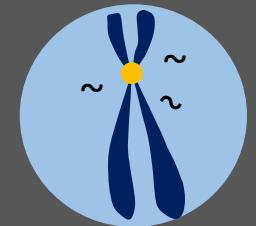


# Cell division requires a balanced level of non-coding RNA from the centromere



港大細胞生物學家發現細胞分裂新機制：  
染色體需「著絲粒RNA」維持其穩定性 避免細胞分裂出錯

**Press Conference: 2019 May 7**

**Dr. Yick Hin LING, Postdoctoral Fellow**

**Dr. Karen Wing Yee YUEN, Assistant Professor**

**School of Biological Sciences  
The University of Hong Kong**



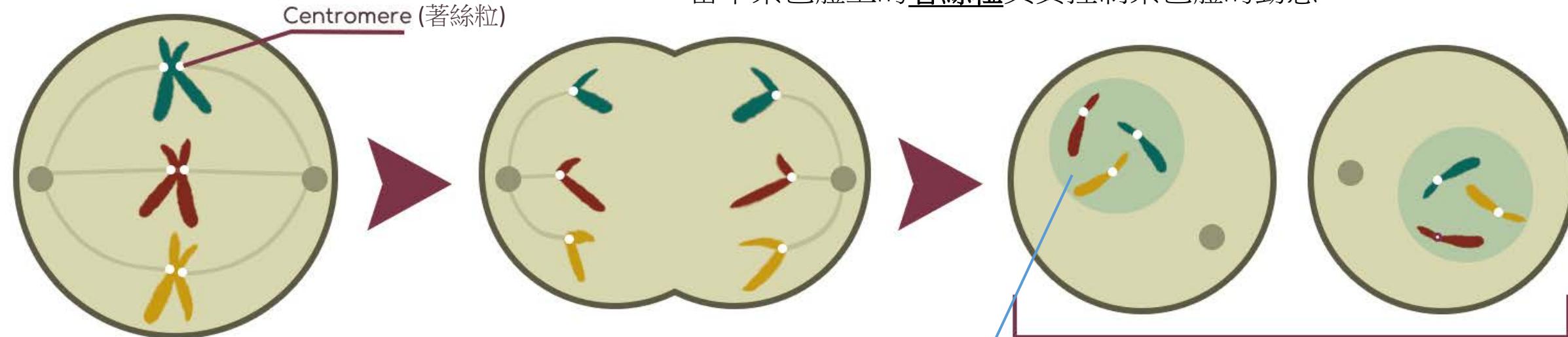
Faculty of Science  
THE UNIVERSITY OF HONG KONG



**HKU SCIENCE**  
*Oak Anniversary*  
明德於櫟 格物以理

# CELL DIVISION (細胞分裂)

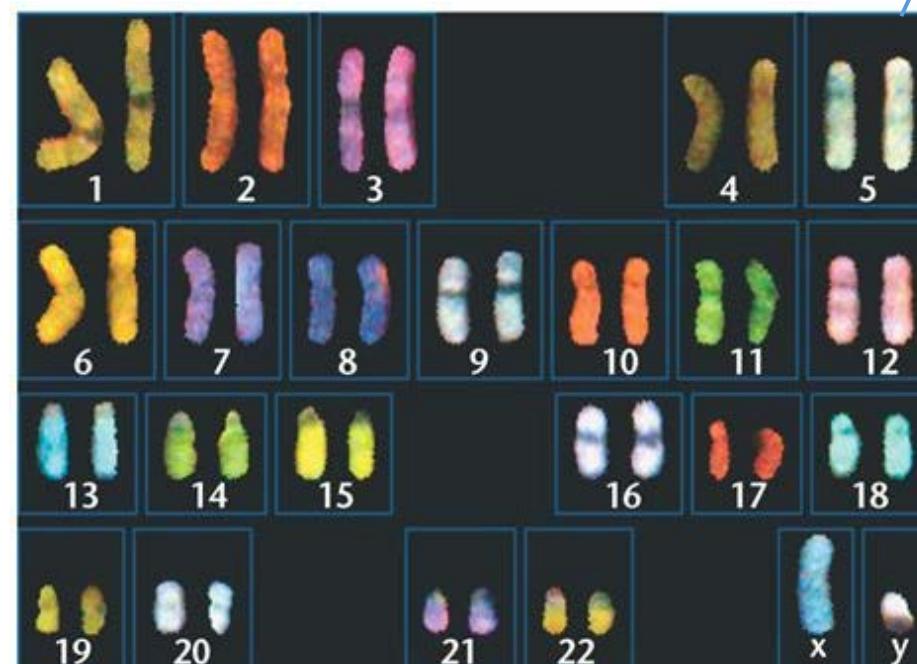
在細胞分裂時，我們的細胞需要準確地分配其染色體到子細胞中。當中染色體上的著絲粒負責控制染色體的動態。



METAPHASE

ANAPHASE

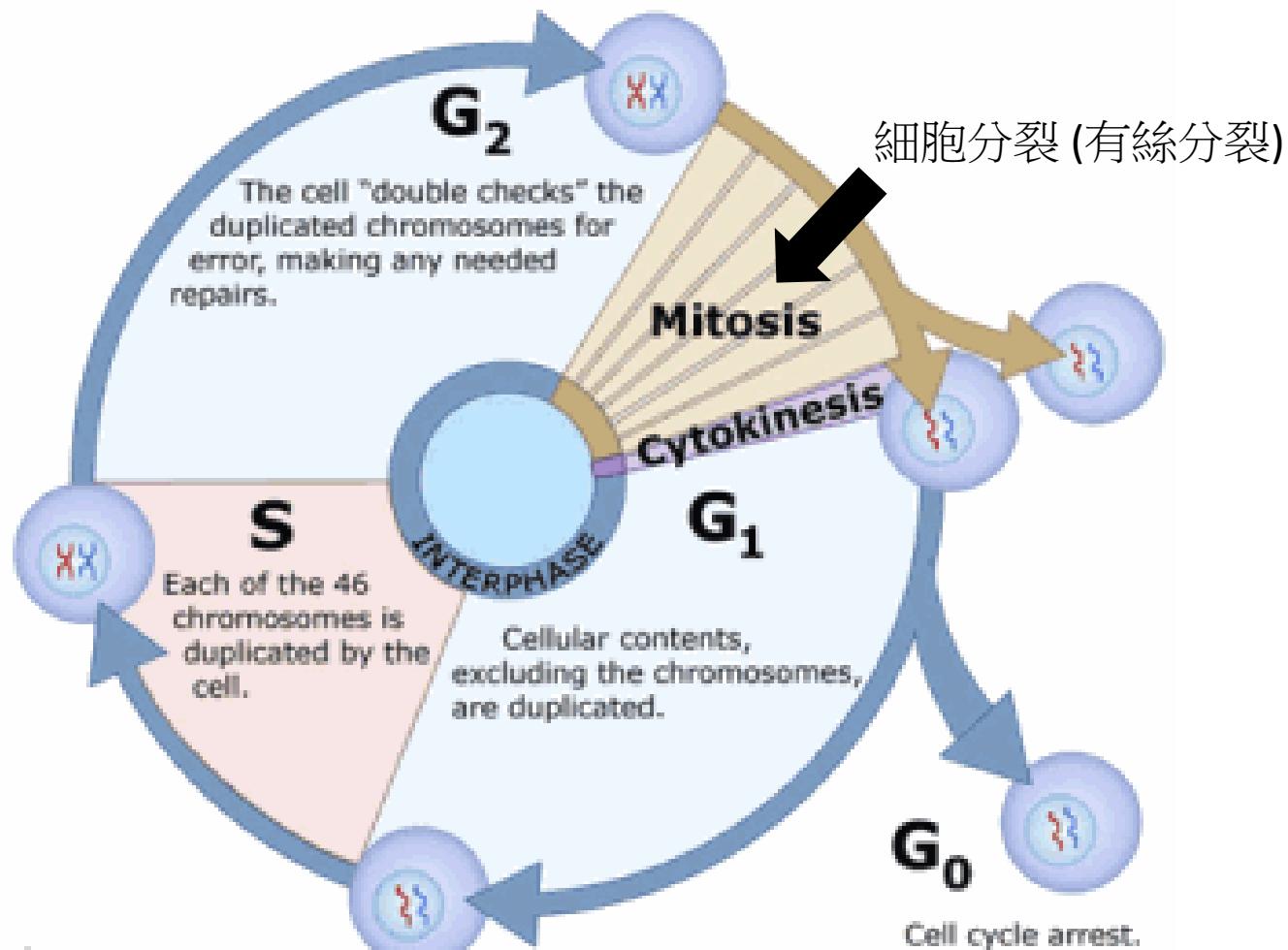
DAUGHTER CELLS  
(子細胞)



Human cells have 23 pairs of chromosomes(染色體)

# Cell division (Mitosis) is part of the cell cycle

細胞分裂是細胞週期中的一個階段

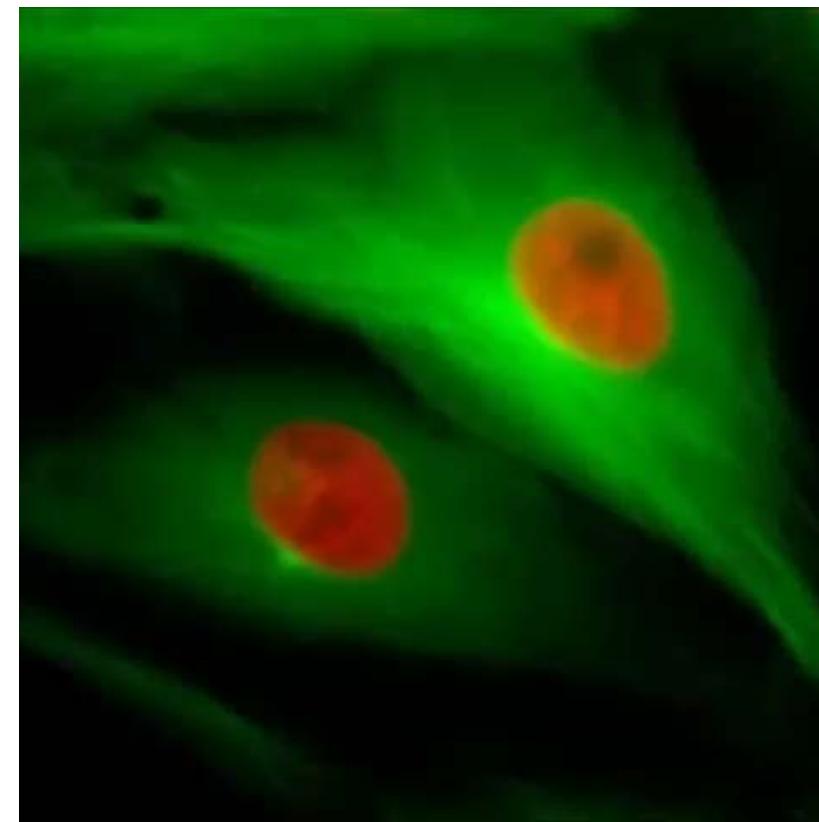


© Clinical Tools, Inc.

**Human**

<https://www2.le.ac.uk/projects/vgec/highereducation/topicscellcycle-mitosis-meiosis>

## Cell division/Mitosis (Mitotic phase)

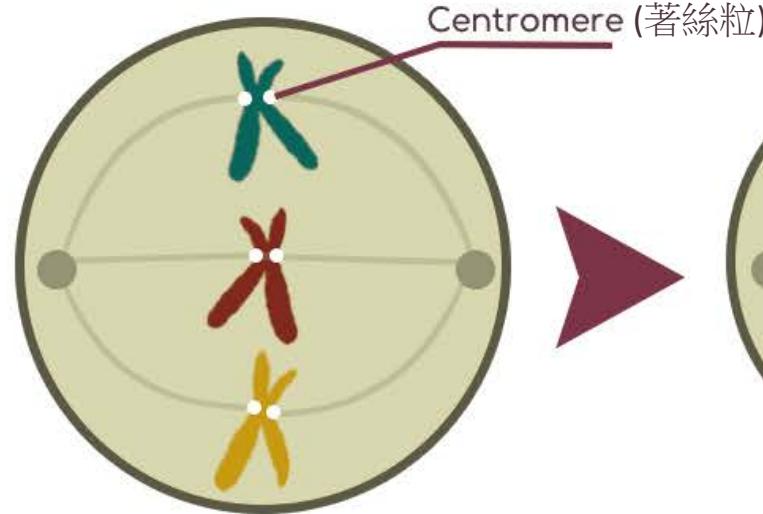


claudiajaffe

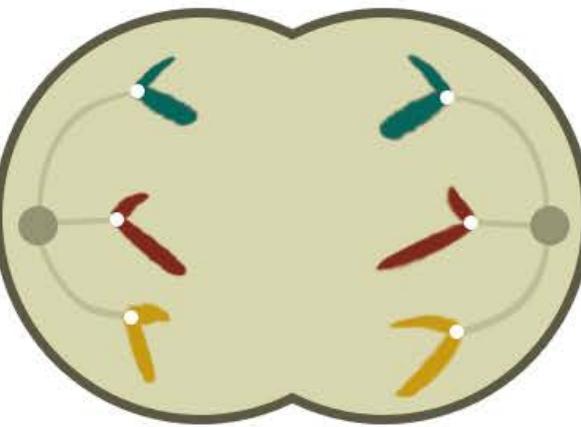
<https://www.youtube.com/watch?v=P7m3WfzgZdI>

# CELL DIVISION (細胞分裂)

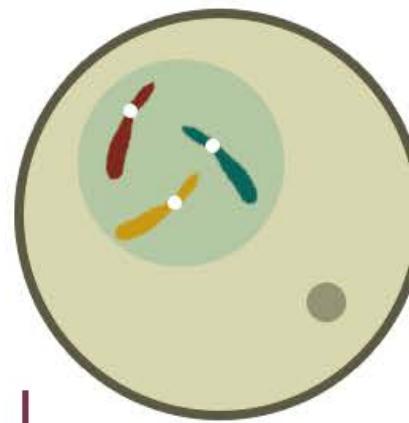
在細胞分裂時，我們的細胞需要準確地分配其染色體到子細胞中。當中染色體上的著絲粒負責控制染色體的動態。



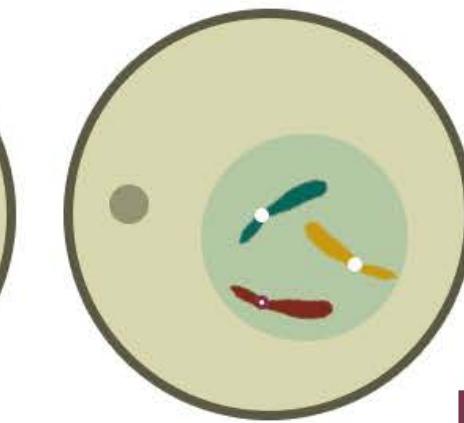
METAPHASE



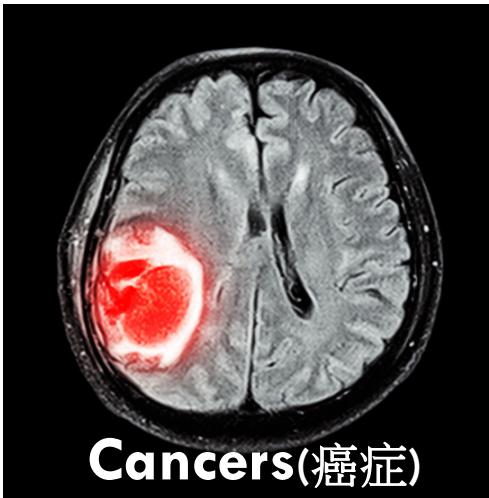
ANAPHASE



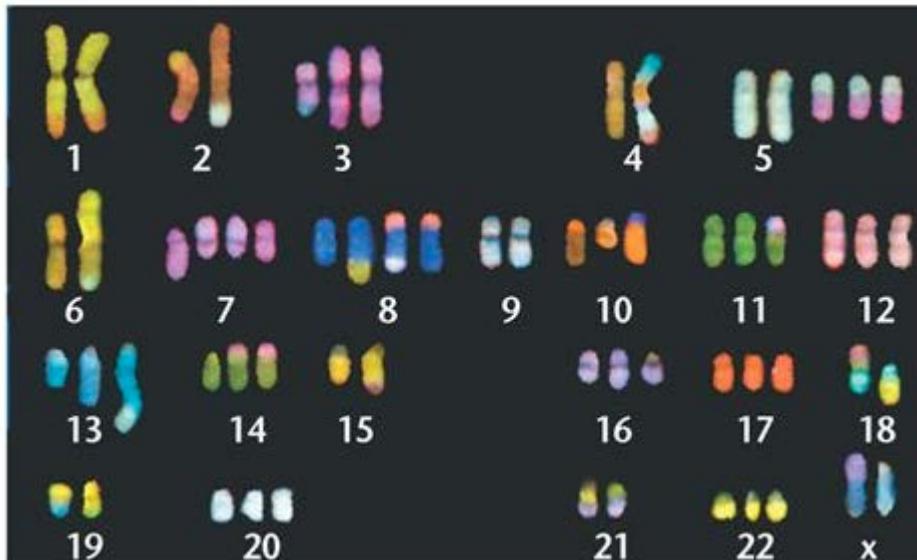
DAUGHTER CELLS  
(子細胞)



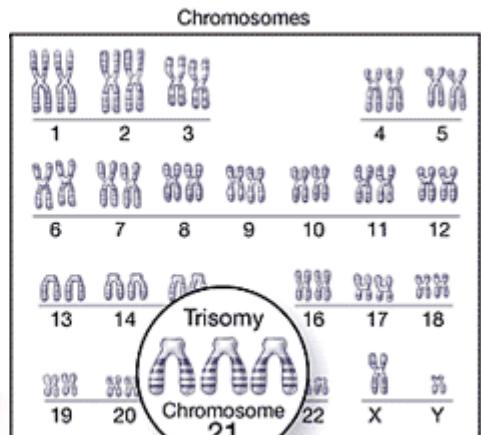
## Errors



Cancers(癌症)

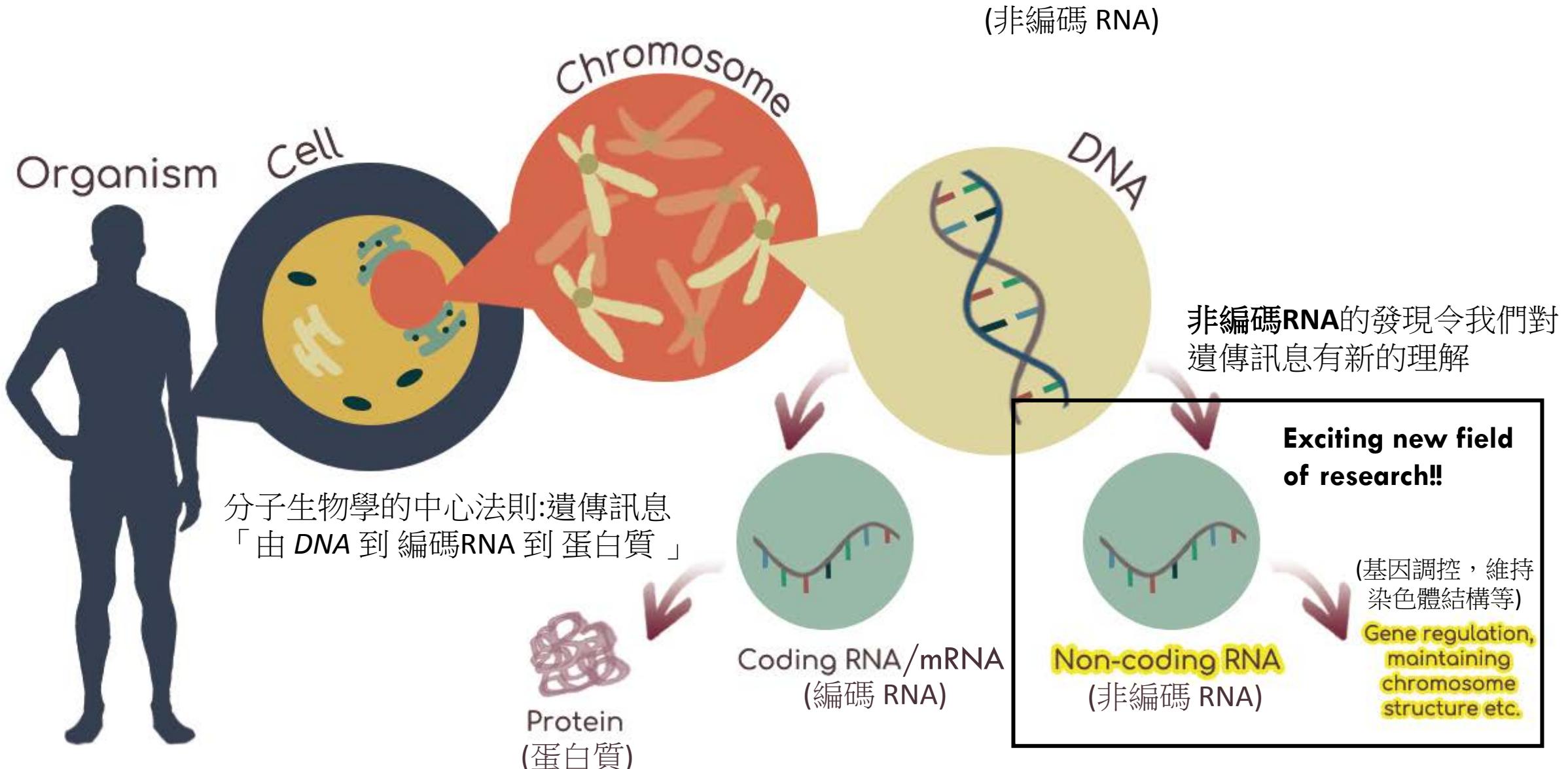


Down's Syndrome  
(唐氏綜合症)



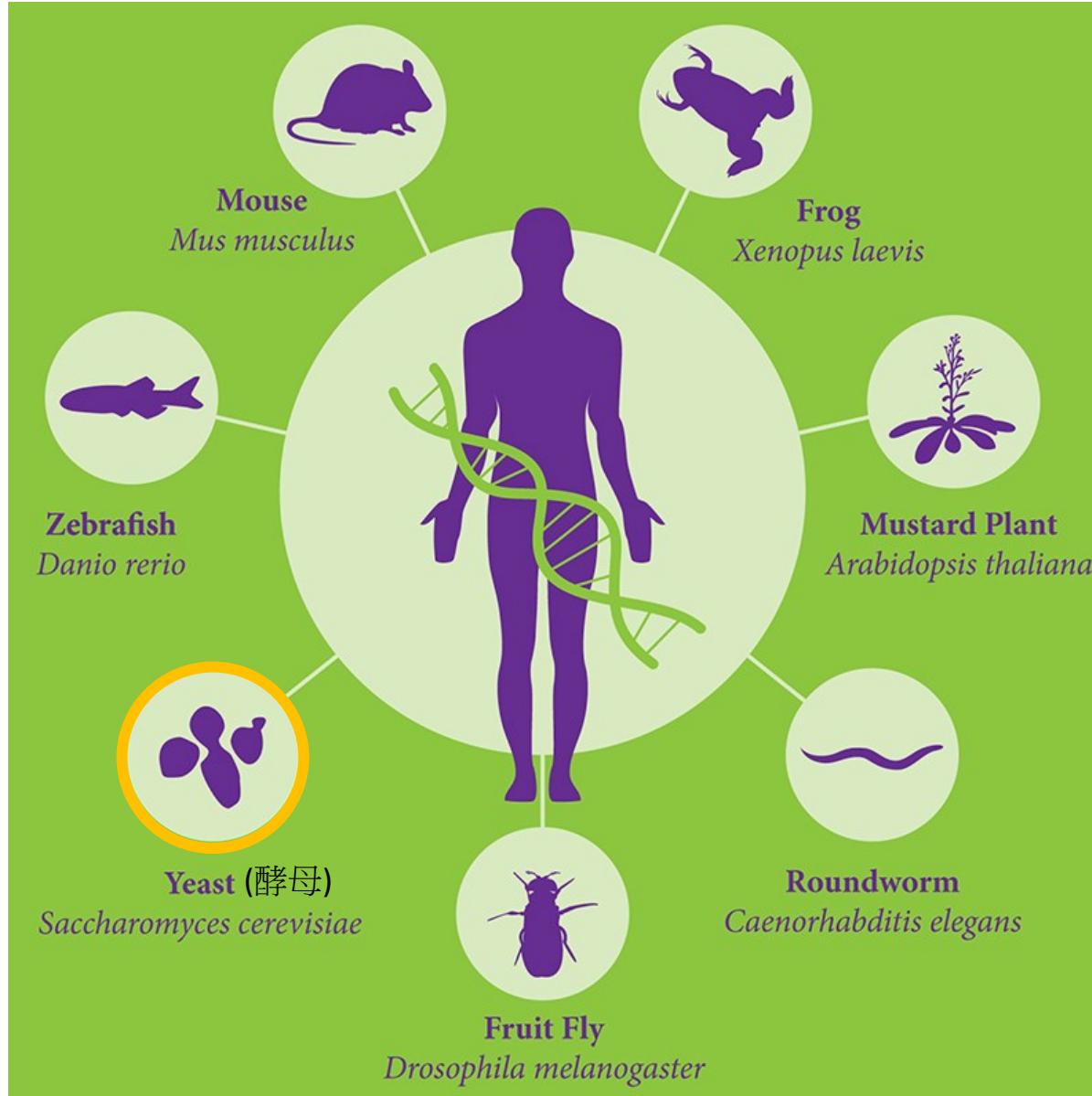
C.Lynn

# Central dogma of molecular biology: DNA → Coding/Messenger RNA → Protein. But new player in regulation: Non-coding RNA



# Common Model Organisms in Cell Biology

(生物模型)



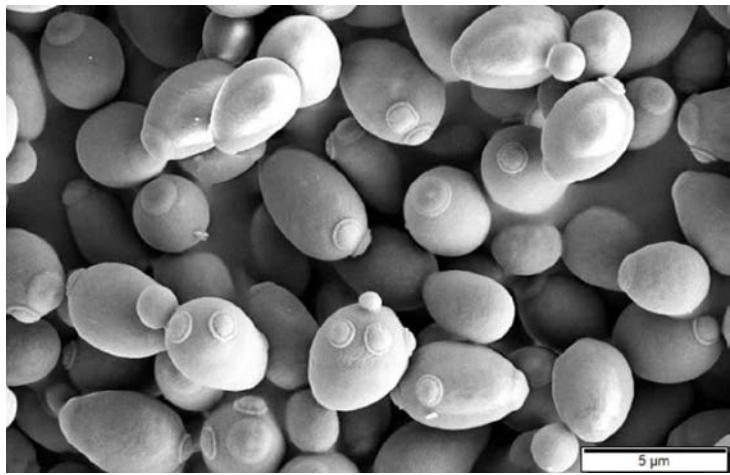
酵母是易於培養的單細胞真核生物，他們的基因和蛋白質與哺乳動物具有很多的相似性，所以是優秀的生物模型

# Baking yeast or Brewing yeast...

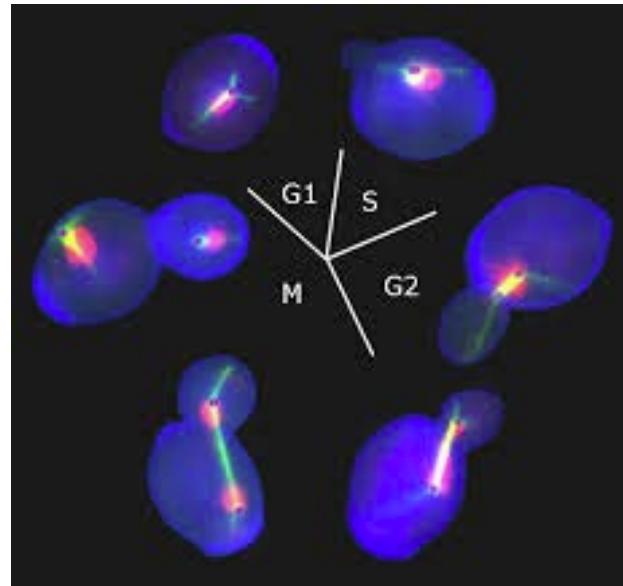


(芽殖酵母)

**is also known as Budding yeast, often used in cell division research**



<https://en.wikipedia.org/wiki/Yeast>



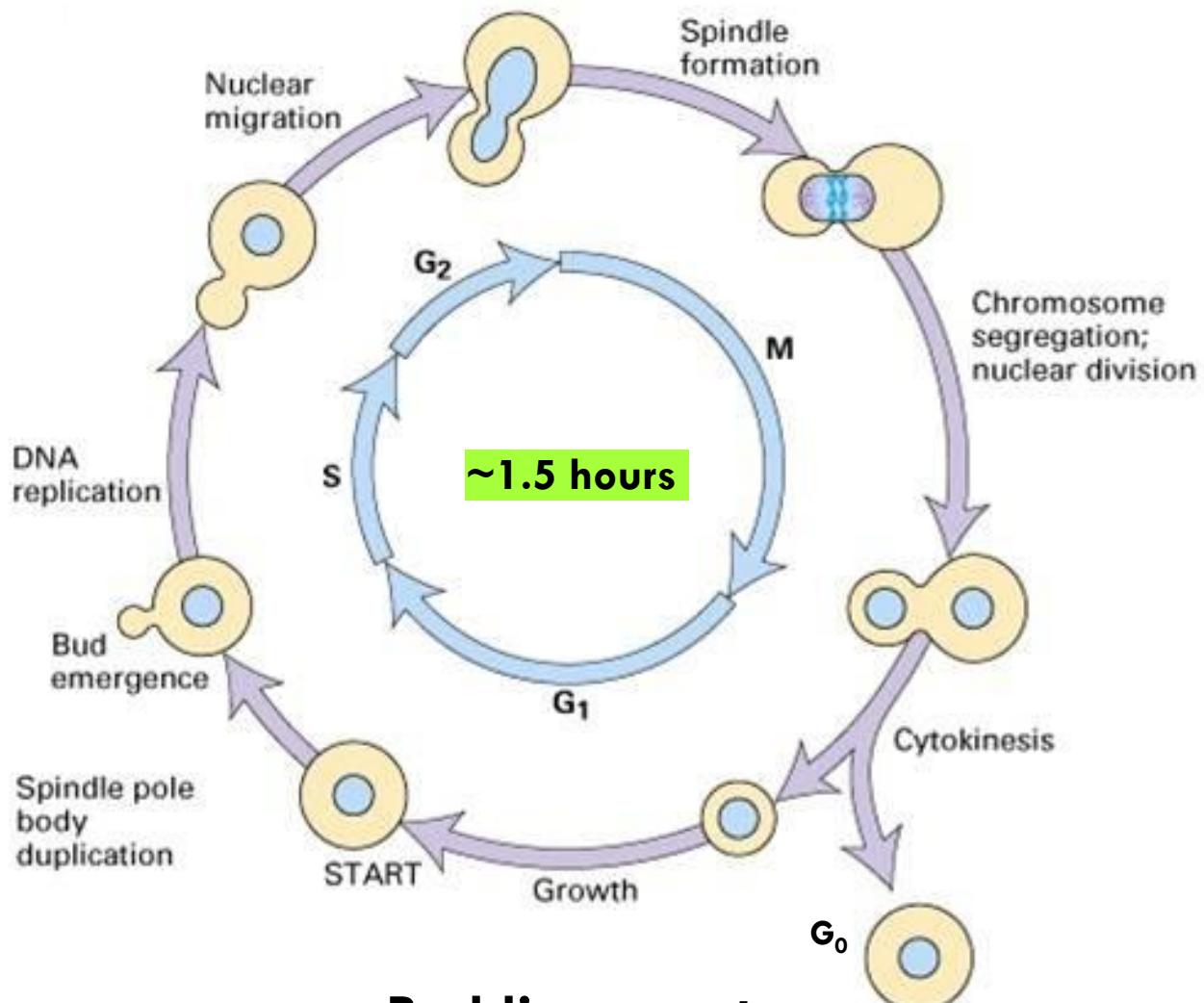
<http://people.virginia.edu/~djb6t/cell/dan333.htm>



UMass Amherst Libraries,  
[https://www.youtube.com/watch?v=GFEgB\\_ytDZY&t=1s](https://www.youtube.com/watch?v=GFEgB_ytDZY&t=1s)

(細胞週期)

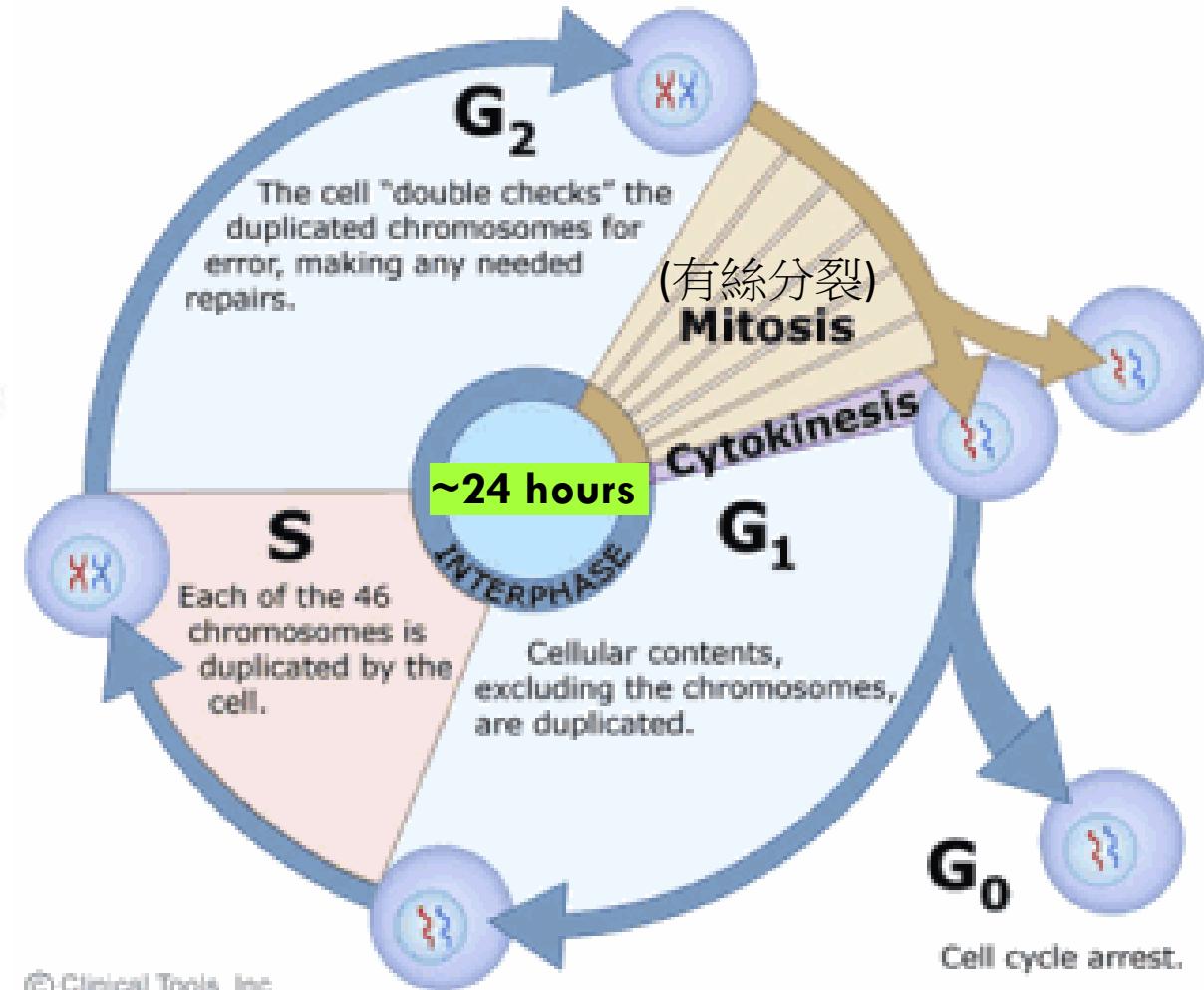
## Same cell cycle phases between yeast and human (G<sub>0</sub>, G<sub>1</sub>, S<sub>ynthesis</sub>, G<sub>2</sub>, Mitotic phase)



**Budding yeast**

<https://voer.edu.vn/m/cell-cycle-regulation-in-the-budding-yeast/1ce212d4>

芽殖酵母和人類的細胞都有相同的細胞週期，而且酵母的細胞週期更快，利用酵母研究細胞分裂，更加方便快捷。



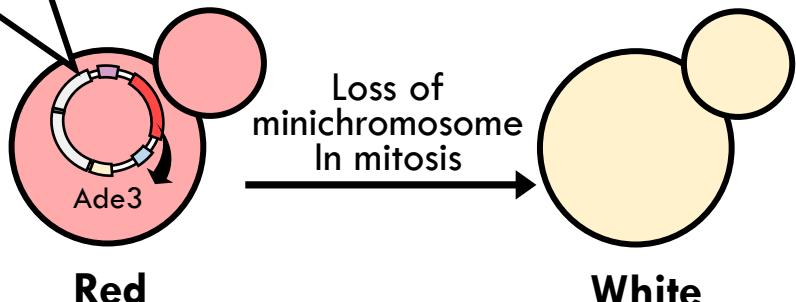
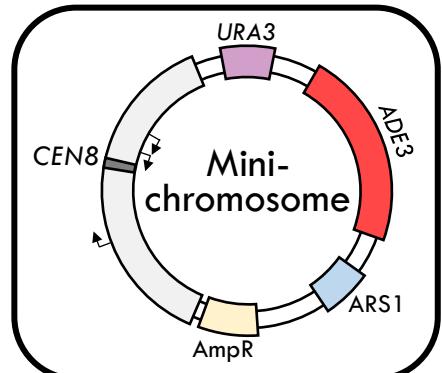
**Human**

<https://www2.le.ac.uk/projects/vgec/highereducation/topics/cellcycle-mitosis-meiosis>

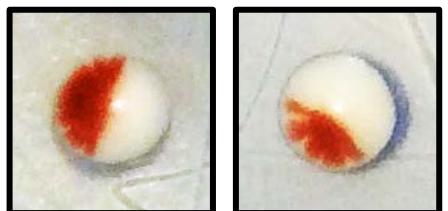
# A simple way to detect error in cell division in budding yeast: using a centromere-containing minichromosome

(著絲粒)

(迷你染色體)

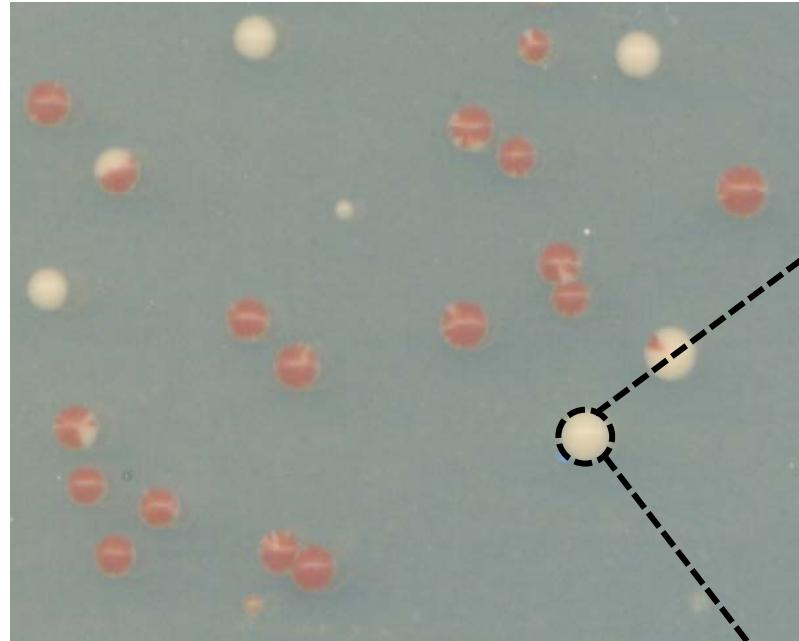


Minichromosome  
is maintained

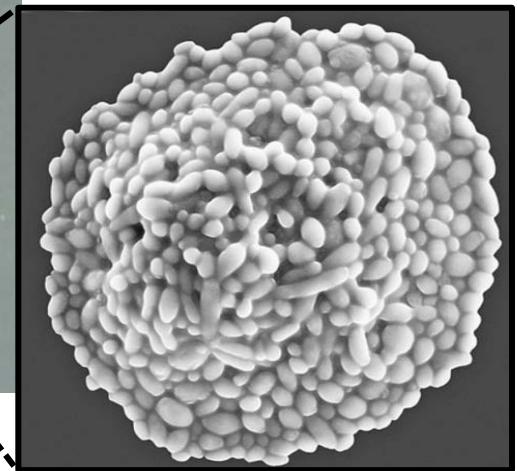


Minichromosome lost  
in 1<sup>st</sup> division

(菌落)  
**Yeast colonies on an agar plate**



我們可以從酵母菌落的顏色  
來判斷細胞分裂有沒有出錯

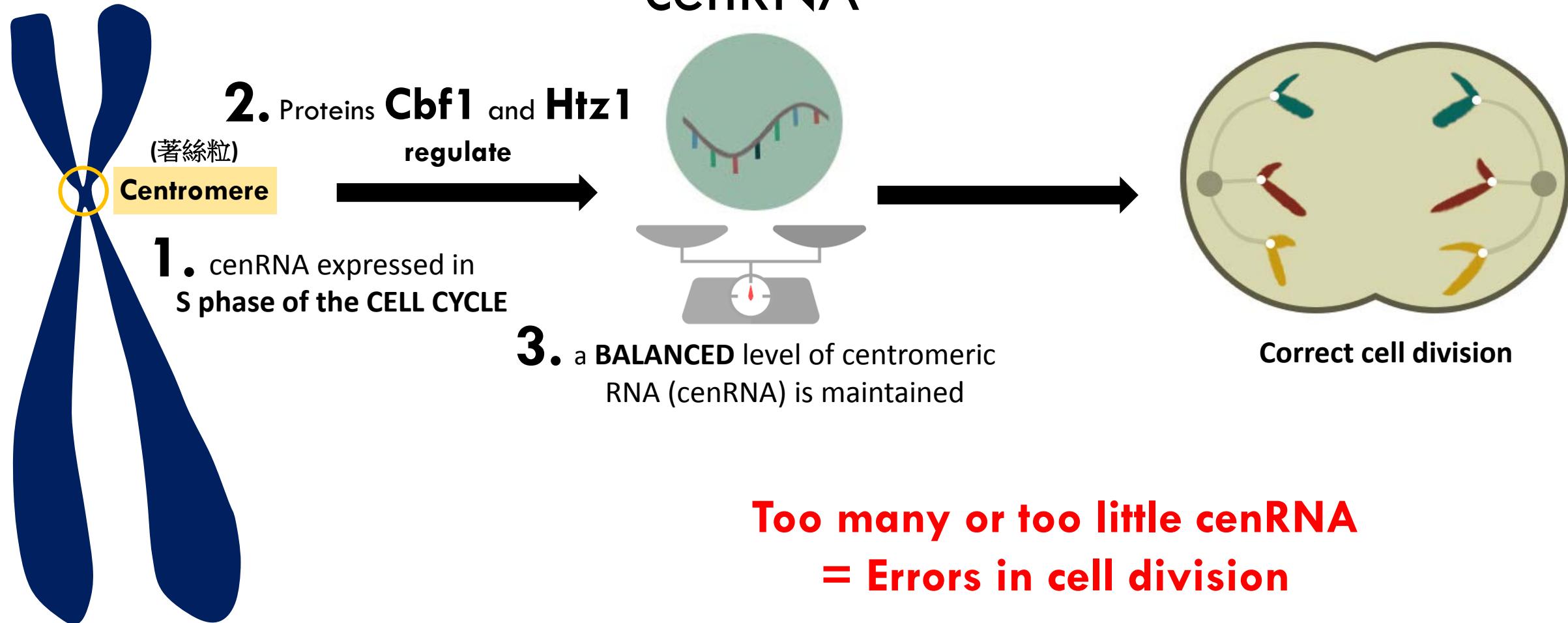


Each colony contains millions of cells,  
originated from a single cell  
(Dennis Kunkel Microscopy)

# Major Findings

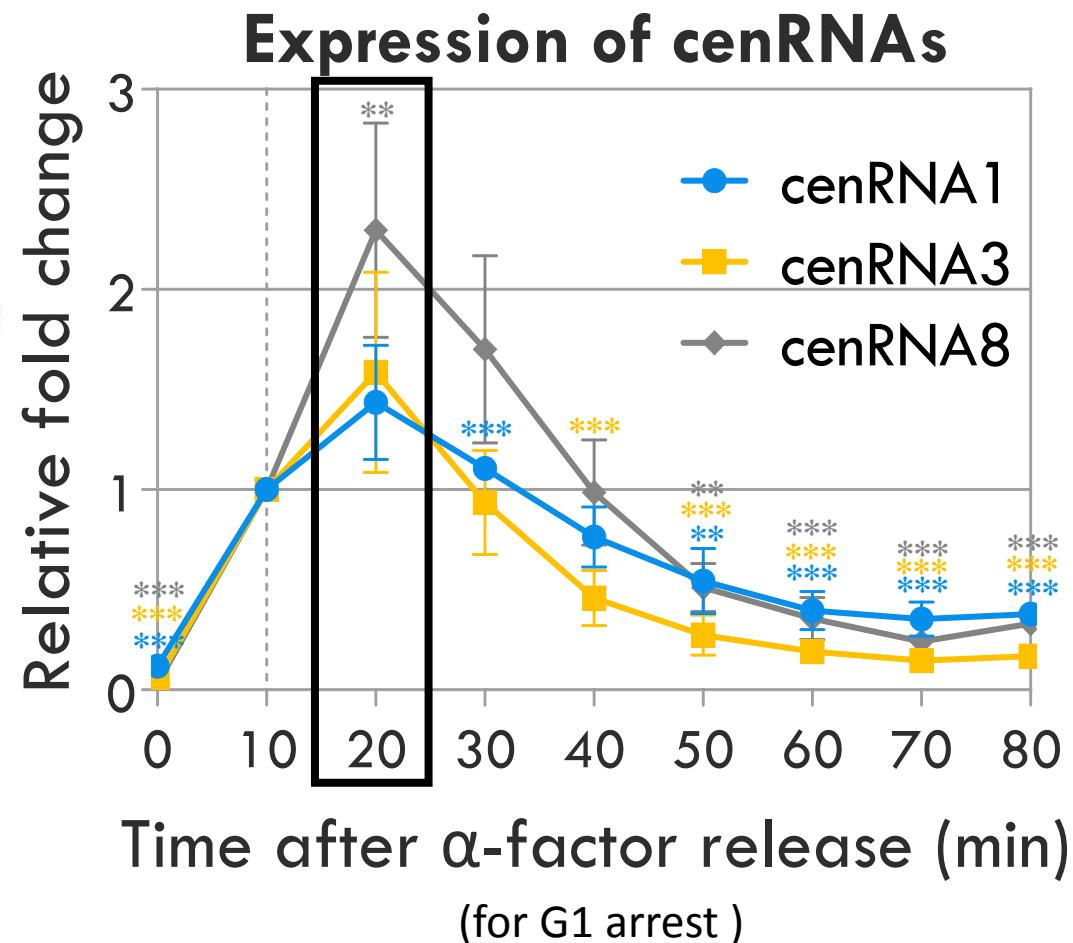
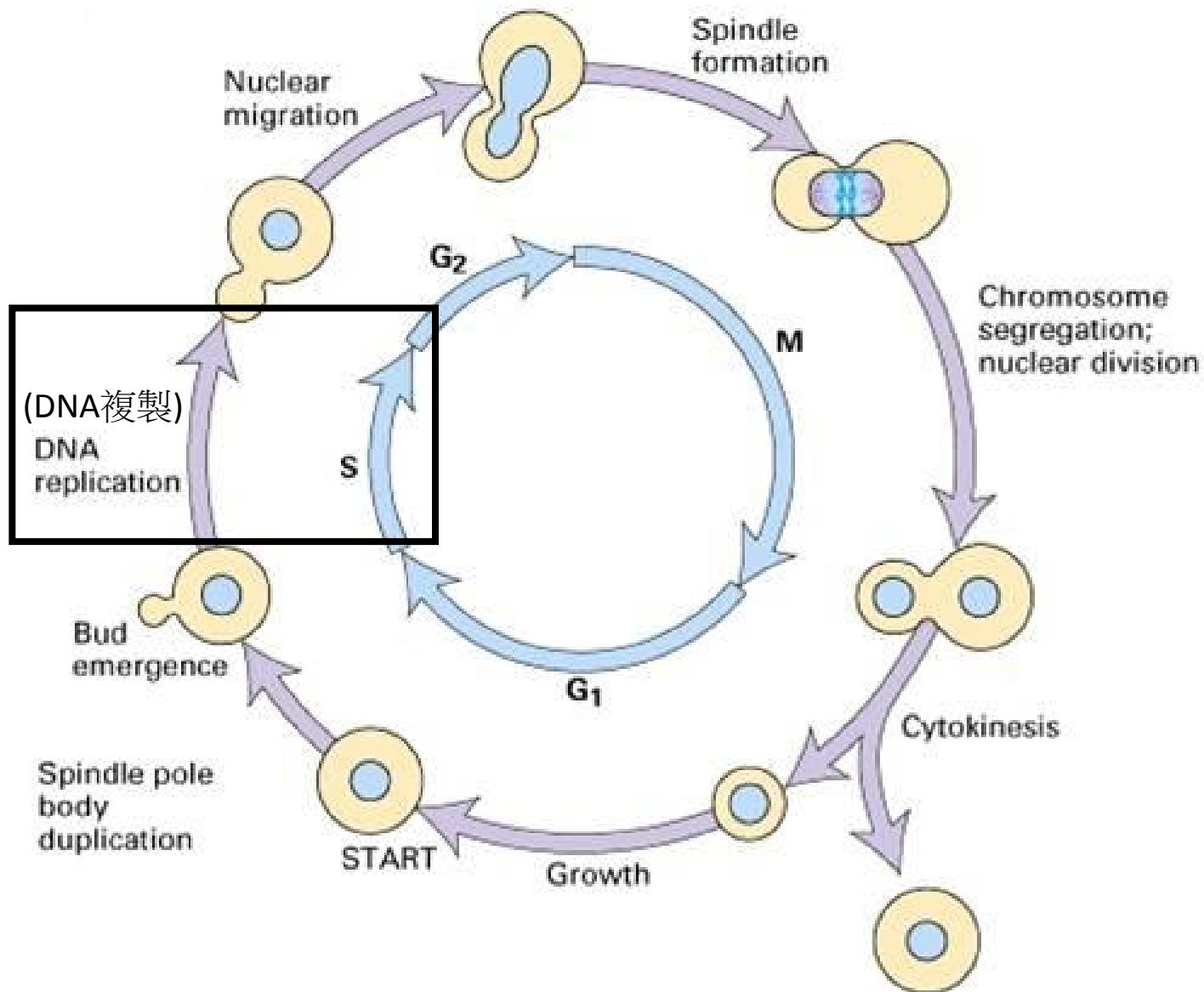
芽殖酵母"著絲粒DNA"會製造出 "著絲粒RNA" (cenRNA), 是一種剛被發現的非編碼RNA

1. "著絲粒RNA" 在細胞週期中的DNA複製期(S phase) 表達
2. "著絲粒RNA" 的水平由**Cbf1**和**Htz1** 蛋白控制
3. 過高或過低的 "著絲粒RNA" 水平會導致細胞分裂出錯



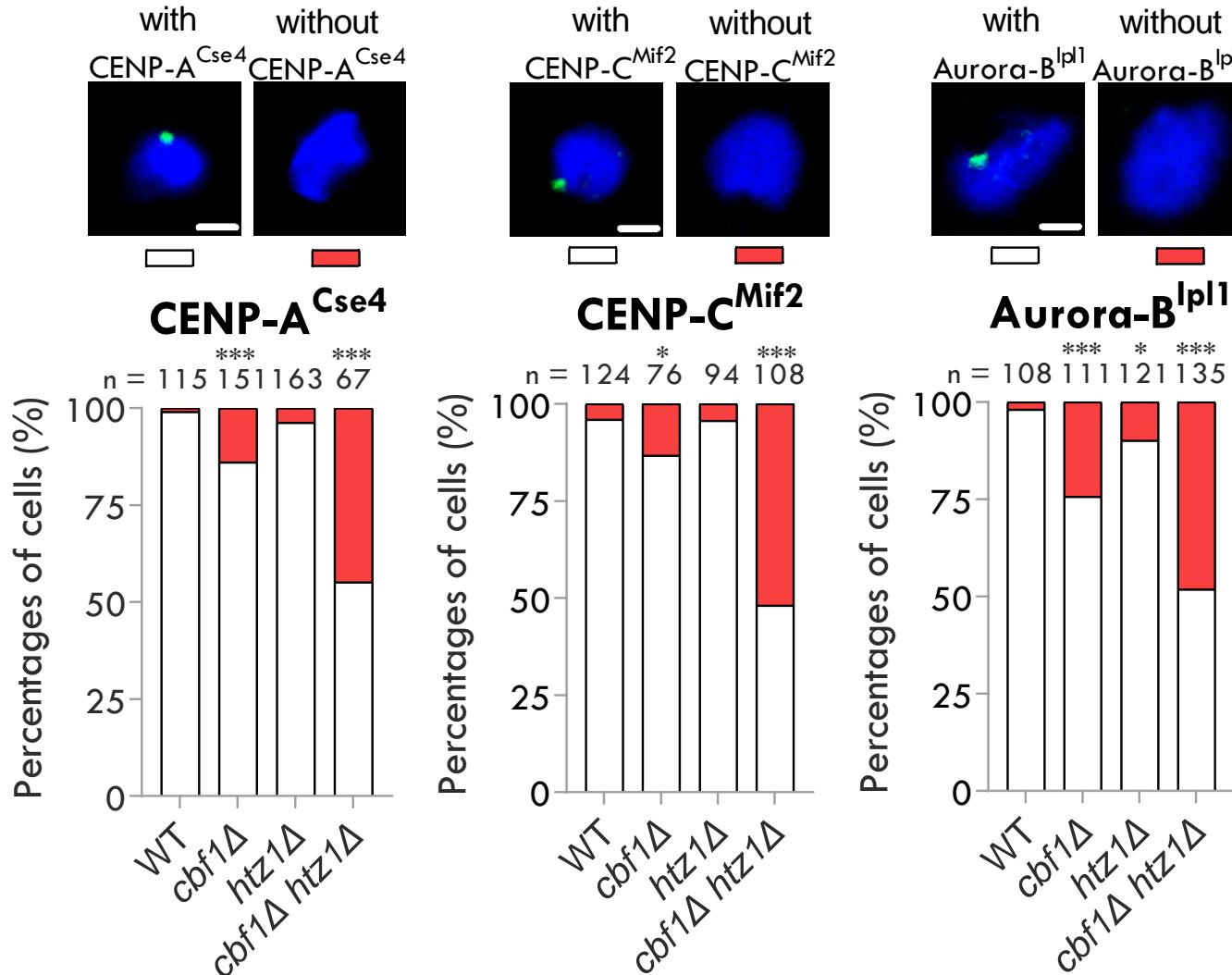
# CenRNA expressed in S<sub>y</sub>nthesis phase of the cell cycle

"著絲粒RNA" 在細胞週期中的S phase 表達



# When too many cenRNA (by removal of Cbf1 and Htz1), centromeric proteins fail to localize to the centromere

(著絲粒蛋白)

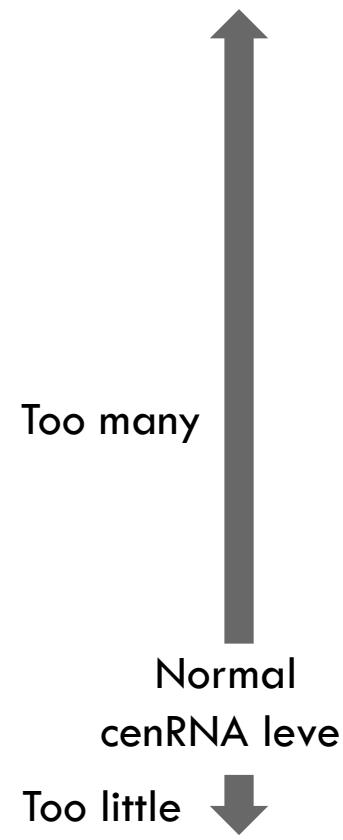


"著絲粒RNA" 的水平由 **Cbf1** 和 **Htz1** 蛋白控制。沒有 **Cbf1** 和 **Htz1** ( $cbf1\Delta htz1\Delta$ ) 的細胞會過度表達 "著絲粒RNA"，令著絲粒失去一些關鍵的蛋白，導致著絲粒功能異常。

(red bar increases  
in  $cbf1\Delta htz1\Delta$ )

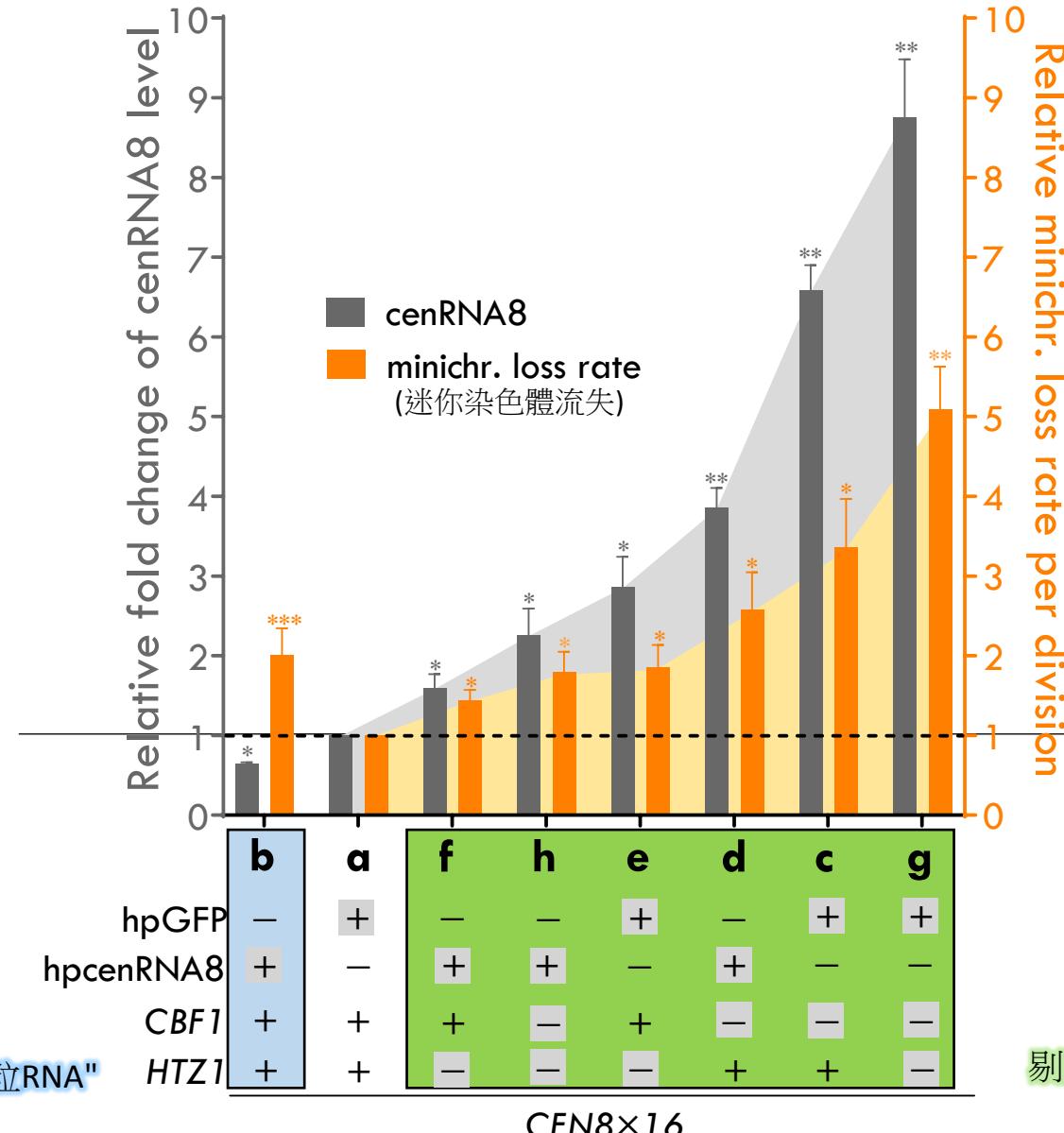
# Too many or too little cenRNA = Cell division error

過高或過低的 "著絲粒RNA" 水平會導致細胞分裂出錯



**Too little cenRNA by cenRNA depletion (RNA interference)**

利用RNA干擾，使細胞缺乏足夠的 "著絲粒RNA"



**Too many cenRNA after removal of Cbf1, Htz1 or both**

剔除Cbf1和Htz1，使細胞過度表達 "著絲粒RNA"

# Significances

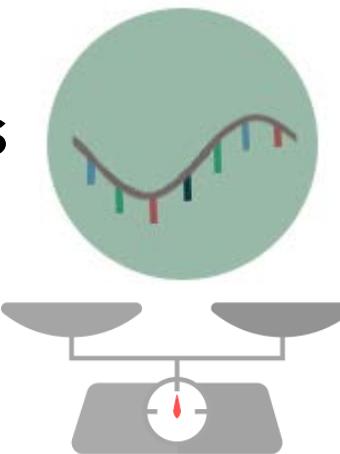
芽殖酵母著絲粒DNA會製造出 "著絲粒RNA" (cenRNA), 是一種剛被發現的非編碼RNA

- CenRNA is cell cycle-regulated (expressed in S phase)

"著絲粒RNA" 在細胞週期中的S phase 表達

- We uncover the regulation (by **Cbf1** and **Htz1** protein) of an important non-coding RNA, cenRNA, in the budding yeast cells

"著絲粒RNA" 的水平由Cbf1和Htz1 蛋白控制



- A balanced cenRNA level is crucial for correct cell division

過高或過低的 "著絲粒RNA" 水平會導致細胞分裂出錯

- CenRNA is an important molecule found in many organisms, including yeasts, fruit flies, frogs, mice and humans.



yeast



fruit fly



amphibians



mice



primates

We all have cenRNA!!!

# Potential applications

- Mis-regulated cenRNA level may result in cells with abnormal chromosome number.
  - Abnormal cenRNA level may cause our cells to mis-divide. Our study will help future researches to investigate the causes of diseases with cell division errors, such as Down's syndrome & cancers.

我們的研究有助了解染色體異常疾病的成因，如先天性的唐氏綜合症、癌症。

- Some cancer cells like ovarian cancer cells contain high level of cenRNA (Zhu et al. 2011, *Nature*).
  - Understanding cenRNA function & regulation will help to understand the causes of cancers.
  - cenRNA may act as a future cancer biomarker.
  - We may also fight cancer by targeting the cenRNA or its regulators.

(生物指標)

我們的研究亦啟發了癌症測試和治療的新方向。

# Acknowledgements

## Funding:



大學教育資助委員會  
University Grants Committee

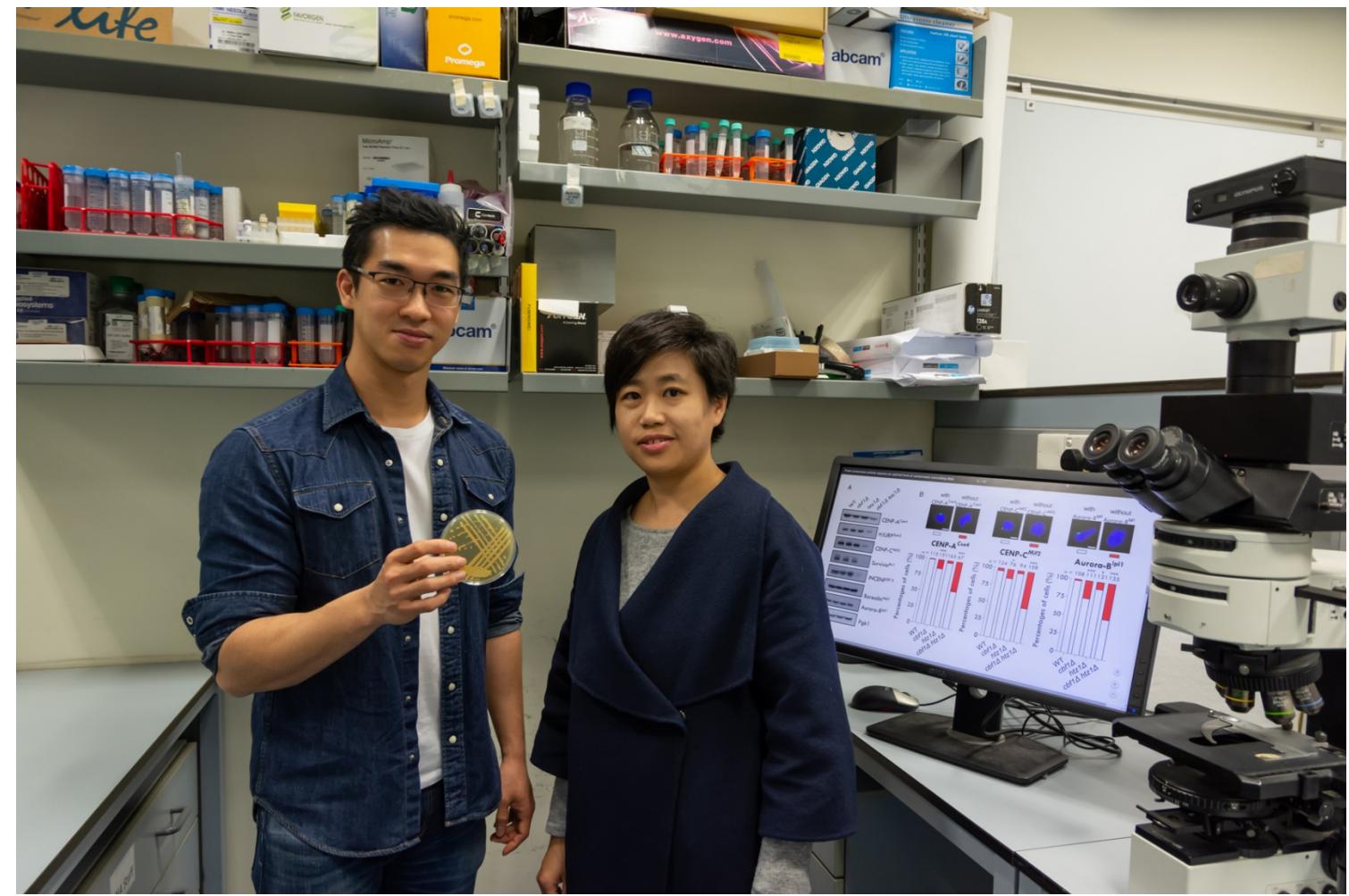
## HK Research Grants Council

- General Research Fund
- Collaborative Research Fund



## The University of Hong Kong

- Seed Funds for Basic Research



**Microscopy:** School of Biological Sciences Core Facility and Faculty of Medicine Core Facility

**Video & Schematics:** Jasmine Lau, undergraduate student helper in Yuen's Lab

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