



# The research of developmental biology in Estonia and beyond

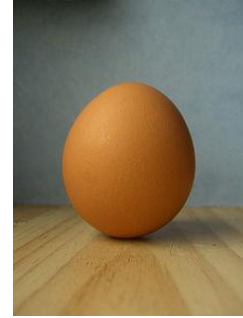
Osamu Shimmi

Chair of developmental biology  
Institute of Molecular and Cell Biology  
University of Tartu

18 May 2023  
Tallinn

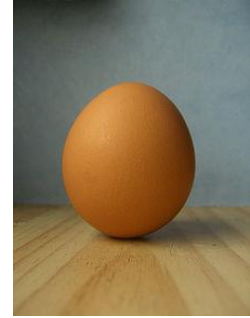
# What is developmental biology?

The fertilized egg: no heart, no eye, no limb



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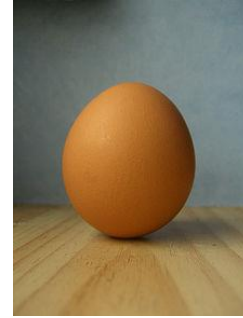


How do we become what we are?

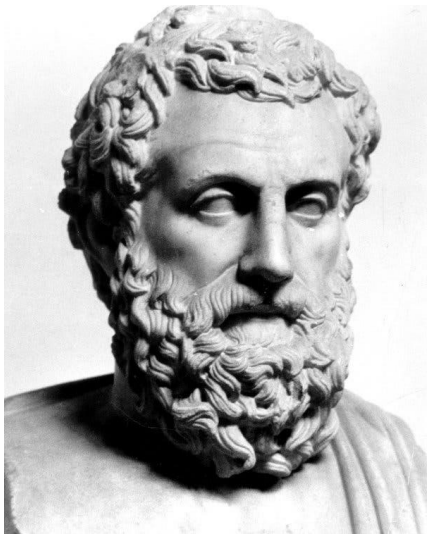


# What is developmental biology?

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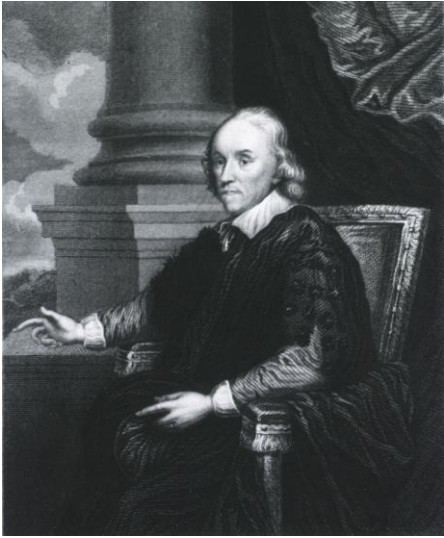
How do we become what we are?



Aristotle

*“The generation of Animals (ca. 350 BCE)”*

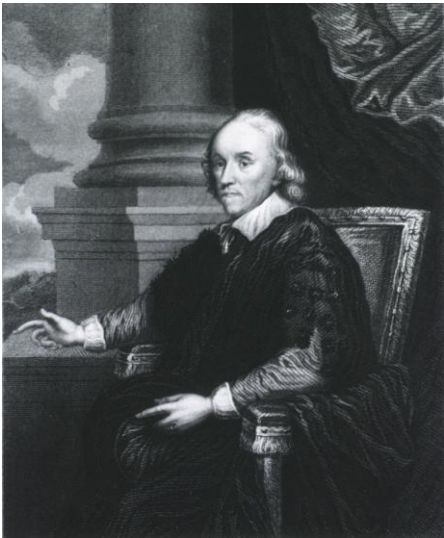
- Some animals are born from eggs (birds, frogs, invertebrates)
- Some by live birth (placental mammals)
- Finding the functions of the placenta and the umbilical cord



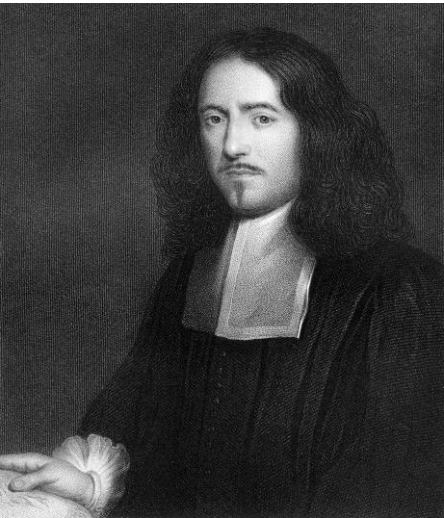
William Harvey  
(1578-1657)

***“Ex ovo omnia (All from the egg)”***





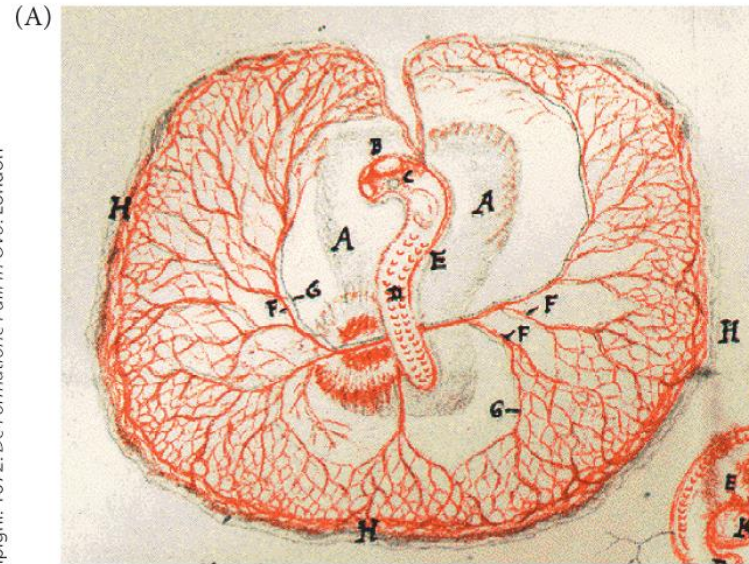
William Harvey  
(1578-1657)



Marcello Malpighi  
(1628-1694)

# “*Ex ovo omnia (All from the egg)*”

Chick developmental anatomy



From M. Malpighi. 1672. *De Formatione Pulli in Ovo*. London

DEVELOPMENTAL BIOLOGY 12e, Figure 1.3  
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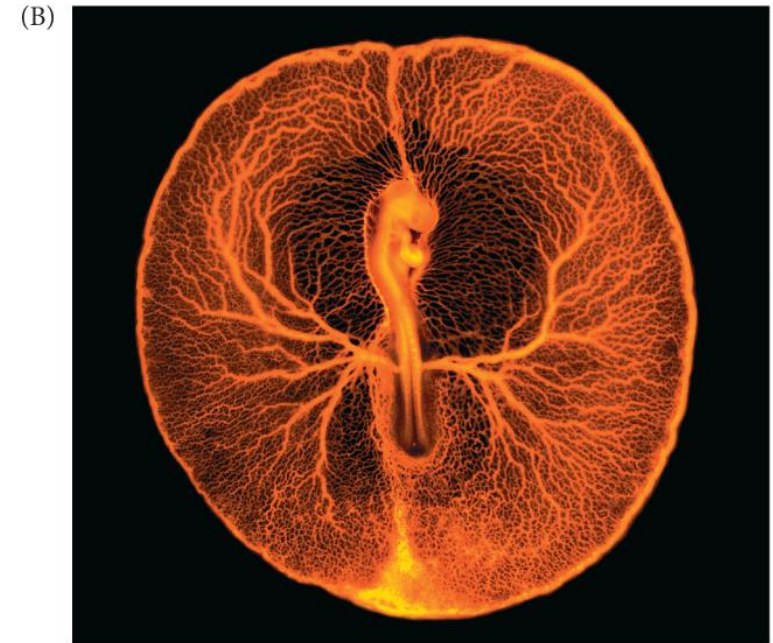


Image courtesy of Vincent Pasque

“Founder of microscopic anatomy”

# A revolution in descriptive embryology (1820- )

The most talented microscopically inclined investigators – three friends of Baltic German – transformed embryology into a specialized branch of science

- Heinz Christian Pander
- Henrich Rathke
- Karl Ernst von Baer Edler von Huthorn

# Heinz Christian Pander

Father of embryology “embruologia isa“

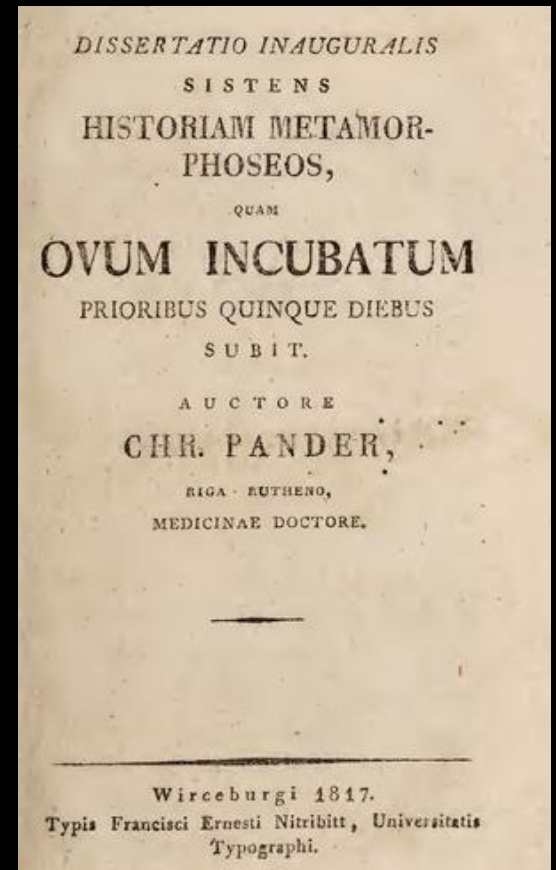
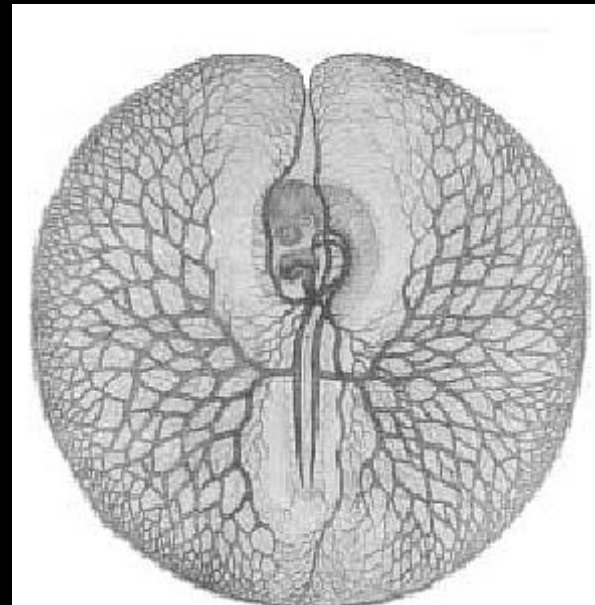
1812-1814 **University of Tartu (Dorpat)** Faculty of Medicine  
> Germany Würzburg (MD)

1817 - *Discovering germ layer using chicken embryo*

Three distinct germ layers

- ✓ Ectoderm  
(neuron, skin)
- ✓ Mesoderm  
(bone, blood cells)
- ✓ Endoderm  
(stomach, lung)

(1794-1865)





# Martin Heinrich Rathke

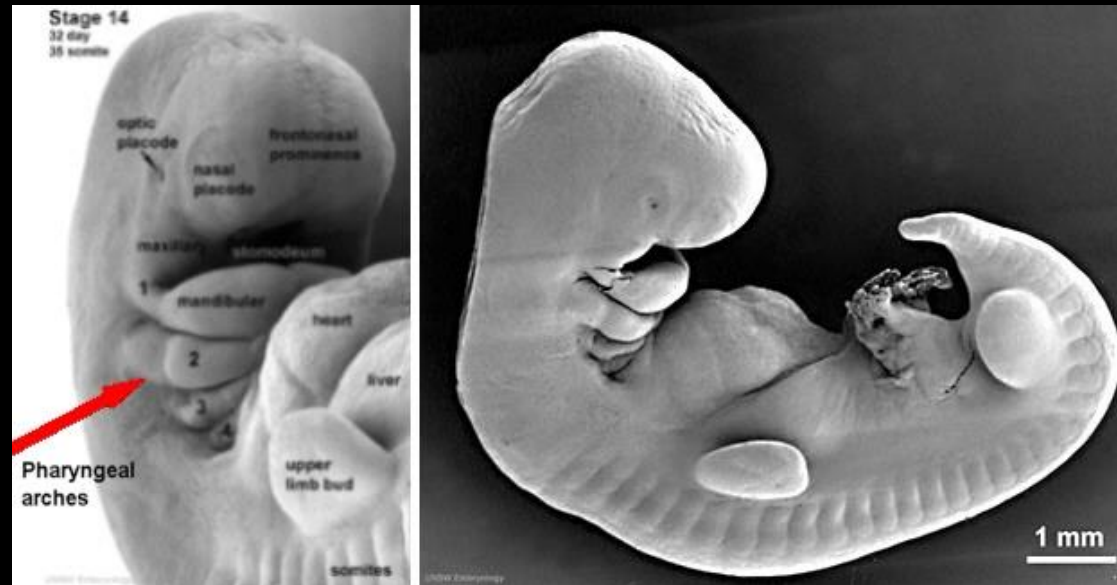
One of the founders of modern embryology

1828-1835 **University of Tartu** (Dorpat) professor of physiology, pathology and medical semiotics

1835- University of Königsberg professor of anatomy and zoology



(1793-1860)



- ✓ Discovery of the pharyngeal arches in bird and mammal embryos
- ✓ Description of the structure later called Rathke's pouch (the anterior lobe of the pituitary gland)

# Karl Ernst Ritter von Baer, Edler von Huthorn

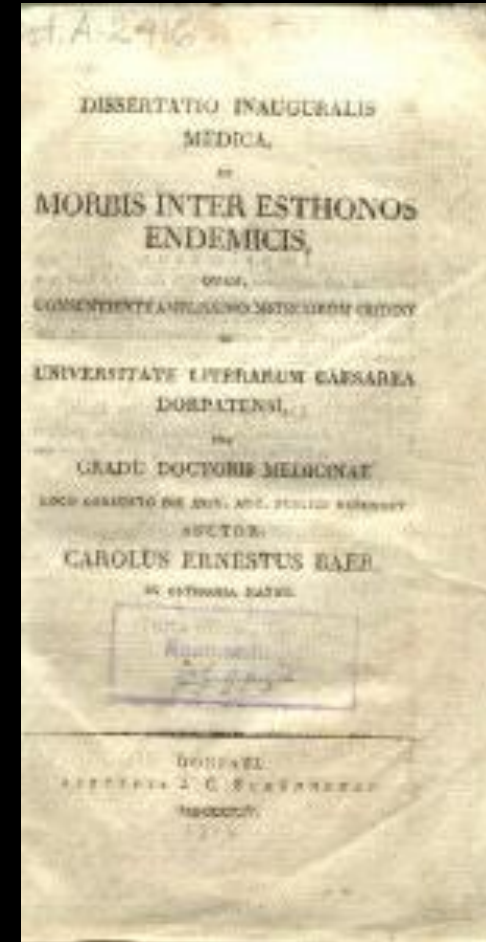


(1792-1876)

1810-1814 **University of Tartu**  
(Dorpat) Faculty of Medicine

- ❖ Naturalist
- ❖ Biologist
- ❖ Geologist
- ❖ Meteorologist
- ❖ Geographer

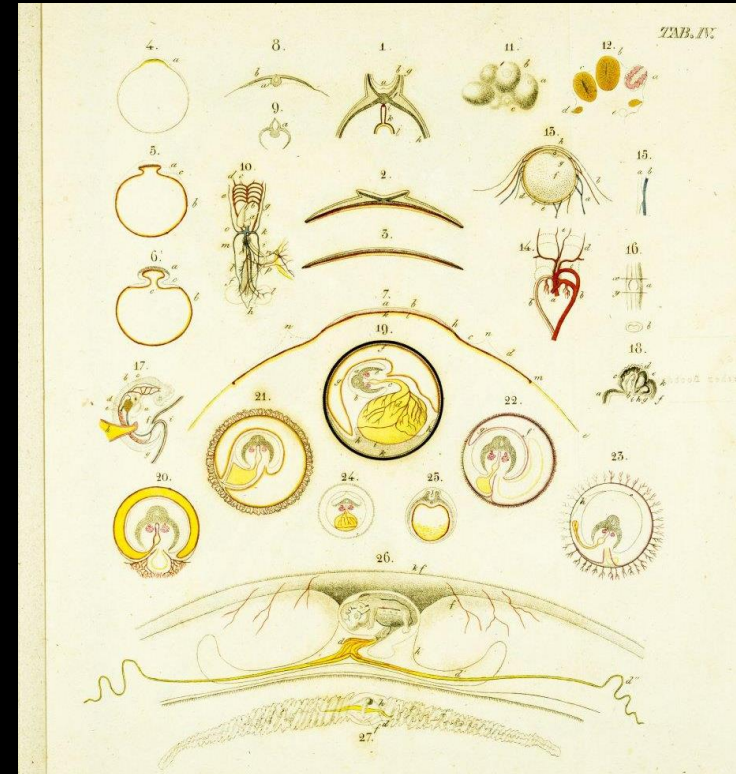
*"Endemic diseases among the Estonians."*



1814, doctoral thesis

# Karl Ernst Ritter von Baer, Edler von Huthorn

Founder of descriptive/comparative embryology



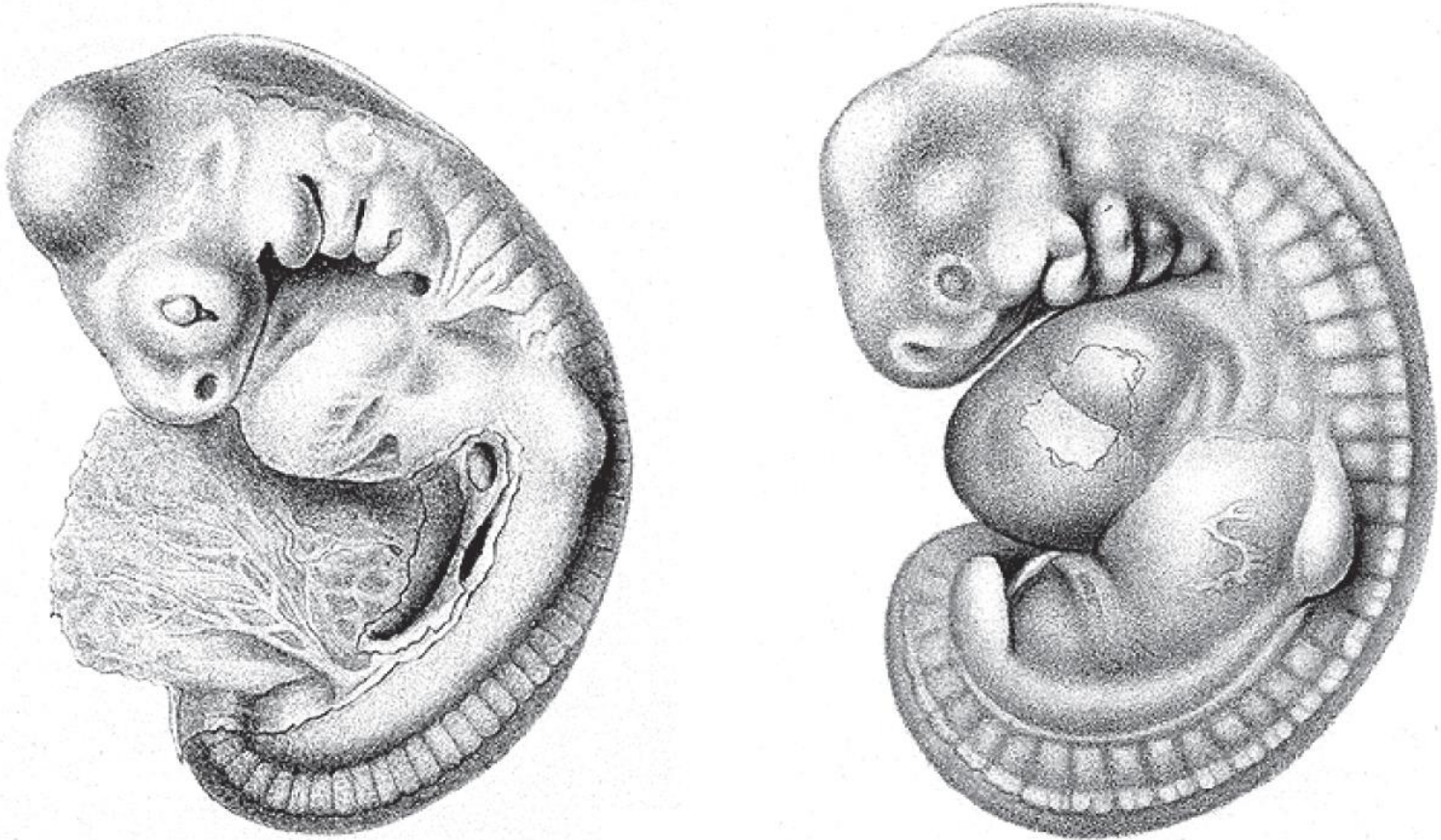
- 1810-1814 **University of Tartu** (Dorpat)  
Faculty of Medicine  
-Berlin, Vienna, Würzburg
- 1821- professor at the Königsberg  
University
- 1841-1852 St Petersburg Academy of  
Science professor

- ✓ Description of the blastula stage of development
- ✓ Discovery of the notochord
- ✓ Discovery of mammalian ovum



# Karl Ernst Ritter von Baer's Laws of Embryology

*Lizard or Human?*



DEVELOPMENTAL BIOLOGY 12e, Figure 1.18  
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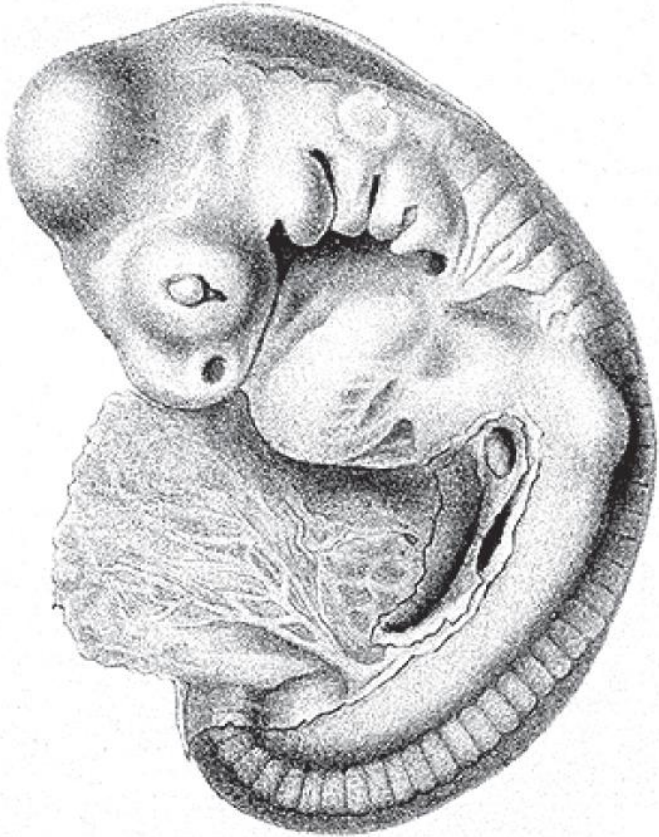
From F. Keibel 1904, 1908. Normentafeln zur Entwicklungsgeschichte der Wirbeltiere, Heft IV, VIII. Gustav Fischer, Jena



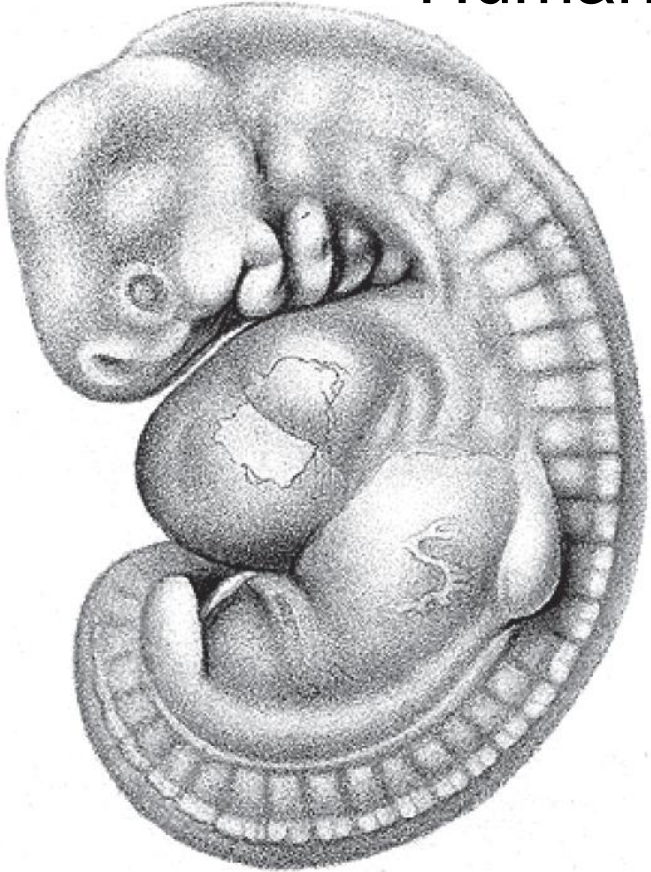
# Karl Ernst Ritter von Baer's Laws of Embryology



Lizard



Human



DEVELOPMENTAL BIOLOGY 12e, Figure 1.18  
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From F. Keibel 1904, 1908. Normentafeln zur Entwicklungsgeschichte der Wirbeltiere, Heft IV, VIII. Gustav Fischer, Jena



# Embryology in Tartu



**Prof. Jüri Kärner** (1940-2010)

1988–1993 TÜ rektor

“ Elus on kaks tähtsat otsust:

1) Läbida korralikult  
gastrulatsioon

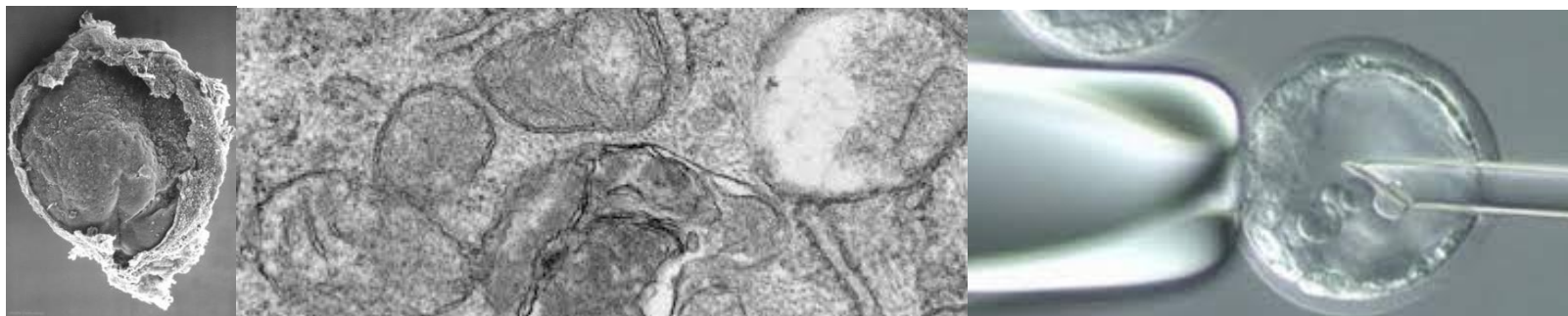
2) Valida endale õige naine

kui siis miskit valesti läheb on  
kõik untsus”



1958 **Prof. Alar Karis**

2007-2012 TÜ rektor  
2021 – EV president



# Embryology in Tartu



**Prof. Jüri Kärner** (1940-2010)

1988–1993 TÜ rektor

"There are two important decisions in life:

1) Go through gastrulation properly

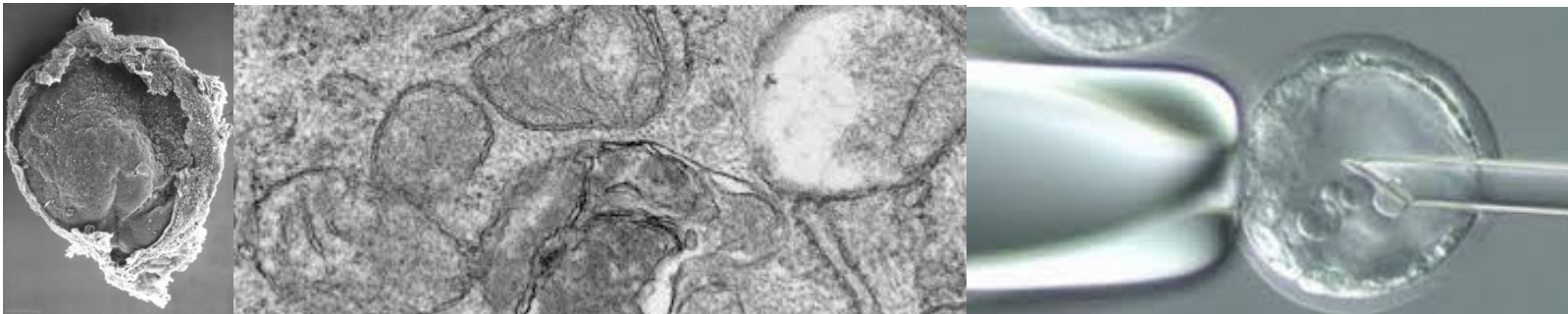
2) Choose the right woman for yourself

if something goes wrong, everything is gone"



1958 **Prof. Alar Karis**

2007-2012 TÜ rektor  
2021 – EV president

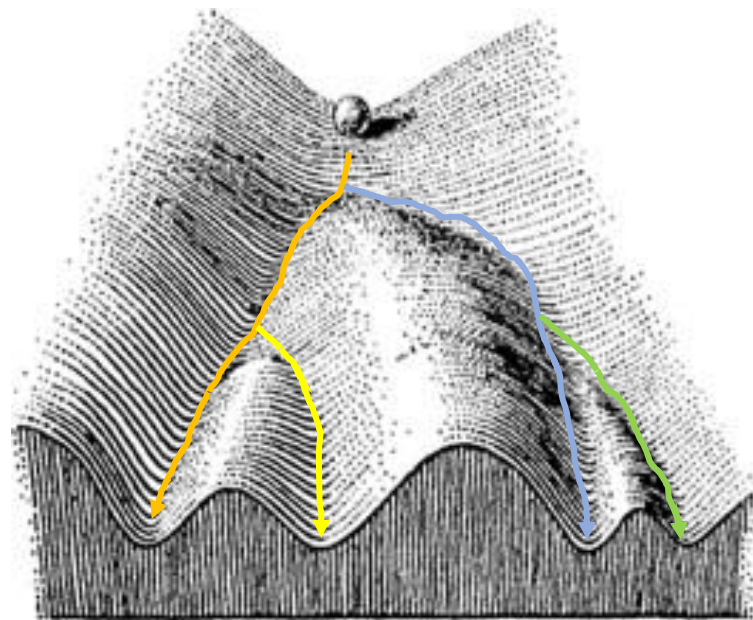
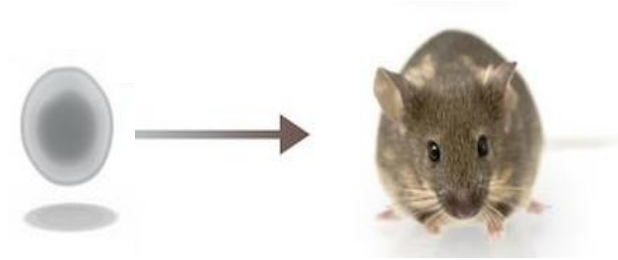




# Cell fate commitment and the Waddington landscape model

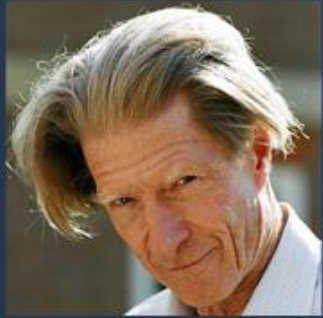


Conrad Waddington (1957)



Schematic representation  
of the development  
potentials

# The Nobel Prize in Physiology or Medicine 2012

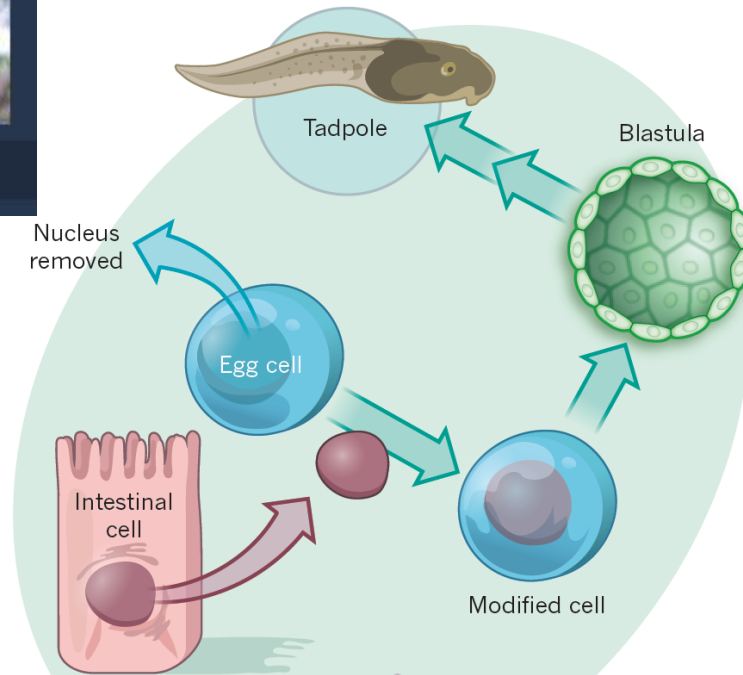


John B. Gurdon



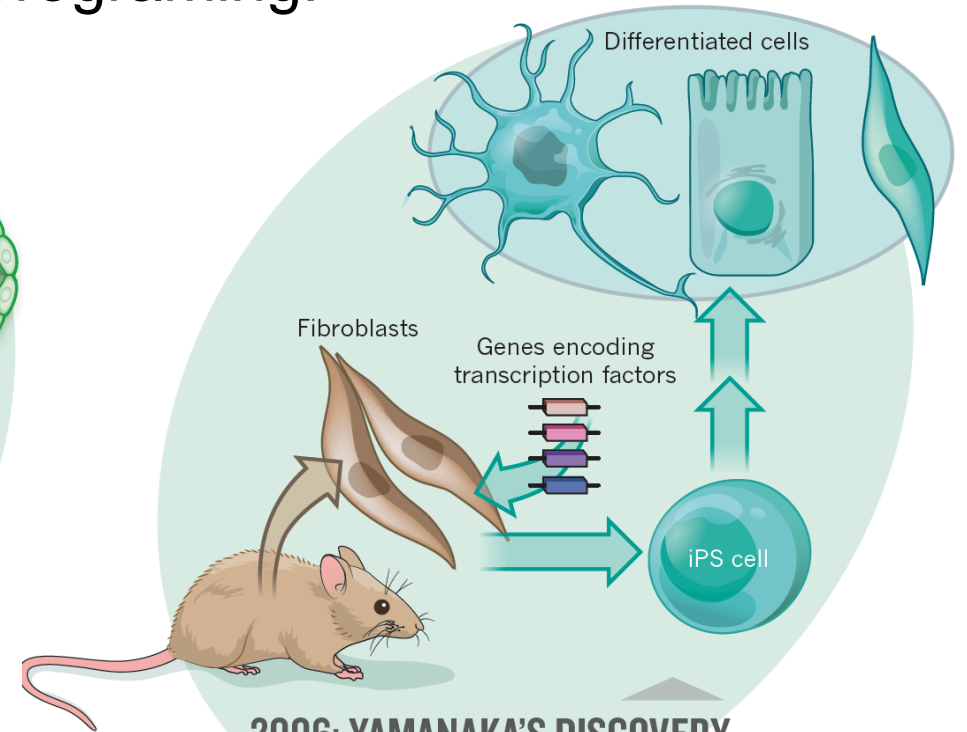
Shinya Yamanaka

## Reprogramming!



### 1962: GURDON'S DISCOVERY

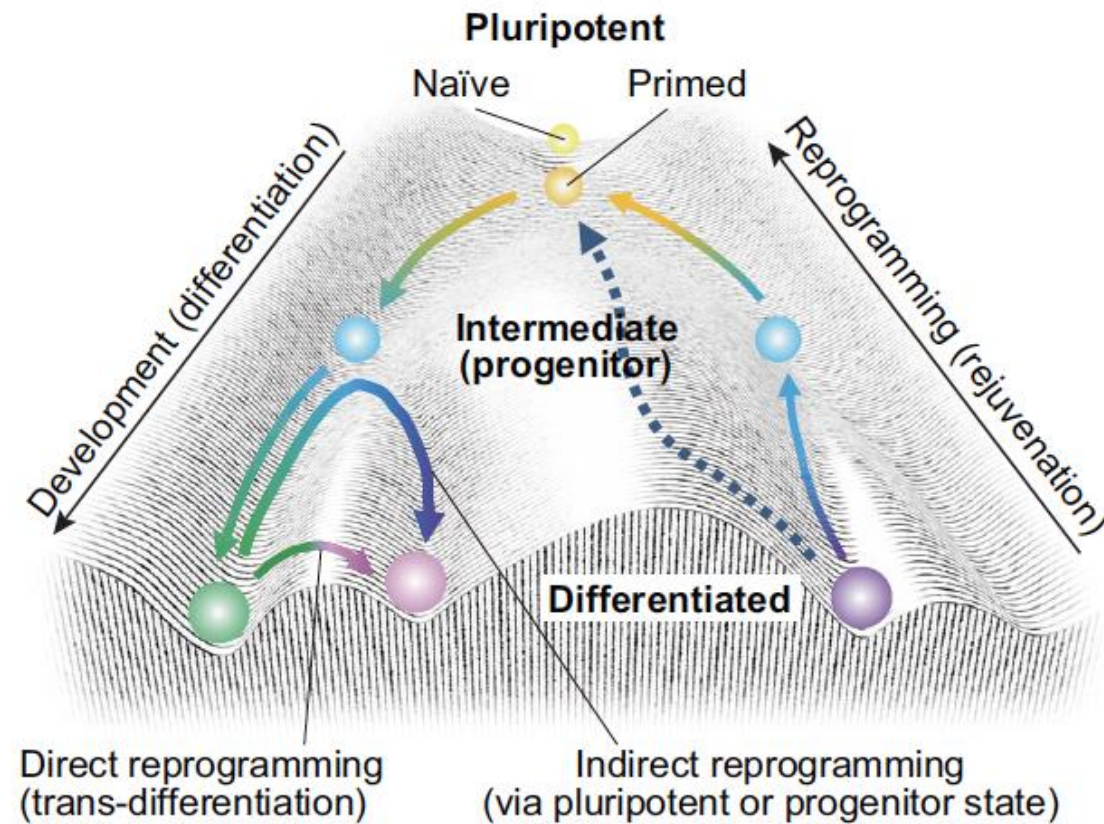
When the nucleus of a differentiated intestinal cell is transferred into a nucleus-free egg, the resulting modified cell can go through normal embryonic development to form a blastula, which can generate a tadpole.



### 2006: YAMANAKA'S DISCOVERY

Introduction of genes encoding just four transcription factors into an intact, differentiated fibroblast can reprogram it into an induced pluripotent stem (iPS) cell that can differentiate into various cell types of the body.

# Cell fate changes on Waddington's landscape



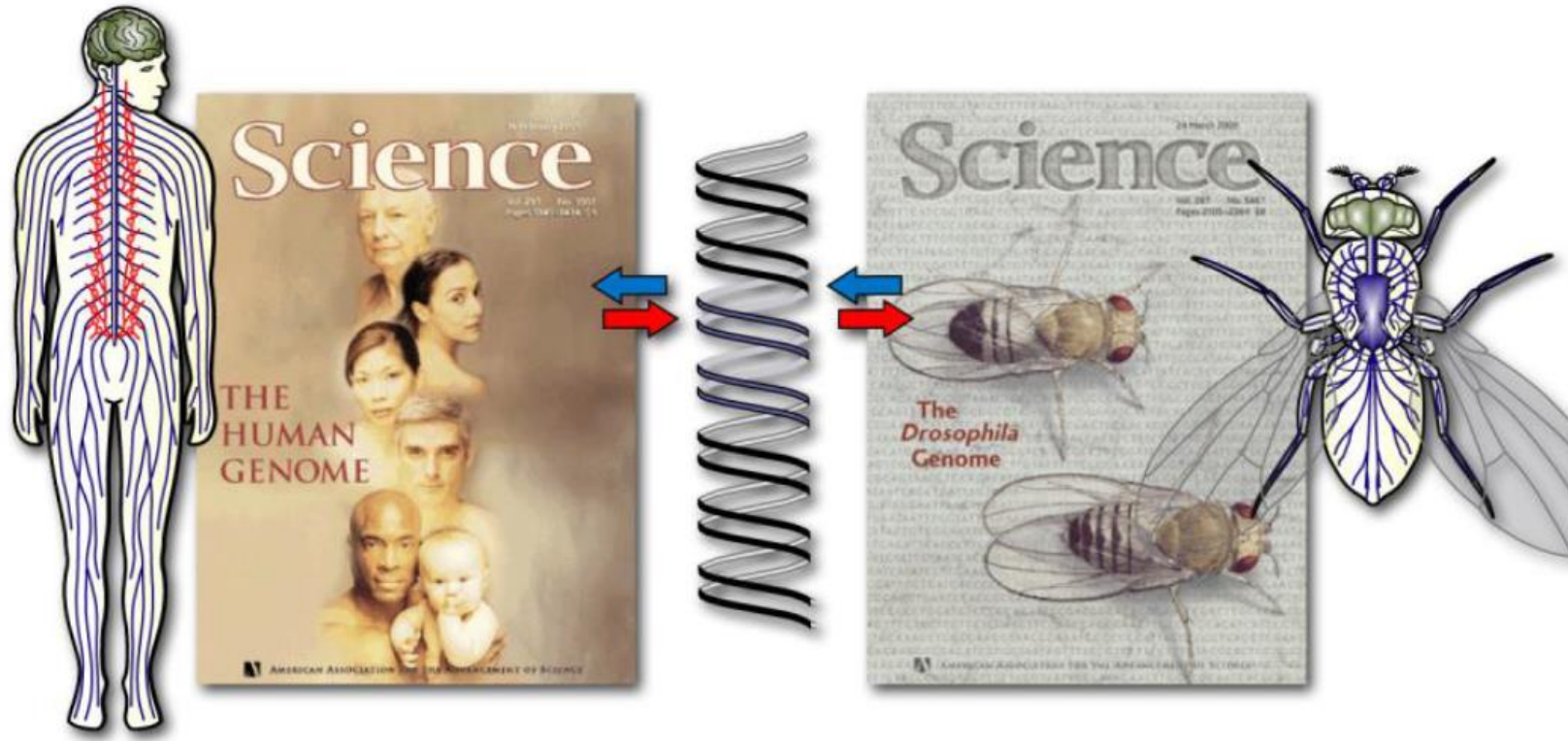


**Simple in vivo model is suitable for  
addressing complex questions in biology!**



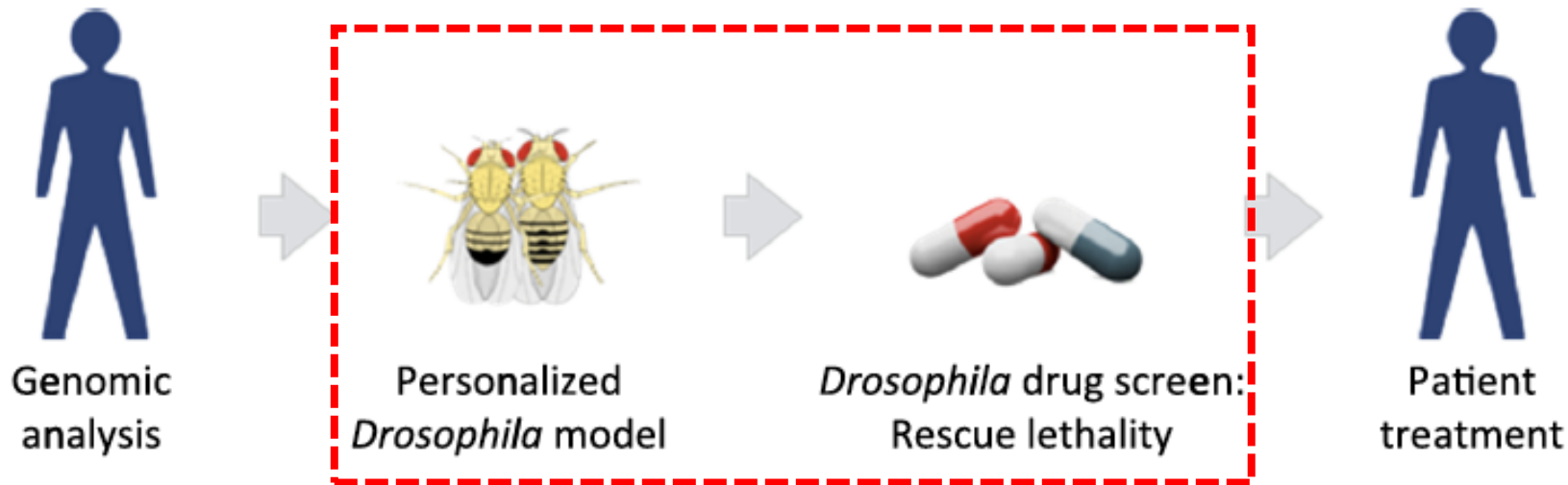
Fruit fly: *Drosophila melanogaster*

**About 75 % of known human disease genes had an identifiable match or orthologue in fruit flies**



CANCER

# A personalized platform identifies trametinib plus zoledronate for a patient with KRAS-mutant metastatic colorectal cancer



(Whole-exome sequencing)

# Acknowledgements



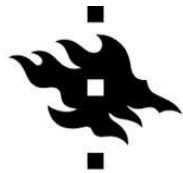
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(Akita Prefectural University)
- Takeshi Imamura  
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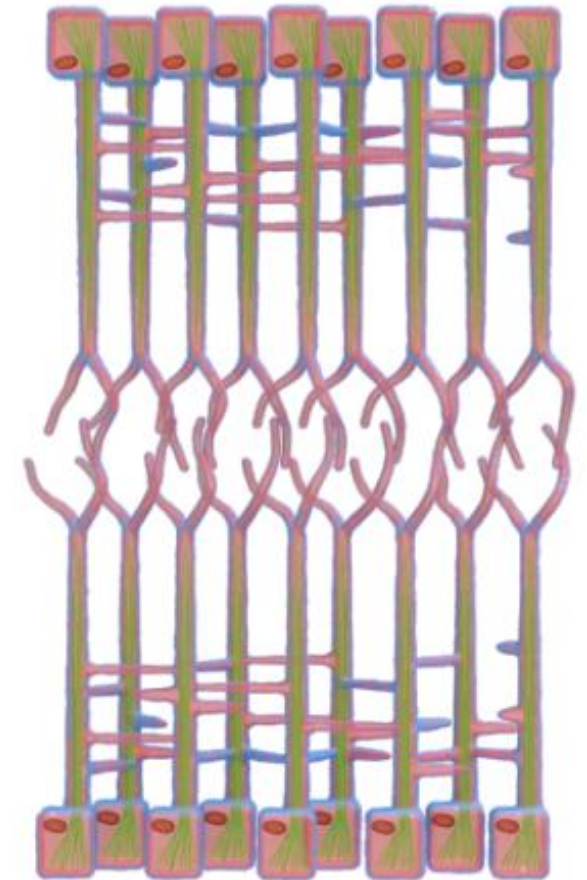
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