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Autoantibodies in Scurfy mice and IPEX Patients Recognize Keratin 14

For many autoimmune disorders the nature of the antigenic targets are unknown. The Scurfy mouse spontaneously develops autoimmune disease due to a loss-of-function mutation in the *foxp3* gene, a transcription factor important for the development and function of regulatory T cells. The skin is one of the main organs affected in Scurfy mice and we have previously shown, that several keratins, including keratin 14, are targets for autoreactive B cells in the skin.

Patients with the rare "Immunodysregulation, Polyendocrinopathy, Enteropathy, X-linked syndrome" (IPEX) suffer from generalized autoimmunity due to the same mutation in the *FOXP3* gene and often present with severe atopic-dermatitis-like skin disease.

We evaluated the keratin 14-reactivity in IPEX patients with or without skin disease. We used sera from IPEX patients for western blot analysis: Two patient sera showed reactivity to keratinocyte extract, and interestingly one of the patients with skin disease yielded the strongest signal. We used the serum of this patient for a 2D-gel electrophoresis followed by Protein Identification and identified keratin 14, keratin 10 and keratin 1 as targets recognized by the autoantibodies. To conclusively demonstrate that the autoantibodies target keratin 14, we expressed 3 protein fragments covering the whole keratin 14 protein and used them for western blot analysis with the IPEX patient serum. As in Scurfy mice, the C-terminal fragment of keratin-14 was predominantly recognized by the patient serum.

In summary we show that autoantibodies from IPEX patients recognize different keratins including keratin 14 and conclude that keratin 14 is an antigenic target in autoimmune skin disease in IPEX patients.