Plants and insects help us understand human infertility

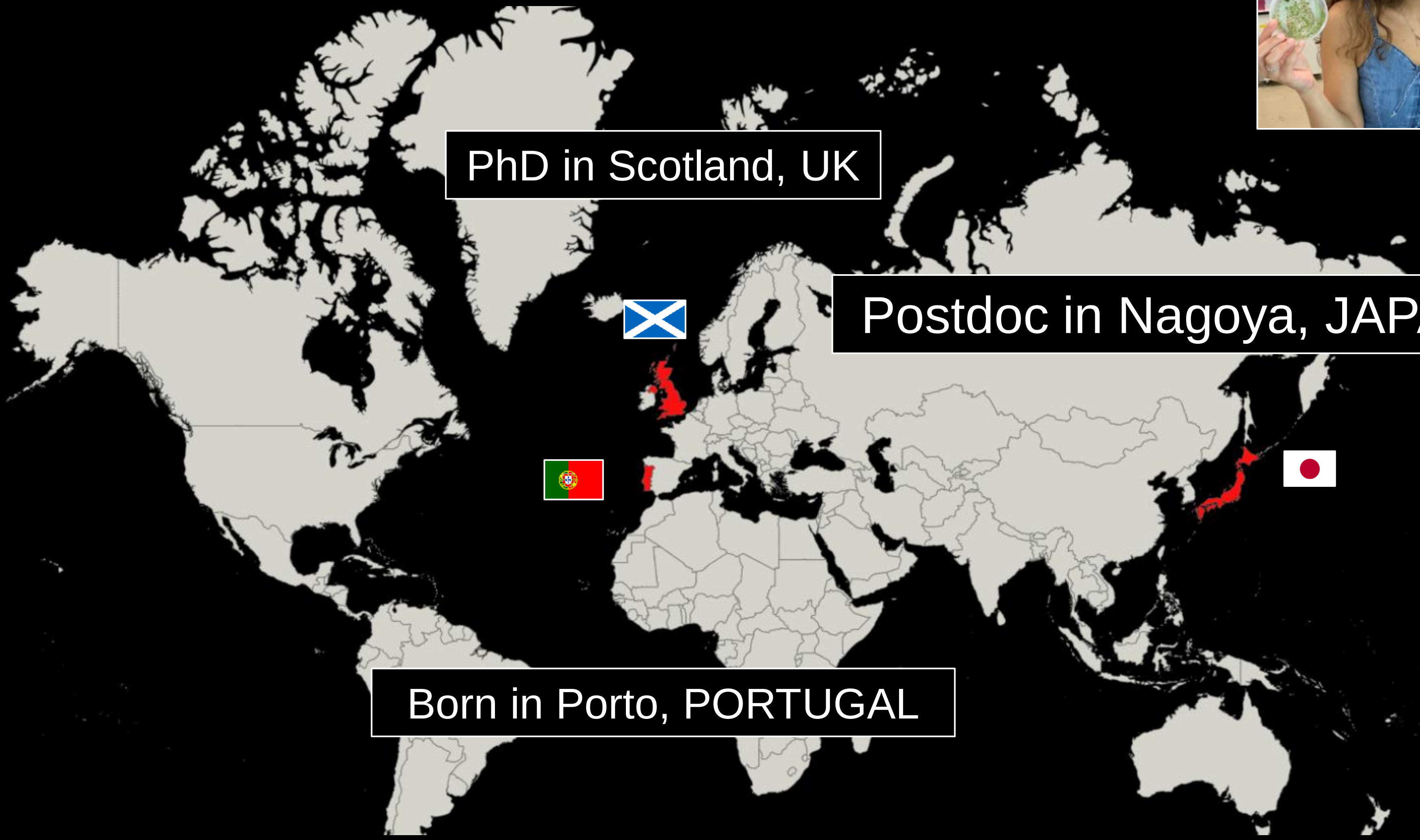
MARIANA COSTA

Postdoctoral researcher

School of Science / Nagoya University

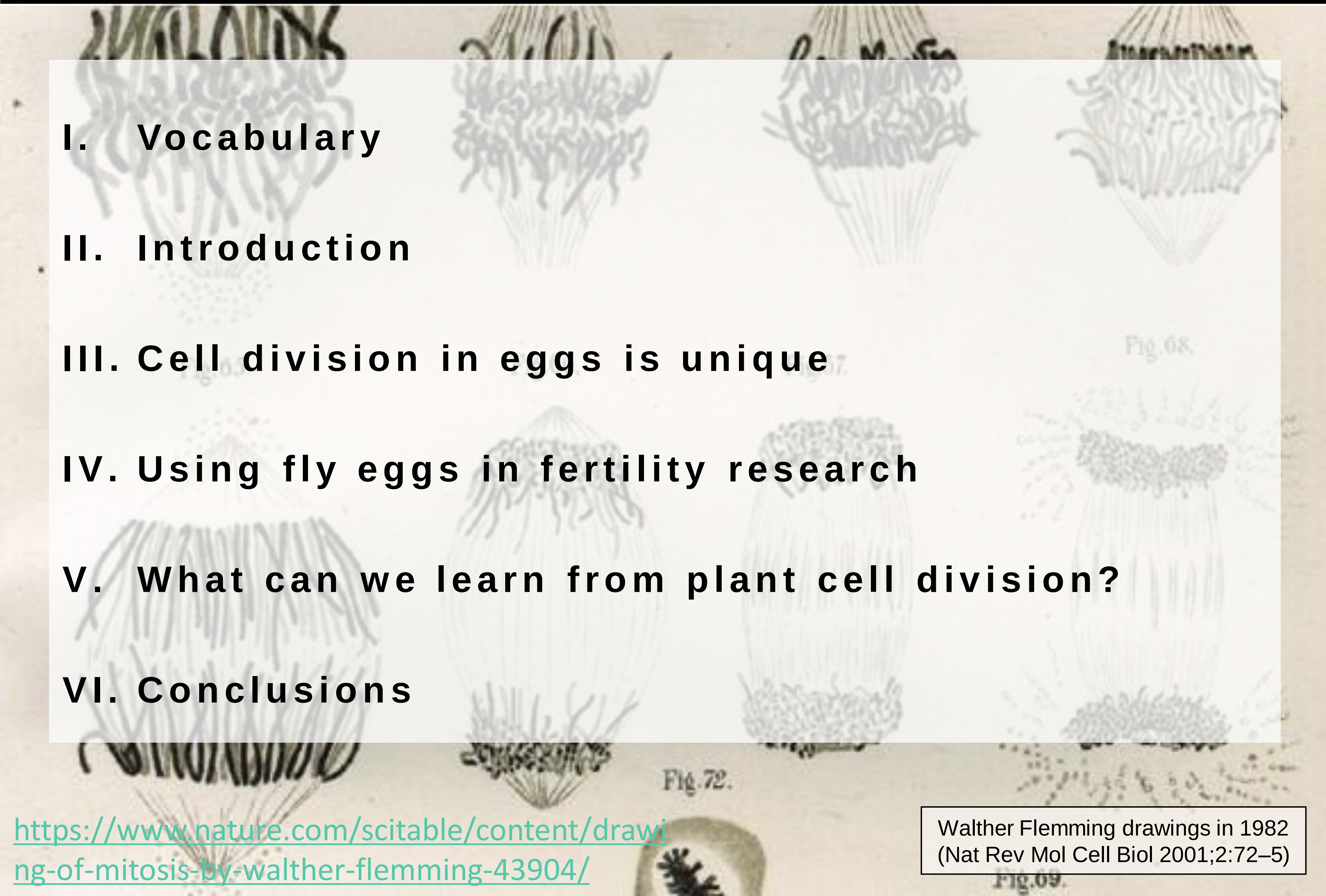
mariana.costa@d.mbox.nagoya-u.ac.jp

A little bit about myself...



SCIENCE CAN TAKE YOU ANYWHERE YOU WANT!

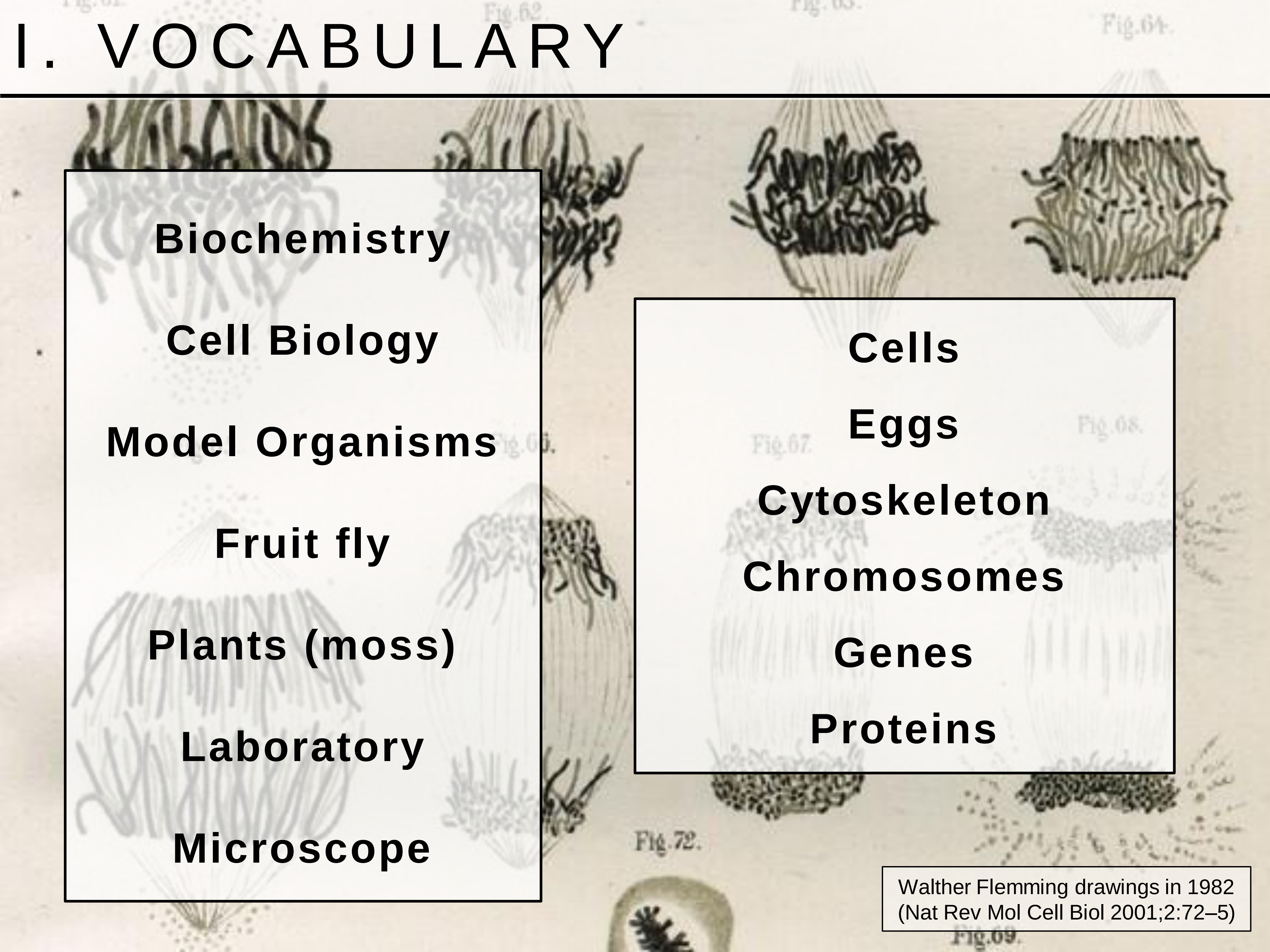
CONTENT



https://www.nature.com/scitable/content/drawing-of-mitosis-by-walther-flemming-43904/

Walther Flemming drawings in 1982
(Nat Rev Mol Cell Biol 2001;2:72–5)

I. VOCABULARY



Biochemistry

Cell Biology

Model Organisms

Fruit fly

Plants (moss)

Laboratory

Microscope

Cells

Eggs

Cytoskeleton

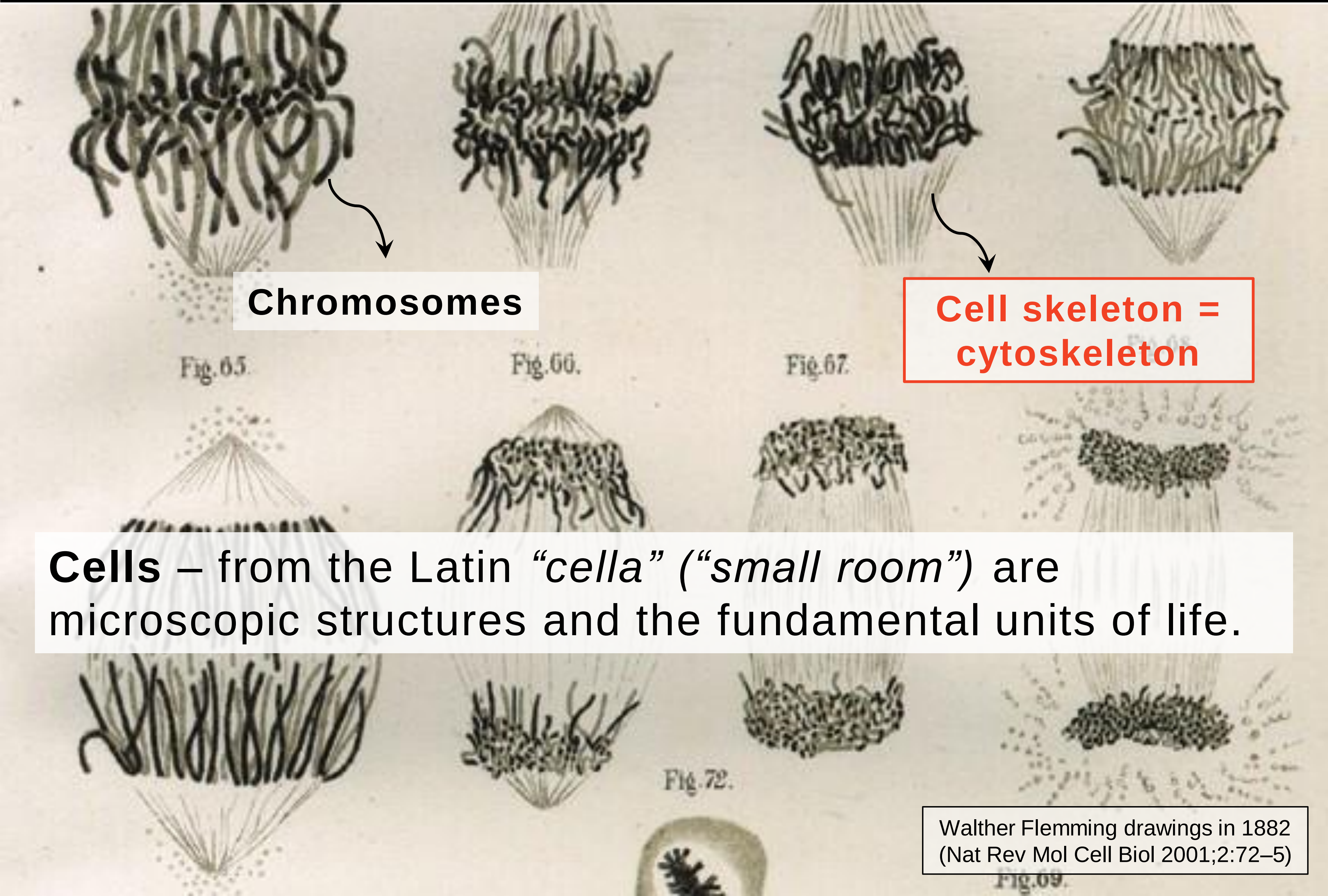
Chromosomes

Genes

Proteins

Walther Flemming drawings in 1982
(Nat Rev Mol Cell Biol 2001;2:72–5)

II. INTRODUCTION



Cells – from the Latin *“cella” (“small room”)* are microscopic structures and the fundamental units of life.

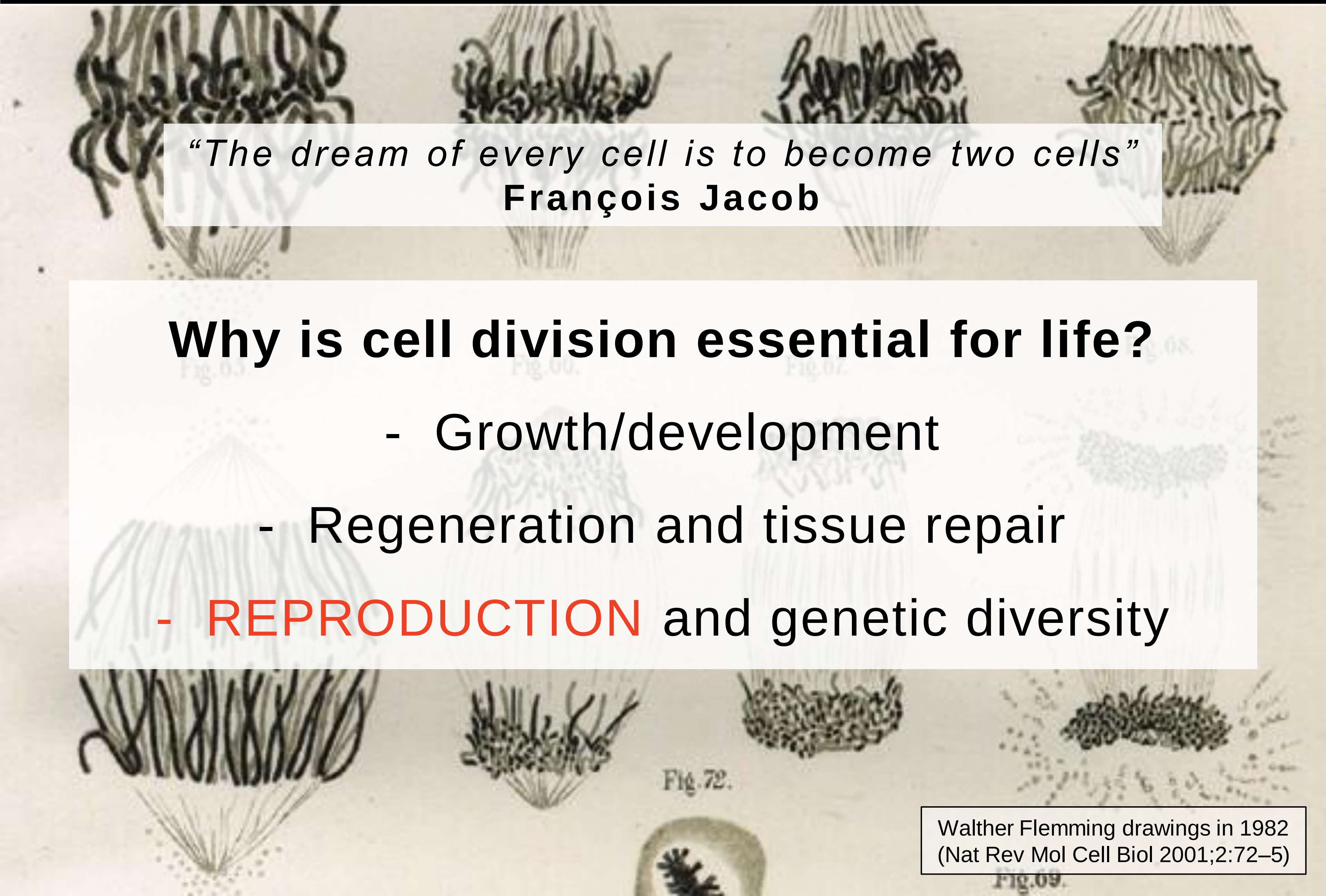
Walther Flemming drawings in 1882
(Nat Rev Mol Cell Biol 2001;2:72–5)

II. INTRODUCTION

"The dream of every cell is to become two cells"
François Jacob

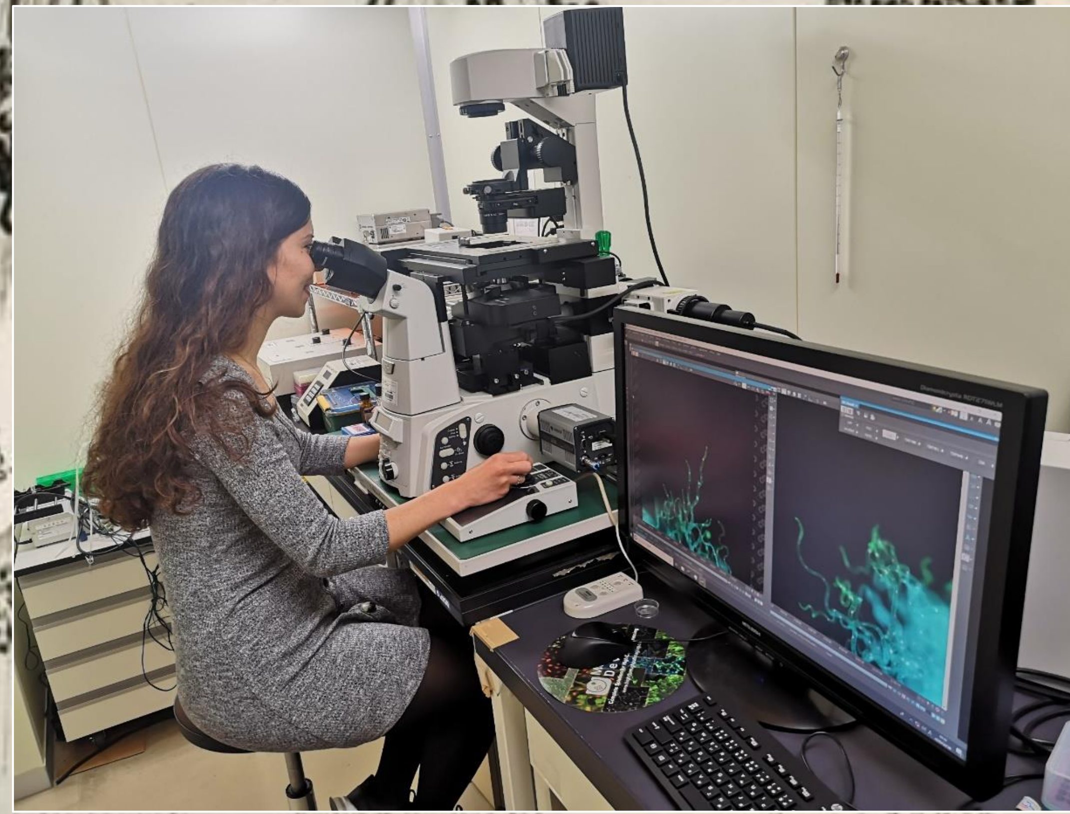
Why is cell division essential for life?

- Growth/development
- Regeneration and tissue repair
- REPRODUCTION and genetic diversity



Walther Flemming drawings in 1982
(Nat Rev Mol Cell Biol 2001;2:72–5)

Applied for a PhD in Cell & Molecular Biology



Walther Flemming drawings in 1982
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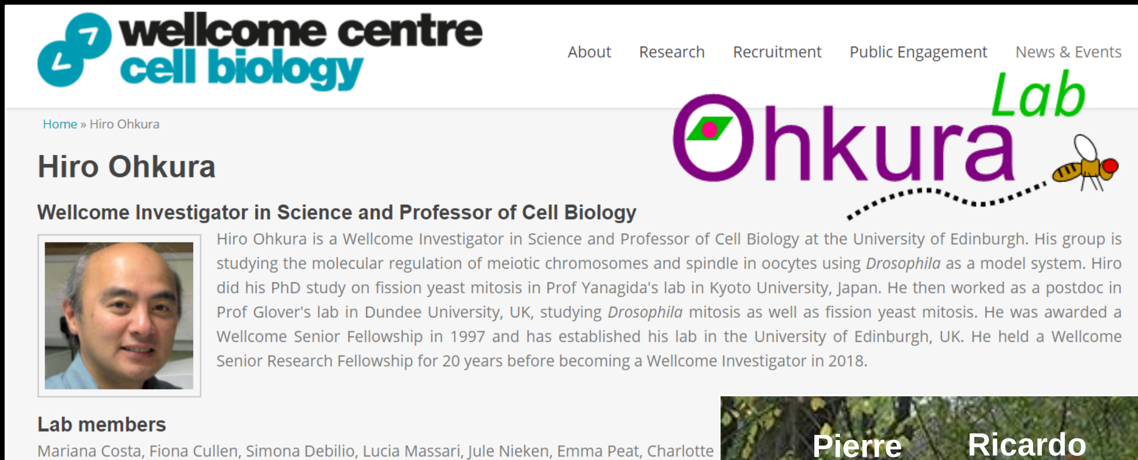
2014-2019 – PhD in Cell & Molecular Biology


wellcome centre cell biology

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Ohkura Lab

Home » Hiro Ohkura

Hiro Ohkura

Wellcome Investigator in Science and Professor of Cell Biology

Hiro Ohkura is a Wellcome Investigator in Science and Professor of Cell Biology at the University of Edinburgh. His group is studying the molecular regulation of meiotic chromosomes and spindle in oocytes using *Drosophila* as a model system. Hiro did his PhD study on fission yeast mitosis in Prof Yanagida's lab in Kyoto University, Japan. He then worked as a postdoc in Prof Glover's lab in Dundee University, UK, studying *Drosophila* mitosis as well as fission yeast mitosis. He was awarded a Wellcome Senior Fellowship in 1997 and has established his lab in the University of Edinburgh, UK. He held a Wellcome Senior Research Fellowship for 20 years before becoming a Wellcome Investigator in 2018.

Lab members

Mariana Costa, Fiona Cullen, Simona Debilio, Lucia Massari, Jule Nieken, Emma Peat, Charlotte

THE UNIVERSITY of EDINBURGH

https://www.ed.ac.uk/files/atoms/files/chapter_one_-_logo_guide.pdf

https://rupress.org/jcb/article/218/9/2854/120953/The-molecular-architecture-of-the-meiotic-spindle

2014 – Moved to Scotland and joined the OHKURA lab as a PhD student

III. Cell division in eggs is UNIQUE

MOTHER

46
chromosomes

♀

FATHER

♂

46
chromosomes

+

23
chromosomes

EGG

SPERM

23
chromosomes

EMBRYO

46
chromosomes

III. Cell division in eggs is UNIQUE

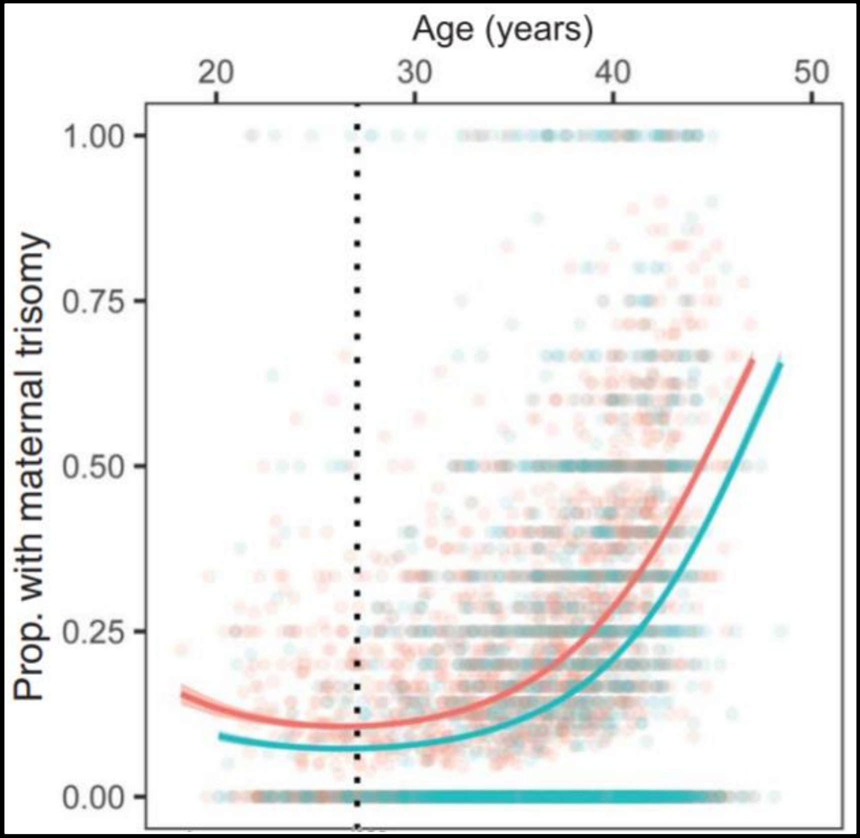
- Women are born with a limited reserve of eggs
- Quality/lifespan of humans increased but women are not more fertile
- The “quality” of eggs decreases with women age
- Women have children later in life
- Women between 30-40 years old: higher chances of miscarriages and congenital abnormalities.

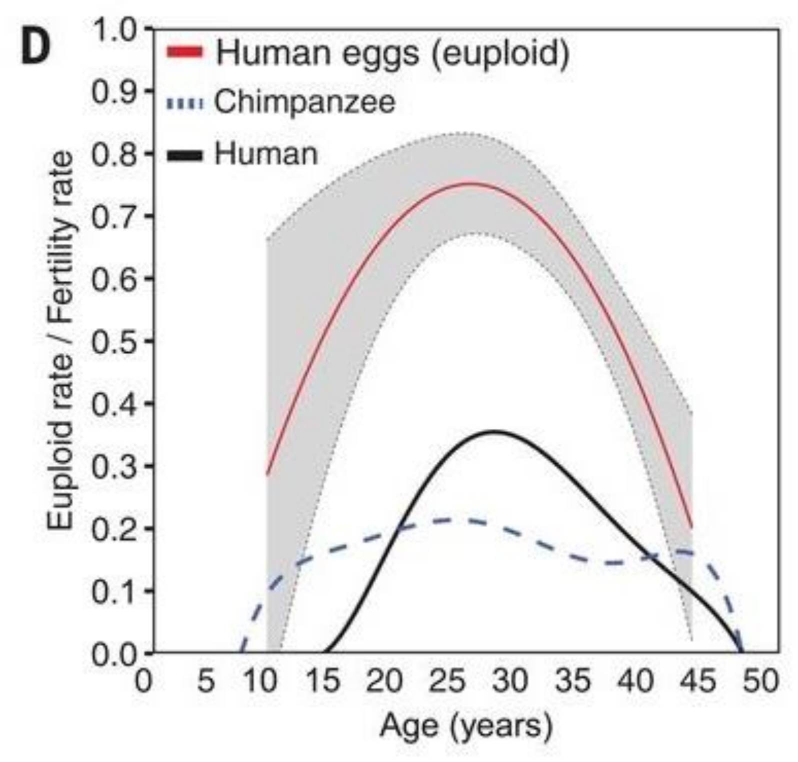
F. Ferri’s Color Atlas and Text of Clinical Medicine, 2nd ed. Philadelphia, PA: Elsevier; 2009

Human egg: Mio, Y. et al. (2012) *J Assist Reprod Genet, 29*(9), 951-956
Info: Webster, A., & Schuh, M. (2017). *Trends Cell Biol, 27*(1), 55-68

III. Cell division in eggs is UNIQUE

- Errors in cell division are more frequent in eggs than in other cells
- Egg cell division lasts for decades → higher chance to accumulate errors
- Errors in cell division can cause infertility, miscarriages and birth defects → Important to study cell division in eggs!



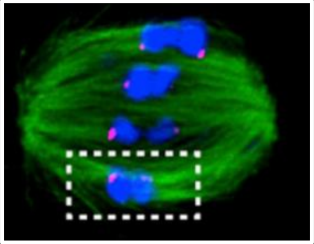


Gruhn, J.R et al. (2019). *Science*. 365:1466-1469.

IV. Using fly eggs in fertility research

It is not easy to study human eggs…

HUMAN

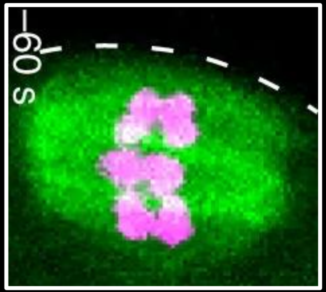


Zielinska, A. P et al. (2019).
Curr Biol, 29(22), 3749-3765 e3747.

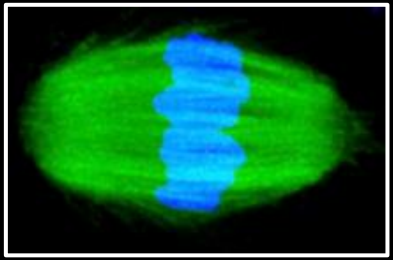
Worm

https://theconversation.com/animals-in-research-c-elegans-roundworm-14163

Laband, K. et al. (2017)
Nat Commun, 8(1), 1499

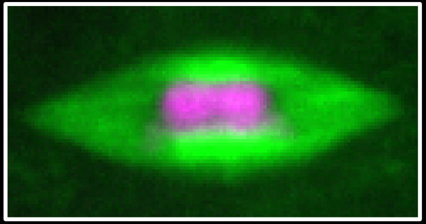


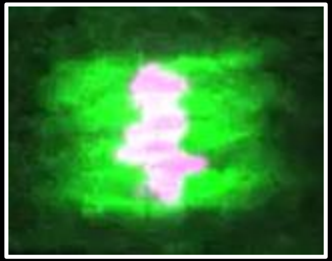
Mouse



https://www.mpg.de/10973935/husbandry-breeding

Fruit fly





Goshima lab

Plants (moss)

IV. Using fly eggs in fertility research

We are all similar at the CELLULAR level

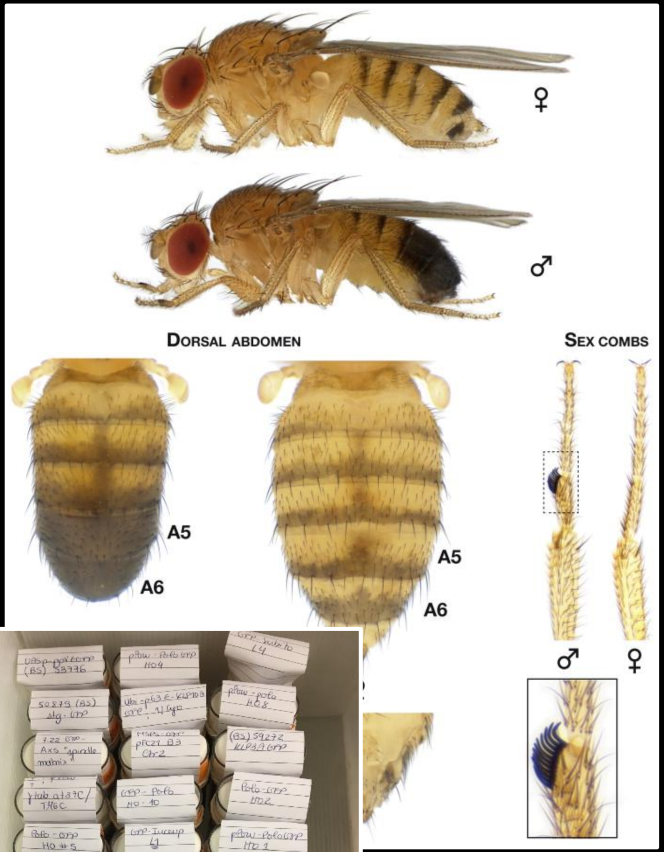
There is so much we can learn from **experimental organisms…**

… that could be applied to HUMAN research in the future!

IV. Using fly eggs in fertility research

<u>ADVANTAGES OF USING FLIES:</u>

- Easy to keep and handle
- Short generation time: HUNDREDS OF EGGS
- 77% of human disease genes have a similar match in fruit flies.
- You can get a Nobel prize !

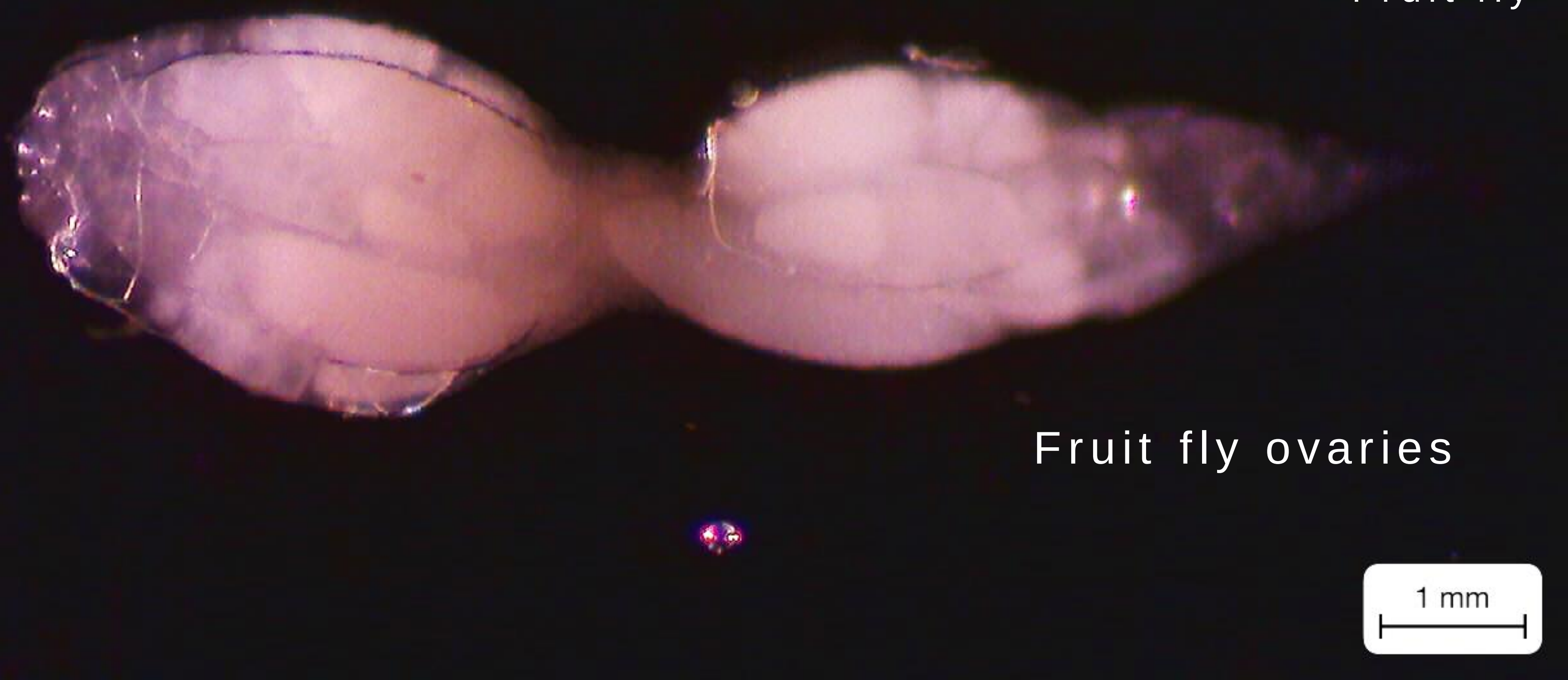


Sylwester Chyb and Nicolas Gompel, in Atlas of Drosophila Morphology, 2013

https://droso4schools.wordpress.com/why-fly/

IV. Using fly eggs in fertility research

Fruit fly



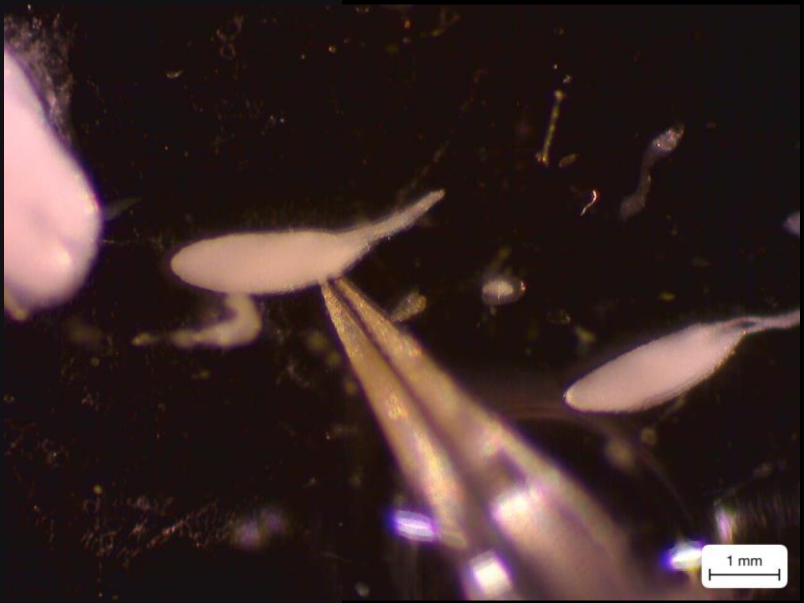
Fruit fly ovaries

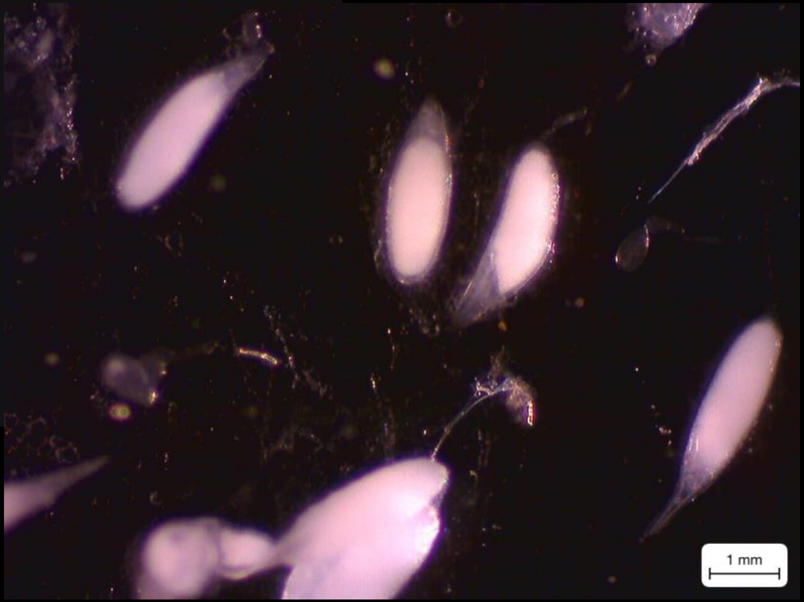
IV. Using fly eggs in fertility research

HOW TO DISSECT FLY OVARIES

IV. Using fly eggs in fertility research

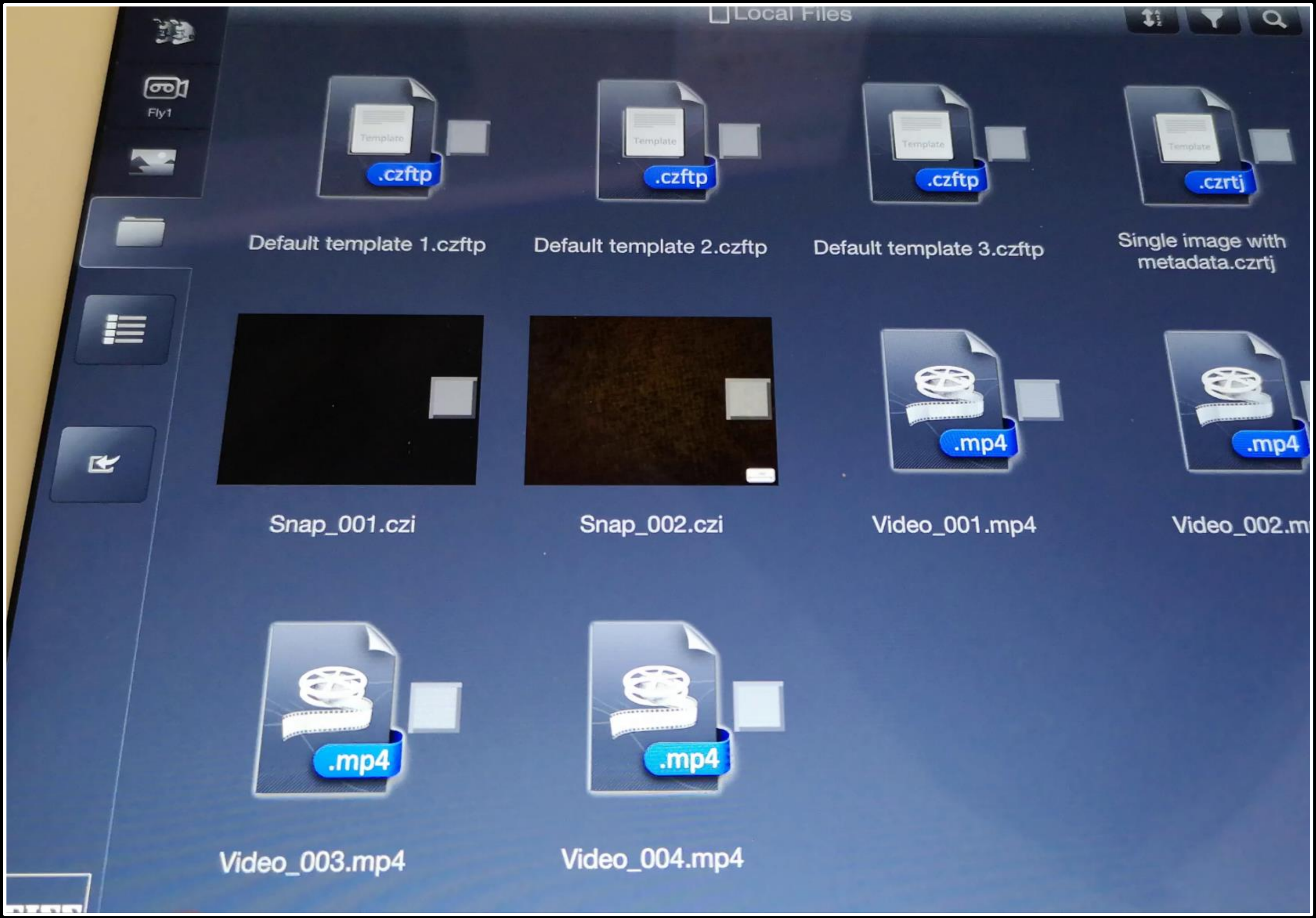
IV. Using fly eggs in fertility research





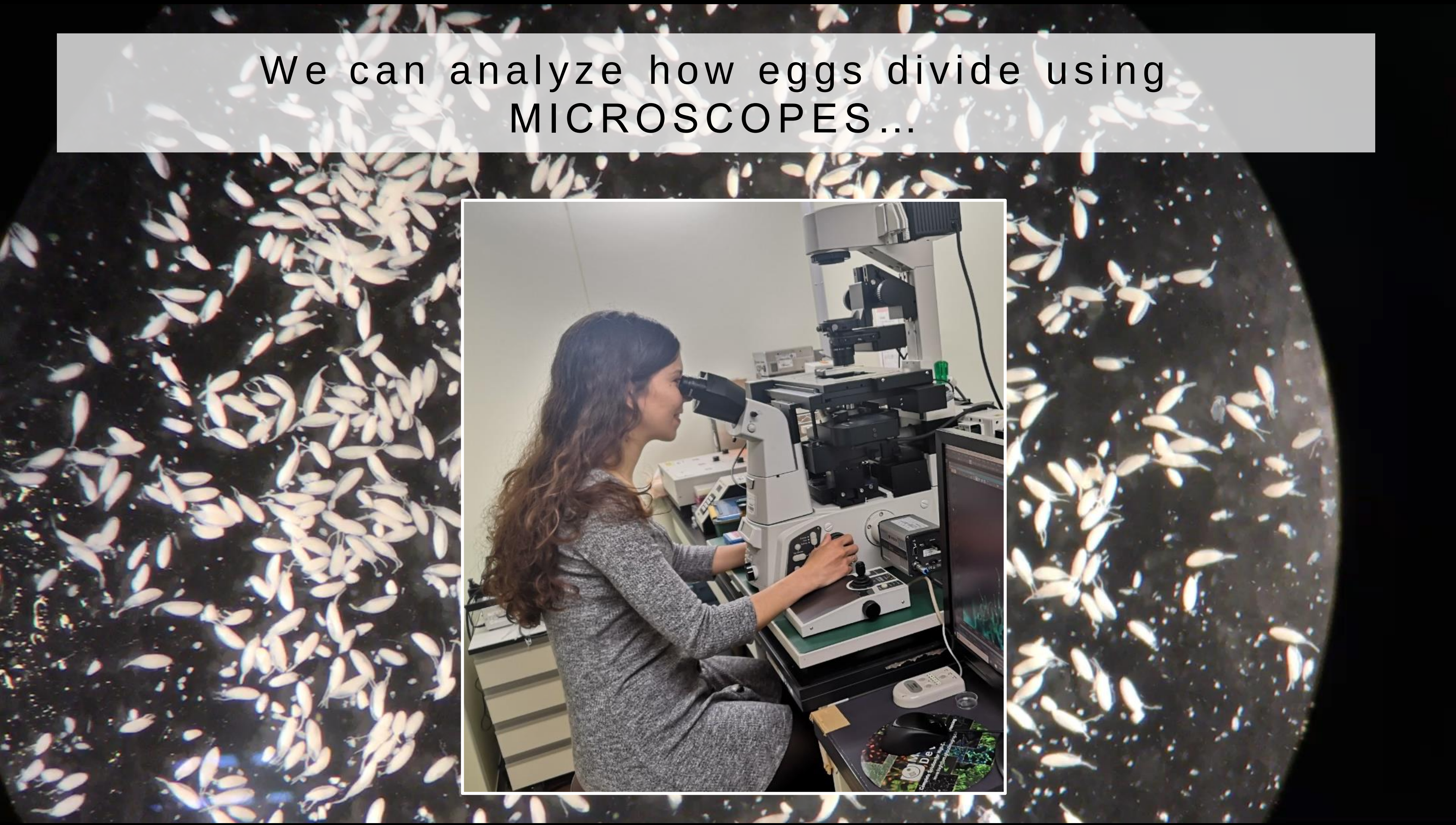
HOW TO DISSECT FLY OVARIES

IV. Using fly eggs in fertility research

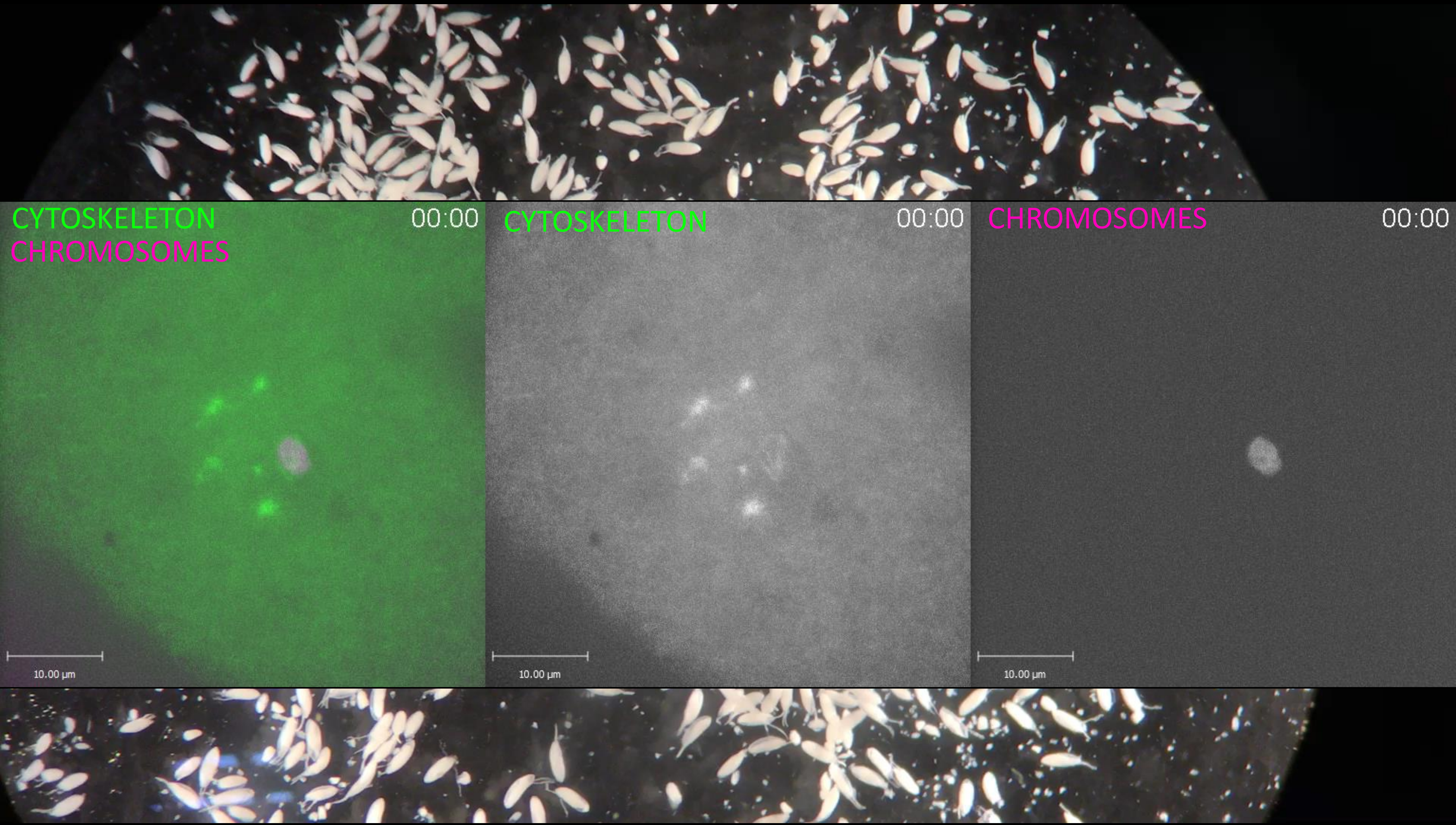


IV. Using fly eggs in fertility research

We can analyze how eggs divide using MICROSCOPES…



IV. Using fly eggs in fertility research



2018/2019 – Finish PhD + publish paper

JCB Journal of Cell Biology

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Volume 218, Issue 9
2 September 2019

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Article Contents

Report | July 05 2019

The molecular architecture of the meiotic spindle is remodeled during metaphase arrest in oocytes

Mariana F.A. Costa, Hiroyuki Ohkura

+ Author and Article Information

Check for updates

J Cell Biol (2019) 218 (9): 2854–2864. https://doi.org/10.1083/jcb.201902110 **Article history**

Review History

Split-Screen Views ⌄ PDF Share ⌄ Tools ⌄

Before fertilization, oocytes of most species undergo a long, natural arrest in metaphase. Before this, prometaphase I is also prolonged, due to late stable kinetochore–microtubule attachment. How oocytes stably maintain the dynamic spindle for hours during these periods is poorly understood. Here we report that the bipolar spindle changes its molecular architecture during the long in *Drosophila melanogaster* oocytes. By generating transgenic flies

Waiting for www.trendmd.com...

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2 September 2019

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All Issues
Cover Image
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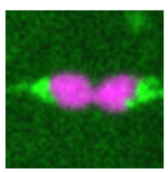


The molecular architecture of the meiotic spindle is remodeled during metaphase arrest in oocytes

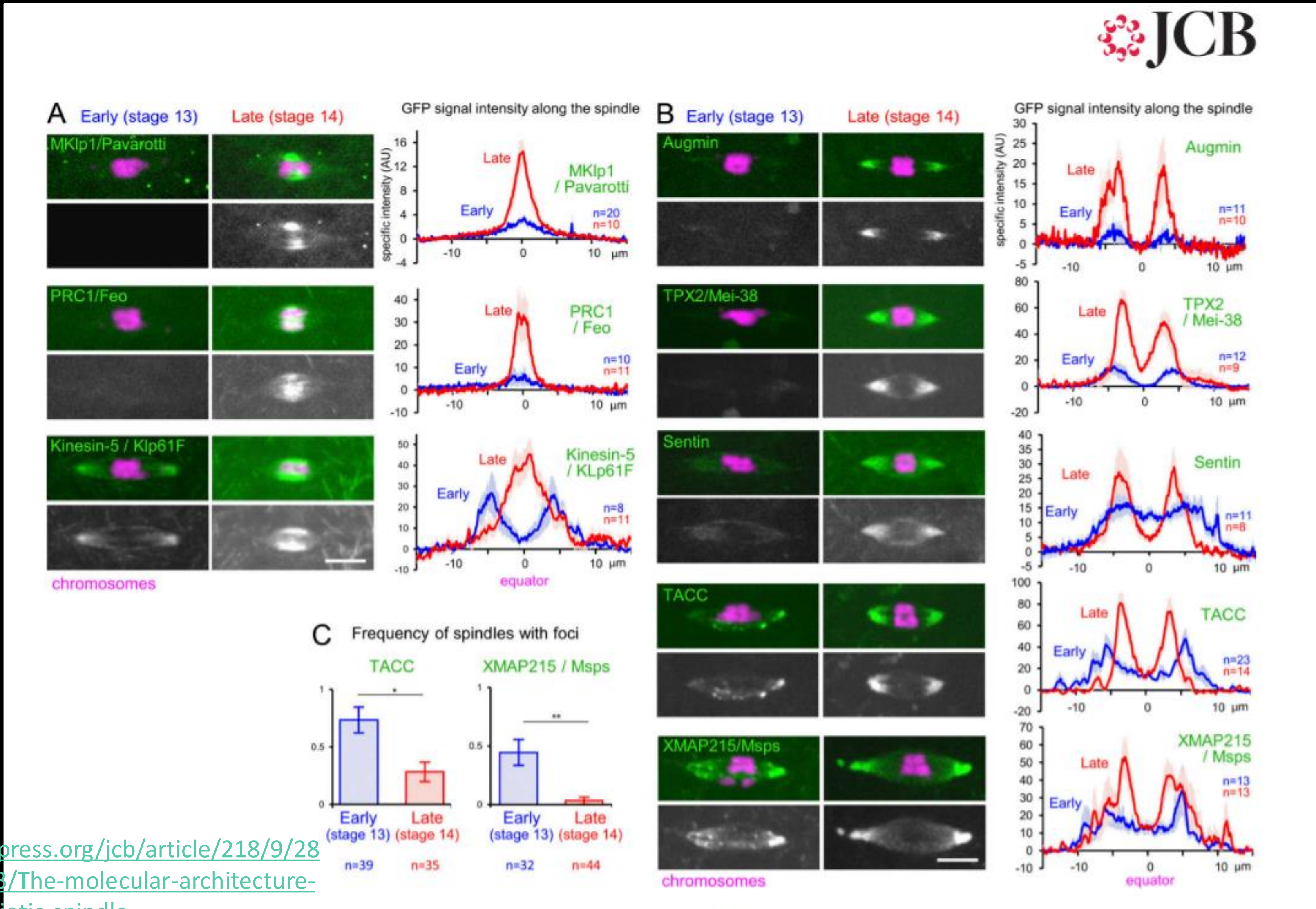
Mariana F.A. Costa, Hiroyuki Ohkura

Costa and Ohkura provide new insight into how the bipolar spindle is stably maintained during metaphase arrest in oocytes. They find that many important spindle proteins change their localization during arrest in *Drosophila* oocytes and show the importance of these changes in stabilizing the spindle during arrest.

View Article

https://rupress.org/jcb/article/218/9/2854/120953/The-molecular-architecture-of-the-meiotic-spindle

2018/2019 – Finish PhD + publish paper



https://rupress.org/jcb/article/218/9/2854/120953/The-molecular-architecture-of-the-meiotic-spindle

Figure 3. **Proteins that accumulate to the spindle equator or poles in late oocytes. (A and B)** Proteins accumulate to the spindle equator (A) or poles (B) in late oocytes. The data are presented as in Fig. 2. **(C)** The frequency of spindles with Msps or TACC foci; mean ± SEM. *, $P < 0.05$; **, $P < 0.01$. AU, arbitrary units.

2018/2019 – Finish PhD + publish paper

From thesis submission to graduation…

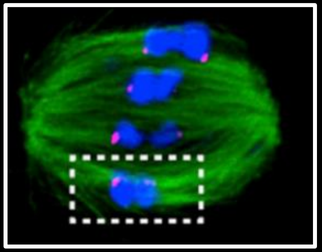
McEwan Hall, Edinburgh (July 2018)

"The important thing is to never stop questioning" **Albert Einstein**

V. What can we learn from plants?

The cytoskeleton in plant cells and animal eggs is very similar!

HUMAN



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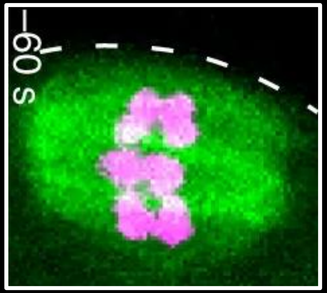
Worm



Laband, K. et al. (2017)
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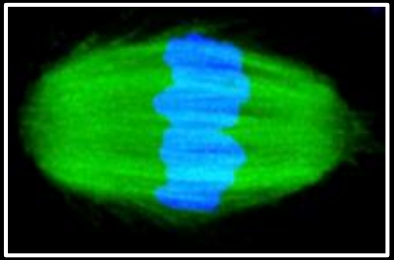
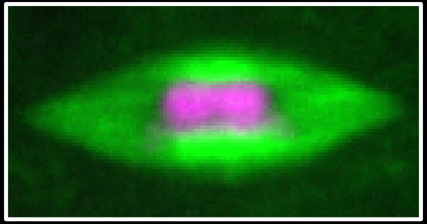
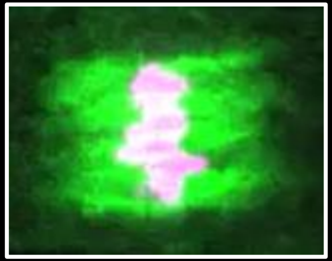
Mouse



Fruit fly

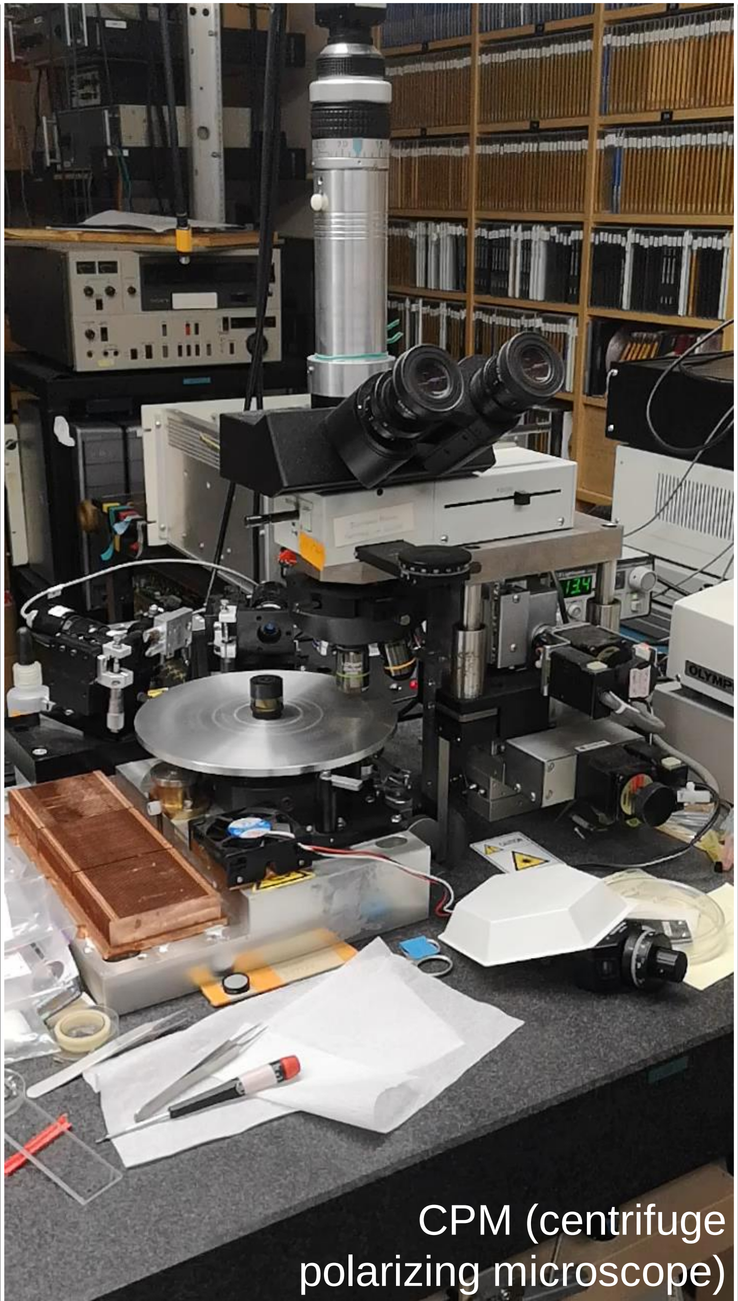


Plants
(moss)



Goshima lab

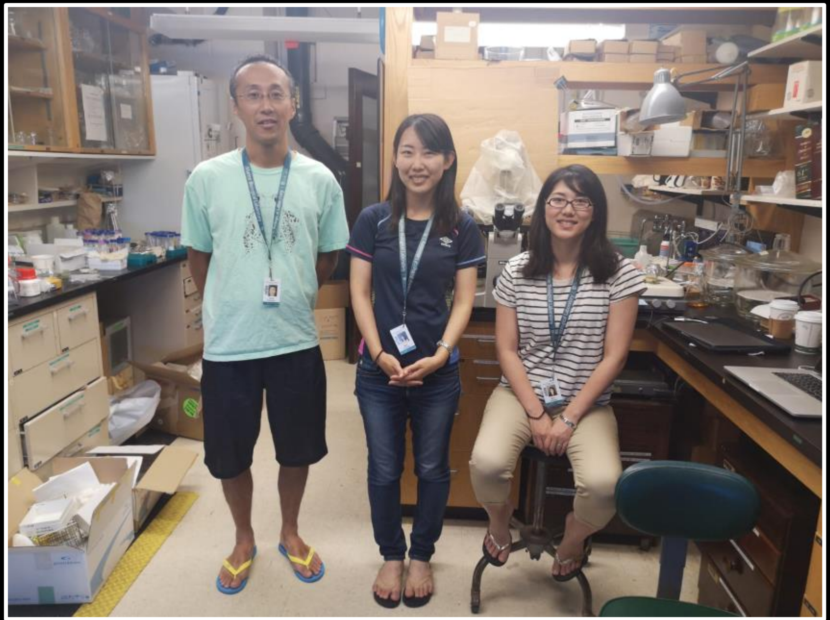
V. What can we learn from plants?

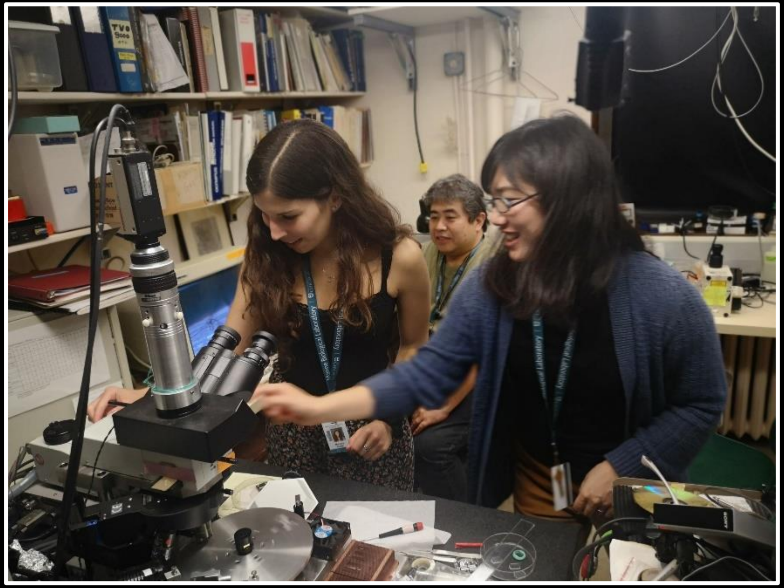


August 2019 (MBL, Woods Hole)
Meet the Goshima lab

V. What can we learn from plants?

August 2019 (MBL, Woods Hole)
Meet the Goshima lab





"Moss team" – Moe Yamada and Mari Yoshida

V. What can we learn from plants?

USING MOSS AS A PLANT MODEL SYSTEM:

- Genome is sequenced
- Efficient genetic tools to make mutants
- High resolution imaging
- Animal cytoskeleton genes are present in moss and can be studied!

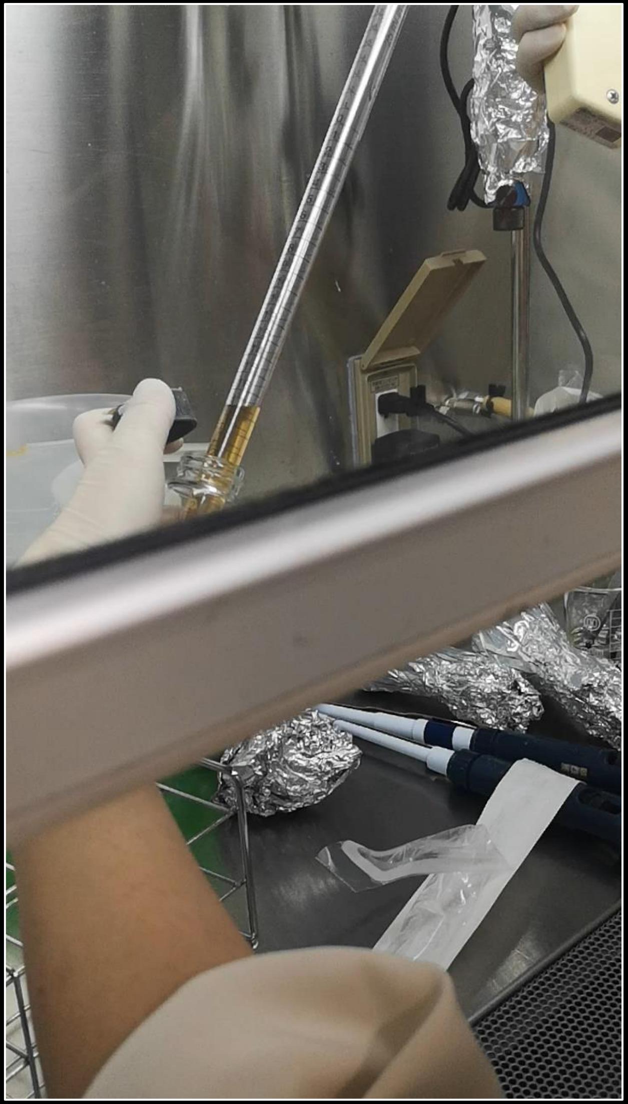
SEPTEMBER 2019

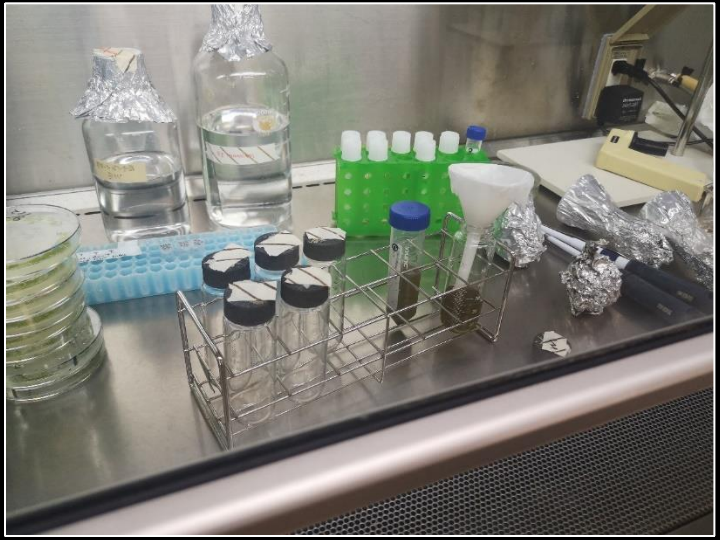
Joined the Goshima lab as a postdoctoral researcher

V. What can we learn from plants?

V. What can we learn from plants?

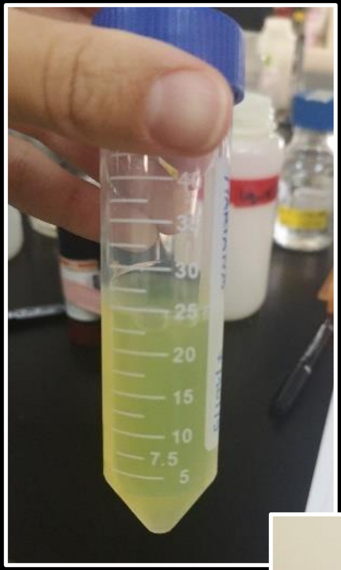
Cell Biology and genetics – manipulate genes in plant cells

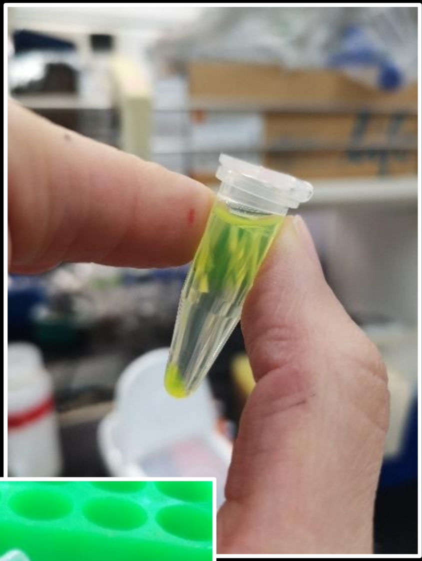




V. What can we learn from plants?

BIOCHEMISTRY solves biological problems combining chemistry and biology

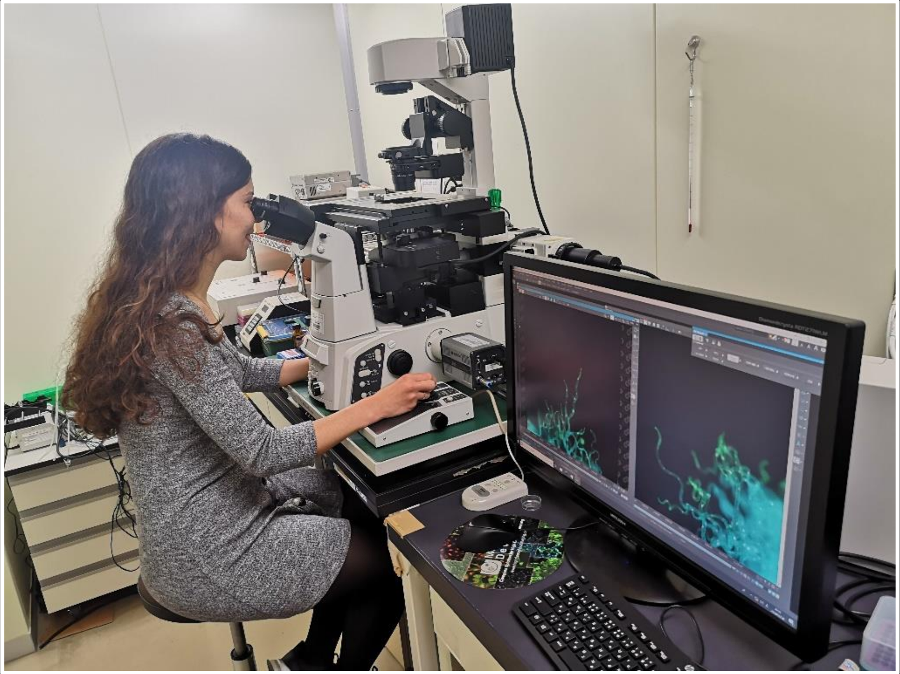


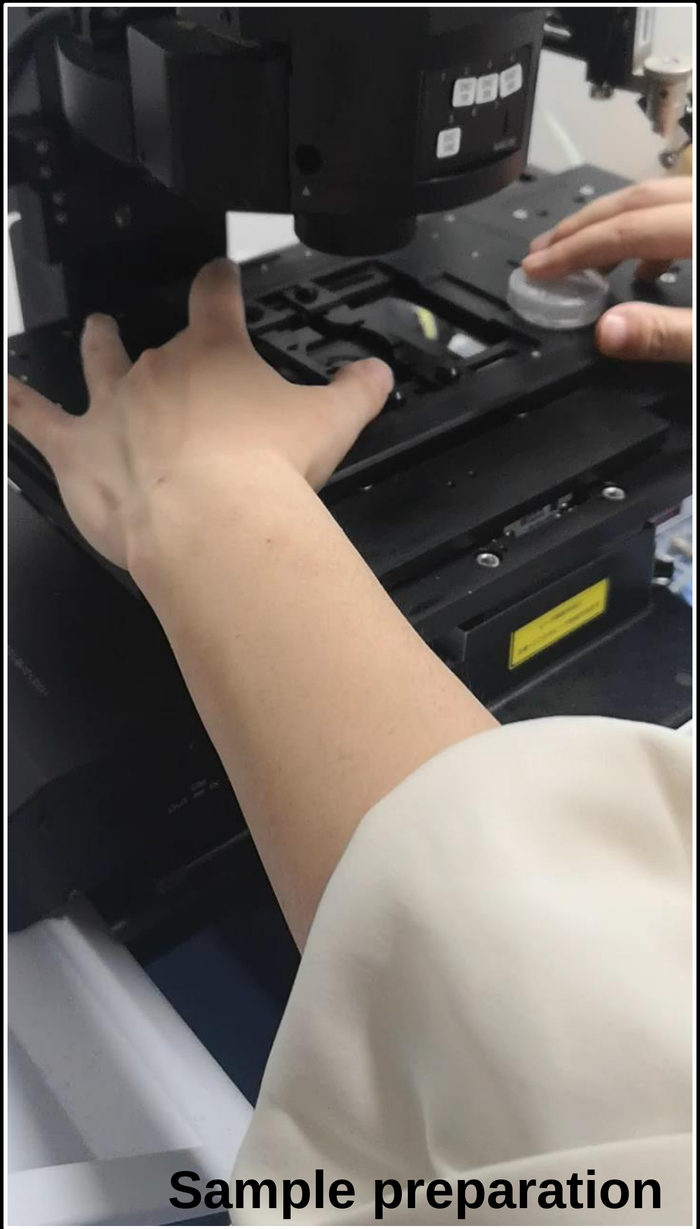


V. What can we learn from plants?

MICROSCOPY:

We can image cells and proteins!



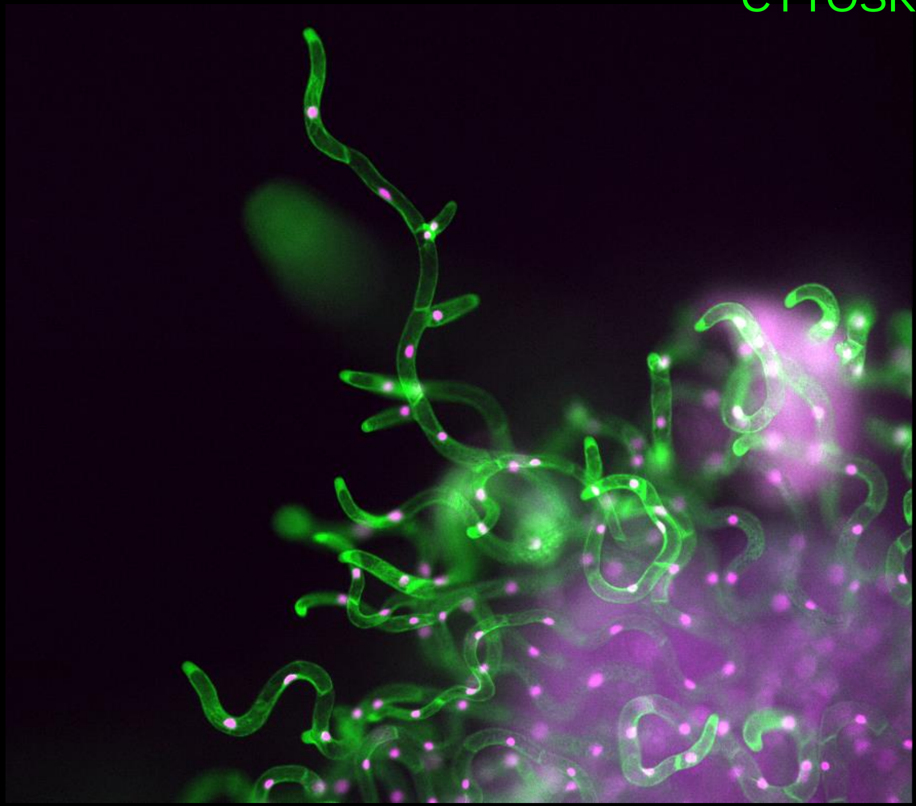


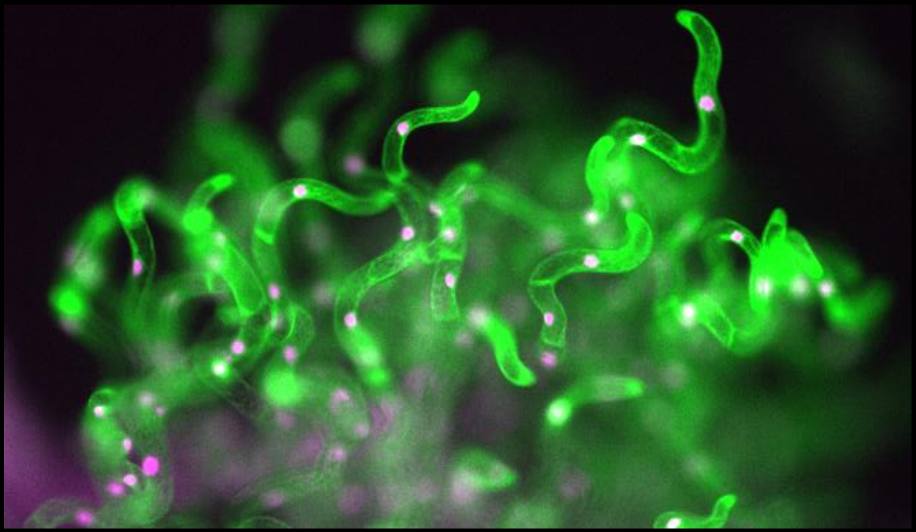
Sample preparation

V. What can we learn from plants?

MICROSCOPY: We can take pictures of the plants using “coloured markers”

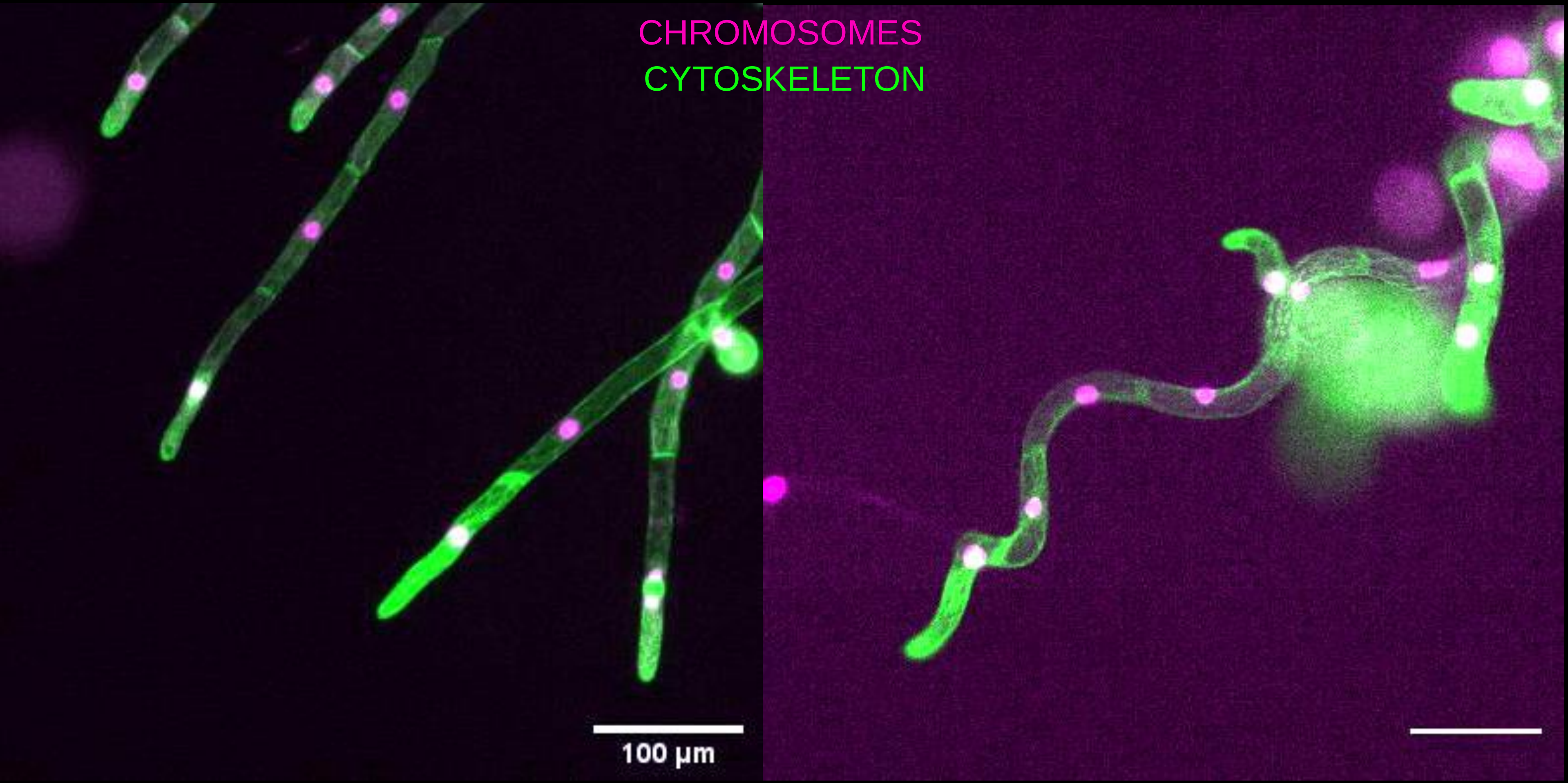
CHROMOSOMES
CYTOSKELETON





V. What can we learn from plants?

MICROSCOPY: We can make videos of the plants growing and visualize cell division



Normal

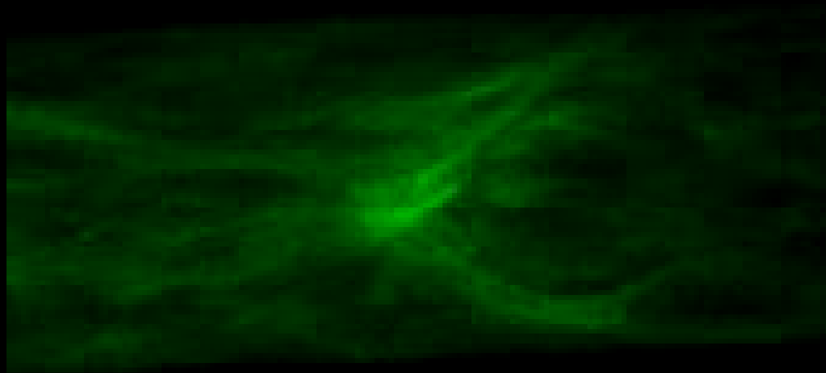
Abnormal (mutant!)

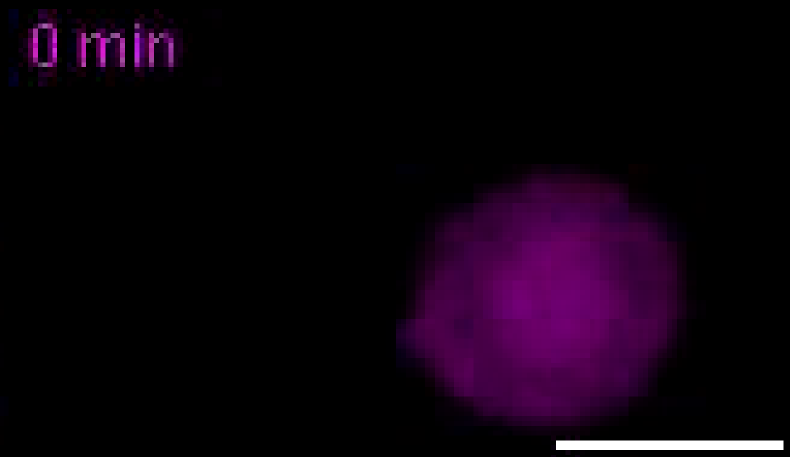
V. What can we learn from plants?

CHROMOSOMES
CYTOSKELETON

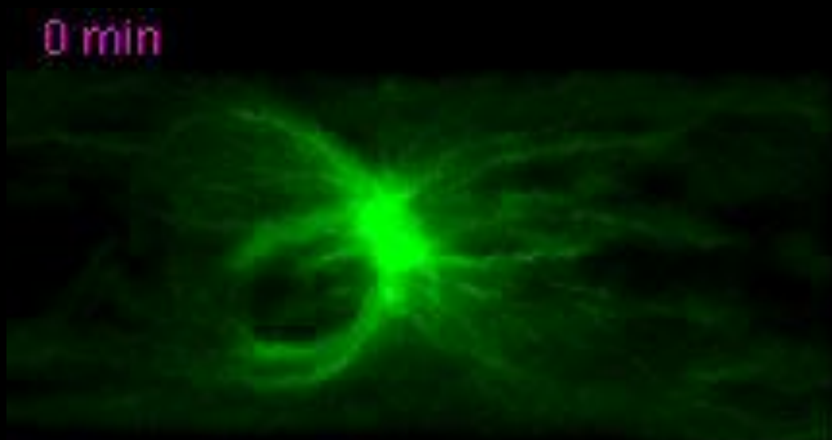
ZOOM IN THE PLANT → CELL

Normal



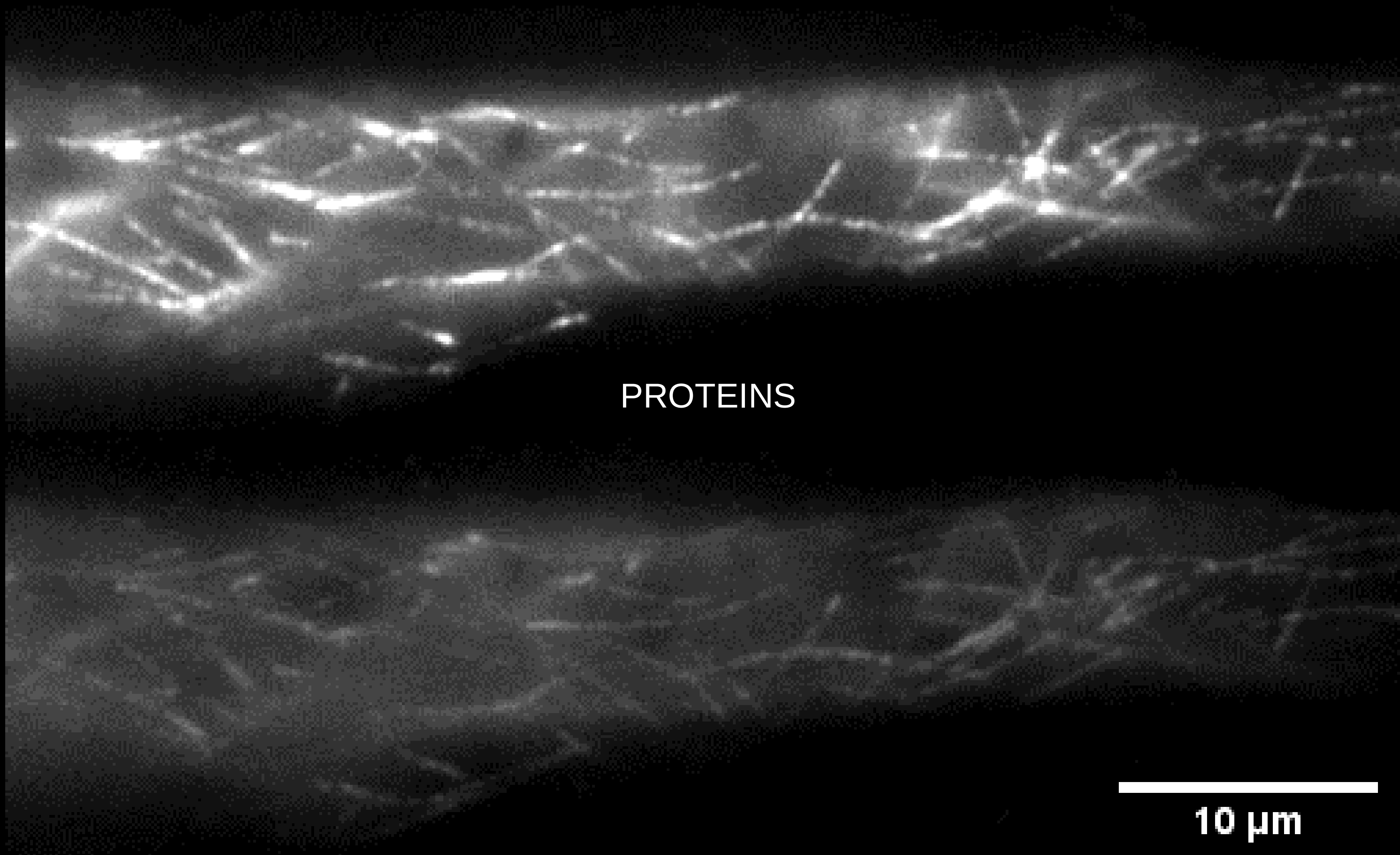


Abnormal (mutant!)



V. What can we learn from plants?

ZOOM IN EVEN MORE → PROTEINS



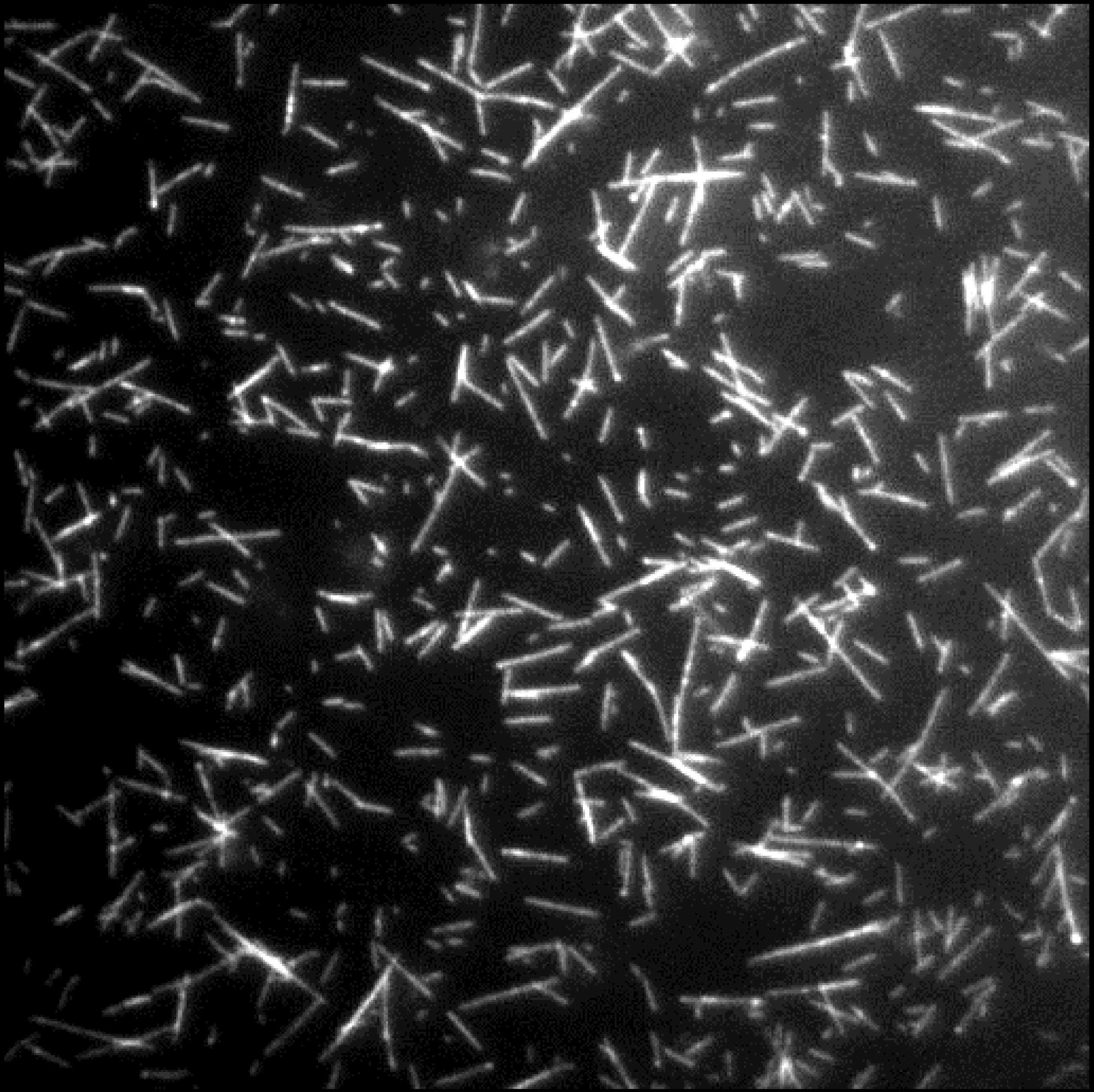
CYTOSKELETON

V. What can we learn from plants?

MIX THE "SKELETON OF CELLS" + PROTEINS REMOVED FROM CELL

↓

Reconstitution of cell behaviour outside the cell!



… TO BE CONTINUED

VI. CONCLUSIONS

✓ Cell division is essential for life

✓ Cell division in eggs is unique, lasts for several decades and therefore is error-prone

✓ Human eggs are not easily available for research

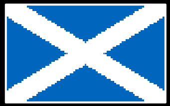
✓ Experimental organisms are essential for research

✓ The "cytoskeleton" of flies and plants is similar to that in eggs

✓ We can use many organisms to answer human biology questions

At the cellular level, we all have similarities…

A C K N O W L E D G M E N T S



Prof Hiro Ohkura – PhD supervisor

Pedro Silva

Liudmila Zhaunova

Pierre Romé

Fiona Cullen

Robin Beaven

Manuel Breuer

Ricardo Bastos

(All other present/ past members of the Ohkura lab)

Prof Gohta Goshima – Postdoc supervisor

Moe Yamada

Peishan Yi

Tomoya Edzuka

Mari Yoshida

Elsa Amelia Tungadi

Juyoung Kim

Kenta Tsuchiya

Rie Inaba

Miki Ueda

Kyoko Zembutsu

"Somewhere, something incredible is waiting to be known"

Carl Sagan