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Anti-AT1R ab and as cause or contributor to skin fibrosis and interstitial lung disease

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Introduction: Systemic sclerosis (SSc) is a complex connective tissue disease which is characterized by autoimmunity, vasculopathy and fibrosis. Recent studies have suggested that autoantibodies (ab) against angiotensin II receptor I (AT1R) might play a pathogenic role in the development of SSc, which need to be further verified by animal models in vivo. However, due to the difficulties in preparation of antigens with native conformational epitopes, induction of functional aab against surface-expressed receptors is a challenging task.

Methods: We Immunized mice with membrane extracts derived from CHO cells overexpressing human AT1R (hAT1R) and evaluated the immunological and histological phenotypes in the immunized mice.

Results: The hAT1R-immunized mice developed functional autoantibodies against AT1R which are able to bind to and to activate the native receptor. Furthermore, hAT1R-immunization induced SSc-like disease symptoms including vasculopathy and interstitial inflammation in the lung as well as perivascular inflammation and fibrosis in the skin. Importantly, the SSc-like disease can be partially transferred by the serum IgG of hAT1R-immunized mice.

Conclusion: Our study provides a new animal model for SSc, which strongly supports the hypothesis of a pathogenic role of functional antibodies against AT1R in this disease.