News Release

Tiny particles in the blood reveal vascular abnormalities and fibrosis-related changes in systemic sclerosis

— Extracellular vesicle analysis provides clues to disease mechanisms and potential biomarkers —

Key Points

- Blood-derived extracellular vesicle (EV) preparations from eight anti-centromere antibody-positive patients and five healthy controls showed distinct protein profiles associated with vascular abnormalities and fibrosis.
- EV preparations from patients were enriched in vascular-associated proteins, including von Willebrand factor (VWF), coagulation factor VIII (F8), and SVEP1; COL1A2 and ECM1 were detected only in patient EV preparations.
- When added to cultured normal human dermal fibroblasts, patient-derived EV preparations altered the expression of genes involved in collagen and the extracellular matrix.

Summary

A research team led by Associate Professor Mariko Ogawa-Momohara of the Department of Dermatology, Nagoya University Graduate School of Medicine, has identified molecular signatures associated with both vascular abnormalities and fibrosis in circulating extracellular vesicle (EV) preparations from patients with systemic sclerosis. The team also found that patient-derived EV preparations changed gene expression in cultured normal human fibroblasts. Systemic sclerosis is an autoimmune disease characterized by vascular injury and fibrosis of the skin and internal organs. These findings suggest that circulating EVs may reflect different aspects of the disease and may contribute to cell-to-cell signaling. The findings were published in Journal of Investigative Dermatology on November 6, 2026.

Research Background

Systemic sclerosis is characterized by immune abnormalities, vascular damage, and progressive fibrosis of the skin and internal organs. In some patients who test positive for anti-centromere antibodies, vascular abnormalities persist for years before clinically apparent skin fibrosis develops. The mechanisms underlying these prolonged changes remain incompletely understood. Extracellular vesicles are small membrane-bound particles released by cells that carry proteins and other molecules and can influence the function of recipient cells. The researchers investigated whether the molecular contents

and biological effects of circulating EV preparations might provide insight into vascular and fibrotic processes in anti-centromere antibody-positive systemic sclerosis spectrum disease.

Research Results

The team isolated EV preparations from plasma samples obtained from eight anti-centromere antibody-positive patients (six with limited cutaneous systemic sclerosis and two with very early diagnosis of systemic sclerosis [VEDOSS]) and five healthy controls. Mass spectrometry identified 995 proteins, of which 571 were included in subsequent analyses. Hierarchical clustering based on differentially abundant EV-associated proteins clearly separated patients from healthy controls. Patient EV preparations showed increased abundance of vascular-associated proteins, including VWF, F8, and SVEP1. Eighteen proteins were detected exclusively in the patient EV preparations, including collagen type I alpha 2 chain (COL1A2) and extracellular matrix protein 1 (ECM1), which are associated with fibroblasts and extracellular matrix regulation. Importantly, the detection of these proteins does not establish which cells released the EVs. To investigate functional effects, EV preparations from three patients and three healthy controls were added to cultured normal human fibroblasts for 72 hours, followed by RNA sequencing. Compared with control EV preparations, patient EV preparations were associated with 282 upregulated and 109 downregulated genes. Upregulated genes included COL3A1, EGR1, TGFB3, and FGF10, and enrichment analysis identified extracellular matrix- and collagen-related categories. TGFB3 was identified as a gene whose expression increased in the recipient fibroblasts, not as a protein detected within the EV preparations.

Research Summary and Future Perspective

These results suggest that circulating EV preparations in anti-centromere antibody-positive systemic sclerosis carry molecular signatures associated with vascular abnormalities and extracellular matrix biology, while also inducing fibrosis-related transcriptional responses in cultured fibroblasts. The findings support further investigation of circulating EVs as potential biomarkers and participants in intercellular communication. Because the study included a small number of participants and the cellular origin of the EVs was not directly established, larger studies with longitudinal sampling, age-matched controls, and additional functional analyses will be needed to determine their clinical utility and mechanistic significance.

Publication

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