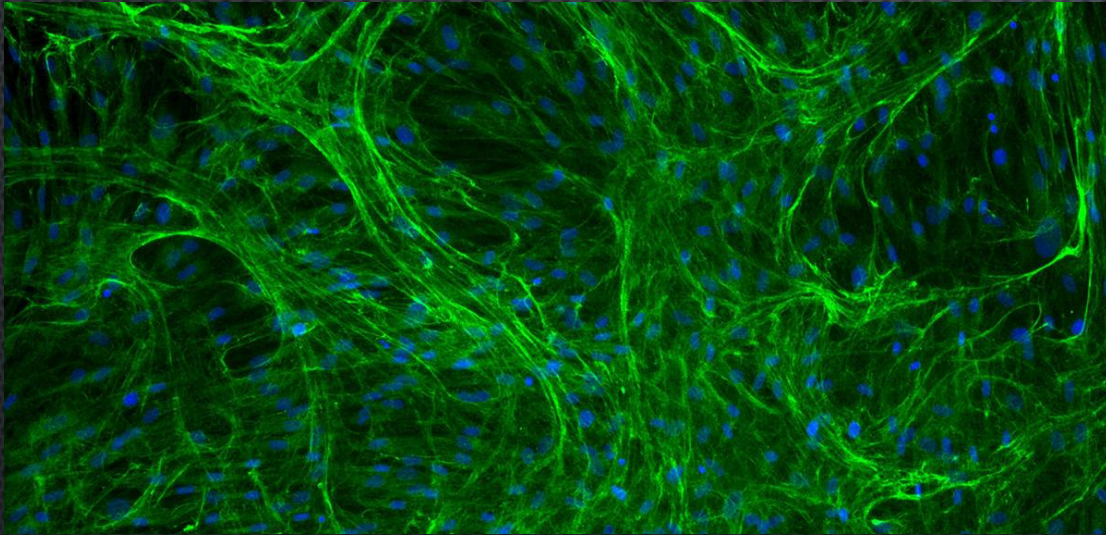




Tissue Biology and Therapeutic Engineering Laboratory
UMR5305 CNRS/UCBL1
Lyon, France



Romain DEBRET, PhD
✉ romain.debret@cnrs.fr



Tropoelastin deposition

Tropoelastin deposition from skin cells *in vitro*
© R. DEBRET/UMR5305/CNRS PHOTOTHEQUE

7th Cutis Laxa Days
February 4th, 2026



Skin elastic fibers

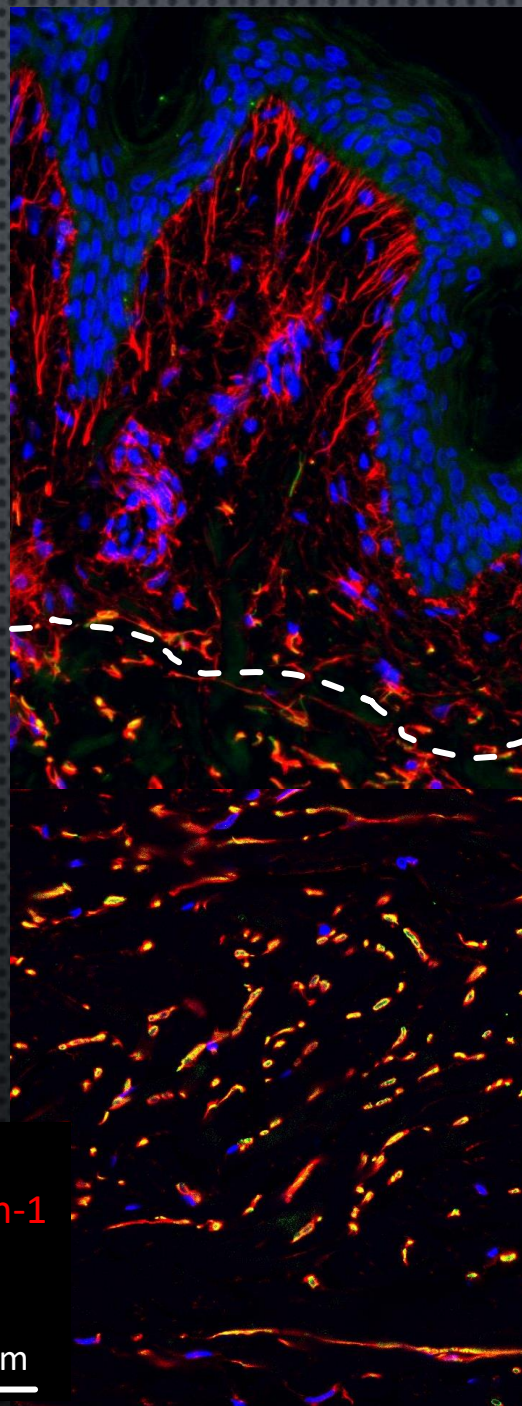
Weak mechanical strains
(papillary dermis)

Strong mechanical strains
(reticular dermis)

Nuclei
Fibrillin-1
Elastin
Merge

Unpublished

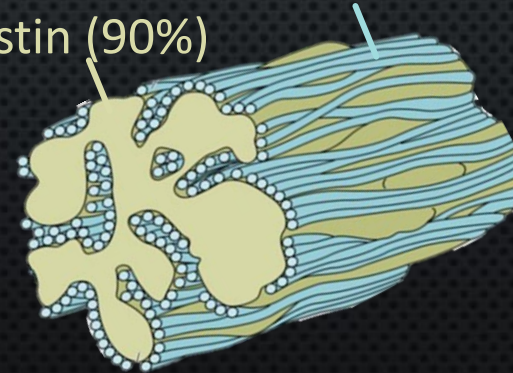
100 μ m



Microfibrils (100%)



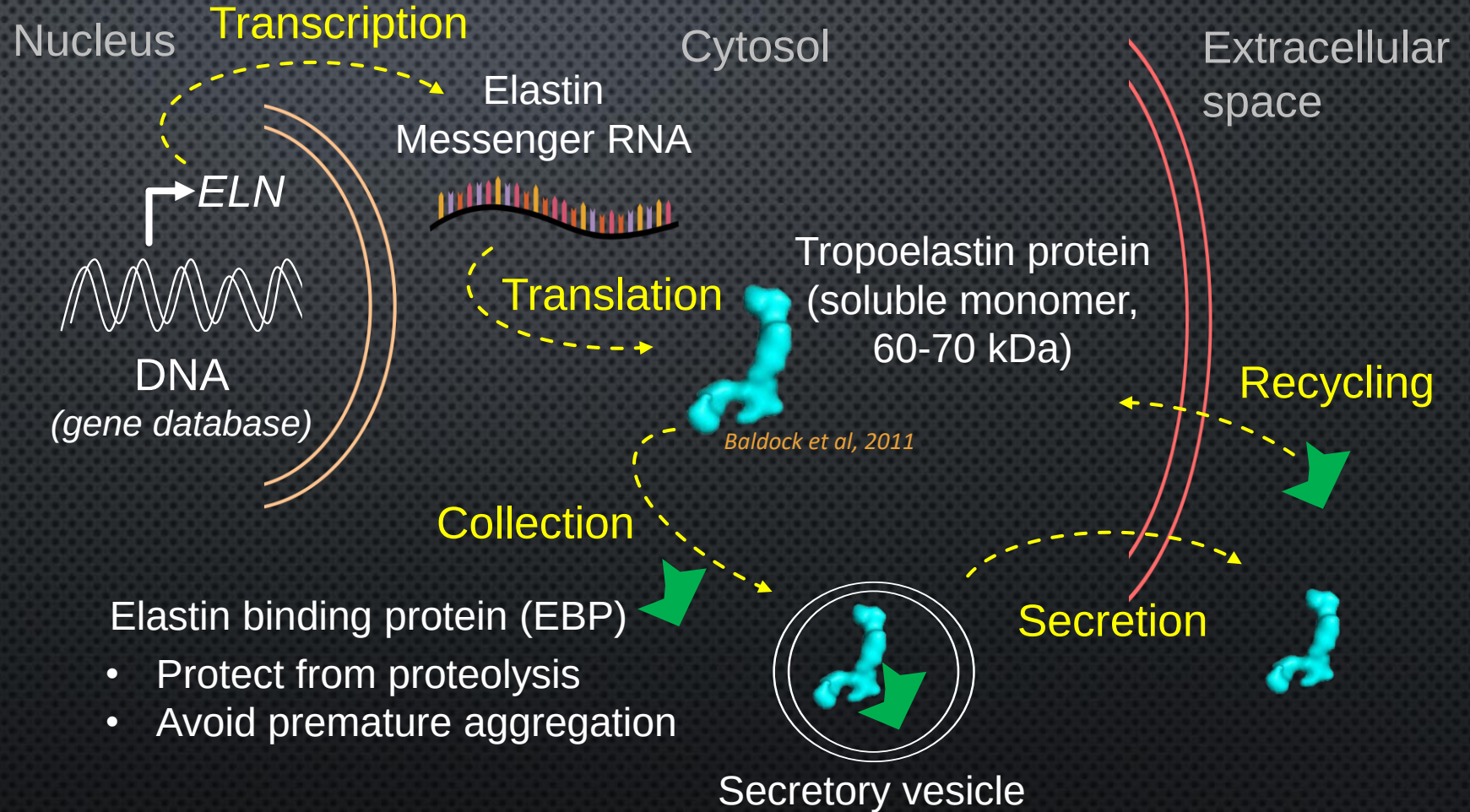
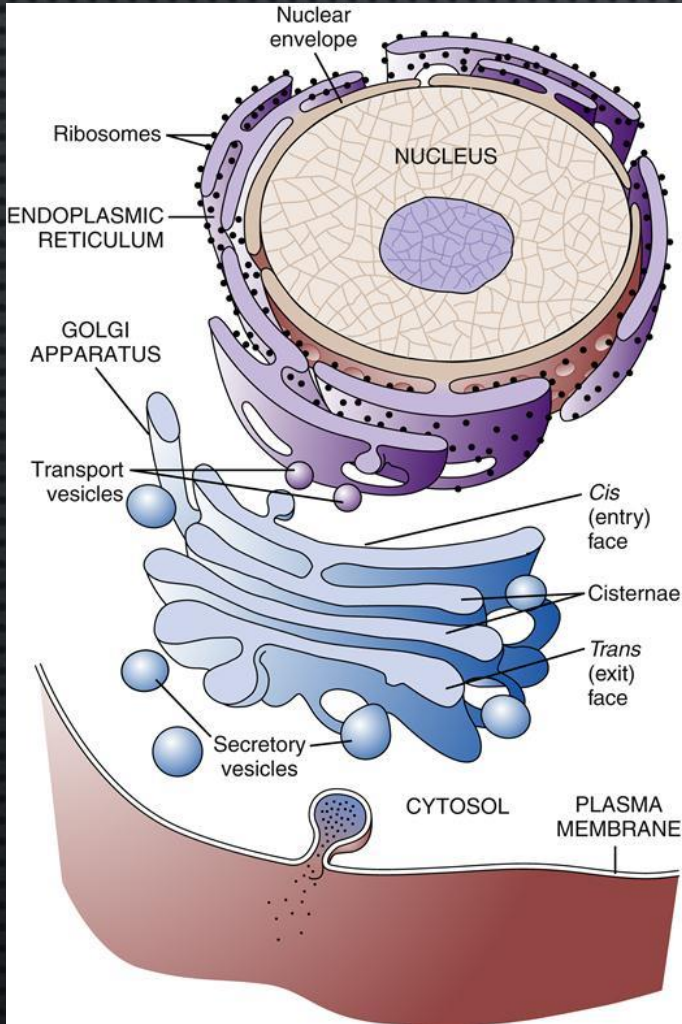
Microfibrils (10%)
Elastin (90%)



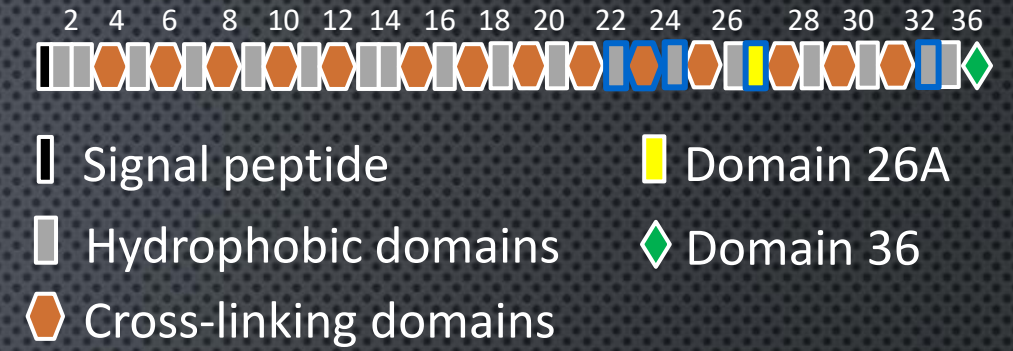
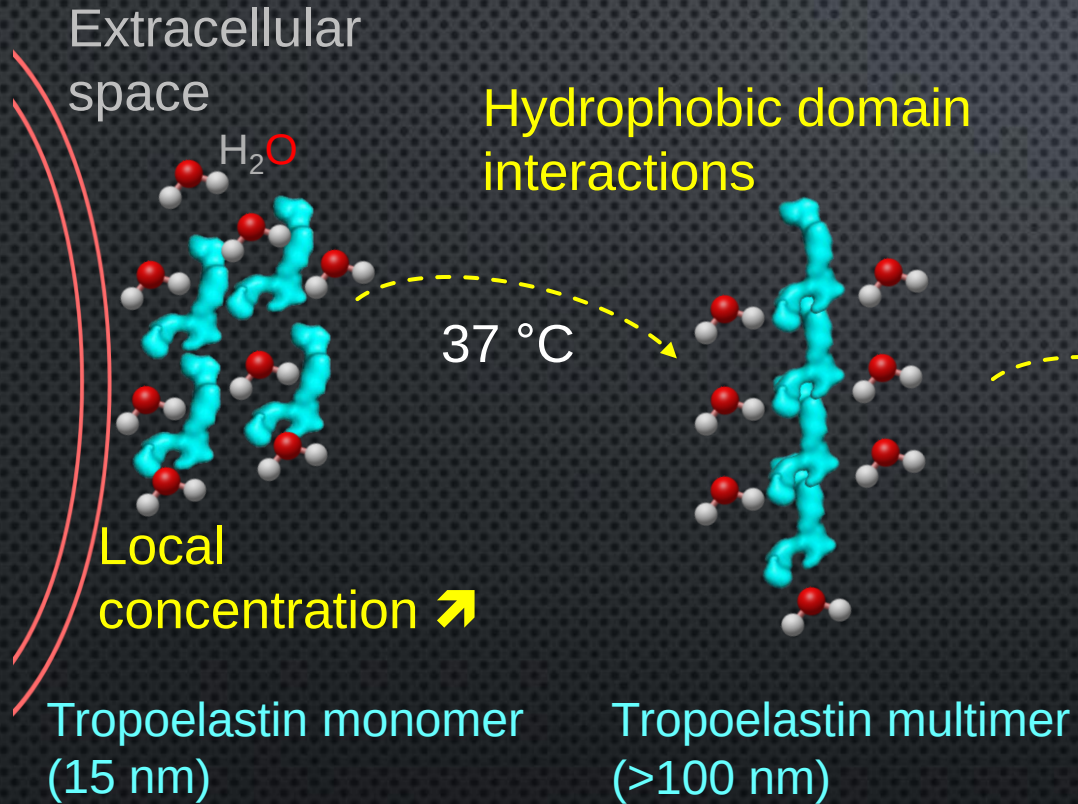
**Elastin is the
main provider
of elasticity**

Stage 1: Synthesis

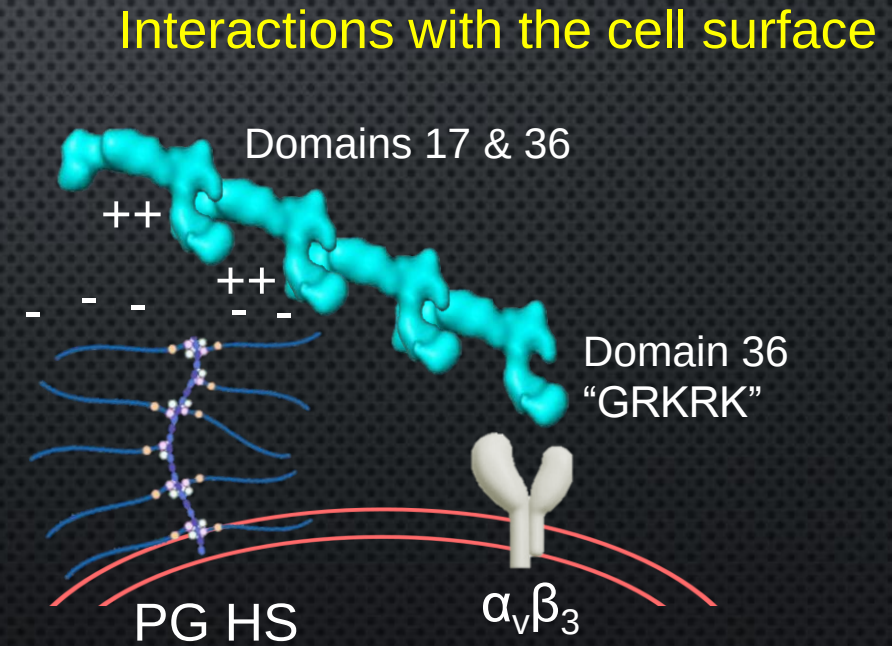
2 main elastogenic cell types: fibroblasts (ex: dermis, lung) and smooth muscle cells (ex: arteries)



Stage 2: Coacervation



Adapted from Wise and Weiss, 2009

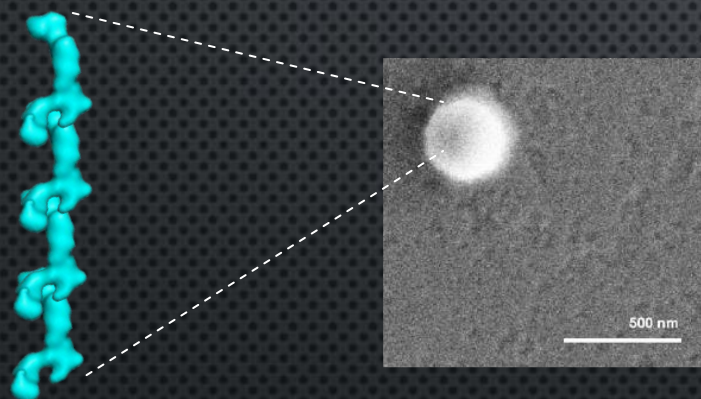


Lee et al, 2017

Bax et al, 2009

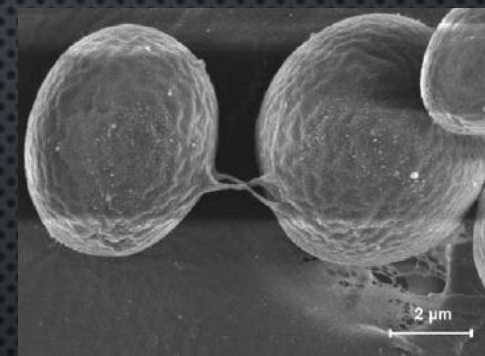
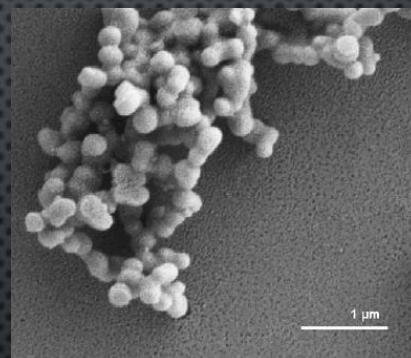
Stage 3: Multimers and spherical aggregates

Tropoelastin spherules
(> 200 nm)



Spherule
coalescence

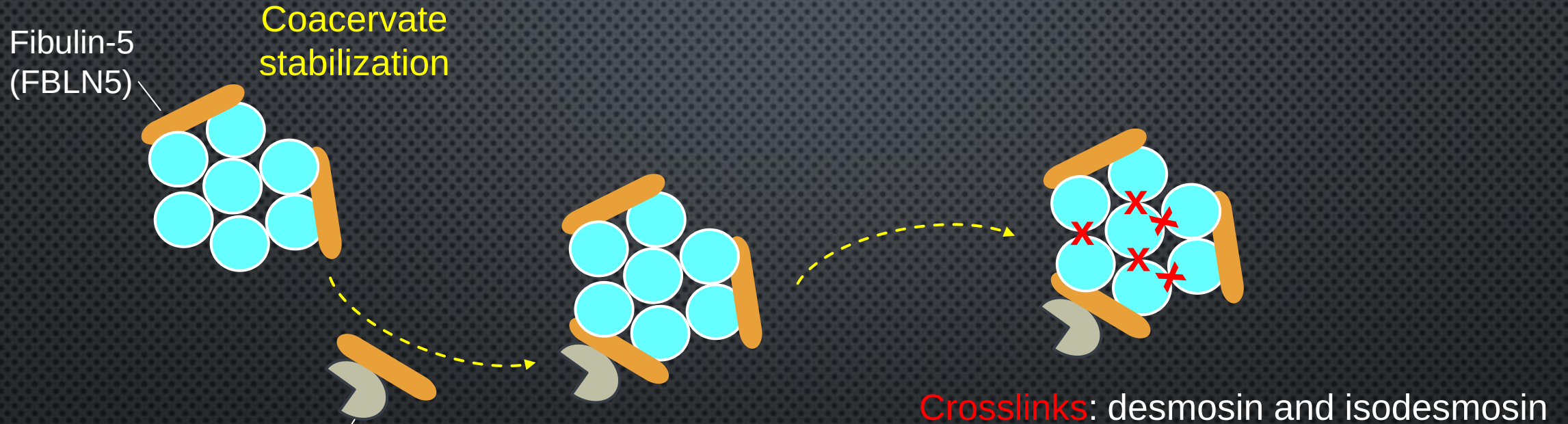
Tropoelastin mature coacervates
(200 nm – $6\text{ }\mu\text{m}$)



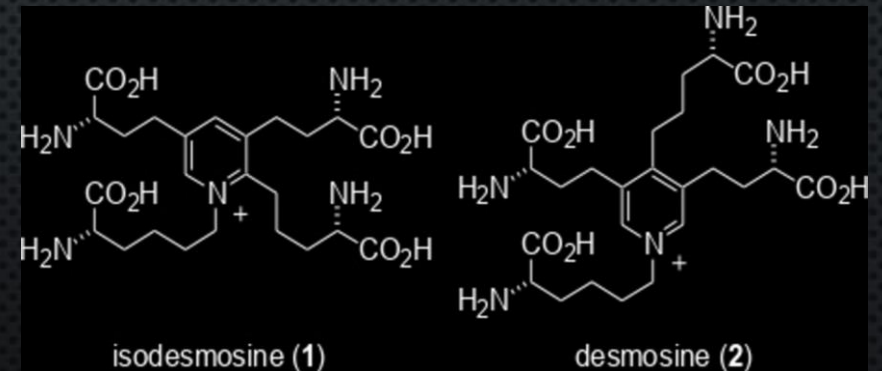
Multimer aggregation

Tu et al, 2010

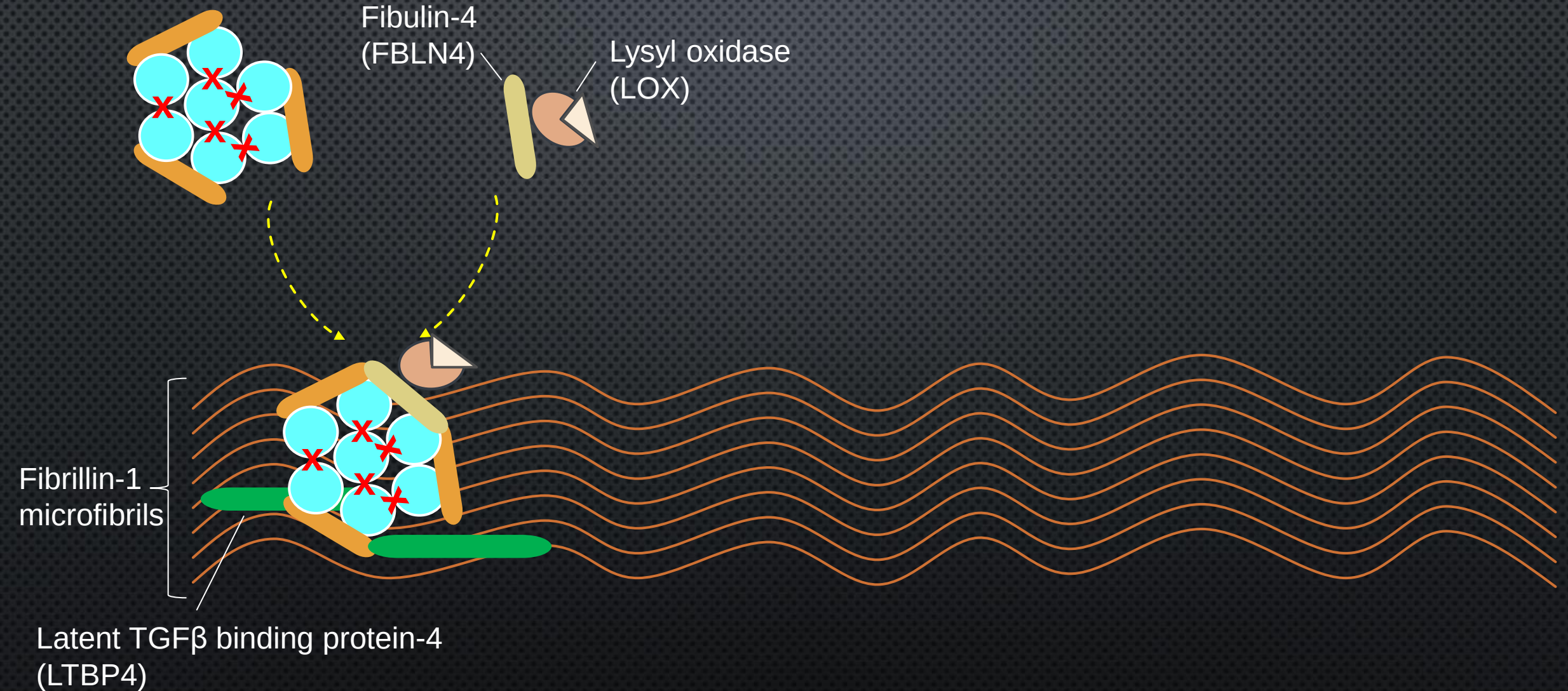
Stage 4: Initial cross-linking



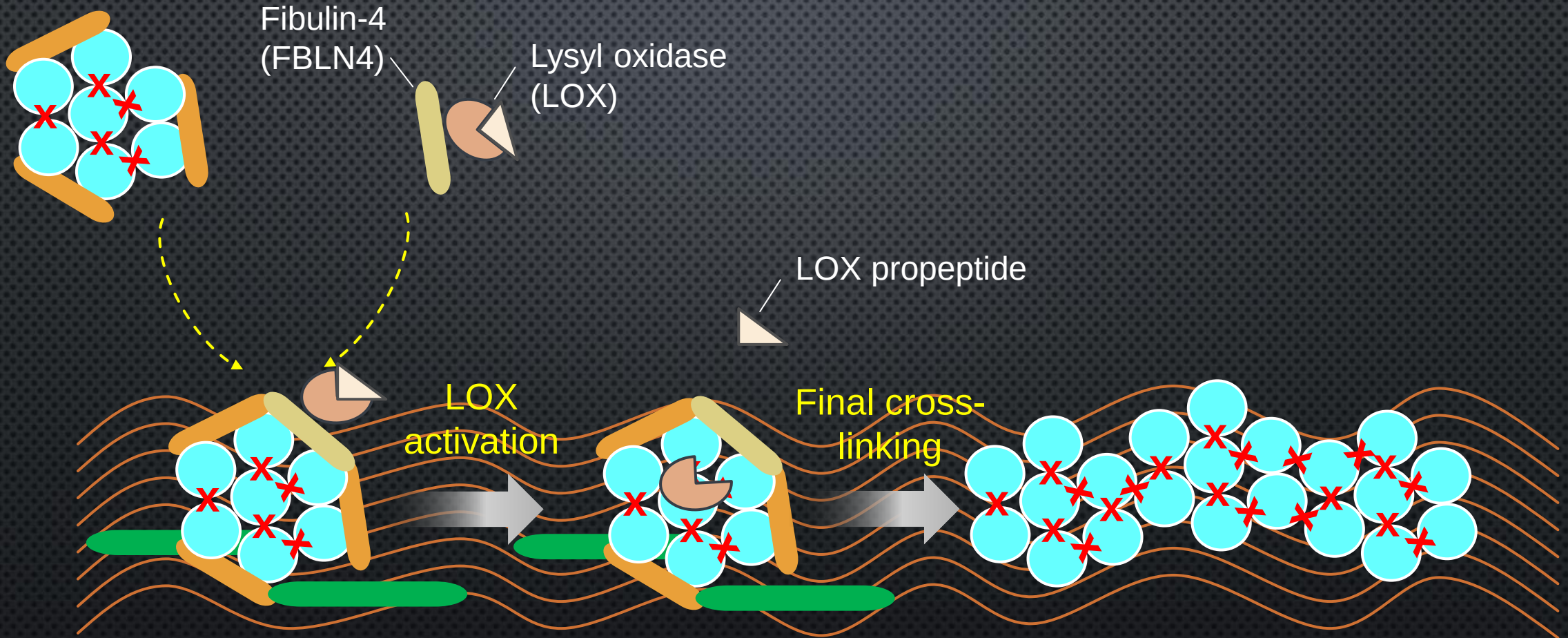
Involve 4 lysin residues from tropoelastin cross-linking domains



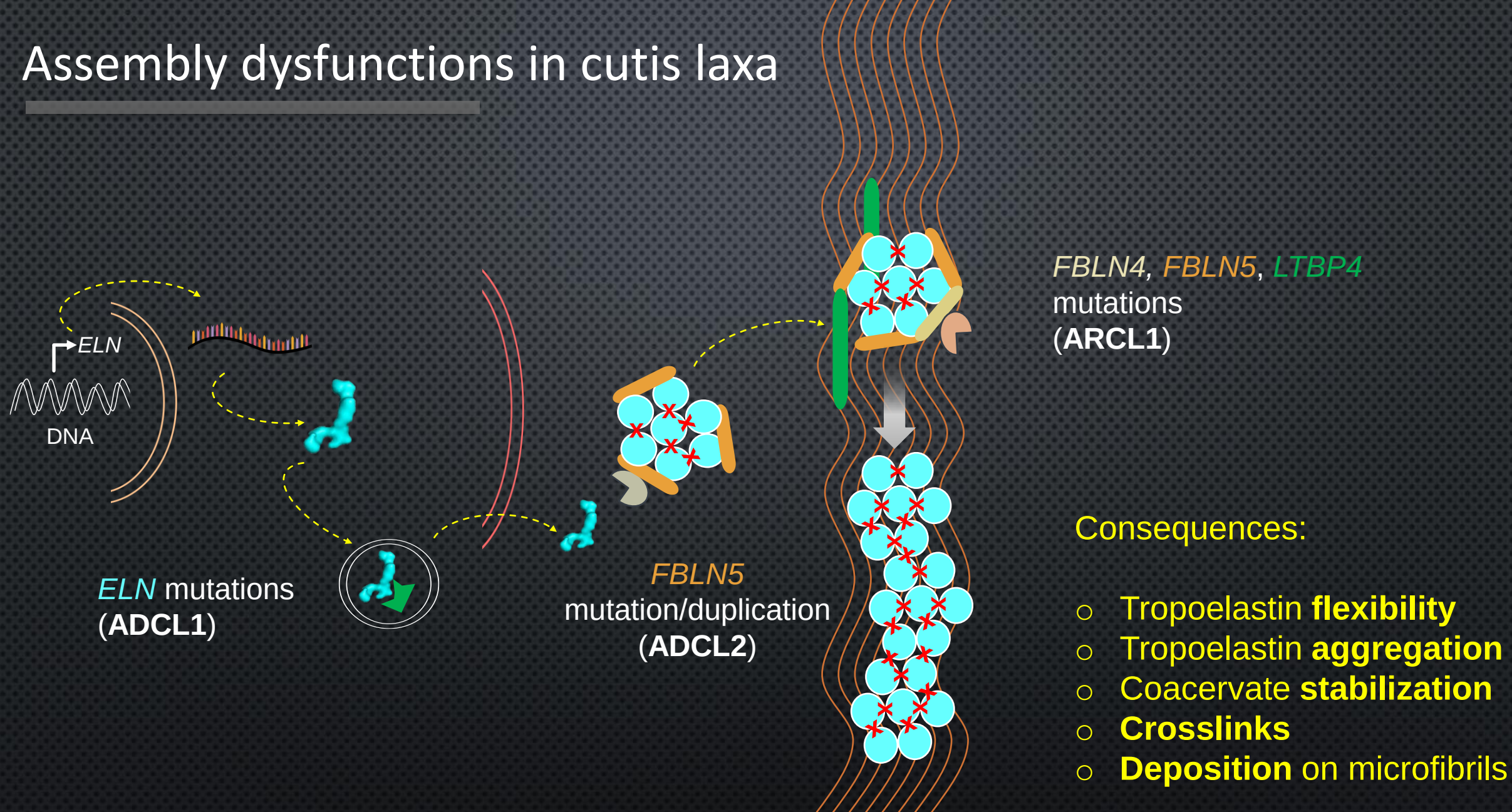
Stage 5: Deposition onto microfibrils



Stage 6: Elastic fiber maturation

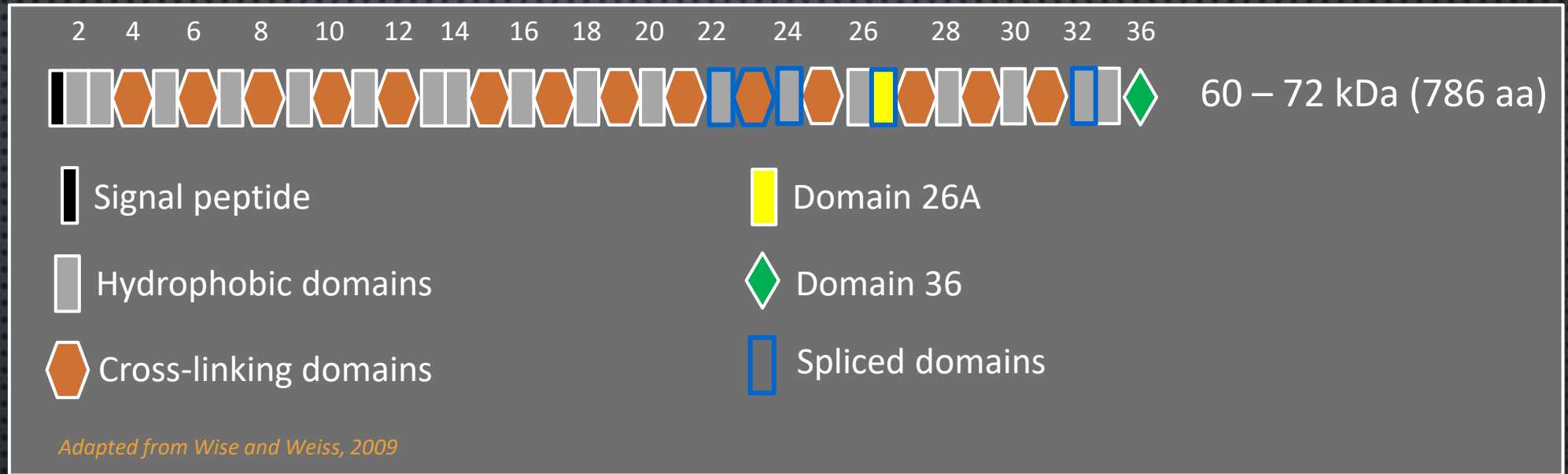


Assembly dysfunctions in cutis laxa

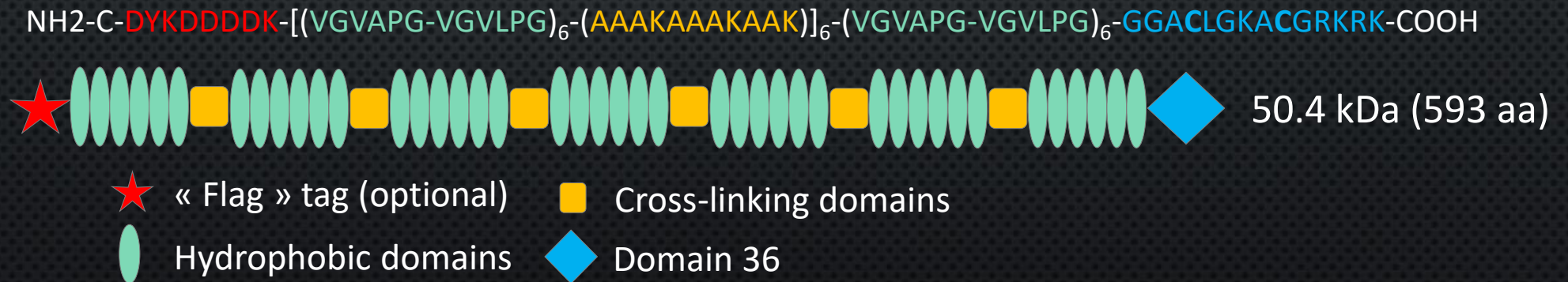


Synthetic elastic protein (SEP)

Human
tropoelastin



SEP



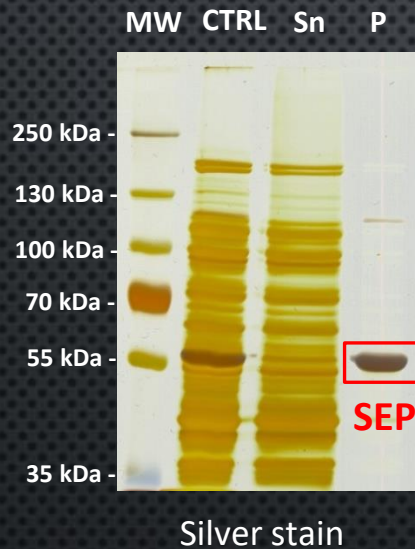
SEP is a simplified tropoelastin

Production and characterization

Bioproduction

Bacterial fermentation

Purification

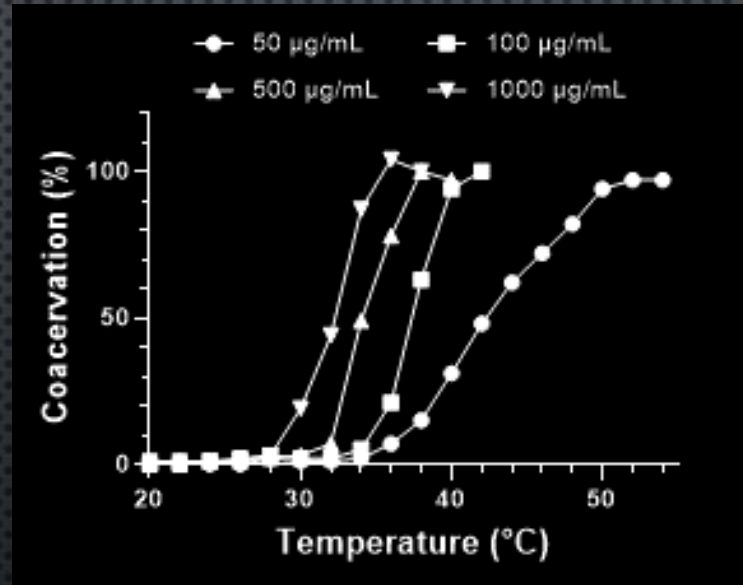


Aqueous
formulation
0.9% NaCl



Hoareau et al, 2023

Thermal responsiveness



Transition temp.
Reversible

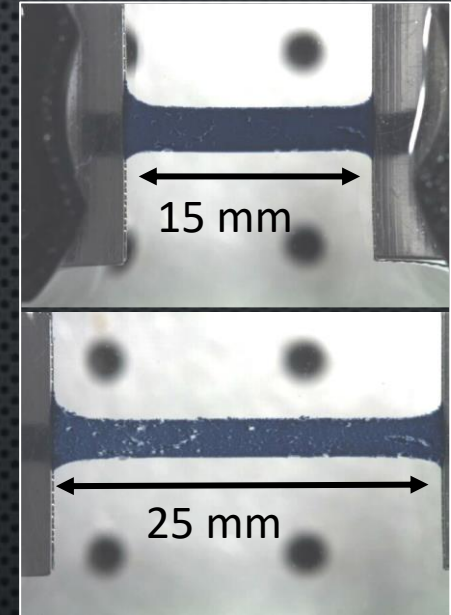
Mechanical properties



Crosslinked SEP

$E = 52.8 \text{ kPa}$

$\lambda_{\text{max}} = 2.8$



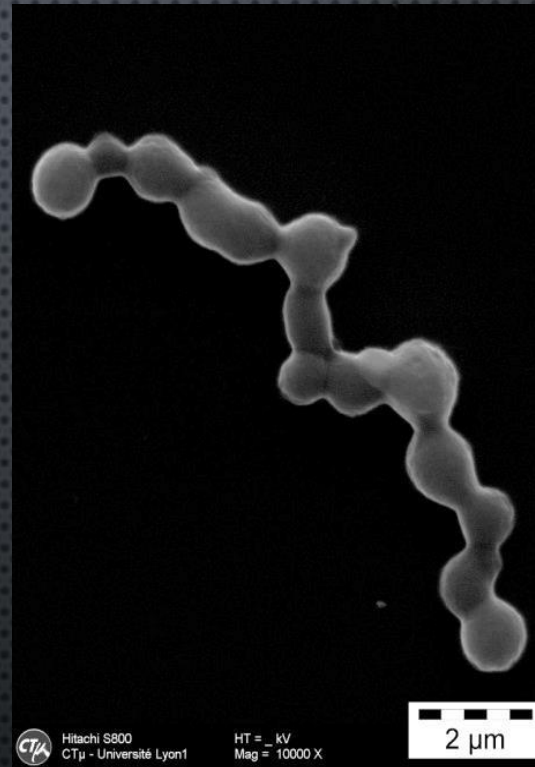
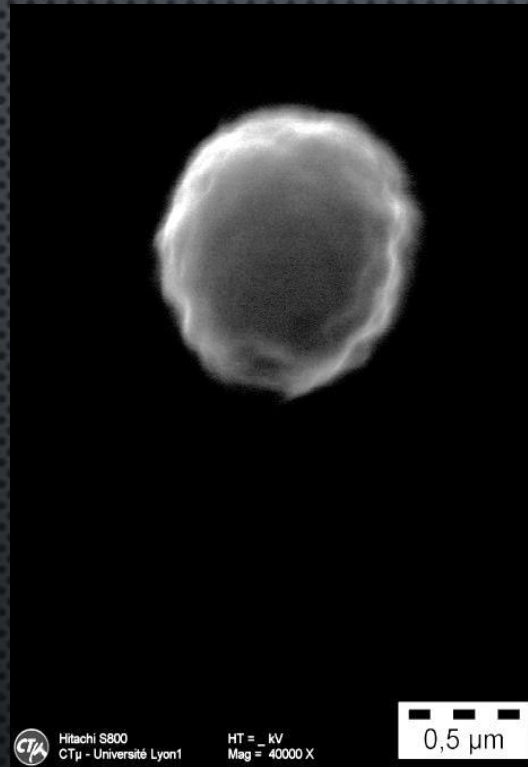
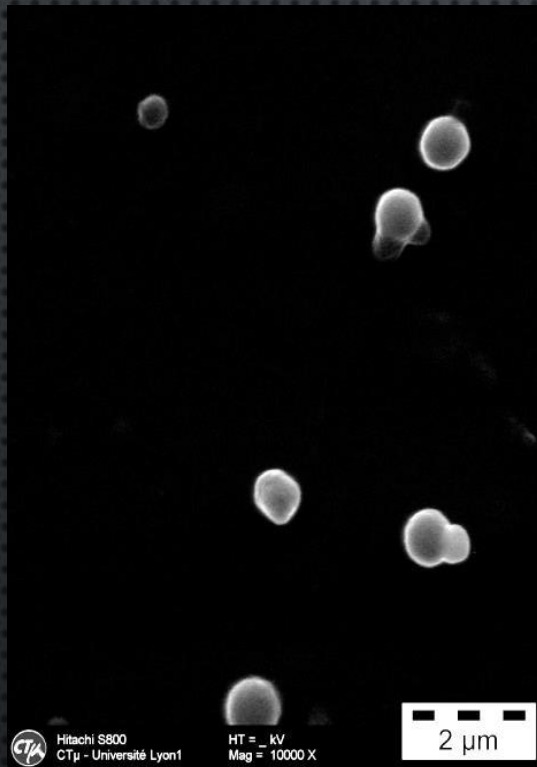
Collaboration S. Avril
(Sainbiose, St Etienne, France)



Elastic behavior

Coacervation structures

Scanning electron microscopy : SEP 2 mg/ml PBS – 37°C

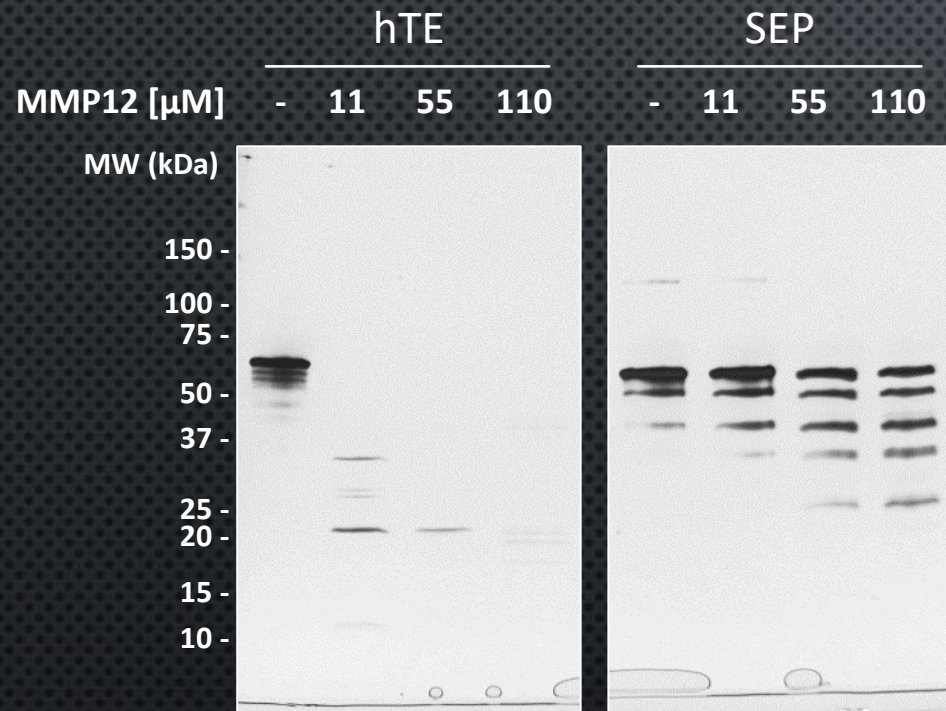


Self-assembly capacity

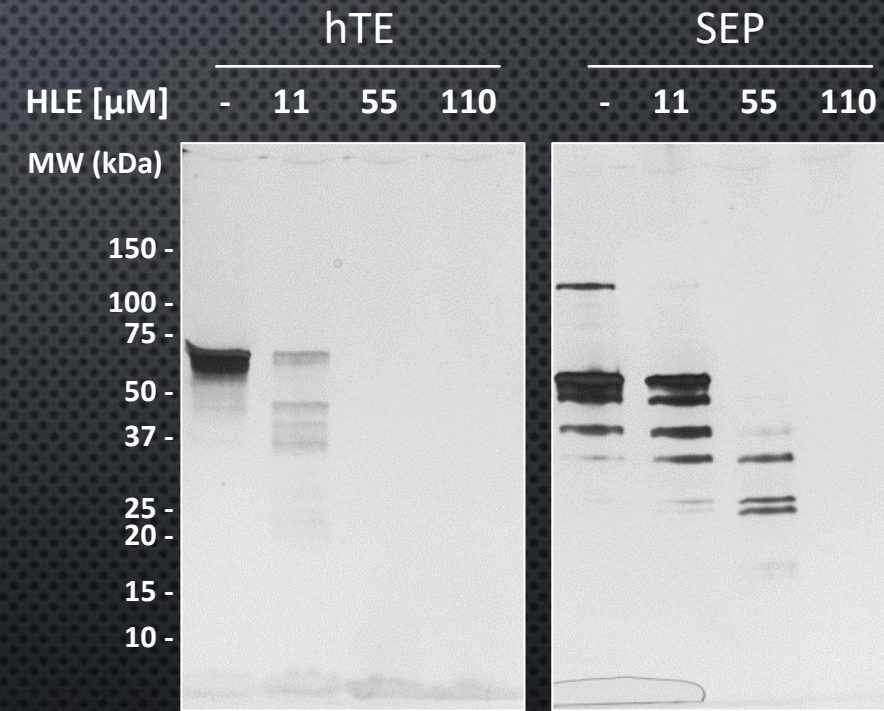
Proteolysis

hTE = human tropoelastin

MMP12



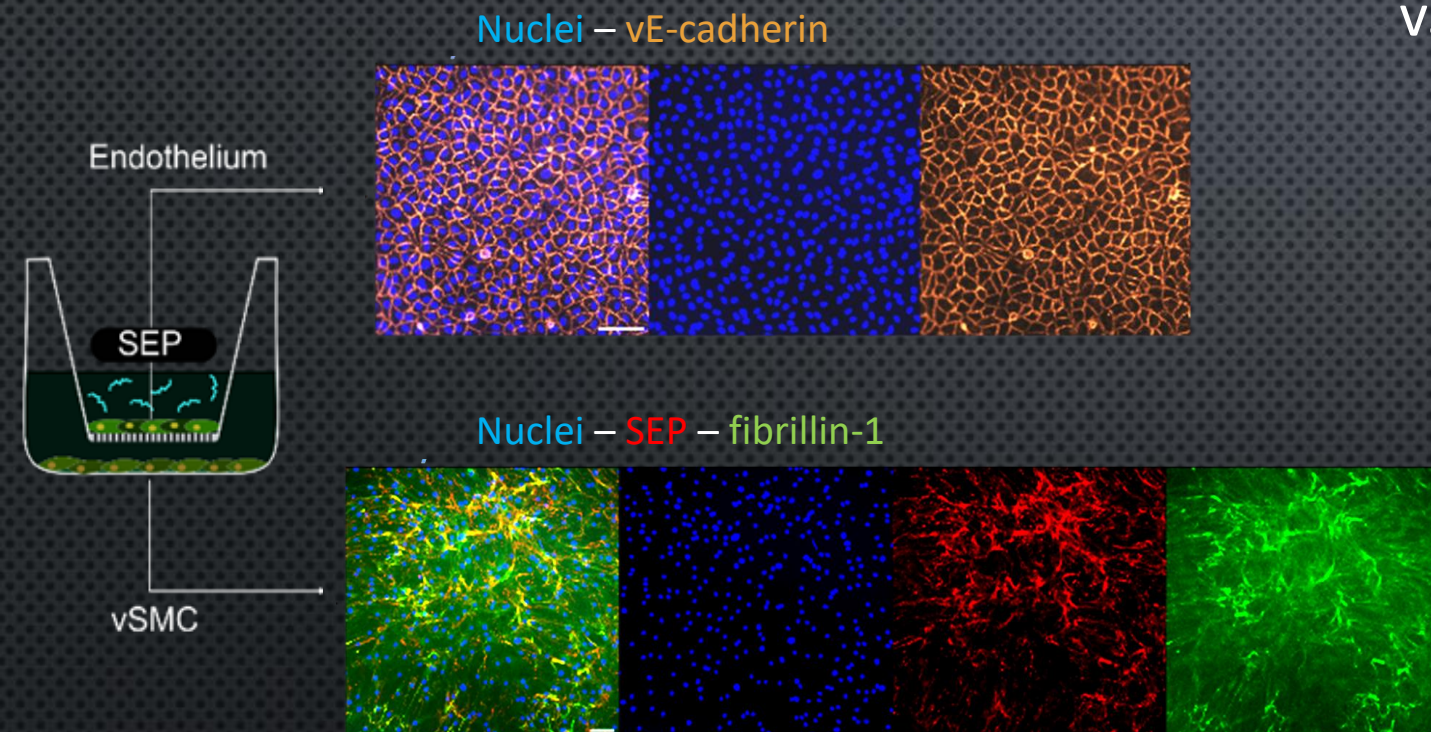
Human leucocyte elastase



SEP has better resistance to proteolysis than hTE

Treatment of human vascular cells

Trans-endothelial passage



Elastic fiber colocalization

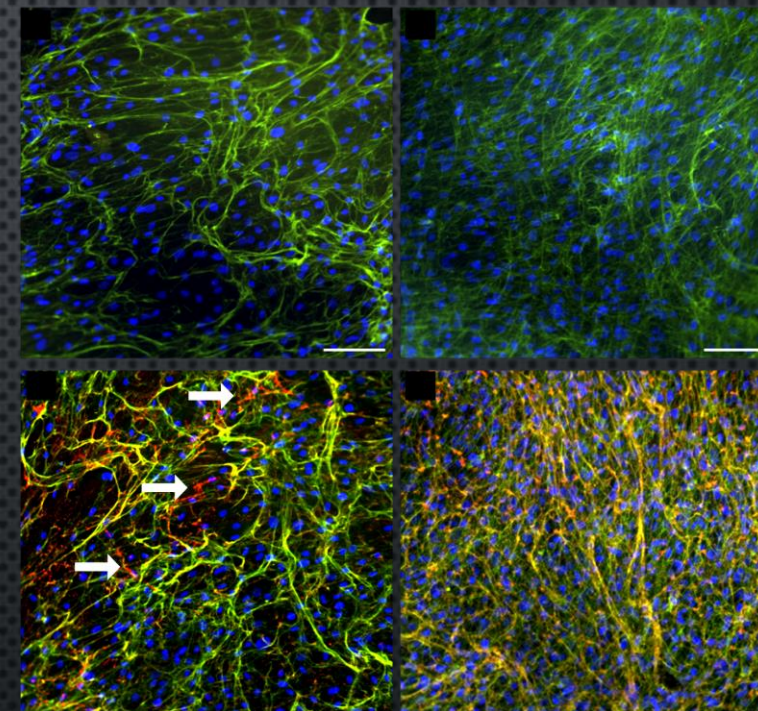
vSMC

J2

J15

Control

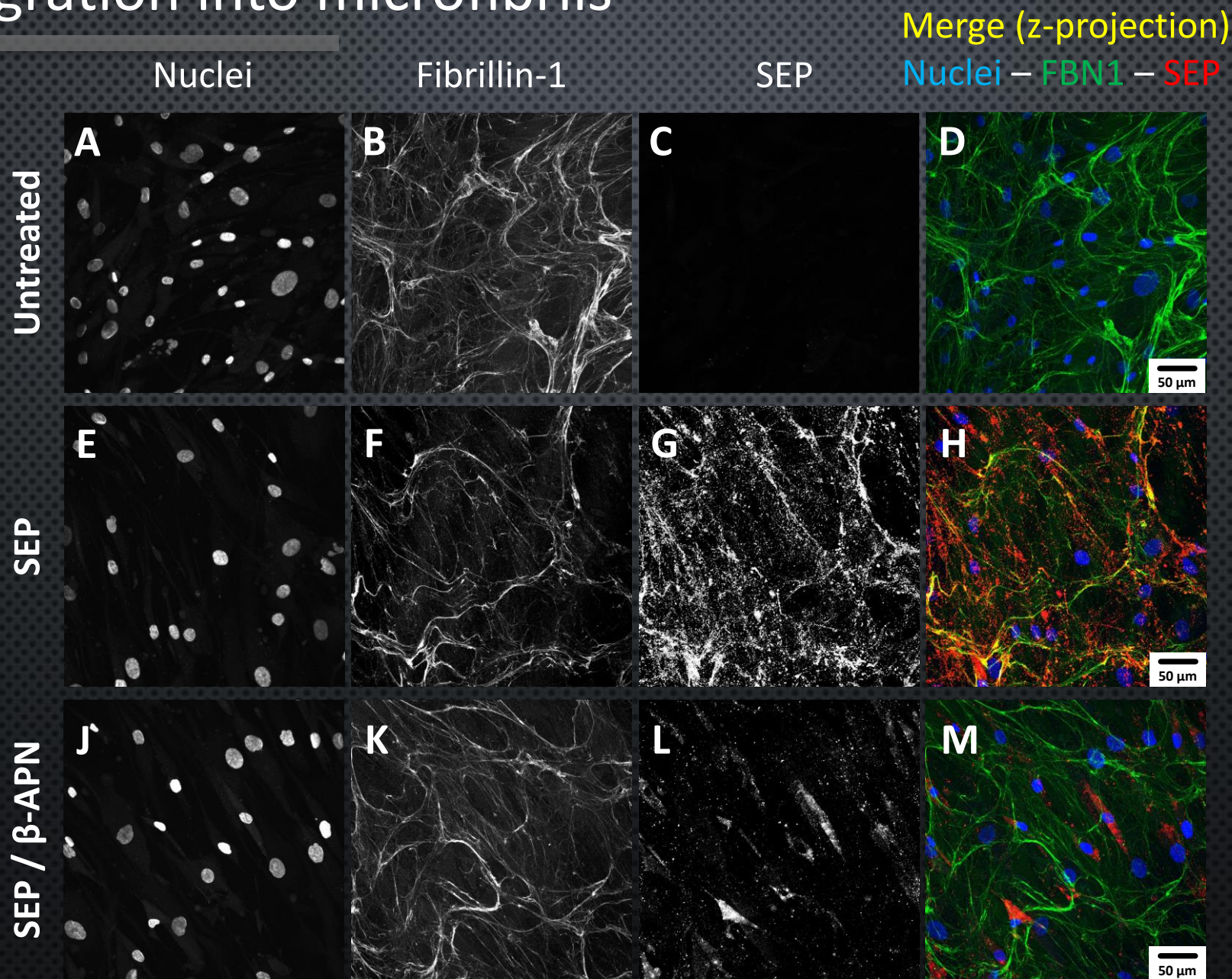
SEP
500 μ g/ml



Nuclei – SEP – Fibrillin-1

Persistence > 15 days in fibers (single treatment)

SEP integration into microfibrils



LOX-dependent
integration
(enzymatic)

SEP effect on murine arterial vasomotion



Model: $Eln^{+/+}$ vs $Eln^{+/-}$  Single-injection 60 $\mu\text{g/g}$

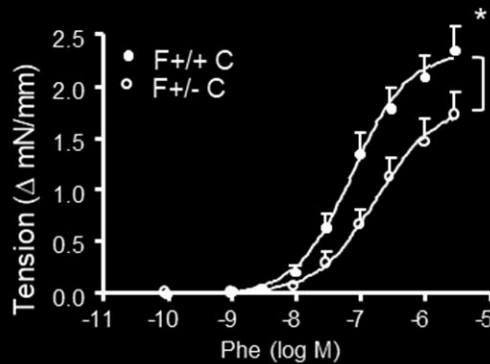


Myography

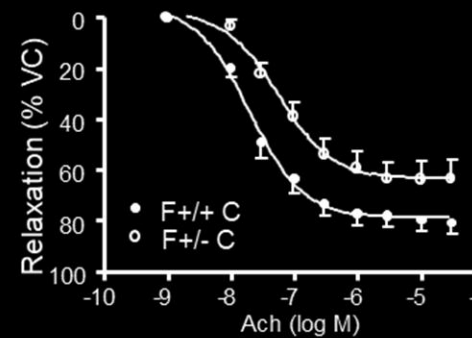
Analysis 3 days post-injection

Improvement of aorta
deficient vasomotion

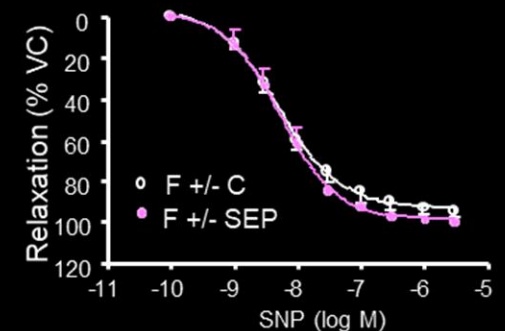
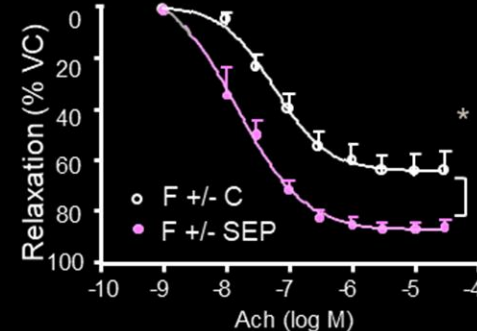
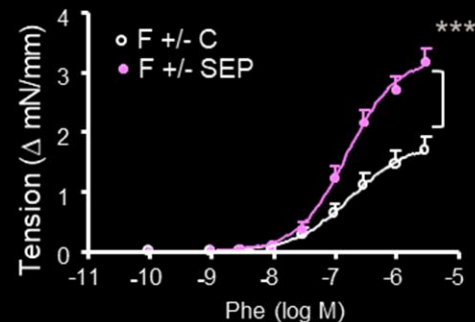
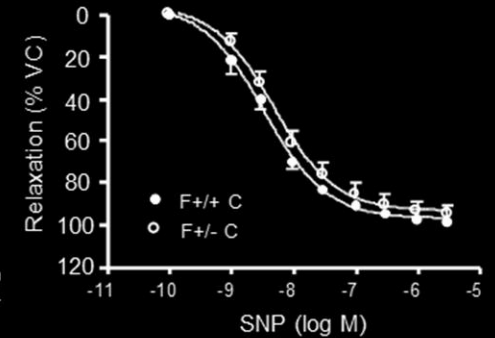
Phenylephrine
(SMC contraction)



Acetyl choline
(endoth.-dependent relaxation)



Sodium nitroprusside
(endoth.-independent relaxation)



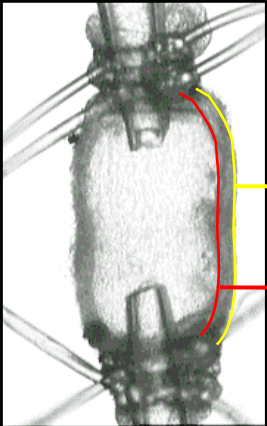
SEP effect on murine arterial mechanical properties



Collaboration G. Faury (HP2, Grenoble, France)



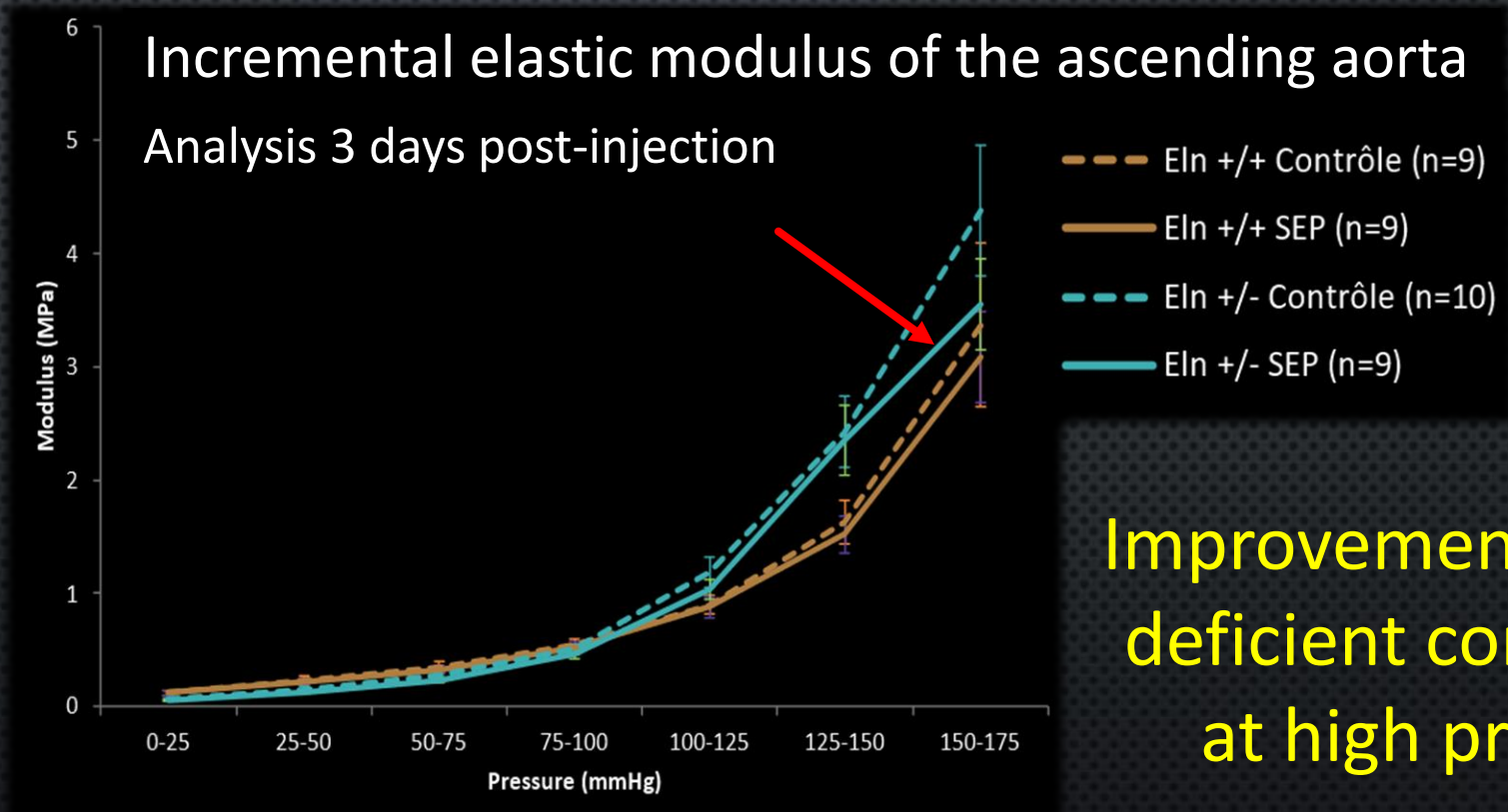
Model: $Eln^{+/+}$ vs $Eln^{+/-}$  Single-injection 60 $\mu\text{g/g}$



$\varnothing$ ext.

$\varnothing$ int.

Cannulated vessel



Improvement of aorta
deficient compliance
at high pressure

Lung emphysema treatment: proof of concept



Collaboration S. Adnot (IRMB, Créteil, France)

SEP oropharyngeal instillation
=> 200 μ g/10g, q.wk. / 3wk

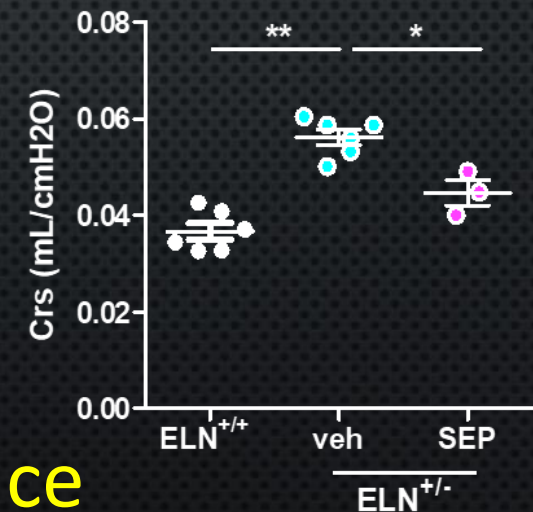
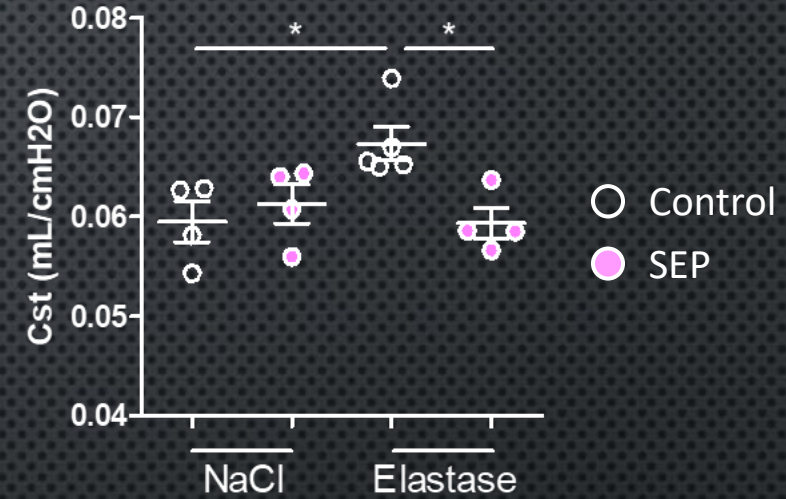


FlexiVent[®]
=> Lung mechanical properties

Mouse model #1
Elastase-induced
emphysema

Mouse model #2
Eln^{+/-}

Dynamic compliance



SEP improves the defective pulmonary compliance

SEP nebulization on lung cells

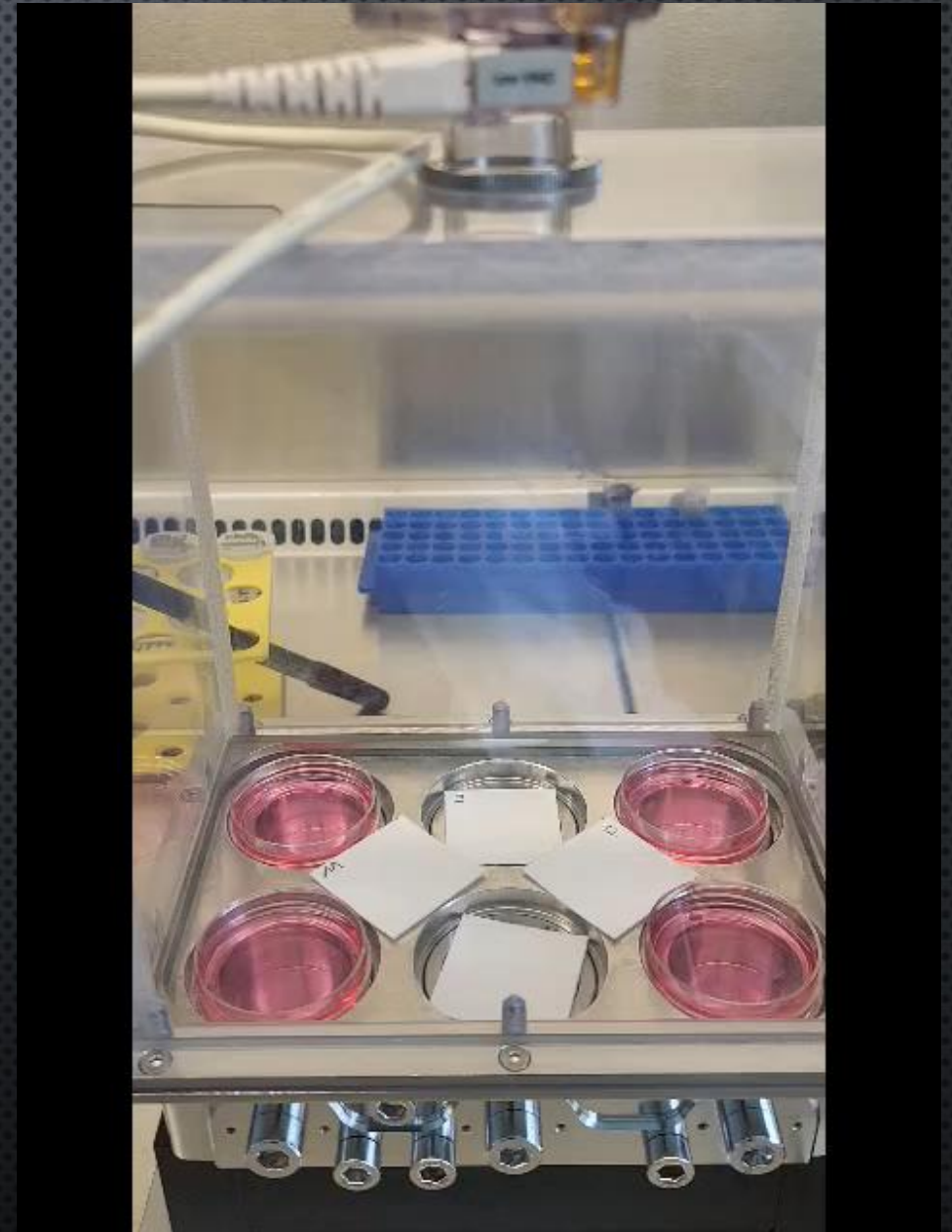
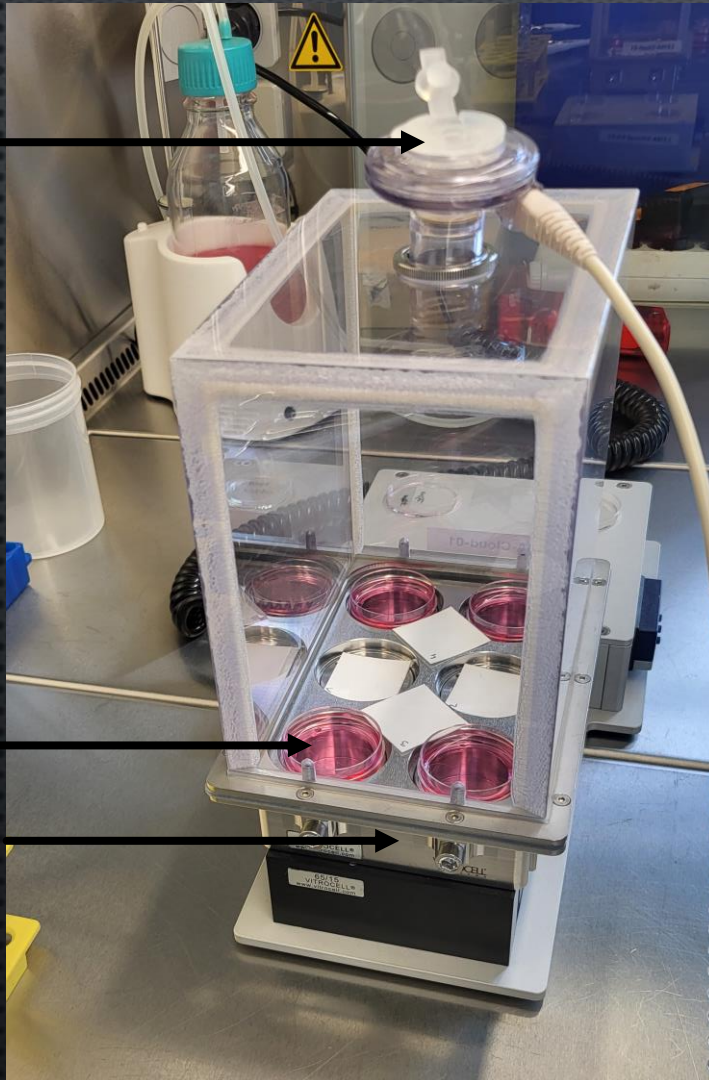
SAINBIOSE
Santé Ingénierie
Biologie Saint-Etienne
UNIVERSITÉ DE SAINT-ETIENNE

Collaboration J. Pourchez (Sainbiose, St Etienne, France)

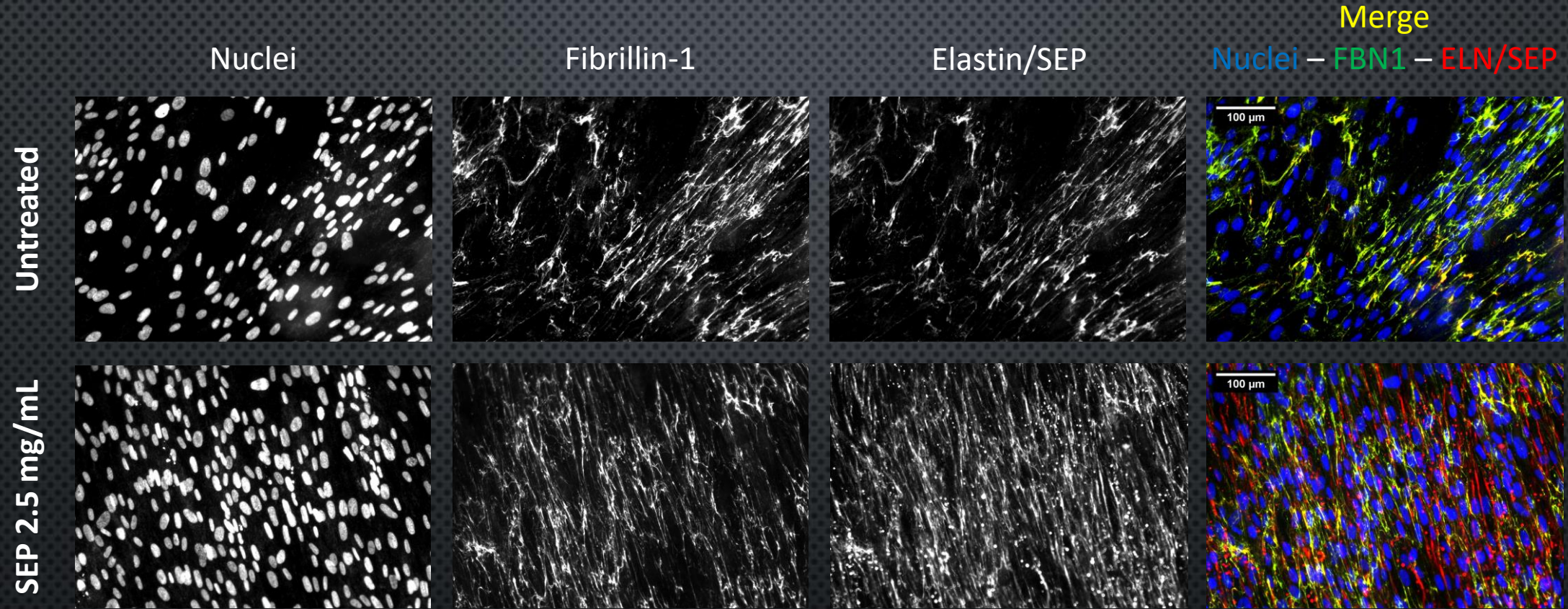
Nebulizer
(contains
fluorescent
SEP)

Lung cells
(MRC5)

Thermoblock



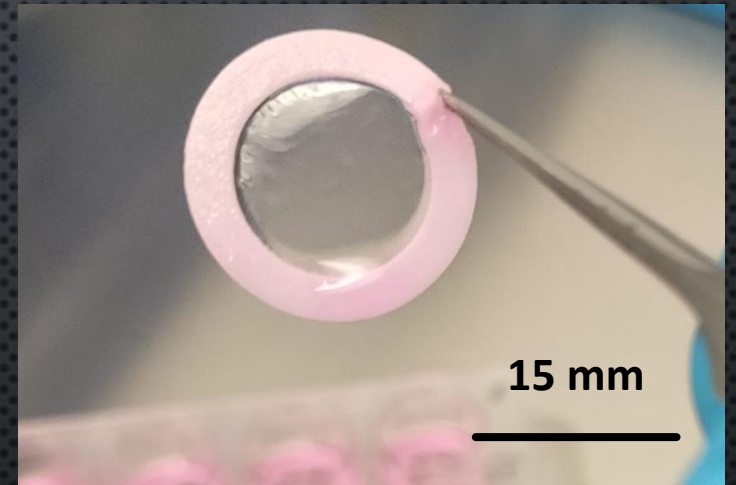
SEP deposition after nebulization



The nebulized SEP is still able to form fibrillar deposits

Treatment of a dermal model

Dermal fibroblasts from 65 y.o. individual

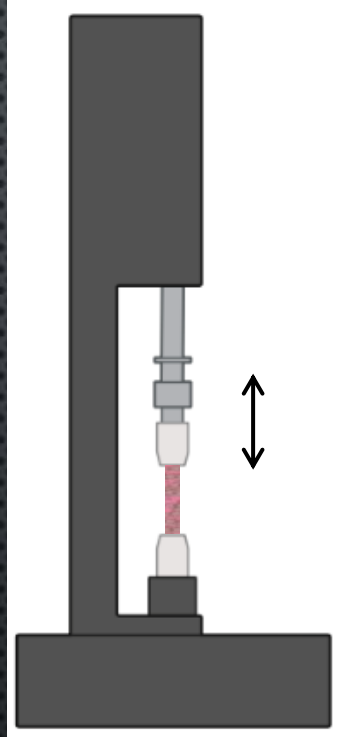


Reconstructed dermal sheet

Mechanical properties of the dermal model



± SEP



DMA
(Dynamic Mechanical Analysis)

	E' (kPa) mean ± SD	Adjusted p-value	Young Modulus (kPa) mean ± SD	Adjusted p-value
Untreated (n=25)	15.61 ± 4.3		5.09 ± 1.9	
SEP 50 µg/mL (n=22)	15.78 ± 5.4	ns	5.17 ± 2.1	ns
SEP 200 µg/mL (n=7)	23.04 ± 2.7	**; 0.004	7.11 ± 1.9	*; 0.038

+ 46% elastic modulus (E')

=> Restores more energy

+ 40% Young's modulus

=> Increased stiffness

Next challenges

1. Defining pharmacokinetics and pharmacodynamics parameters

=> How the SEP diffuses in the body and what is the relation between dose and efficacy

2. Developing vehicles to cross the skin barrier on large surfaces

=> molecules > 500 Da do not cross the epidermis (SEP is 50 000 Da)

3. Evaluating the benefit with cells from cutis laxa patients

=> at the structural and the mechanical levels

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Jorgan Guard (Msc 2024)
Joseph Combecave (Msc 2026)

Thibault Massias (Postdoc 2024-...)

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(HP2, Grenoble)



Serge Adnot
(IMRB, Créteil)



Stéphane Avril
Jérémy Pourchez
(Sainbiose, St Etienne)



Chrystel Faure
(CBMN, Bordeaux)



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Private partner:



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