298 **Fli1-deficient adipocytes promote the spontaneous development of dermal fibrosis and vasculopathy mimicking systemic sclerosis through adipocyte-to-myofibroblast transdifferentiation and defective vasculogenesis**

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[Introduction]

Systemic Sclerosis (SSc) is a multisystem connective tissue disease characterized by autoimmunity, vasculopathy and extensive organ fibrosis. Although its pathogenesis still remains unknown, recent studies revealed that the deficiency of Fli1, which is a Ets family transcription factor, is a potential predisposing factor of SSc.^{1,2} On the other hand, current issues showed the association of adipocytes with SSc. For instance, some kinds of adipokines are associated with fibrotic responses and/or vasculopathy in SSc.³⁻⁴

<references>

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[Purpose/method]

To further clarify the association of adipocytes with SSc, we generated adipocyte-specific *Fli1* knockout (*Fli1* AdipoKO) mice by using the Cre/loxP system and investigated whether these mice recapitulate the cardinal features of SSc.

[Results]

➤ ***Fli1* AdipoKO mice spontaneously developed dermal fibrosis through adipocyte-to-myofibroblast transdifferentiation**

In double immunofluorescence for α-SMA and perilipin, double positive fusiform cells were evident in *Fli1* AdipoKO mice, suggesting that adipocyte-to-myofibroblast transdifferentiation contributes to dermal fibrosis in *Fli1* AdipoKO mice.

➤ ***Fli1* AdipoKO mice spontaneously exhibited vascular structural and functional abnormalities due to defective vasculogenesis**

Decreased α-SMA expression and dilated blood vessels suggested pericyte dysfunction in *Fli1* AdipoKO mice.

Decreased number and decreased α-SMA expression of blood vessels were remarkable in *Fli1* AdipoKO mice, suggesting defective vasculogenesis in the mice.

In bone marrow, decreased number of adipocytes with abnormal shapes was prominent in *Fli1* AdipoKO mice. Furthermore, bone marrow-derived mesenchymal stem cells (BM-MSCs) exhibited de-differentiated phenotype. Collectively, Fli1-deficient adipocytes can change BM-MSCs into de-differentiated phenotype, resulting in defective vasculogenesis and further leading to an SSc-like phenotype.

[Conclusion]

Fli1-deficient adipocytes promote the spontaneous development of dermal fibrosis and vasculopathy mimicking SSc through adipocyte-to-myofibroblast transdifferentiation and defective vasculogenesis.

[Conflicts of interest]

None declared.