



What is scleroderma and why me?

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Structure

- Are my children at risk to get scleroderma?
- Scleroderma is damaged vessels
- Scleroderma is inflammation
- Scleroderma is too much extracellular matrix
- Why does my neighbour have such a different disease from me?

Are my children at risk to get scleroderma?

Autosomal Dominant Inheritance

Father with Condition

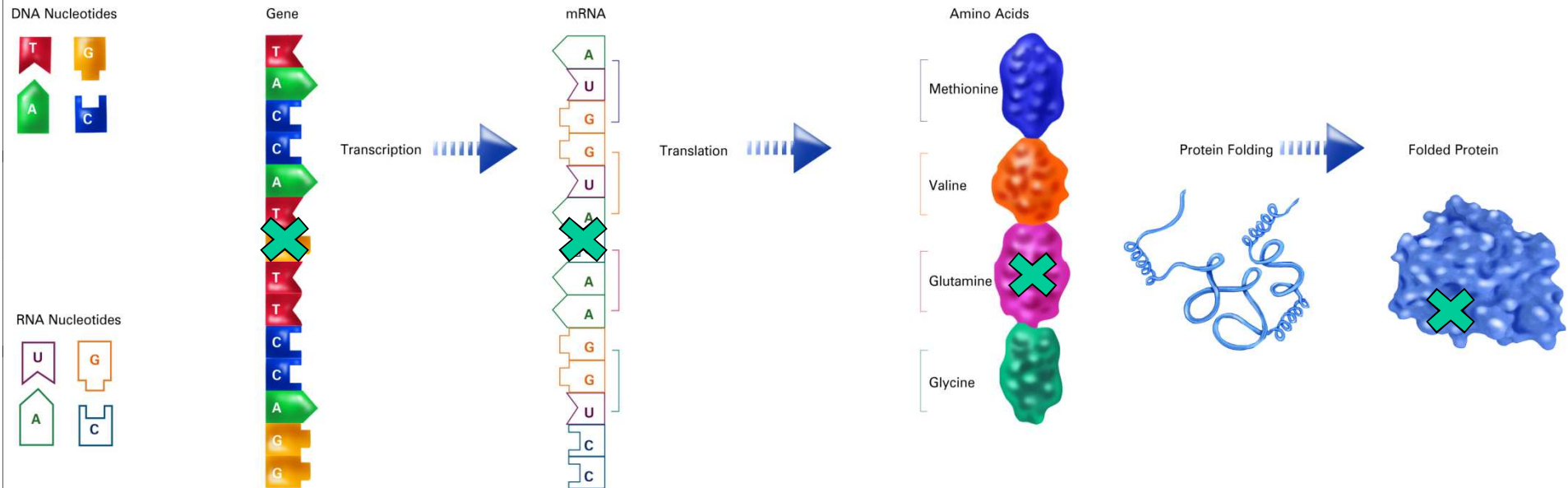
Normal Mother

This is not scleroderma !!!



Great! So I do not need to worry at all?

Well:



Change of function



Increased risk
to get
scleroderma

Genetic changes in SSc

Table 1 Recent candidate gene associations with susceptibility to scleroderma

Gene	Reference	Cohorts (single/multiple)	Number of subjects	
			SSc	Controls
<i>BANK1</i>	Rueda <i>et al.</i> [20**]	Multiple	2380	3270
<i>CTGF</i>	Fonseca <i>et al.</i> [16]	Multiple	500	500
<i>C8orf13-BLK</i>	Gourh <i>et al.</i> [22*]	Multiple	1639	1416
<i>IL-23R</i>	Agarwal <i>et al.</i> [23*]	Single	1402	1038
<i>IRF5</i>	Dieude <i>et al.</i> [26**]	Multiple	881	760
<i>STAT4</i>	Rueda <i>et al.</i> [28**]	Multiple	1317	3113
<i>TBX21</i>	Gourh <i>et al.</i> [30*]	Multiple	1402	1038
<i>TNFSF4</i>	Gourh <i>et al.</i> [32*]	Single	1059	698

Agarwal et al, *Curr Opin Rheumatol.* 2010 Mar;22(2):133-8

Confusing!

Are my children now at risk or not?



Did I do anything wrong?

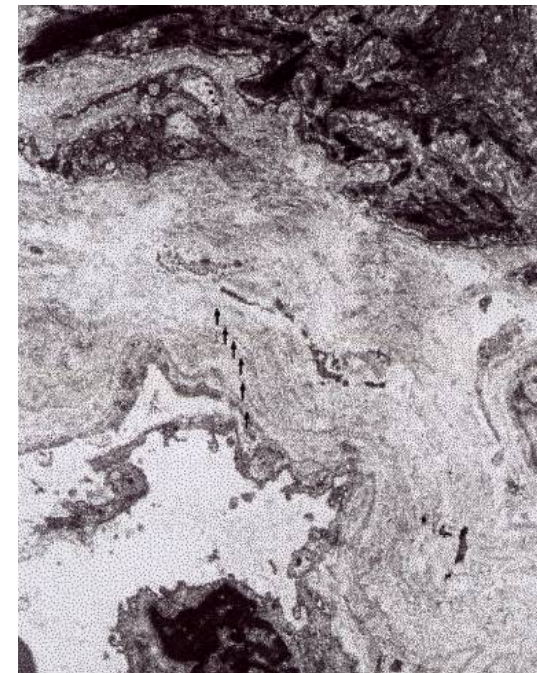
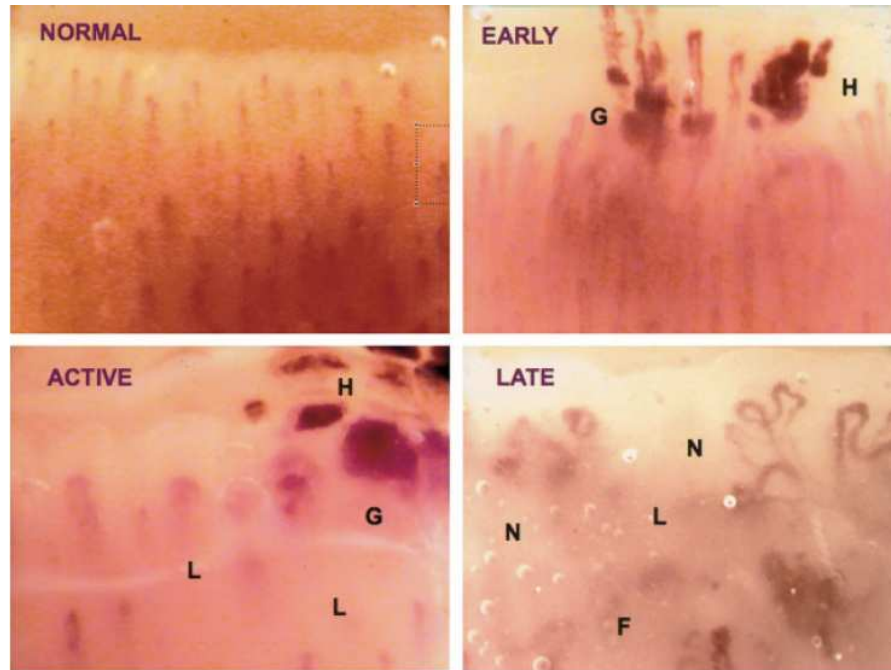
- **Not that we know**

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Scleroderma is damaged vessels

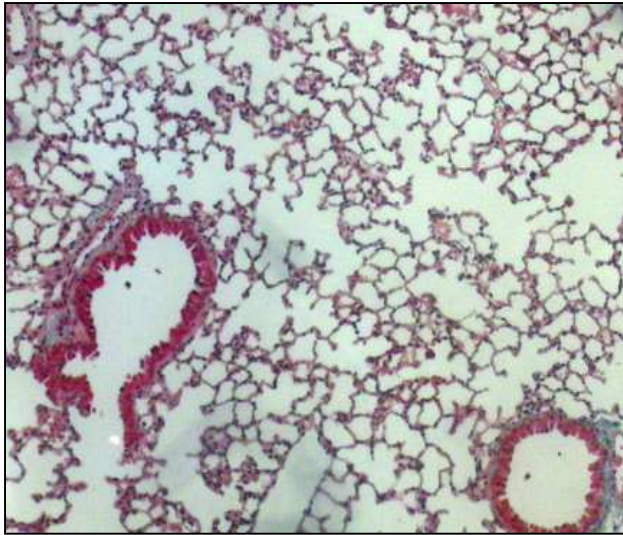
Capillaries and small arteries



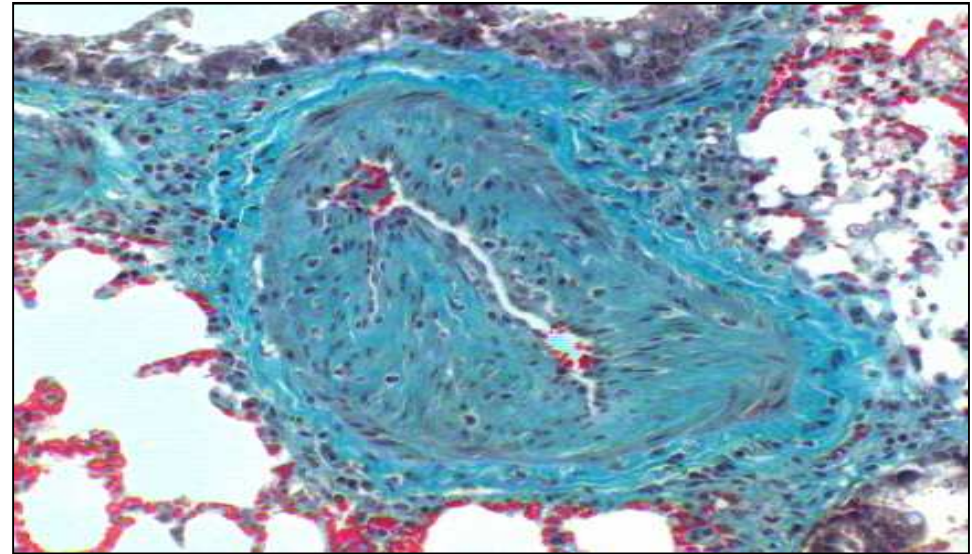
Destruction (Capillaries)
(Dilatation, Instability)
(Malformation, Rarefaction)

Fibroproliferation (small arteries)
(Intimal hyperplasia)

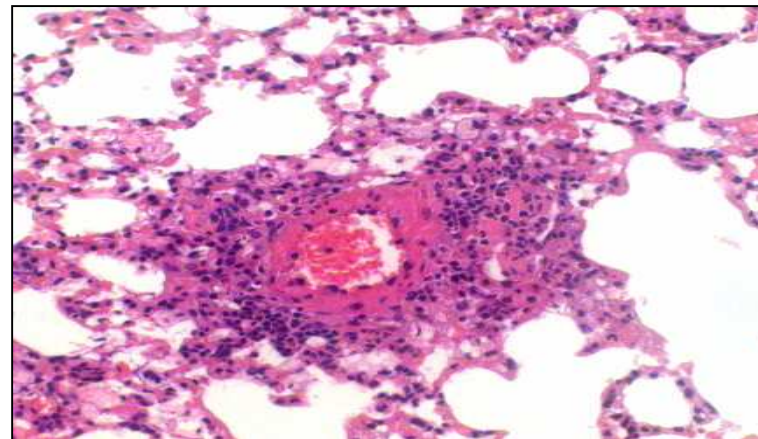
Damaged Vessels: Pulmonary arterial hypertension



wt



Fra-2

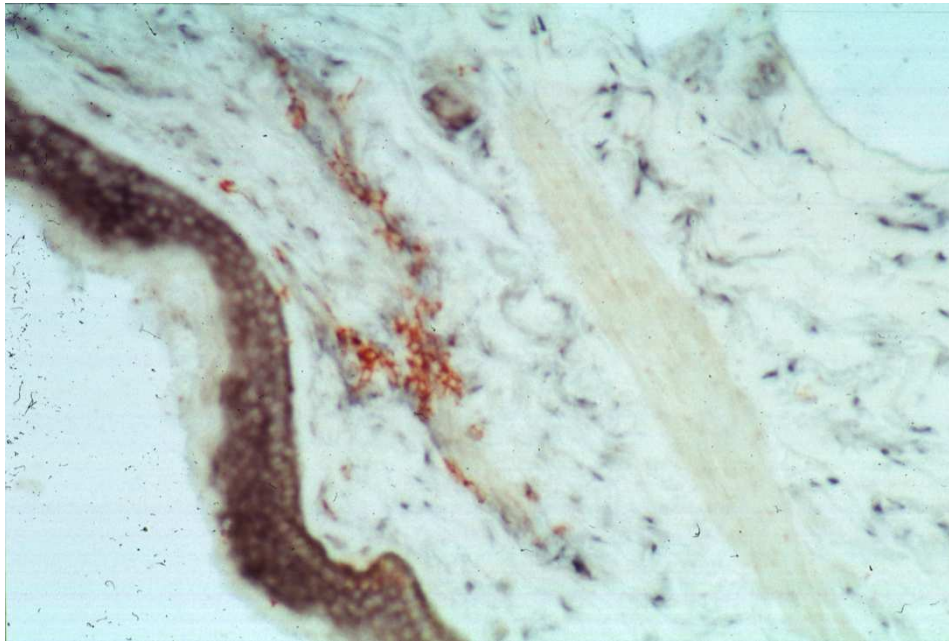


Fra-2

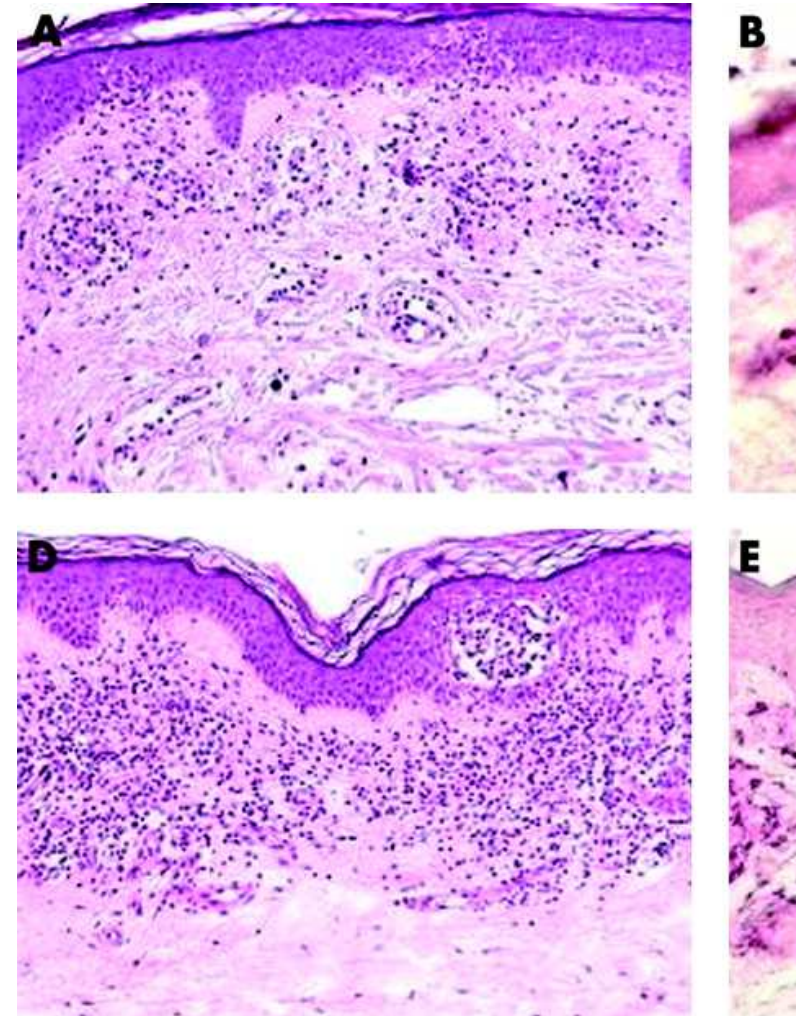
Damaged vessels are found in many organs

Involvement	Clinical manifestation
Skin	Ulcers
Lungs	PAH
Kidneys	Renal crisis
GI tract	
Skeletal muscle	
Myocardium	

Scleroderma is inflammation

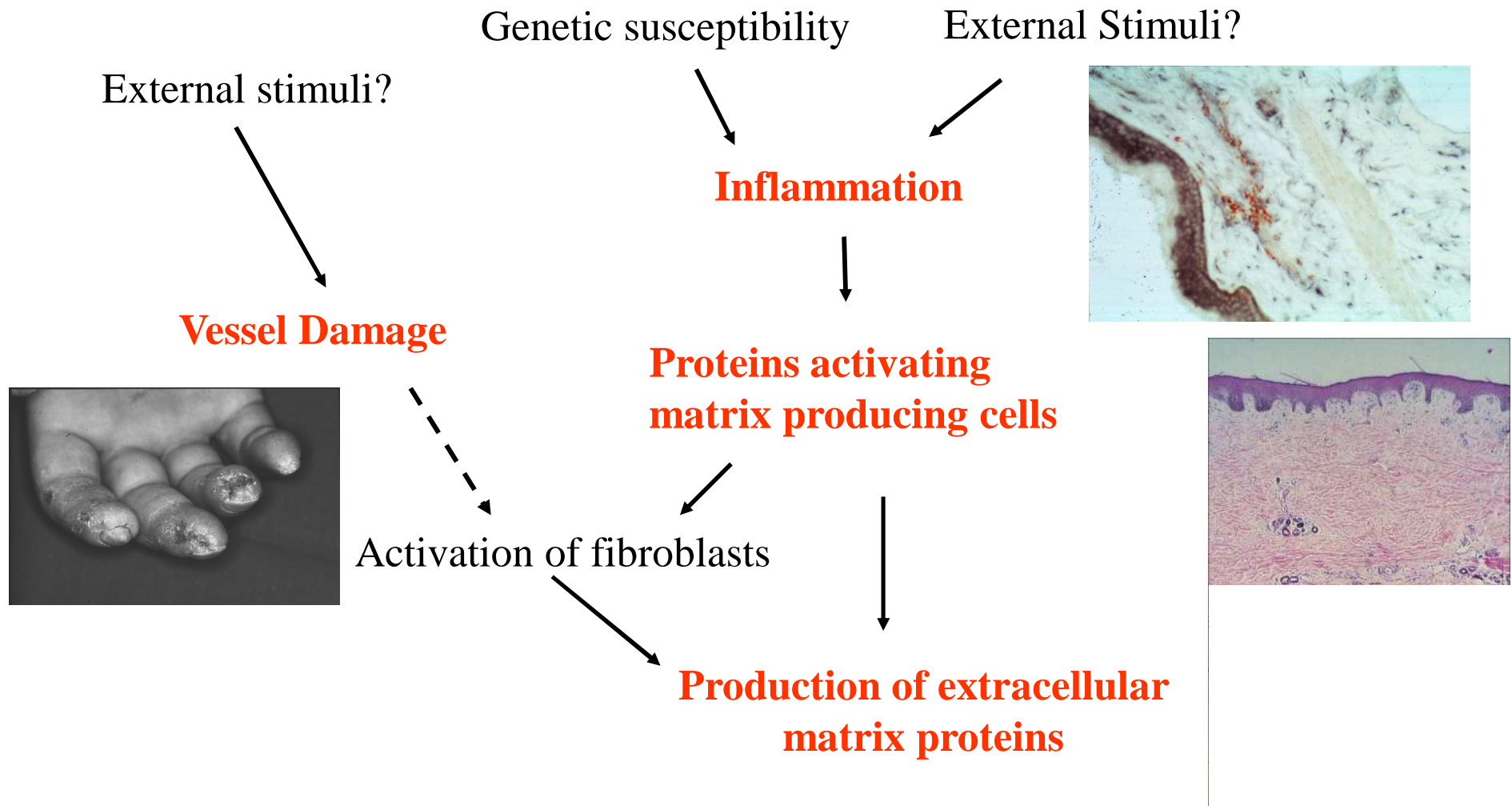


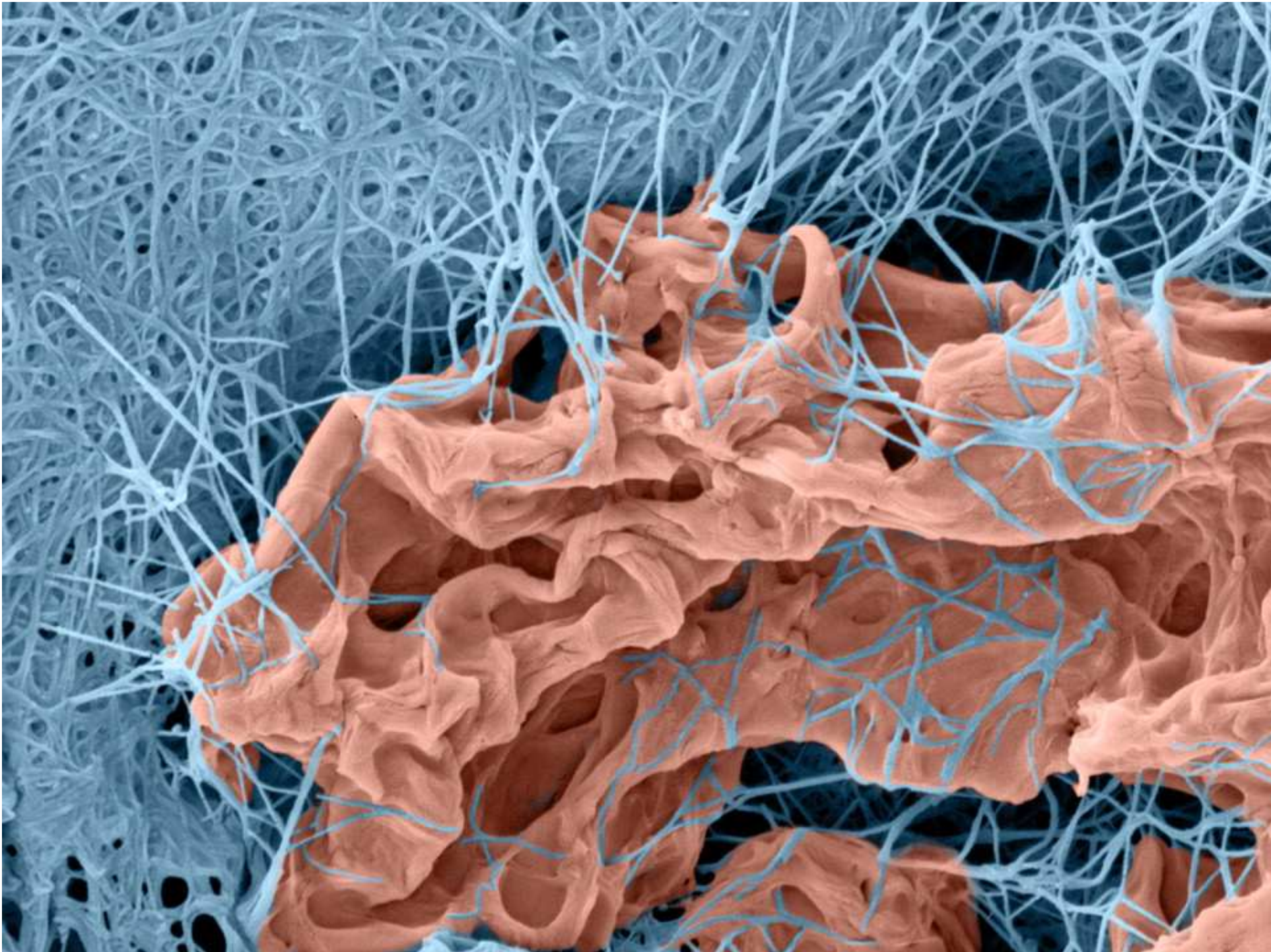
Scleroderma



Psoriasis

Scleroderma is too much extracellular matrix







Thanks for your attention!