Connective tissue

Connective tissue

- **origin:** from mesenchyme = embryonic connective tissue, may originate from all three germ layers, but mostly from the mesoderm

- **function:** to provide structural support, to connect, to provide vascular and nerve supply, to store energy, immunity, healing...

- **consists of:** cells surrounded by extracellular matrix (ECM), which consists of fibres and groud substance

Types of connective tissue

- connective tissue proper
- cartilage
- bone
- blood and lymph

Cells of the connective tissue

- fixed
- wandering (migratory)

- „-blasts“
  - mostly precursors, may undergo further differentiation
  - produce amounts of ECM
  - still able to undergo mitosis
  - e.g., fibroblast, osteoblast, chondroblast, adipoblast

- „-cytes“
  - diferentiated cells
  - e.g., fibrocyte, osteocyte, chondrocyte, adipocyte

Fixed cells of connective tissues

- fibroblast/fibrocyte
- myofibroblast
- reticular cells
- adipocyte
  - univacuolar (white adipose tissue)
  - multivacuolar (brown adipose tissue, non-shivering thermogenesis)
- chondrocyte
- osteocyte
- melanocyte (from the neural crest)
- endotelial cells, pericytes

- modified fibroblasts in healing tissues; they have contractile filamentsand dense bodies similar to smooth muscle cells
- →**myofibroblasts** (wound contraction in scars)
- when too much ECM synthesis→ hypertrophic keloid scars

Pigment cells - melanocytes

- from the neural crest ectomesenchyme
- at the junction between dermis and epidermis
- Golgi complex → melanosomes → granules in the extracellular space → keratinocytes
- iris, choroid

Pigment cells - melanocytes

- melanin (eumelanin – brown/black, pheomelanin – red/brown, neuromelanin – substantia nigra, locus coeruleus)
- tyrosine → DOPA →... → melanin
- tyrosinhydroxylase decifiency - albinism

Migratory cells of connective tissue

- **macrophages** (histiocytes; from blood monocytes; phagocytosis; presentation of antigens)
- **mastocytes** (heparinocytes; granules with heparin, histamin)
- **plasma cells** (from B lymphocytes; produce immunoglobulins)
- **other white blood cells (leukocytes):** (lymphocytes, neutrophilic, eosinophilic and basophilic granulocytes)

Mastocytes = heparinocytes

- metachromatic granules
  - heparin
  - histamin
- membrane receptor for IgE (type I allergy)

Macrophages = histiocytes

- bone marrow → monocytes → diferentiation under Th-Ly → macrophages
- fagosomes, lysosomes
- respiratory burst

→

Macrophages = histiocytes

- antigen
- fagosome + lysosome → fagolysosome
- hydrolases
  - peptid fragments
  - bound with MHC II → presenting antigen (Antigen Presenting Cells)
  - T-lymphocytes stimulated → interleukins → more effective phagocytosis, stimulation of B-ly → clonal expansion, plasma cells formed

→

Plasma cells = plasmocytes

- B-lymphocytes stimulated by antigens → migration into CT → plasma cells
- excentric nucleus, rich GER+Golgi
- immunoglobulins (humoral immunity) classes IgM, IgG, IgA, IgE, IgD

More CT cells

- endothelium
- pericytes
- eosinophilic granulocytes
- neutrophilic granulocytes

Extracellular matrix

- **fibres**
  - collagen
  - elastic
  - reticular (type III collagen)
- **ground substance**
  - glycosaminoglycans (GAG)
    - hyaluronic acid
    - sulphated esters of GAG
  - structural and adhesive glycoproteins
    - fibronectin
    - laminin
    - chondronectin

Collagen

- white at macroscopic level; eosinophilic at microscopic level
- unbranched fibres
- swells in acids and alkali; when boiled, dissolves into adhesive colloid solution (gelatin, glue); digested by pepsin
- overlap of ¼ of molecule length → cross striation (axial periodicity)í
- tropocollagen 1.5 nm → microfibrils 40 nm → fibres 1 μm → bundles of fibres 5-10 1 μm

Collagen

- the most abundant protein of the body, 30% of dry weight
- Gly-Pro-X or Gly-X-Hyp
- prolyl-, lysyl-, glycyl-hydroxylasa (cofaktor = C vitamin)

- **type I –** produced by fibroblasts and osteoblasts, forms thicker fibres; loose and dense connective tissue; dermis, fibrous capsules, tendons, aponeuroses, bone
- **type II –** produced by chondrocytes; fibrils within hyaline and elastic cartilage
- **type III –** produced by fibroblasts, reticulocytes, smooth muscle cells, endothelial cells; forms reticular fibres, loose connective tissue, vascular wall, interstitial tissue of liver, spleen, kidney, lungs...
- **type IV –** produced by epithelial and endothelial cells, myocytes, Schwann glia cells, forms sheets of the basal lamina
- **type V –** produced by fibroblasts in fetal membranes

osteogenesis imperfecta

- autosomal dominant
- defficiency in quality and quantity of type I collagen ← substitution of Gly → defect of the tropocollagen trihelix
- fragile and deformed bones, blue sclerae, wrong position of joints, hypotonic muscles

Ehler Danlos syndrome

- synthesis of type I/III collagen defficiency
- cutis hyperelastica
- unstable joints, hypermobility, subluxation, pain, muscle weakness
- chest deformed
- fragile blood vessels, aneurysms, heart valve problems (mitral prolaps)

Reticular fibres

- contain more hexoses than collagen → argyrophilic
- fine fibres made of type III collagen microfibrils
- supporting network surrounding blood vessels, nerves, muscle cells and fibres, adipocytes, lung alveoli;
- in the basal membranelů, lymph nodes, spleen, kidney....
- during maturation and growth is sometimes replaced by type I collagen

Elastic fibres

- yellow at macroscopic level
- at microscopic level: branched fibres (0.5-4 µm) and membranes
- yellow ligaments, wall of vagina, bronchioles, interalveolar septa, elastic arteries (fenestrated membranes of aorta)
- stained with orcein, resorcin-fuchsin
- hydrolysed by the pancreatic elastase
- central amorphous protein core (elastin) + microfibrils (fibrilin)
- aminoacids: glycine, proline, iso/desmosine, valine etc.

Marfan syndrome

- autosomal dominant
- mutation in FBN1 gene coding fibrillin-1
- mild to severe
- long extremities, arachnodactylia, heart valve problems, aortic aneurysms, lund problems, wrong suspension of the eye lens, scoliosis, ...

Ground substance

- **surrounds the cells and fibres**

- protein-poylsaccharide complexes, glycoproteins and proteoglycans (mucopolysaccharides)

- glycosaminoglycans (GAG)
  - hyaluronic acid
  - suphated GAGs
- structural (multiadhesive) glycoproteins
  - fibronectin
  - laminin
  - chondronectin

Glycosaminoglykans

- komple molecules containing: **hexosamine, uronic acids and proteins**

- **hyaluronic acid** = glucosamin + glucuronic acid
  - non-sulphated GAG
  - 3-4 mil. Da
  - fast turnover
  - intercellular spaces of fetal and adults organs (umbilical cord, vitreous body, synovial fluid, cartilage); tixotropie
  - bacterial hyaluronidase → depolymerization; invasive bacteria

- sulphated esters of GAGs
  - chondroitin sulphate = galactosamin + glucuronic acid, cartilage, bone, cornea, skin, notochord
  - dermatan sulphate (dermis, tendons)
  - heparan sulphate (lung, liver, basal laminae)
  - keratan sulphate (cornea, intervertebral discs)

Glycosaminoglycans

- a) proteoglycan = protein core with sulphated polysaccharides
- b) glycoprotein

Hurler syndrome

- AR lysosomal storage disease
- mukopolysaccharidosis type I
- deficiency of alpha-L iduronidase (degradation of GAG) → heparan- and dermatan-sulphate accumulates
- facia dysmophia, gargoylism; organ deformities, respiratory obstruction, early death

Structural and adhesive glycoproteins

- **fibronectin** (binds cells with collagen and GAG)
- **laminin** (basal laminae of epithelium, endothelium, muscle cells)
- chondronectin (chondrocytes bound to collagen)

Staining

- **hematoxylin-eosin:** collagen is eosinophilic, elastic fibres stain weakly or not at all
- **trichrome stains** (blue and green, according to the colour of collagen)
- **elastin** stained with**:**
  - orcein (brown)
  - resorcin-fuchsin (dark blue)
  - Verhoeff's iron hematoxylin (black)
- reticula fibres stain with **PAS** (perjodic acid-Schiff, purple-magenta) or with silver impregrnation (black)
- **PAS** = oxidation of vicinal diols with perjodic acid → aldehyde proved using Schiff's reagent → purple