Morphology and Development

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https://rps.unibo.it

Morphology and Development (I.C)

Morphology and Development (I.C.)			
84283	Embryology	BIO/17	2
83151	Histology	BIO/17	4
84282	Histology Laboratory	BIO/17	1
84281	Stem Cell Biology	BIO/17	1

- Introduction to the course/Exam
- Methods of Microscopy
- Tissue Classification
- Stem Cell/Differentiation
- Embryonic Origin of Tissues

Exam

Written test

- Histology
- Embryology
- Stem Cells

Those who are **not satisfied with their score** (which must be **18 or higher**) may arrange an oral exam.

Exam's dates:

	84280 - Morphology And Development (I.C.) - Modulo 84282-Histology Laboratory (Cds. 6734 - Bo)	Morphology and Development	19/06/2026 08:30	Aula Golgi, Histology Laboratory Room	Scritto	> Pubblicata	0	Iscritti Modifica Duplica	Cancella
	84280 - Morphology And Development (I.C.) (Cds. 9210 - Bo) 84280 - Morphology And Development (I.C.) (Cds. 6734 - Bo)	Morphology and Development	19/06/2026 10:30	Aula Magna Maestri	Scritto	> Pubblicata	0	Iscritti Modifica Duplica	Cancella

EXAM AULA MAGNA I MAESTRI - **Pad. 23 -** June 19th at 10:30

Laboratory assessment AULA Golgi - June 19th at 8:30

	84280 - Morphology And Development (I.C.) - Modulo 84282-Histology Laboratory (Cds. 6734 - Bo)	Morphology and Development	17/07/2026 08:30	Aula Golgi, Histology Laboratory Room	Scritto	> Pubblicata	0	Iscritti Modifica Duplica	Cancella
	84280 - Morphology And Development (I.C.) (Cds. 9210 - Bo) 84280 - Morphology And Development (I.C.) (Cds. 6734 - Bo)	Morphology and Development	17/07/2026 10:30	Aula Magna Maestri	Scritto	> Pubblicata	0	Iscritti Modifica Duplica	Cancella

Morphology and Development - **final exam**

Question **1**

Not yet answered

Marked out of 4.00

Flag question

Edit question

The protein filamin associates to:

Select one:

a. Cell cortex

b. Filopodia

c. Gel-like networks

d. All of them

e. Lamellopodia

Multiple-choice question

About 20–25 questions, each worth between 1 and 2 points.
No penalty for incorrect answers

FINAL SCORE FORMULA

$$\frac{(\text{EMBRYOLOGY} \times \mathbf{2}) + (\text{HISTOLOGY} \times \mathbf{4})}{8} + \text{LABORATORY} + \text{STEM CELL}$$

$$28x2+27x4+30+28 = 222/8$$

$$27.75 \rightarrow 28$$

Important information about

ATTENDANCE REQUIREMENTS

Attendance to this learning activity is mandatory; the minimum attendance requirement to be admitted to the final exam is **60% of lessons**. For Integrated Courses (IC), the 60% attendance requirement refers to the total amount of I.C. lessons. Students who fail to meet the minimum attendance requirement will not be admitted to the final exam of the course.

Professors **may** authorise excused absences **upon receipt of proper justifying documentation, in case of illness or serious reasons.** Excused absences do not count against a student's attendance record to determine their minimum attendance requirement.

The physiology of learning

	Learning Zone	Performance Zone alias EXAM
GOAL	Improve	Do as best as you can
Activity for	Improvement	Execution
Concentrate on	Haven't mastered yet	Have mastered
Mistakes to be	Expected	Minimized or nullified

Edoardo Briceno -TedxManhattan

Goals

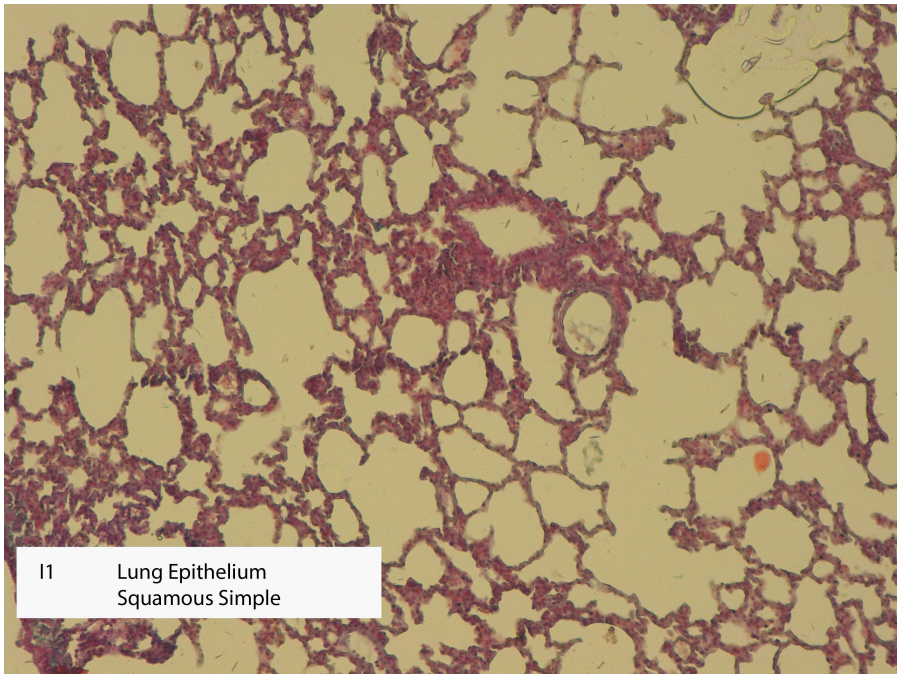
To understand:

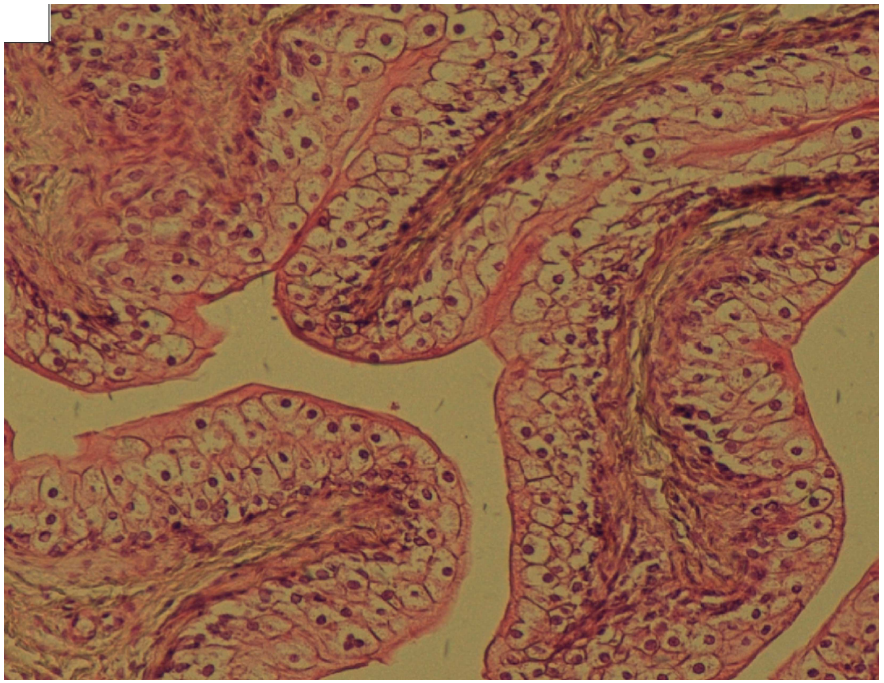
- **How cells and tissues are arranged in the normal organ system of the body.**
- **How these cells and tissues are specialized to perform the function(s) most effectively**

The knowledge gained will provide a cellular and ultrastructural "framework" for several other topics (anatomy, physiology, biochemistry, etc.) that you'll learn in the following years .

Histology is also a FUNDAMENTAL part of PATHOLOGY.

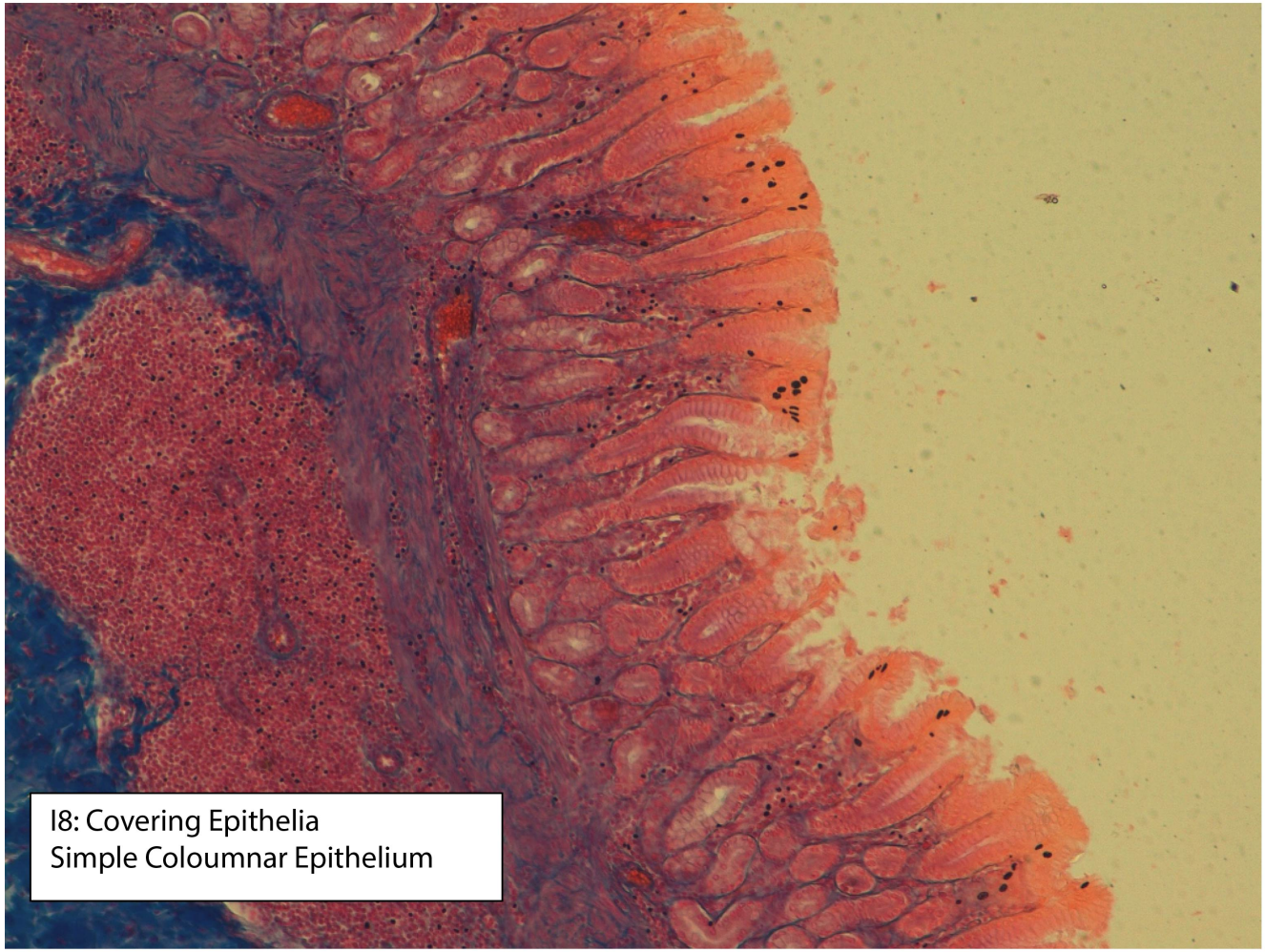
Histology is learning a new language



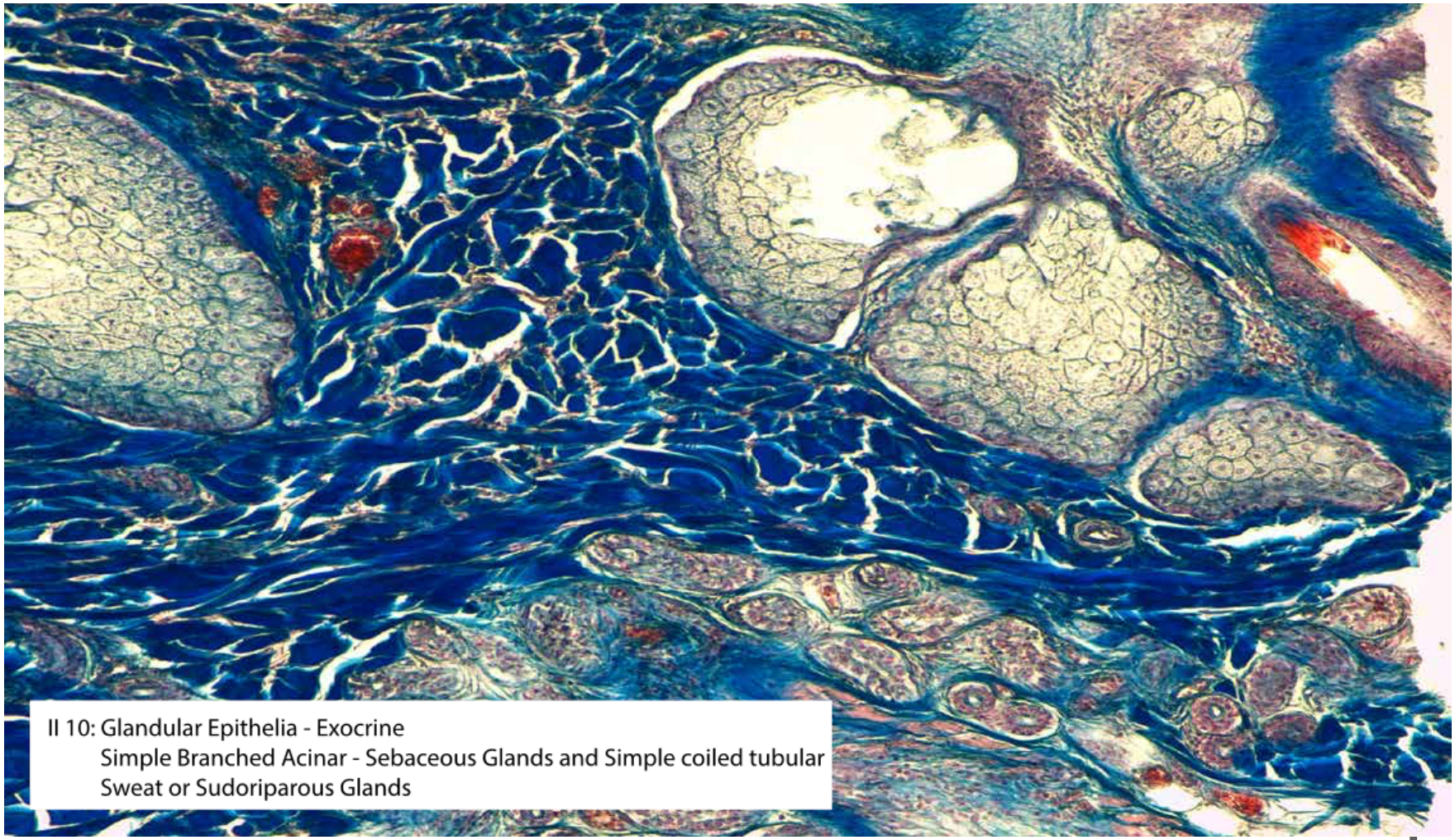


By the end of the course, you should possess the ability to interpret any type of tissue sample.

I 5: Covering Epithelia
Stratified Squamous keratinized epithelium- skin



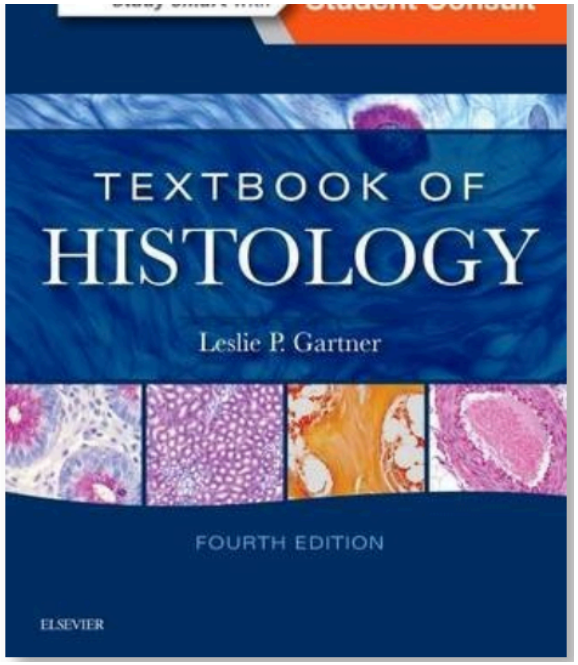
I8: Covering Epithelia
Simple Coloumnar Epithelium



Il 10: Glandular Epithelia - Exocrine
Simple Branched Acinar - Sebaceous Glands and Simple coiled tubular Sweat or Sudoriparous Glands

Recommended Book

Textbook of histology Leslie P. Gartner



The ppt of each lesson will be uploaded on **Virtuale**

Virtual Microscopy

https://unibo.smartzoom.com/s1241/course1776/f2017/f7823/

Introducing myself

Tampa, Florida,
USA in 2008

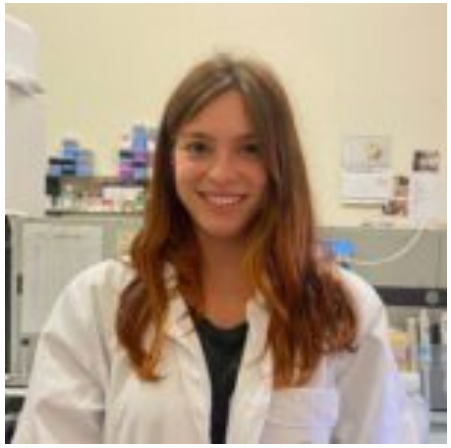
- PhD in Biotechnology of Development and Human Reproduction

Weizmann Institute of Science, Israel
2009-2014

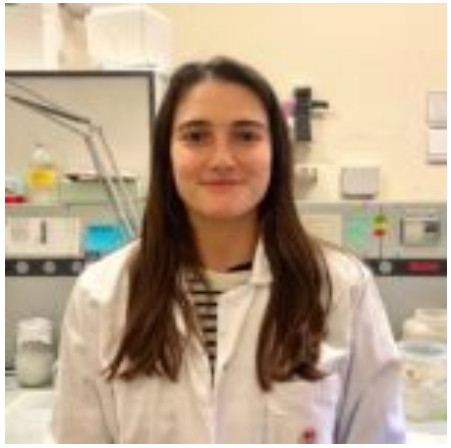
- In 2022 Associate Professor in Histology

From 2023 Full Professor in Histology

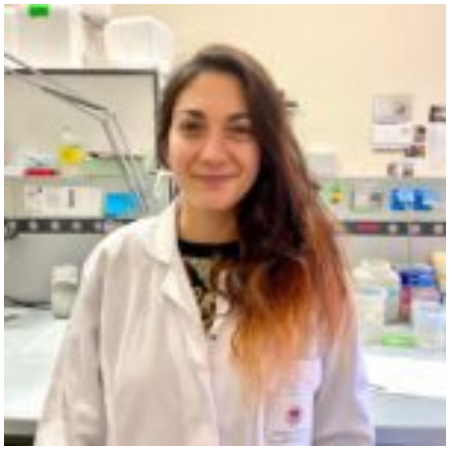
The histology Team



Prof. ssa Michela Sgarzi
michela.sgarzi2@unibo.it
G5 Group



Alessandra Morselli, Ph.D
Tutor



Prof. ssa Martina Mazzeschi
martina.mazzeschi2@unibo.it
G6 Group

The histology laboratory – Aula Golgi- Via Belmeloro 8

6 Groups

G1. ABDUR RASHID **to** CASABIANCA

G2. CAVANI **to** ER

G3. EREN **to** KECSETI

G4. KILIŚ **to** NICORA

G5. NOBILI **to** SIQUEIRA BUENO with Prof. Sgarzi

G6. SPINOLA MEDAGLIA GABRIEL **to** ZHANG with Prof. Mazzeschi

Histology Lab Schedule

1-Covering Epithelia
2-Glandular Epithelia - Exocrine
3-Glandular Epithelia - Endocrine
4-Connective Tissue Proper - Hematopoietic system
5-Connective Tissue - Bone and Cartilage
6-Nerve Tissue and Muscle Tissue
7-Summary- Rehearsal/Recap

8- Self-evaluation – **MAY 18 (G1, G2, G5)** and May **9 (G3, G4, G6)**

Histology Laboratory test

Laboratory test – examples will be provided during the laboratory classes

Self-evaluation – MAY 18 (G1, G2, G5) and May 19 (G3, G4, G6)

Histology

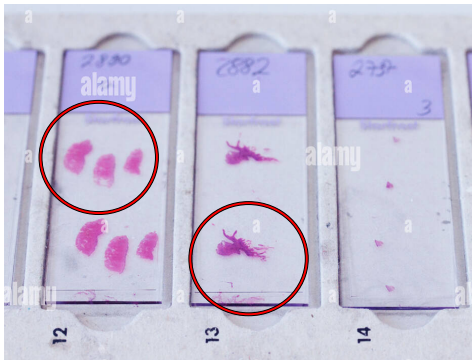
From greek (histós), meaning web or tissue and λόγος (lógos), science of tissue

Is the branch of the anatomical sciences that studies the cellular organization of body tissues and organs

The light microscope is the tool used most widely for applications of histology

A new vocabulary

The slide: is a piece of glass upon which a sample (specimen) is placed or layered



Specimen: the sample

Magnification (power): 4X, 10X up to 100X

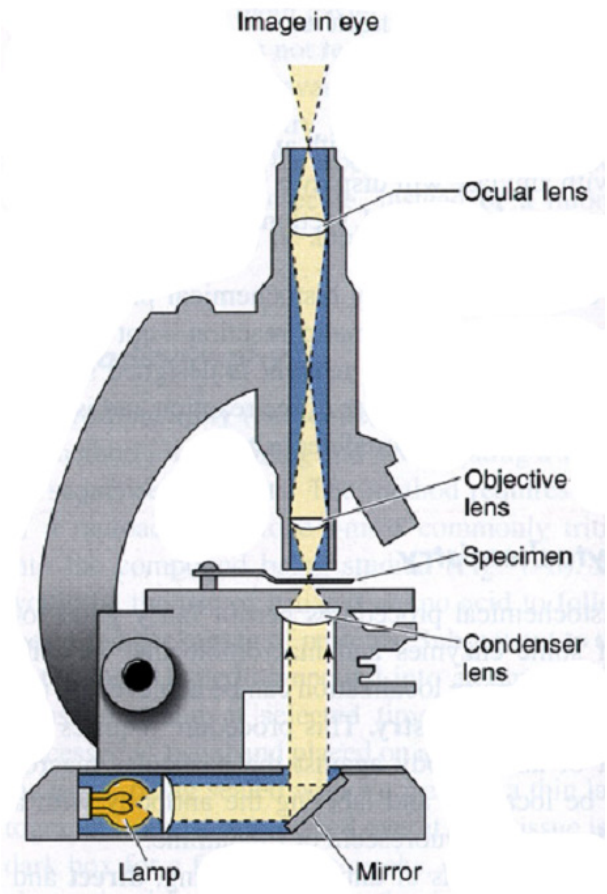
Artifact: any unintended result or error that occurs during the collection or the preparation of the tissue

BASIC TISSUES

EPITHELIUM
CONNECTIVE TISSUE
MUSCLE TISSUE
NERVOUS TISSUE

Basic tissues combine to form larger functional units, called ORGANS.

Light Microscopy

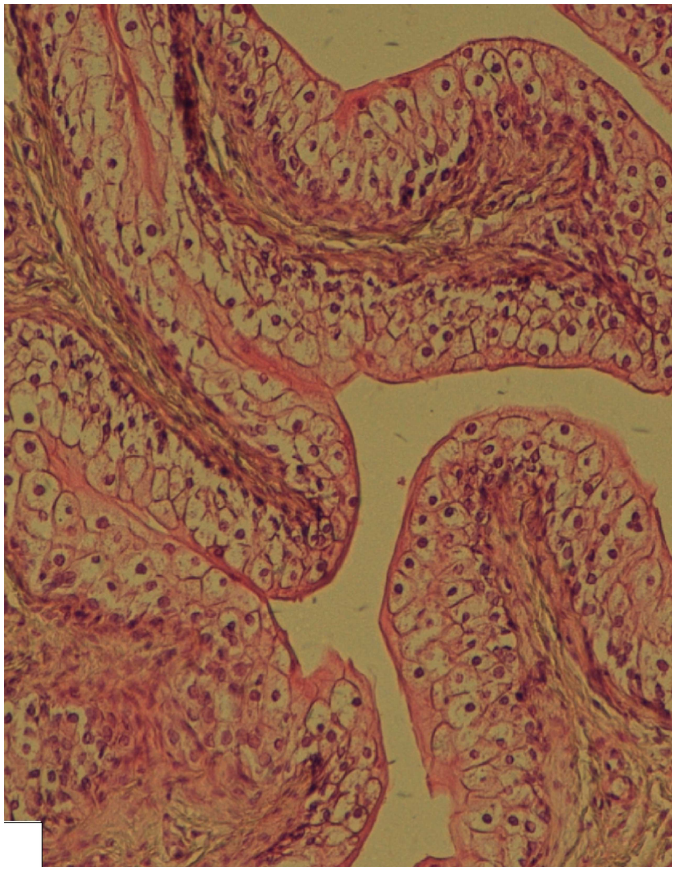


1. ILLUMINATION SOURCE
2. CONDENSER LENS
3. SPECIMEN STAGE
4. OBJECTIVE LENS (4X, 10X, 40X to 100X)
5. PROJECTION (OCULAR) LENS
6. OBSERVER

YIELDS A 2-DIMENSIONAL IMAGE CAPABLE OF **0.2 μm RESOLUTION**.

CELLULAR FEATURES ARE STAINED DIFFERENTIALLY BASED PRIMARILY UPON CHEMICAL PROPERTIES.

Light Microscopy

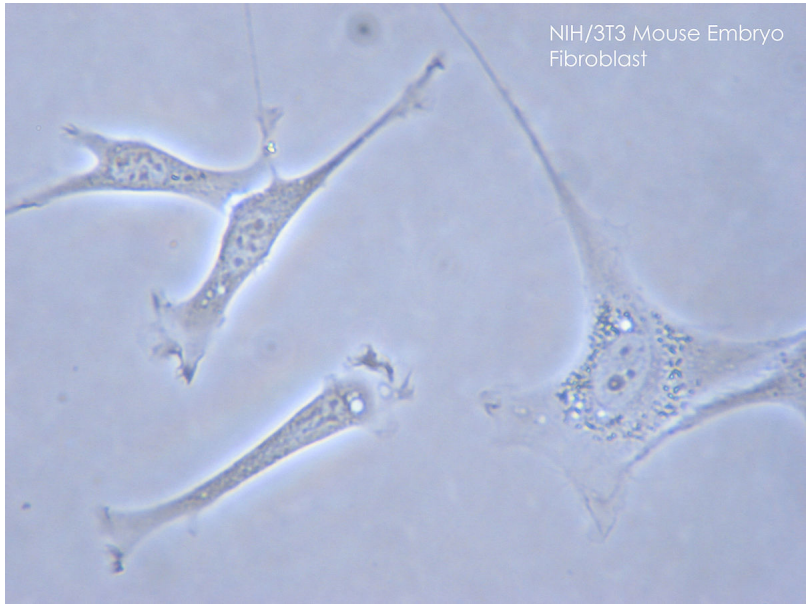


Resolution: 0.2 µm

The smallest distance between two points on a specimen that can still be distinguished as two separate entities.

The **resolution** of the **light microscope** cannot be smaller than the half of the wavelength of the visible **light**, which is 0.4-0.7 µm.

Tissue Preparation for Light Microscopy



1. Stabilize cellular structures by chemical fixation.
2. Dehydrate and infiltrate tissues with paraffin or plastic
3. Embed fixed tissues in paraffin or plastic blocks.
4. Cut into thin slices of 3-10 micrometer thick; collect sections on slides

Tissue Preparation for Light Microscopy

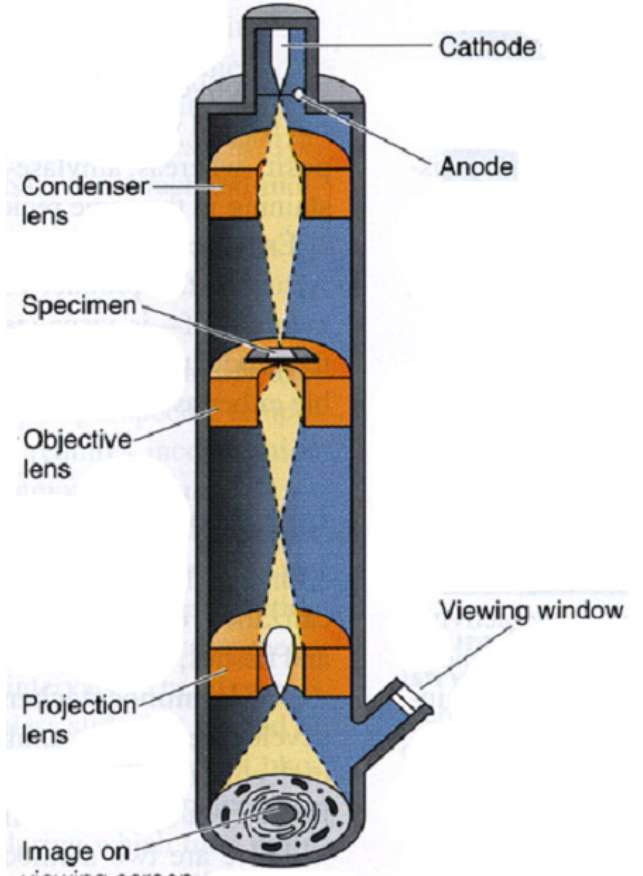
1. Stabilize cellular structures by chemical fixation.
2. Dehydrate and infiltrate tissues with paraffin or plastic.
3. Embed fixed tissues in paraffin or plastic blocks.
4. Cut into thin slices of 3-10 micrometer thick; collect sections on slides.
5. Re-hydrate and stain with Hematoxylin (**a basic dye**): Stains acidic structures (e.g. nucleic acids) blue/purple.

What do you expect to be stained by Hematoxylin?

6. Counter-stain with Eosin (an **acidic dye**): Stains basophilic structures (e.g. proteins, membranes) red/pink.

H&E staining is routine, but additional dyes and staining techniques may be used to visualize other structures.

Transmission Electron Microscopy



Transmission electron microscope

ILLUMINATION SOURCE (**generates electron beam**)

2. CONDENSER LENS
3. SPECIMEN STAGE
4. OBJECTIVE LENS
5. PROJECTION LENS
6. VIEW SCREEN
7. VIEWING WINDOW & OBSERVER

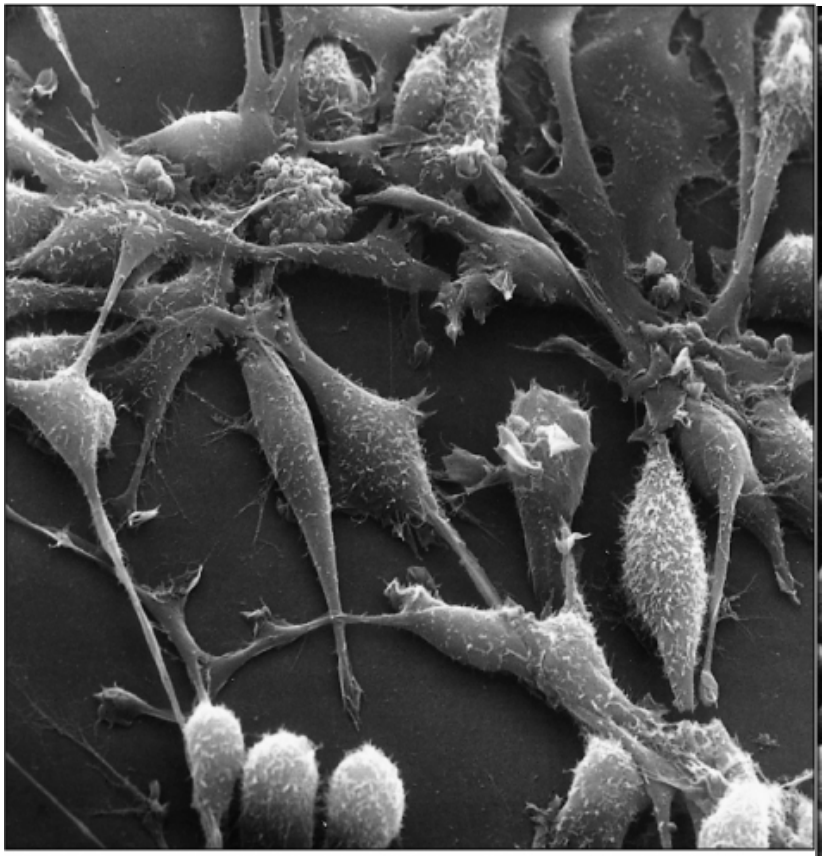
YIELDS A 2-DIMENSIONAL IMAGE CAPABLE OF **0.2 nm RESOLUTION.**

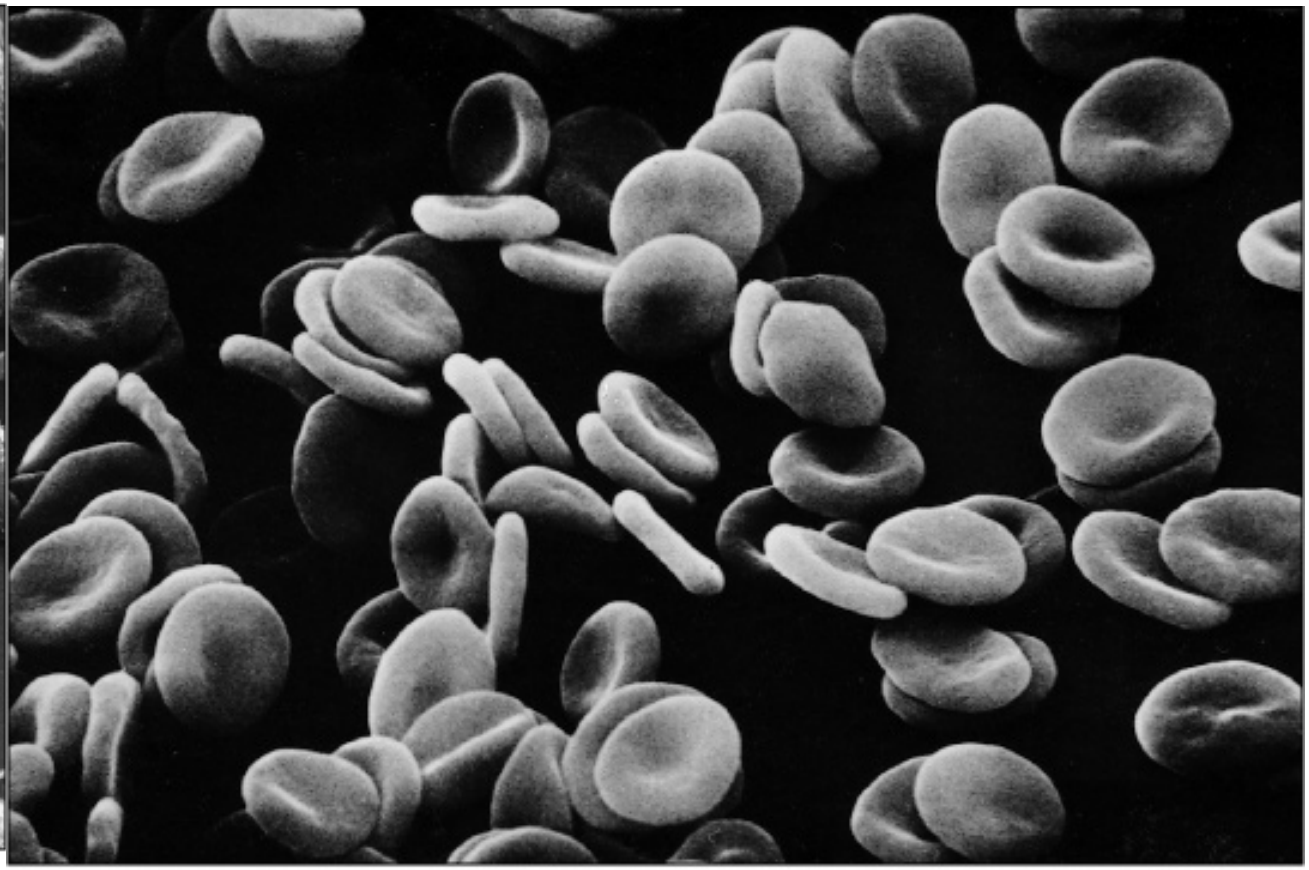
CELLULAR FEATURES ARE STAINED WITH ELECTRON-DENSE, HEAVY METAL STAINS YIELDING ONLY A BLACK AND WHITE IMAGE

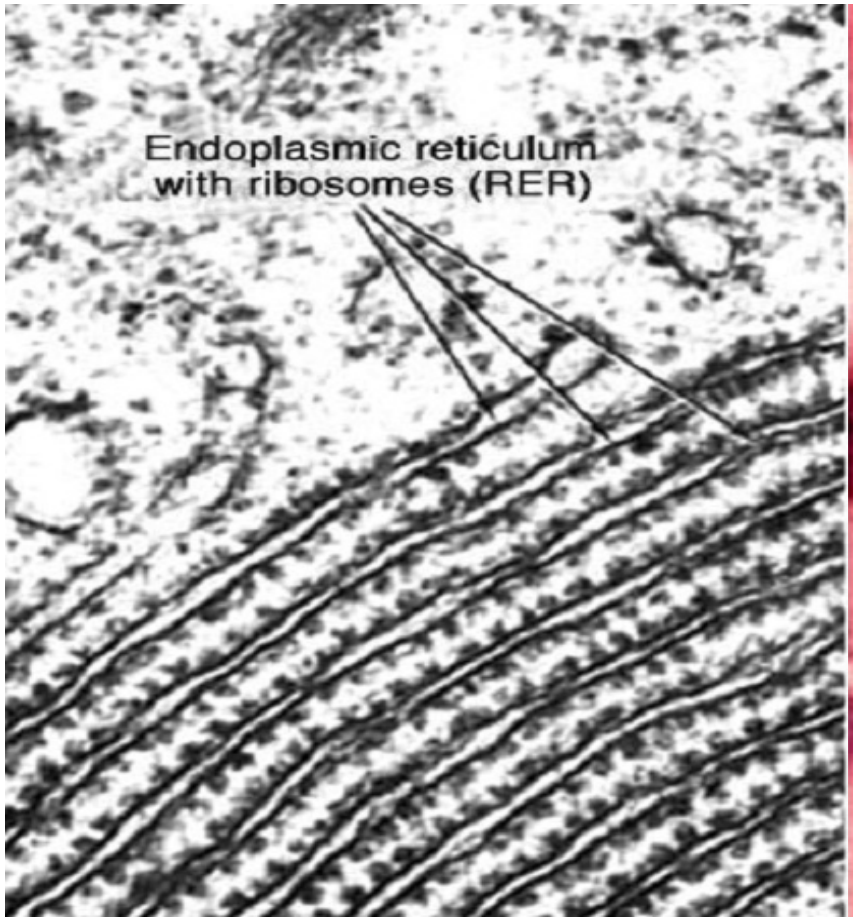
Tissue Preparation for Electron Microscopy

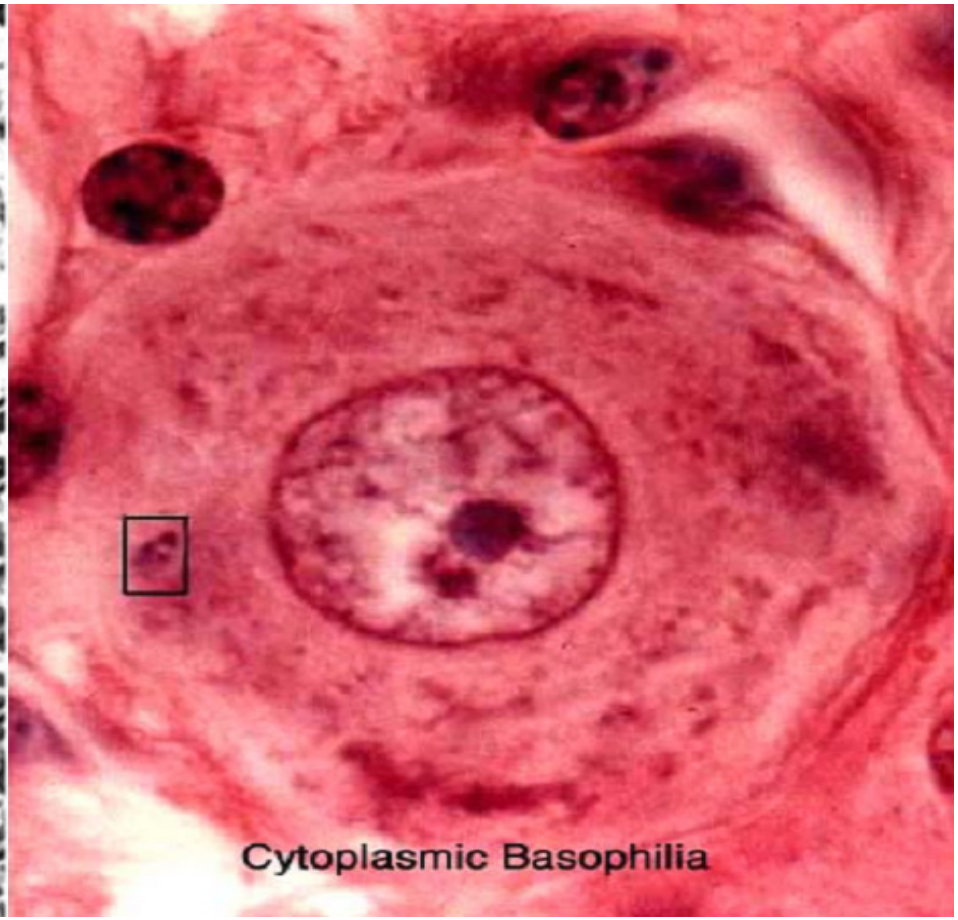
1. Tissues are fixed with glutaraldehyde (cross-links proteins) and osmium tetraoxide (cross-links lipids); OsO_4 is also an electron-dense “stain”
2. Dehydrate and infiltrate tissues w/o plastic.
3. Embed and block fixed tissues in plastic.
4. Cut into ultra-thin slices (50 nanometers thick); collect sections on slides.
5. Stain sections with heavy metal salts that bind nucleic acids & proteins.
6. Visualize in TEM; heavy metal “stains” block electrons to create contrast

0.2-0.1 nm resolution



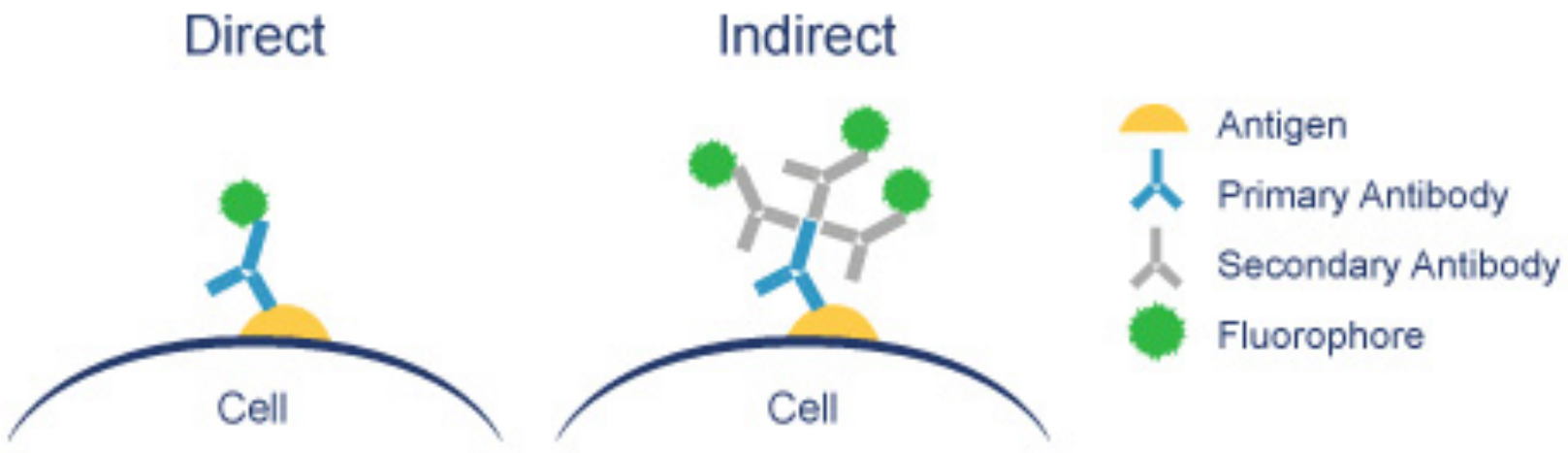




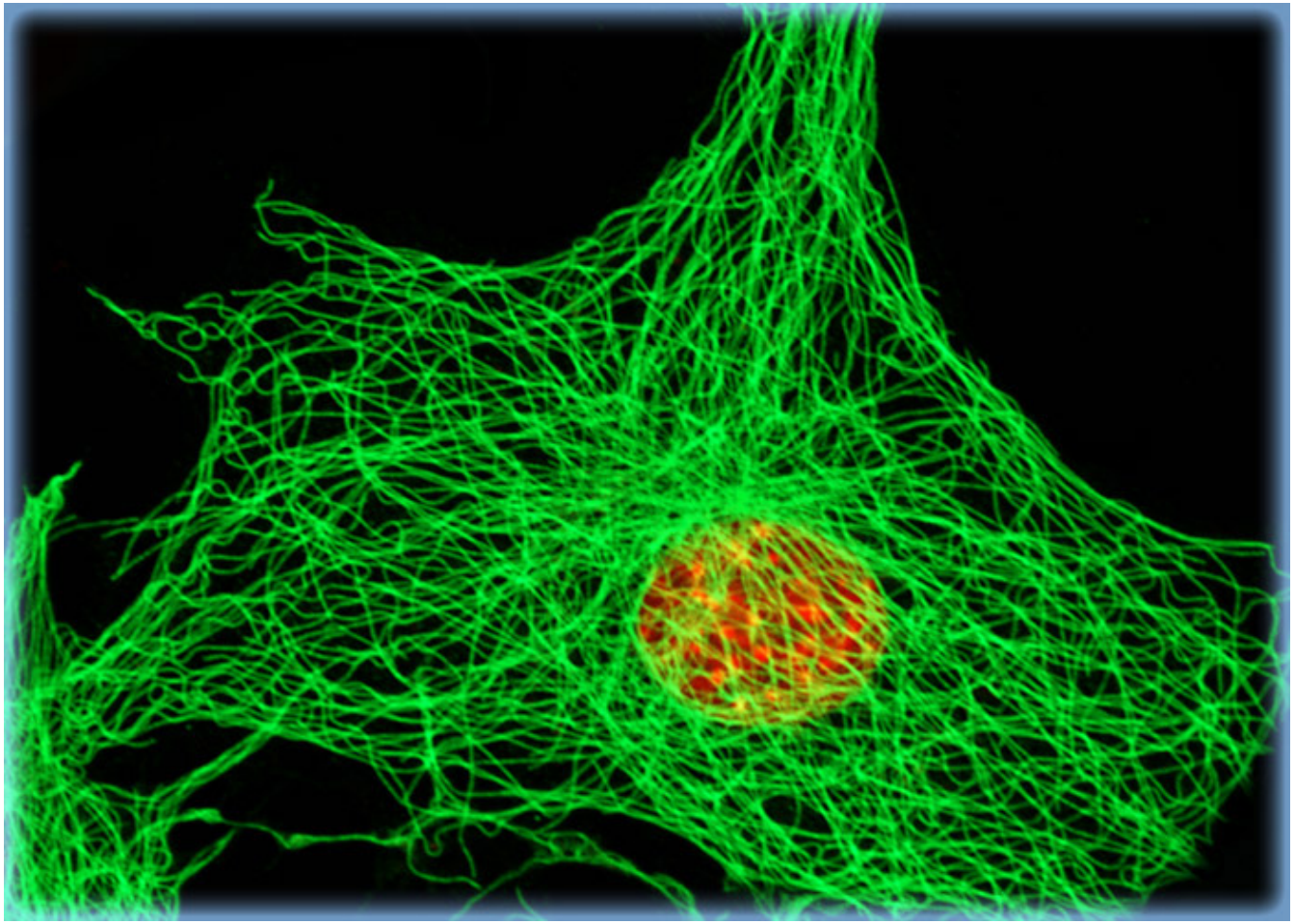


Immunofluorescence microscopy

Antigen/Antibody reaction, where the antibodies are tagged
With a fluorescence dye and the antigen/antibody complex is visualized using fluorescence microscope

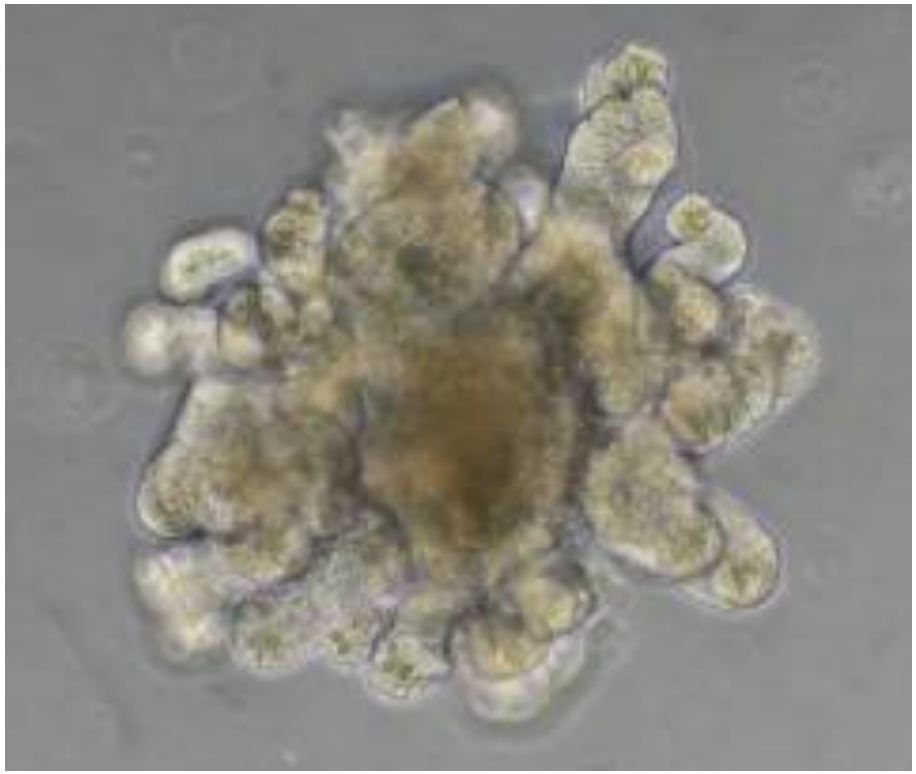


Confocal Microscopy



Resolution 0.2 μm

Confocal Microscopy for 3D



Organoids light microscope

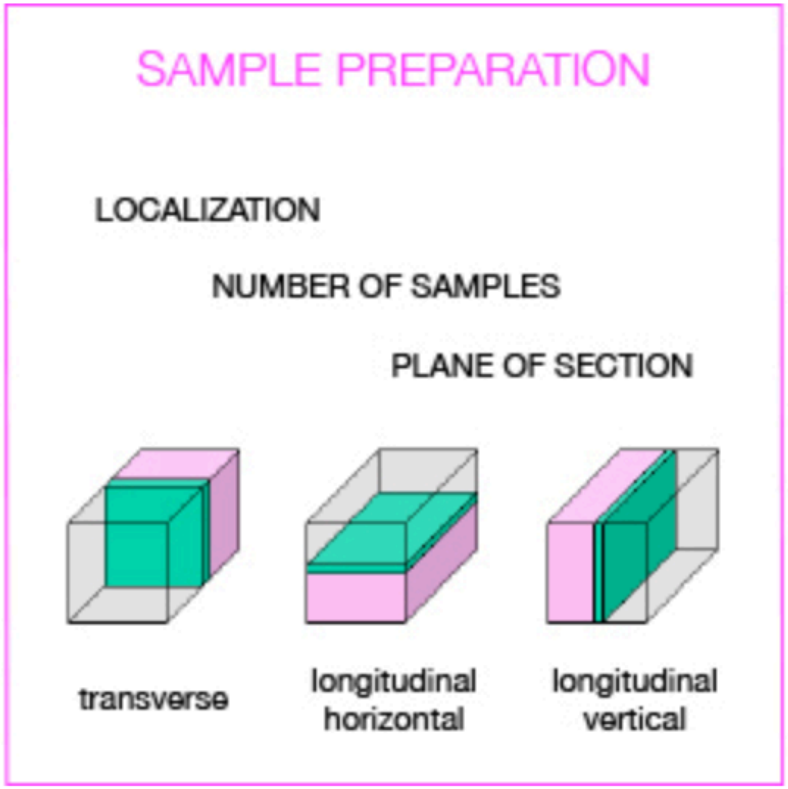
Organoids confocal

https://app.jove.com/it/v/20255/formalin-fixed-paraffin-embedded-ffpe-tissue-preservation-method-for

Cross or transverse section:
cutting through an object at a **right angle** to a specified axis or plane.

Longitudinal horizontal section: "longitudinal horizontal section" refers to a cut that follows the long axis (longitudinal) and is divide the object into an upper and lower parts (horizontal).

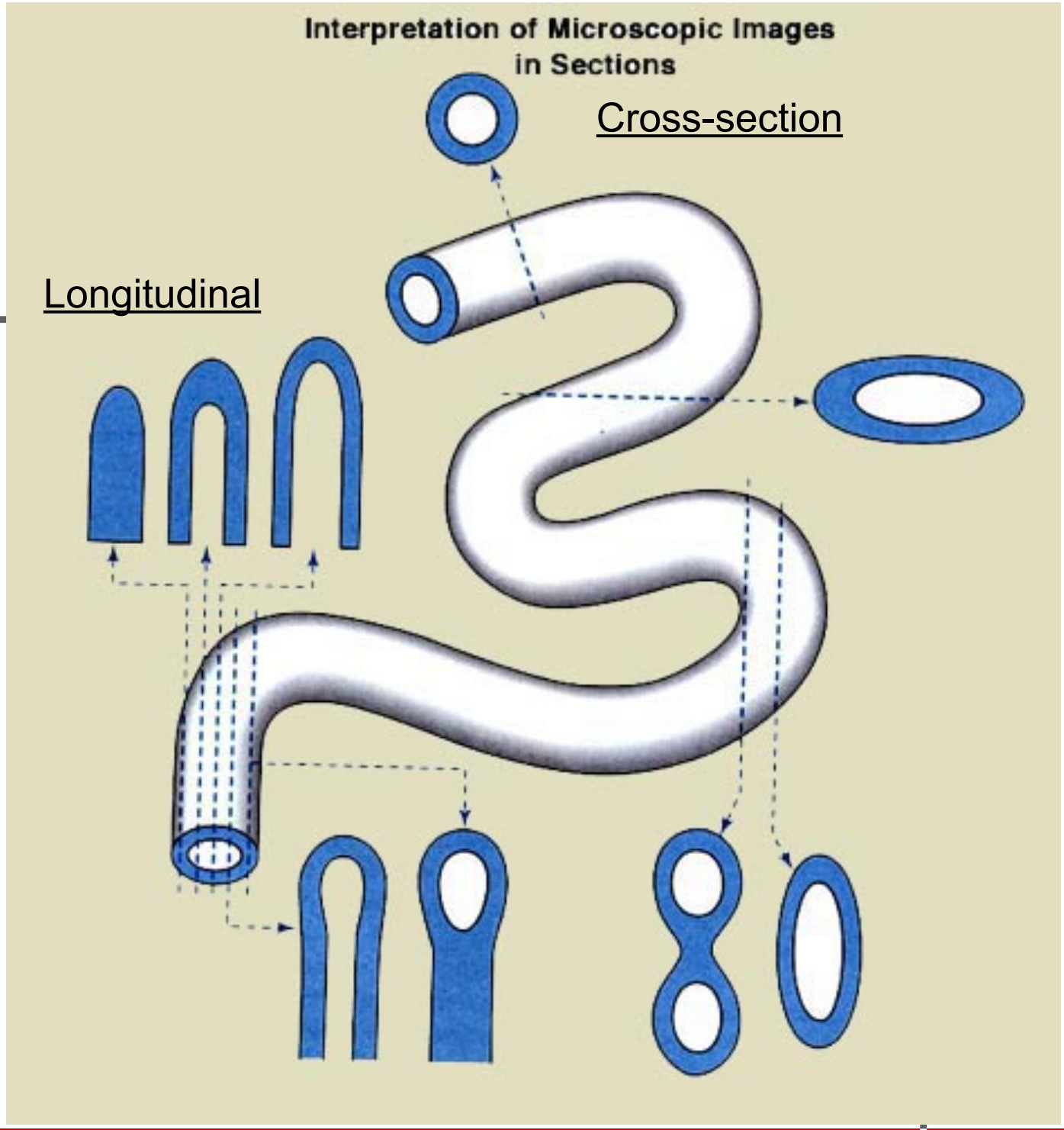
Longitudinal vertical or Sagittal Section: The sagittal plane is oriented parallel to the body's midline and divides the sample into two symmetrical halves, with the left half on one side of the plane and the right half on the other.



Sagittal

The challenge:

3D structures, but viewed only in 2D…

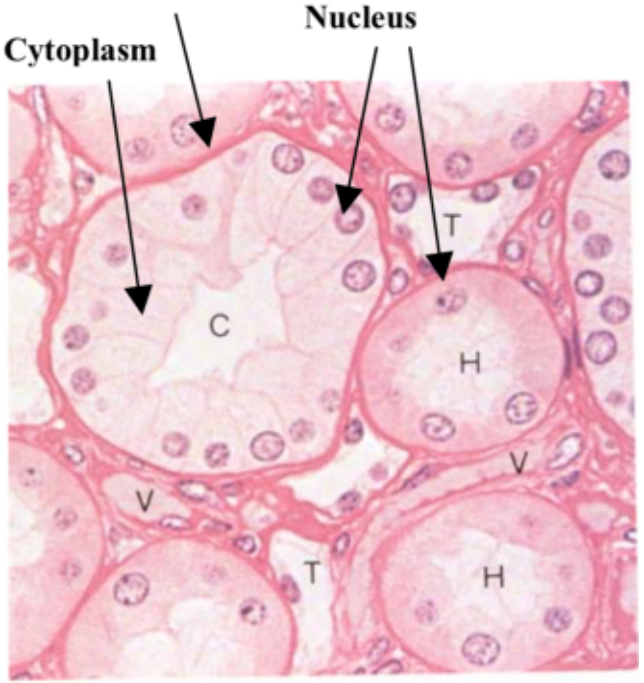


H&E

(Haematoxylin and Eosin staining)

Haematoxylin binds to basophilic substances (**DNA**, negatively charged) and stains nuclei in blue-violet

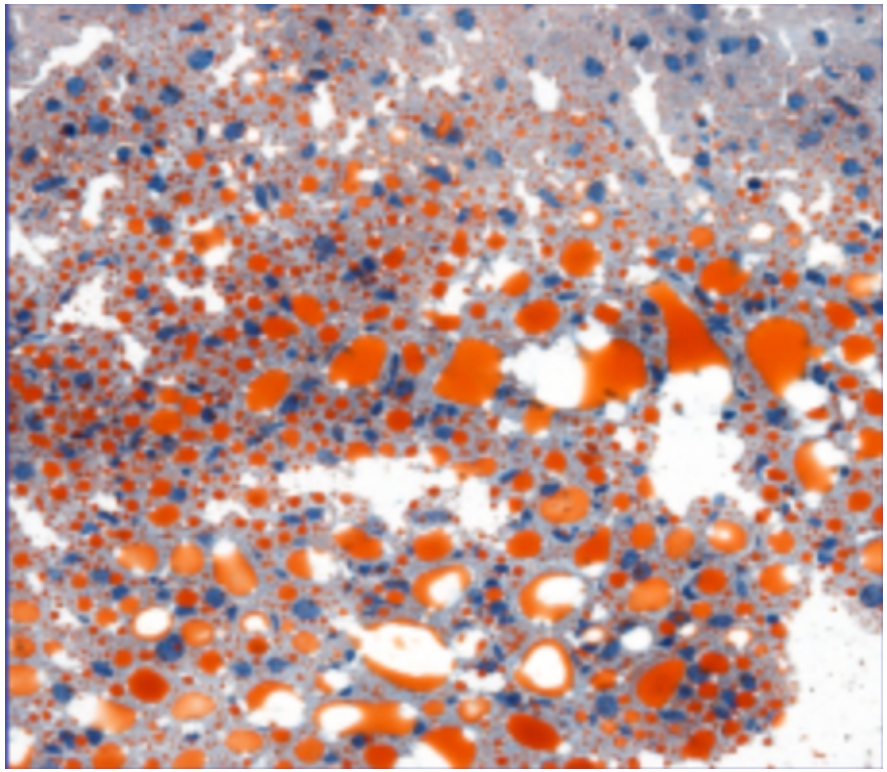
Eosin binds to acidophilic substances (most **proteins**, positively charged) and stains cytoplasm in red or pink



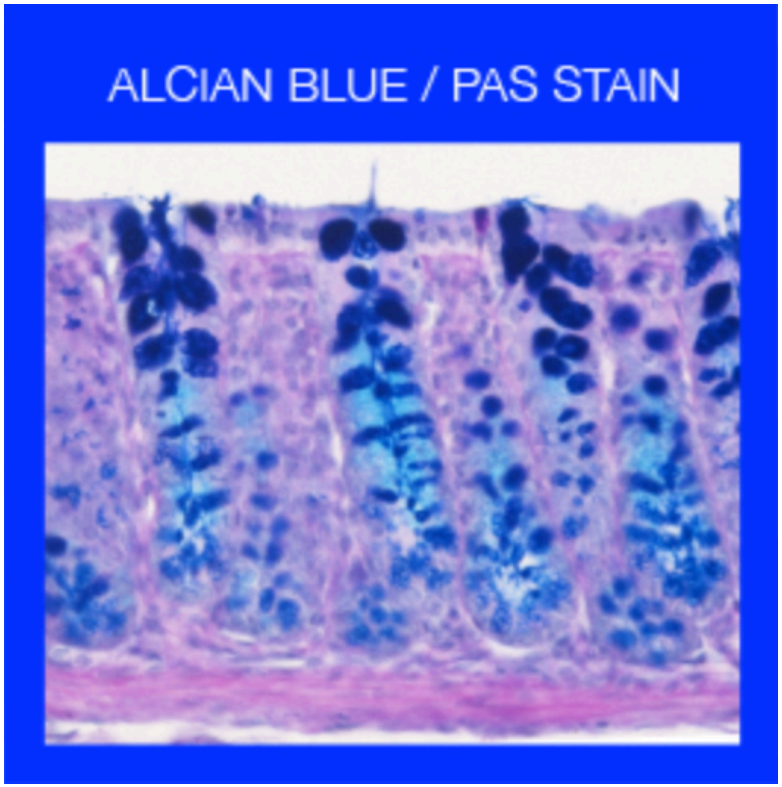
H&E: KIDNEY (Cross section of medulla)

The Picro-Sirius Red is used in the histological visualization of **collagen I and III fibers** in paraffin-embedded tissue sections.

What are special stains? Red Oil



ORO is used to demonstrate the presence of **fat or lipids in <u>fresh frozen</u>** tissue sections. It is performed on fresh frozen sections because fixatives containing alcohols, or routine tissue processing, will remove lipids.



Alcian Blue stains strongly acidic mucins blue, nuclei pink to red, and cytoplasm pale pink.

Periodic acid–Schiff (PAS) detects polysaccharides such as glycogen, glycoproteins, glycolipids, proteoglycans as well as neutral and acidic mucins, allowing for example the identification of hepatic glycogen, intestinal goblet cells and basal laminae.

Golgi's Black reaction

Golgi's "black reaction" (*reazione nera*) was based on the fixation of nervous tissue blocks in potassium dichromate (2–2.5%) for a variable number of days or weeks (from 1 to 50 days or even longer), followed by immersion in silver nitrate which led to the precipitation of silver chromate fully impregnating cells in the nervous tissue

https://unibo.smartzoom.com/s1241/course1776/f1858/i1876/

The importance of staining

The Golgi Dispute

The fertile controversy between Camillo Golgi and Ramon y Cajal about the structure of the nervous system.

The nervous system was still considered as a network formed by anastomosing nerve cells, in analogy to the vascular network- **the reticular theory of nerve cells continuity** :(a "reticulum") of interconnected nerve fibers, rather than individual, discrete cells.

Cajal, paladin of the **neuron doctrine**, which stated that neurons are individual elements representing the structural and functional units of the nervous system.

Both won the Nobel Prize in 1906
The metallic impregnation invented by Camillo Golgi in 1873 has allowed the visualization of **individual neurons** in their entirety, leading to a breakthrough in the knowledge on the structure of the nervous system.

The dispute illustrates a classic scientific lesson:

The same experimental data can lead to radically different interpretations depending on theoretical assumptions.

The technical limits of microscopy:
Golgi and Cajal worked with **optical microscopes**, resolution limit of about **200 nanometers (0,2 um)**.

Key consequence:
Synapses are extremely small (≈20–40 nm gaps between neurons).
Under a light microscope, these gaps **cannot be resolved**.
Separate neurons therefore **appear to touch or fuse together**.

The decisive evidence came later
The debate lasted decades because no available technology could directly show synapses.

The issue was finally resolved with:
Electron microscopy (1950s)
This revealed:
- **a synaptic cleft between neurons**
- **vesicles releasing neurotransmitters**
- **membranes remaining separate**

Tissues

Cells work together in functionally related groups called tissues

Types of tissues:

1. Epithelial – lining and covering or secrete
2. Connective – support
3. Muscle – movement
4. Nervous – control

Tissues

Tissues are made by two elements:

Cells

Extracellular matrix

Extracellular Matrix (ECM)'s actions

- Modify the morphology and functions of cells
- Modulate survival of cells
- Regulate the migration of cells
- Direct mitotic activity
- Form junctional associations with cells

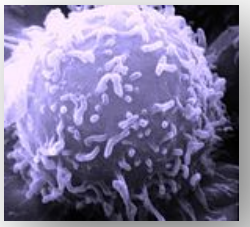
The ECM of connective tissue proper is composed of: gel-like *ground substance* with several fibers embedded

Cells

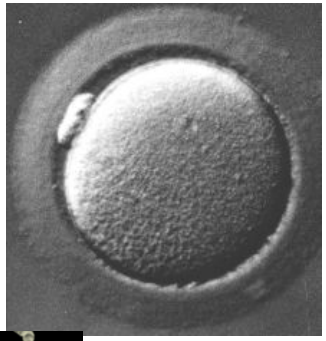
- Size
- Shape
- Function
- Chemical products

Classification by size

- Lymphocytes about 5-6 µm

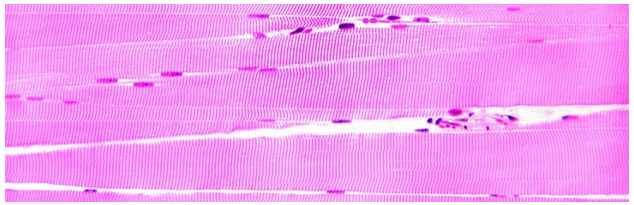


- Oocyte 150 µm



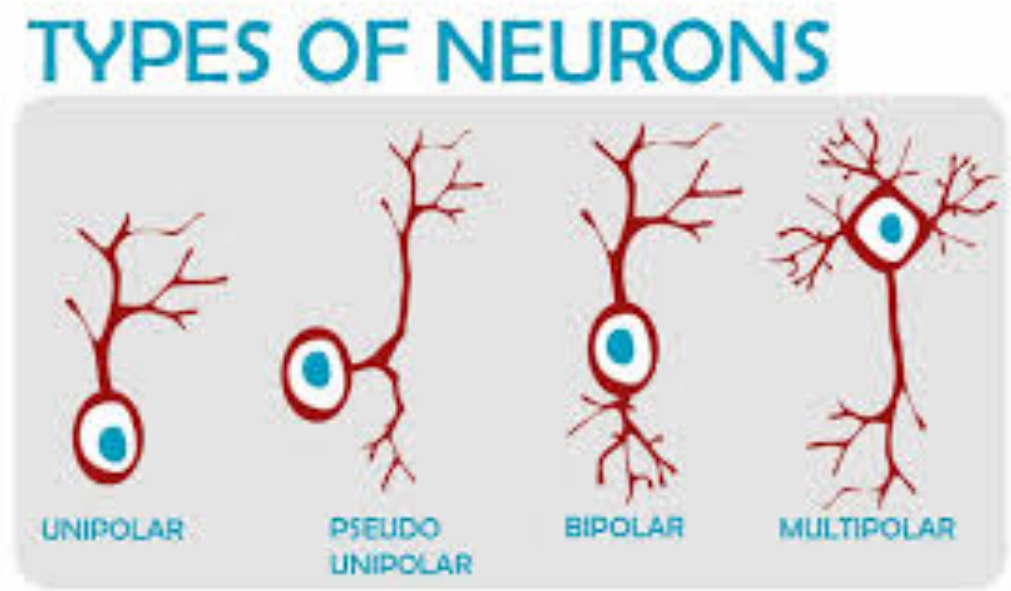
- Neurons about mm

- Muscle fiber-syncytium few cm



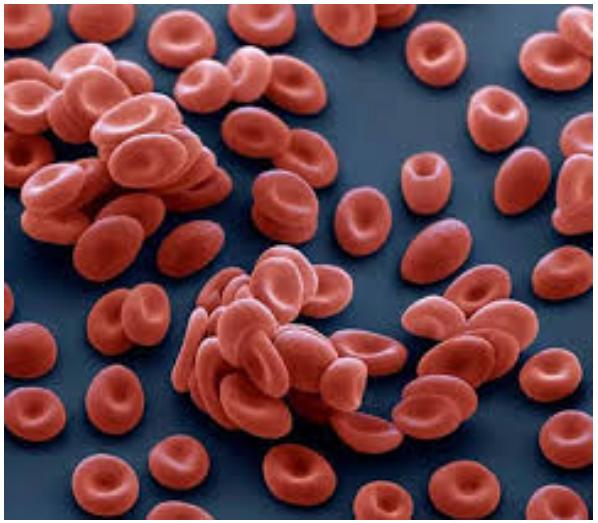
Classification by shape

- Shape and function are correlated



Classification by type of secretion

- Growth factors
- Gas or CO2



Differentiation

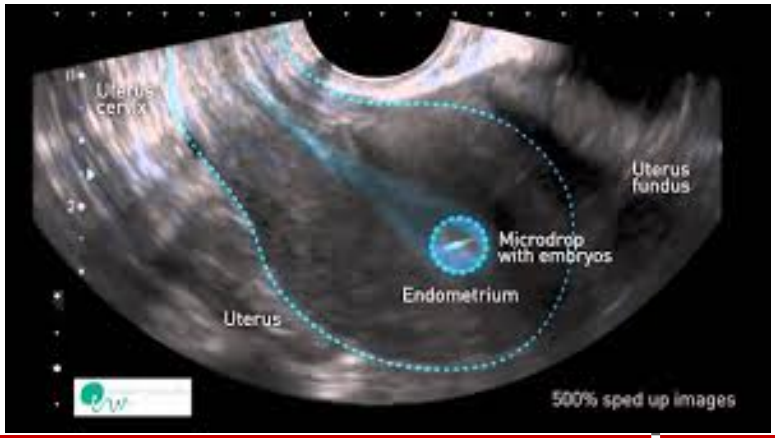
The process by which unspecialized cells (stem cells) become specialized to carry out distinct functions.

Stem cells can divide without limits as needed and, under specific conditions, can differentiate into specialized cells

Differentiation

The first embryonic cells that arise from the division of the zygote are the ultimate **stem cells**; these stem cells are described as **totipotent** because they have the potential to differentiate into any of the cells needed to enable an organism to grow and develop.

Blastocyst stage embryo transfer (BET) leads to pregnancy when transfereed in a stimulated endometrium.



Differentiation

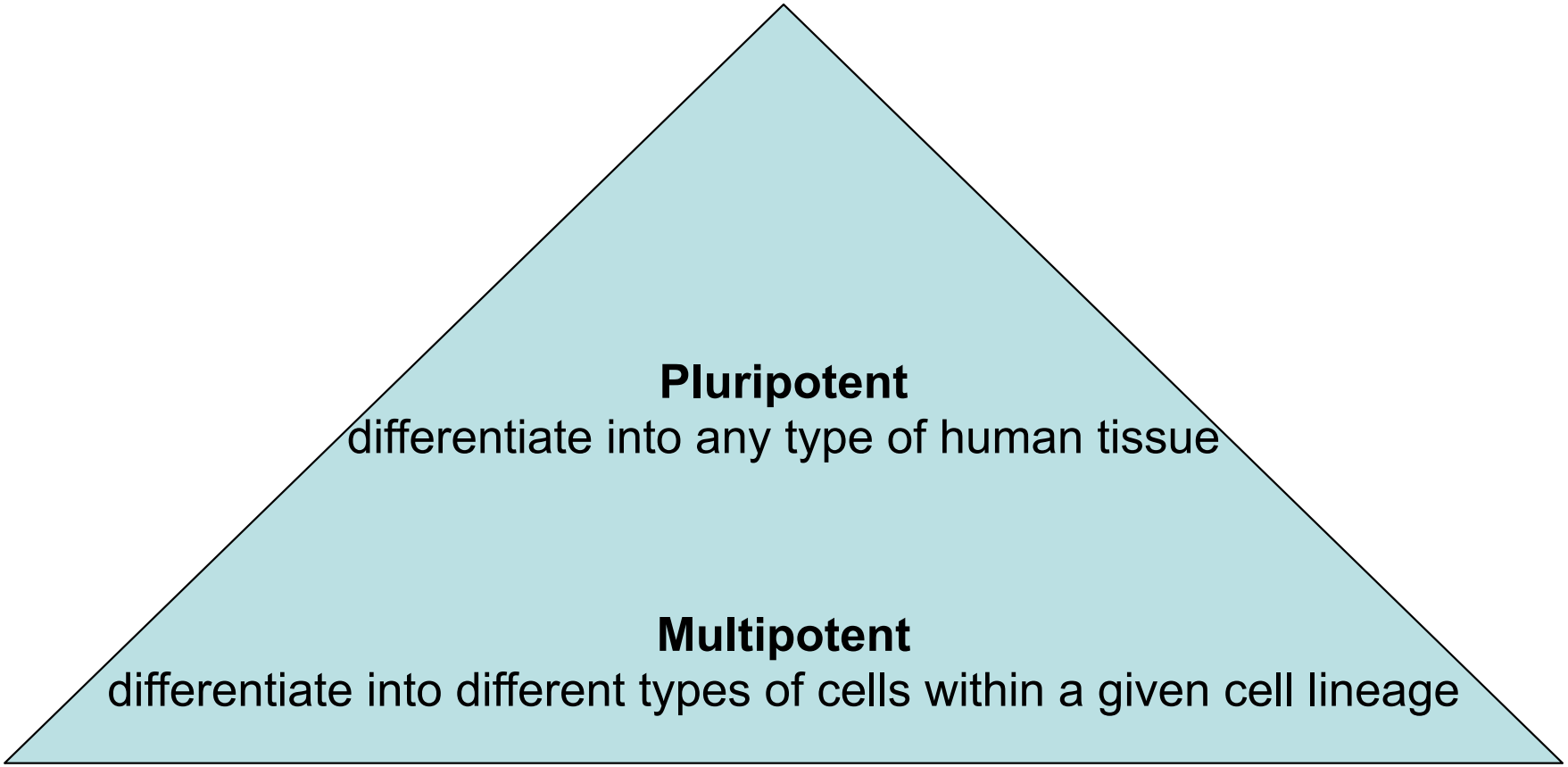
The embryonic cells that develop from totipotent stem cells and are precursors to the **fundamental tissue layers** of the embryo are classified as pluripotent.

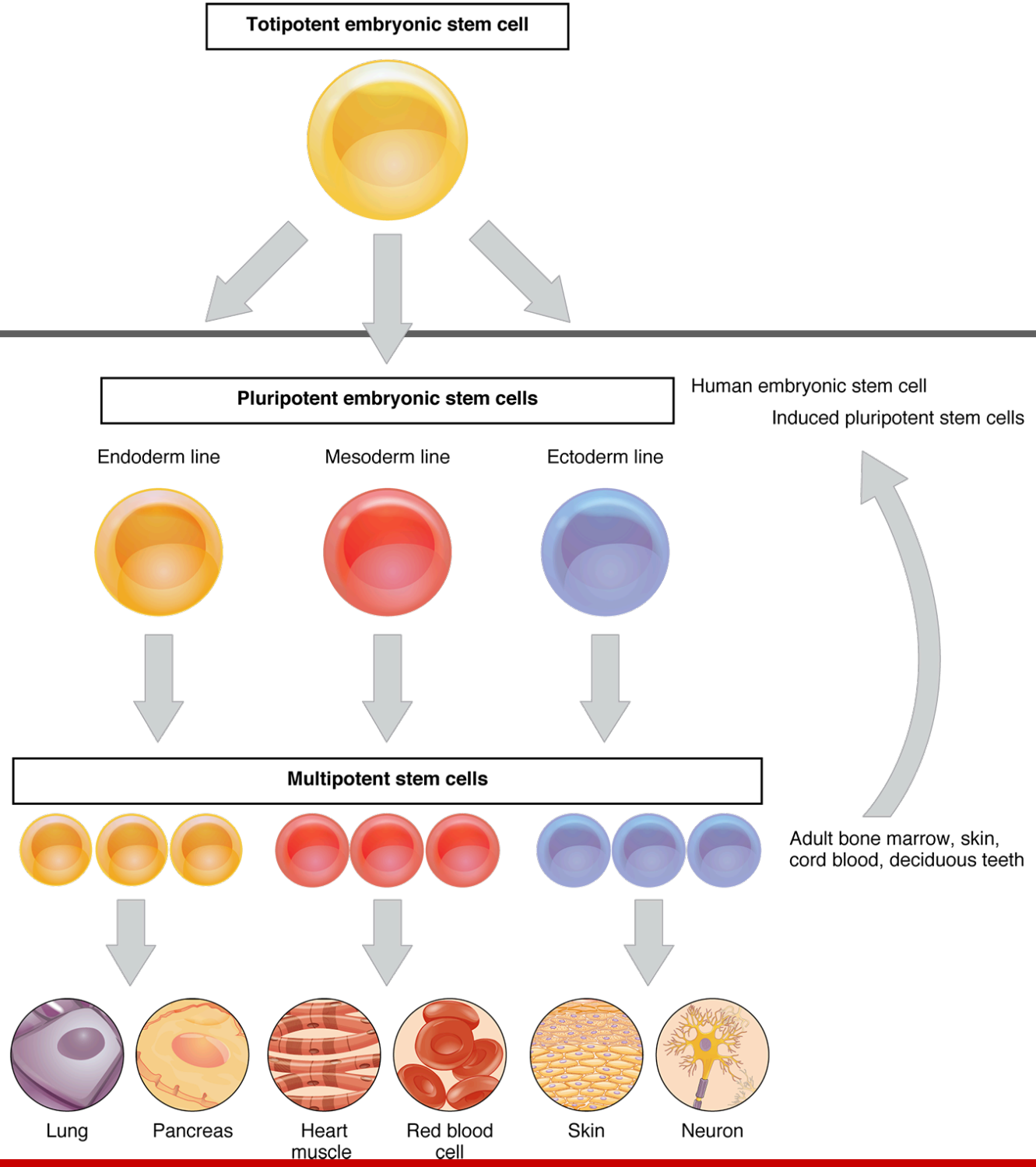
A **pluripotent** stem cell has the potential to differentiate into any type of human tissue but cannot support the full development of an organism.

These cells become slightly more specialized, and are referred to as **multipotent cells**.

A **multipotent** stem cell has the potential to differentiate into different types of cells within a given cell lineage or small number of lineages, such as a red blood cell or white blood cell.

Totipotent
differentiate to enable an organism to grow





Embryonic Origin of Tissues

After fertilization the zygote gives rise to rapid mitotic cycles, generating many cells to form the embryo.

The first embryonic cells generated have the ability to differentiate into any type of cell in the body and, as such, are called **totipotent**, meaning each has the capacity to divide, differentiate, and develop into a new organism.

Embryonic Origin of Tissues

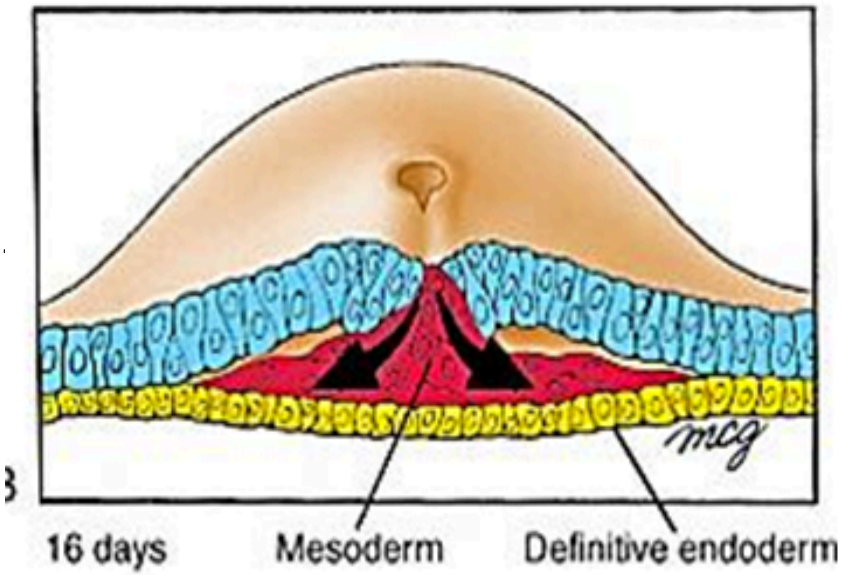
The zygote, or fertilized egg, is a single cell formed by the fusion of an egg and sperm.

As cell proliferation progresses, three major cell lineages are established within the embryo.

Each of these lineages of embryonic cells forms the distinct germ layers from which all the tissues and organs of the human body eventually form.

Each germ layer is identified by its relative position: **ectoderm** (ecto- = “outer”),

Mesoderm (meso- = “middle”), and **endoderm** (endo- = “inner”).



Differentiation MODEL

Because all cells in the body, beginning with the fertilized egg, contain the same DNA, how do the different cell types come to be so different?

All cells contain the same full complement of DNA, but each type of cell only “reads” the portions of DNA that are relevant to its own function. In biology, this is referred to as the **unique genetic expression.**

In order for a cell to differentiate into its specialized form and function, it manipulates those genes (and thus those proteins) that will be expressed, and not those that will remain silent.
The primary mechanism by which genes are turned “on” or “off” is through transcription factors and methilation.
A **transcription factor** is one of a class of proteins that bind to specific genes on the DNA molecule and either promote or inhibit their transcription

THE RIGHT COMBINATION OF **TRANSCRIPTION FACTORS MAY DRIVE STEM CELL REPROGRAMMING.**

Cell

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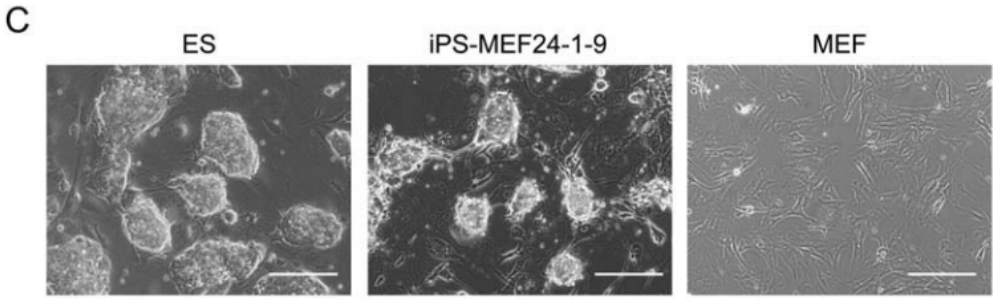
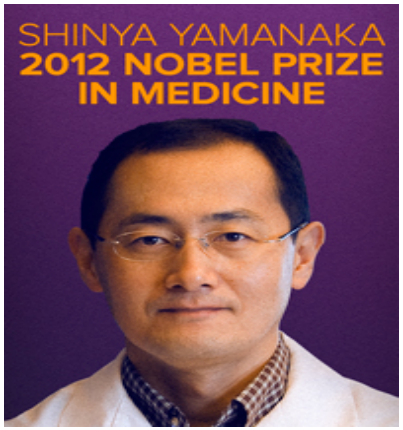
Article

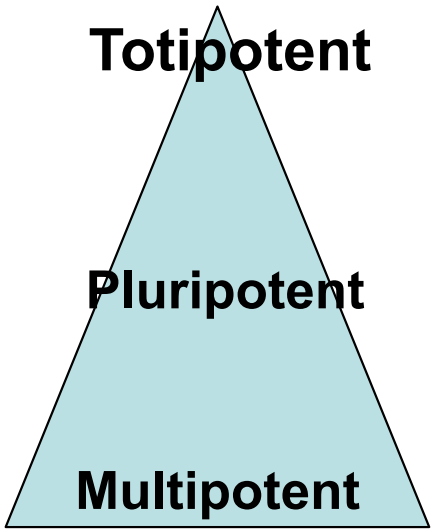
Induction of Pluripotent Stem Cells from Adult Human Fibroblasts by Defined Factors

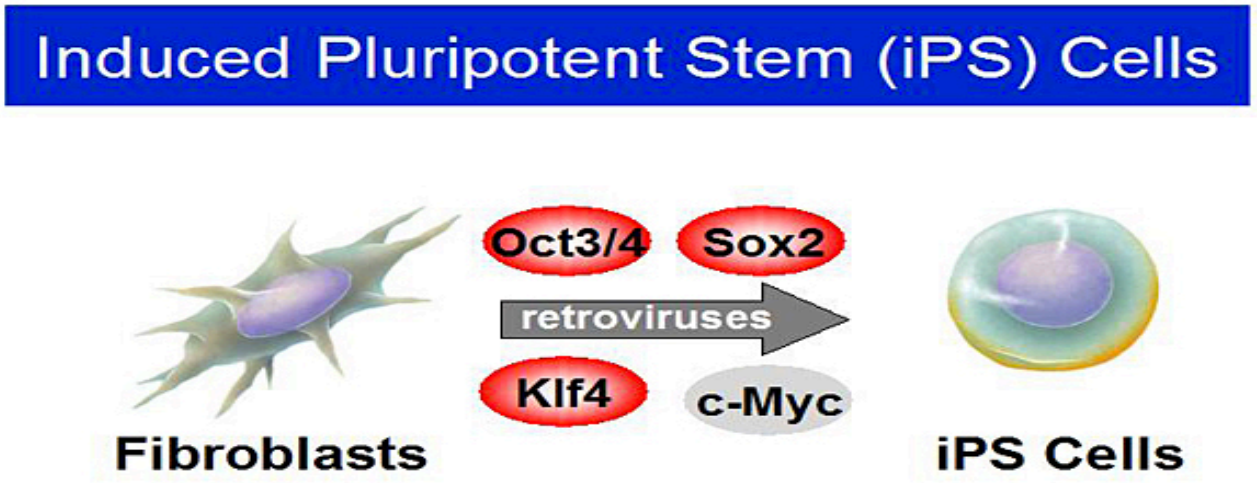
Kazutoshi Takahashi [1], Koji Tanabe [1], Mari Ohnuki [1], Megumi Narita [1, 2], Tomoko Ichisaka [1, 2], Kiichiro Tomoda [3], Shinya Yamanaka [1, 2, 3, 4]



IPS- Induced Pluripotent Stem Cells







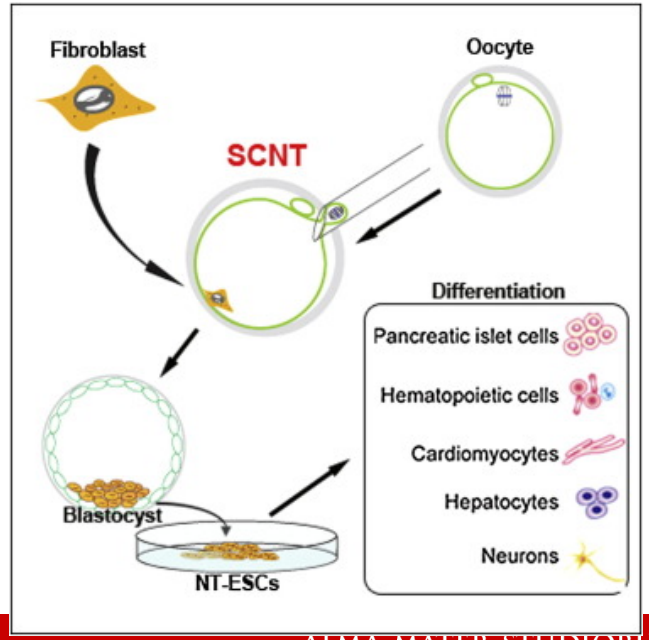
Mouse iPS cells reported in 2006

Human iPS cells reported in 2007

How Yamanaka did it?

Differentiated cells can be reprogrammed to an embryonic-like state by transfer of nuclear contents into oocytes or by fusion with embryonic stem (ES) cells.

This means that unfertilized eggs and ES cells contain factors that can confer pluripotency
to somatic cells

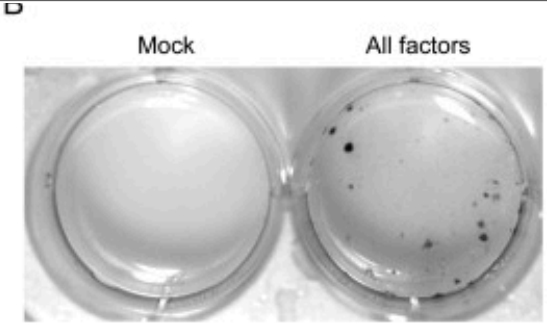


How Yamanaka did it?

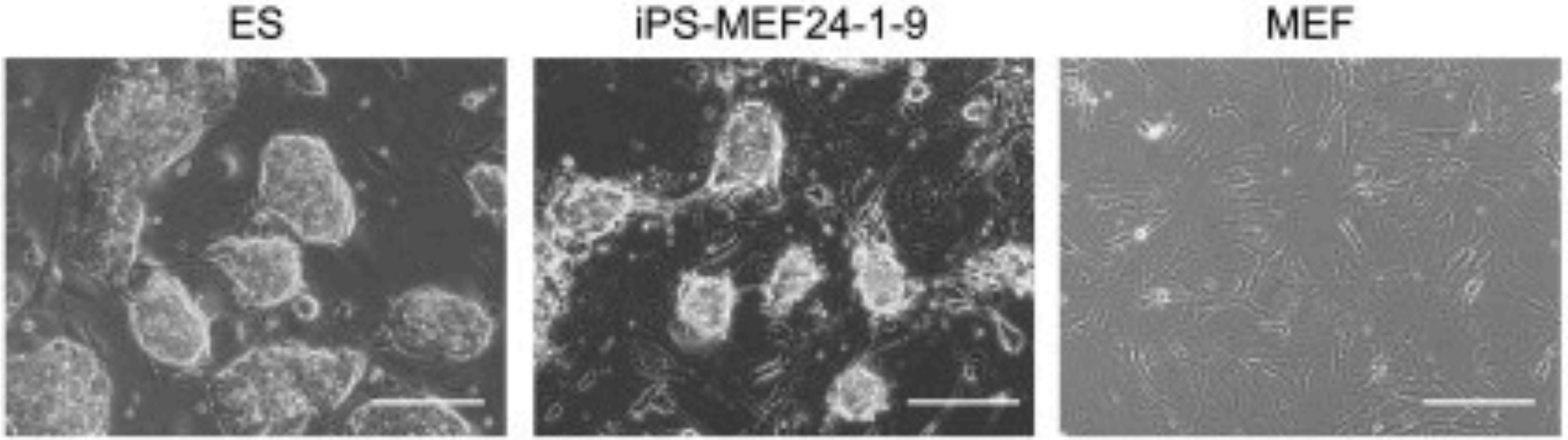
Pluripotent stem cells can be directly generated from mouse embryonic fibroblasts (MEF) cultures by the addition of **only a few defined factors**. Which factors?

Transcription Factors

- He started with 24 TF (Transcription Factors)
- Adding single TF ----> no iPS
- All together ------→ yes iPS

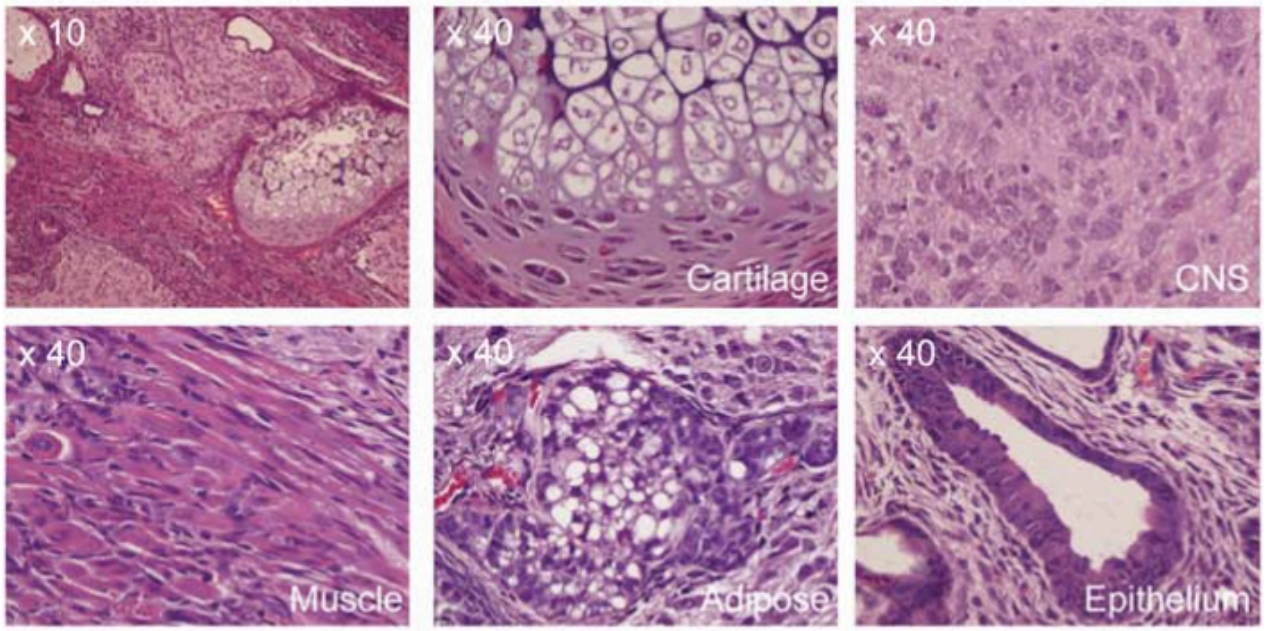


mouse embryonic fibroblasts



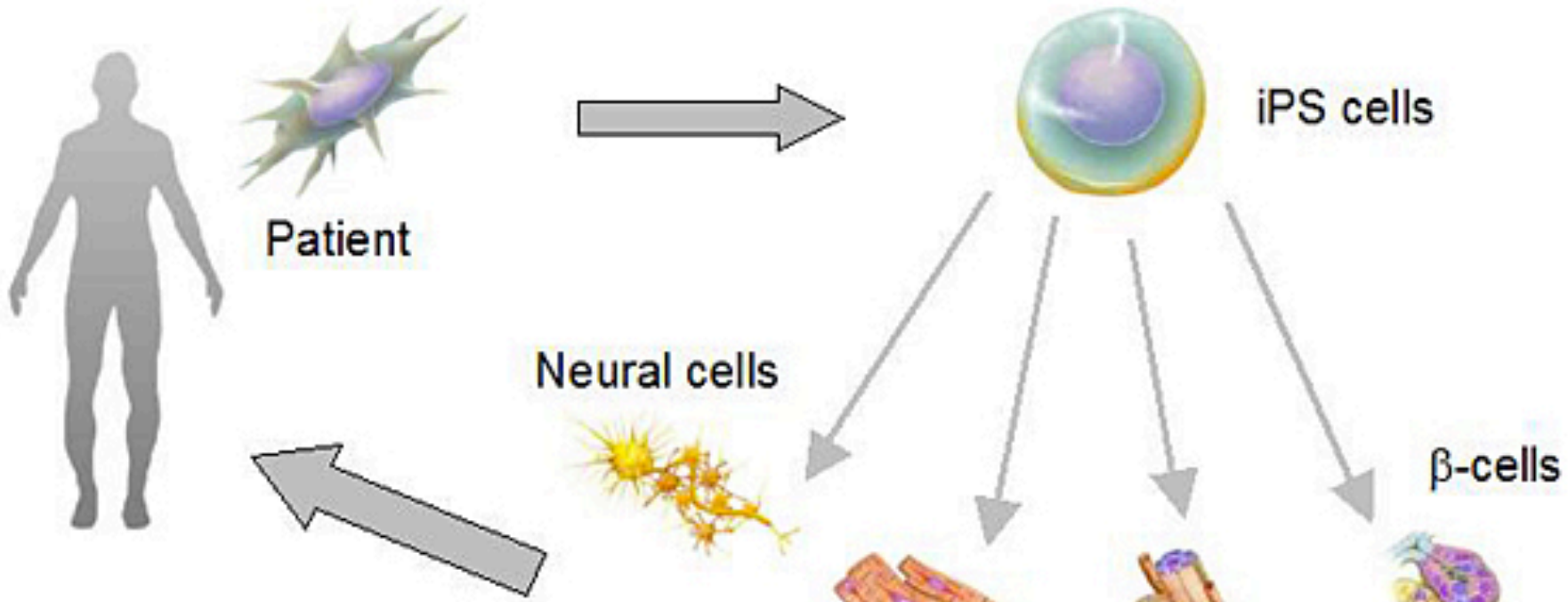
Yamanaka's Experiment

Next, to determine which of the 24 candidates were critical, he examined the effect of withdrawal of individual factors from the pool of 24 candidate genes.



Various tissues present in teratomas
derived from iPS-MEF4-7 cells.

Applications of iPS Cells



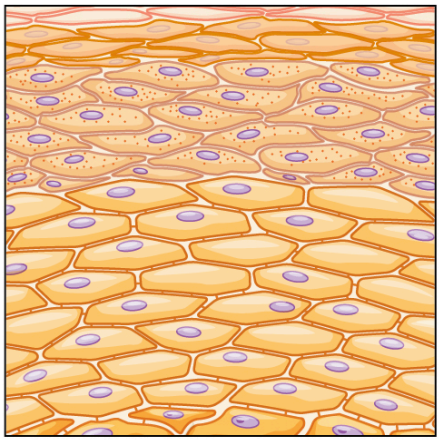
Regenerative medicine (in vivo USE)

Toxicology
Disease Model, Drug Screening
(in vitro USE)

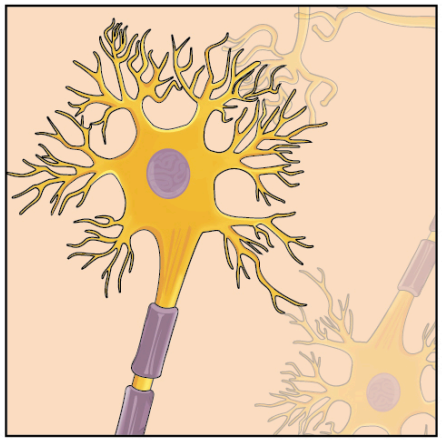
Ectoderm derivation

Each of these lineages of embryonic cells forms a distinct germ layers from which all the tissues and organs of the human body eventually form. Each germ layer is identified by its relative position: **ectoderm** (ecto- = “outer”),

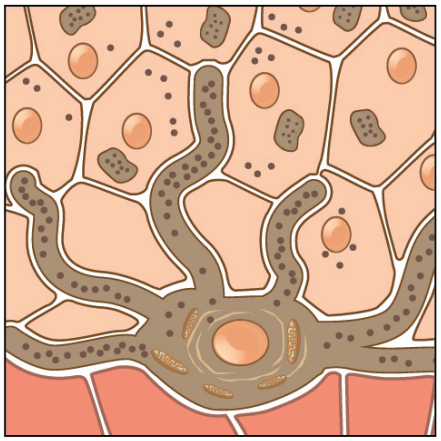
Germ Layer	Gives rise to:
Ectoderm	Epidermis, glands on skin, some cranial bones, pituitary and adrenal medulla, the nervous system, the mouth between cheek and gums, the anus



Skin cells



Neurons



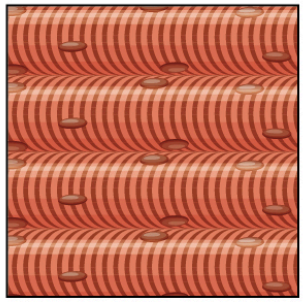
Pigment cell

Mesoderm derivation

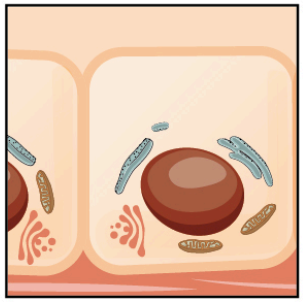
Mesoderm (meso = “middle”).

Mesoderm	Connective tissues proper, bone, cartilage, blood, endothelium of blood vessels, muscle, synovial membranes, serous membranes lining body cavities, kidneys, lining of gonads

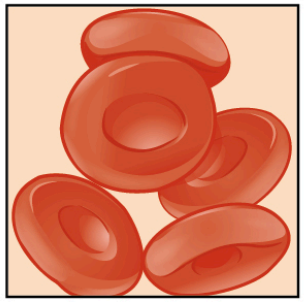
Cardiac muscle



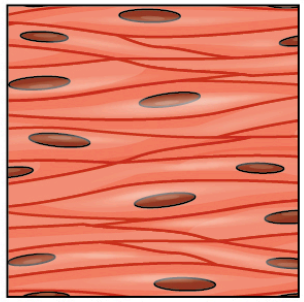
Skeletal muscle



Tubule cell of kidney



Red blood cells

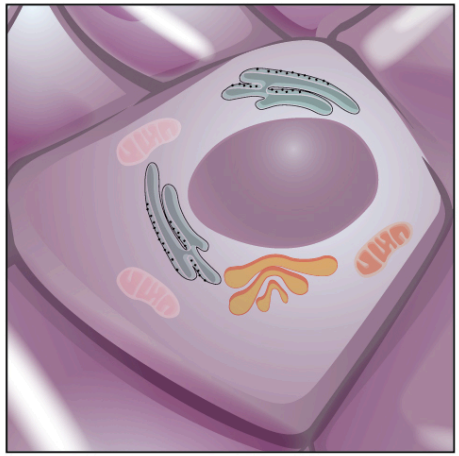


Smooth muscle

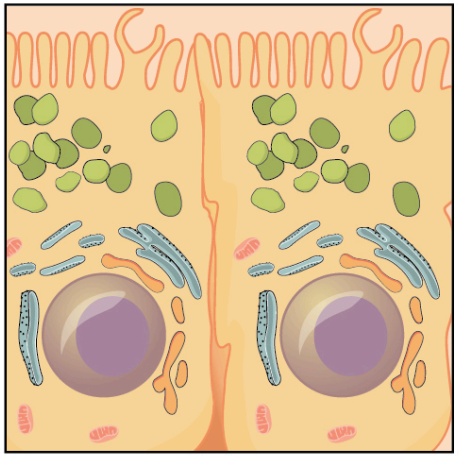
Endoderm derivation

endoderm (endo- = “inner”).

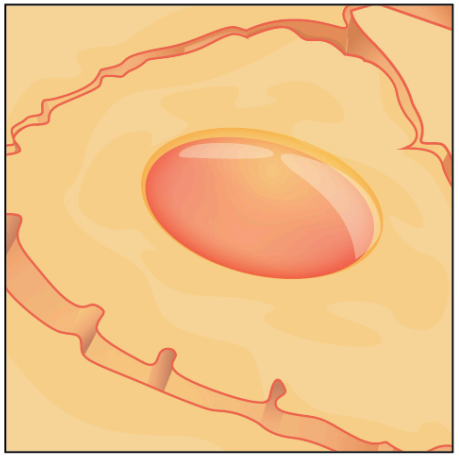
Endoderm	Lining of airways and digestive system except the mouth and distal part of digestive system (rectum and anal canal); glands (digestive glands, endocrine glands, adrenal cortex)



Lung cell



Thyroid cell



Pancreatic cell

Take home message

- Methods of Microscopy
- Tissue Classification
- Stem Cell/Differentiation
- Embryonic Origin of Tissues