# 物理學家與斑馬魚的距離

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物理研究所通俗演講

6 June, 2023

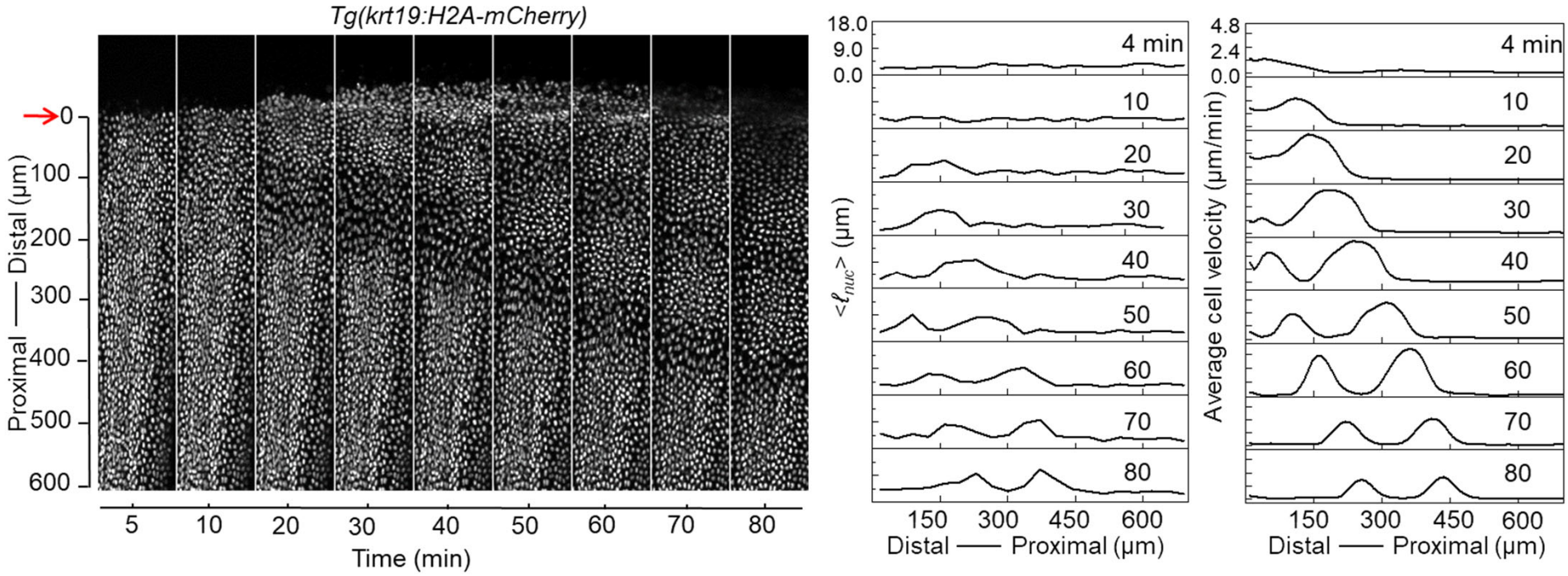
# 今天的目標

1. 為什麼要跟物理學家合作?

2. 生物和物理學家合作的挑戰?

3. 物理學家和斑馬魚的距離?

# 在斑馬魚尾鰭發現「機械波」




De Leon *et al*., *Nature Physics* (accepted)

# 「機械波」的生物意義

1. 首次在活體動物身上驗證「機械波」的存在。

2.回答一個困擾生物學家超過250年的奇特現象-為什麼再生速度總是跟受傷程度成正比?會再生的動物可以利用「機械波」偵測受傷發生的位置，以控制相對應的傷口癒合和再生反應。

# 從前從前... 2017的夏天

**From:** Keng-hui Lin [mailto:kenghui@gate.sinica.edu.tw]
**Sent:** Wednesday, August 9, 2017 4:28 PM
**To:** Chen-Hui Chen <chcchen@gate.sinica.edu.tw>
**Subject:** Re: input on our findings

Dear Chen-hui,

It sounds like we have overlapped research interests and I would love to see the wave-like behaviors you observe. I have more time this Friday. Will 1:30 pm work for you?

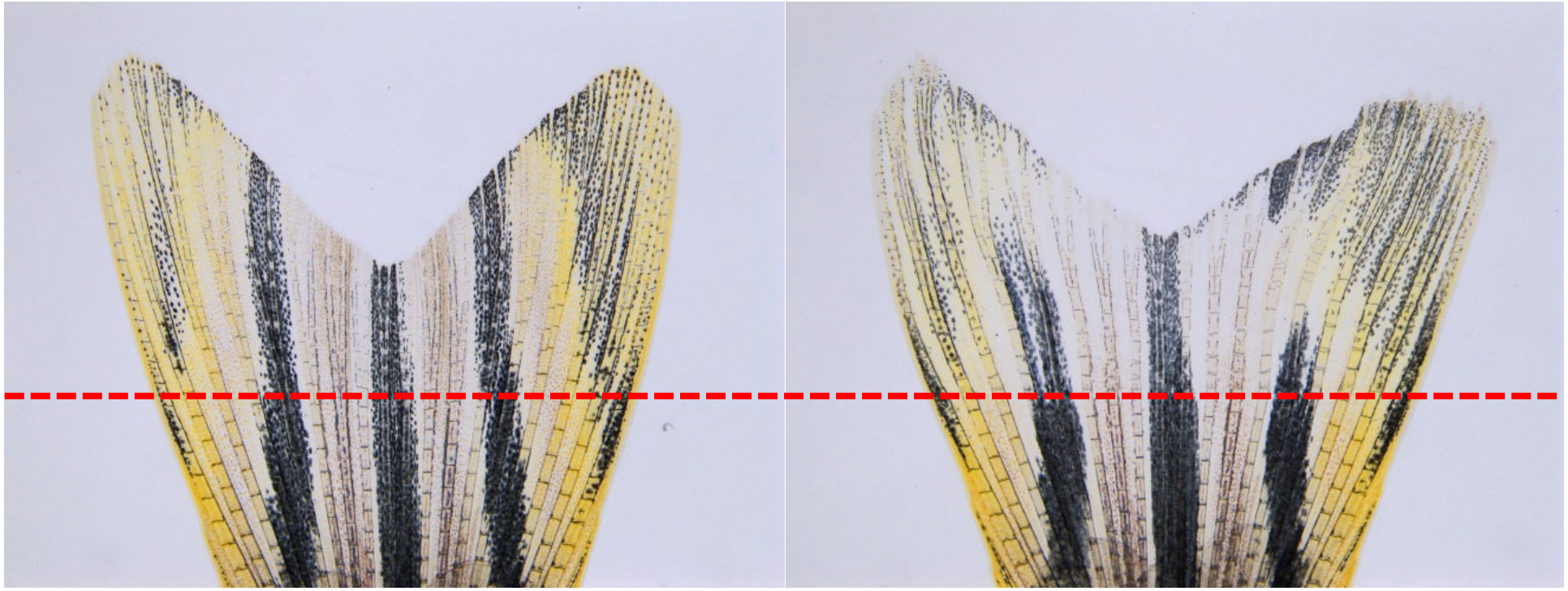
Keng-hui

> Chen-Hui Chen <chcchen@gate.sinica.edu.tw> 於 2017 年 8 月 9 日 上午 11:17 寫道：
>
> Dear Dr. Lin,
>
> Let me introduce myself. I am an assistant research fellow at ICOB, AS.
> My lab is interested in wound healing response and tissue regeneration using zebrafish as our model system.
>
> Using live imaging approach, we recently identify unexpected cell behaviors that remind me of basic physics in waves.
> Is it possible that I could stop by to show you our imaging data, and have your input on our findings?
>
> Many thanks,
> Chen
>
> _____
> Chen-Hui Chen, Ph.D.
> Assistant Research Fellow at ICOB

# 利用斑馬魚尾鰭研究再生

Before amputation

21 dpa



# 利用斑馬魚尾鰭研究再生

Before amputation

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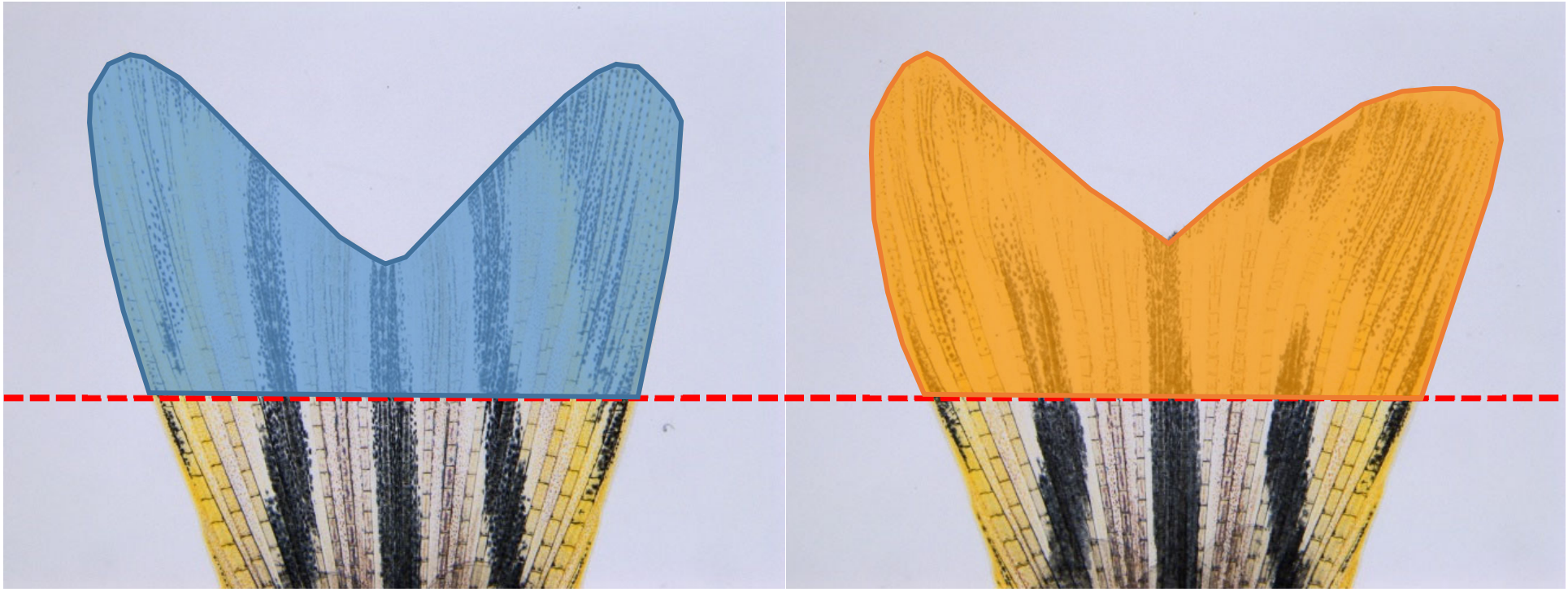
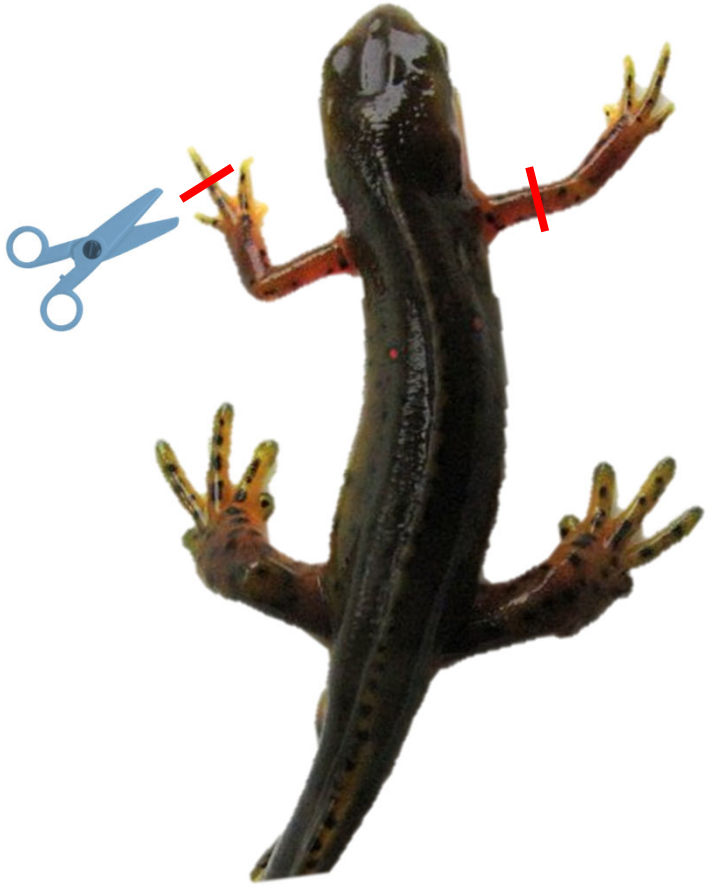


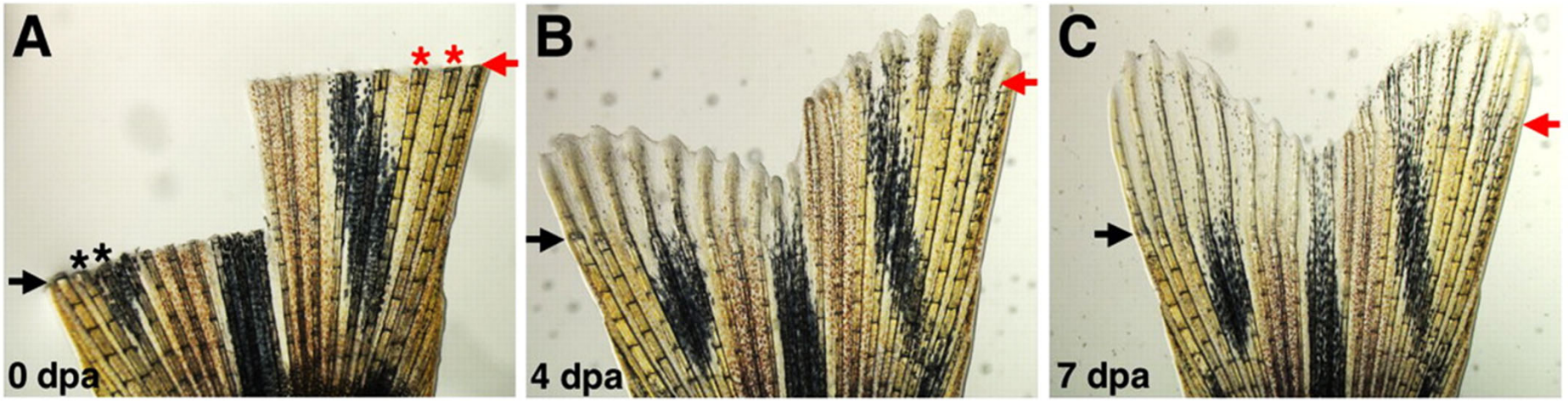
# Regeneration speed vs. injury levels

Lazzaro Spallanzani
(1729- 1799)



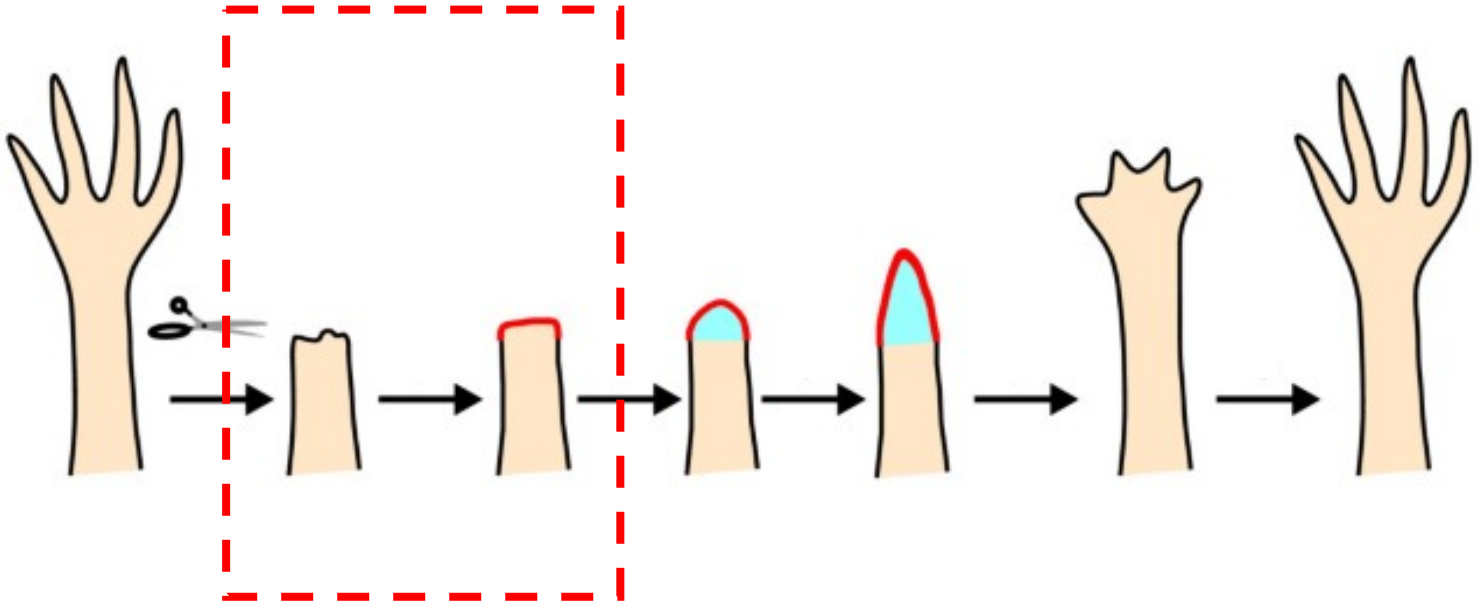
# Set up my lab at ICOB in 2016…

# How do animals sense amputation levels and have different response?



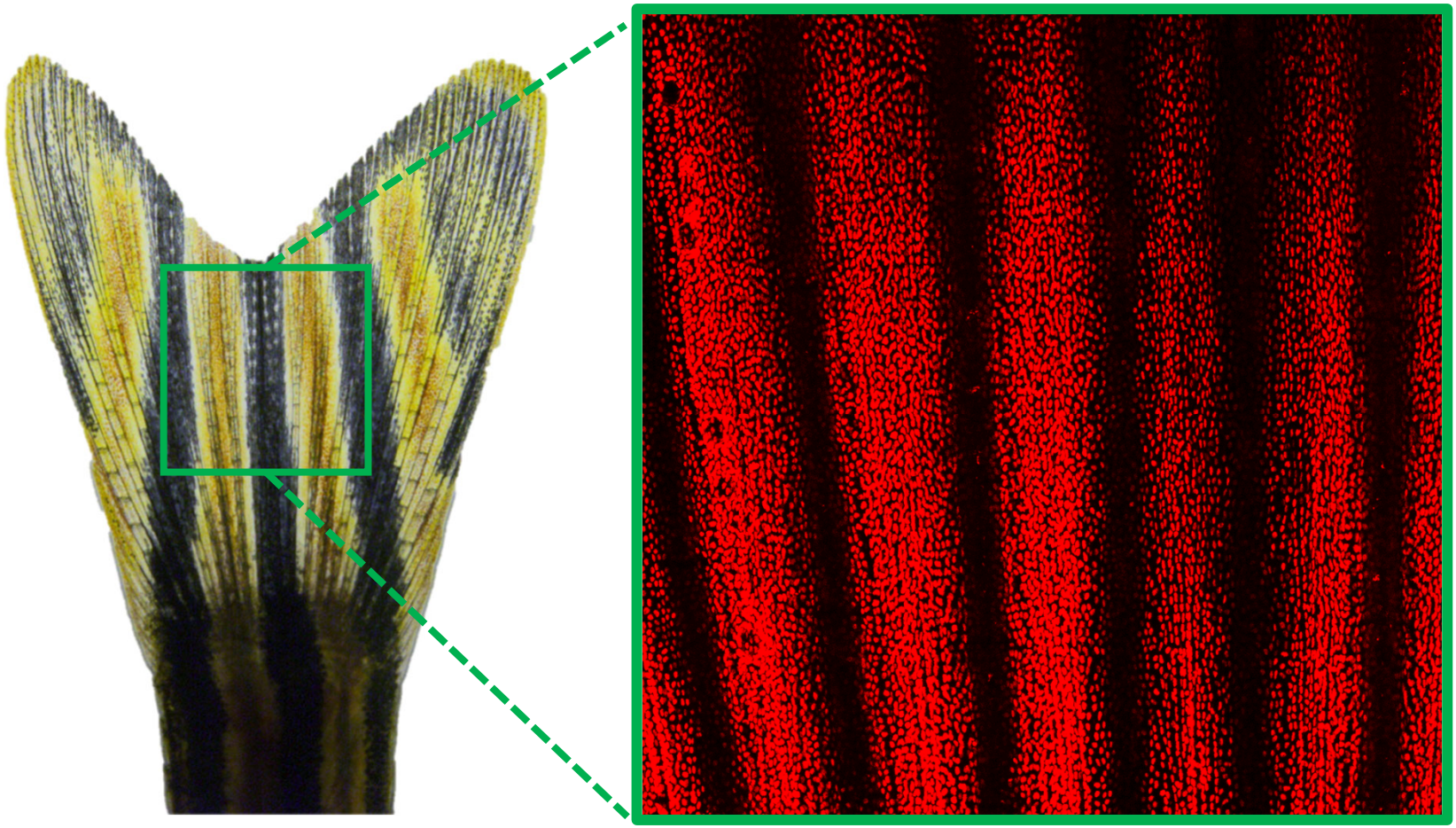

Lee *et al., Dev* (2005)

# Wound healing is key to regeneration



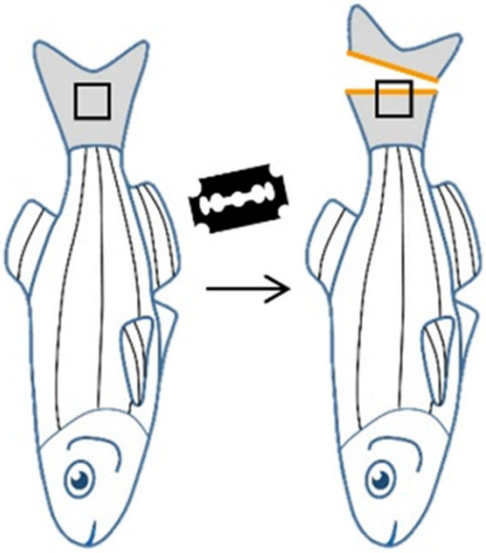
Whited *et al*., 2009

# Live imaging of wound healing response

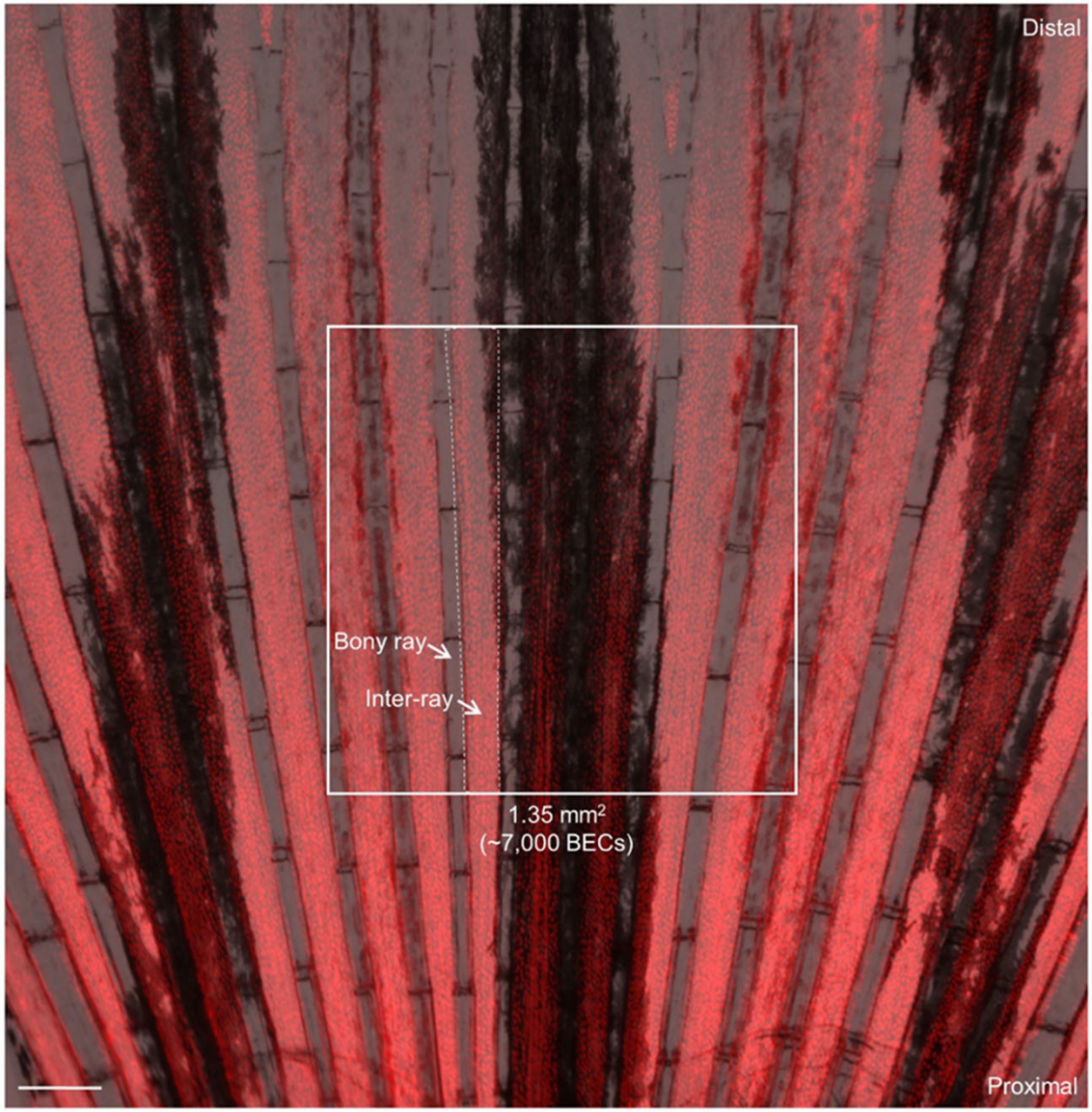


*Tg(krt19:H2A-mCherry)*

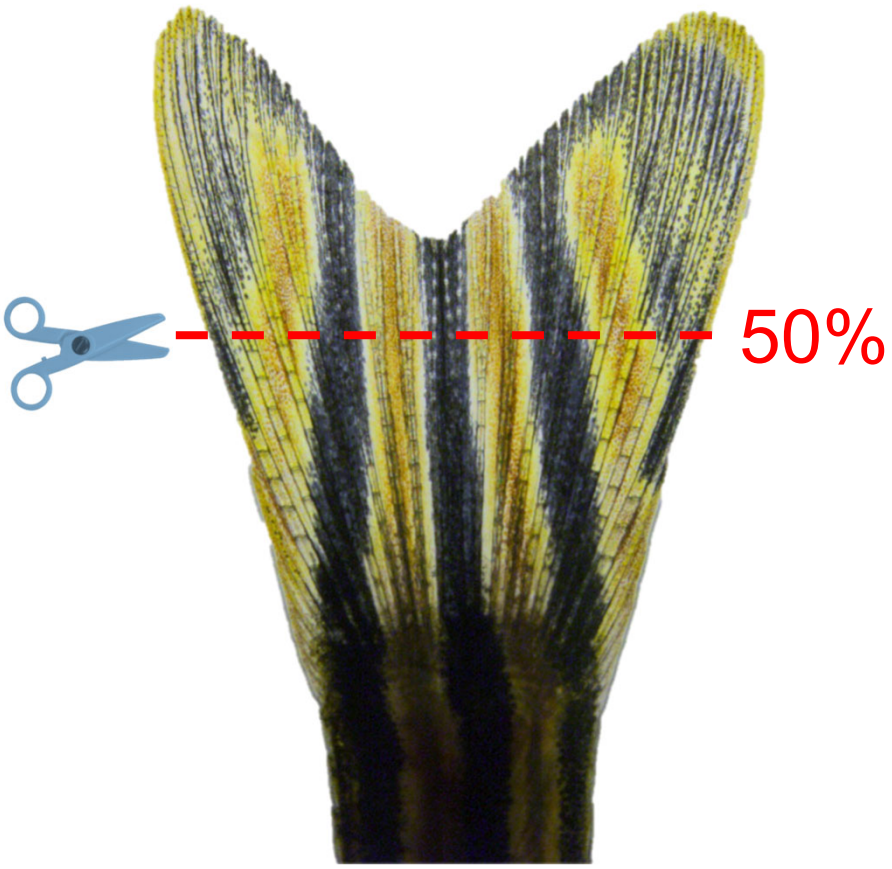
# Monitoring of 7,000 cells in a live animal

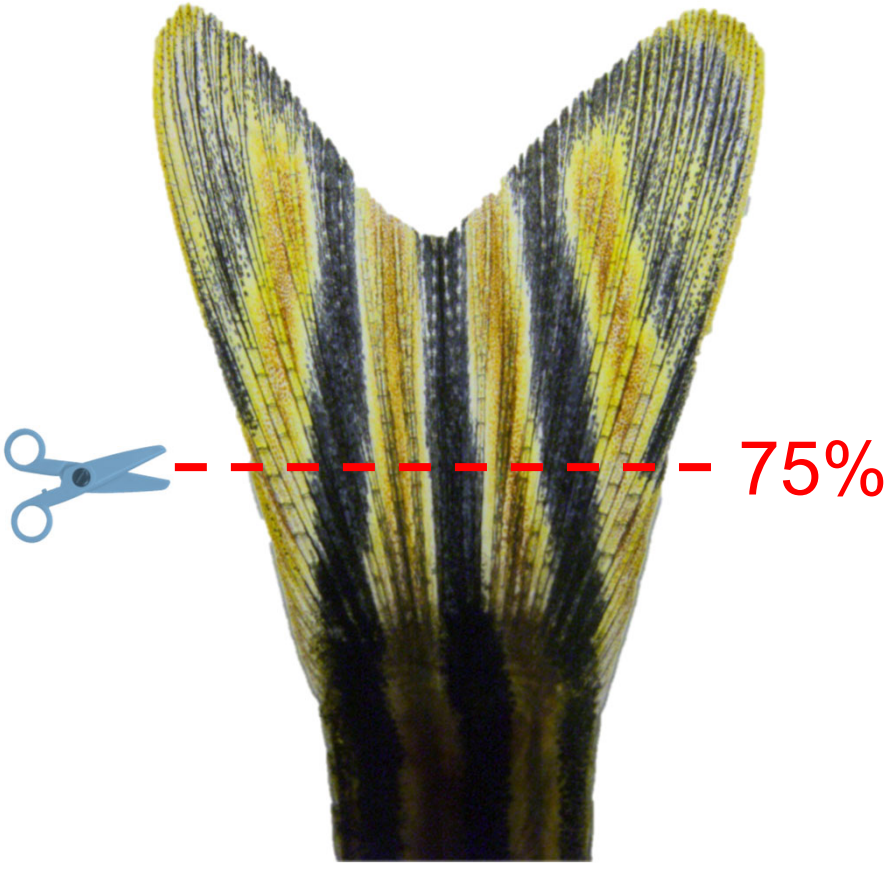


Marco De Leon

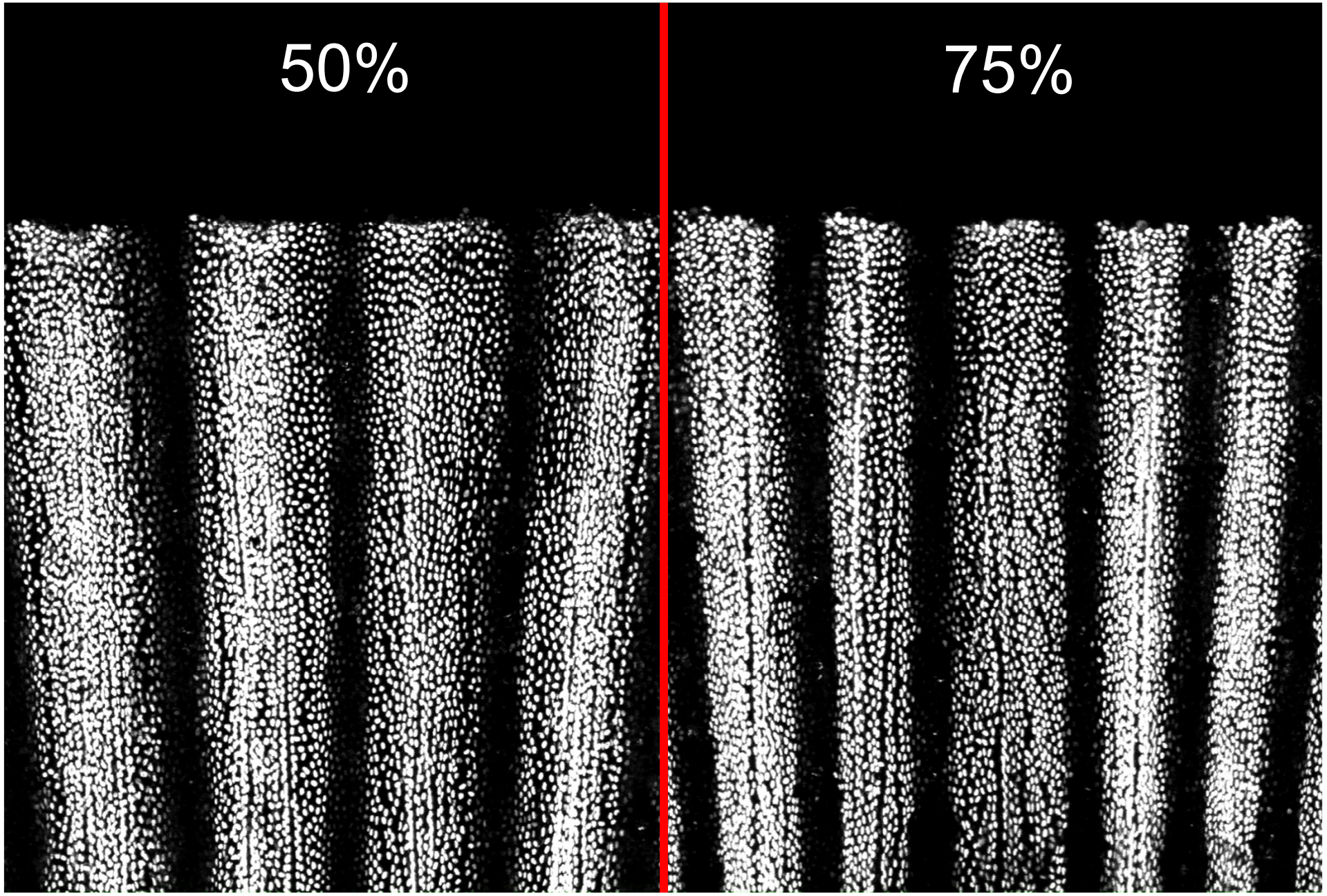


# Distal amputation vs. Proximal amputation

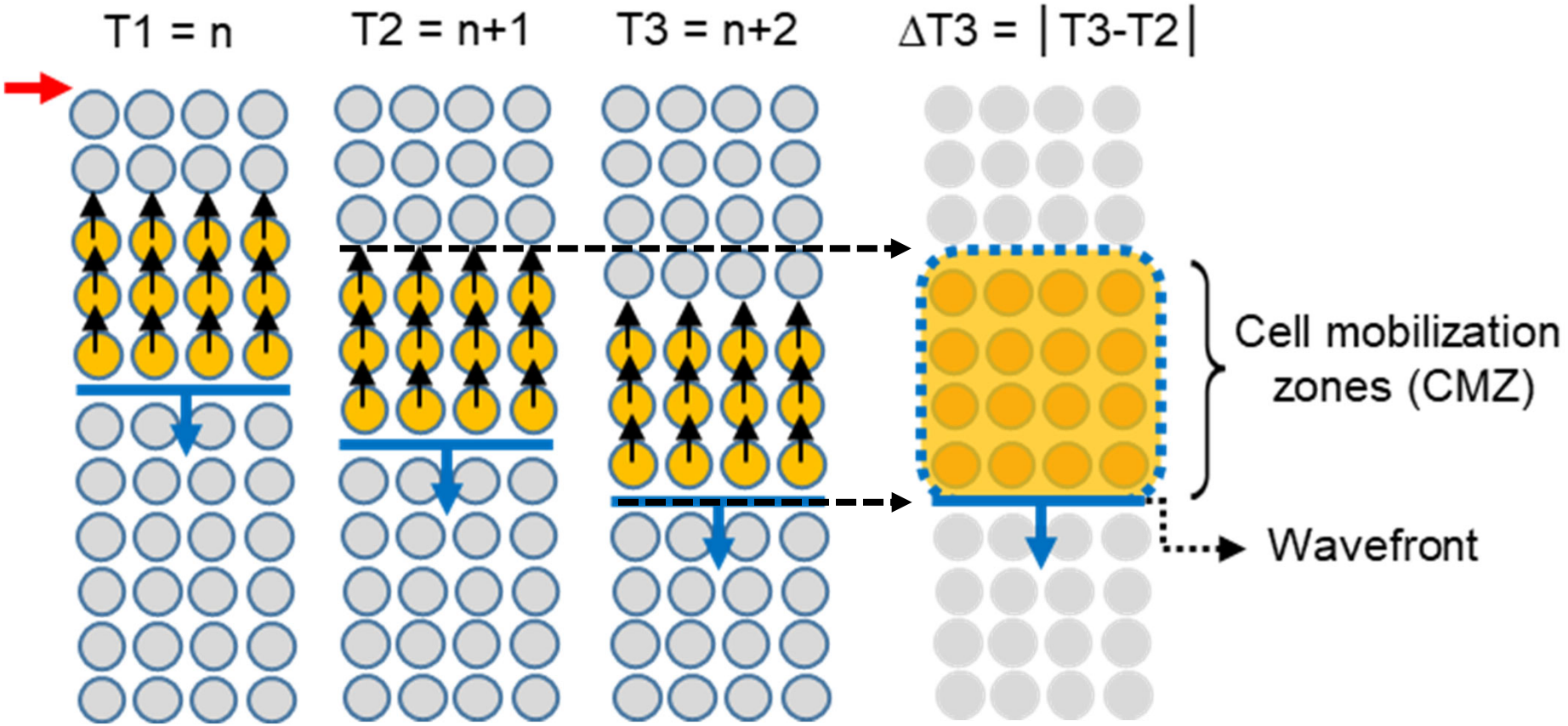


# Amputation levels regulate wound response



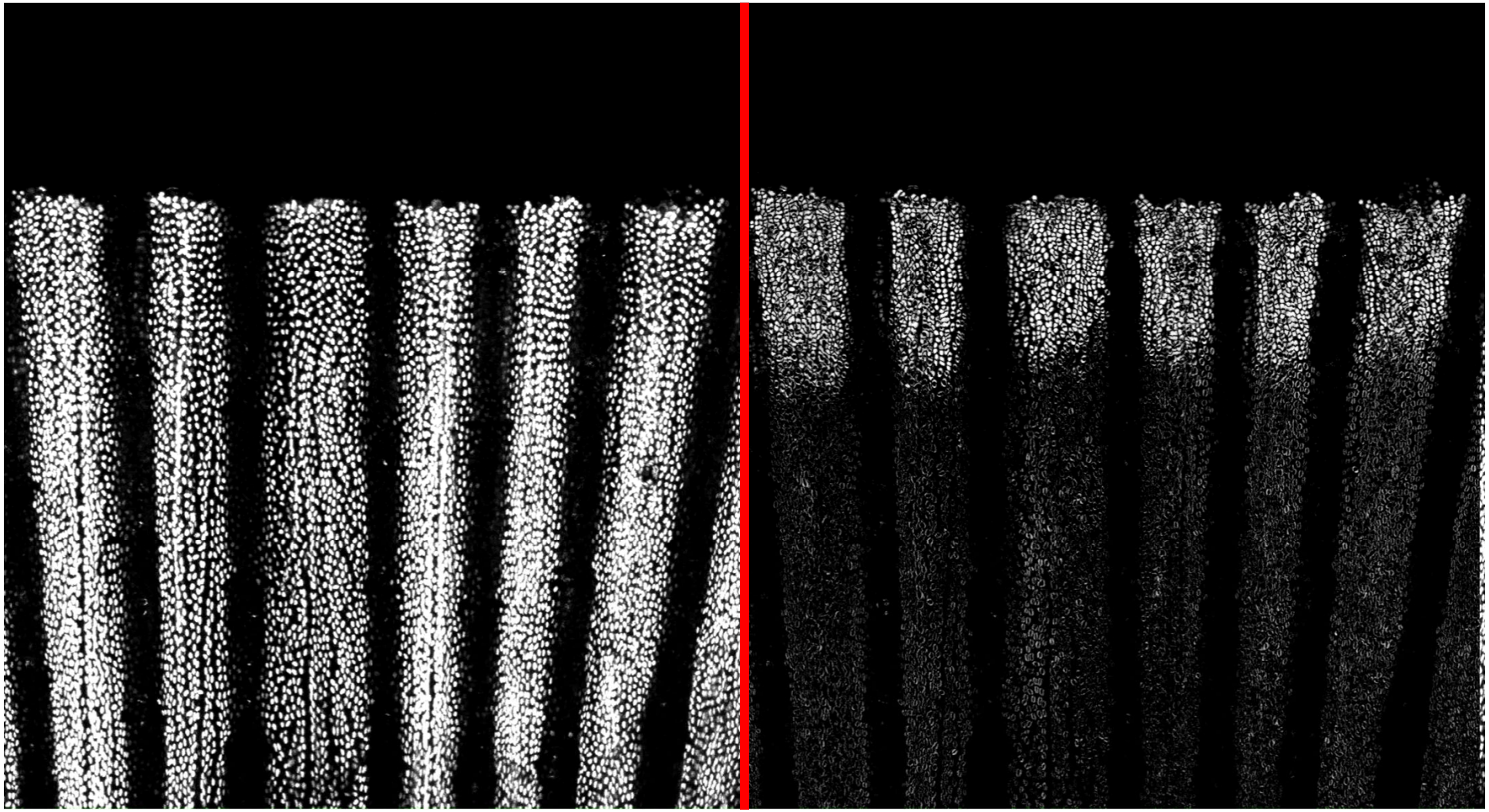
# Amputation triggers “waves” to mobilize cells



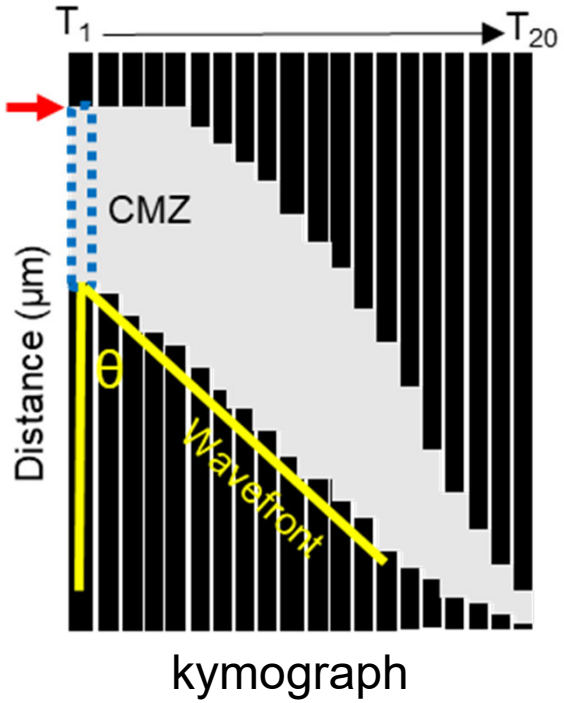
# The wave travels over ~600 µm in an hour

Live cell imaging

“White wave” analysis

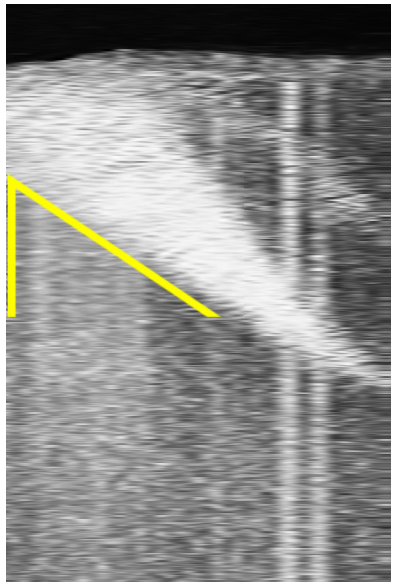


# CMZ travels at a constant speed




kymograph

50%



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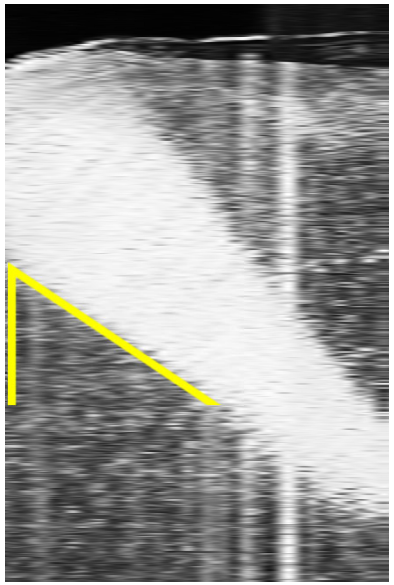
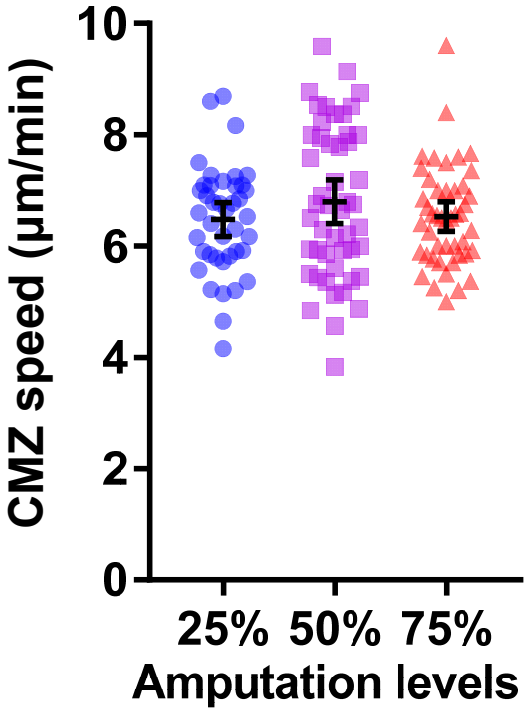


# CMZ travels at a constant speed

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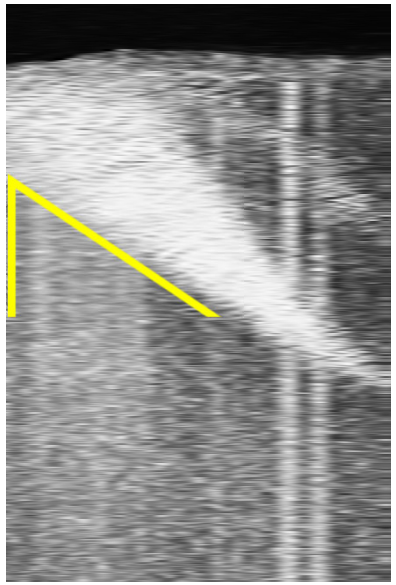
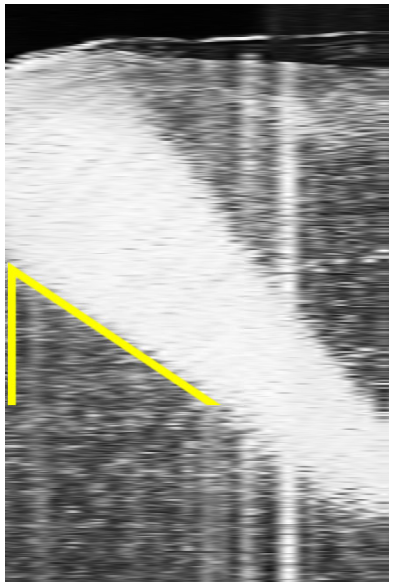
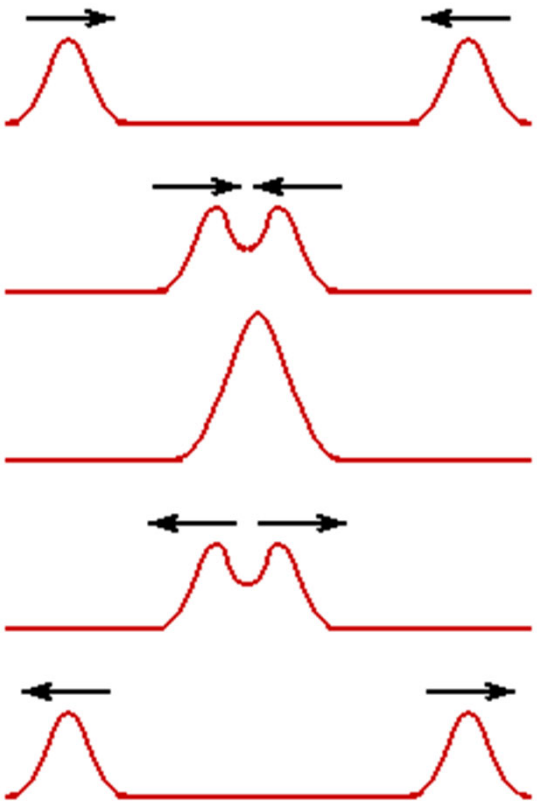
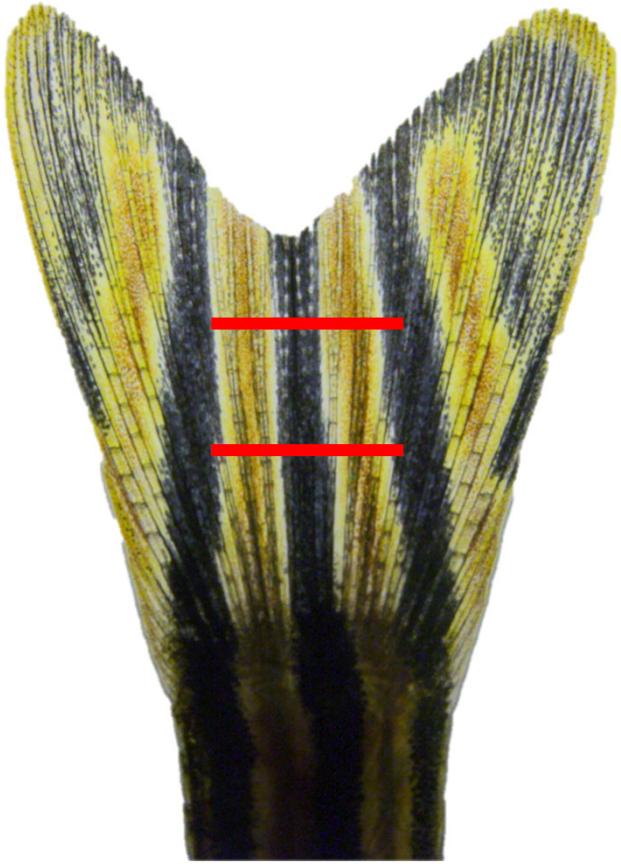


75%

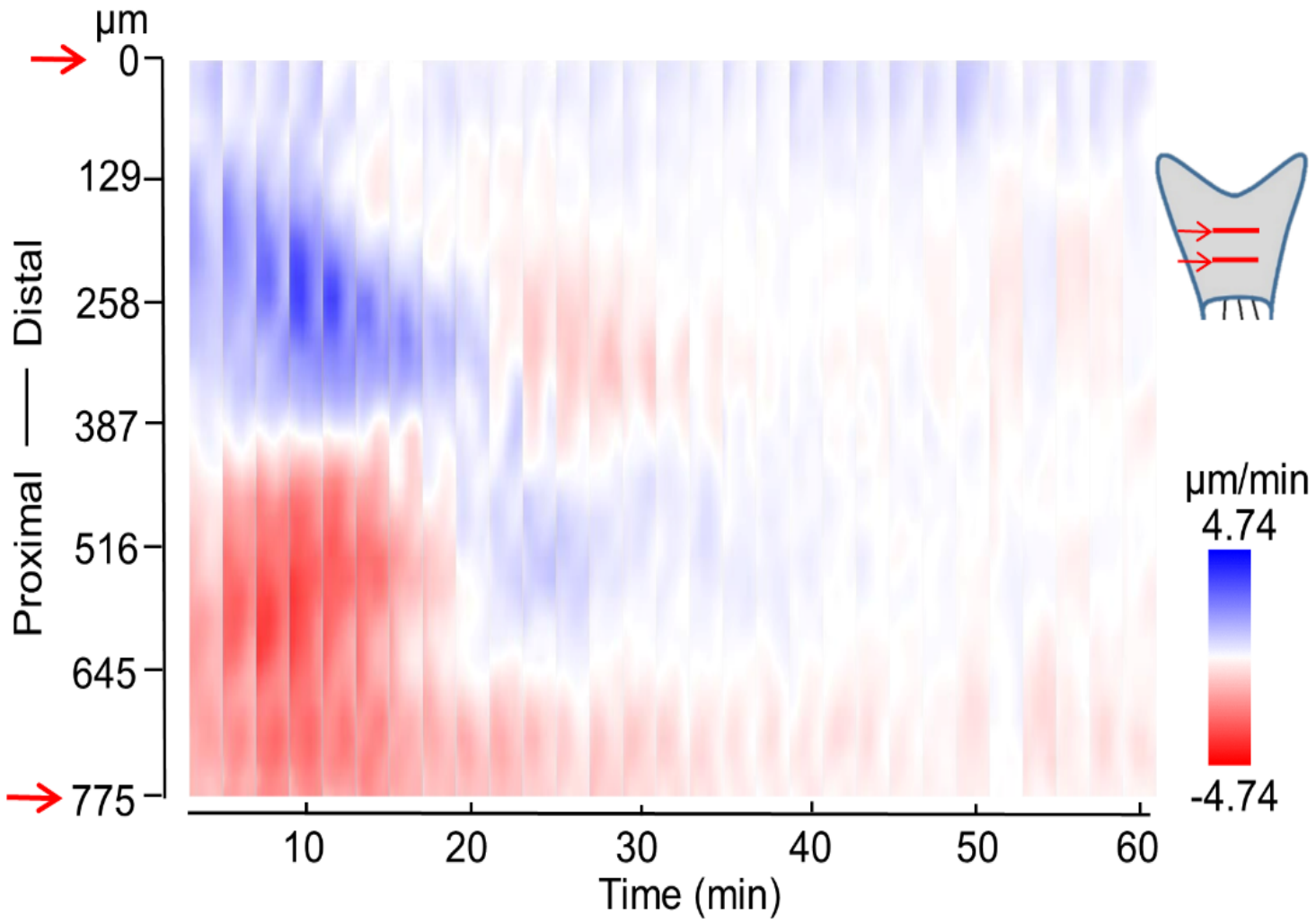


# Mechanical waves vs. Chemical waves





# *Mechanical waves* direct amputation-level dependent tissue responses




De Leon et al., accepted

# Physicists rock!

Dr. Lin, Keng-Hui

A soft matter physicist

Dr. Wen, Fu-Lai

A theoretical physicist

但是...

但是... 為什麼我們用了六年?

# 看問題的角度 完全不同

物理學家: 沒有我們不知道的東西

生物學家: 沒有我們真正知道的東西

# 漫長的溝通、磨合期

Keng-Hui: 興趣廣泛 充滿活力 對數字敏銳
有很強的主見 喜歡一直挑戰新的東西

Chen: 興趣集中 堅持固定的作息 很在意細節
有很強的主見 喜歡想故事和寫論文

有耐心 願意花時間溝通
了解對方獨特的能力和能耐
最後 相信對方 尊重對方的堅持

# 學生的長期掙扎

Marco De Leon

兩倍的學習 + 兩倍的挑戰 + 兩倍的時間

# 學生的長期掙扎

Marco De Leon

兩倍的學習 x 兩倍的挑戰 x 兩倍的時間

# 學生的長期掙扎

Marco De Leon

兩倍的學習 x 兩倍的挑戰 x 兩倍的時間

= 精神上的沉重壓力

# 跨領域研究投稿的挑戰-投稿前

Keng-Hui:

Chen:

# 跨領域研究投稿的挑戰-投稿前

Keng-Hui: observe、agree

Chen: determine、define、find 、identify、support 、indicate

speed 、velocity、mobility 、 motility、apparent speed 、 length scale 、local 、global 、 instant、lasting 、intriguingly、remarkably 、unexpectedly

# 跨領域研究投稿的挑戰-投稿後

# 跨領域研究投稿的挑戰-投稿後

**From:** Developmental Cell
**Sent:** Thursday, February 10, 2022 1:59 AM
**To:** Chen-Hui Chen <chcchen@gate.sinica.edu.tw>
**Subject:** Editorial Decision on Developmental Cell manuscript

Dear Dr. Chen,

I apologise for the unusually lengthy delay in contacting you with this editorial decision on your manuscript and am sorry for any inconvenience caused.

I am enclosing the comments that reviewers provided on your paper. As you will see, the overall recommendation is against publication in *Developmental Cell*. Based on the reviewers' reports, it seems that a substantial amount of further work would be required to resolve the issues raised in the reviews. in particular, both reviewers note there is no evidence for the mechanical wave and both question your model/assumptions. Given that such work likely falls beyond the scope of what is feasible to include in this manuscript, I am sorry to say I cannot offer to consider a revision.

I appreciate that this outcome will be disappointing, but I hope you will find the reviewers' comments useful and constructive nonetheless. I do want to stress that this decision does not imply any lack of interest on our part about the field in general or your work in particular. I hope, therefore, that you will feel free to continue to submit future papers to *Developmental Cell*.

Yours sincerely,

# 生物和物理學家合作的挑戰

1. 看問題的角度 完全不同
2. 漫長的溝通、磨合期
3. 學生的長期掙扎
4. 跨領域研究投稿的挑戰

# 兩方面都需要「不尋常的勇氣」

1. 看問題的角度 完全不同
2. 漫長的溝通、磨合期
3. 學生的長期掙扎
4. 跨領域研究投稿的挑戰

# 很深刻的個人體會

1. 產生獨一無二的研究成果
2. 深刻的認識你的合作夥伴
3. 到達一個人走不到的境界
4. 帶來解決關鍵問題的機會

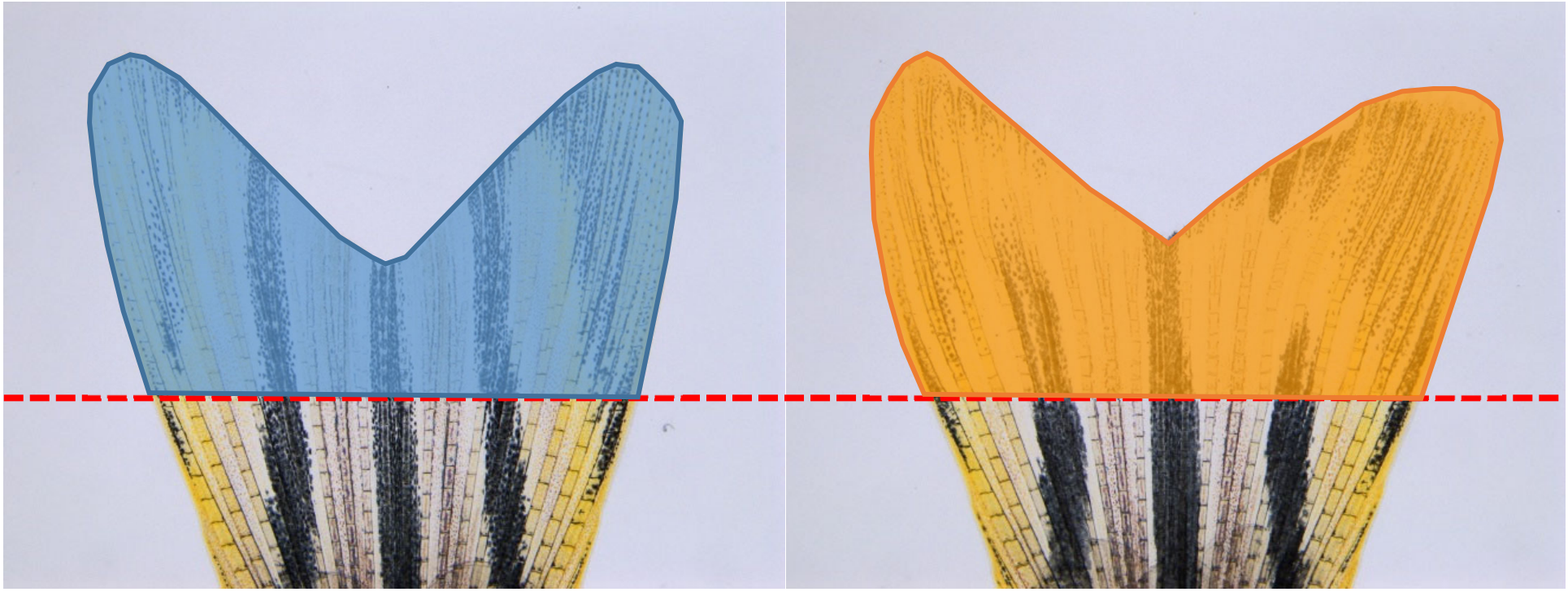
# 這是你想要的嗎?

1. 產生獨一無二的研究成果
2. 深刻的認識你的合作夥伴
3. 到達一個人走不到的境界
4. 帶來解決關鍵問題的機會

# 再生領域的關鍵問題

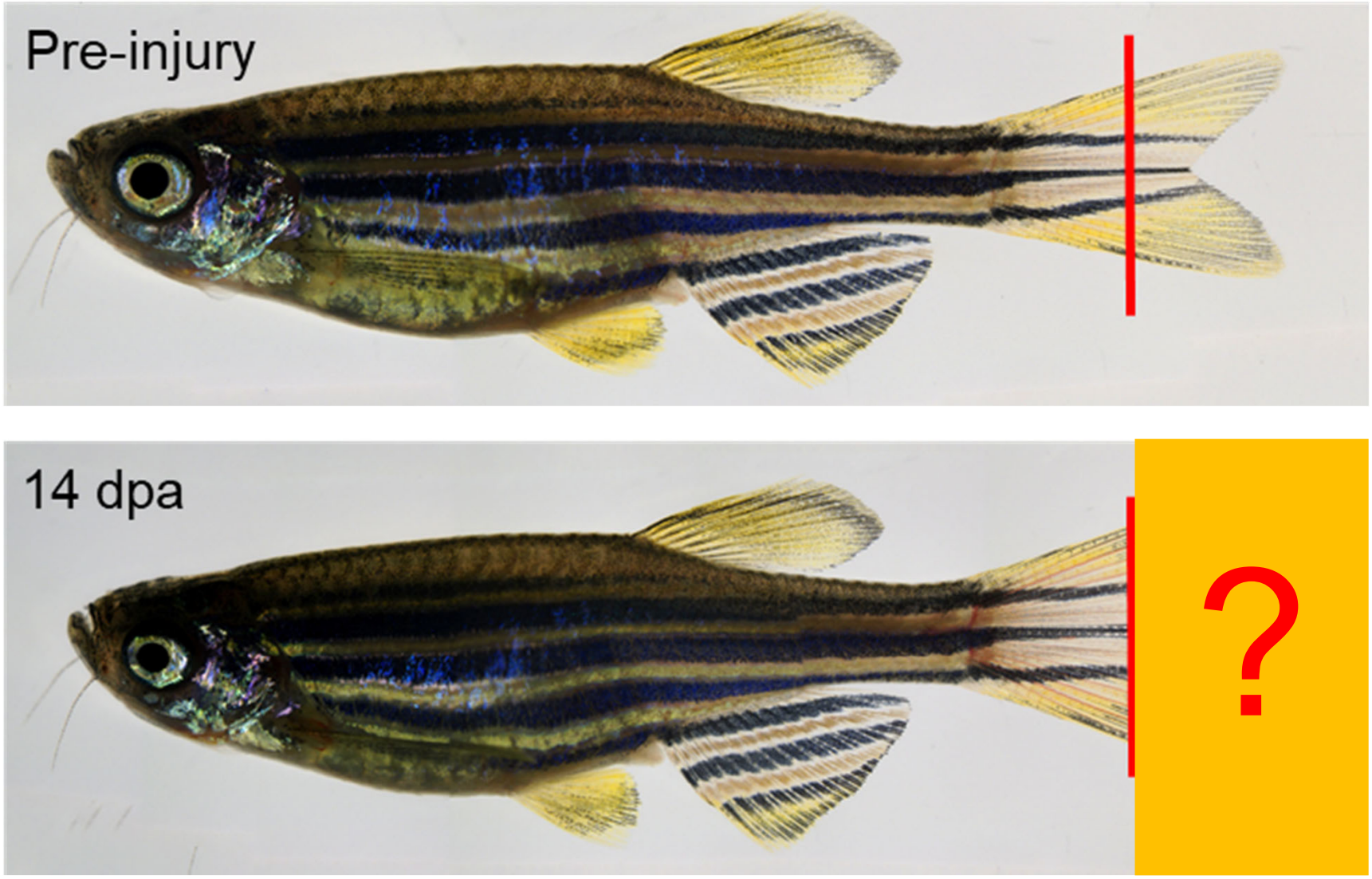
Before amputation

21 dpa



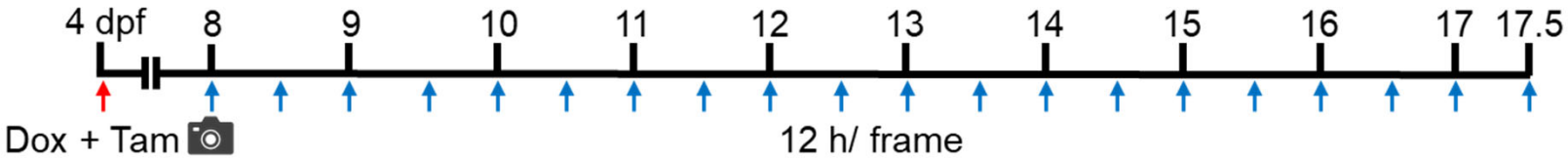
# Chen lab: what do we have?

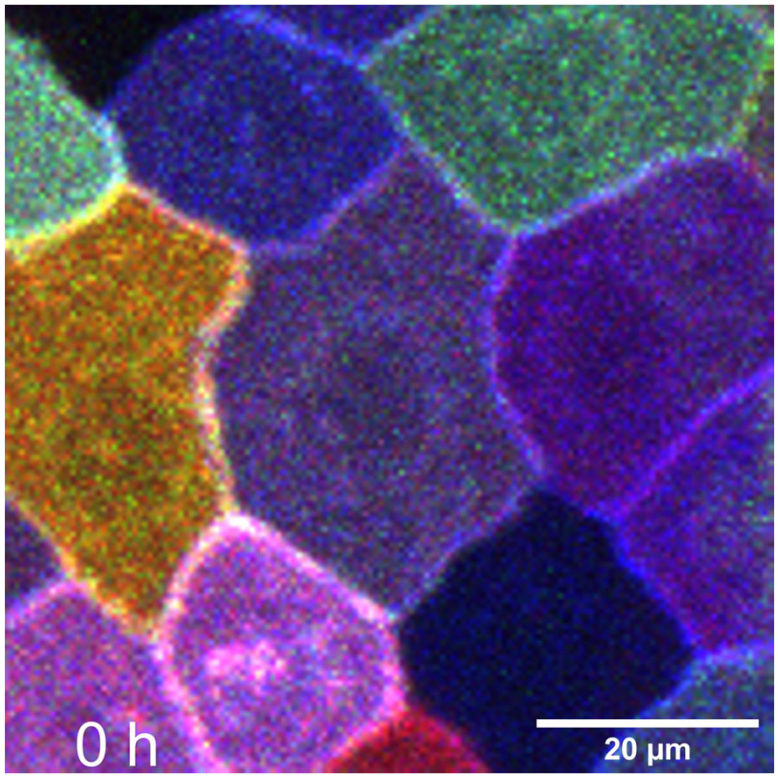
## - “Exciting questions and the fish”



# Chen lab: what else do we have?

## - “Asynthetic fission”

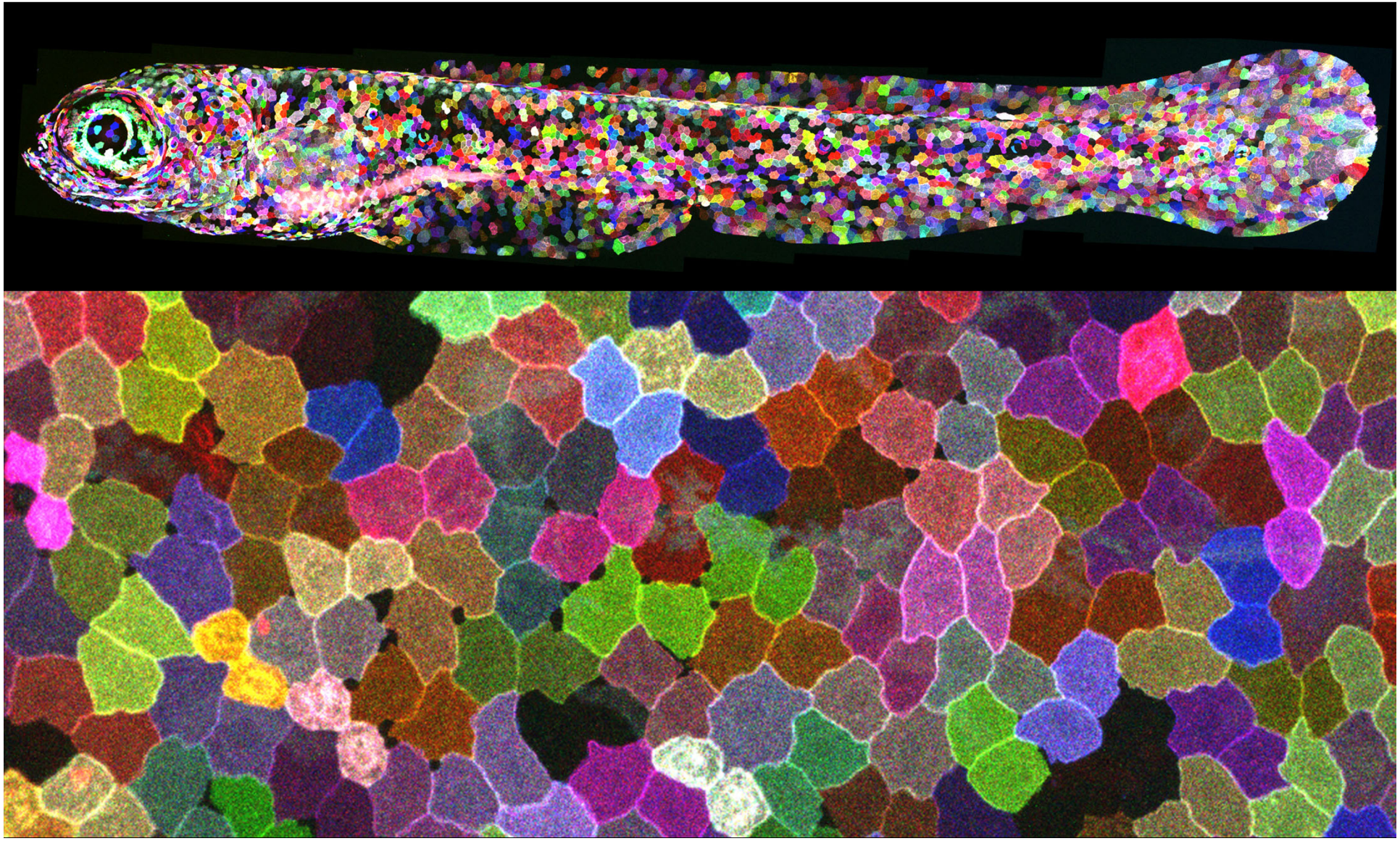


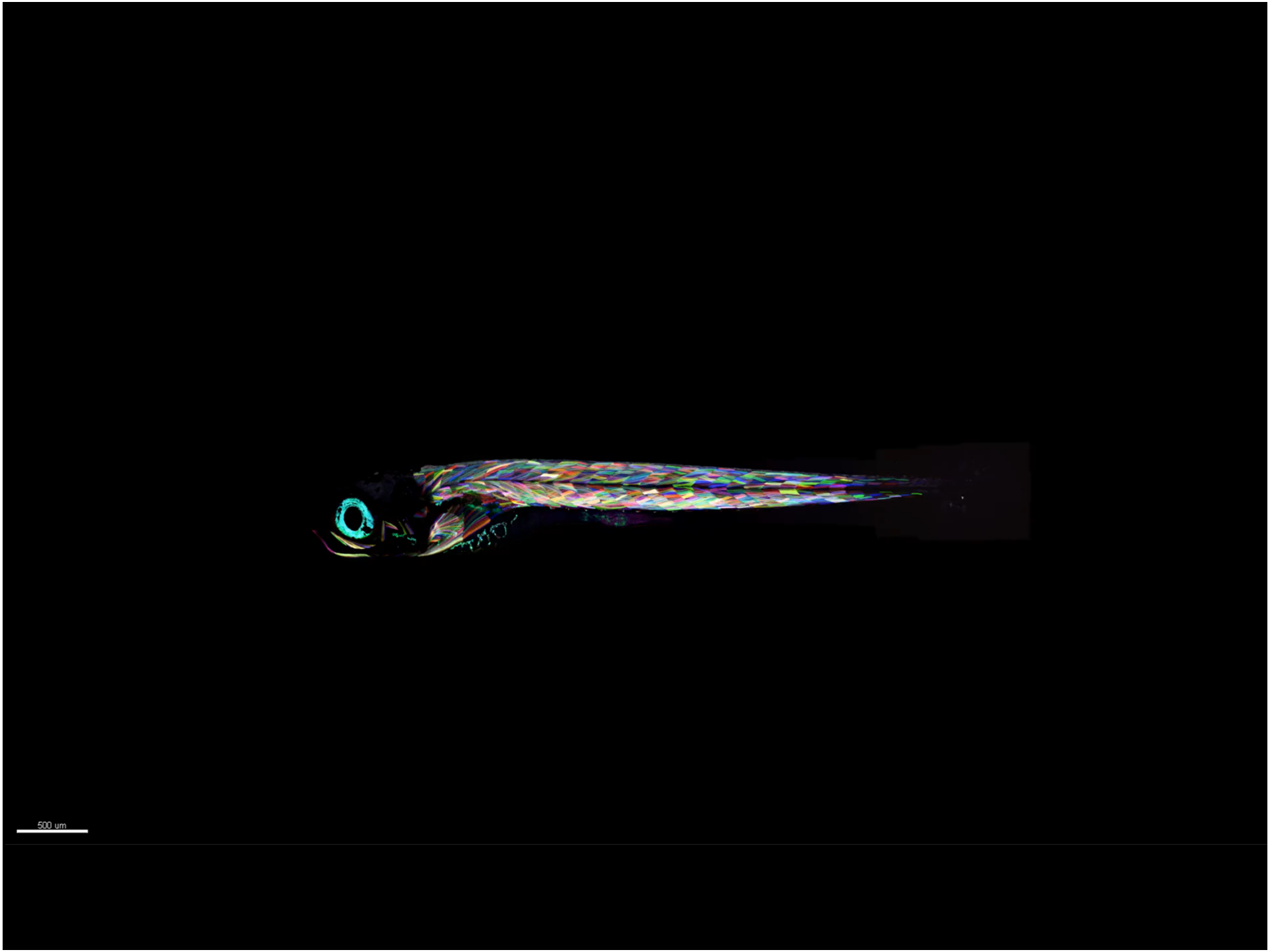




Chan *et al*., *Nature* (2022)

# Chen lab: what else do we have?

## - “Multicolor tools”




500 um

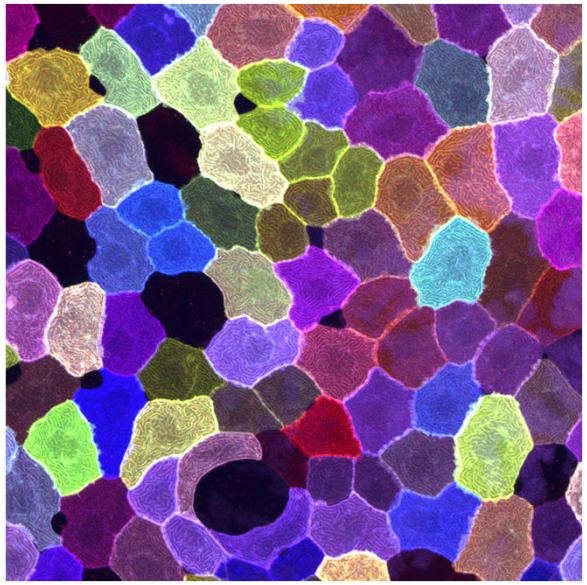
# What can “a” cell do *in vivo*?

Proliferation

Differentiation

Migration

Apoptosis



Hypertrophy

Cell-Cell fusion

Endoreplication

De-differentiation

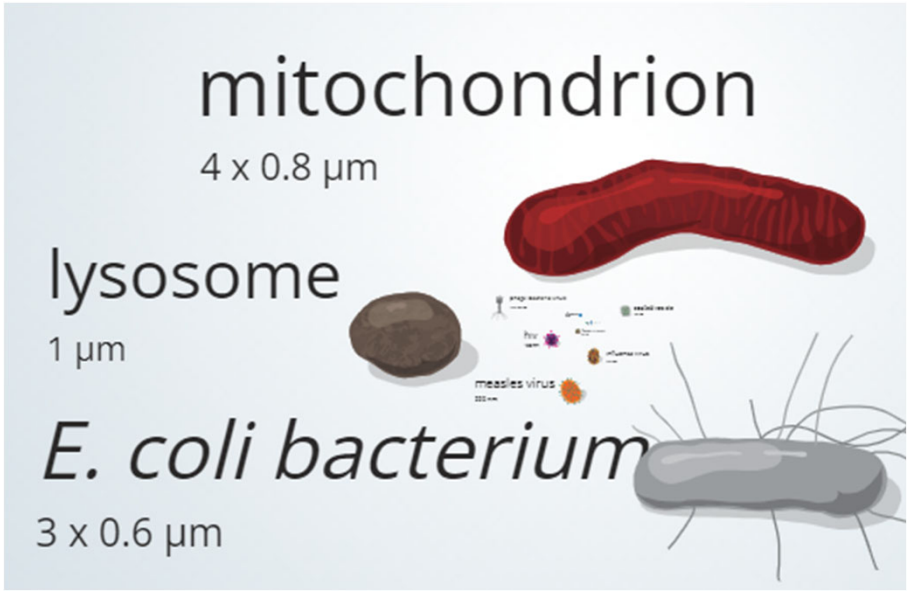
Trans-differentiation

Cell extrusion

*Asynthetic fission*

*SWAP*

# Do you want to *go big* or *go small*?



http://learn.genetics.utah.edu/content/cells/scale/

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3. 物理學家和斑馬魚的距離?

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2. 兩方面都需要「不尋常的勇氣」

3.物理學家和斑馬魚沒有距離

# Acknowledgements

Marco De Leon

Institute of Cellular and Organismic Biology

TZCAS
Taiwan Zebrafish Core Facility at Academia Sinica

中央研究院
Academia Sinica

NSTC
國科會