Ceramide deficiency in the epidermis leads to development of psoriasis-like lesions associated with IL–23–dependent proliferation of γδ–17 cells

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It has been recognized that ceramide levels are decreased in the epidermis of patients with atopic dermatitis and psoriasis. However, the underlying mechanism by which ceramide deficiency leads to skin inflammation still remains unclear. Here, we generated Sptlc2 targeted mice under control of the keratin 5 promoter, by which their keratinocytes were devoid of serine palmitoyltransferase (SPT), the rate-limiting enzyme for de novo sphingolipid synthesis. K5–SPT–KO mice have demonstrated barrier dysfunction. From 2 weeks of age, they develop the skin lesion, showing psoriasis-like histopathologic changes. Transcriptional levels of IL–17 and IL–22 were increased in the skin and draining lymph nodes. Strikingly, K5–SPT–KO mice showed increased numbers of gd–T cells that produce IL–17 (gd–17) in the skin lesion and lymph nodes and most of them also produce IL–22, similar to Th17 cells. In vivo administration of anti–IL–12/23p40 antibody ameliorated the skin lesions and reduced the number of gd–17 cells in K5–SPT–KO mice. Therefore, we conclude that ceramide deficiency in the epidermis results in the development of psoriasis-like lesions, mediated by IL–23–dependent gd–17 cells in mice.