



北京大学
PEKING UNIVERSITY



生命科学学院
School of Life Sciences



Decoding **Regeneration**: Unveiling The Hidden Mechanisms in Diverse Organisms

UHPB Journal Club

Jiaxi Liu (刘家希)
School of Life Sciences

2025.12.06



Yan Song (宋艳)

- Vice Dean & Principal Investigator, School of Life Sciences, Peking University
- Principal Investigator, PKU-THU Joint Center for Life Sciences (CLS)

Research Interests:

- Inheritance of neuronal cell fate memory
- Brain-specific gene expression programs
- Decoding temporal regulation in neural development



Wei Wang (王伟)

- Principal Investigator & Assistant Professor, National Institute of Biological Sciences, Beijing (NIBS)
- Assistant Professor, Tsinghua Institute of Multidisciplinary Biomedical Research (TIMBR).

Research Interests:

- Molecular basis of regeneration
- Evolution of regenerative capacities in vertebrates
- Regeneration and rejuvenation



Cheng-Ran Xu (徐成冉)

- Principal Investigator, School of Basic Medical Sciences Peking University
- Principal Investigator, Peking-Tsinghua Center for Life Sciences (CLS)

Research Interests:

- Directed differentiation of embryonic stem cells & Tissue and organ regeneration
- Mechanisms of mammalian liver and pancreas development
- Regulation of gene networks by cell signaling and epigenetic mechanisms during development and regeneration

Regeneration in our life



Doctor Who

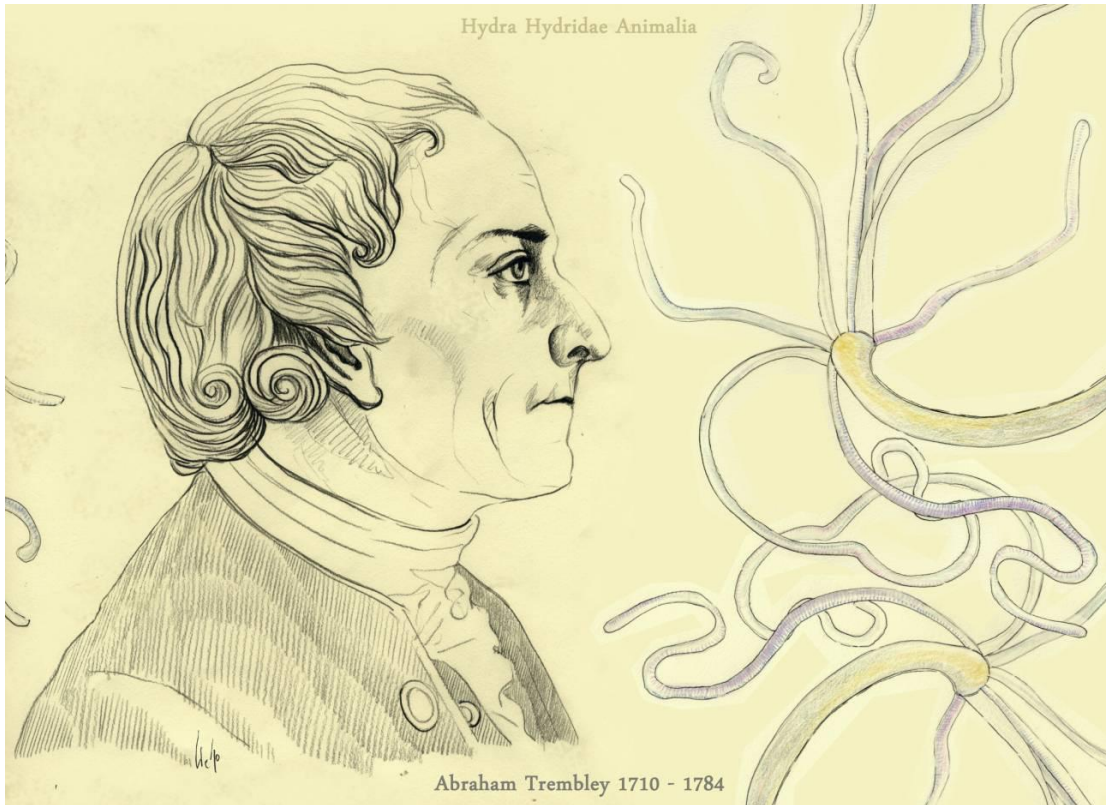


Gecko (Credit: Feast or Famine)

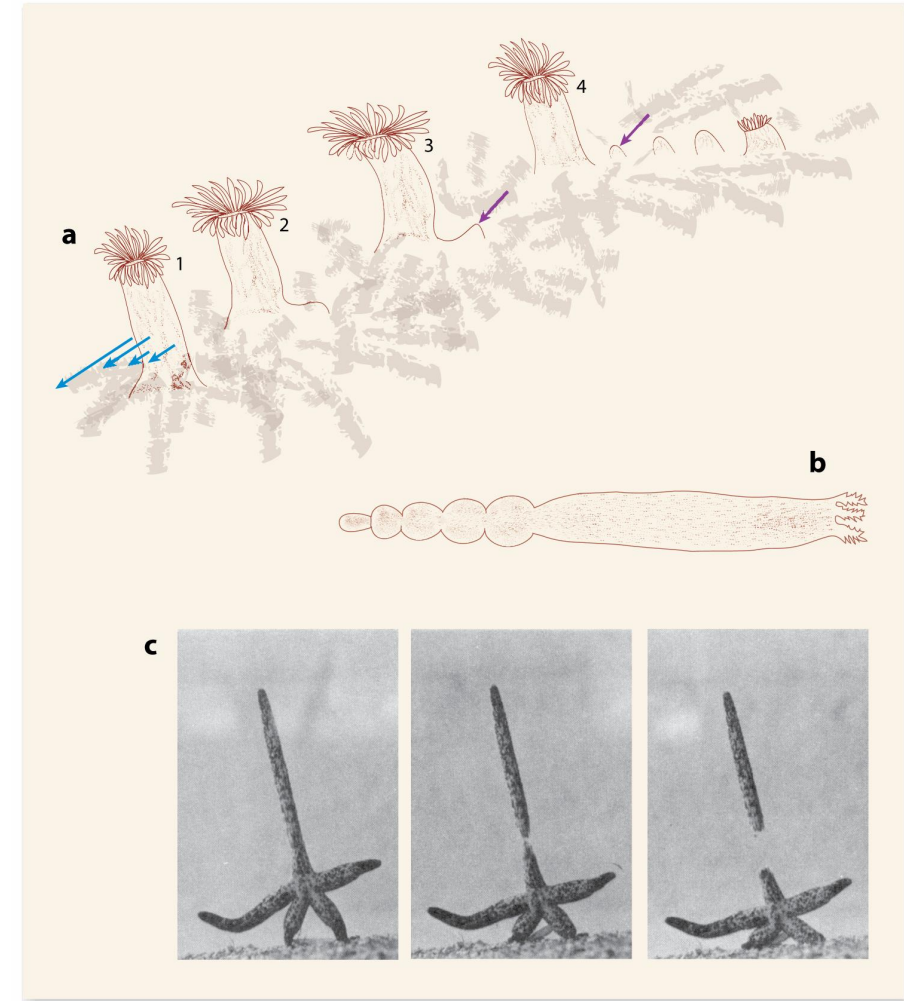


Maine Lobster

Historical Foundations of Regeneration

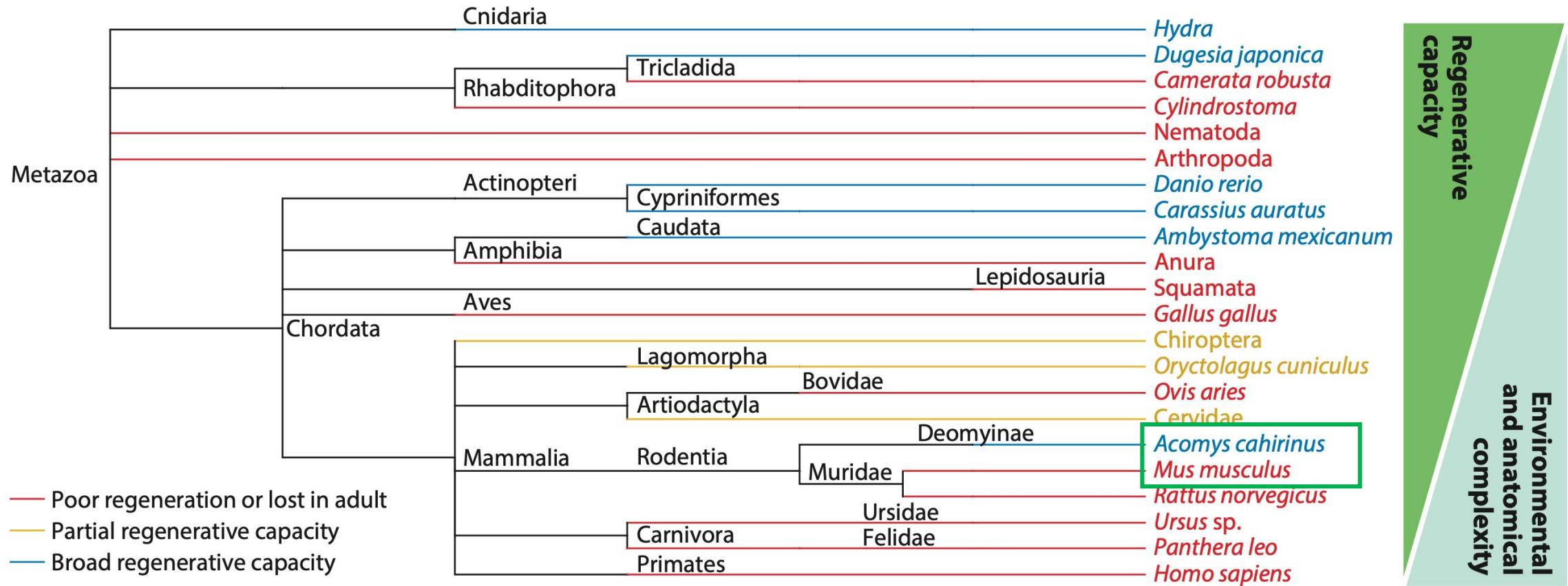


Abraham Trembley (1710-1784)



 Brockes JP, Kumar A. 2008.
Annu. Rev. Cell Dev. Biol. 24:525-49

Regeneration Across the Animal Kingdom



The ability to regenerate is **widespread** in the animal kingdom

Key Questions in Regeneration



Biologists have long been captivated by questions such as:

- Where do the new cells **come from**? ———**cell sources**
- Why do some animals/organs regenerate while most **mammals** do not? ———**evolution**
- How does the process **start**? /How do wounded tissues **“know”** what to remake? ———**signal control**

Classical Model Organisms



invertebrate

Hydra



planarians



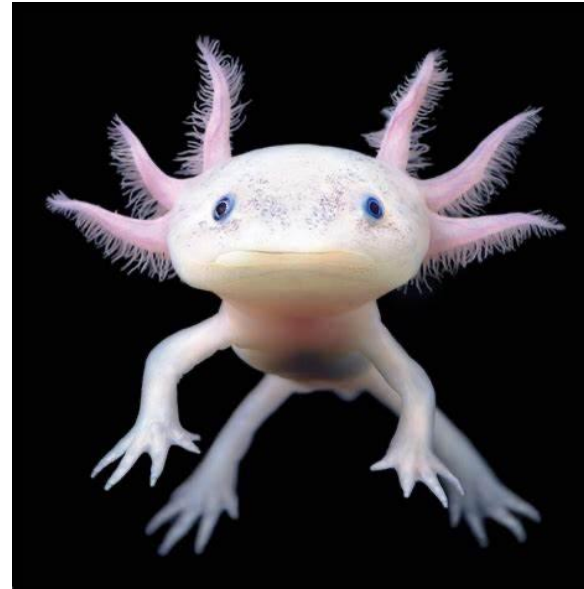
adult **pluripotent** stem cells

vertebrate

zebrafish



Axolotl



AcoMys



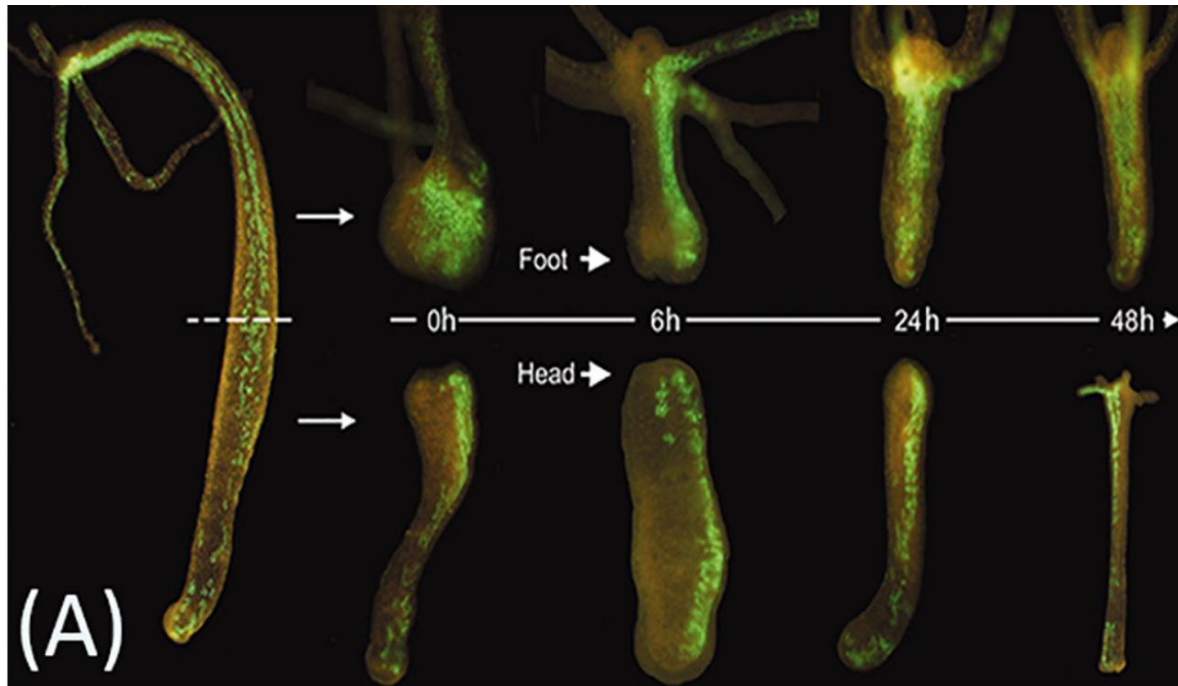
lineage-restricted progenitors from different tissues

Model Organisms – invertebrates



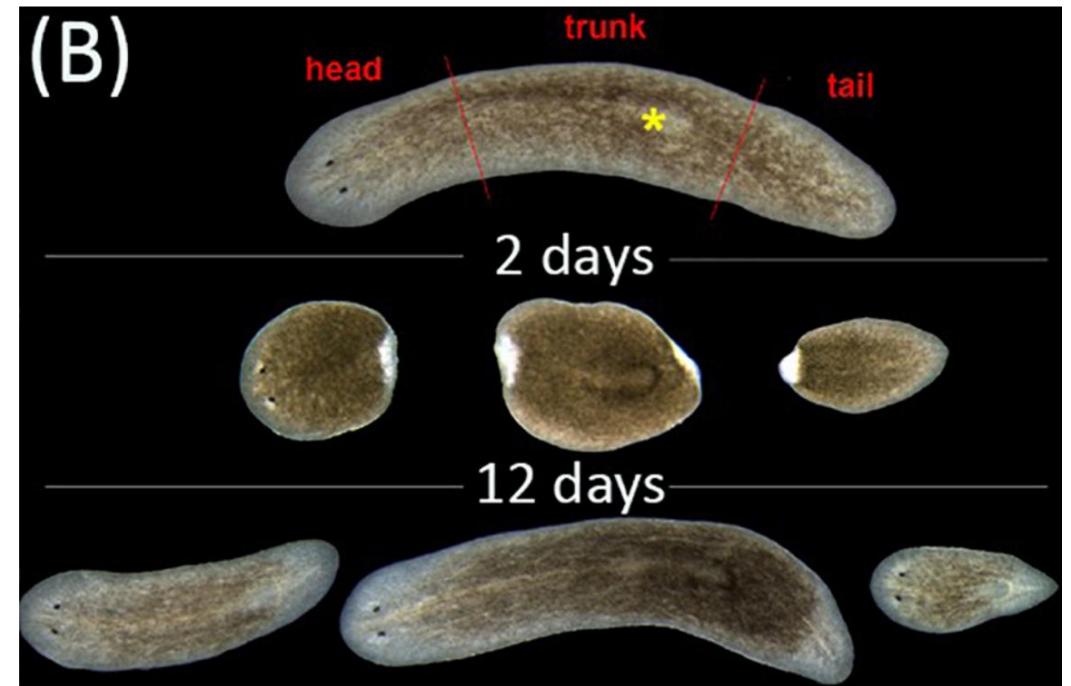
Small fragments of Hydra or planarians tissue can regenerate a complete organism

Hydra



Wittlieb, J. et.al. *Proc. Natl. Acad. Sci.* 2006

planarians



Adell, T. *Biomed Res.* 2014



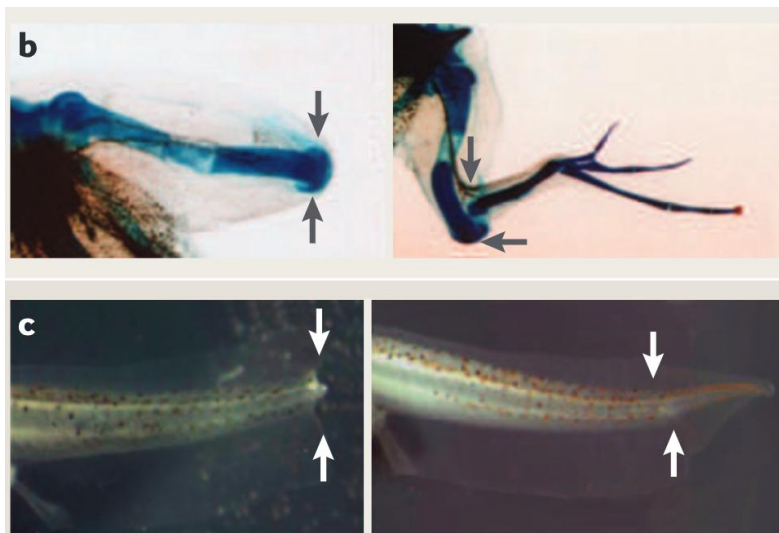
Model Organisms – vertebrates (no mammals)

Salamanders

- limbs
- tail
- lower jaw
- the lens of the eyes
- the heart
- brain (main1)



Monaghan et.al. *Regeneration*. 2014



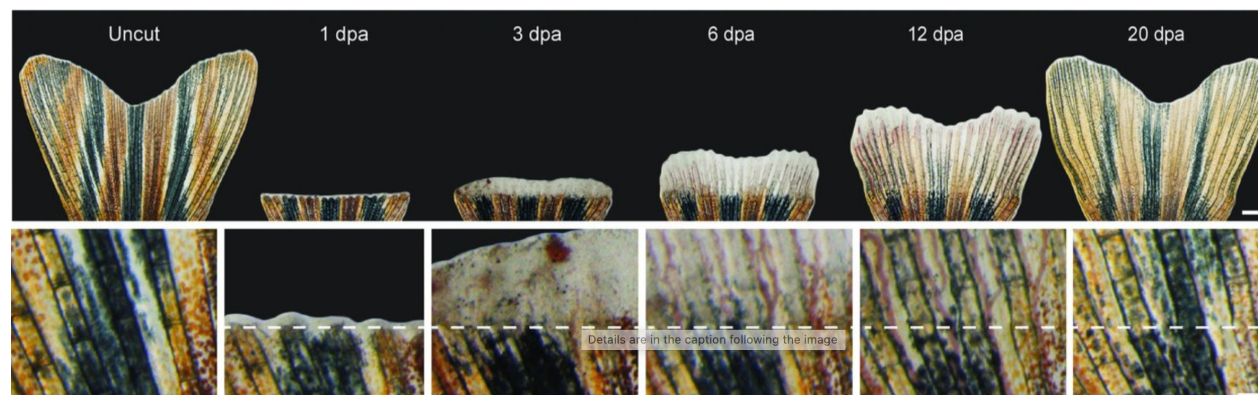
Xenopus

- limb
- tail

Sánchez Alvarado A. *Nat Rev Genet*. 2006

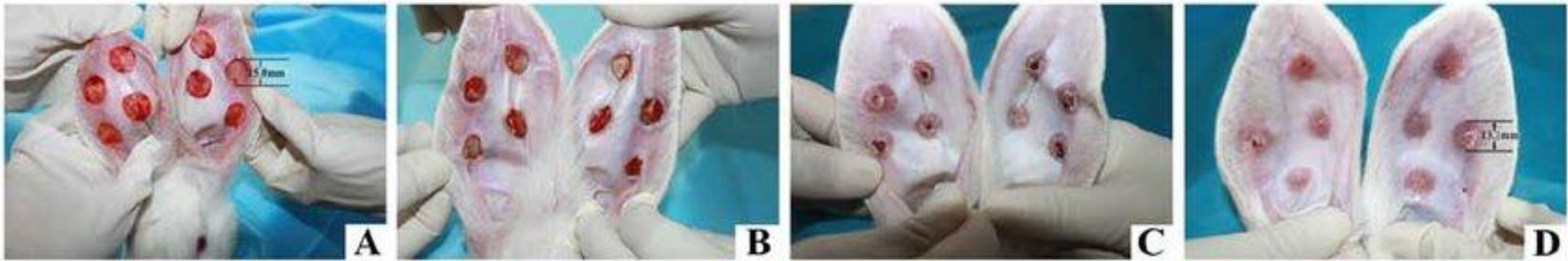
Zebrafish

- Myocardium
- fin ray
- spinal cord

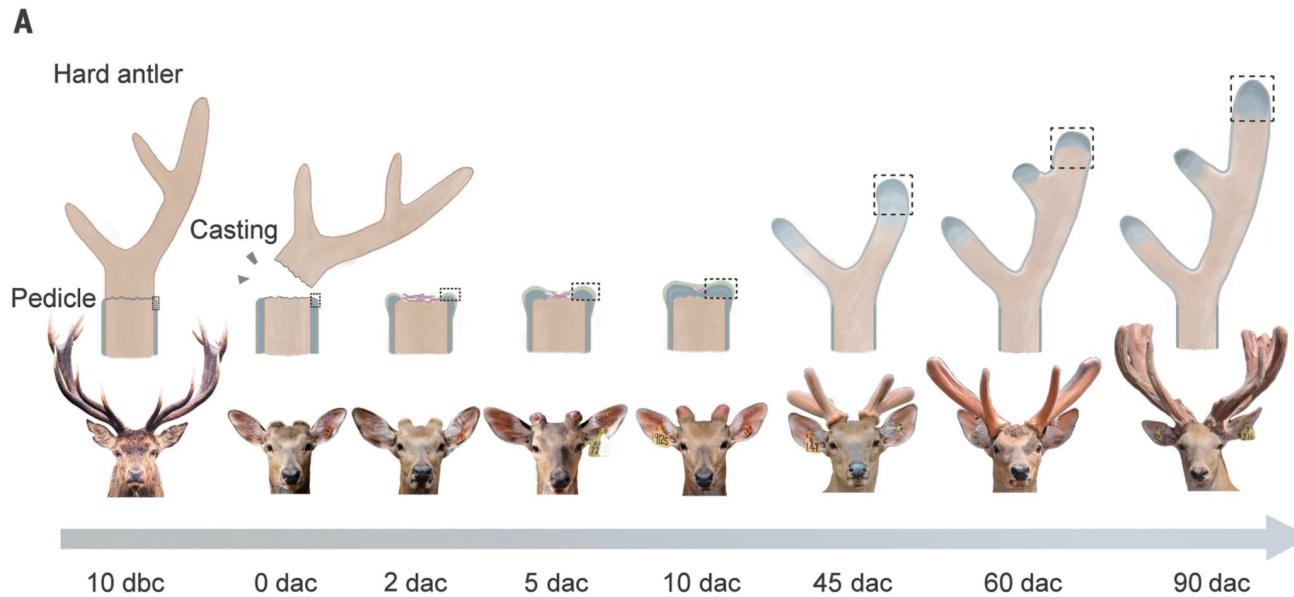


Pfefferli C et.al *Regeneration (Oxf)*. 2015 11

Regeneration in Mammals



Zhao JC et.al. *Exp Ther Med*. 2018



Qin T et.al. *Science*. 2023



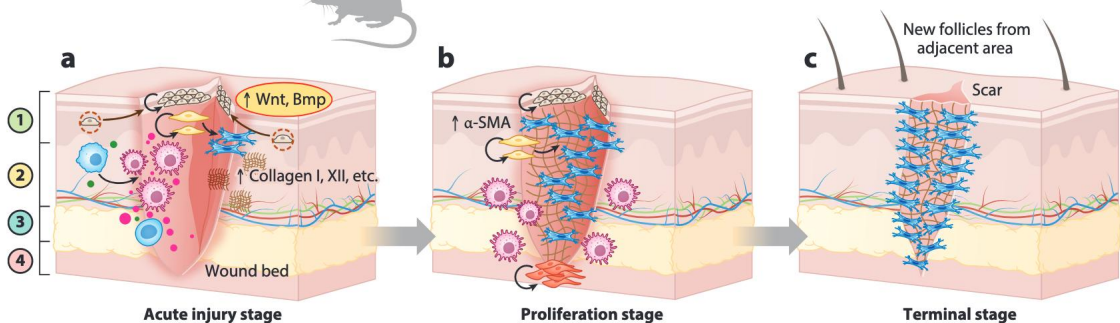
from rika.com

Regeneration in Mammals – Limitations

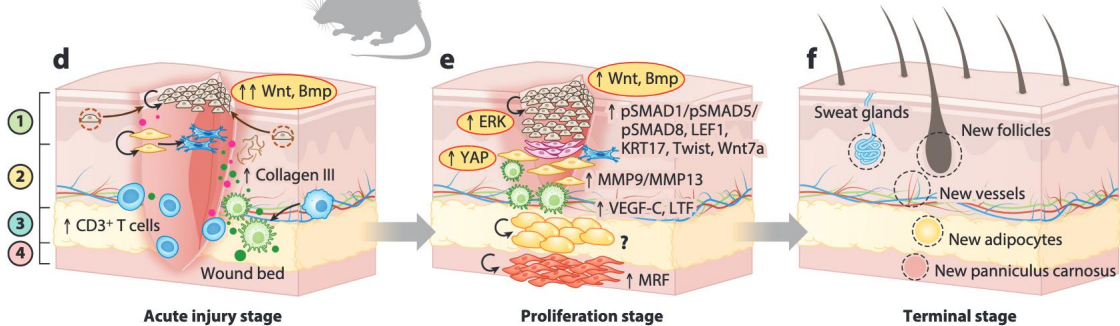


Differences in ear pinna healing between house mice and rabbits (main2)

Adult house mouse (*Mus musculus*)



Adult spiny mouse (*Acomys spp.*)



Skin structure	Cell type					
1 Epidermis	 T cell	 M1 macrophage	 Fibroblast	 Keratinocyte	 Papilla progenitor	
2 Dermis	 Monocyte	 M2 macrophage	 Myofibroblast	 Adipocyte	 Muscle cell/satellite cell	
3 Hypodermis						
4 Muscle						
Extracellular matrix			Cytokines			
 Loose ECM			 Proinflammatory cytokines			
 Dense ECM			 Anti-inflammatory cytokines			

Model organisms	Overall	Skin or ear pinna	Bone	Central nervous system	Visceral organs	Skeletal and other muscles
Axolotl <i>Ambystoma mexicanum</i>	■	●	●	●	●	●
House mouse <i>Mus musculus</i>	■	●	●	○	○	●
Bat <i>Eptesicus fuscus</i>	■	●	●	●	●	●
Rabbit <i>Oryctolagus cuniculus</i>	■	●	●	○	○	●
Deer <i>Cervus nippon</i>	■	●	●	●	●	●
Spiny mouse <i>Acomys spp.</i>	■	●	●	●	●	●

Regeneration model types	Regeneration potential levels				
Classic nonmammalian regeneration models	○	●	●	●	●
Classic mammalian nonregeneration models	○	○	○	○	○
Promising mammalian regeneration models	○	●	●	●	●

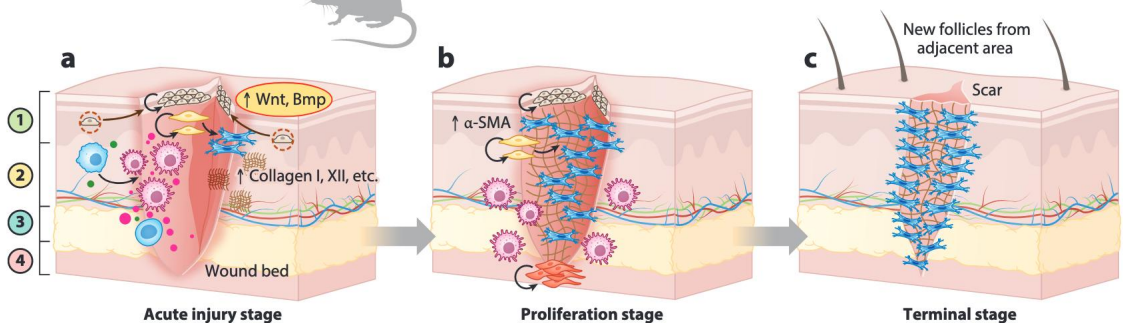
None Low Moderate High Unknown

Regeneration in Mammals – Limitations

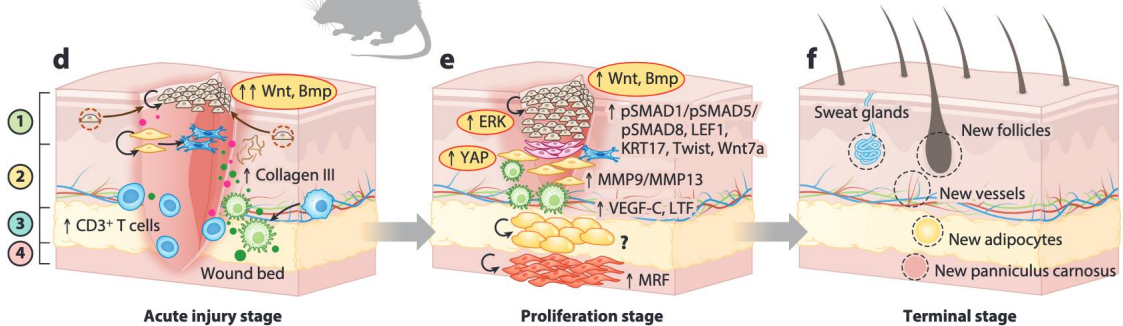


Differences in ear pinna healing between house mice and rabbits (main2)

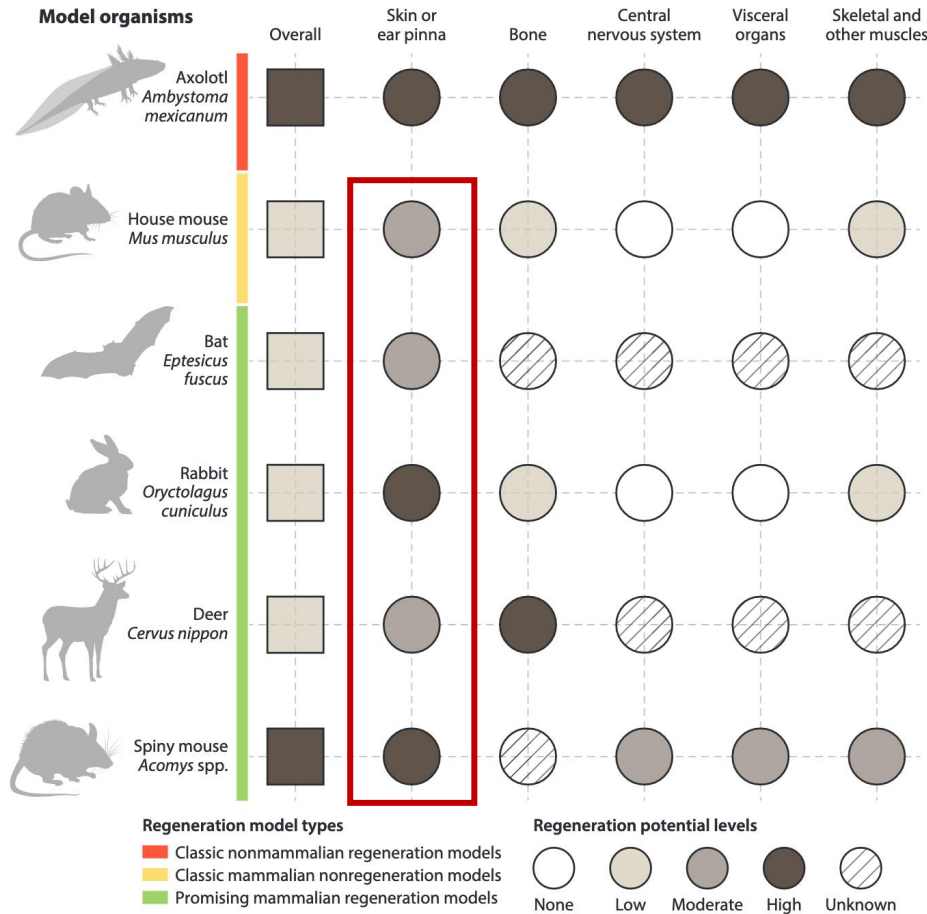
Adult house mouse (*Mus musculus*)



Adult spiny mouse (*Acomys spp.*)



Skin structure	Cell type	Extracellular matrix	Cytokines
1 Epidermis	T cell	Loose ECM	Proinflammatory cytokines
2 Dermis	Monocyte	Dense ECM	Anti-inflammatory cytokines
3 Hypodermis	M1 macrophage		
4 Muscle	M2 macrophage		
	Fibroblast		
	Myofibroblast		
	Keratinocyte		
	Adipocyte		
	Papilla progenitor		
	Muscle cell/satellite cell		

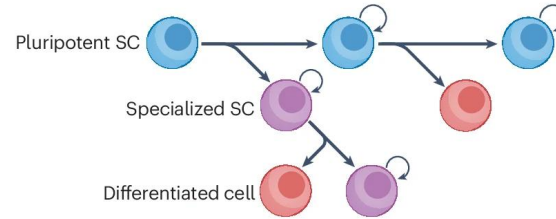




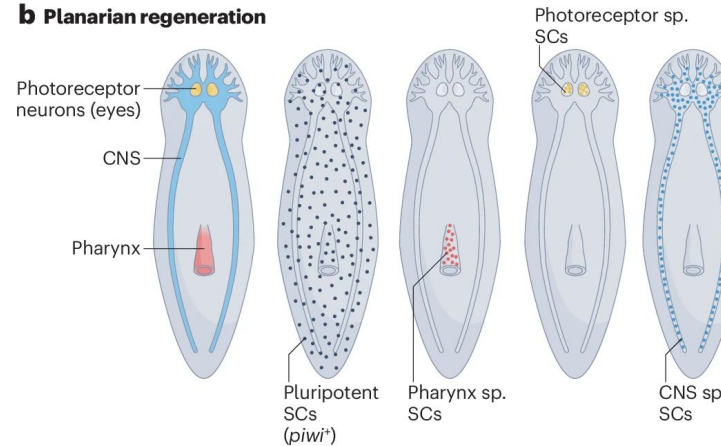
Cellular Sources for Regeneration

- stem cell
- dedifferentiation
- transdifferentiation
- other: self-duplication

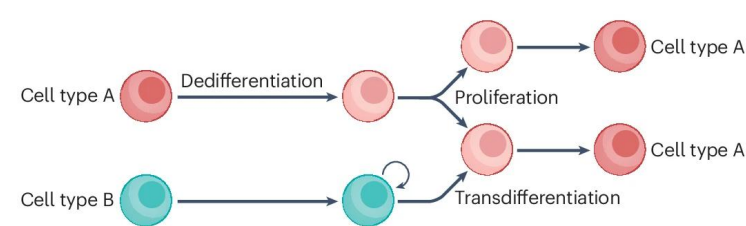
a Stem cell source



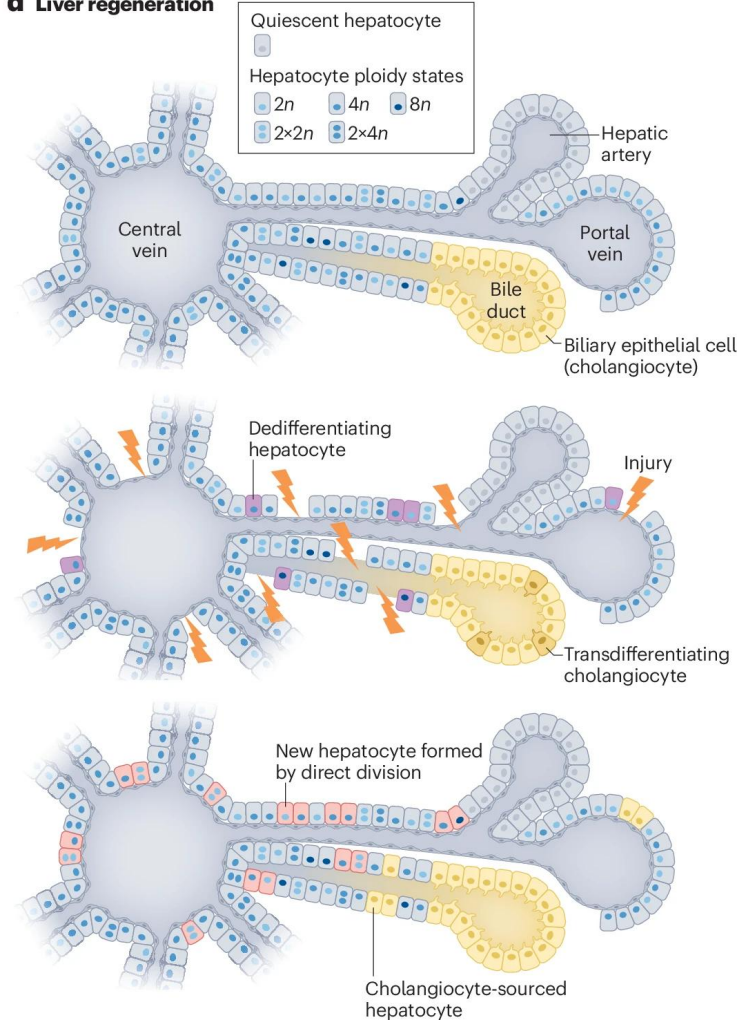
b Planarian regeneration



c Transdifferentiation and dedifferentiation of somatic cells



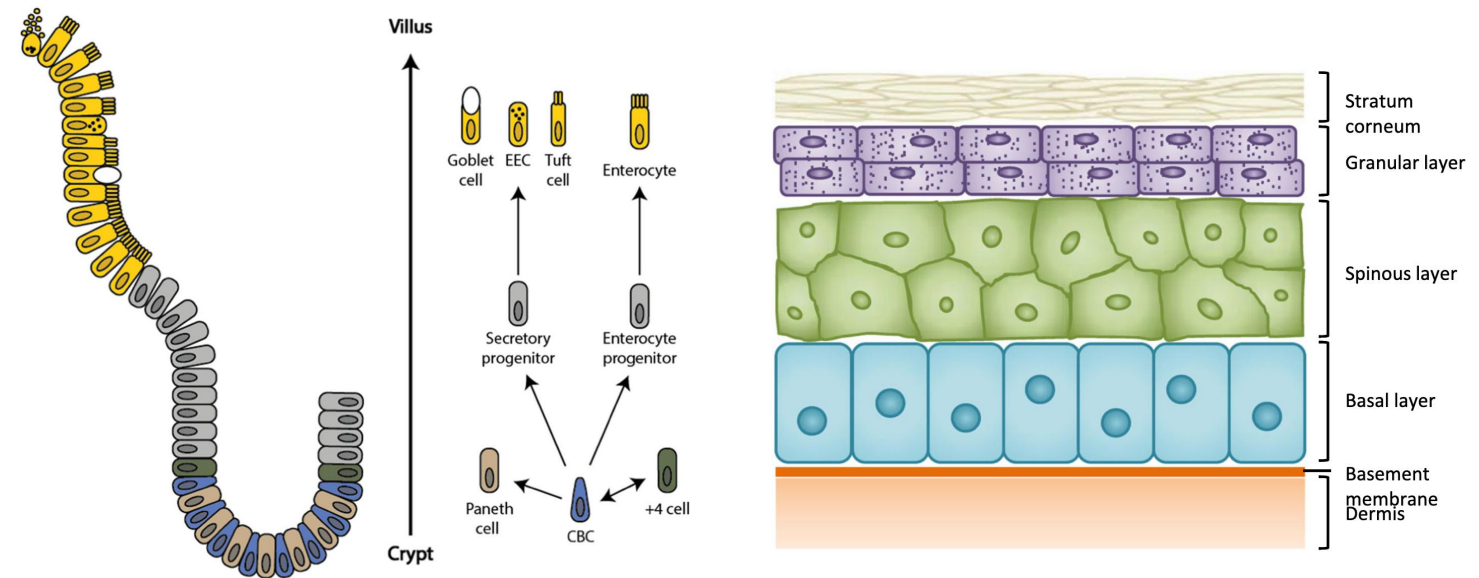
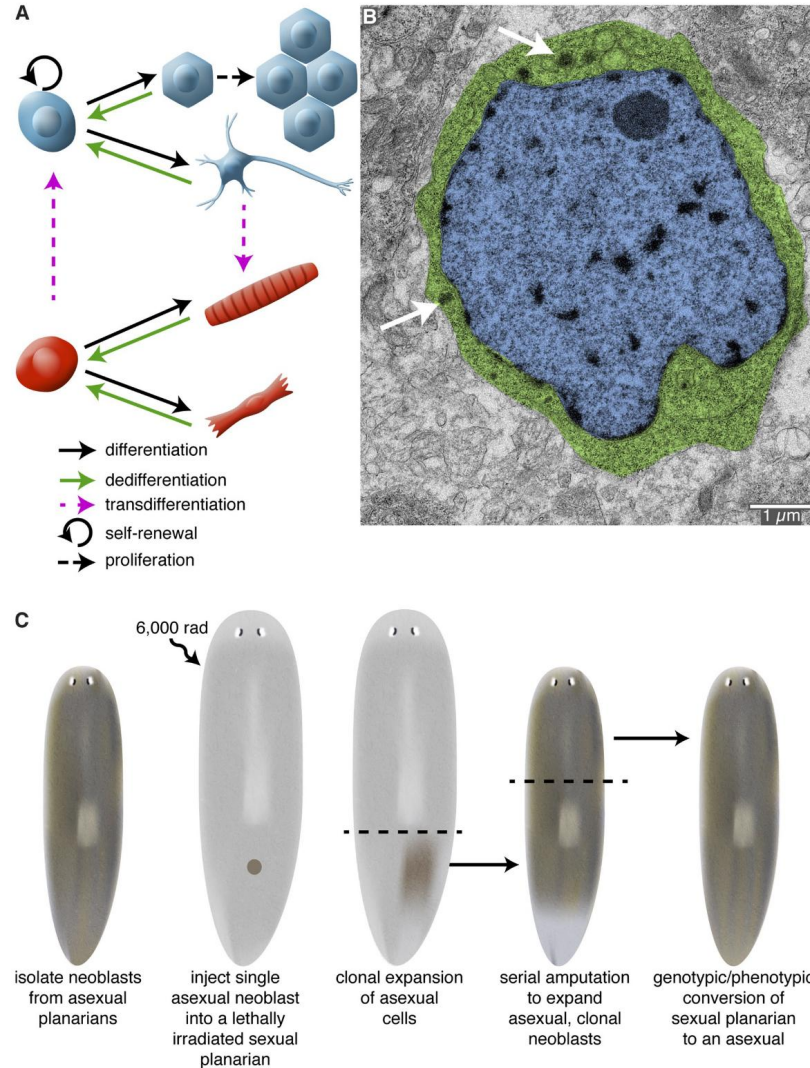
d Liver regeneration



Stem Cell–Driven Regeneration



- Planarians accomplish regeneration with use of adult **pluripotent stem cells** (**neoblasts**)
- several vertebrates utilize a collection of **lineage-restricted progenitors**

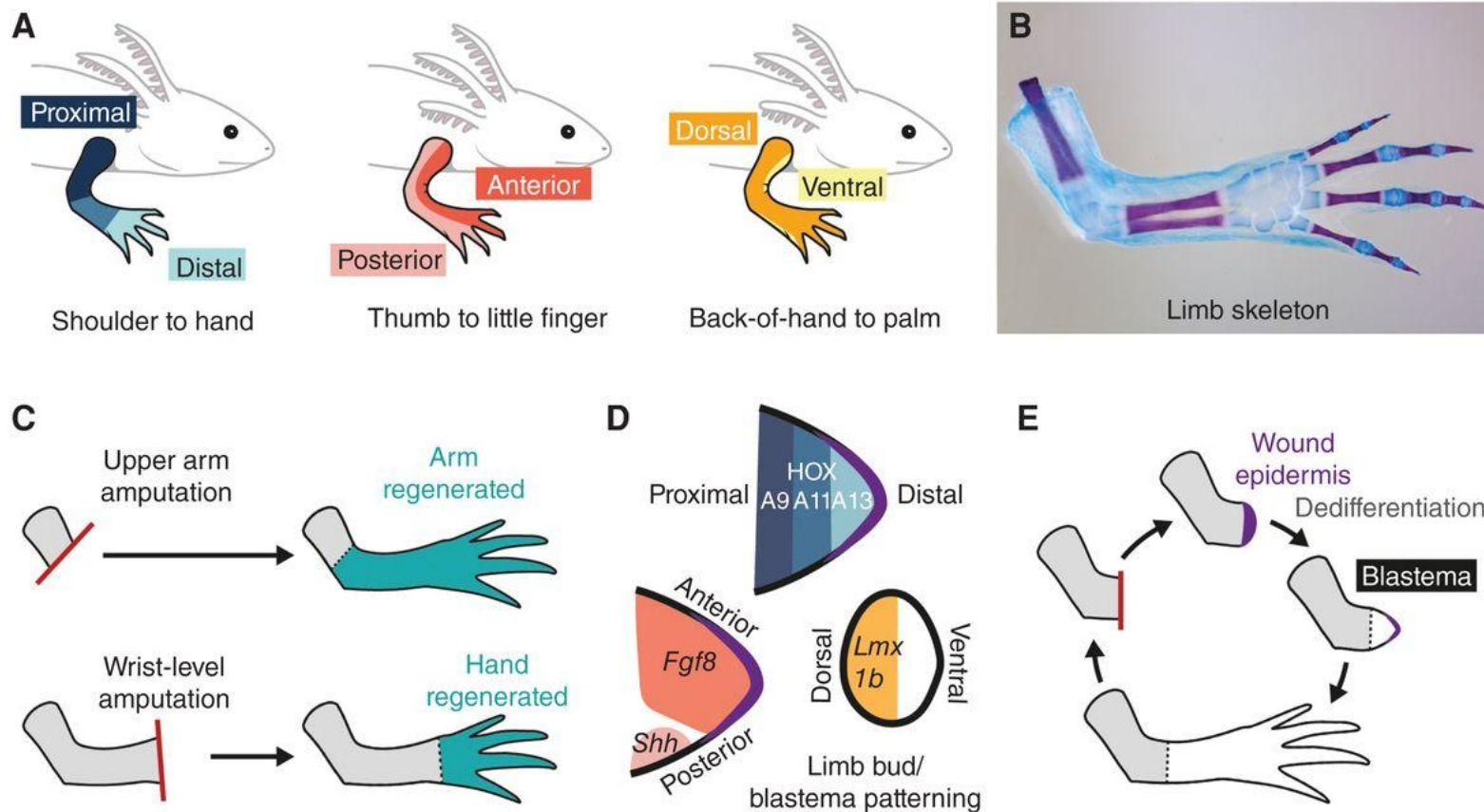


lismaa SE et.al. *NPJ Regen Med.* 2018

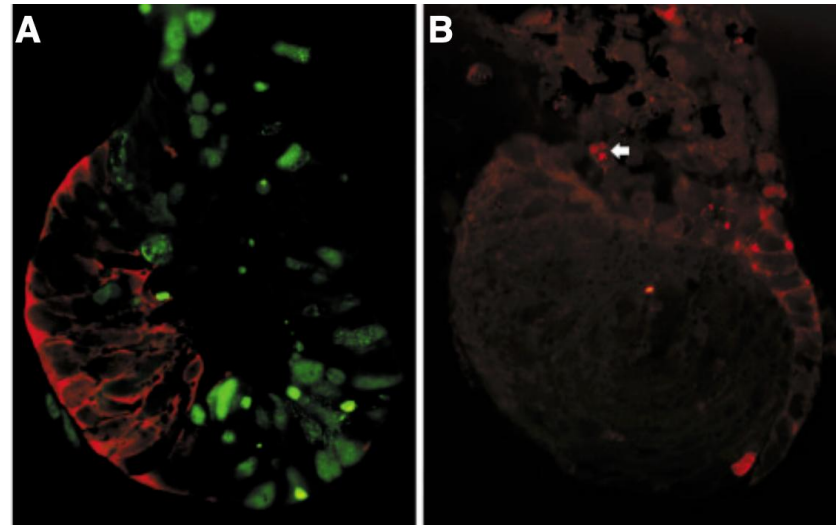
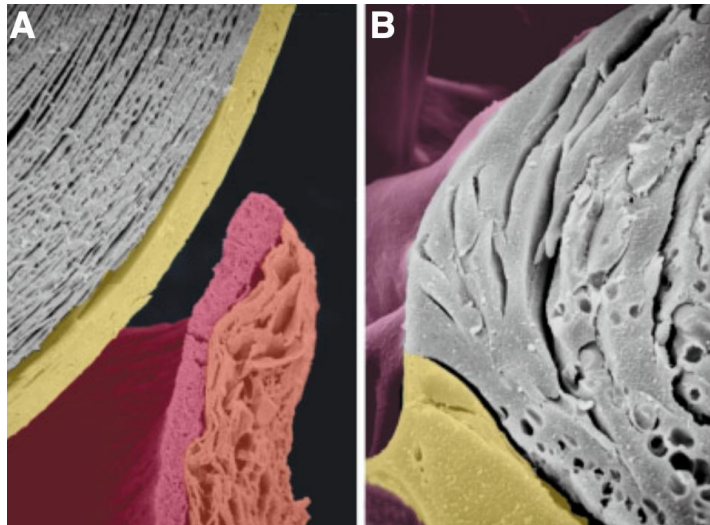
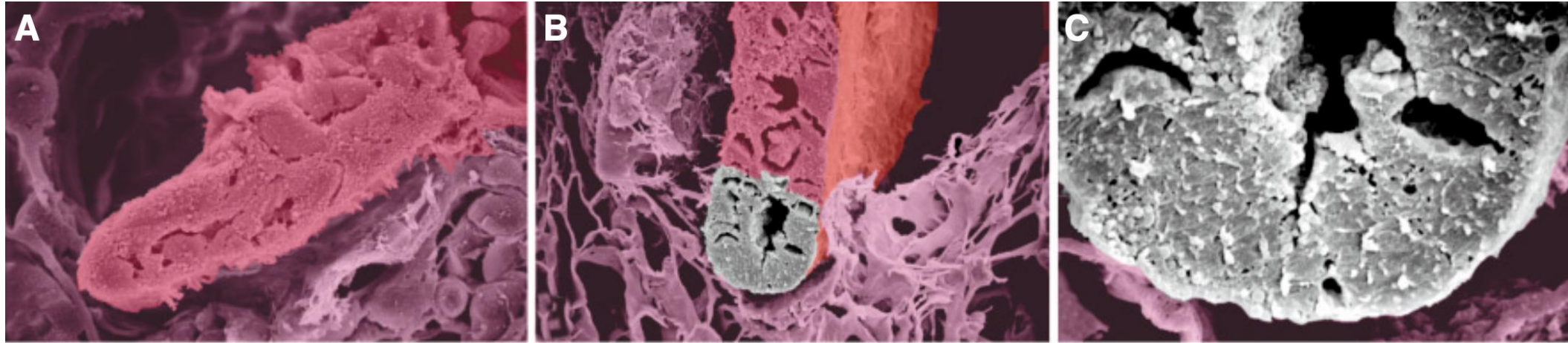
Dedifferentiation and Blastema (Salamanders)



Regeneration generally involves formation of a **wound epithelium** after injury, followed by the generation of regenerative **progenitor cells** (a **blastema**)



Transdifferentiation and Cellular Plasticity

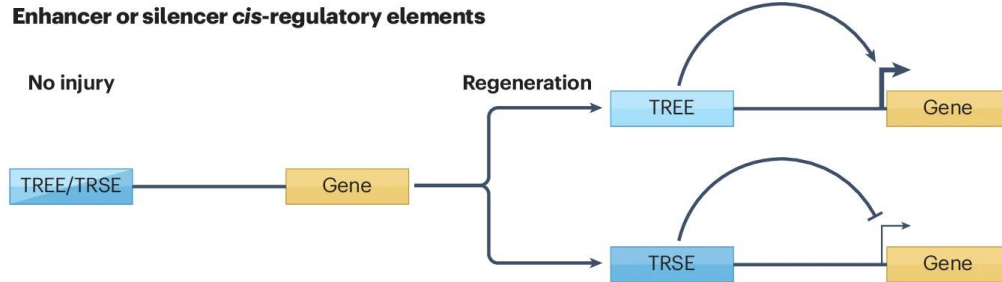


Tsonis PA et.al *Int J Dev Biol.* 2004

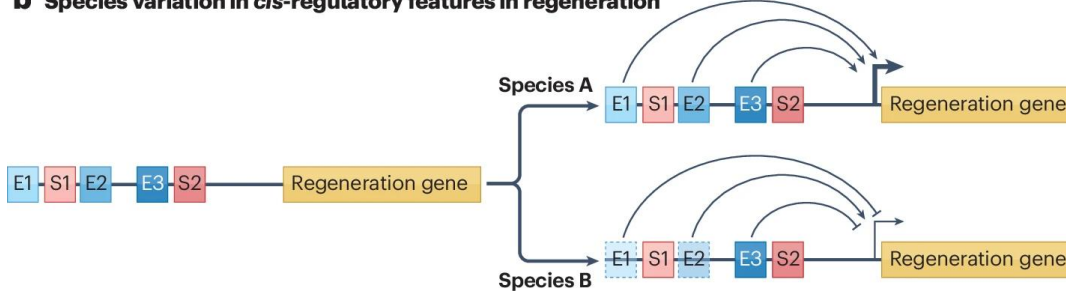
Gene regulation mechanisms



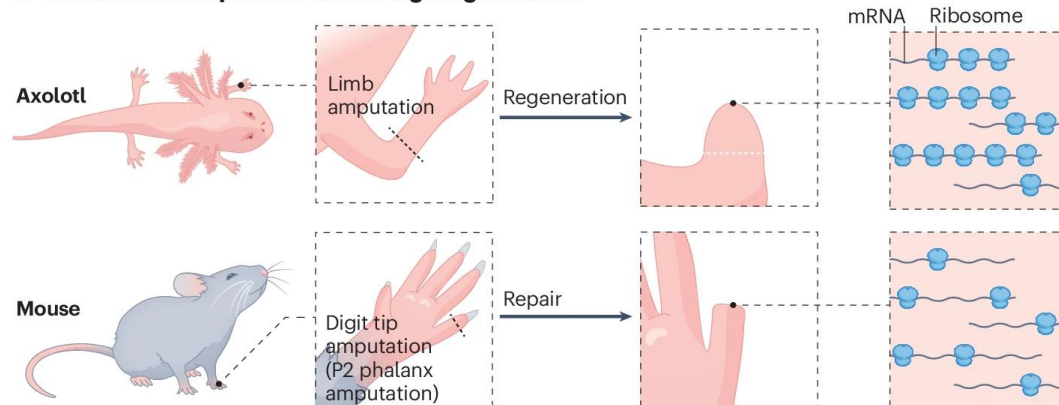
a Enhancer or silencer *cis*-regulatory elements



b Species variation in *cis*-regulatory features in regeneration

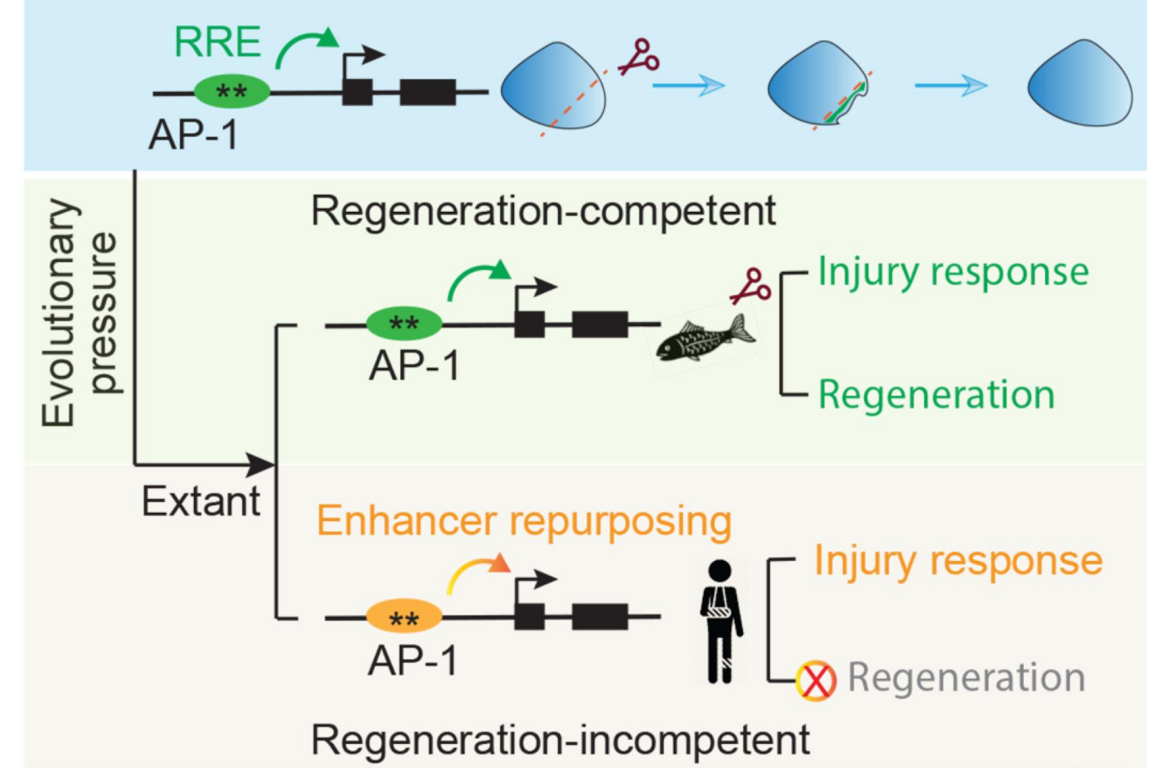


c Translational response in limb or digit regeneration



Loss of regenerative capacities

Ancestral regenerative response = injury + regeneration



Wang W, *Science*. 2020

Microenvironment and metabolic state regulation

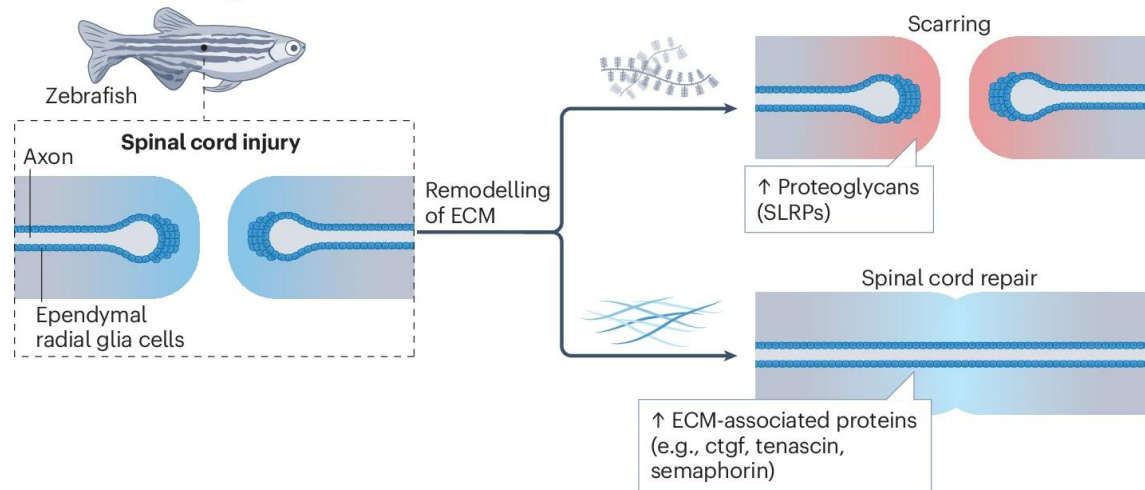


Immune activity, ECM remodeling, and metabolic state collectively shape whether tissue undergoes true regeneration or fibrotic repair.

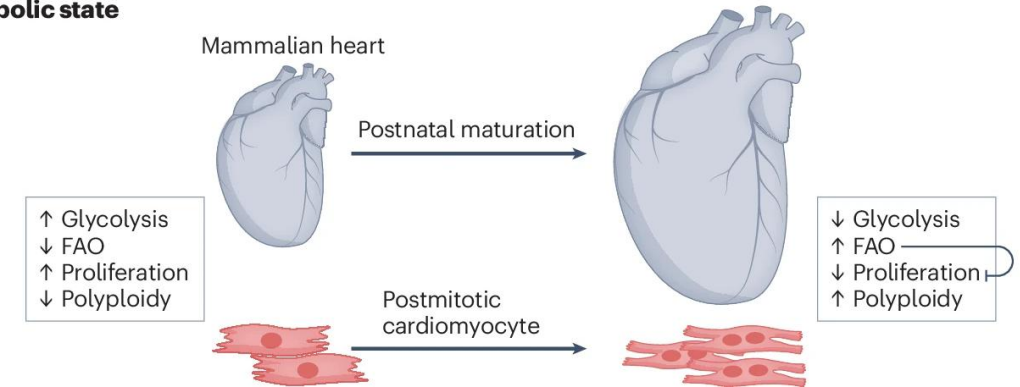
a Pro-regenerative immune response (macrophages)



b ECM remodelling



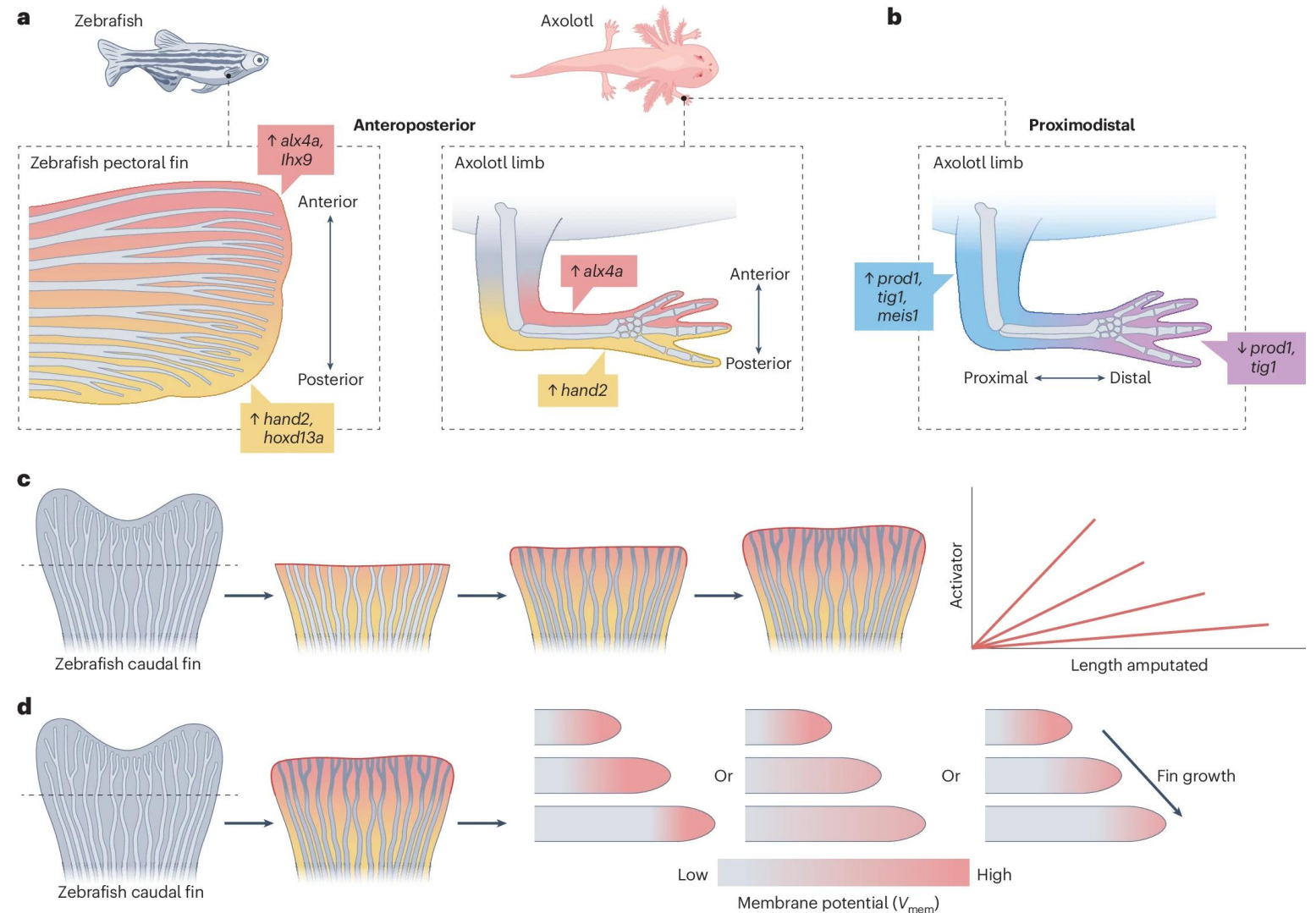
c Metabolic state





Patterning and Scaling in Regeneration

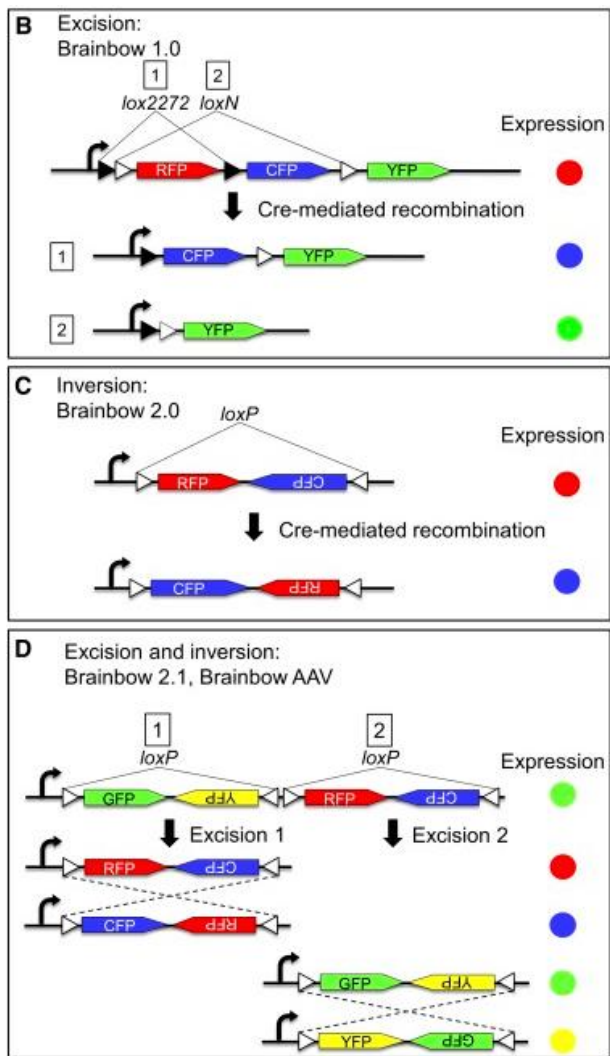
Positional identity and scaling mechanisms guide regenerating tissues to rebuild structures with correct orientation, shape, and size.



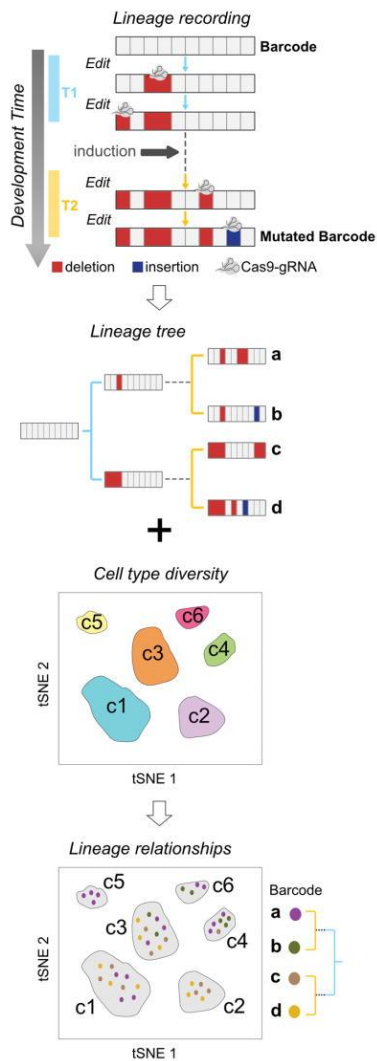


Tools: Single-cell omics to discover key events

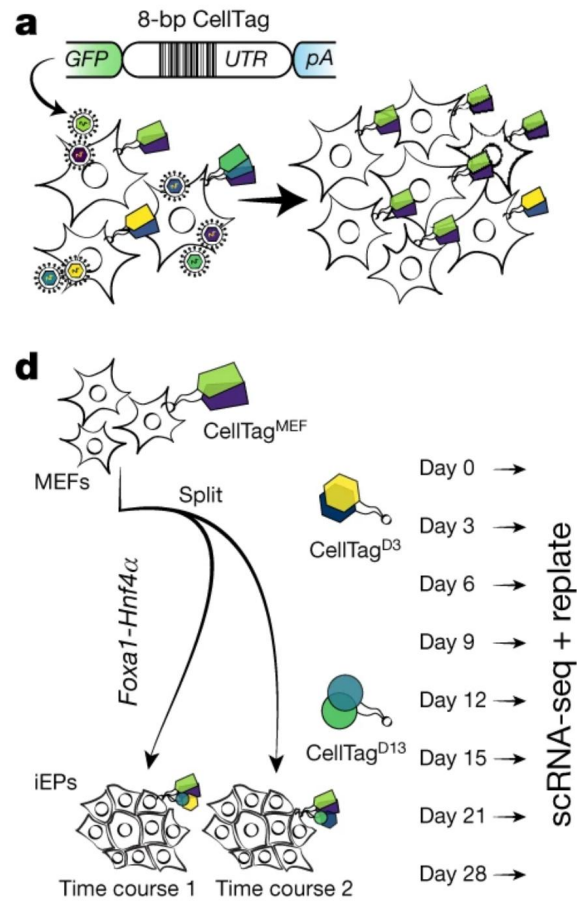
Brainbow



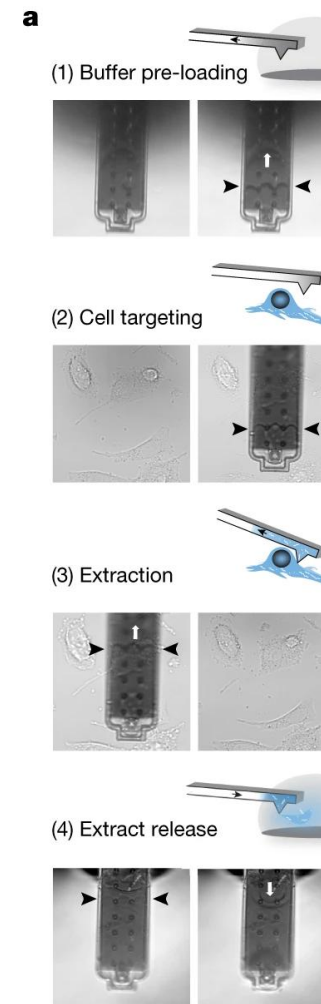
scGESTALT



CellTagging

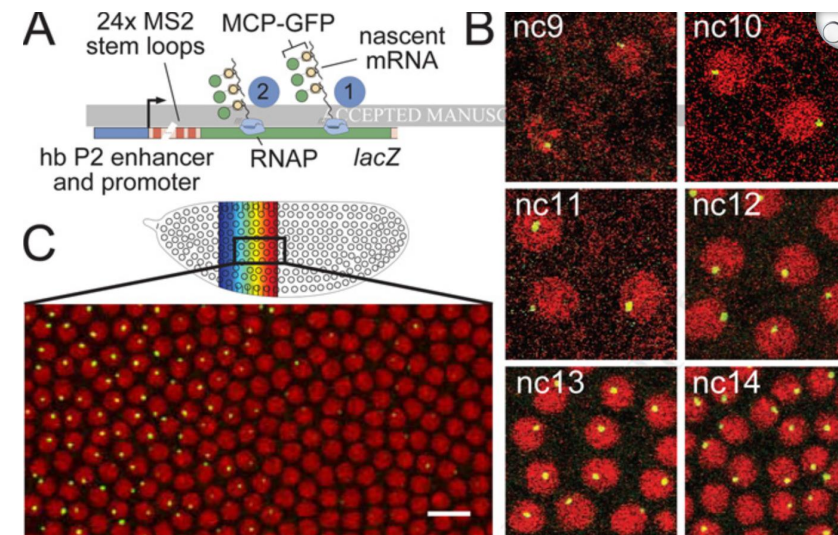
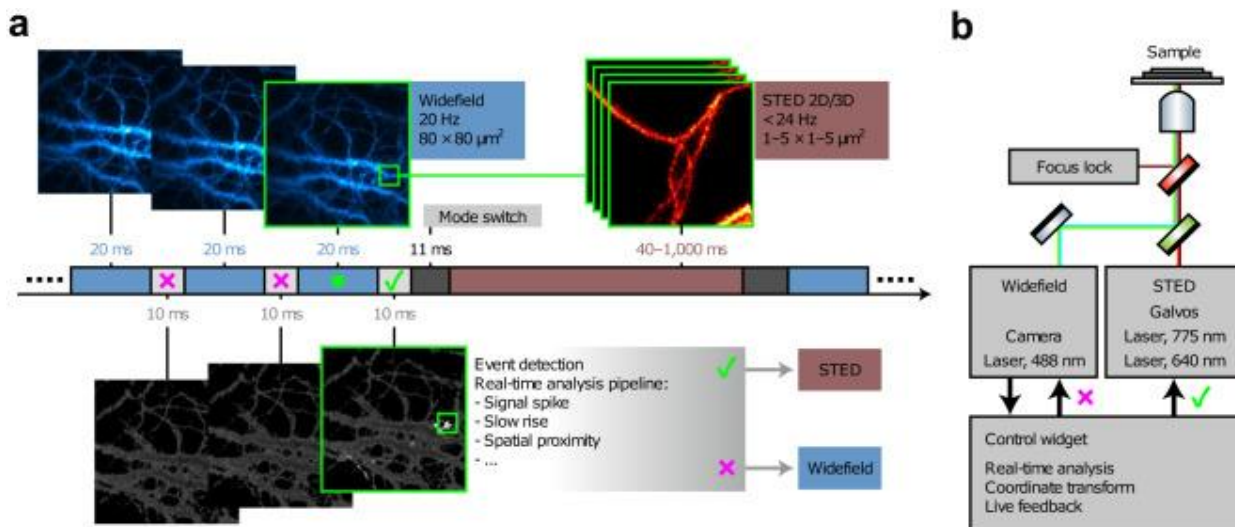


Live-seq



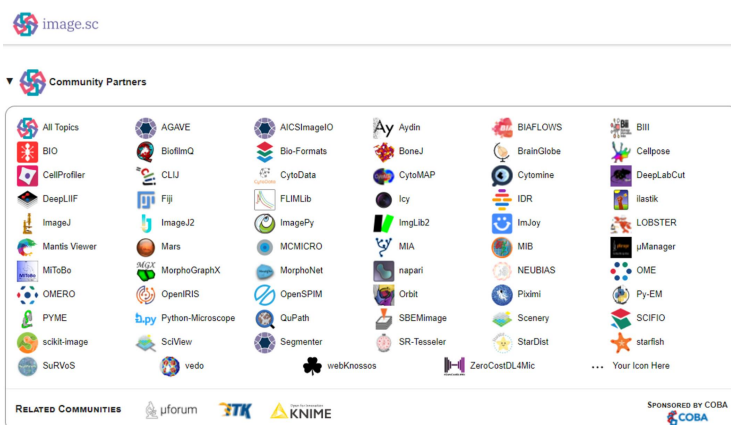


Tools for analysing dynamic cell behaviours

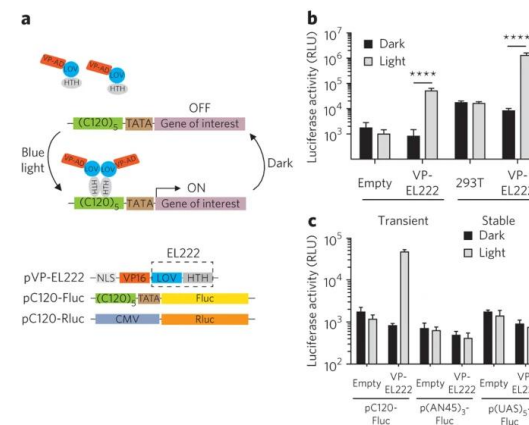


Garcia HG *Curr Biol.* 2013

Balasubramanian H et.al. *Commun Biol.* 2023



Haase et.al. *FEBS Lett.* 2022



Motta-Mena LB et.al. *Nat Chem Biol.* 2014



Q&A



生命科学学院
School of Life Sciences



*Thanks
For your Listening!*

Jiaxi Liu (刘家希)
School of Life Sciences

2025.12.06