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Proteomic analysis of Systemic Sclerosis serum identifies the toll-like receptor agonists S100A8/A9 as a novel possible pathogenic marker

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Background

Systemic sclerosis (SSc) is an autoimmune disease characterized by fibrosis of the skin and the internal organs. The etiology is still unknown but prominent features are vascular injury and chronic inflammation resulting in fibrosis. There are no markers available that predict SSc susceptibility and/or prognosis. This study is the first study that exploits a proteome-wide profiling to identify new targets in the pathogenesis of SSc.

Method

40 SSc patients were included for initial proteomic identification. Patients were stratified as having diffuse SSc (dSSc) (n= 19) or limited SSc (lSSc) (n=21) according to the extent of skin involvement. As controls 20 healthy donors were included. First we run a training set on the SELDI-TOF-MS and next the validation set was measured. For replication a cohort compromising 30 difSSc patients and 60 limSSc was available.

Results

Analysis revealed a list of 29 masspeaks of interest of which 21 could be predicted using Tagident. One of the main significant peaks was S100A8. We next aimed to replicate the increased expression of S100A8. Further stratification for SSc disease phenotype reveals it to be increased solely in limSSc patients with lung fibrosis. This finding is replicated with an ELISA in 60 limSSc patients S100A8/A9 being 415 pg/ml in limSSc without lung fibrosis and 659 pg/ml in limSSc with lung fibrosis ($p<0.05$). Furthermore we show an increased presence of S100A8 in SSc skin sections.

Conclusion

This is the first study identifying new targets in SSc using proteome wide profiling in serum. S100A8 revealed to be increased in limSSc patients with lung fibrosis specifically. As S100A8 is an important protein in inflammatory processes it is interesting to further investigate its contribution to the pathogenesis of SSc and more specifically lung fibrosis.

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