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Patterns of 31 new autoantibodies against G-protein-coupled receptors and growth factors

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Background: Systemic sclerosis (SSc) is a rare autoimmune disease with a significant disease burden. Scl70 and centromere ab are disease specific and prognostic antibodies. Functional ab against G protein-coupled receptors (GPCR) regulate immune function and were reported in the pathogenesis of various inflammatory diseases. Objectives: We analyzed 31 ab against GPCRs in a retrospective cohort of 71 SSc sera compared to 196 sera from healthy controls (HC). Ab levels were related to disease manifestations in order to hypothesize functional ab in SSc.

Methods: SSc patients were retrospectively characterized by mRSS, organ involvement, lab tests, spirometry and imaging. 30/71 had active disease (EUSTAR activity score). Ab patterns were analyzed using new statistical approaches: factor analysis, principal component analysis (PCA), linear discriminant analysis (LDA), cluster analysis and biserial correlation.

Results: SSc subgroups (diffuse/ limited cutaneous) differ in ab levels forming separate clusters (LDA method). Moreover, latent factors group ab and clinical disease manifestations. Factor analysis reveals VEGFR2 ab and the signaling molecule YBX1 ab to be more unique with the lowest communalities. The biserial correlation shows moderate associations between ab patterns and SSc symptoms. Compared to association of ETAR ab with Raynaud's and skin sclerosis HGFR ab are inversely correlated.

Conclusions: We describe 31 new ab against GPCR and growth factors in SSc. Ab levels can be clustered by latent factors. Some ab were linked to the absence of SSc manifestations. Thus, we postulate that a dysbalance of functionally protective autoantibodies, that can be found in healthy individuals and the appearance of SSc specific ab such as Scl70 contribute to its pathogenesis. Considering the preliminary character of our data, the functional impact of ab against GPCR and growth factors has to be validated in vitro and statistical correlations to be confirmed in a prospective independent patient cohort.