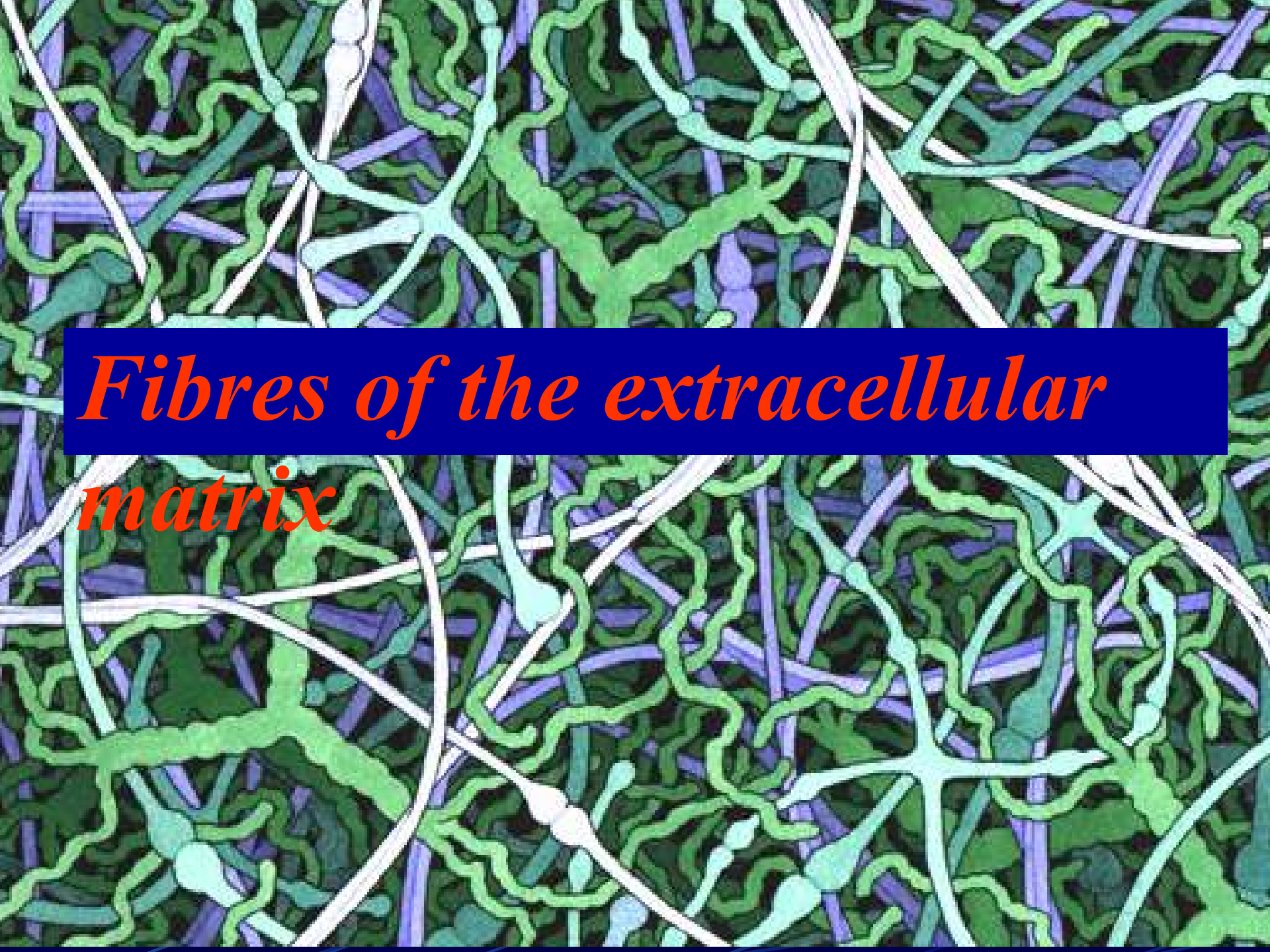

Matrix



Fibres of the extracellular matrix

The matrix of connective tissue

fibres

ground substance

Fibres in matrix

collagen

reticulin

elastin

Collagen

most abundant protein in animal world

25% of protein of mammals

Noncollagen collagens – C1q, SP – A, SP - D

Distribution of collagen

fibrous component of ordinary connective tissue

cartilage

bone

cornea

sclera

vitreous body

nucleus pulposus

tendons

aponeurosis

ligaments

fascia

sheaths of muscles & nerves

meninges

dermis

Light microscopic features of collagen

fresh collagen white & glistening

faint longitudinal striation

no branching

stains lightly with eosin

stain strongly with aniline blue & aldehyde fuschin

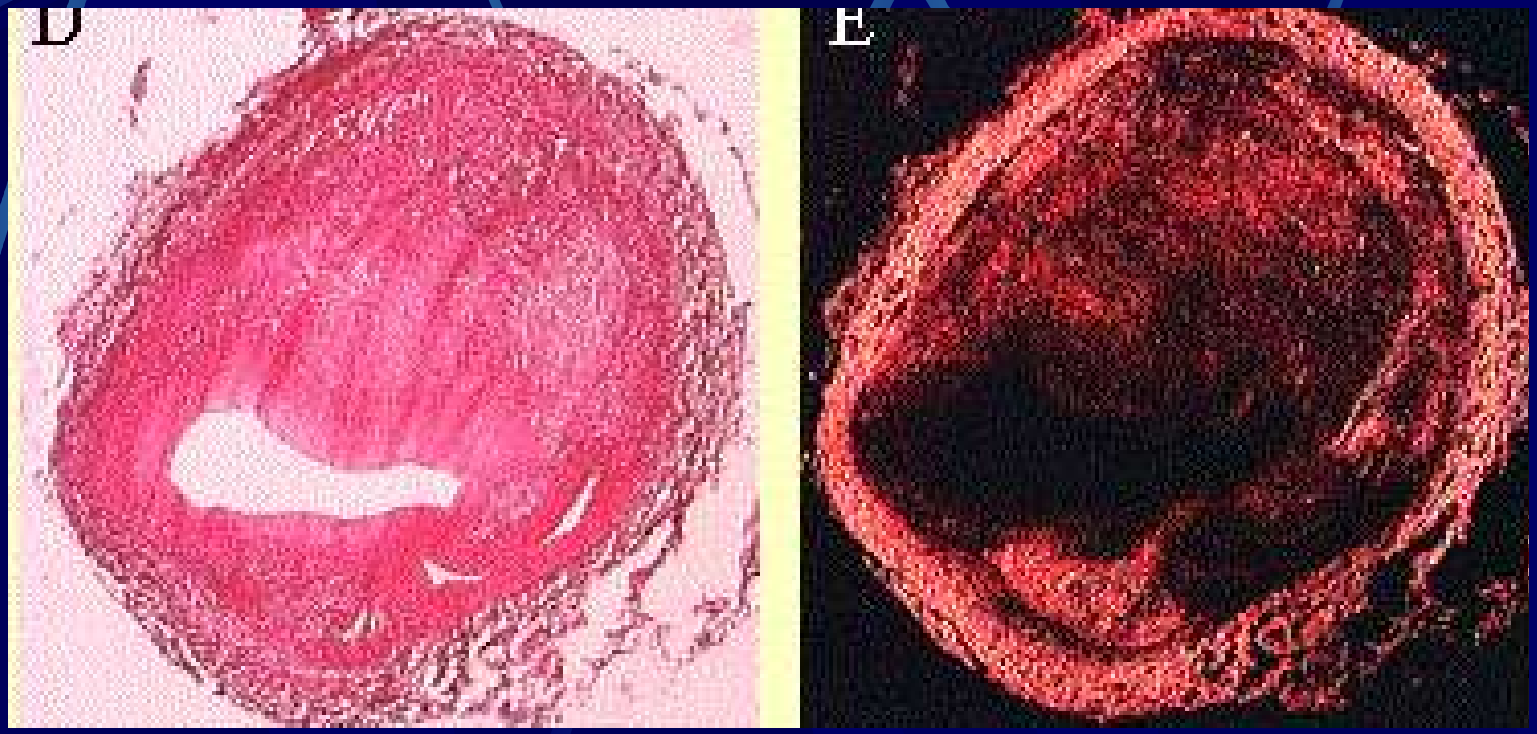
birefringence under polarizing microscope with enhancement by Sirius Red

LS through tendon

H & E

Collagen viewed by polarizing microscope

Sirius red



Arrangement of collagen in different structures

ligament

dense irregular connective tissue

tendon

Electron micrograph of collagen

collagen fibrils (20 – 200 nm)

fine microfibrils

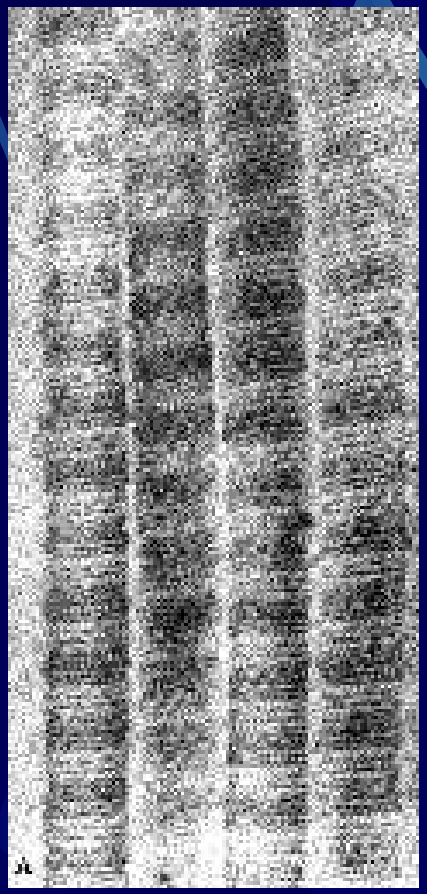
(aggregates of filamentous tropocollagen molecules)

visible strations

polarity of collagen in fibril

TEM of skin collagen fibril

uranyl acetate

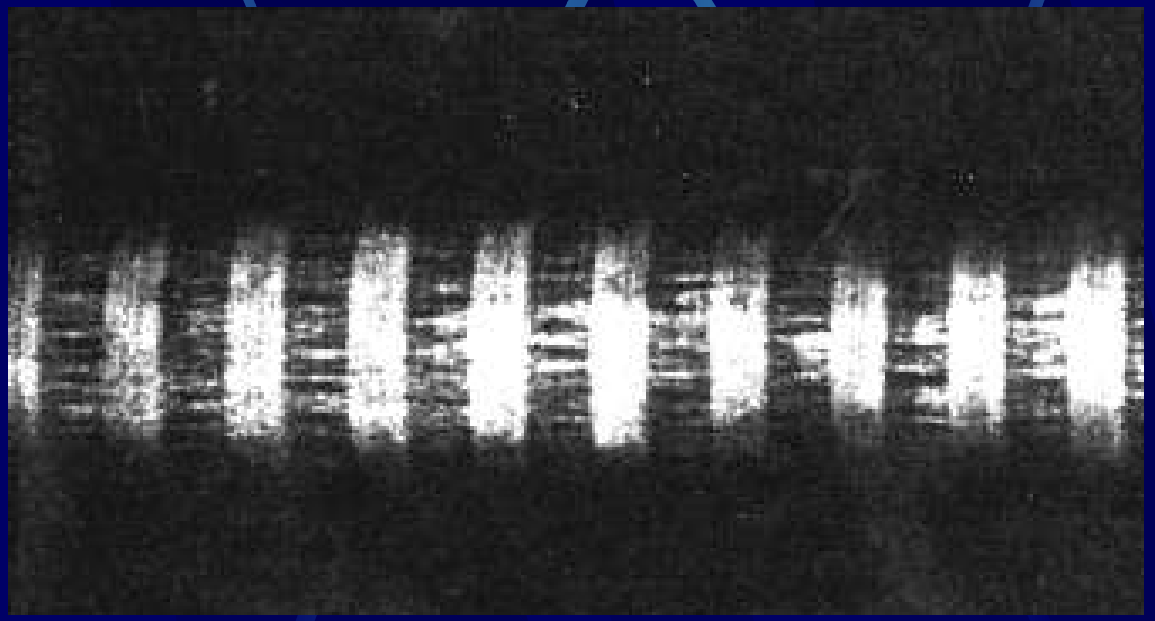


* 100, 000

Type I collagen fibril

phosphotungsate

1,40,000



Types of collagen

Type	Tissue
I	most connective tissue, bone
II (100 nm & 20 nm)	cartilage,vitreous humour, notochord
III	lung, vascular system, skin, reticulin
IV	lamina densa of basement membrane
V	~ collagen I
VII	anchoring fibrils
VIII	endothelium
IX	~ collagen II
XI	~ collagen II
XIV	~ collagen I
XVII	skin , hemidesmisomes
XVIII	liver, kidney

Classification of collagen, based primarily on the structure that they form

Class	Type
Fibril – forming	I, II, III, V, XI
Network like	IV, VIII, X
FACIT	IX, XII, XIV, XVI, XIX
Beaded filaments	VI
Anchoring fibrils	VII
Transmembrane domain	XIII, XVII

Molecular structure of collagen

triple helix

fibril forming vs. FACITs

Molecular structure of collagen

collagen type I – 1000 AA / chain

α chain in L handed helix of 3 residues / turn

3 α chains wound into R handed superhelix

300 nm / 1.4 nm

Molecular structure of collagen

$(Gly – X – Y)_n$

100 X = proline, 100 Y = (OH) proline

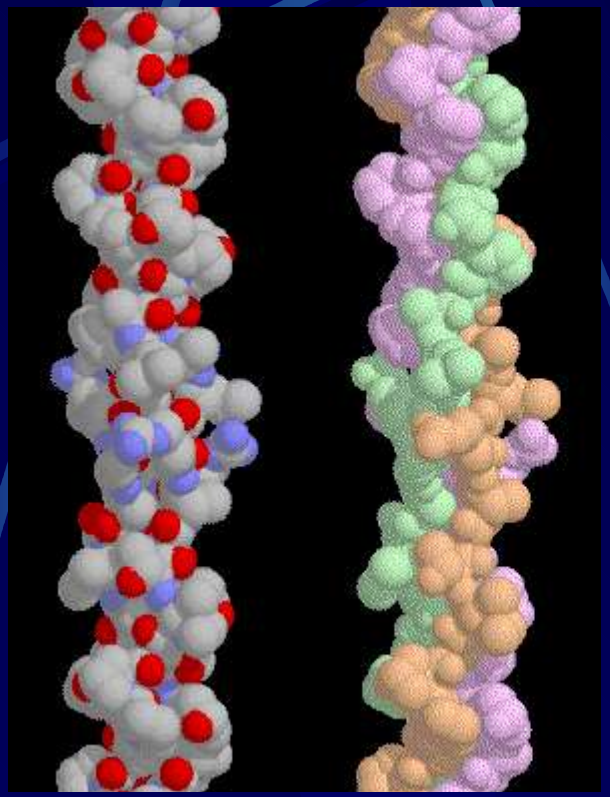
proline ---- **prolyl hydroxylase** ----------→ (OH) proline
vit. C, ketoglutarate

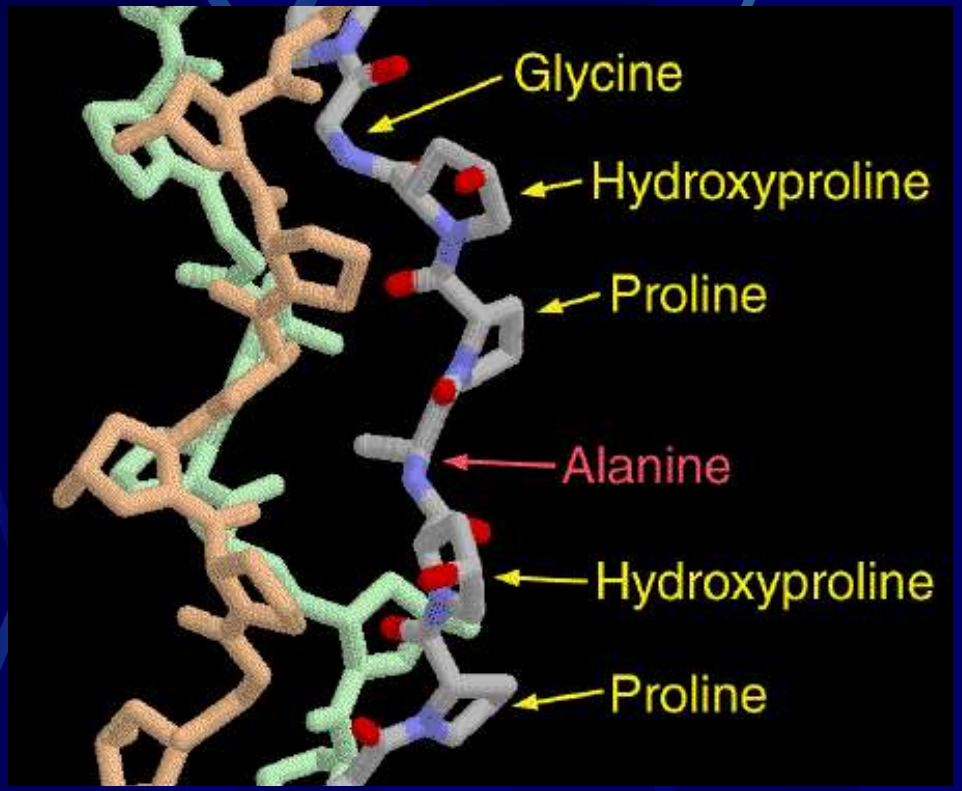
(OH) lysine in Y position by lysyl hydroxylase

(OH) lysine ~ O - glycosidic linkage ~
galactose / galactosyl - glucose

Triple helix

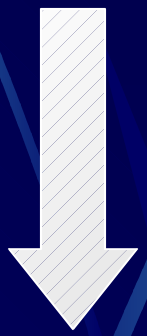
$(Gly – X – Y)_n$





Covalent cross links

ε– amino gr. of lysine / (OH) lysine



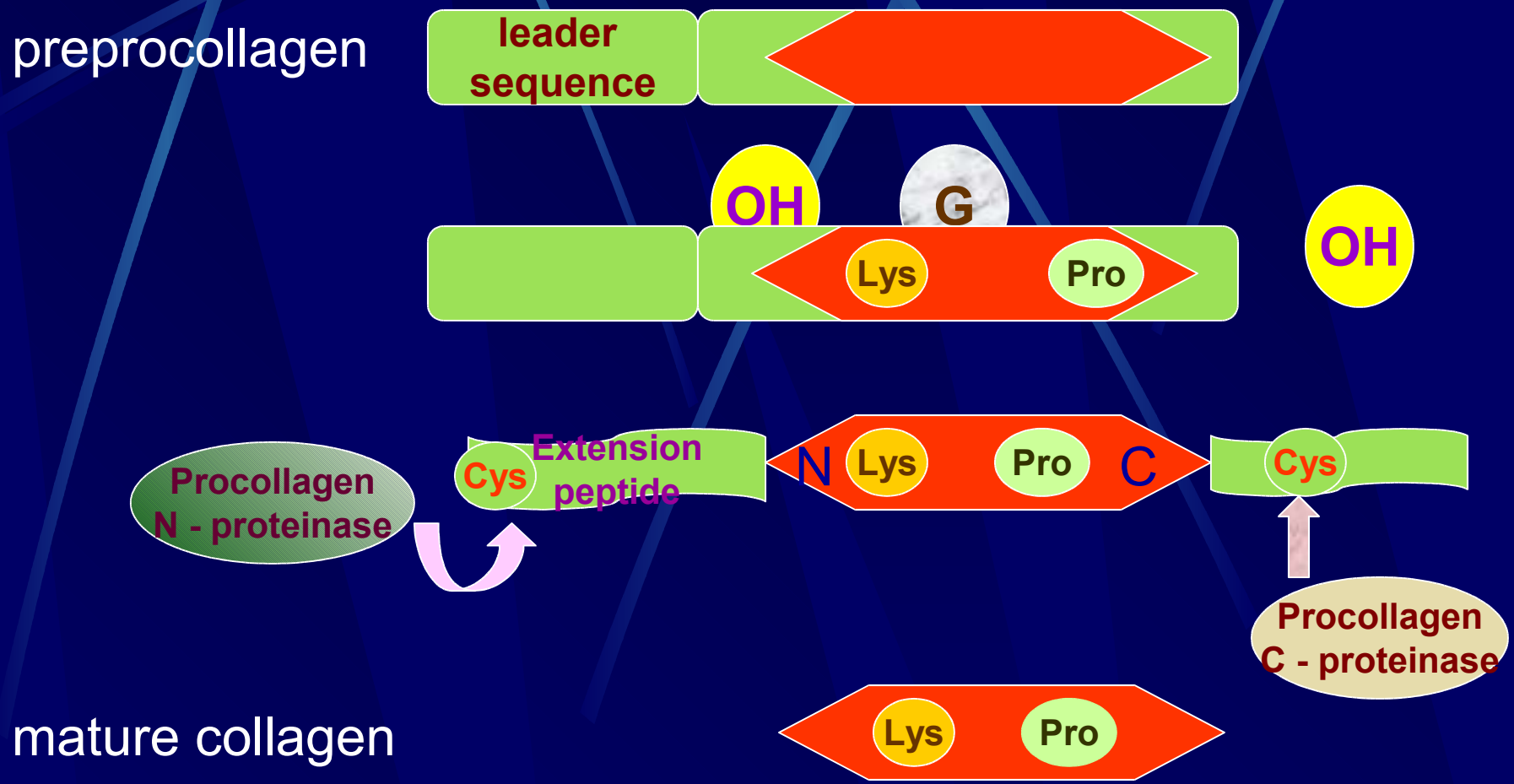
lysyl oxidase, Cu++

oxidative deamination

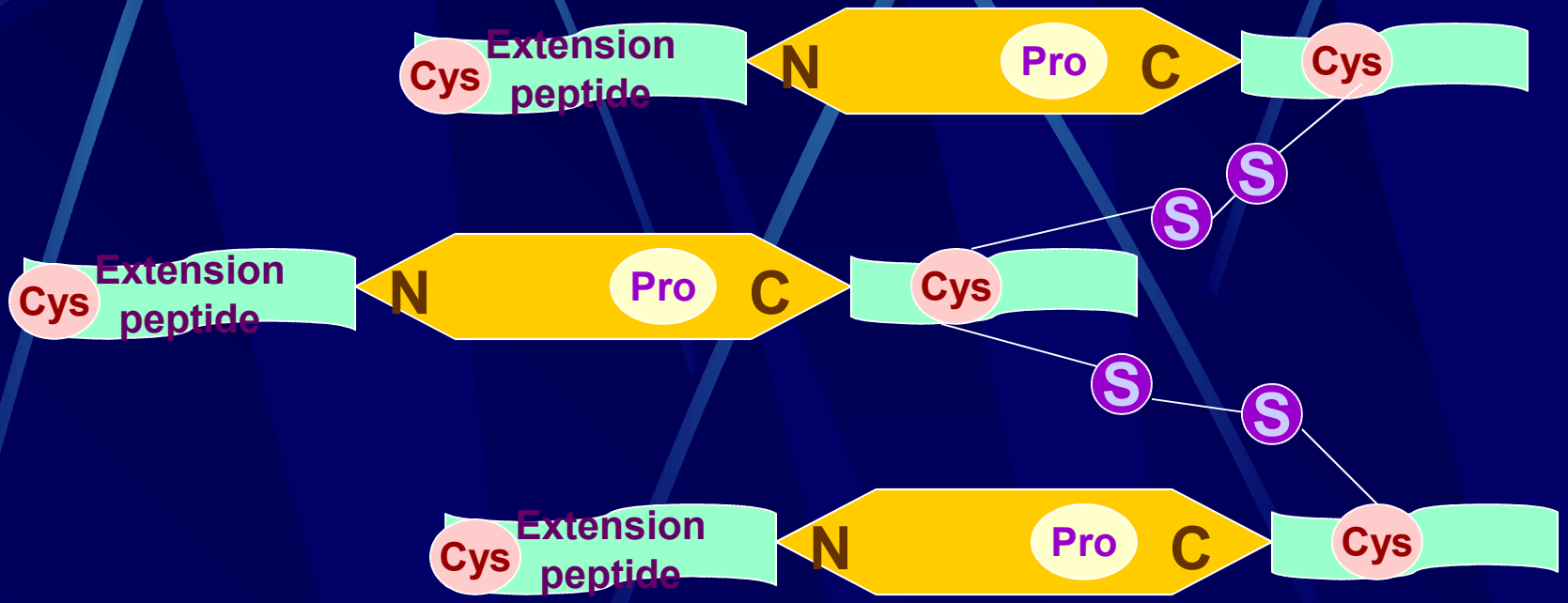
- CHO

Aldol condensation / Schiff bases

Posttranslational modification of collagen polypeptide



Zipping of collagen to form triple helix



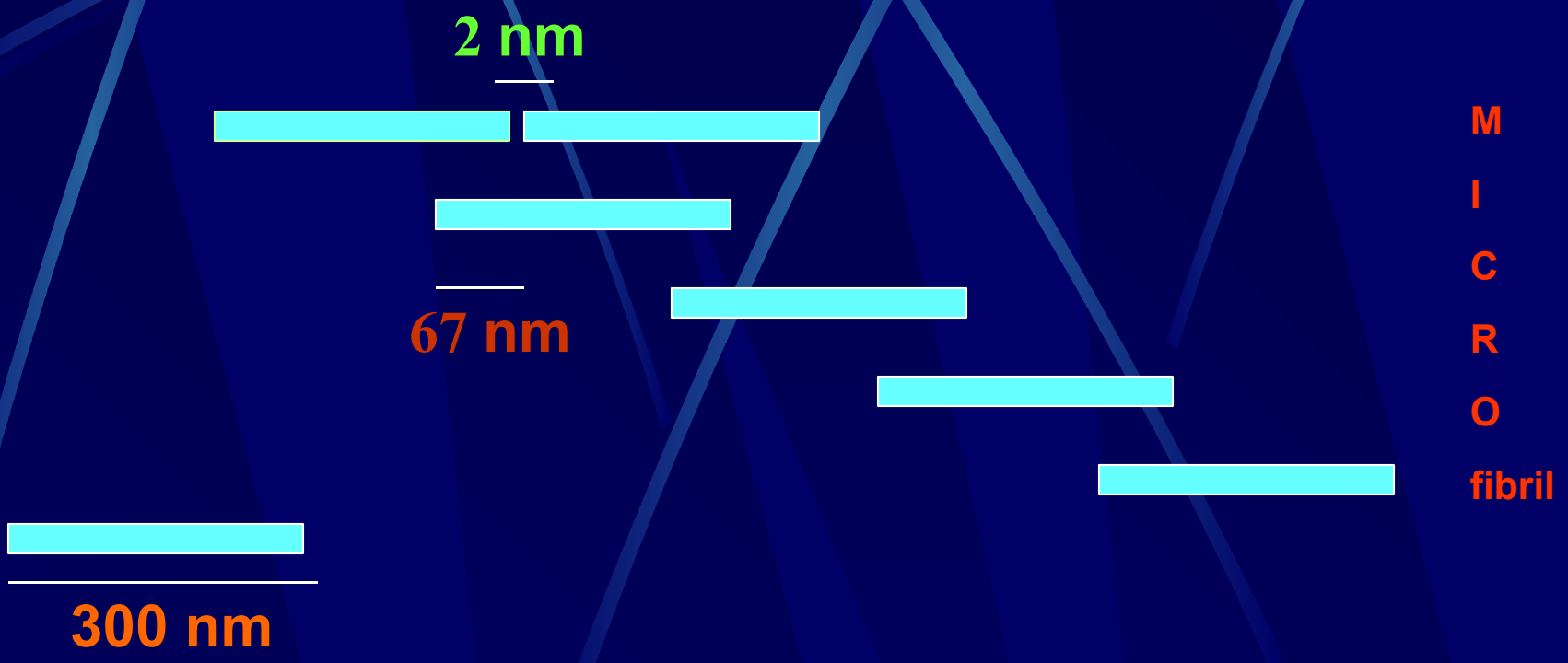
SELF ASSEMBLY

How does collagen form microfibril?

solubility of collagen = 1 mg/ml

entropy facilitates microfibril formation

Quarter staggered alignment



Proteoglycans aiding assembly of collagen

decorin, biglycan, fibromodulin

osteopontin, osteocalcin – chelate Ca++

Collagen turnover

↑Collagen turnover

- starvation
- prolonged immobilization
- low gravitational stress

Usually low except bone

↑Collagen deposition

- cirrhosis of liver
- pulmonary fibrosis
- atherosclerosis
- nephrosclerosis
- wound healing

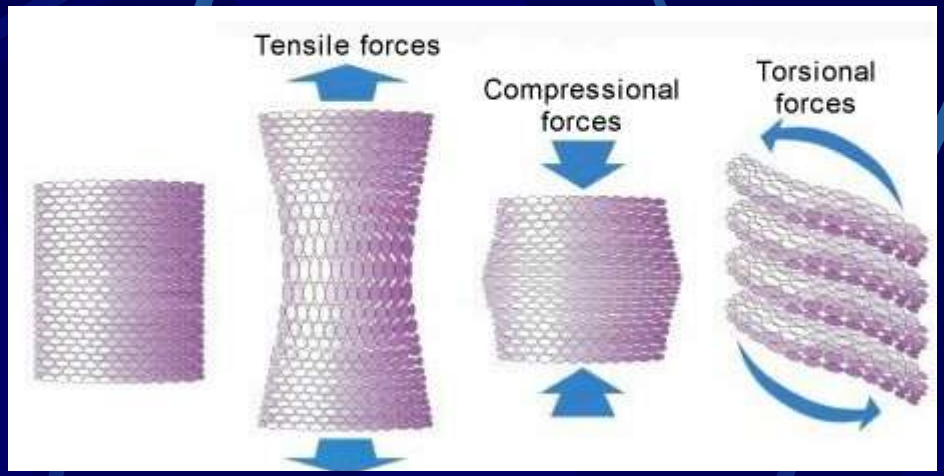
Mechanical properties of collagen

flexible

high tensile strength

little elastic recoil

Direction of fibre formation in collagen



lines of stress

piezoelectric current

successive layers of collagen in cornea at 90 degrees to each other

Diseases resulting from defective collagen synthesis

Disease	Mechanism	Key features
Ehlers – Danlos syndrome (11 varieties)	III	Type 4 – spontaneous rupture of arteries / bowel
	lysyl hydroxylase	Type 6 – ocular rupture, hyperextensibility of joint
epidermolysis bullosa	VII	anchoring fibrils
scurvy	deficiency of vit. C	bleeding gums, subcutaneous haemorrhage, poor wound healing

Reticulin fibres

supporting feldwork

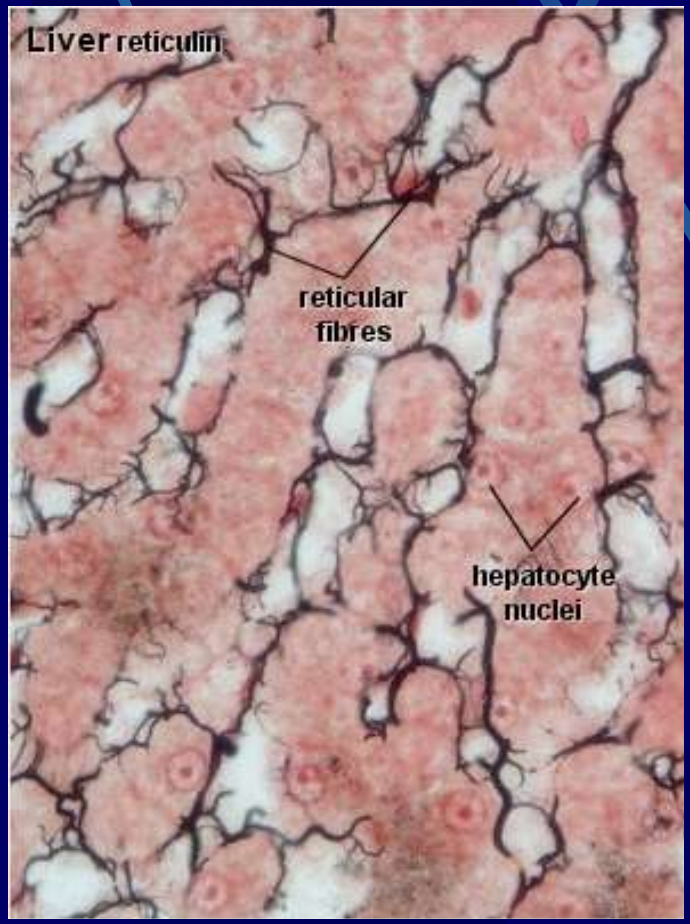
glands, kidney, lymph nodes, spleen, basement membrane, bone marrow, papillary layer of dermis

type III collagen

incomplete removal of extension peptide – limit growth in diameter

strongly argyrophilic

Argyrophilic reticulin fibres in liver



Elastin confers extensibility & recoil on lung, blood vessel & ligaments

1 genetic type

synthesized as soluble monomer of tropoelastin

(70 Kda)

(OH) proline

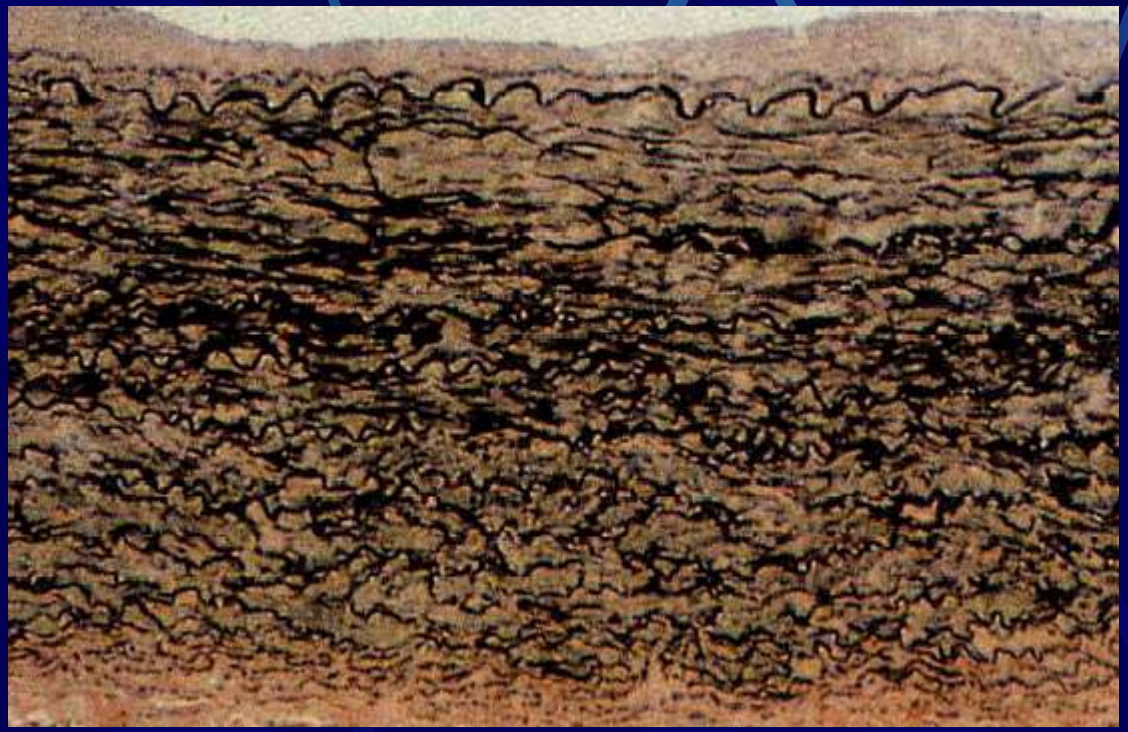
3 lysine derived – CHO + unmodified lysine

desmosines

mature extracellular form highly stable

TS of young human aorta

Verhoeff's stain



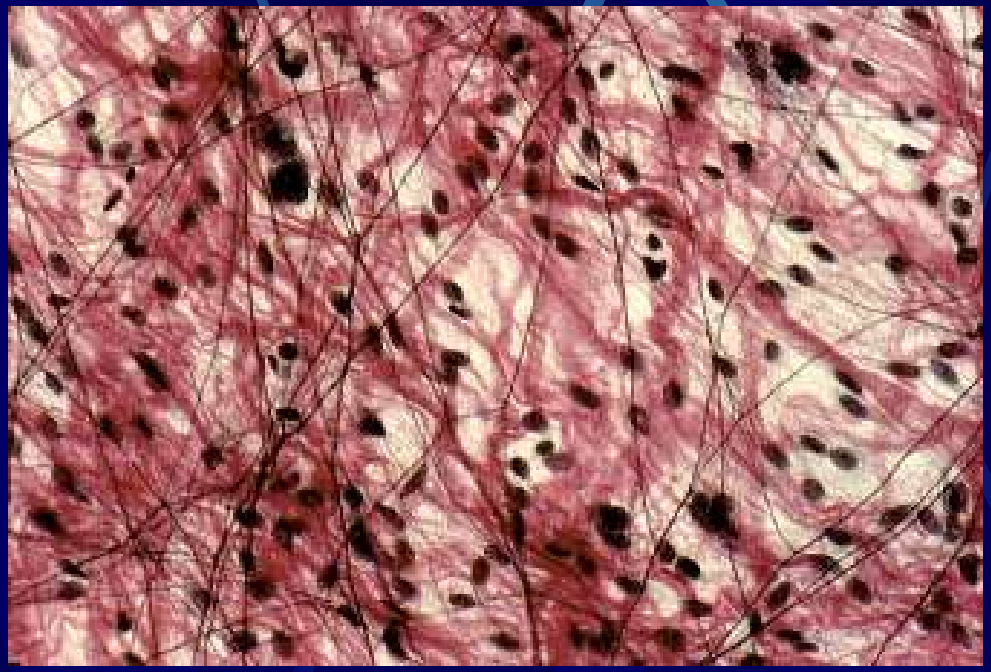
LS through elastic ligament of ox

Verhoeff's & van Gieson

* 200

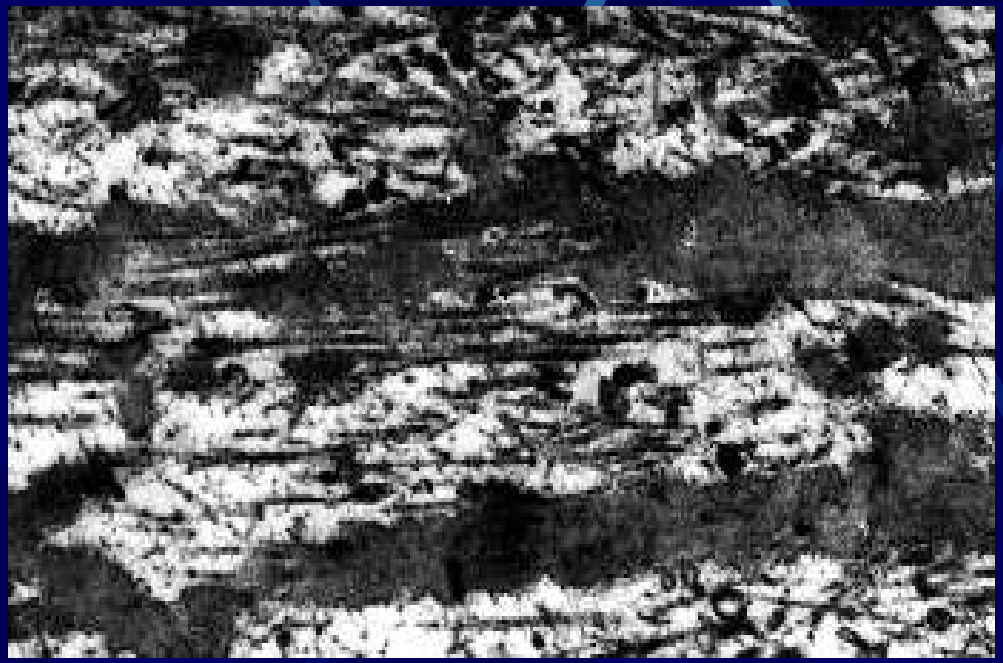
Elastin & collagen in mesentery

Verhoeff's & van Gieson



Developing elastin fibres & surrounding collagen fibres

phosphotungstate



* 20,000

Elastic tissue microfibrillar component

Fibrillin = glycoprotein

350 Kda

scaffold for deposition of elastin

other proteins in microfibril = emelin, elaunin,

oxytalan

Diseases affecting elastin

Disease	Features
William's syndrome	Del 7q11.23
scleroderma	accumulation of elastin
↓ in elastin	pulmonary emphysema,cutis laxa, aging of skin

Paginini

Rachmaninoff

Diseases affecting fibrillin

Disease	Molecular disorder	Features
Marfan's syndrome	AD, chr.15 (fibrillin gene)	Ectopia lentis, aneurysm, hyperextensibility of jts, arachnodactyly
Congenital contractural arachnodactyly	Chr 5 (fibrillin gene)	

Where lies the future of collagen?

Recombinant Collagen

Vasostat

Skin graft

Facial rejuvenation surgery


Thank you