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THE ROLE OF PDGF AND TSP-1 IN THE DEVELOPMENT OF SYSTEMIC SCLERODERMA

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Abstract
Systemic scleroderma (SSc), also called systemic sclerosis, is a chronic autoimmune disease. It causes:
- Thickening and hardening of the skin
- Damage to small blood vessels
- Fibrosis of internal organs (like lungs, heart, kidneys)

Keywords: Systemic scleroderma, PDGF, TSP-1, fibrosis, angiogenesis, vascular damage, autoimmune disease, TGF-beta, fibroblasts, treatment.

Introduction

One of the earliest and most important events in scleroderma is damage to small blood vessels. This damage makes it hard for blood to reach tissues, which leads to low oxygen (hypoxia) and scarring.
Two key molecules that control blood vessel growth are:
- PDGF (Platelet-Derived Growth Factor) – helps new blood vessels grow and stimulates fibroblasts
- TSP-1 (Thrombospondin-1) – stops new blood vessel growth and increases fibrosis
In systemic scleroderma, these two molecules are out of balance, which causes more fibrosis and tissue damage.
What is PDGF and What Does It Do?
PDGF is a protein released by blood platelets and damaged cells. It plays a big role in:
- Healing wounds
- Growing new blood vessels (angiogenesis)
- Activating fibroblasts – the cells that make collagen

But in SSc, the PDGF system works abnormally:
- PDGF is overproduced
- It causes too much fibroblast activity
- This leads to excess collagen, which causes fibrosis

PDGF also sends signals inside the cell using pathways like:
- PI3K/Akt
- MAPK

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These pathways make fibroblasts live longer and produce more collagen and other scar-forming proteins.

What is TSP-1 and What Is Its Role?

TSP-1 is a large protein found in the extracellular matrix (the space around cells). Its main job is to:

- Stop the growth of new blood vessels (anti-angiogenic)
- Activate TGF-β – a powerful molecule that causes fibrosis
- Control inflammation and tissue remodeling

In systemic scleroderma:

- TSP-1 is found at high levels in the blood and tissues
- It prevents new capillaries from forming
- It promotes fibrosis by activating TGF-β

So, even though the body tries to make new blood vessels (with PDGF), TSP-1 blocks this process, making the blood supply worse.

How the Imbalance Between PDGF and TSP-1 Affects the Disease

In healthy people, PDGF and TSP-1 are in balance. But in systemic scleroderma:

PDGF - Angiogenic (builds vessels), activates fibroblasts → Overexpressed → fibroblast overactivity, fibrosis

TSP-1 - Angiostatic (blocks vessels), activates TGF-β → Overexpressed → no angiogenesis, more fibrosis

As a result:

- Capillaries are destroyed and not replaced
- Tissues become hypoxic (lack oxygen)
- More scarring (fibrosis) occurs
- Organs become damaged (lungs, skin, heart, kidneys)

Clinical Signs Caused by PDGF/TSP-1 Imbalance

This imbalance helps explain many symptoms of scleroderma, such as:

- Digital ulcers (painful sores on fingers due to poor blood flow)
- Raynaud's phenomenon (color changes in fingers in response to cold)
- Pulmonary arterial hypertension (high pressure in lungs)
- Interstitial lung disease (lung scarring)
- Heart problems (fibrosis of heart muscle)

Can PDGF and TSP-1 Be Used as Biomarkers?

Yes, recent research shows that:

- PDGF and TSP-1 levels are higher in people with severe SSc
- They can help predict disease activity and organ involvement
- High TSP-1 means more fibrosis
- High PDGF means active fibroblasts

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These molecules could help doctors monitor the disease and choose better treatments.

New Treatments: Targeting PDGF and TSP-1

Scientists are now working on new drugs that block these harmful pathways. Some examples:

Drug Name: Imatinib | Target: Blocks PDGF receptor | Effect: Reduces fibroblast activity, slows fibrosis

Drug Name: Nintedanib | Target: Blocks PDGF, VEGF, FGF receptors | Effect: Used in lung fibrosis (also tested in SSc)

Drug Name: TSP-1 inhibitors | Under study | Effect: May help improve blood flow, reduce scarring

These drugs may slow the disease and protect organs. More clinical trials are needed.

Conclusion

Systemic scleroderma is a complex disease with problems in the immune system, blood vessels, and connective tissue. Two important molecules in this disease are:

- PDGF – causes fibrosis and abnormal blood vessel growth
- TSP-1 – blocks blood vessel formation and increases fibrosis

Their imbalance is a major reason why patients suffer from poor blood flow, chronic tissue damage, and organ failure. Studying and targeting these molecules can help find better diagnostic tools and treatments.

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