Background: Systemic sclerosis (SSc) is an autoimmune disease characterized by vascularopathy, inflammation, and extensive fibrosis of the skin and organs. Exosomes (EXOs) are cell-derived vesicles 30-150 nm in size that contain miRNAs, microRNAs and proteins.

Objectives: Here, we aimed to investigate the roles of EXOs in SSc pathogenesis, especially in angiogenesis.

Methods: EXOs were respectively isolated from plasma, cultured peripheral blood mononuclear cells (PBMCs) and neutrophil supernatants, and were identified by transmission electron microscopy. The expression of S100A8/A9 was measured by real-time PCR (qPCR) with ELISA. Potential migration and scratch assays in human dermal microvascular endothelial cells (HDMECs) were used to study the influence of neutrophil EXOs and neutrophil EXOs S100A8/A9. We also performed a genome-wide transcriptome analysis on PBMCs from 19 SSc patients and 18 matched normal controls (NC) using Illumina BeadChip arrays. The ingenuity pathway analysis (IPA) tool and Database for Annotation, Visualization and Integrated Discovery (DAVID) were used for bioinformatics analysis.

Results: Plasma EXOs and neutrophil EXOs from SSc patients suppressed the proliferation and migration of HDMECs. Using a microarray analysis we found 28% genes upregulated in PBMCs could exist in EXOs, especially the S100 protein family, including S100A8/A9. High levels of S100A8/A9 were consistently verified in SSc plasma, PBMCs, plasma EXOs, PBMC EXOs and neutrophil EXOs. Particularly, S100A9/A9 expression in neutrophil EXOs was distinctly higher than that in PBMC EXOs in SSc patients. Furthermore, we found that neutrophil EXOs S100A8/A9 inhibit the proliferation and migration of HDMECs, and that neutrophil EXOs bind to Toll-like receptor 4 (TLR4) pathway.

Conclusion: S100A8/A9 is one of components of neutrophil EXOs that regulates vascular endothelial cell angiogenesis in SSc patients, most likely by activating the TLR4 signalling pathway.

Disclosure of Interests: None declared