RESEARCH

MEIOTIC DRIVE

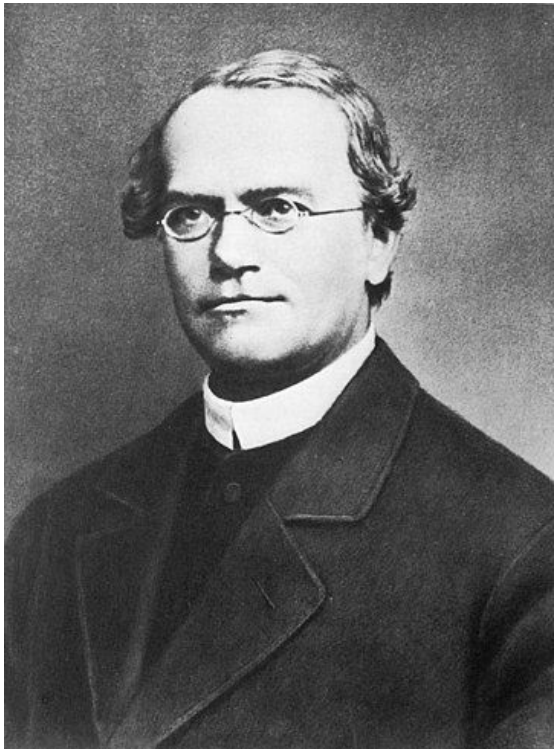
Spindle asymmetry drives non-Mendelian chromosome segregation

Takashi Akera,[1] Lukáš Chmátal,[1] Emily Trimm,[1] Karren Yang,[1] Chanat Aonbangkhen,[2] David M. Chenoweth,[2] Carsten Janke,[3,4] Richard M. Schultz,[1] Michael A. Lampson[1]*

王擎天, 朱柏昇, 張家瑜

Mendelian inheritance (1866)

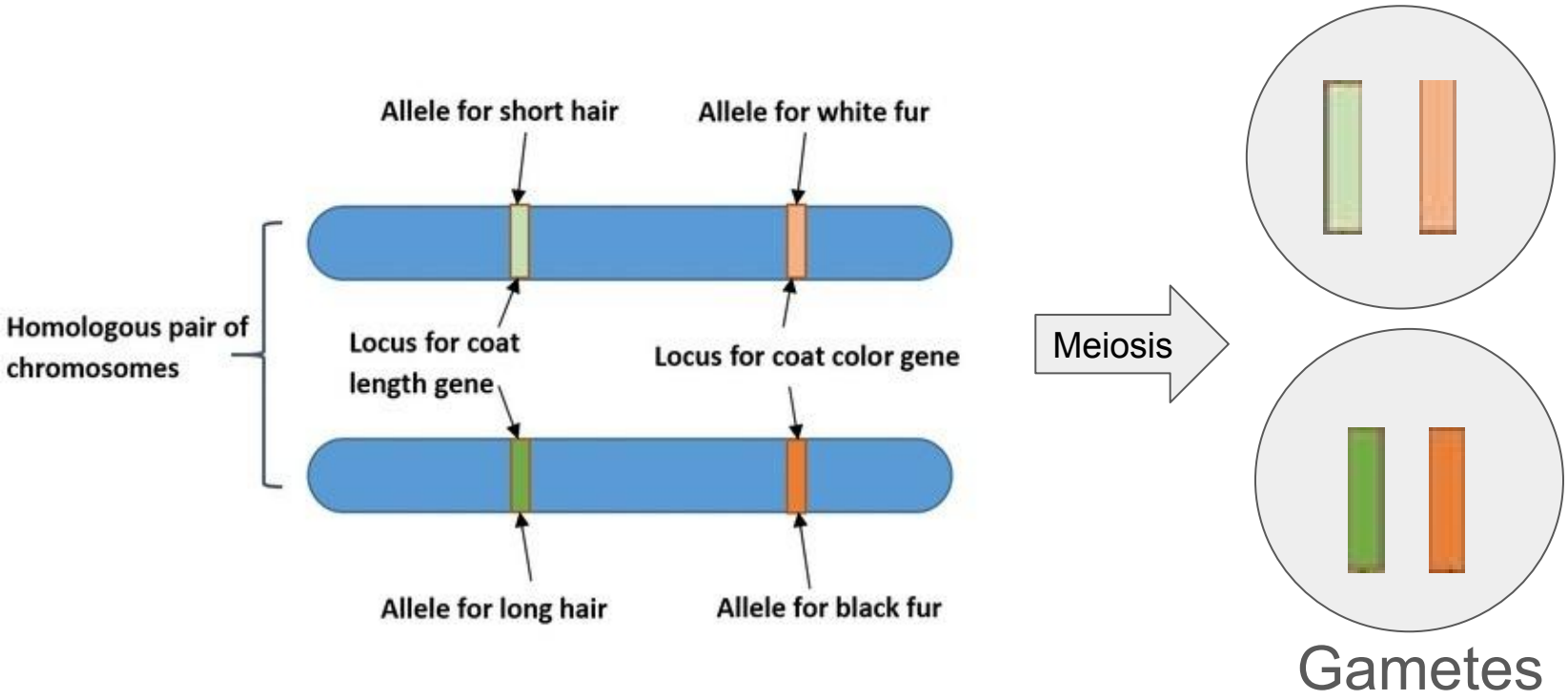
- Law of Segregation
- Law of Independent Assortment
- Law of Dominance



Gregor Mende (1822 - 1884)
wikipedia

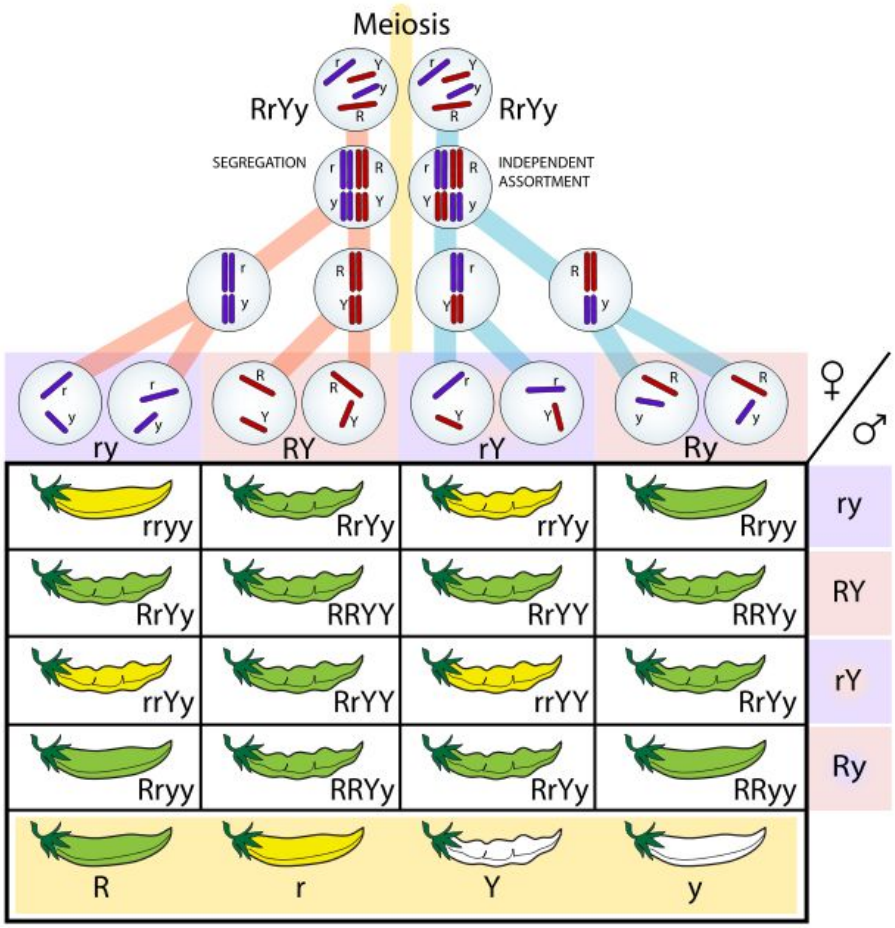
Law of segregation(分離定律)

- Every individual organism contains two alleles(等位基因) for each trait
- Alleles segregate during meiosis each gamete contains only one of the alleles



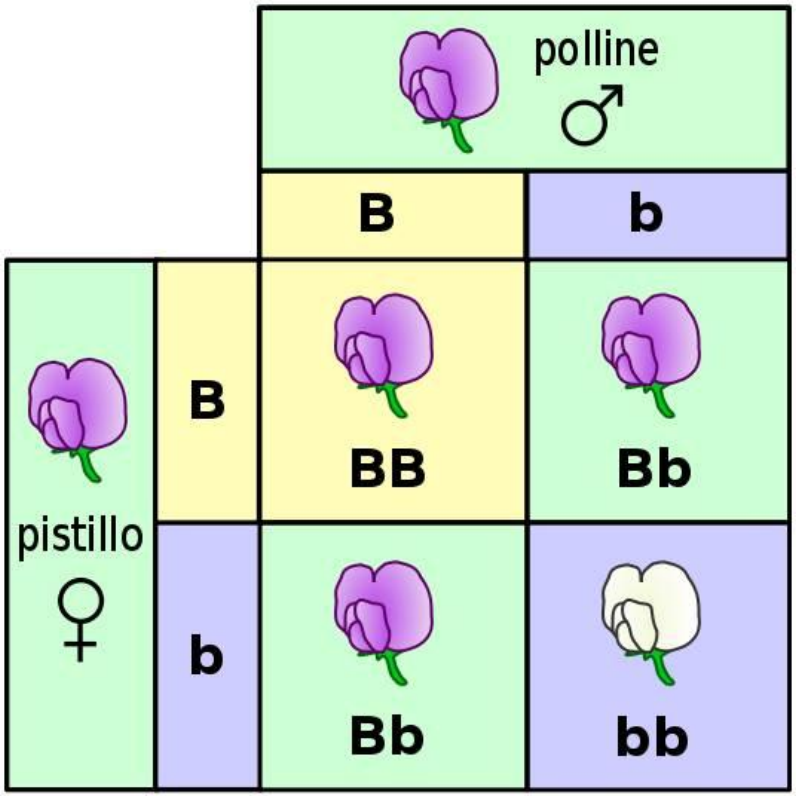
Law of Independent Assortment(獨立分配定律)

- The separation and combination of genetic elements that control different traits do not interfere with each other

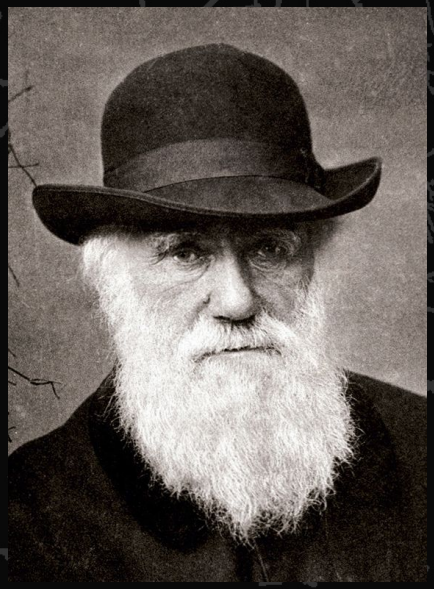


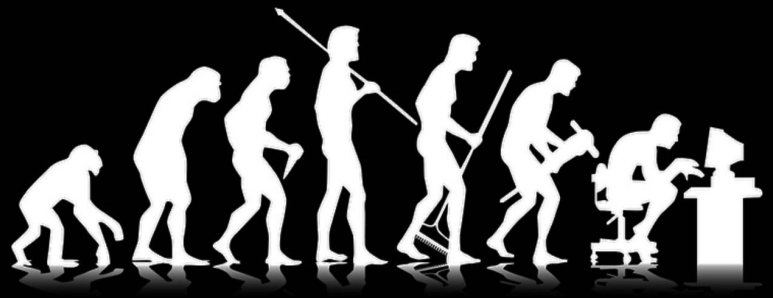
Law of Dominance (顯性法則)

- Recessive alleles will always be masked by dominant alleles.



Theory of Evolution



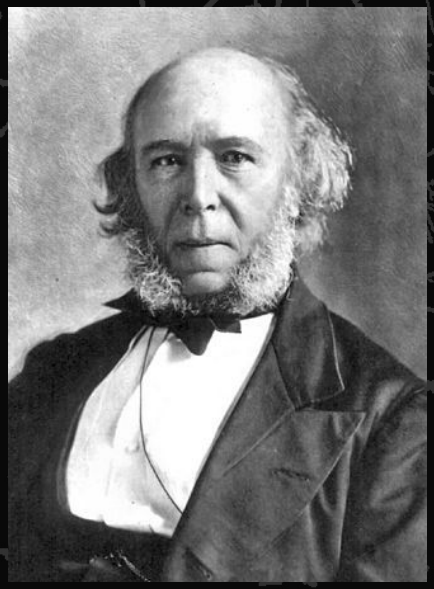


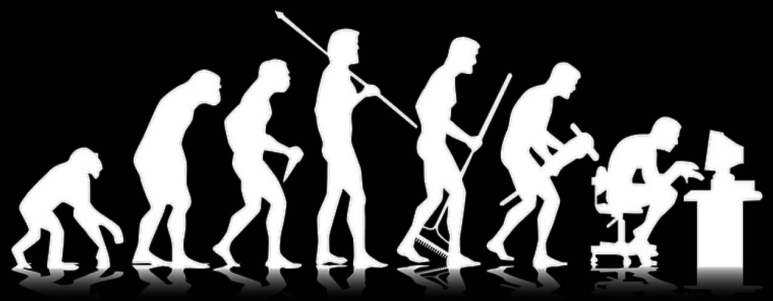
*"Survival of the **fittest**"*

Charles Darwin, On [illegible] of Species (1859)?

wikimedia
http://www.macleans.ca/wp-content/uploads/2013/02/5519745603_e6be133cf8.jpg

Theory of Evolution





*"Survival of the **fittest**"*

Herbert Spencer, Principles of Biology (1864)

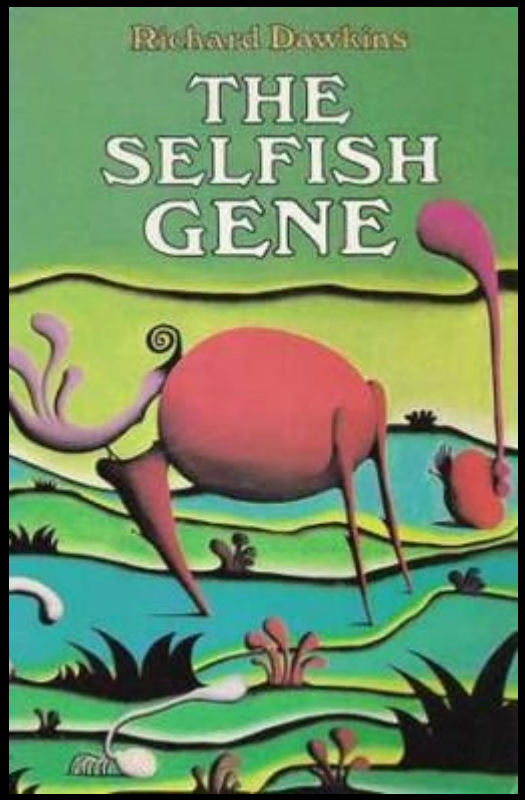
"Survival of the **successful reproducers**"

- Evolution is **change** in the **heritable characteristics** of biological **populations** over successive generations.
- In evolution, fitness simply means **reproductive success** and reflects how well an organism is adapted to its environment.
- All life on Earth shares a **common ancestor.**

wikimedia
http://www.macleans.ca/wp-content/uploads/2013/02/5519745603_e6be133cf8.jpg

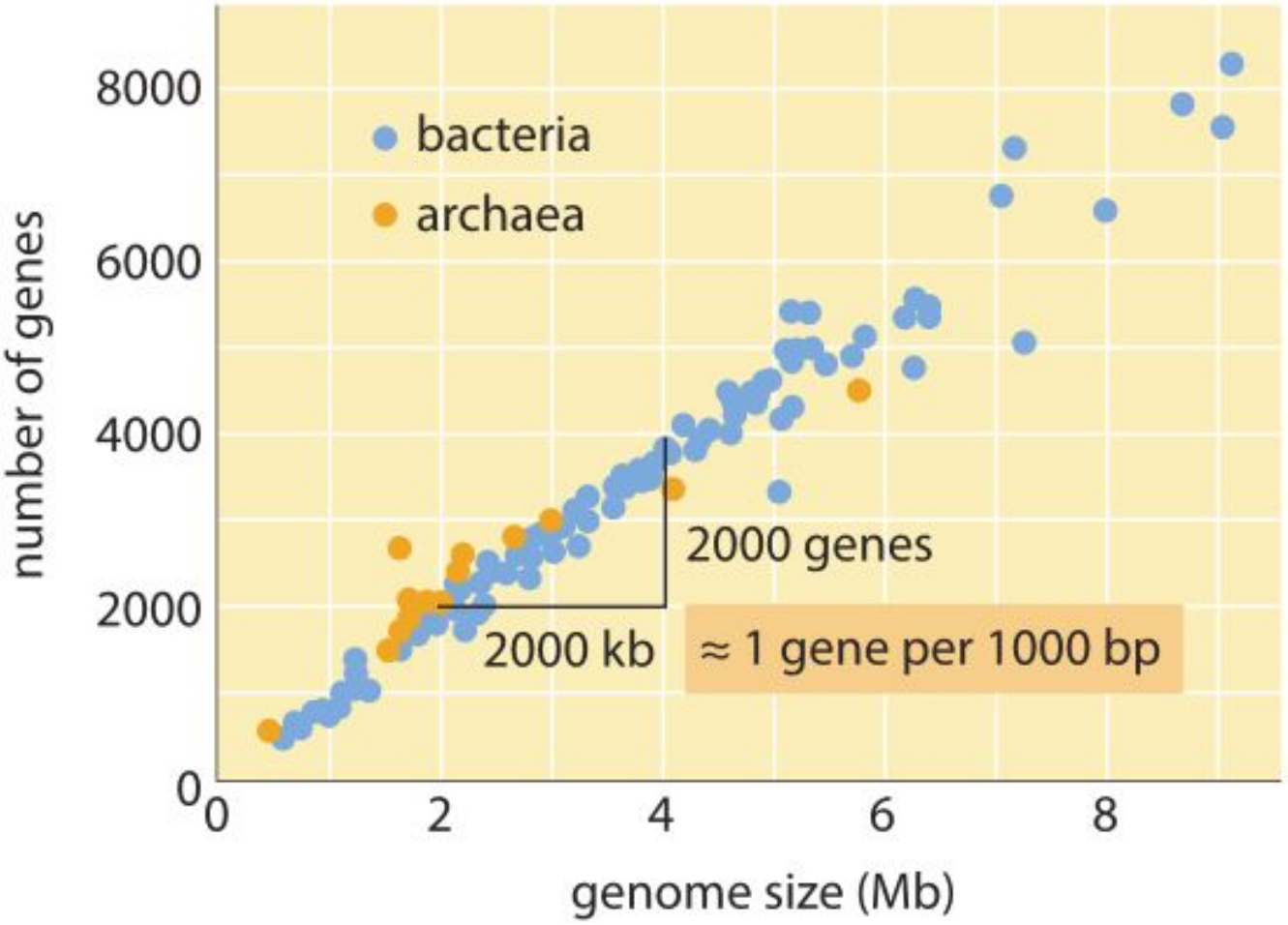
The selfish gene (The Immortal Gene)

- Richard Dawkins,1966
- **Gene centered view** of Evolution
  - Evolution occurs through the differential **survival of competing genes**, increasing the allele frequency of those alleles whose **phenotypic trait effects successfully promote their own propagation**.



wikipedia

Numbers of genes

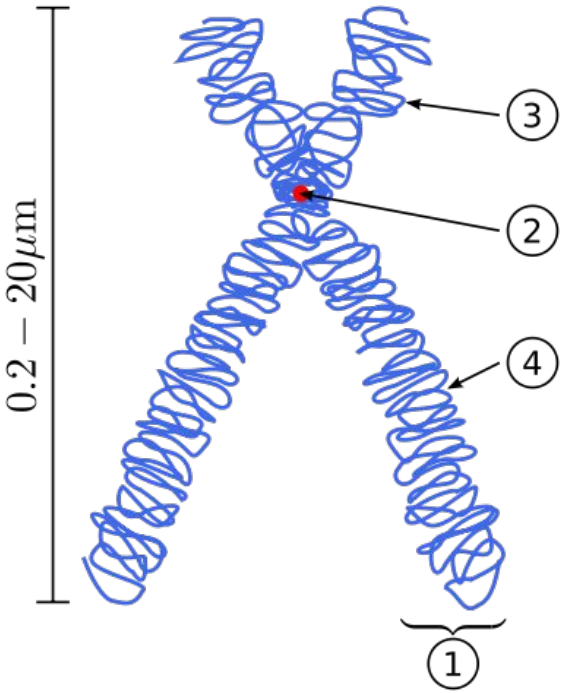


(M. Lynch, The Origins of Genome Architecture)

Organism	# of protein coding genes	# of genes by prediction	
HIV	9	10	viruses
Influenze A virus	11	14	
Bacteriophage	66	49	
Buchnera sp.	610	640	prokaryotes
T. maritima	1900	1900	
E. coli	4300	4600	
S. cerevisiae	6600	12000	eukaryotes
C. elegans	20000	100000	
D. melanogaster	14000	140000	
M. musculus	20000	2800000	
H. sapiens	21000	3200000	

Chromosome theory (1902)

"Chromosomes are the carriers of genetic material (genes)."

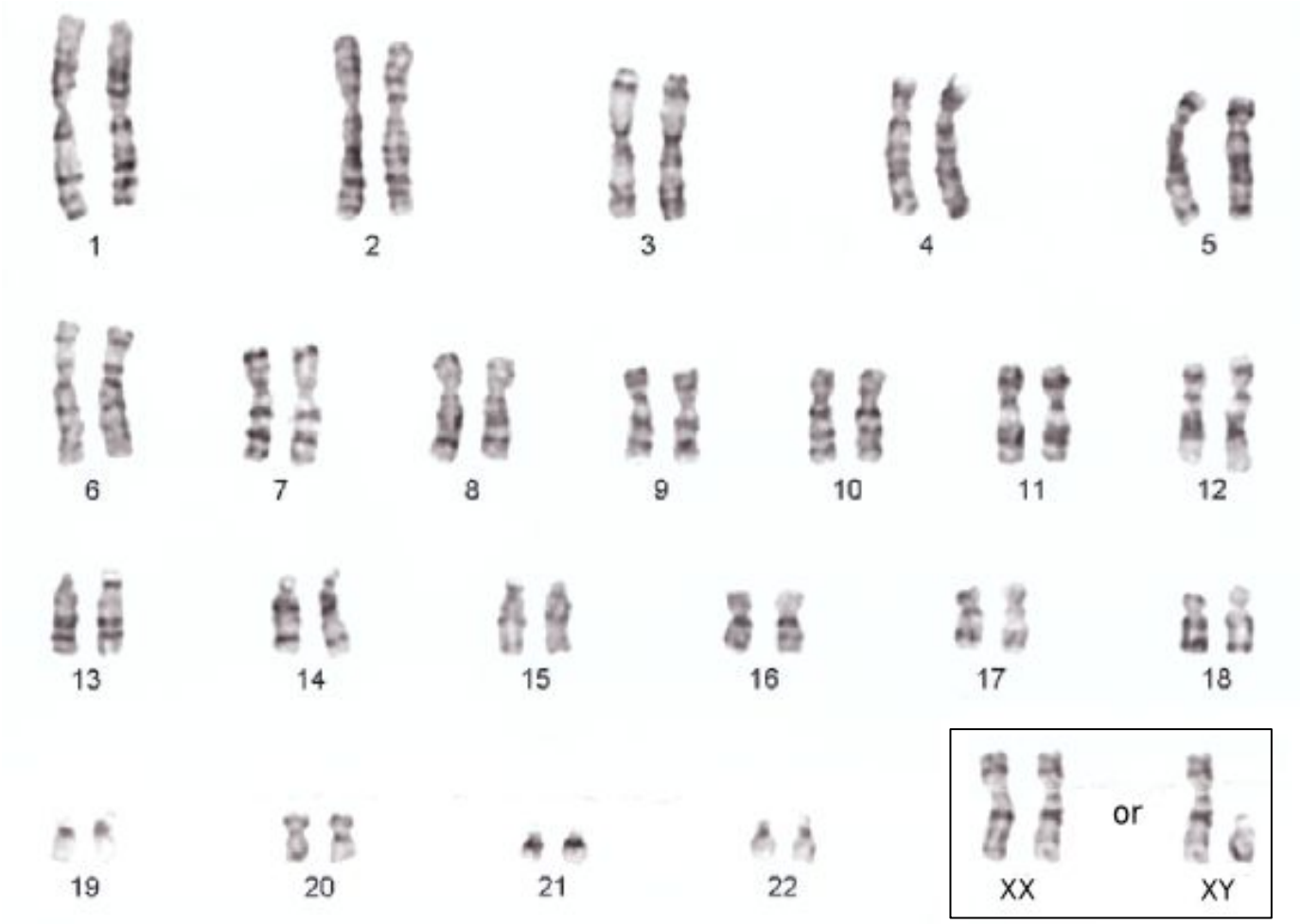


Sister chromatids

1. Chromatid
2. Centromere
3. Short (p) arm
4. Long (q) arm

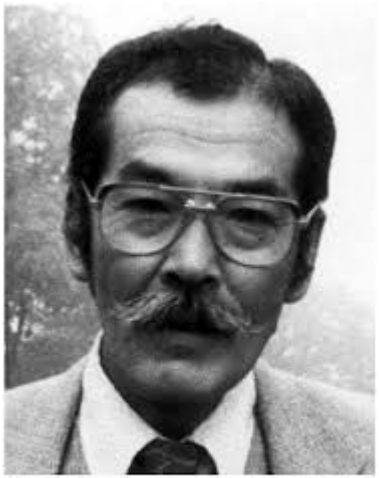
Walter Sutton (left)
Theodor Boveri (right)

Chromosome structure



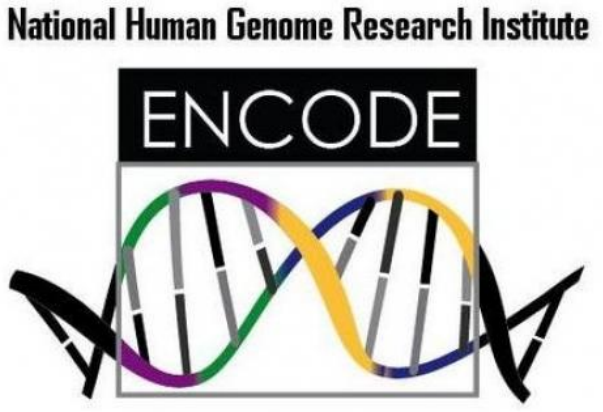
Junk DNAs (1)

- Susumu Ohno (大野乾)
- Noncoding region of the genome.
- Any DNA sequence that does not play a **functional role** in development, physiology, or some other organism-level capacity



L: https://www.nap.edu/read/10470/chapter/14
R: http://www.imm.ox.ac.uk/_asset/image/junkdna.jpeg

Junk DNAs (2)



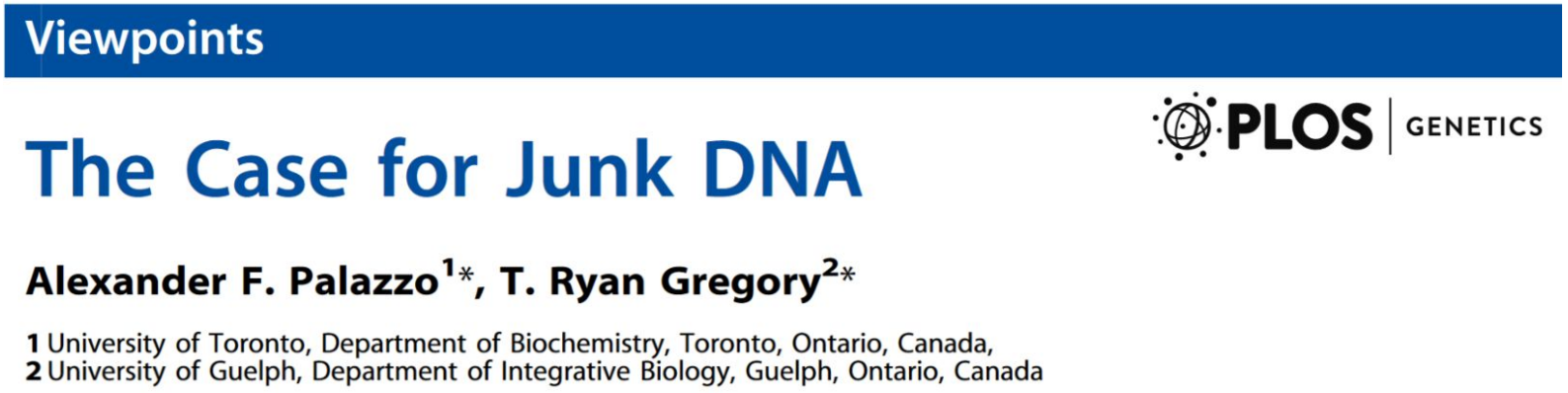
- ENCODE Project
- Goal:
  - Mapping and characterizing the functionality of the entire human genome.

*“ These data enabled us to assign biochemical functions for **80%** of the genome, in particular outside of the well studied protein-coding regions. ”*

The ENCODE Project Consortium

2012, *Nature*

Junk DNAs (3)



Viewpoints

PLOS | GENETICS

The Case for Junk DNA

Alexander F. Palazzo[1]*, T. Ryan Gregory[2]*

1 University of Toronto, Department of Biochemistry, Toronto, Ontario, Canada,
2 University of Guelph, Department of Integrative Biology, Guelph, Ontario, Canada

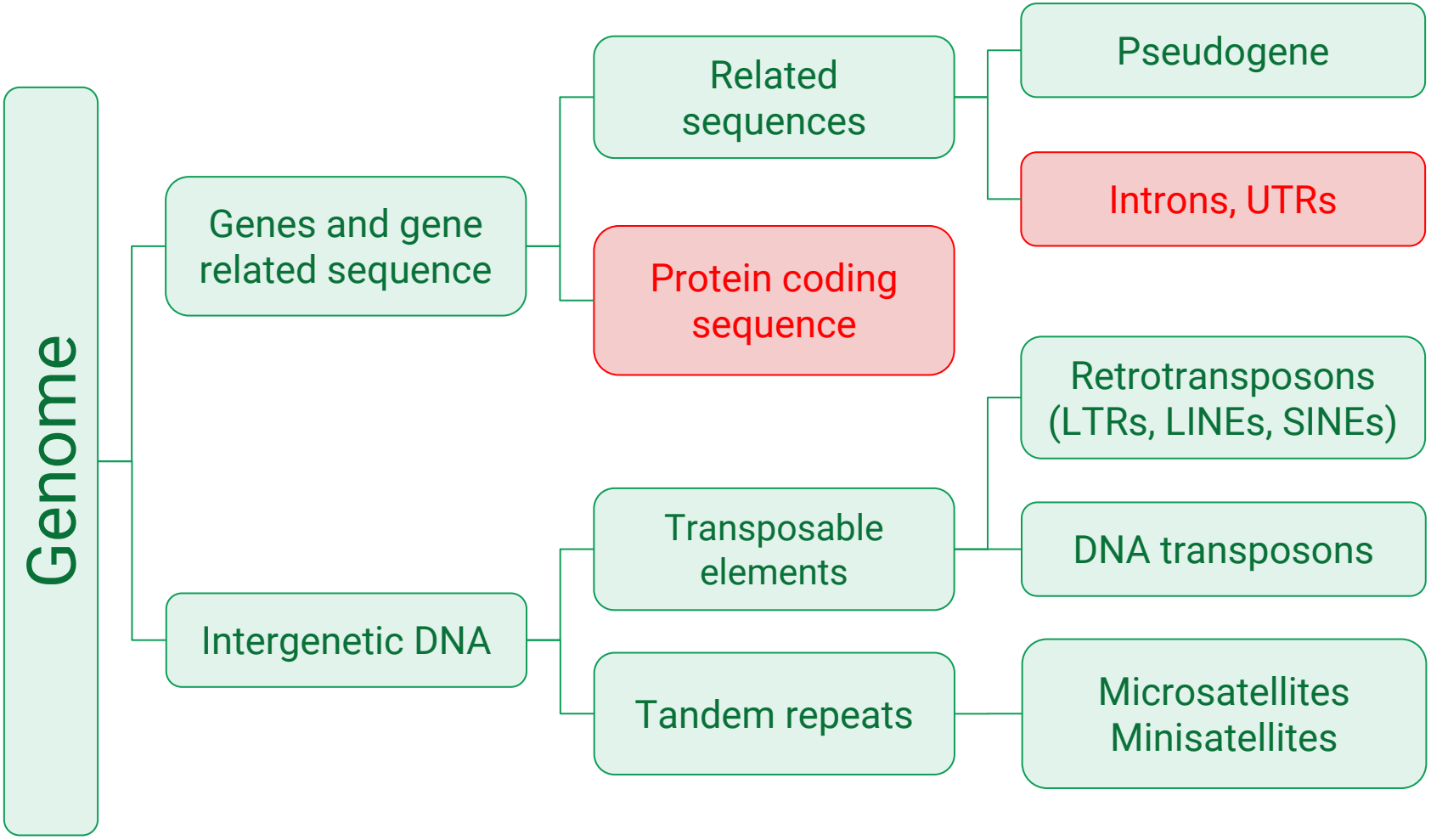
" … We examine several lines of evidence that support the notion that a substantial percentage of the DNA in many eukaryotic genomes lacks an organism-level function and that ***the junk DNA concept remains viable post-ENCODE****."*

Alexander F. Palazzo , T. Ryan Gregory

2014, *PLOS Genetic*

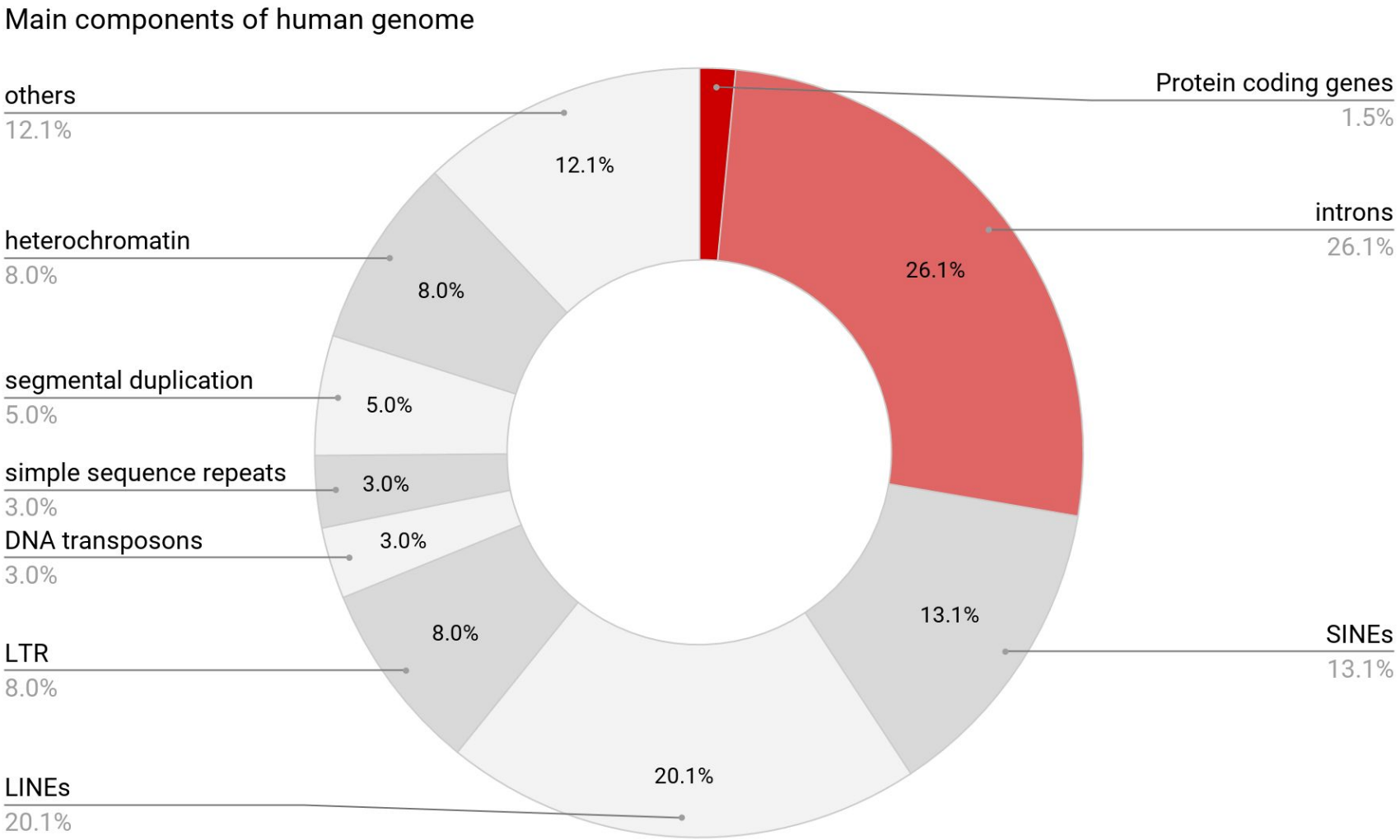
Genome structure (1)

Genome: The genetic material of an organism.



(T. Ryan Gregory, *Nature Reviews Genetics,* 2005)

Genome structure (2)



(T. Ryan Gregory, *Nature Reviews Genetics,* 2005)

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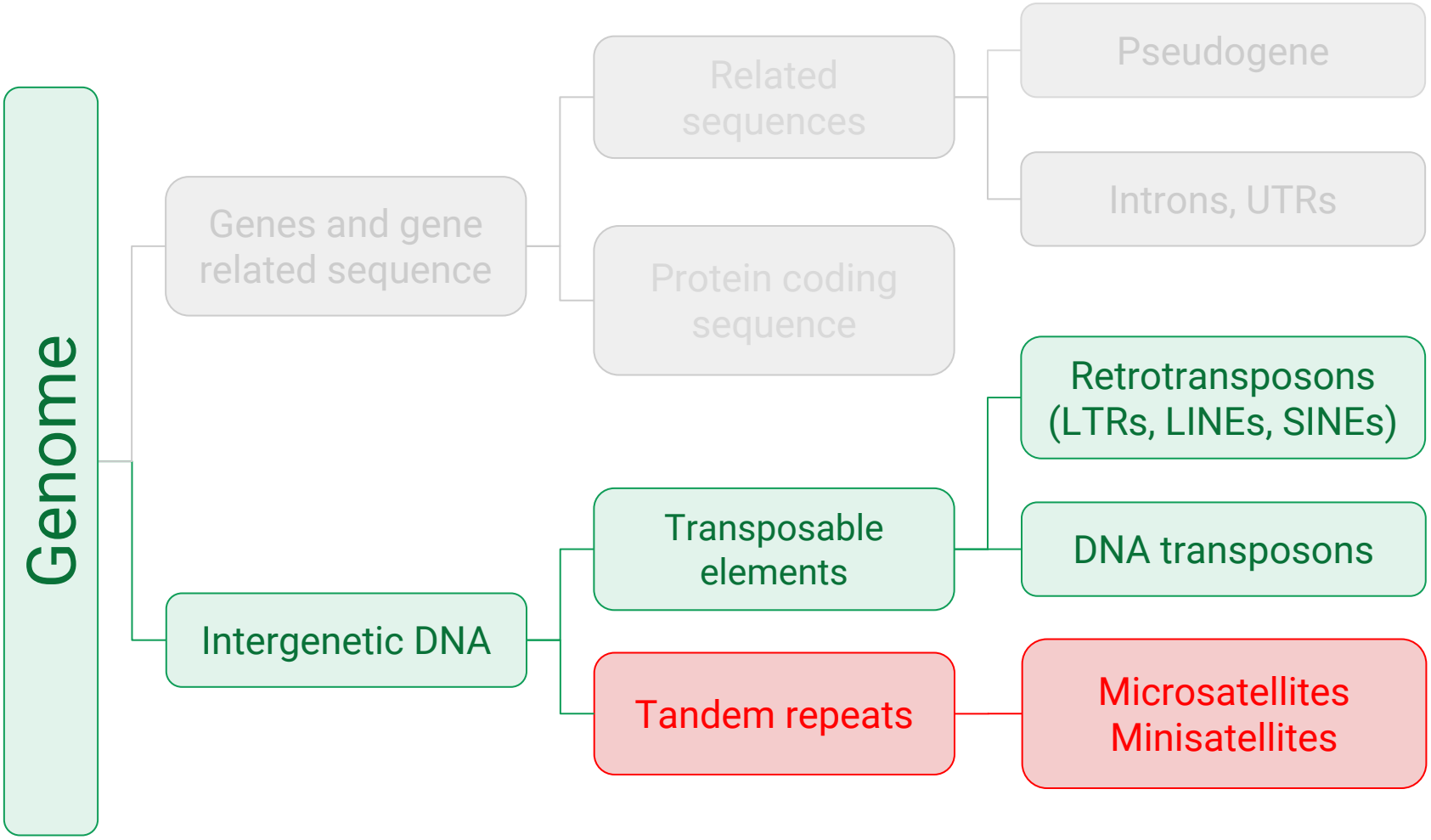
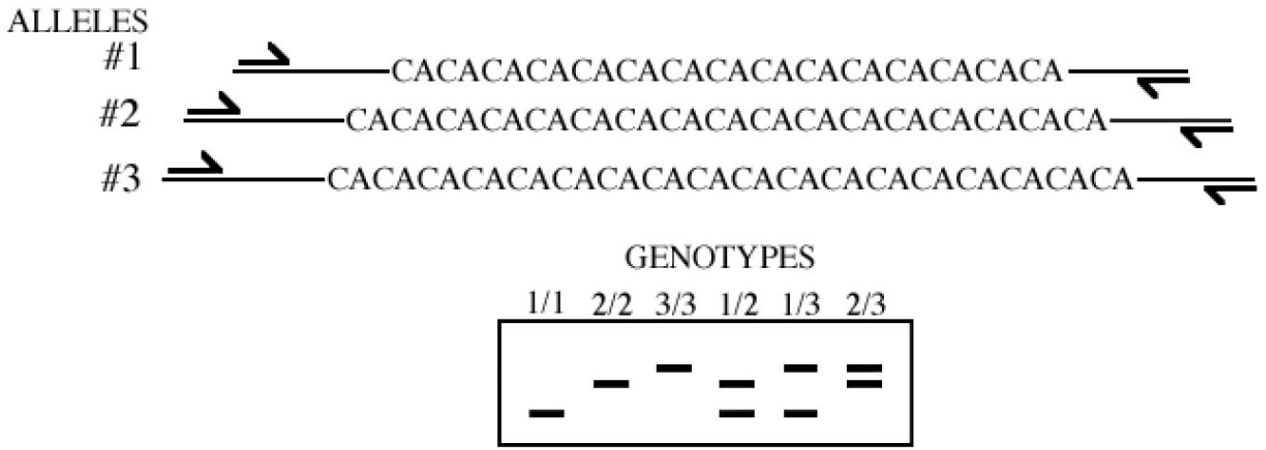


(T. Ryan Gregory, *Nature Reviews Genetics,* 2005)

Tandem repeats (TRs, Simple sequence repeat)

- Microsatellites (1-10nt)
- Minisatellites (> 10nt)
- Repeat 5 - 50 times
- 50,000-100,000 dinucleotide microstaellites in human genome

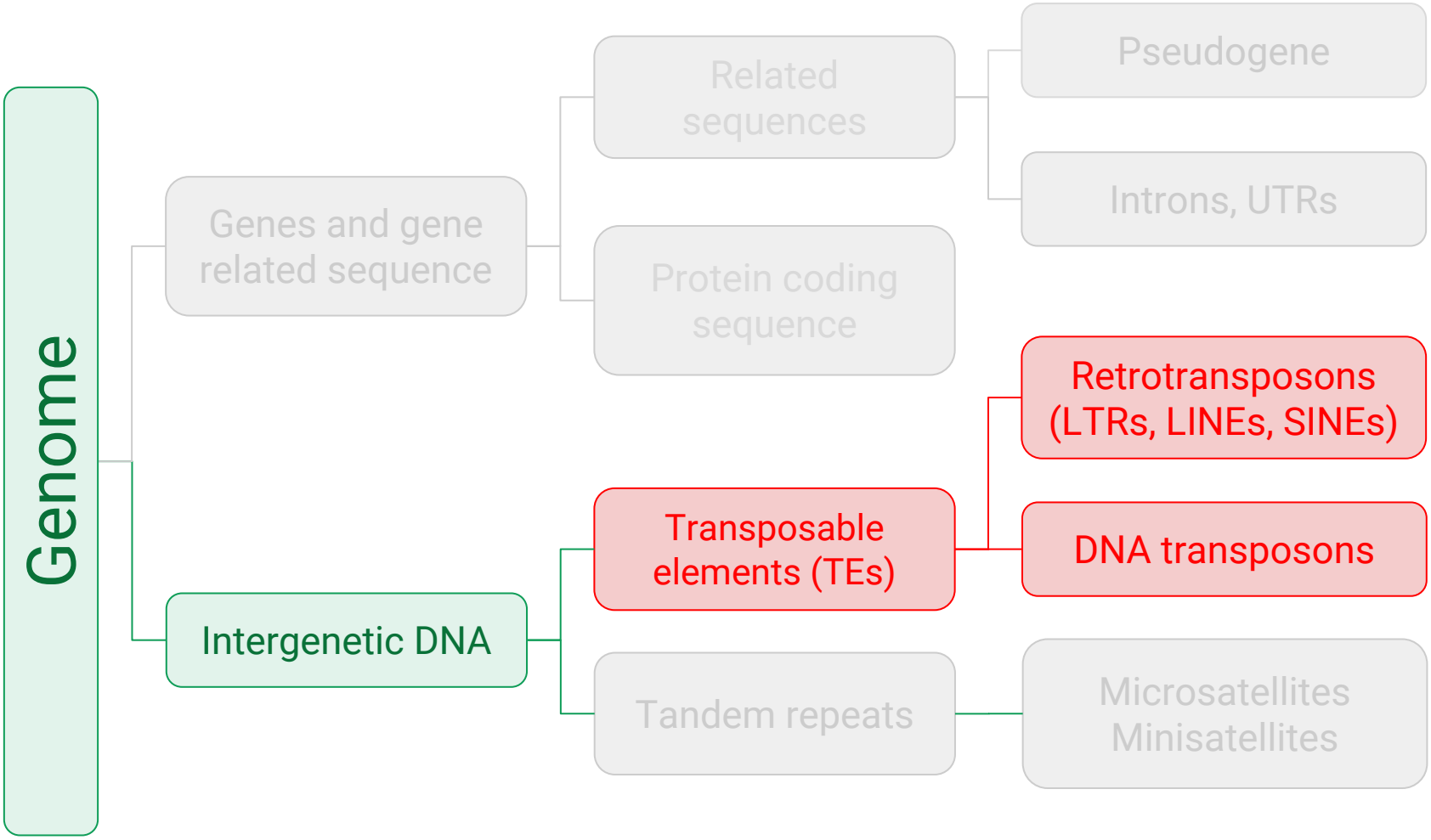


Tandem repeats (TRs)

- Mutation rate
  - 10^{-2} - 10^{-6} / sexual generation
  - points mutation (10^{-10} - 10^{-11}/ sexual generation)
  - (10^{-6}) x (2 x 3 x 10^{9}) = 6 x 10^{3} mutations per gen.
- Telomeres
  - TTAGGG 2,500 times in human
  - 11 kilobases at birth → 4 kilobases in old age
- Huntington's disease
  - Expansion of CAG in gene coding region of Huntingtin protein

Genome structure (1)

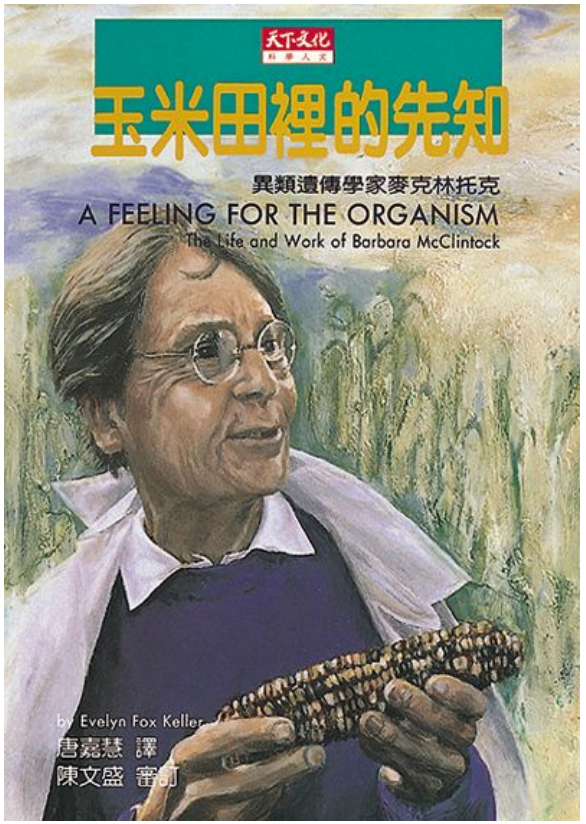
Genome: The genetic material of an organism.



(T. Ryan Gregory, *Nature Reviews Genetics,* 2005)

Transposable Elements (TE, transposons) (1)

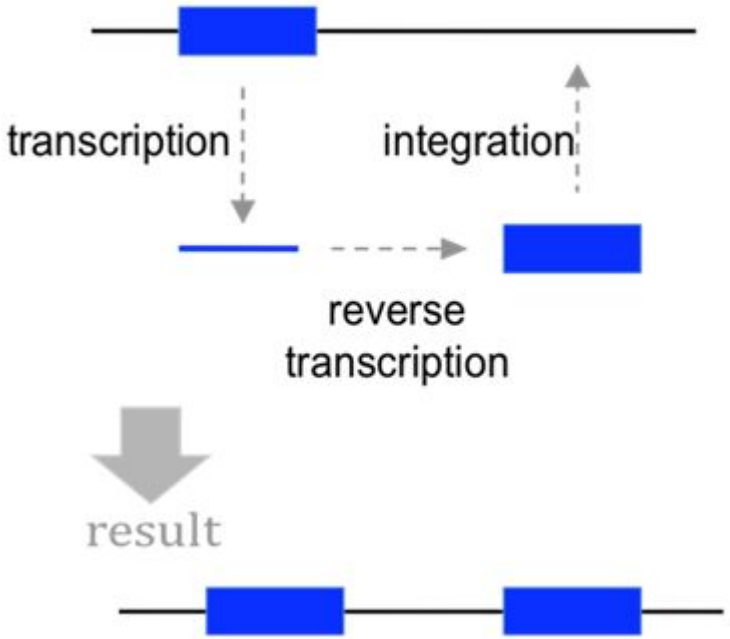
- Barbara McClintock (1902 - 1992)
- First discovered in Maize (1948)
- 1983 Nobel Prize
- A DNA sequence that can change its position within a genome.

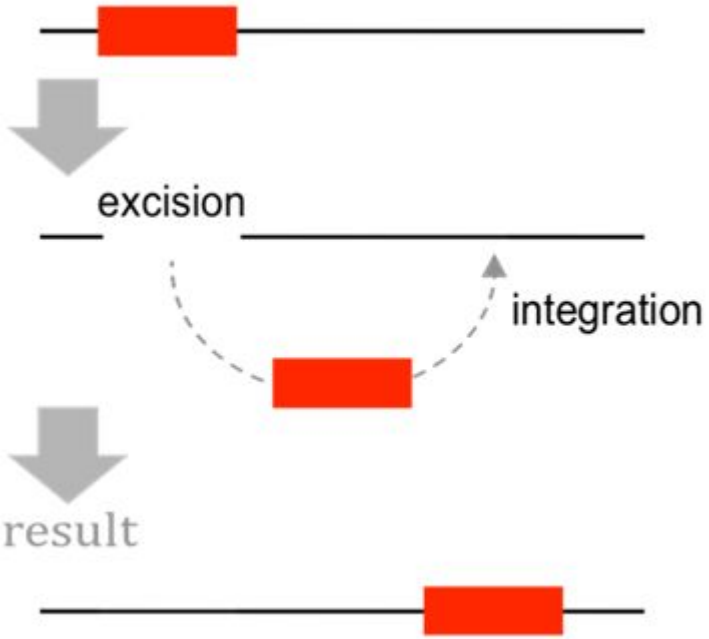


https://images-na.ssl-images-amazon.com/images/I/817ocdJh0-L.jpg
https://bookzone.cwgv.com.tw/public/upload/books/BCS/BCS019/cover/thumb/BCS019.png

Transposable Elements (TE, transposons) (2)

- Retrotransposons
  - copy and paste
  - LTRs, LINEs, SINEs
  - Retroviruses
- DNA transposons
  - cut-and-paste
  - Transposase

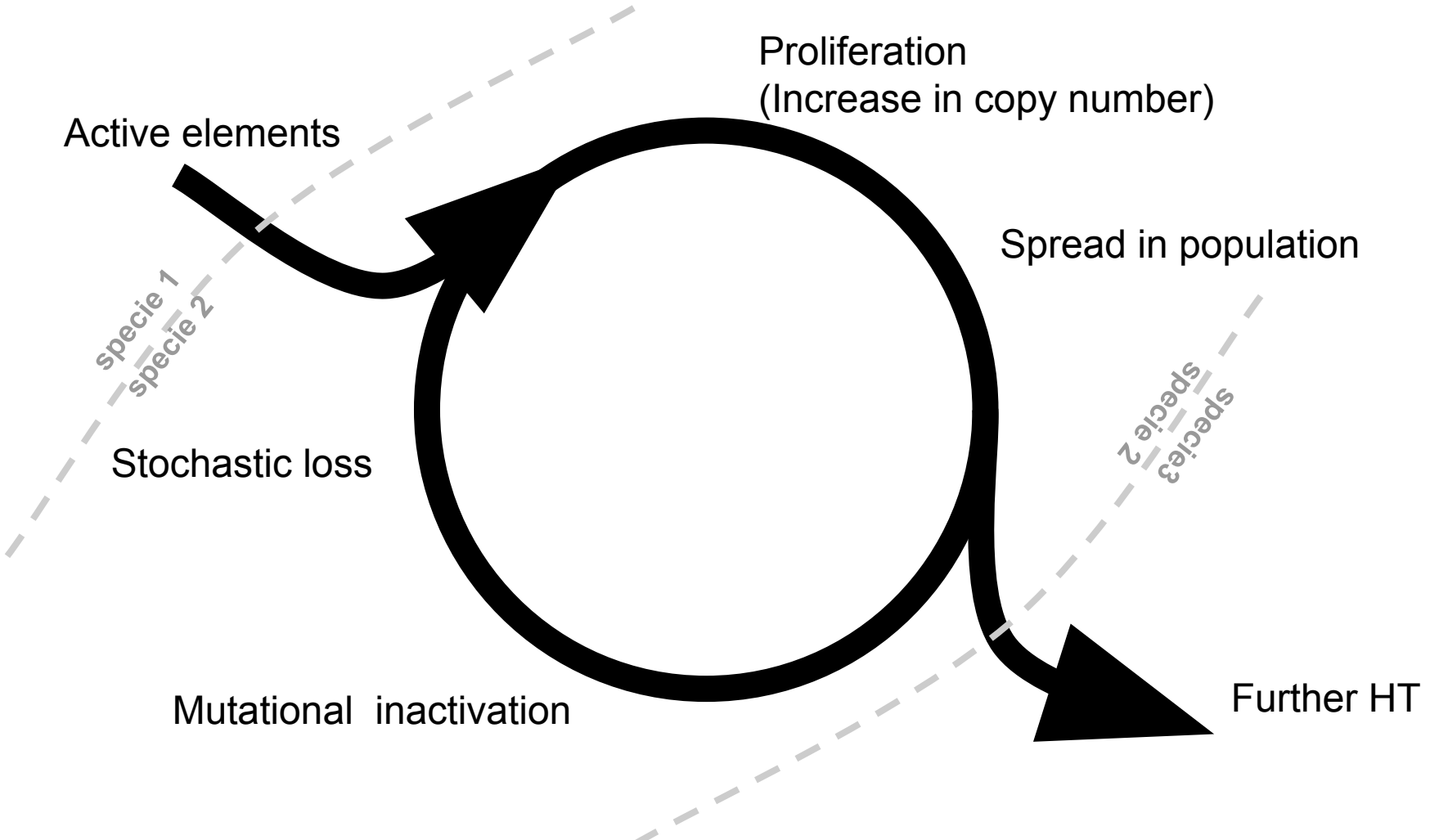




http://cubocube.com/dashboard.php?a=1182&b=1264&c=103

Horizontal Transmission of TEs (1)

- Mariner-like element



Horizontal Transmission of TEs (2)

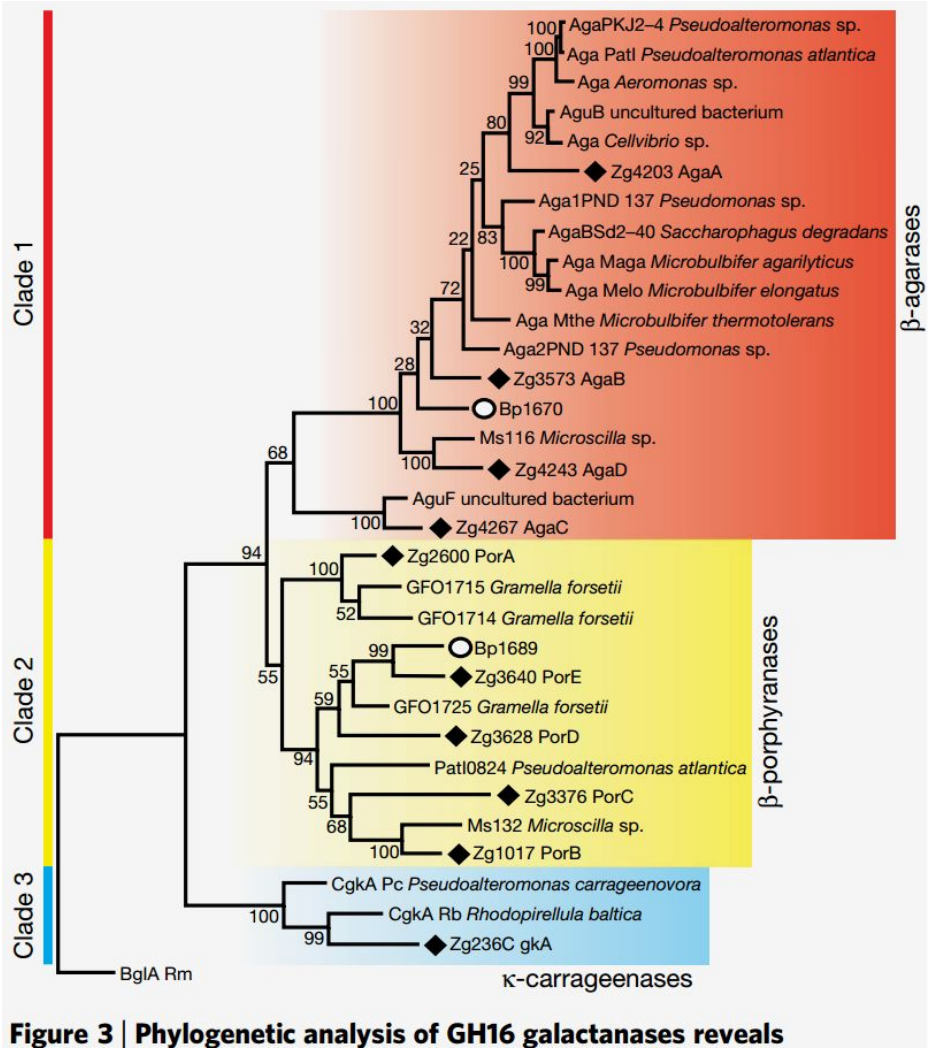


Figure 3 | Phylogenetic analysis of GH16 galactanases reveals

(Hehemann, *Nature, 2010*)

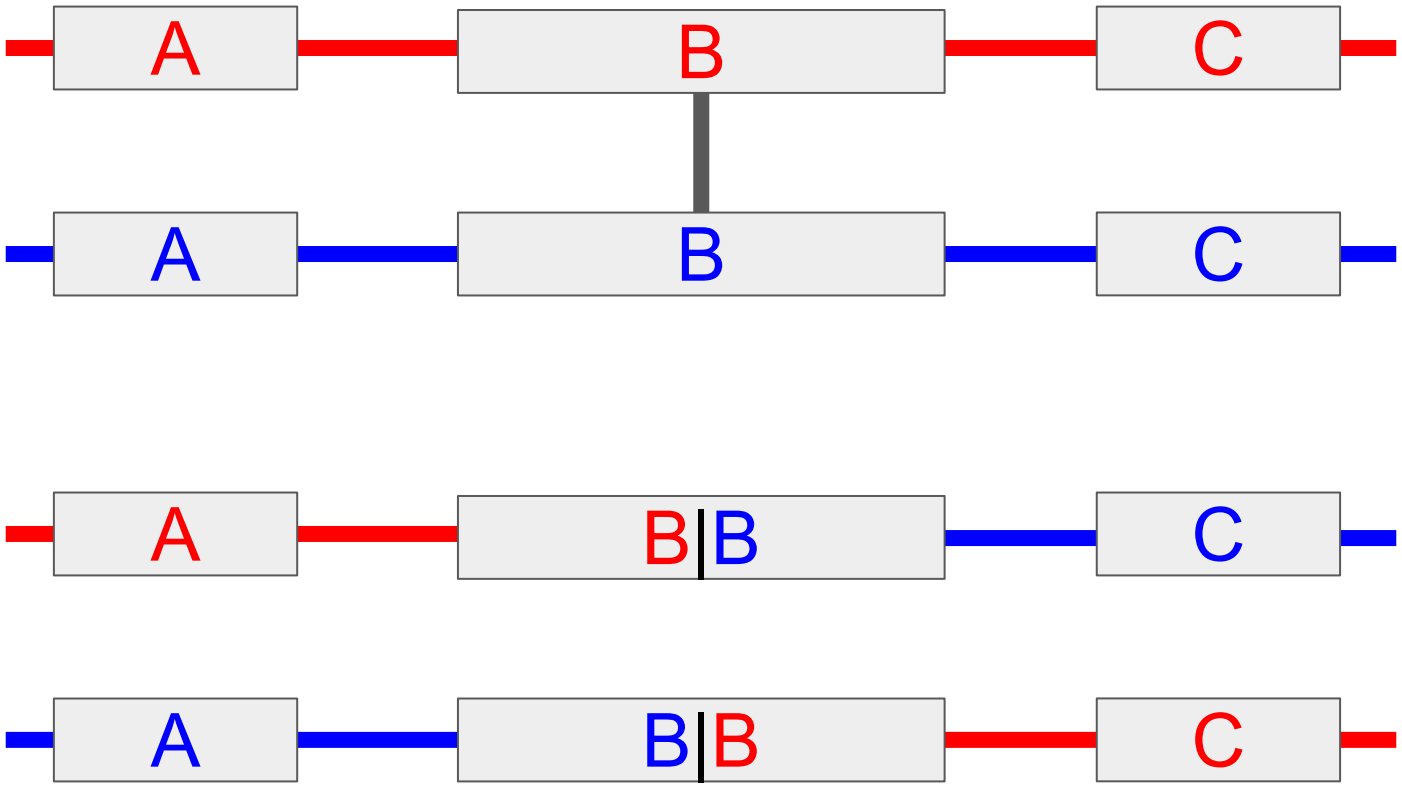
Transfer of carbohydrate active enzymes from marine bacteria to Japanese gut microbita

Hehemann, *Nature, 2010*

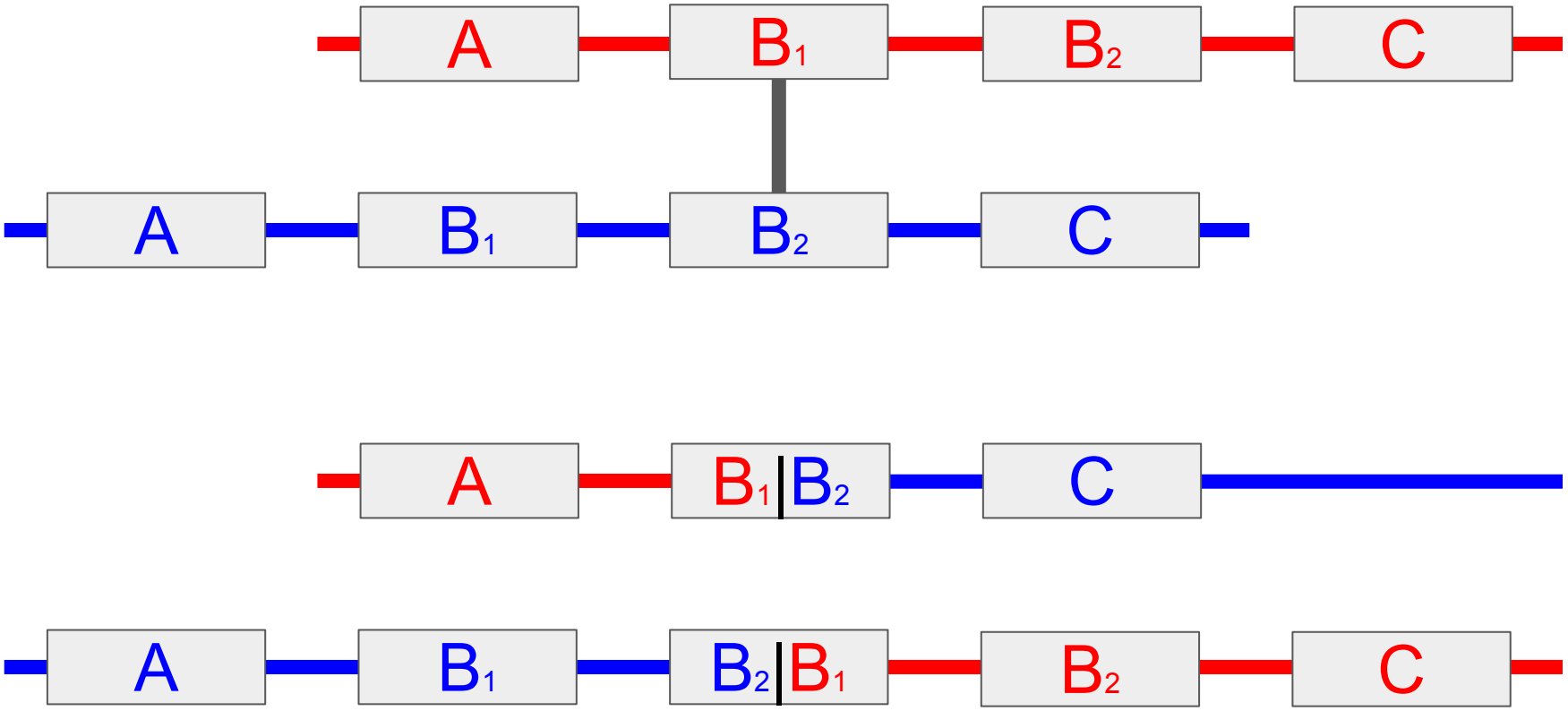
"The consumption of food with associated environmental bacteria is the most likely mechanism that promoted this CAZyme update into the human gut microbe."

Hehemann

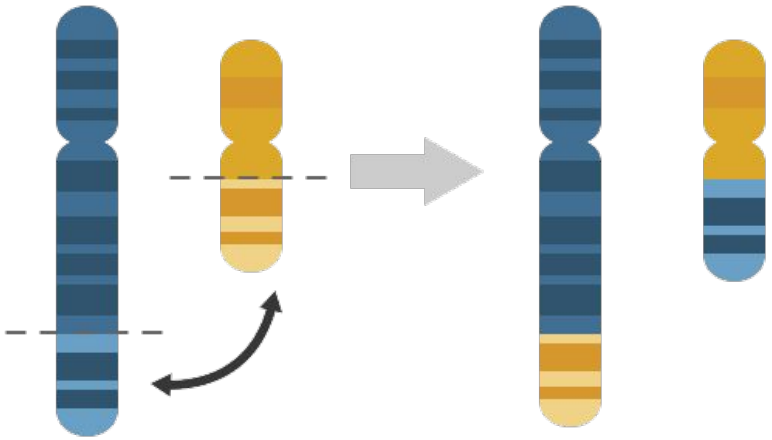
Crossing over

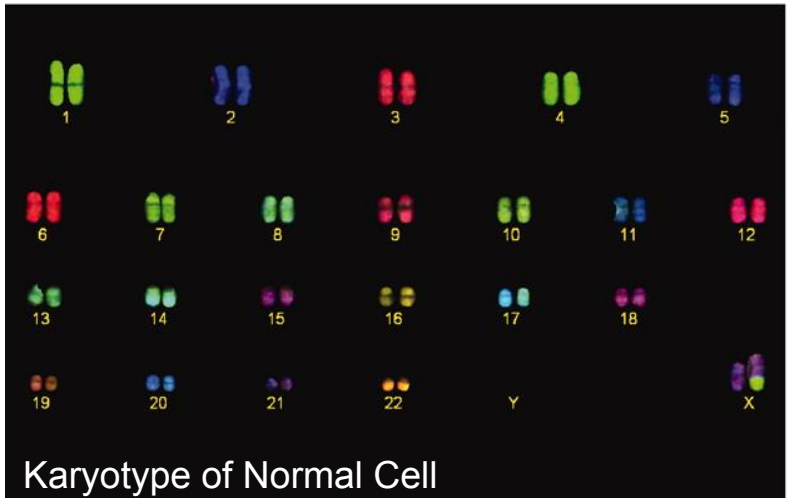


Unequal crossing over

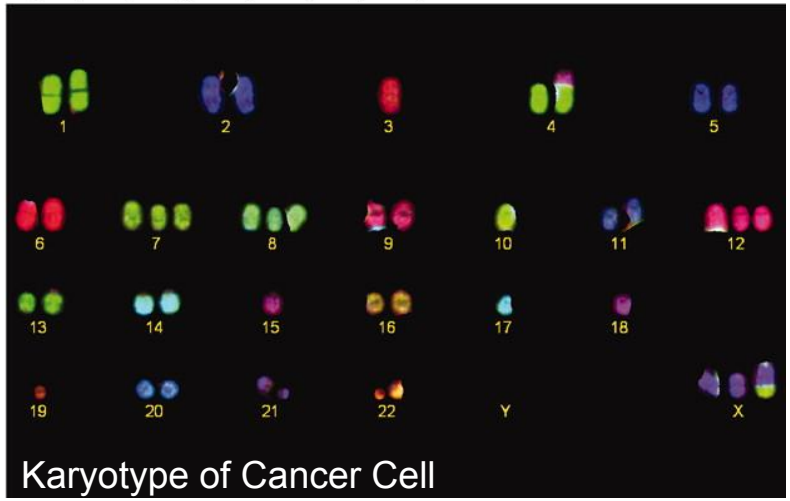


Chromosome translocation





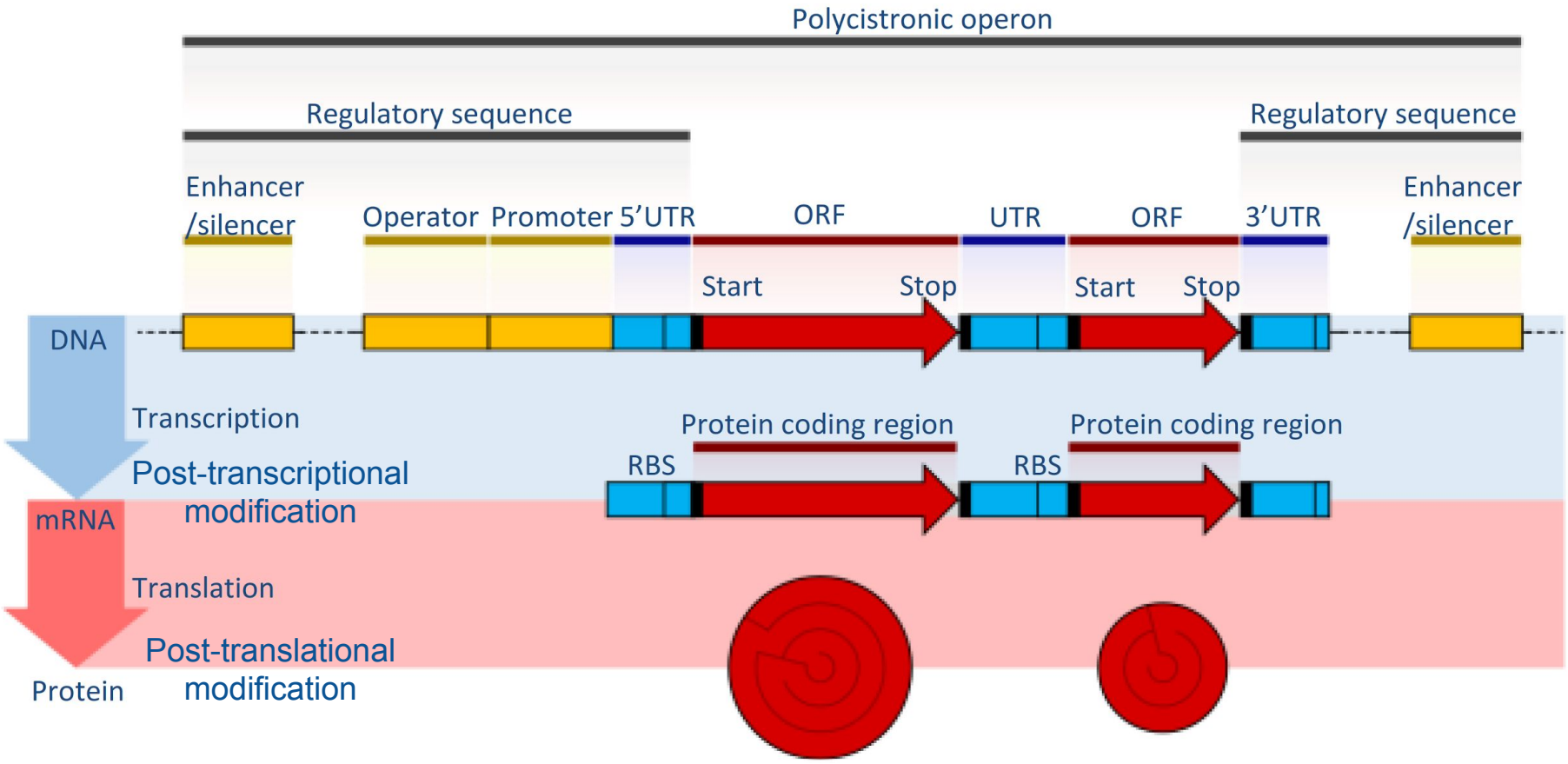
Karyotype of Normal Cell



Karyotype of Cancer Cell

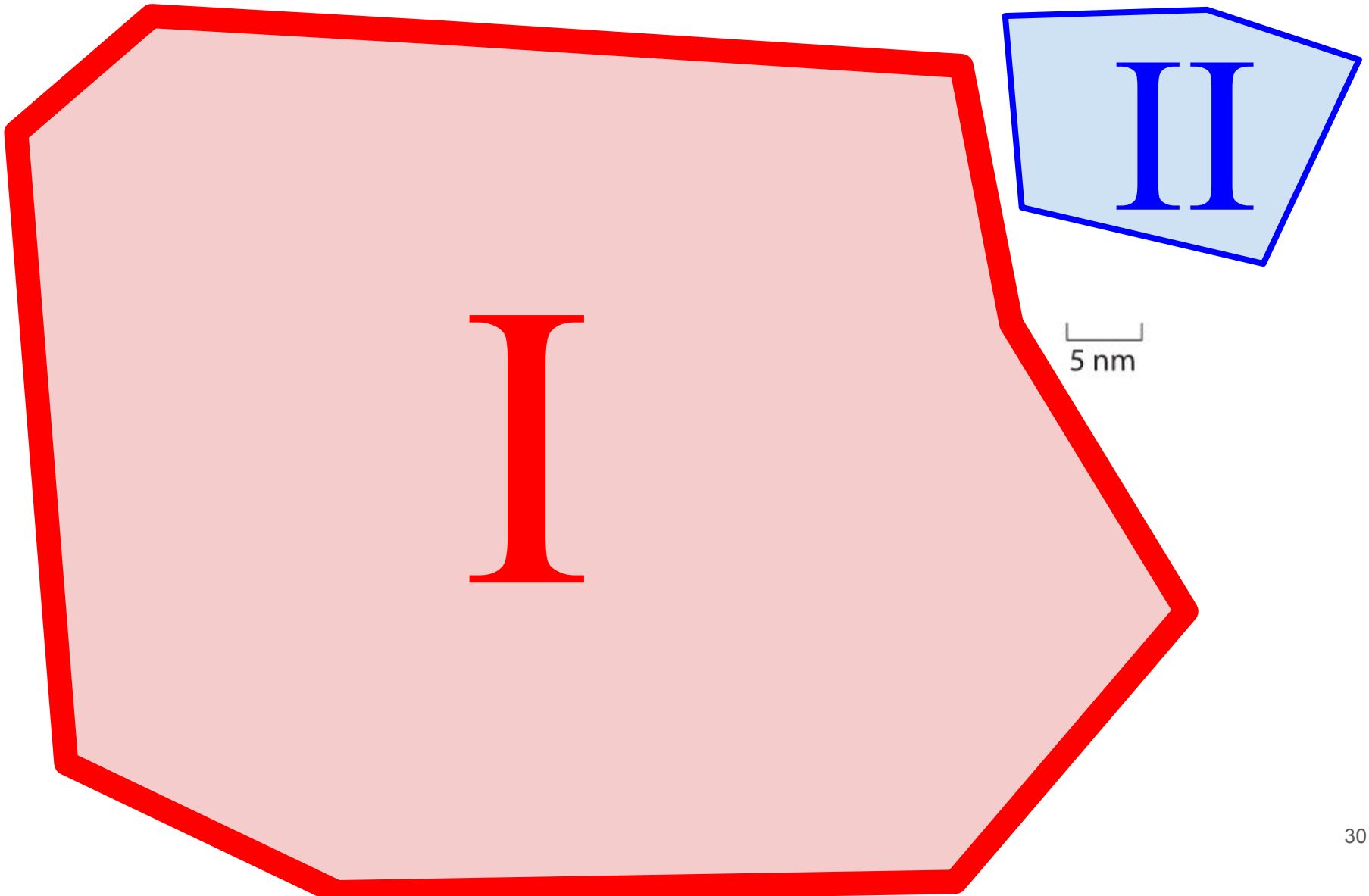
L: https://www.yourgenome.org/facts/what-is-a-chromosome-disorde
R: Janssen et al, Science 30 Sep, 2011

The structure of a eukaryotic protein-coding gene



UTR: UnTranslated Regions
ORF: Open Reading Frame

Which is bigger, mRNA or the protein it codes for?



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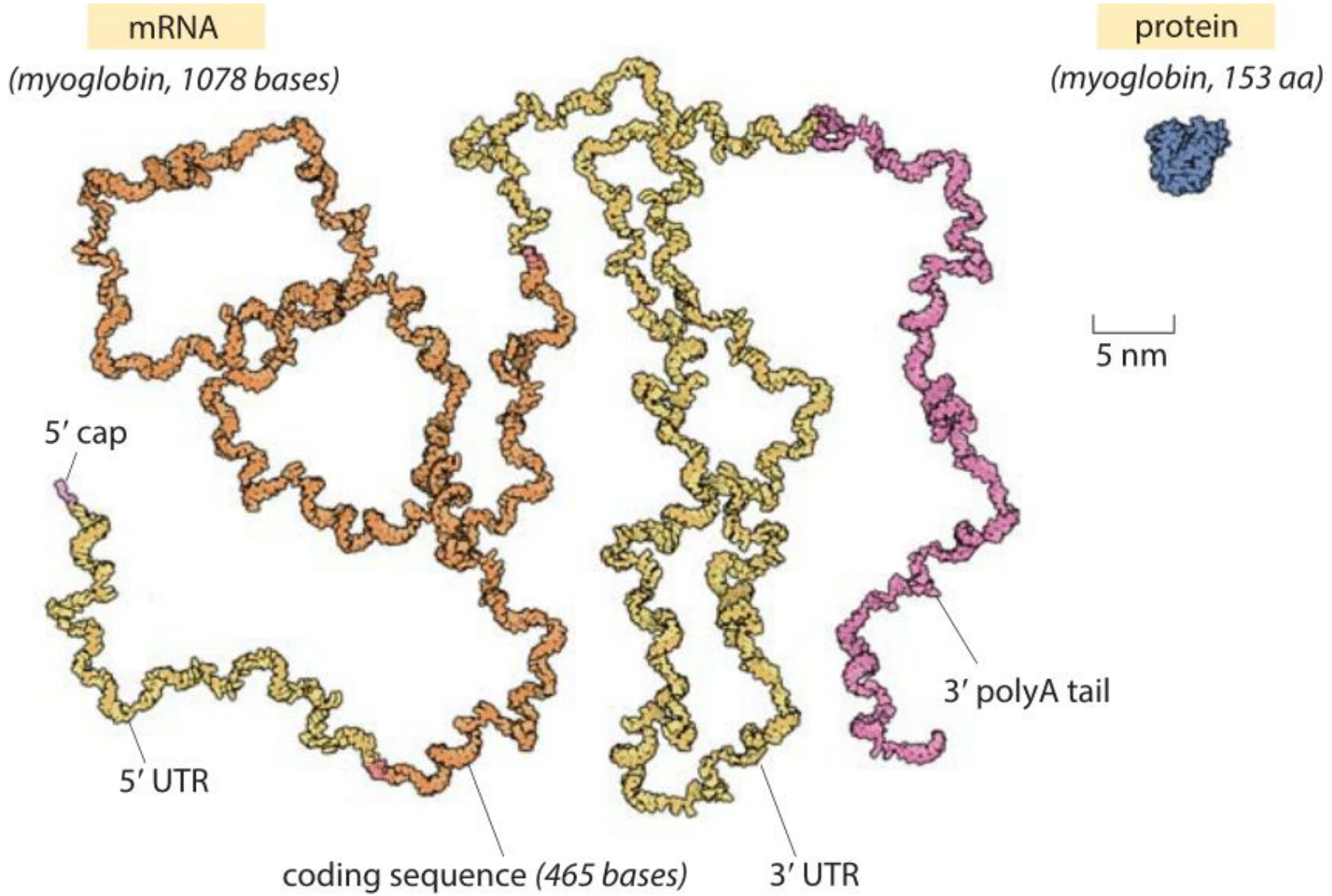
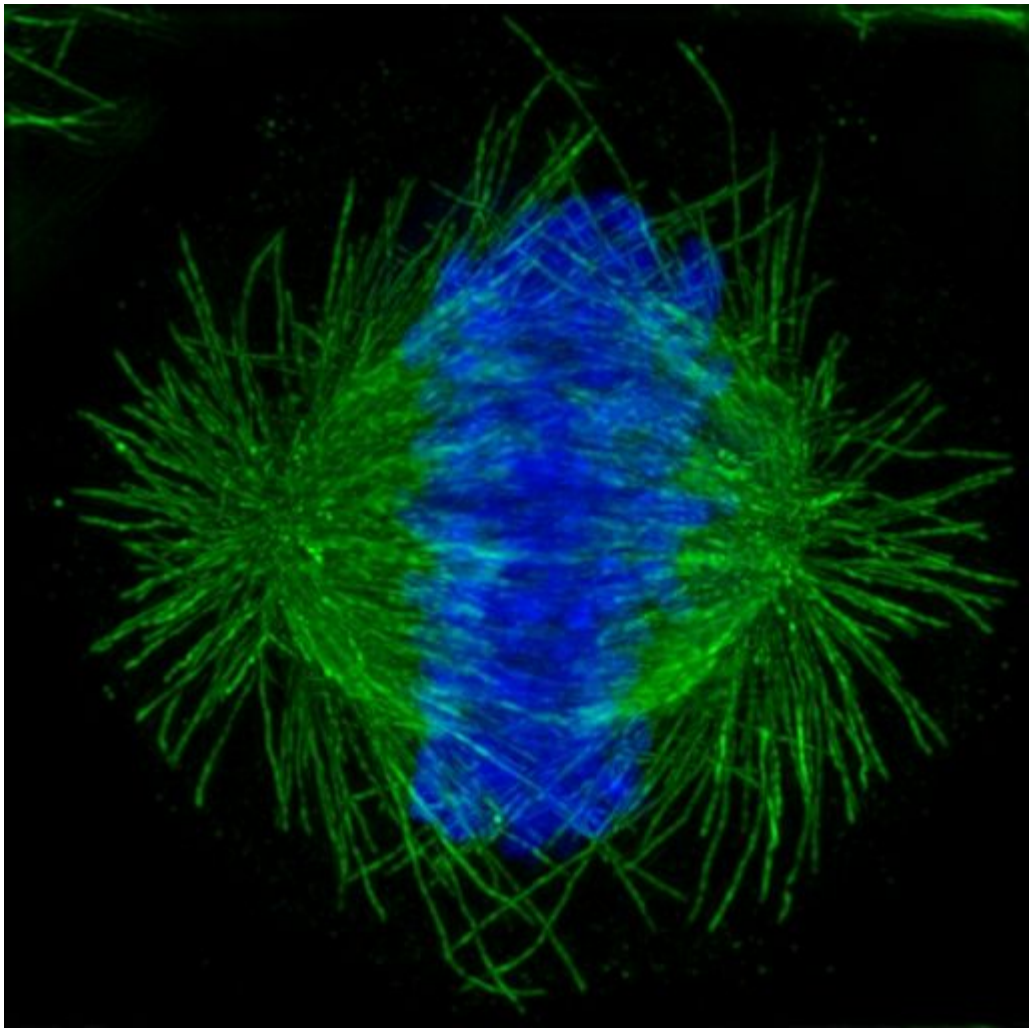


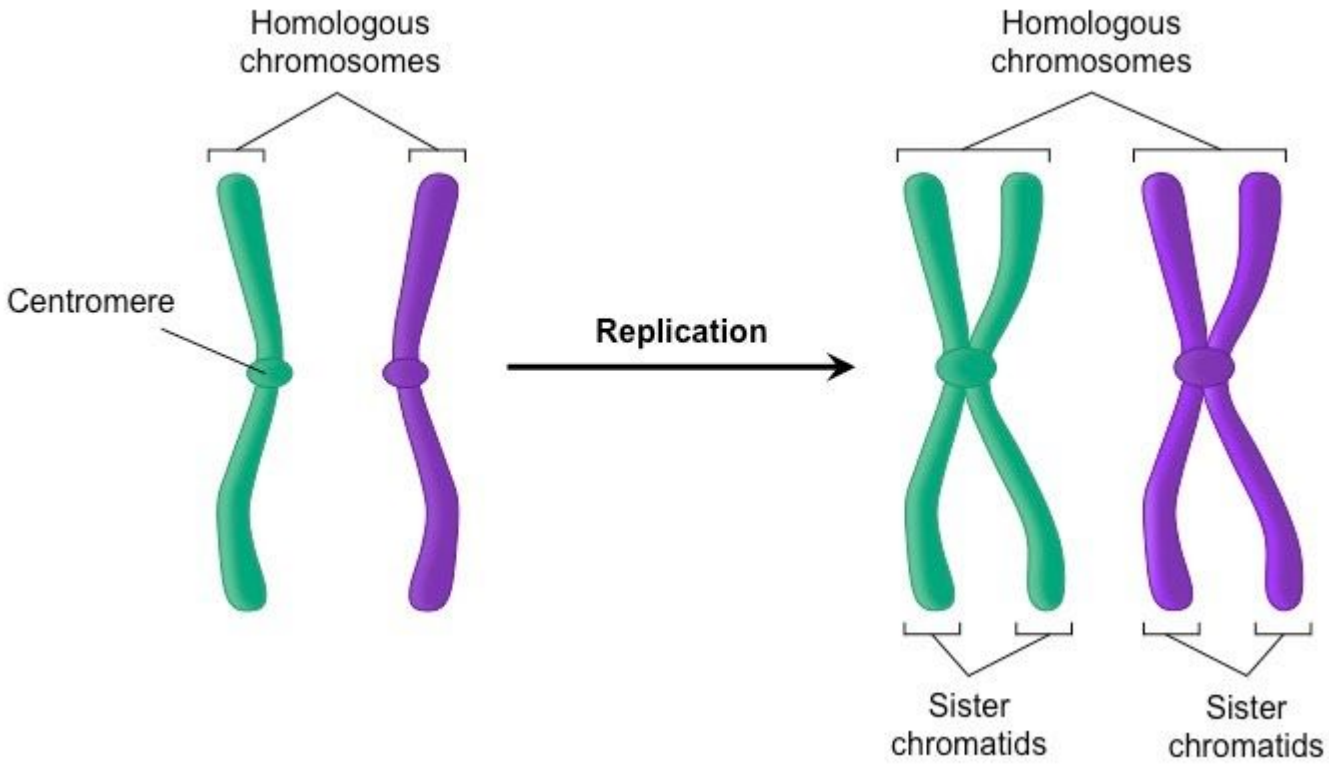
Cell division

- mitosis
- meiosis



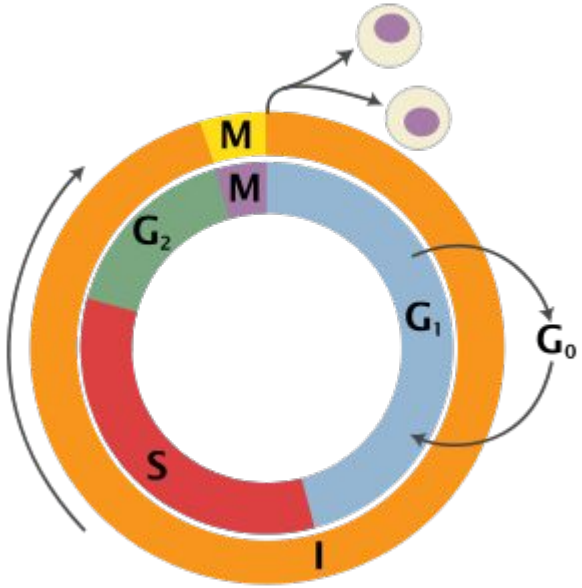
http://www.lunenfeld.ca/about-us/discovery-corner-stories/hela-cell-undergoing-mitosis

Sister chromosome and homologous chromosome

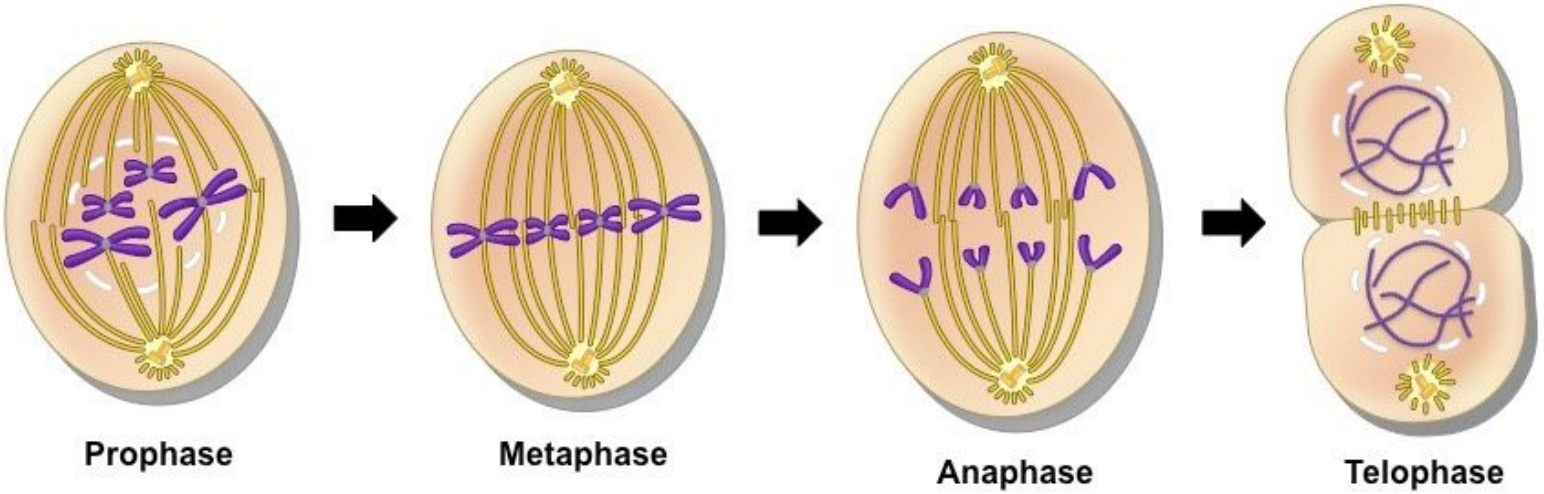


http://ib.bioninja.com.au/standard-level/topic-3-genetics/33-meiosis/sister-chromatids.html

Mitosis

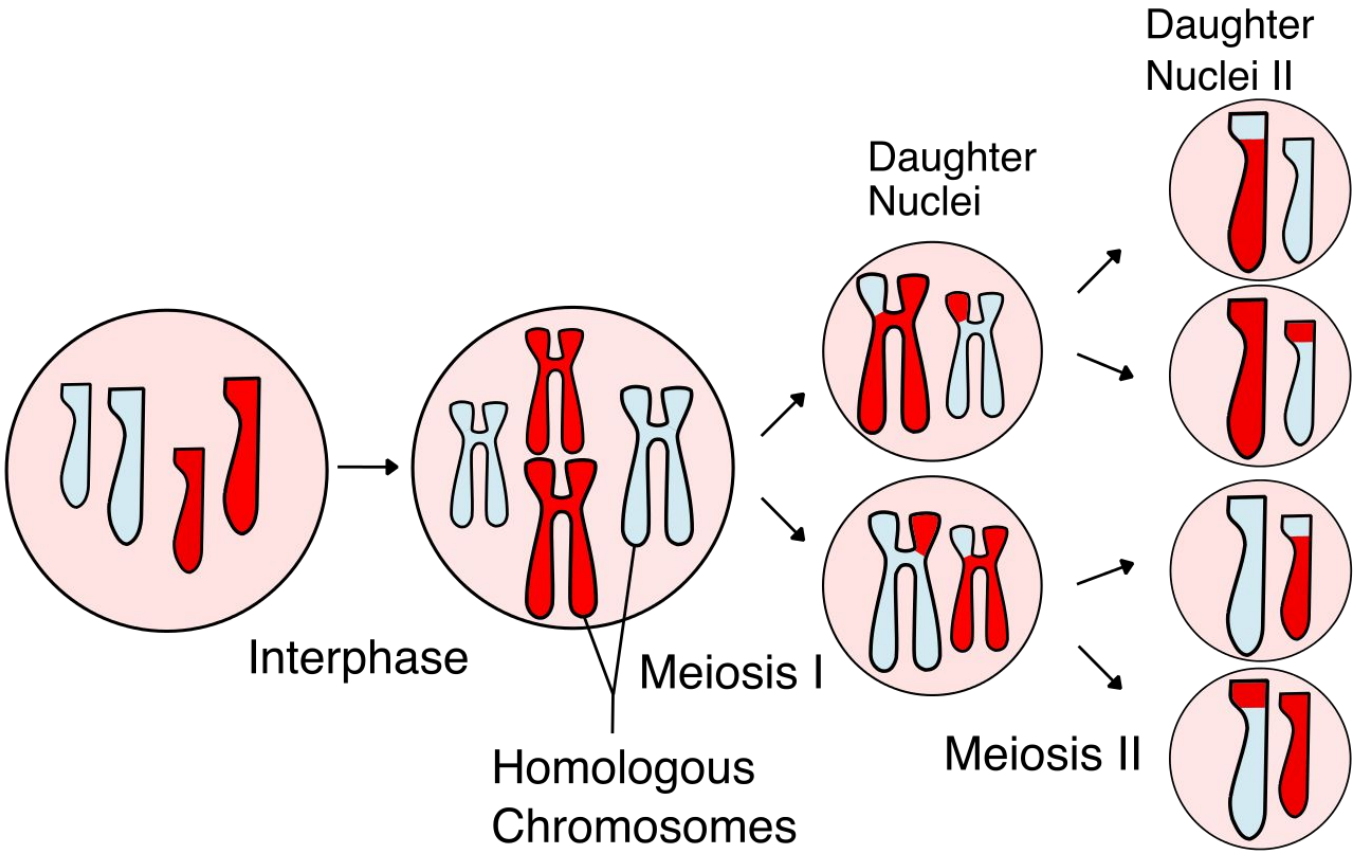


https://en.wikipedia.org/wiki/Cell_cycle



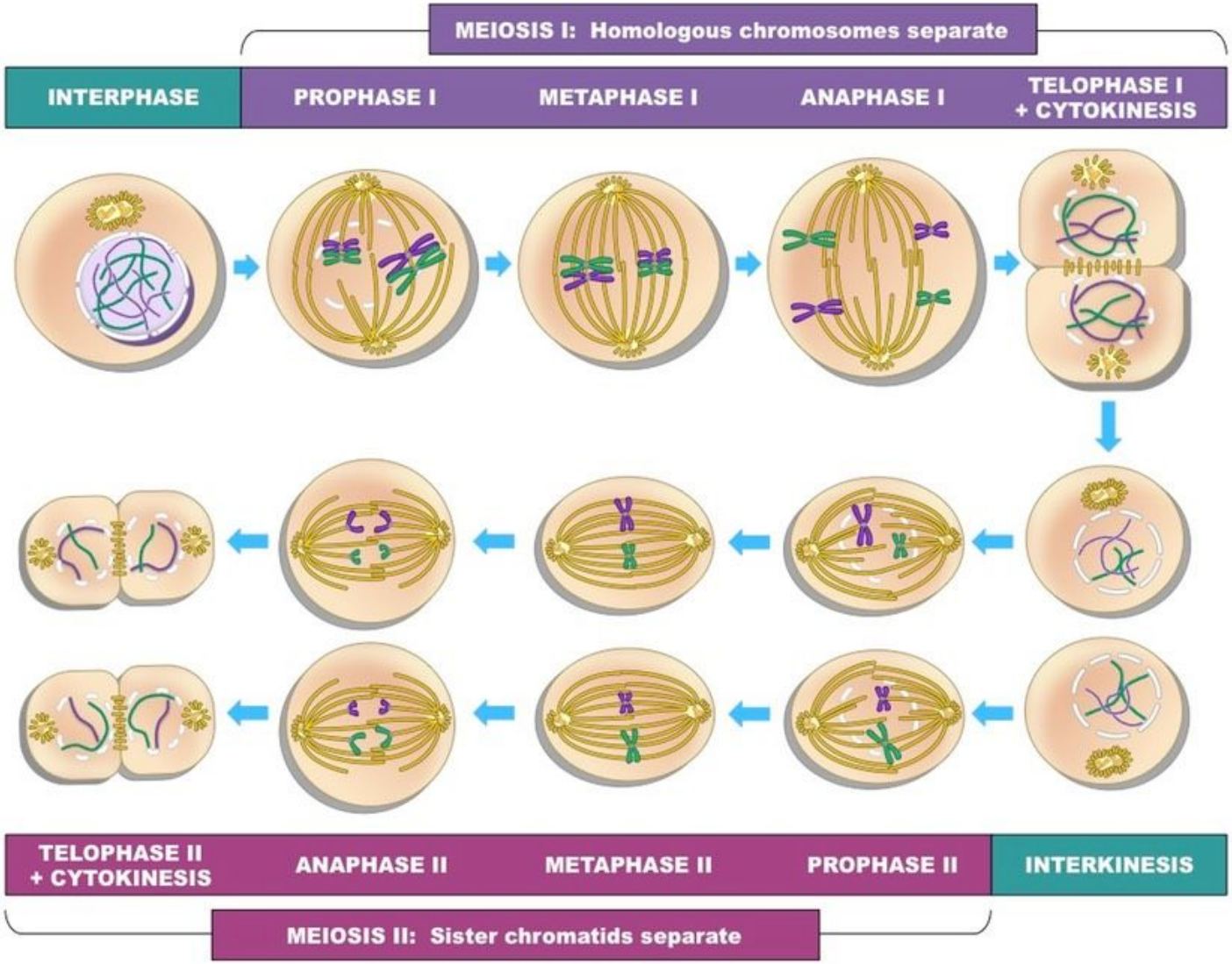
http://ib.bioninja.com.au/standard-level/topic-1-cell-biology/16-cell-division/mitosis.html

Meiosis



https://upload.wikimedia.org/wikipedia/commons/thumb/9/96/Meiosis_Overview_new.svg/1280px-Meiosis_Overview_new.svg.png

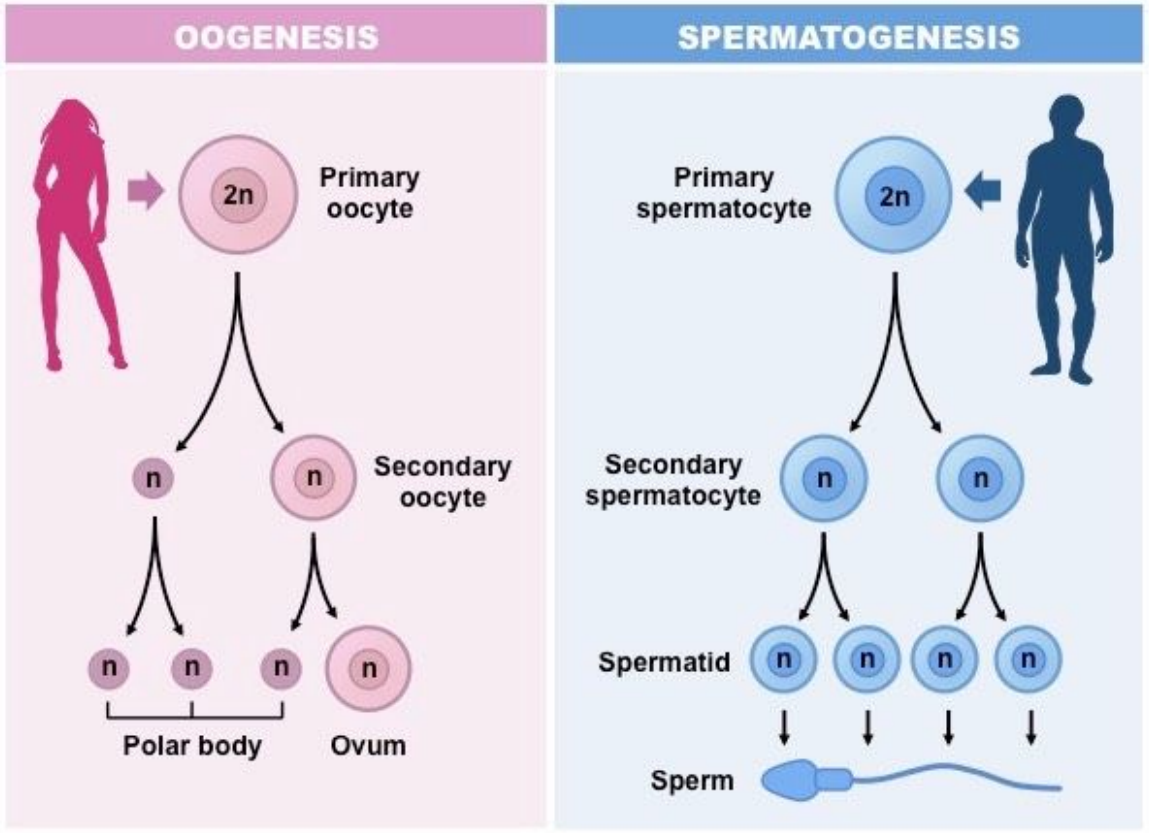
Meiosis



http://ib.bioninja.com.au/standard-level/topic-3-genetics/33-meiosis/stages-of-meiosis.html

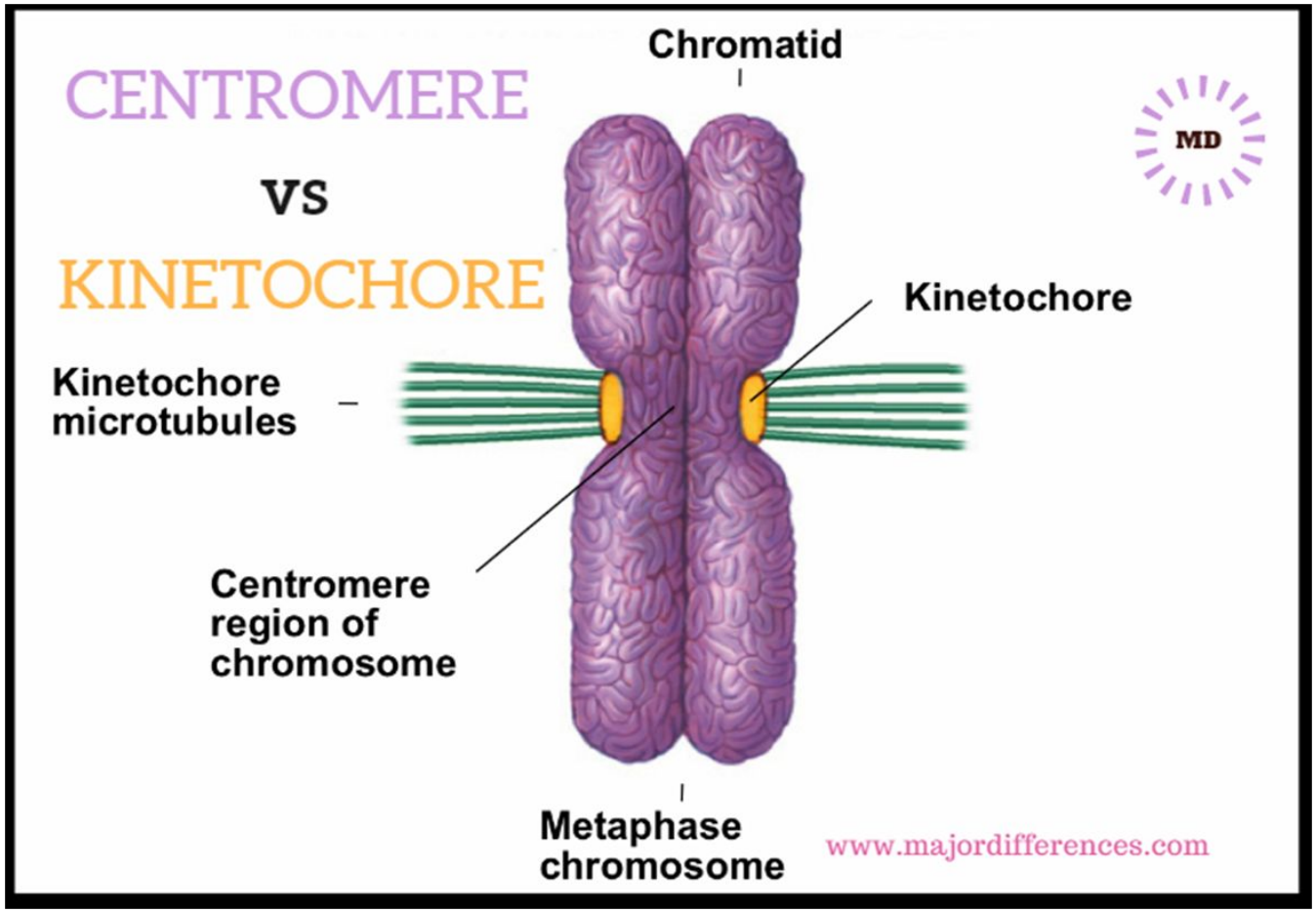
Gametogenesis

- spermatogenesis
- oogenesis



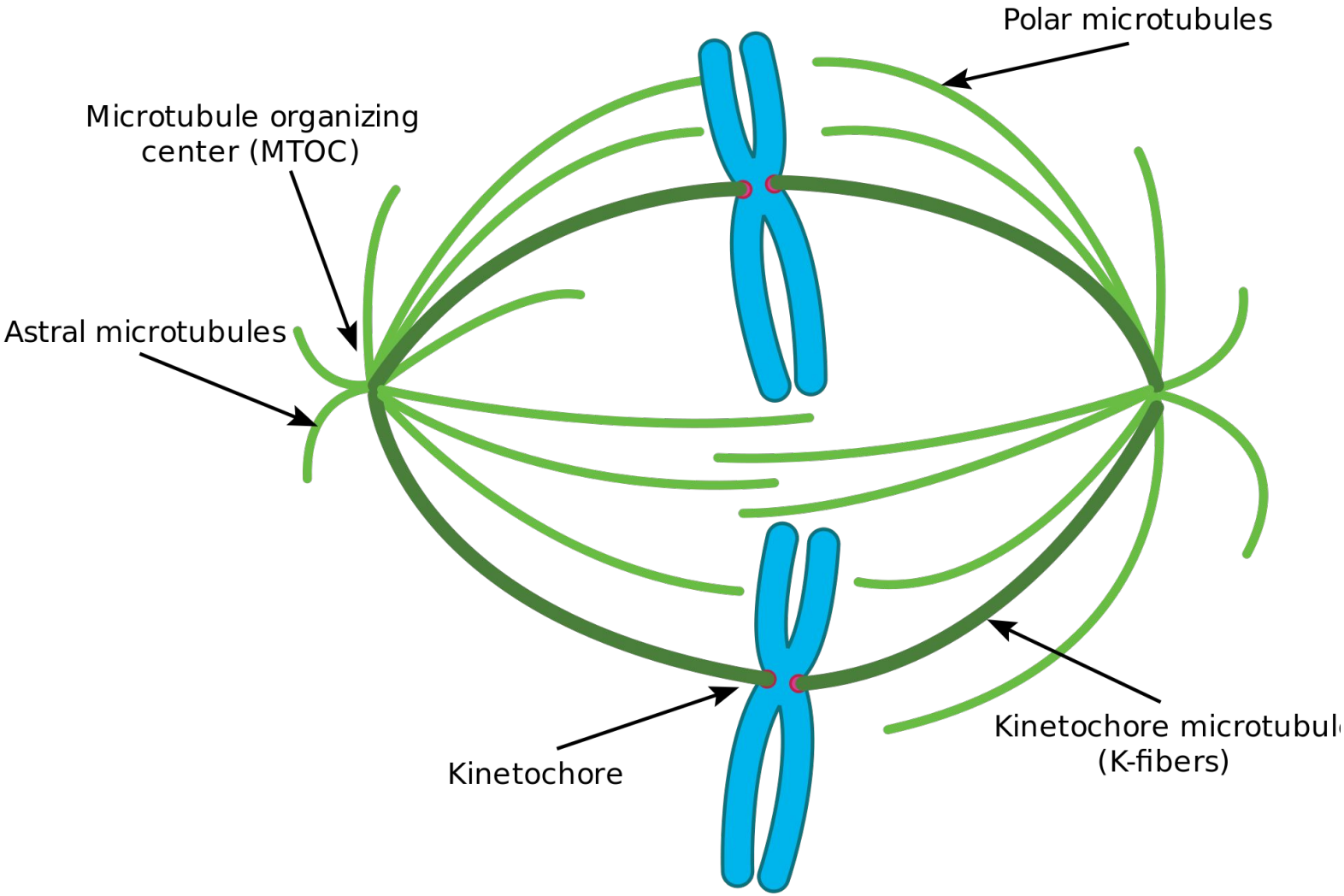
http://ib.bioninja.com.au/higher-level/topic-11-animal-physiology/114-sexual-reproduction/gametogenesis.html

Centromere and Kinetochore



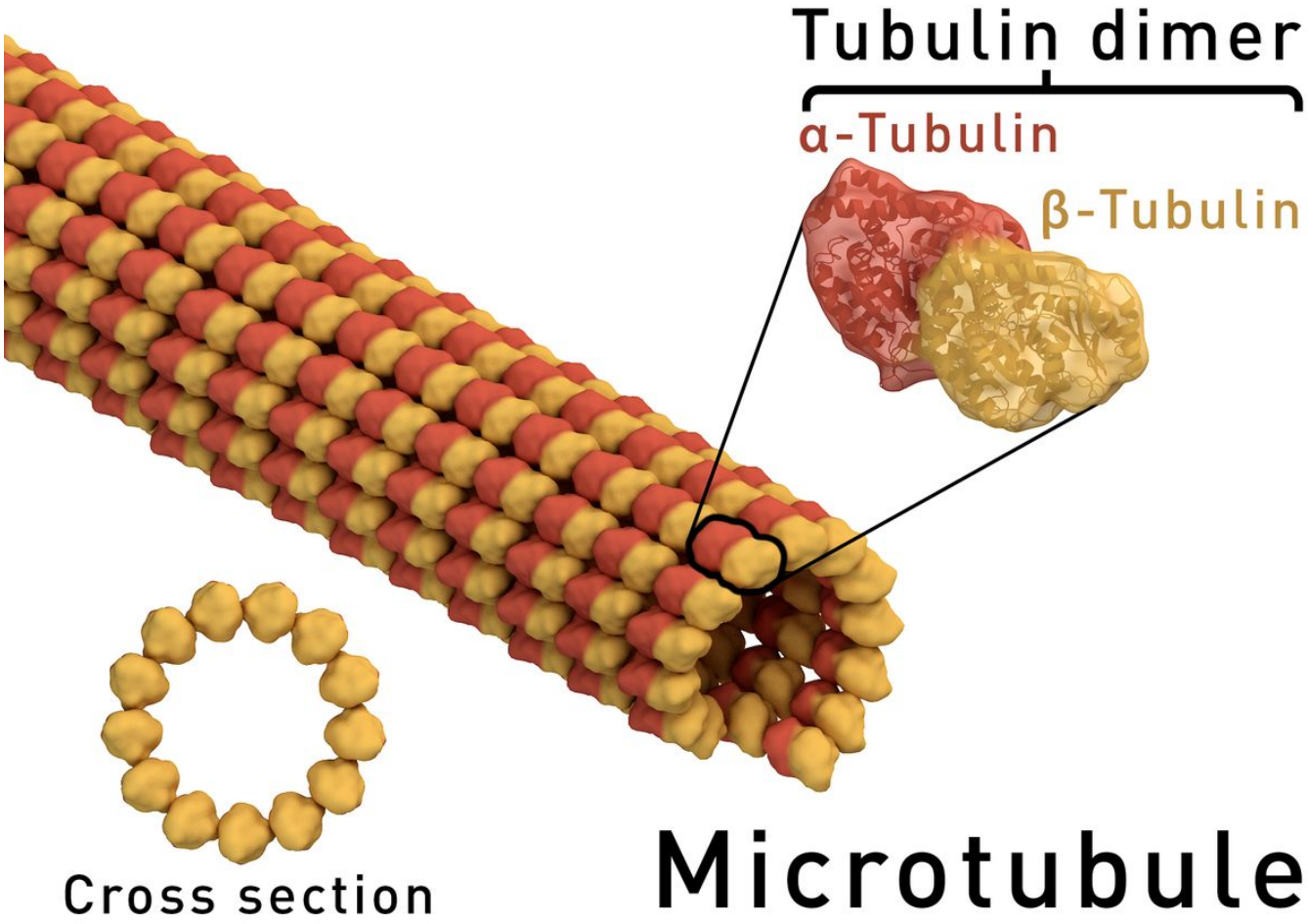
http://www.majordifferences.com/2017/03/differences-between-centromere-and-kinetochore.html#.WjUstN-Wbcs

Spindle fibers



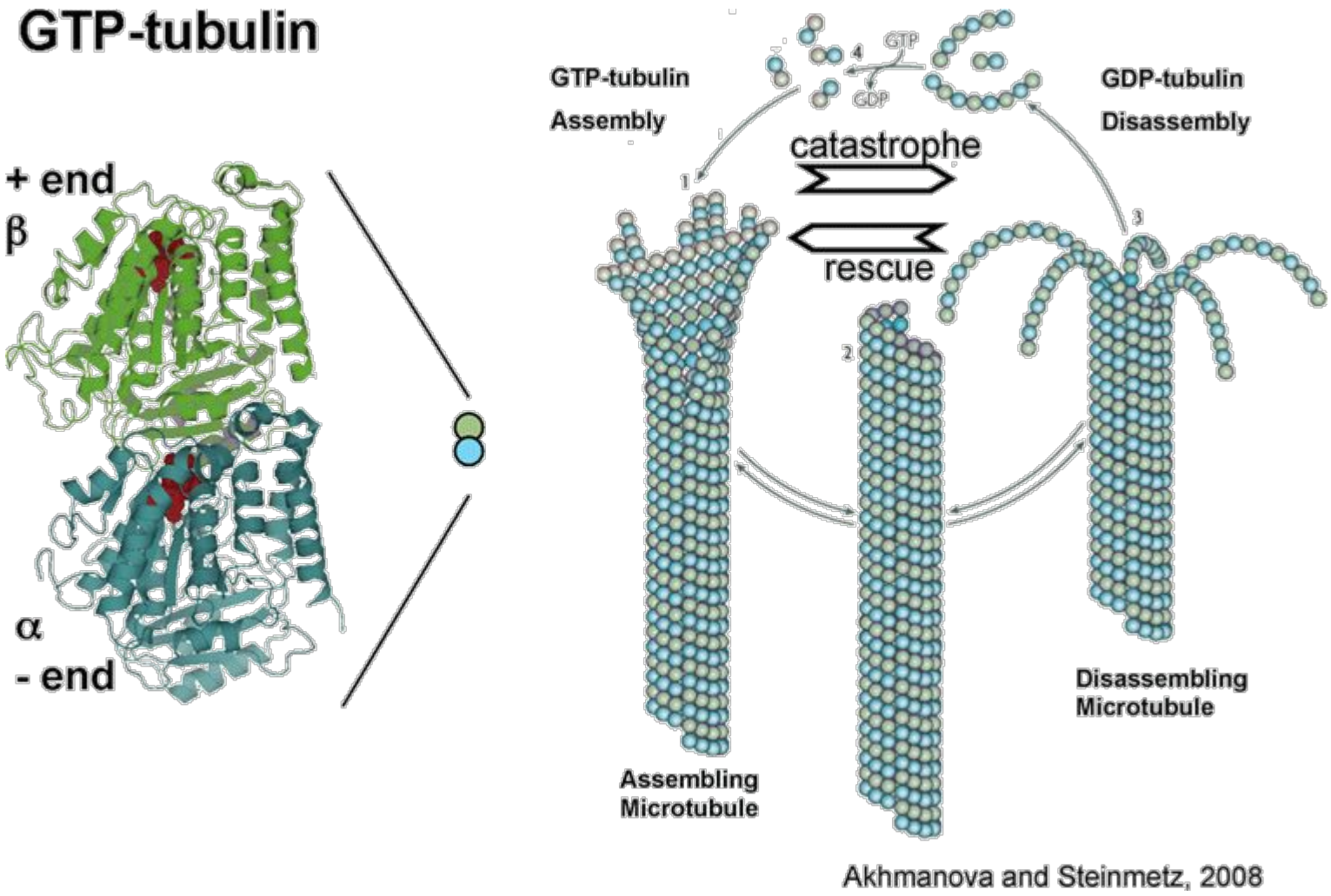
https://en.wikipedia.org/wiki/Microtubule

Microtubule and tubulin



https://en.wikipedia.org/wiki/Microtubule

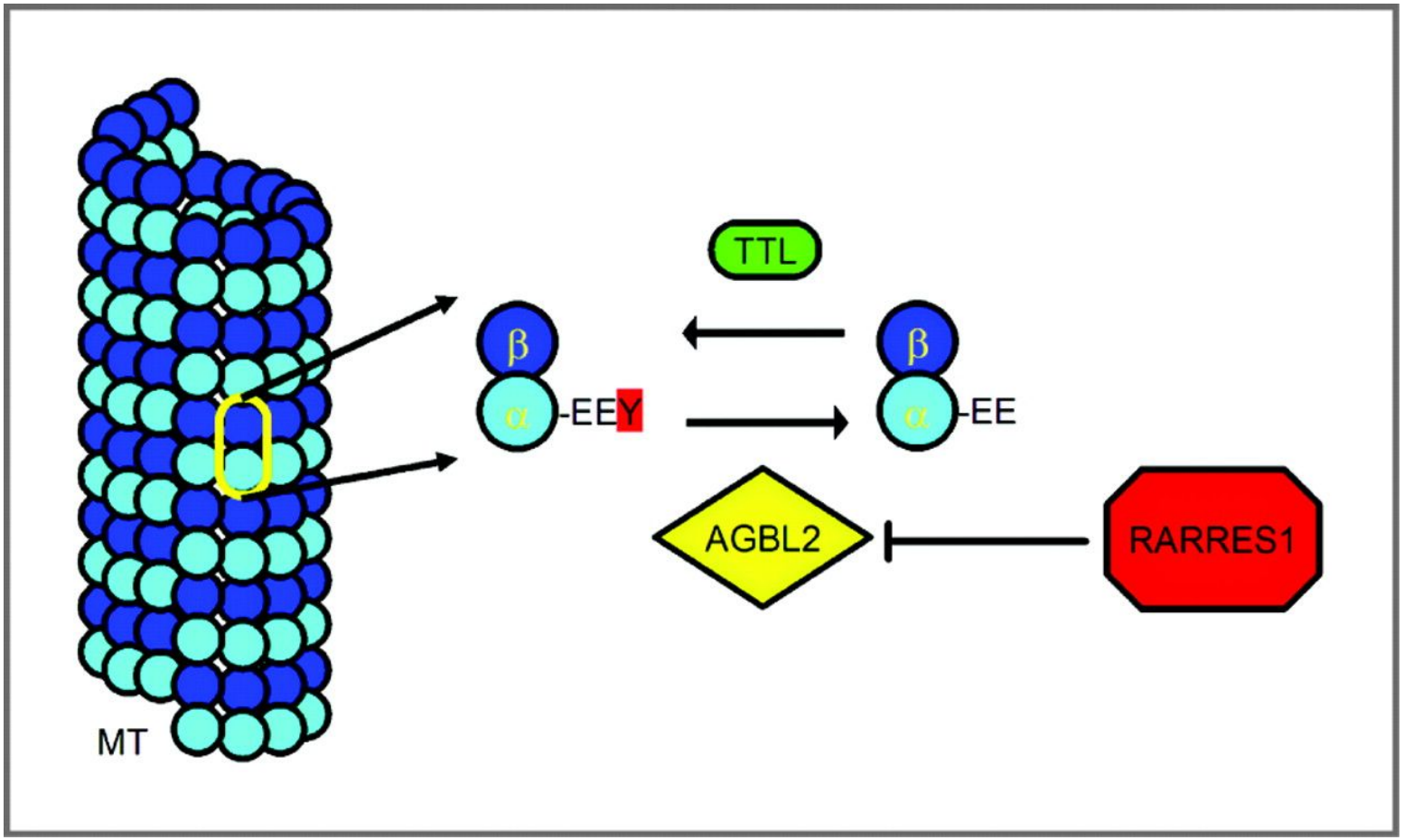
Assembly and Disassembly



https://www.mcb.ucdavis.edu/faculty-labs/al-bassam/research.html

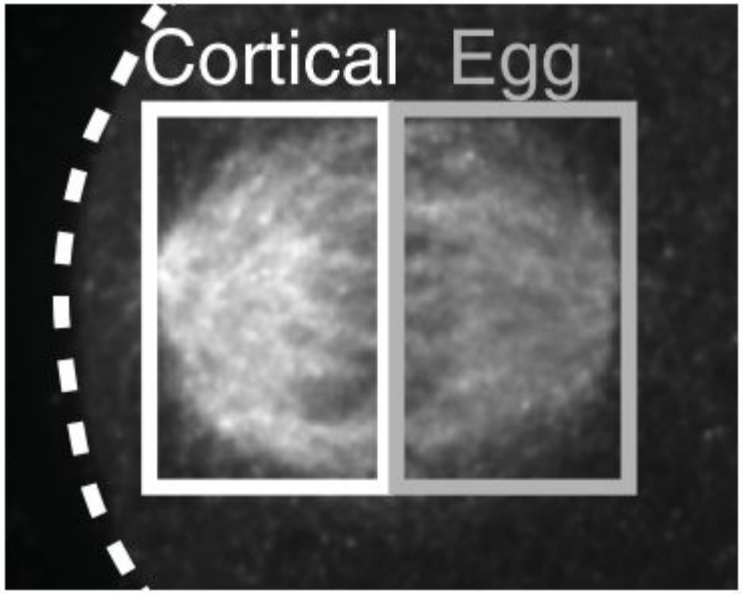
Tyrosine and alpha-tubulin

TTL:**tubulin-tyrosine ligase**



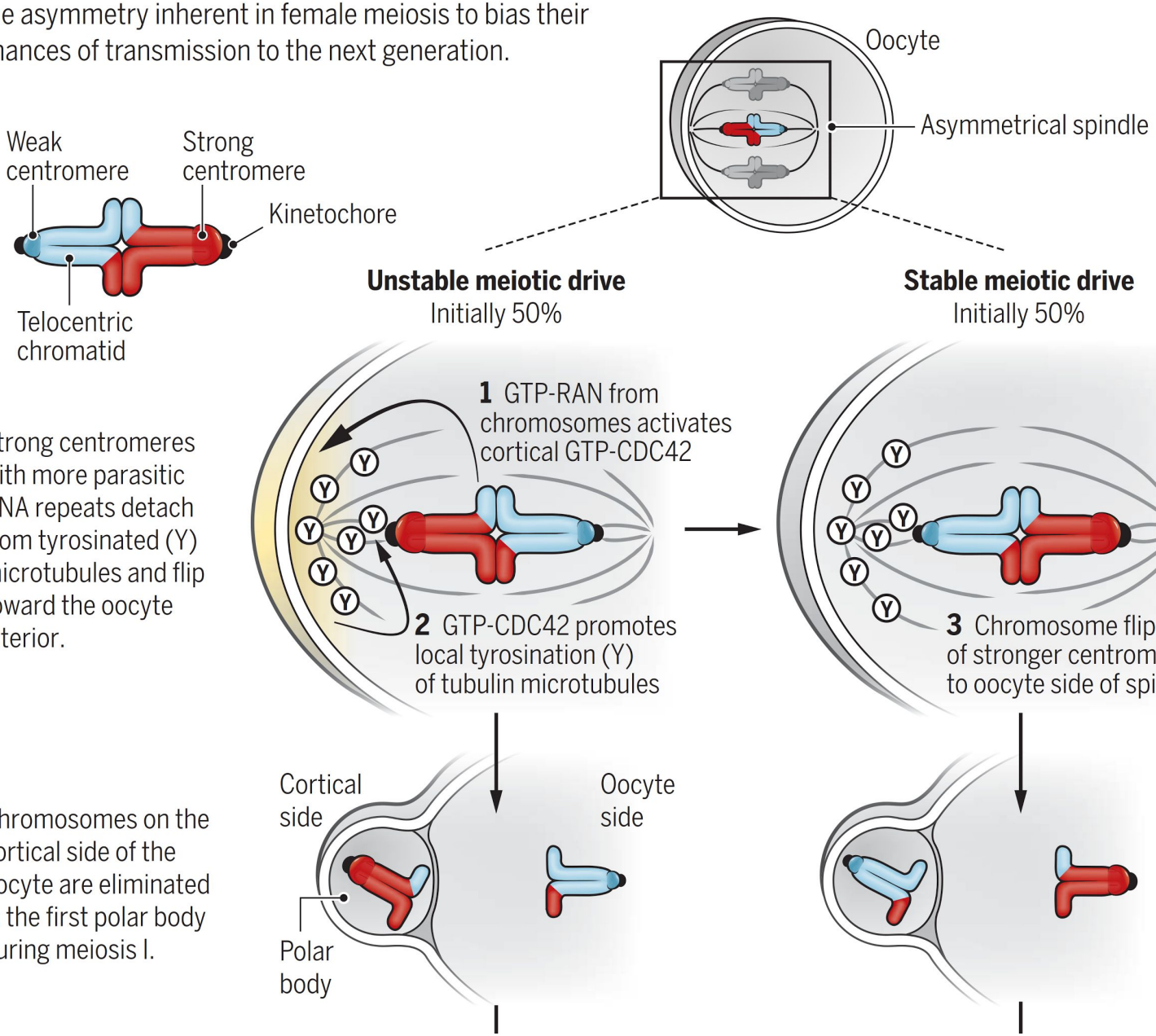
http://cancerres.aacrjournals.org/content/71/4/1219

Cortical side and egg side



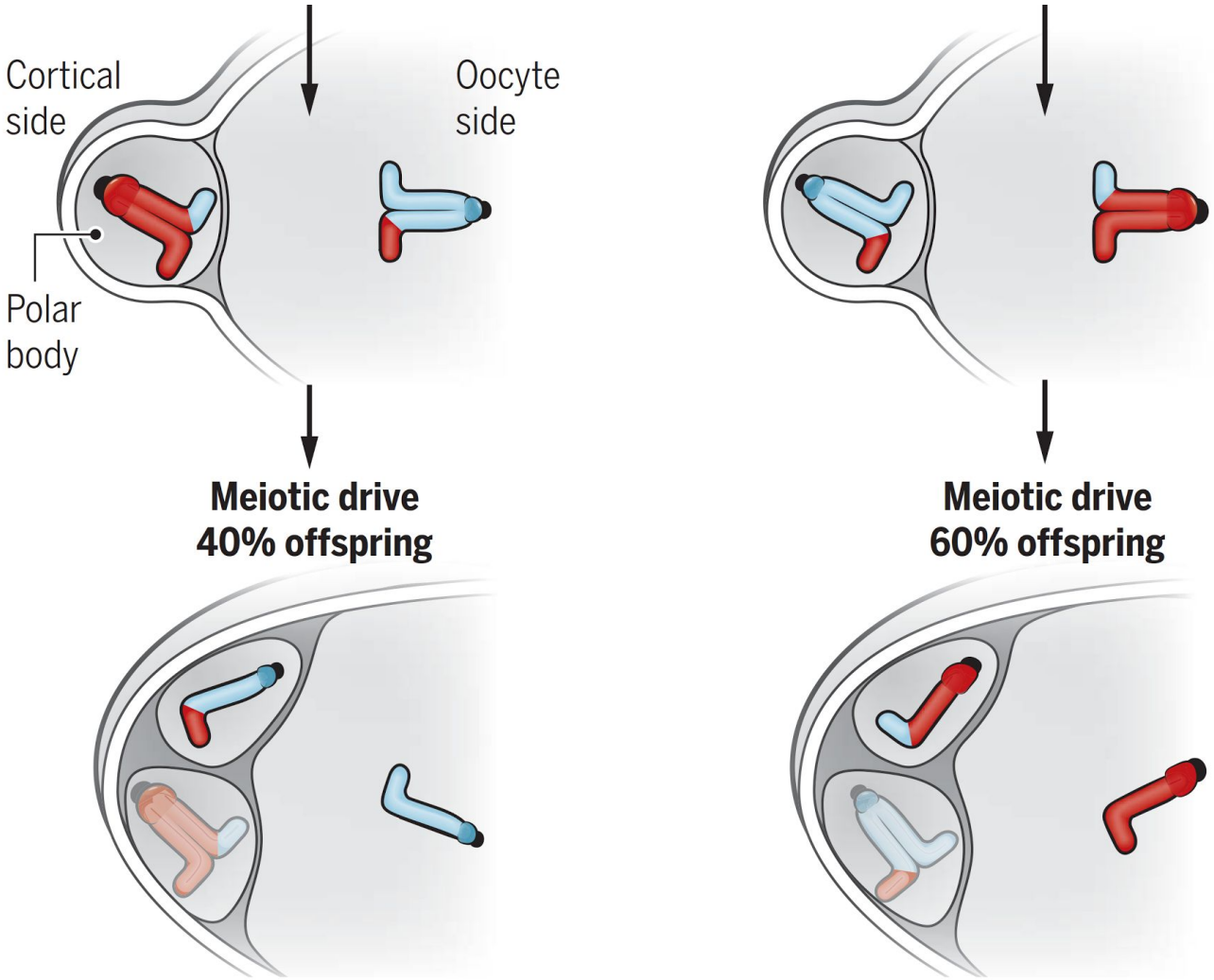
Preferential inheritance during female meiosis

A parasitic DNA sequence in centromeric repeats exploits the asymmetry inherent in female meiosis to bias their chances of transmission to the next generation.

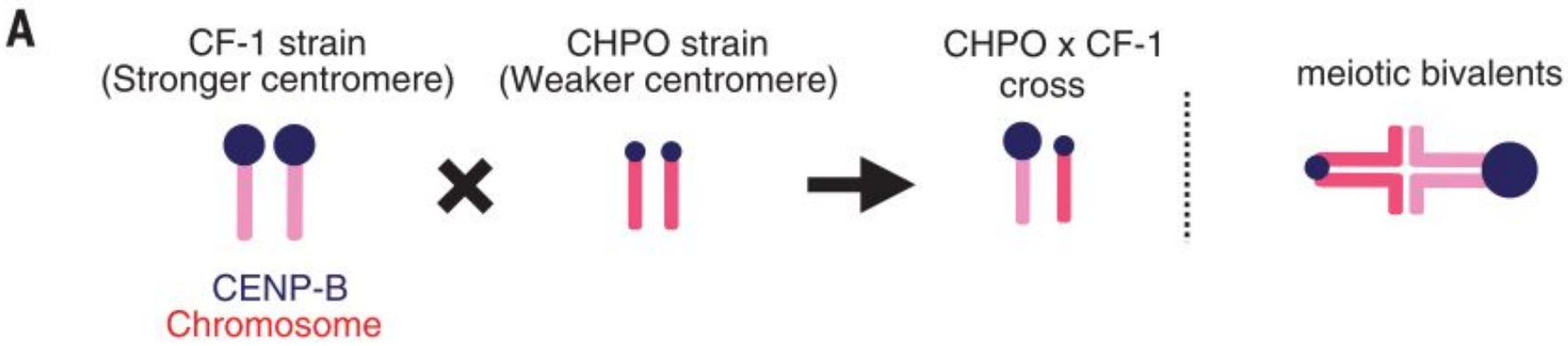


Chromosomes on the cortical side of the oocyte are eliminated in the first polar body during meiosis I.

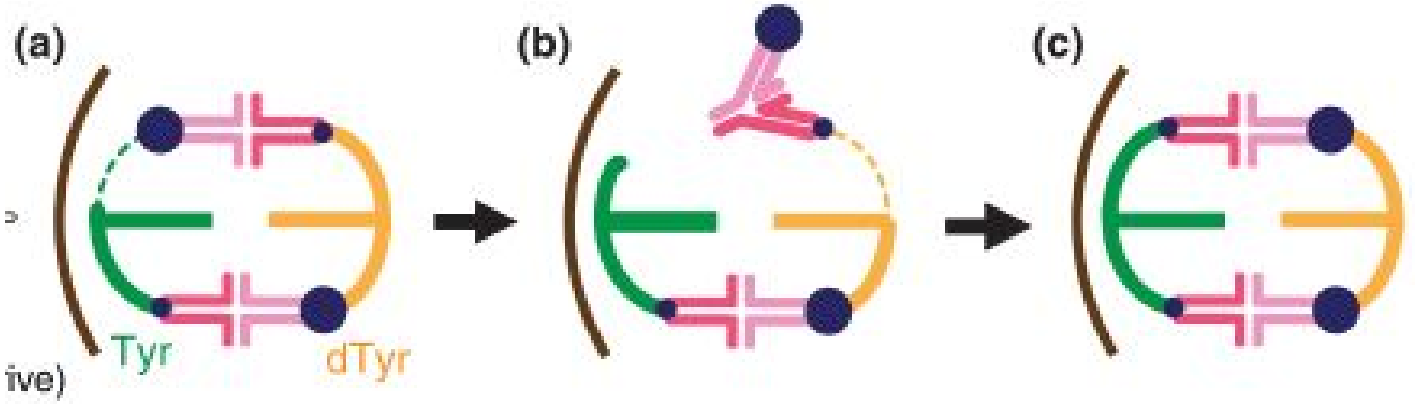
After meiosis II, one of the chromatids with more parasitic DNA repeats is preferentially inherited.

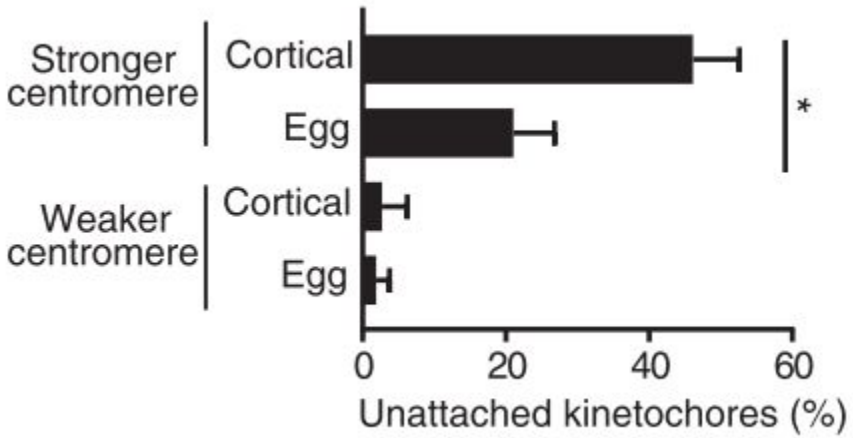


Strong centromere and week centromere

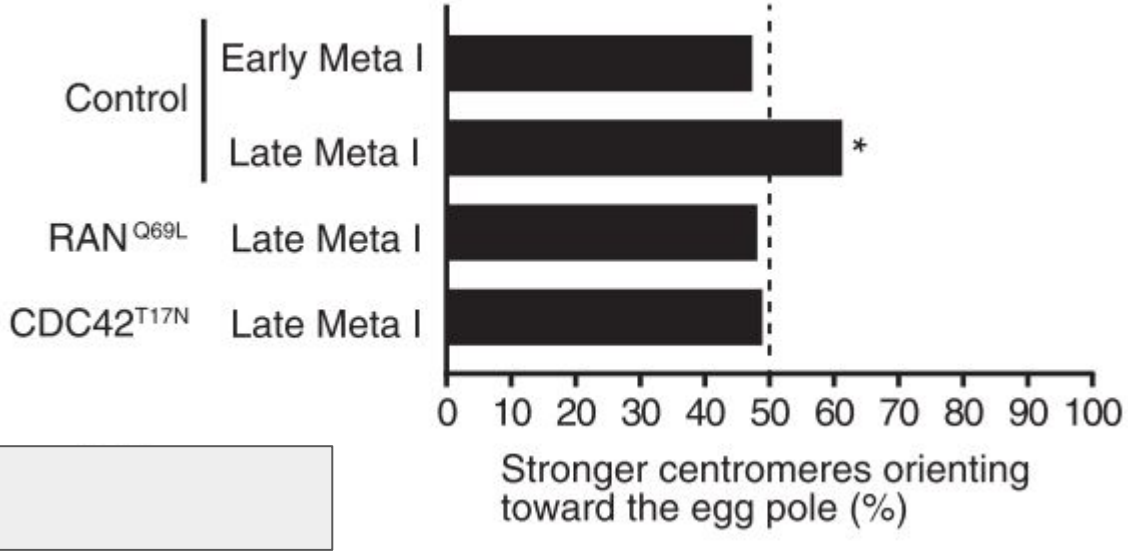


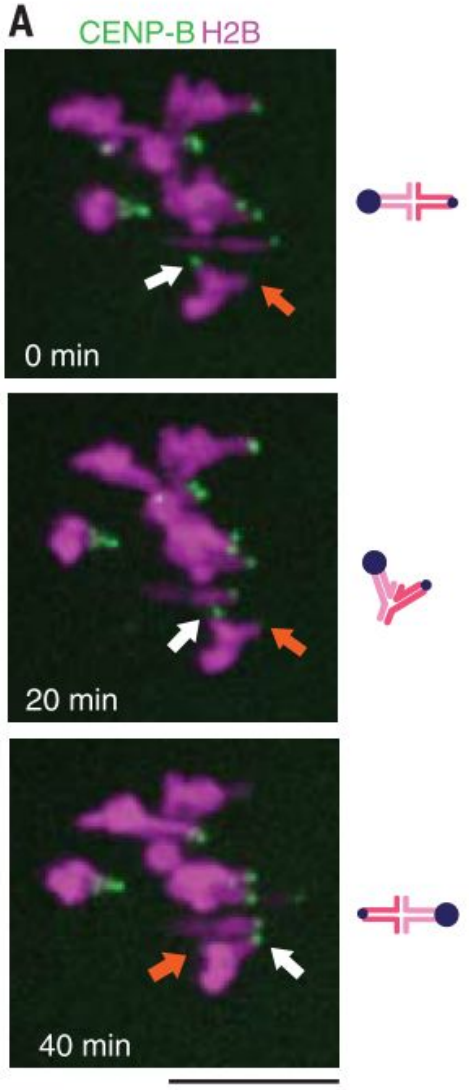
Chromosome Flipping -I



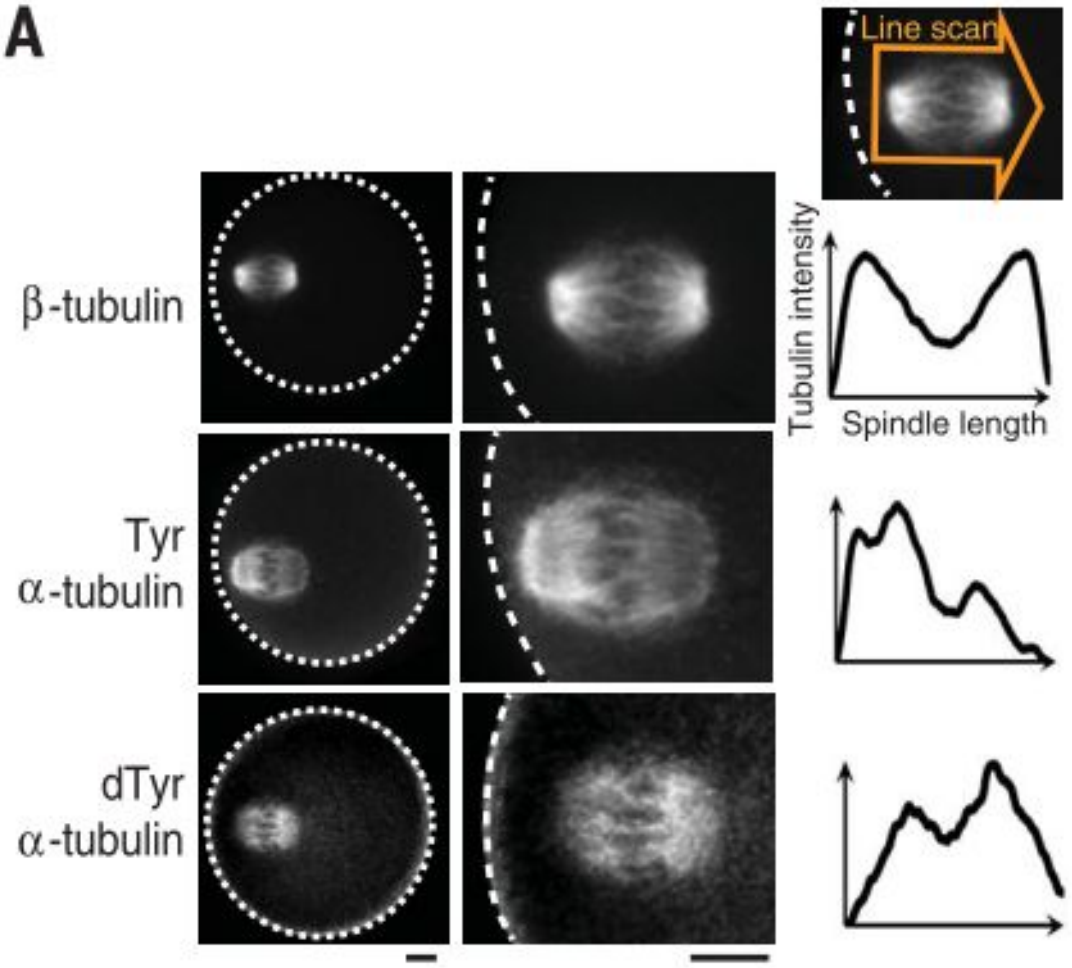


Chromosome Flipping -II





Spindle asymmetry

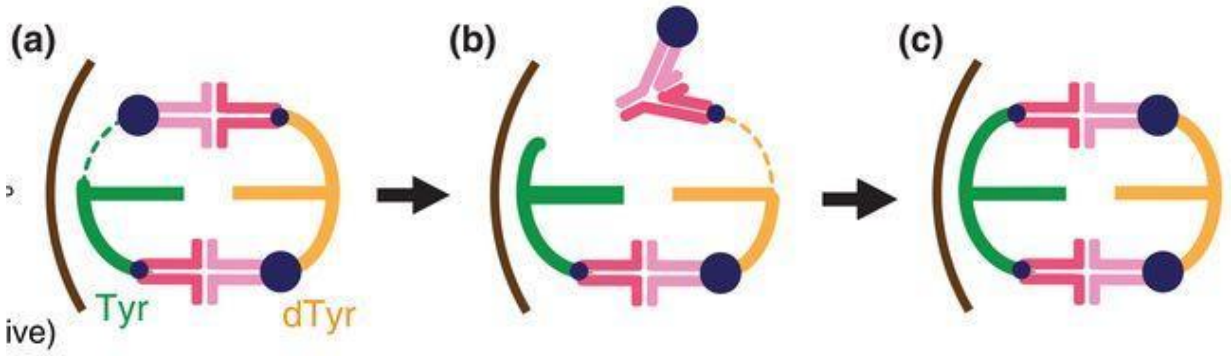


Conclusion

- Microtubule tyrosination promotes unstable interactions between selfish centromeres and the cortical side of the spindle.
- Spindle asymmetry drives non-Mendelian chromosome segregation
- Selfish centromeres have bigger chance to face toward egg side,and pass their genetic information into next generation.

Take home message

- Selfish meiotic drivers exploit the asymmetry inherent in female meiosis to bias their transmission.



Video link

https://www.youtube.com/watch?v=uNRBZ6ARQp4