



基因分子生物學 (2)
再生研究：斑馬魚的角度

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ICOB at Academia Sinica
20 Jan, 2024

Topics for today

1. 為什麼要研究再生?
2. 如何利用斑馬魚研究再生?
3. 人類有一天也可以斷肢再生嗎?

Some vertebrates are highly-regenerative



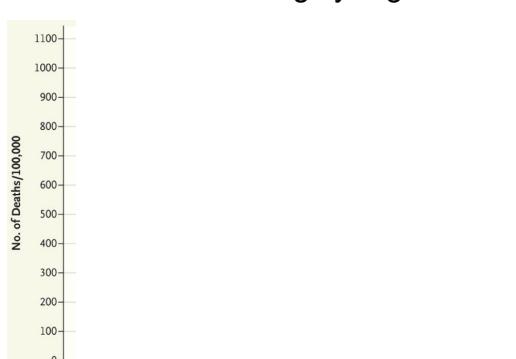
HHMI

Don't try this at home!



www.inquisitr.com

What if humans were highly-regenerative?

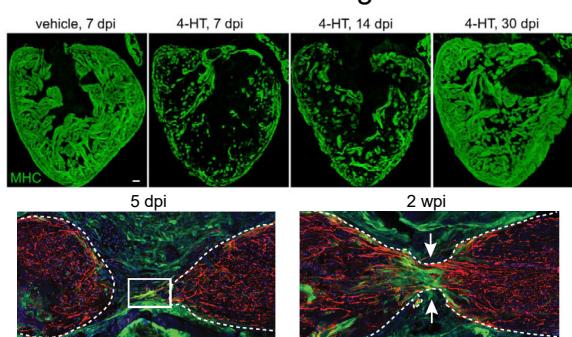


No. of Deaths/100,000

1900 2010

NEJM, 2012

Zebrafish are highly-regenerative to repair their internal organs



vehicle, 7 dpi 4-HT, 7 dpi 4-HT, 14 dpi 4-HT, 30 dpi

MHC

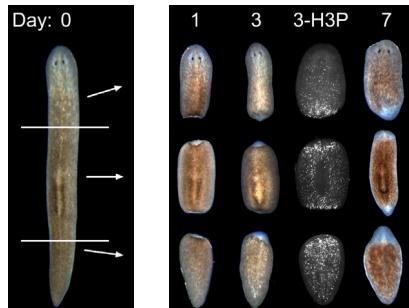
5 dpi 2 wpi

Wang et al., 2011; Mokalled et al., 2016

Challenges in studying regeneration

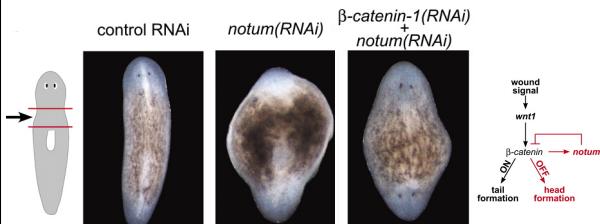


Something about planarians



http://pearsonlab.ca/?page_id=6

Regeneration genes



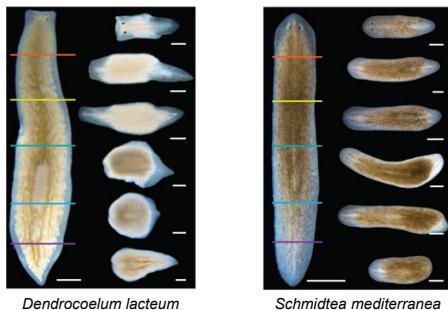
<http://scienceintheclassroom.org/research-papers/heads-or-tails/university>

Regeneration and Immortality



<http://www.ub.edu/planaria/index.html>

Some planarians can't regenerate



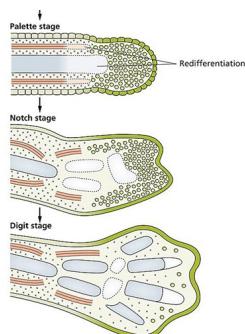
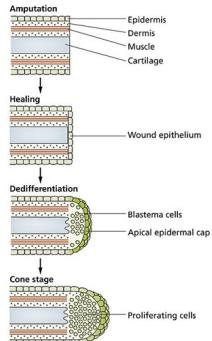
<http://www.nature.com/nature/journal/v500/n7460/full/nature12414.html>

Models of highly-regenerative vertebrates



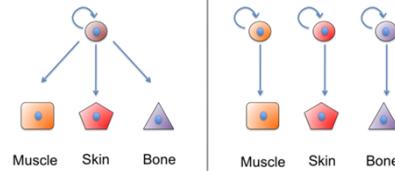
mentalfloss.com

What is the “blastema”?



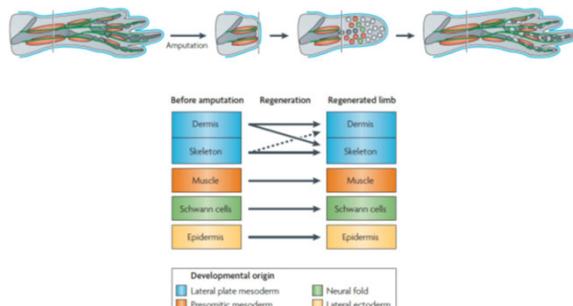
Stem cells and regeneration

A. Multipotent stem cell makes all the tissues needed
OR
B. Several different stem cells are needed to make the different tissue types



<http://www.eurostemcell.org/image/possible-regeneration-models>

Stem cells and regeneration



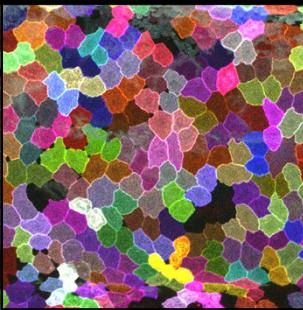
NRG 2010



Highly regenerative
Accessible to many genetic tools
Great for cell imaging studies

My research program at ICOB

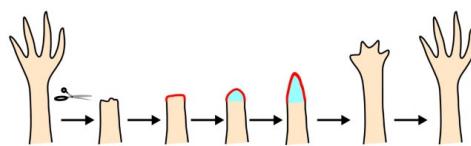
Direction#1
Collective cell behavior



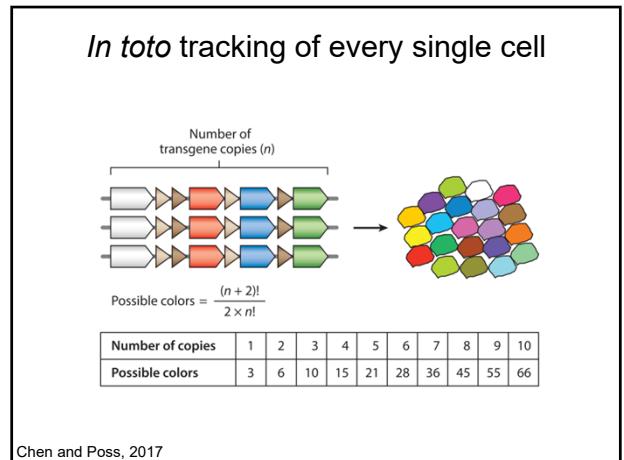
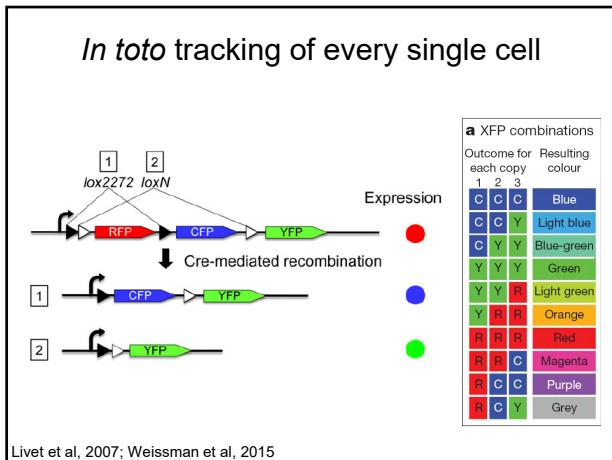
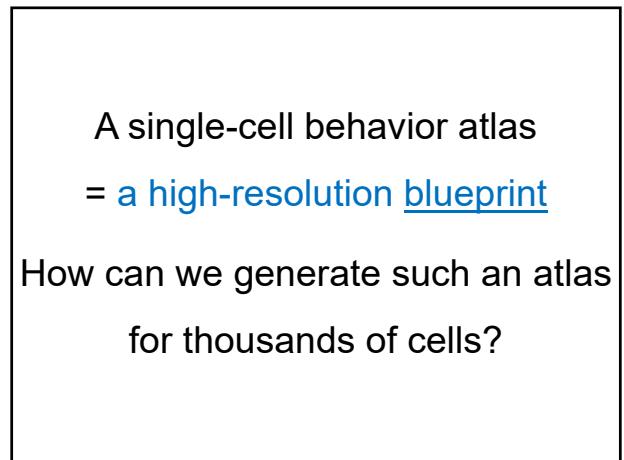
Direction#2
Regeneration mutants

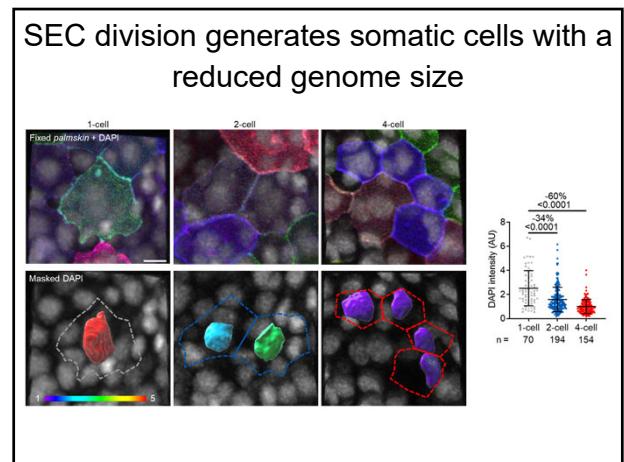
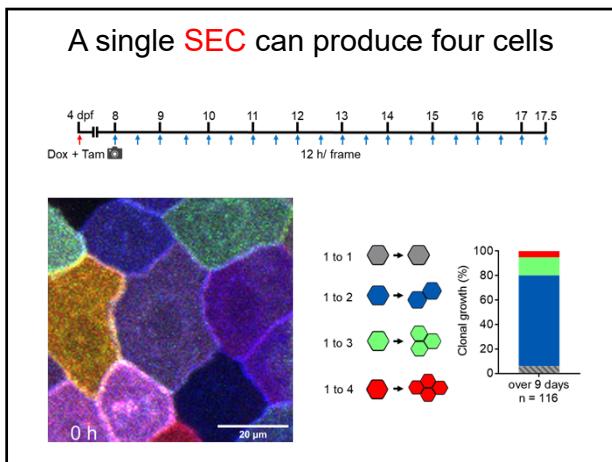
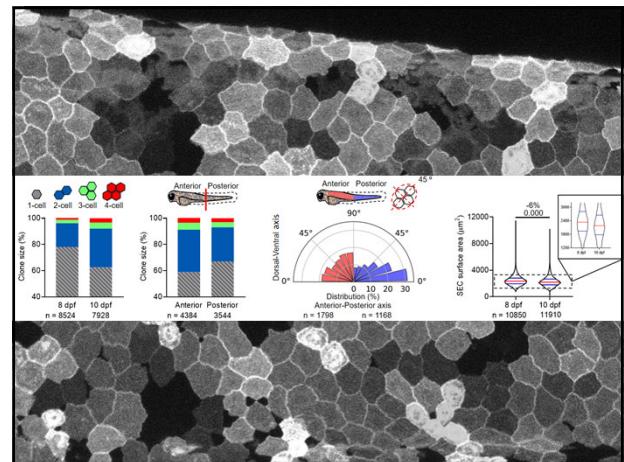
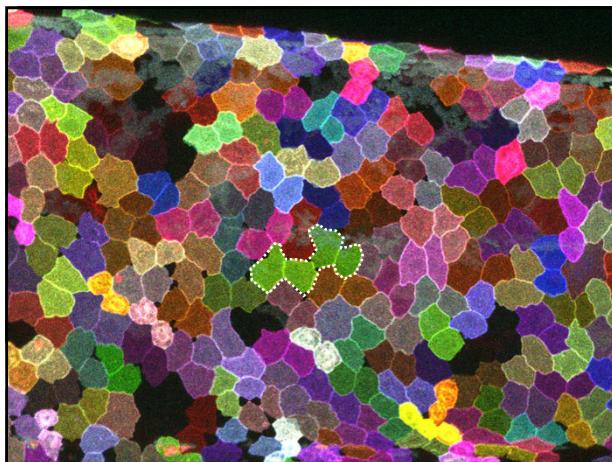
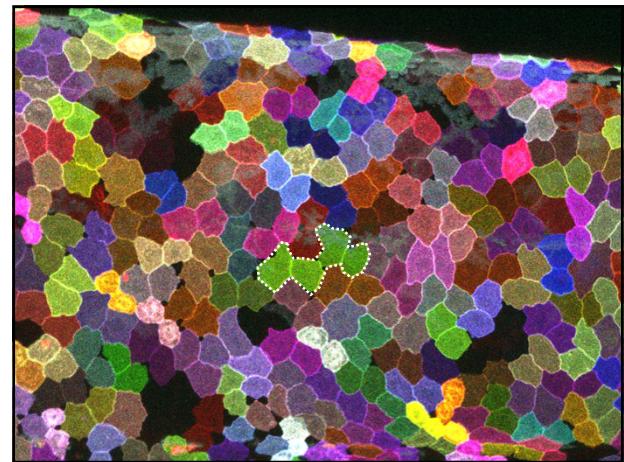
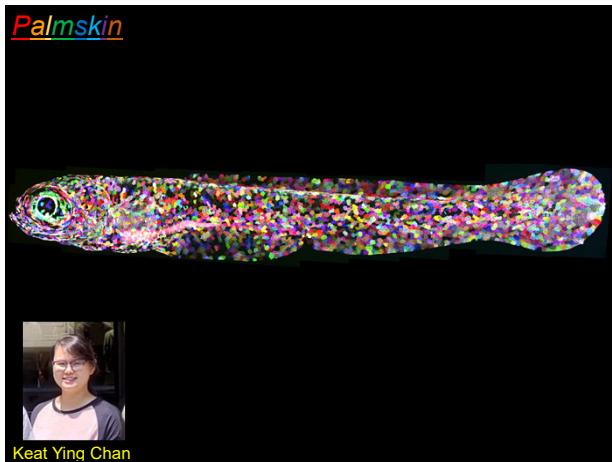


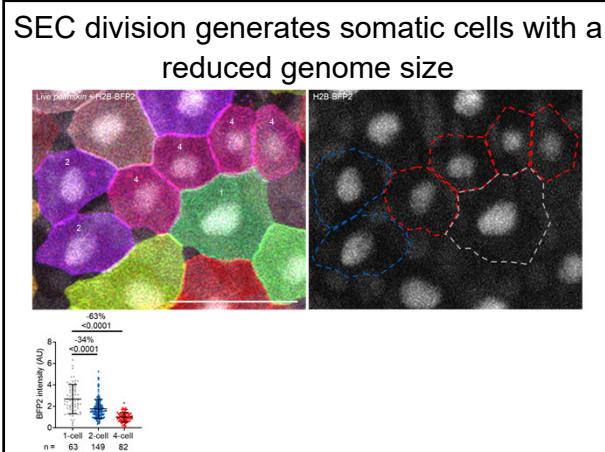
Construct single-cell behavior atlases



Whited et al, 2009







How did we come up with the name?

Asynthetic Fission

“*a*” as a prefix means “opposite”

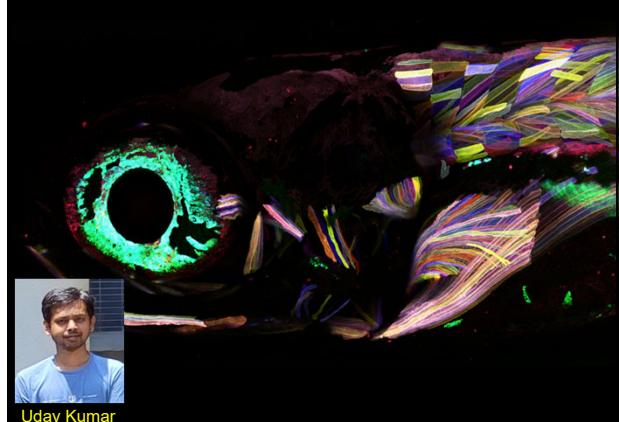
“*fission*” means “splitting into two or more”

Chan et al., Nature (2022)

基礎研究

1. 正常細胞分裂- 發育 生長 繁殖 再生
2. 不正常細胞分裂- 癌症 疾病 老化
3. 明顯的例外- 基礎細胞分裂機制的研究
4. 斑馬魚是脊椎動物- 其它細胞或物種

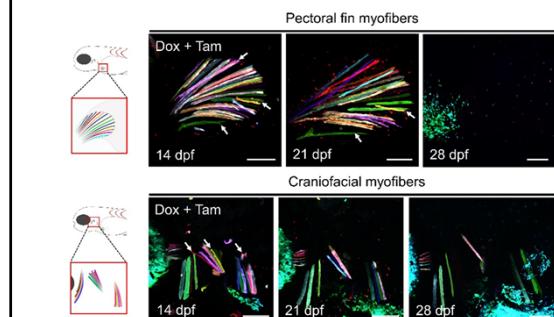
Palmuscle



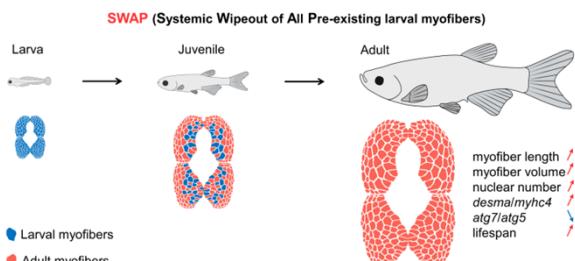
Palmuscle



Palmuscle enables long-term tracking of all myofibers in a growing individual



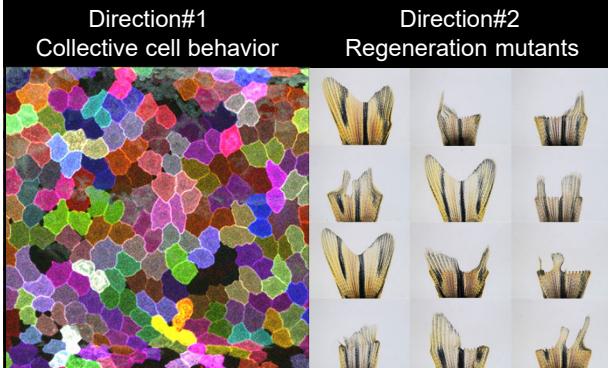
In toto approach identifies a new muscle growth mechanism



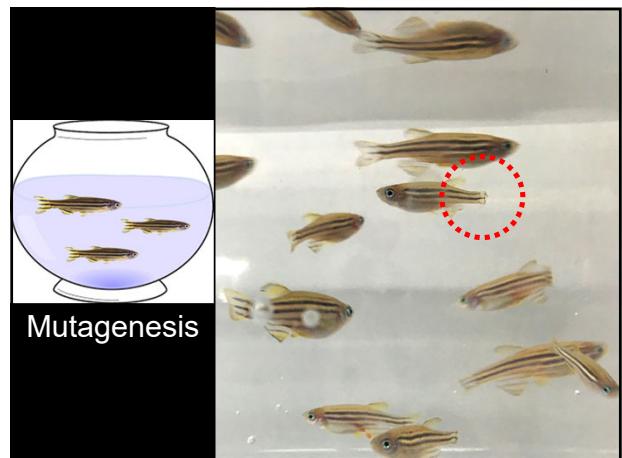
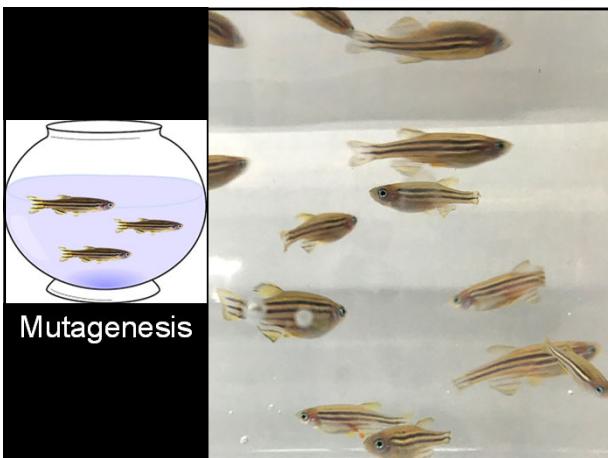
Kumar et al., under review

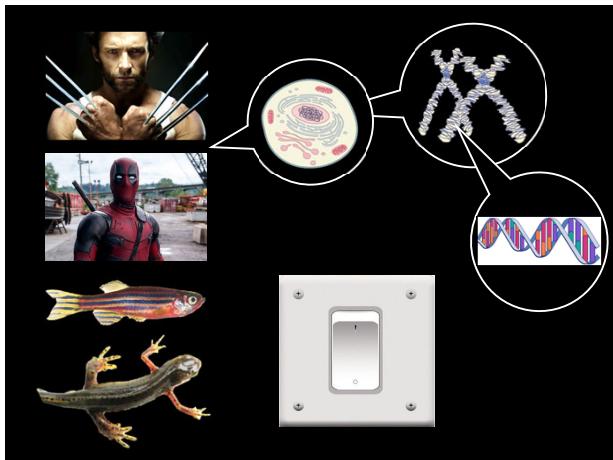
Any questions for the first part?

My research program at ICOB



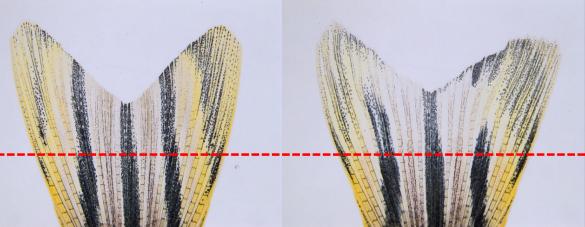
Find **Wolverines** or **Deadpools** that are unable to regenerate!





Zebrafish tailfin regeneration is robust

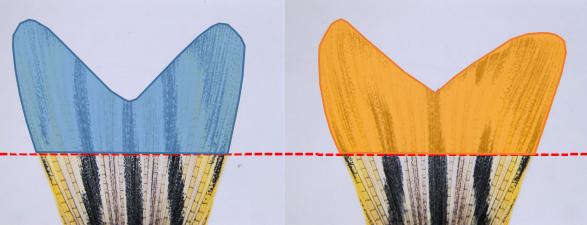
Before amputation 21 dpa



Zebrafish tailfin regeneration is robust

Before amputation

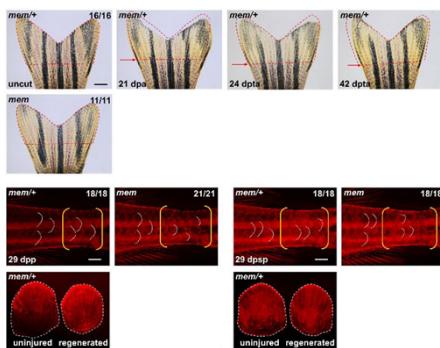
21 dpa



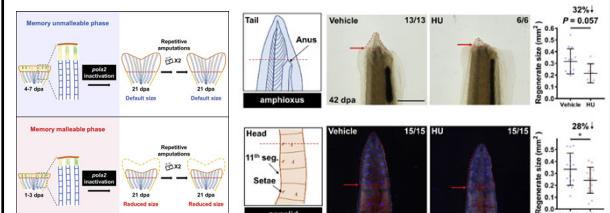
A fish that cannot remember what to regenerate



The gene can create new, long-lasting memory in distinct tissues



Pola2 resets positional memory during regeneration



Wang et al., Current Biology (2019)

Regeneration speed vs. injury levels

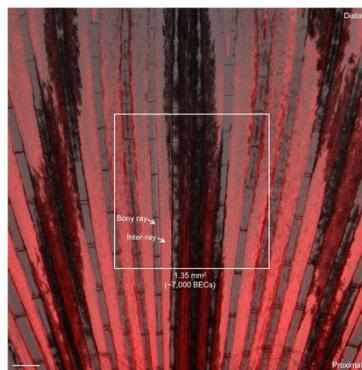
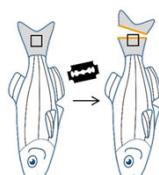


How do animals sense amputation levels and have different response?

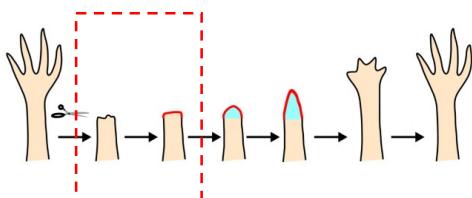


Lee et al., Dev (2005)

Real-time monitoring of 7,000 cells in a live animal

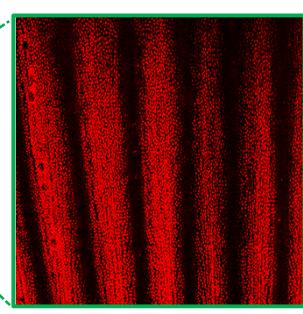
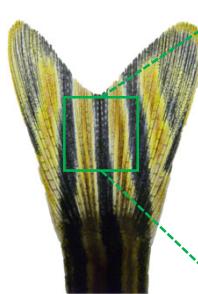


Wound healing is key to regeneration

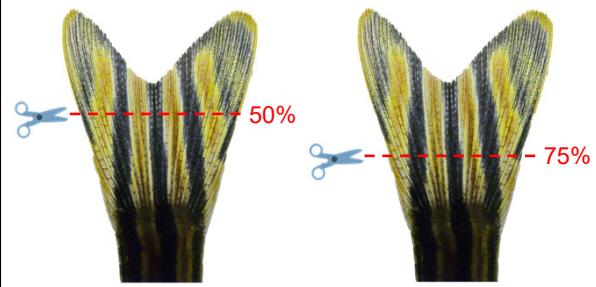


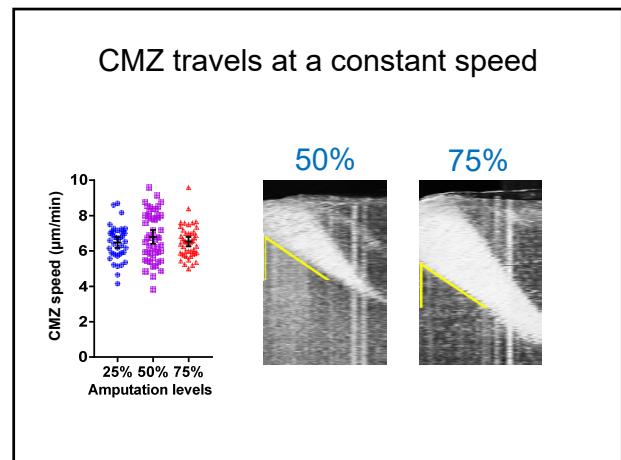
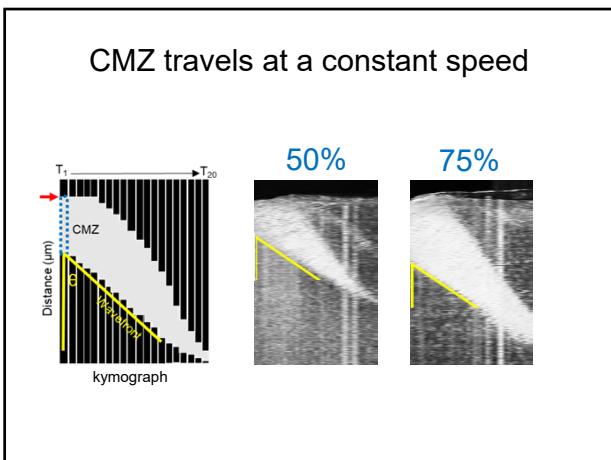
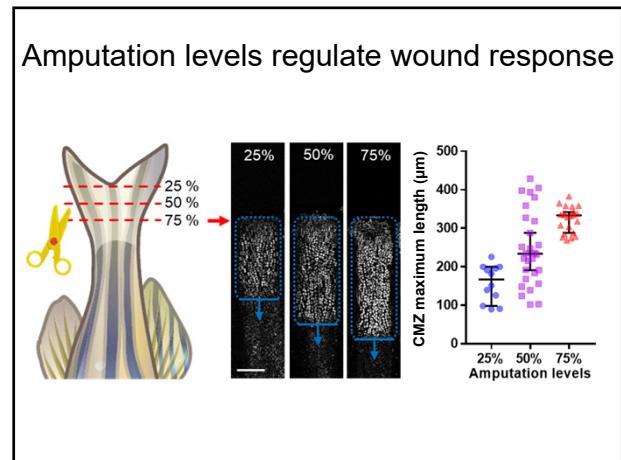
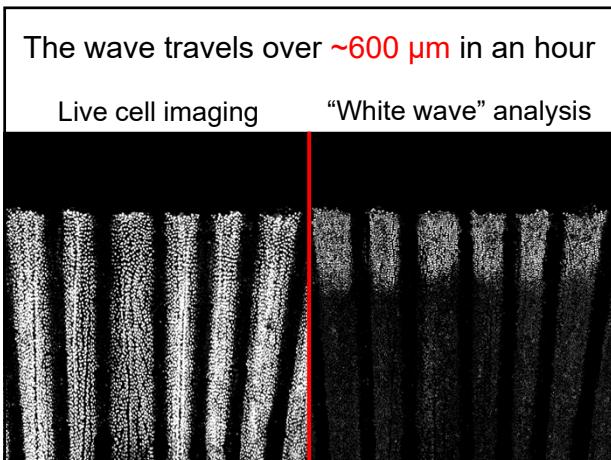
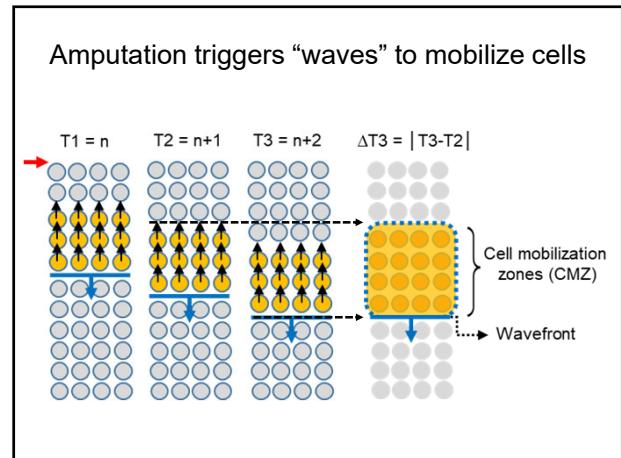
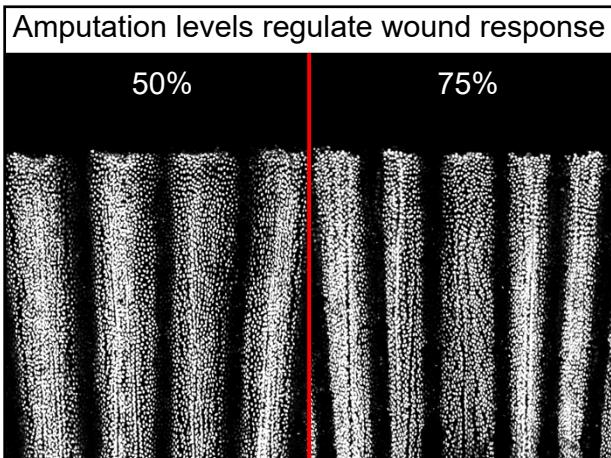
Whited et al, 2009

Live imaging of wound healing response



Distal amputation vs. Proximal amputation





Time to talk to a physicist!

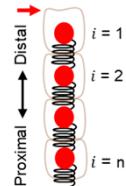


Dr. Lin, Keng-Hui
A soft matter physicist at Academia Sinica

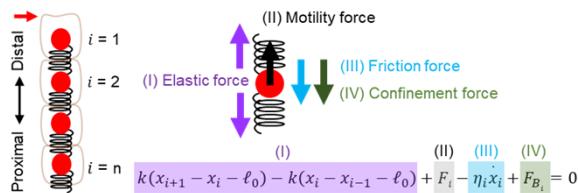


Dr. Wen, Fu-Lai
A theoretical physicist at NCKU

One-Dimensional Active Spring (ODAS)

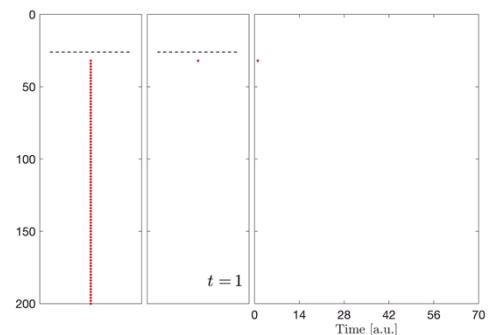


One-Dimensional Active Spring (ODAS)

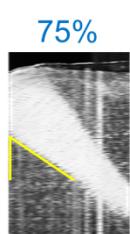
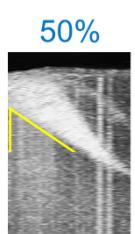
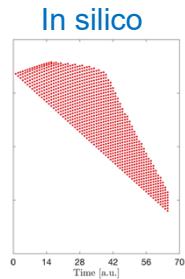


$$k(x_{i+1} - x_i - \ell_0) - k(x_i - x_{i-1} - \ell_0) + F_i - \eta_i \dot{x}_i + F_{B_i} = 0$$

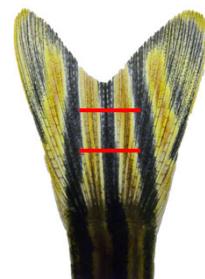
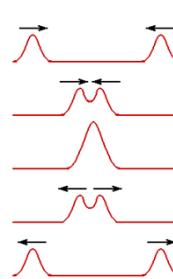
One-Dimensional Active Spring (ODAS)



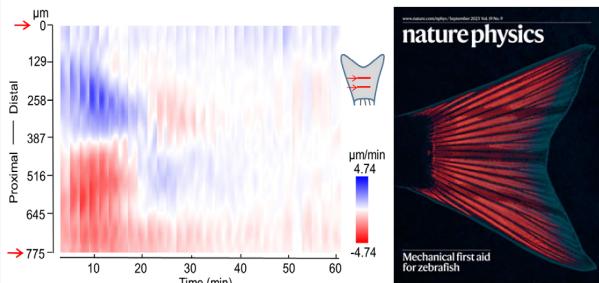
One-Dimensional Active Spring (ODAS)



Mechanical waves vs. Chemical waves

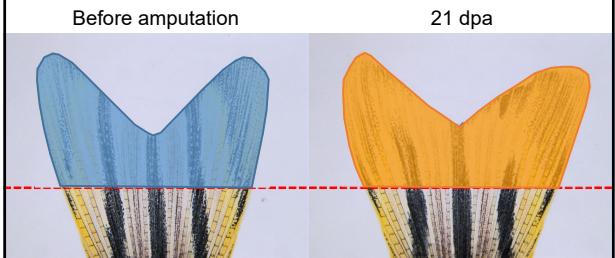


Mechanical waves direct amputation-level dependent tissue responses

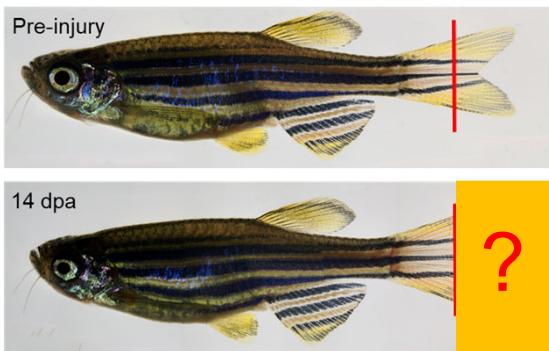


De Leon et al., Nature Physics (2023)

How does regeneration stop?



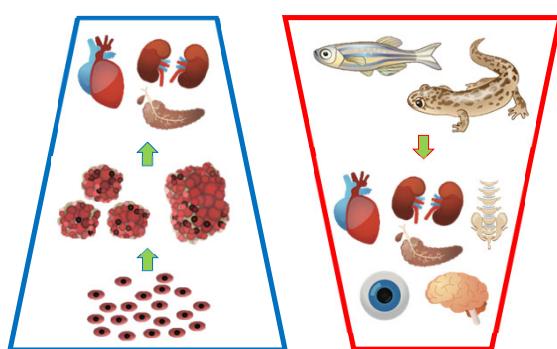
A fish that cannot stop regeneration



Can we make non-regenerative animals regenerative?



Bottom-up vs. **top-down** approaches



Topics for today

1. 為什麼要研究再生?
2. 如何利用斑馬魚研究再生?
3. 人類有一天也可以斷肢再生嗎?

Topics for today

1. 為什麼要研究再生? 迷人&重要
2. 如何利用斑馬魚研究再生? 問對問題
3. 人類有一天也可以斷肢再生嗎? 可能

