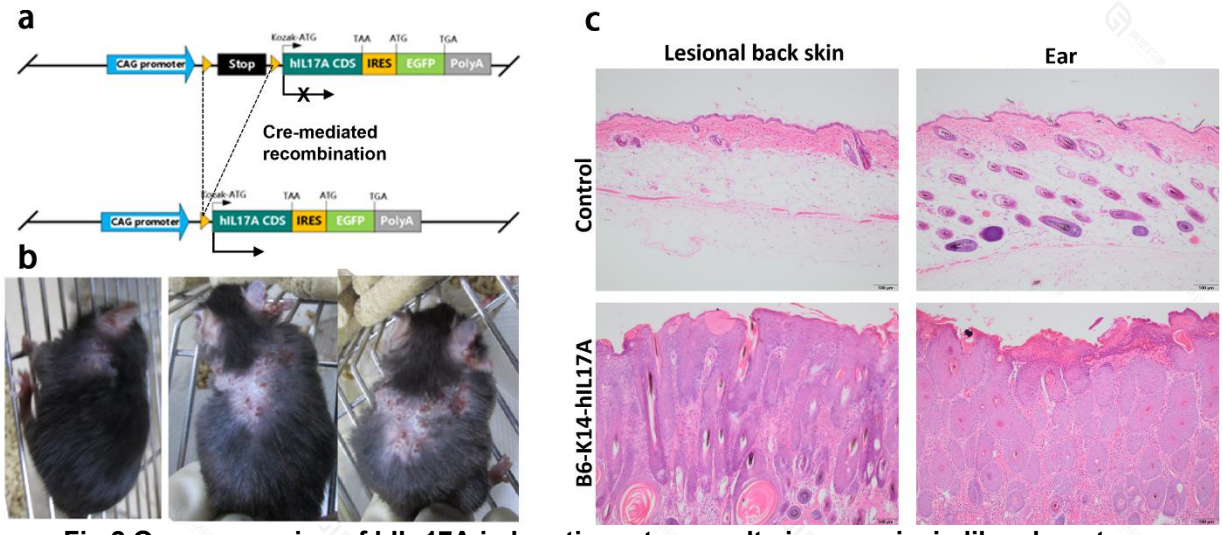


**Fig.2 Overexpression of hIL-17A in keratinocytes results in a psoriasis-like phenotype.**
B6-CAG-LSL-hIL17A-IRES-EGFP mice (T037029) were breeding with B6-K14-Cre mice (T004833) to

generate B6-K14-hIL17A model (T051527) with specific overexpression of hIL17A in keratinocytes. (a) Schematic diagram of overexpression of hIL17A in keratinocytes. (b) A psoriasis-like phenotype was observed in B6-K14-hIL17A model. (c) H&E staining of the back skin and ear of B6-K14-hIL17A. Acanthotically thickened epidermis, loss of the stratum granulosum, and anelongation of the papillary dermis as well as areas of hyper and parakeratosis and multiple neutrophilic abscesses in the horny layer were observed in B6-K14-hIL17A model. Those signs closely resemble human psoriasis lesions in terms of the phenotypic and histological characteristics.

## References


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3. Teunissen, B. Marcel, et al. Interleukin-17 and interferon-γ synergize in the enhancement of proinflammatory cytokine production by human keratinocytes. *Journal of Investigative Dermatology.* 1998, 111, 645-649.
4. Aggarwal, Sudeepta, et al. Interleukin-23 promotes a distinct CD4 T cell activation state characterized by the production of interleukin-17. *Journal of Biological Chemistry*. 2003, 278, 1910-1914.
5. Hedrick, N. Michael, et al. CCR6 is required for IL-23–induced psoriasis-like inflammation in mice. *The Journal of clinical investigation*. 2009, 119, 2317-2329.