

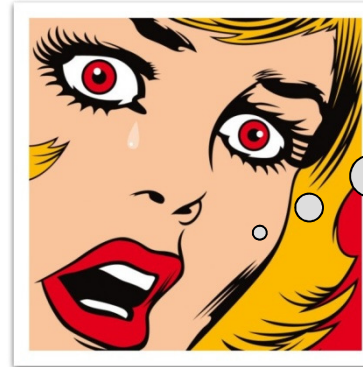
Gametogenesis: the process of meiosis

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Meiosis

Myths and truths



Oh, no!
Meiosis

Impossible to memorize the whole process!

Too many names, phases, stages, events, mechanisms ...

Still some obscure phenomena and unresolved points.

Too many papers on yeast!

Gender particularities to make it more difficult!

Learning objectives

- To get an updated overview of mammalian meiosis.
- To review crucial meiotic events playing strategically roles to drive the process.
- To highlight the consequences of meiotic anomalies in male and female gametogenesis.
- To underline issues that are still in the *dark side* and that hopefully will see the light in the next future.

1. An overview

Essential process for sexually reproducing eukaryotic organisms.

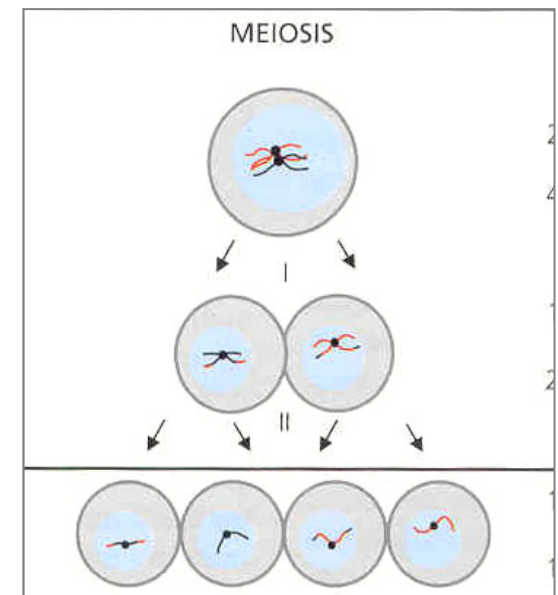
Termed by Farmer and More (1905): “reduction”.

Embedded in the process of mammalian gametogenesis, producing haploid gametes from diploid precursor cells.

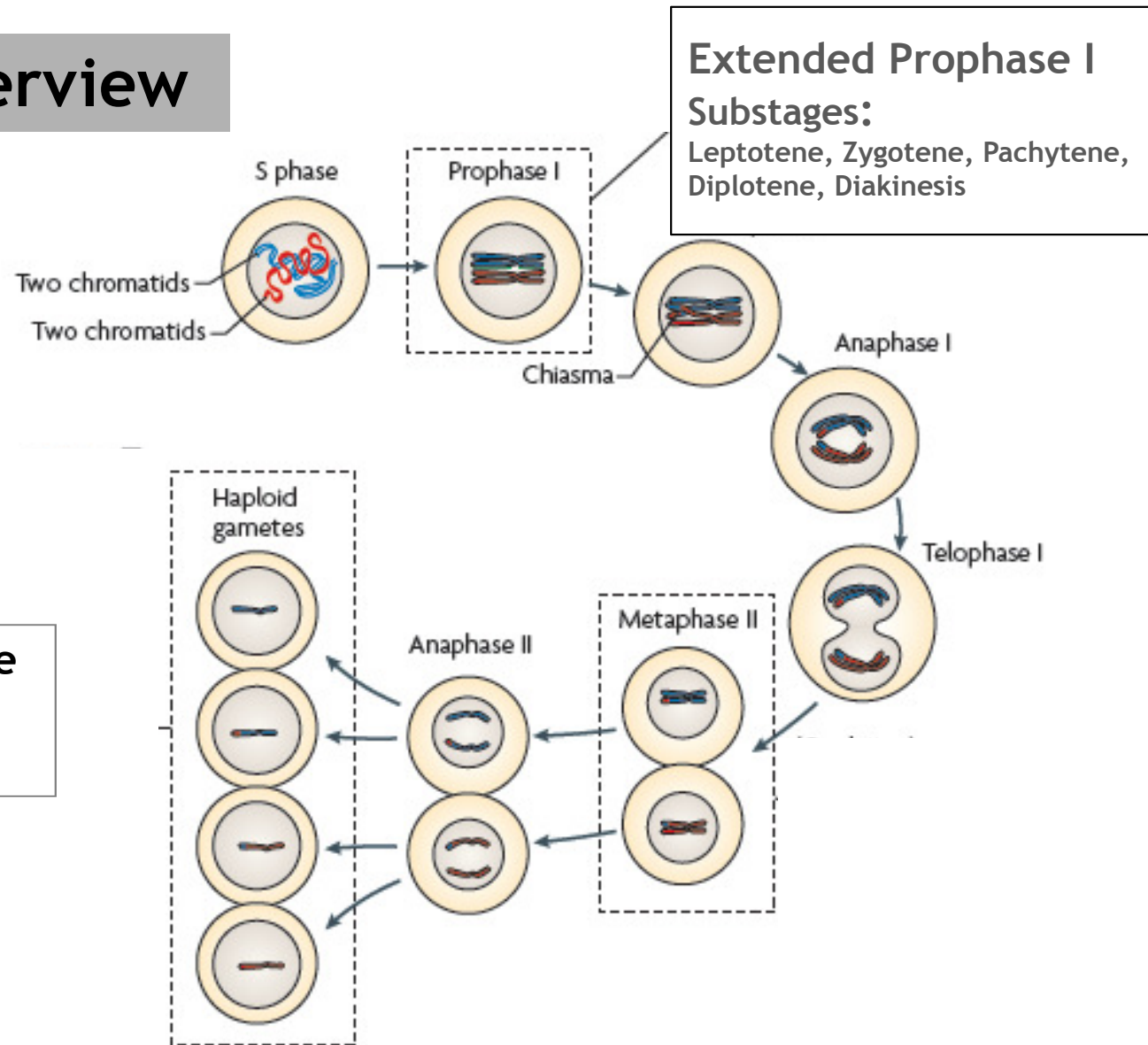
Specialized cell division program.

Correct execution of meiosis is essential for fertility.

Meiotic anomalies could result in an impairment of gamete production and to abnormalities in the integrity of the genome.



1. An overview



Most features are conserved from fungi to human

Crucial events

Prophase I

Leptotene

Zygotene

Pachytene

Diplotene

Diakinesis



Find your homologue! You must first pair to achieve a correct separation

- Synapsis

- Recombination



Essential for meiotic success

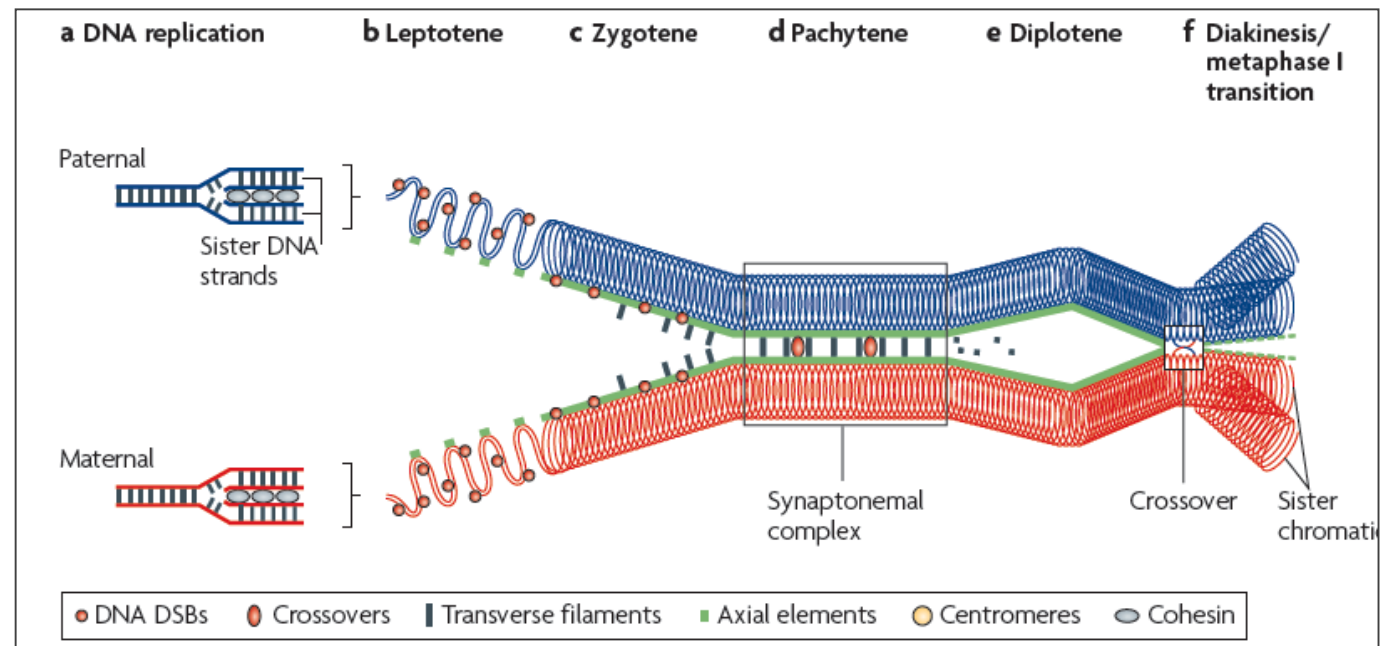
Crucial events

- Synapsis
- Recombination

Chromosome pairing
Homologue chromosome recognition

Synaptonemal complexes (SCs)

Transient structures.
Link the axes of the
aligned chromosomes



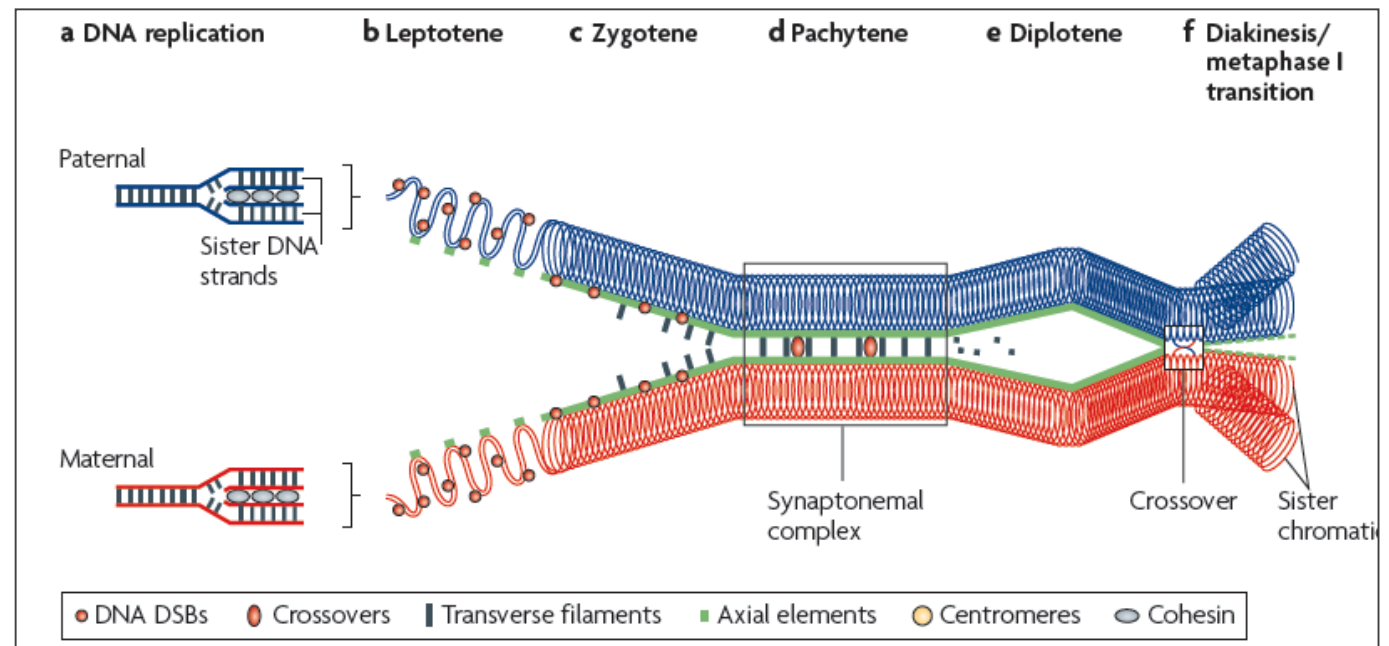
Crucial events

- Synapsis
- Recombination

Chromosome pairing
 Homologue chromosome recognition

Double-strand breaks (DBs)
 Crossovers
 Chiasmata

Synaptonemal complexes (SCs)

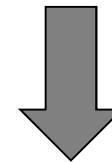


Crucial events

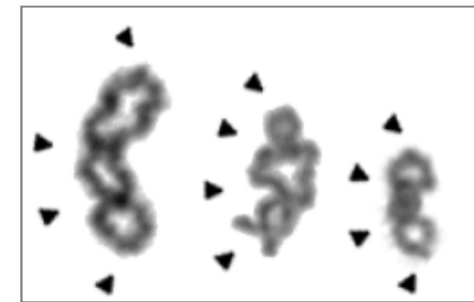
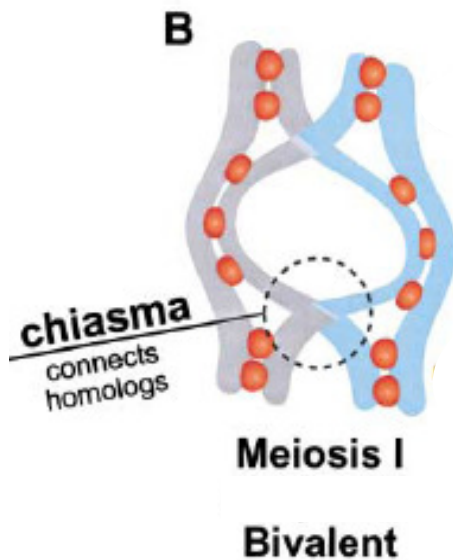
- Synapsis
- Recombination



Essential for meiotic success



Chiasma and arm cohesion



Metaphase I bivalents from human spermatocytes. Arrows point to chiasmata

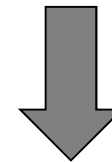
“Added value” of recombination

Crucial events

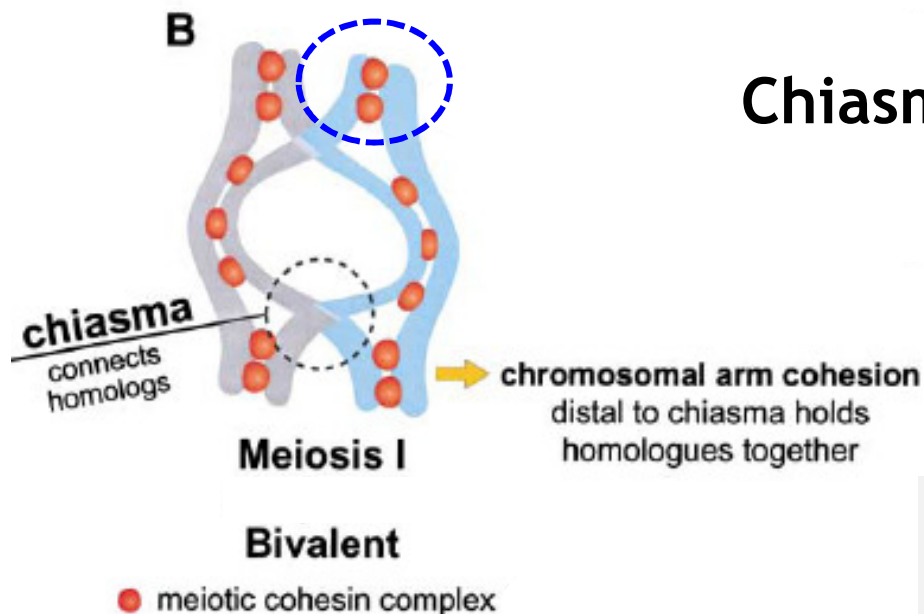
- Synapsis
- Recombination



Essential for meiotic success

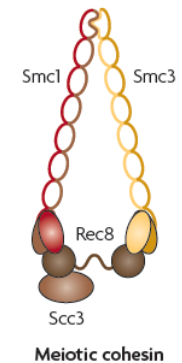


Chiasma and arm cohesion



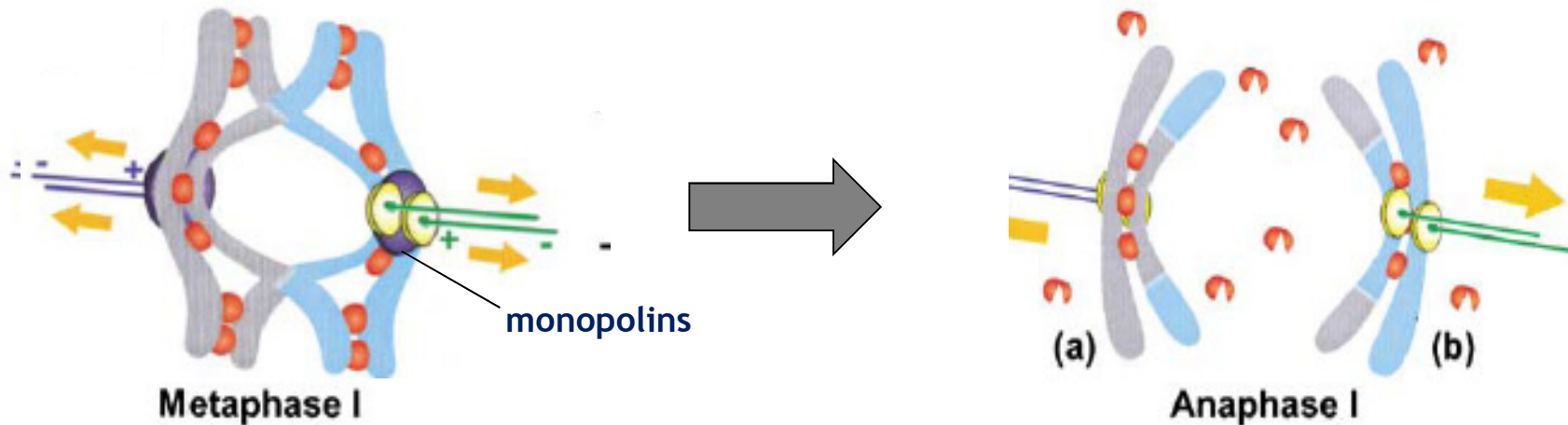
Meiotic cohesin

Chromatid cohesion is established during premeiotic DNA replication



The way to segregation

Chiasma and arm cohesion promote proper disjunction at meiosis I



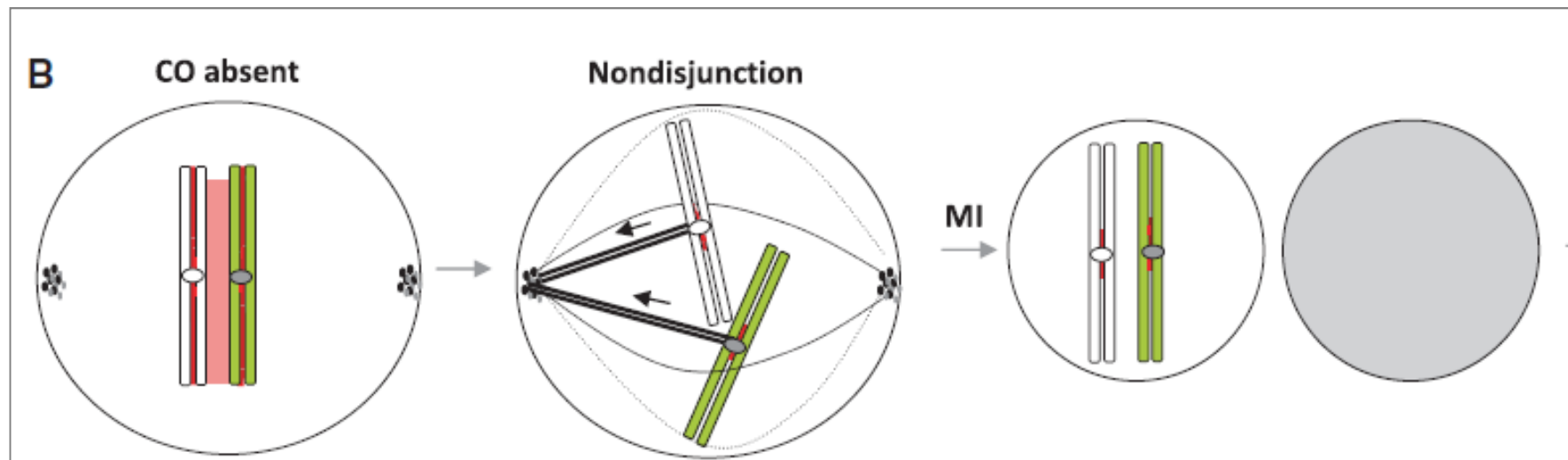
Syntelic attachment of sister kinetochores
Bi-orientation of homologues
Cohesion + Chiasmata
Spindle microtubule tension

Cleavage of cohesins
Centromeric cohesion protection

The way to segregation

Chiasma and arm cohesion promote proper disjunction at meiosis I

If not ...

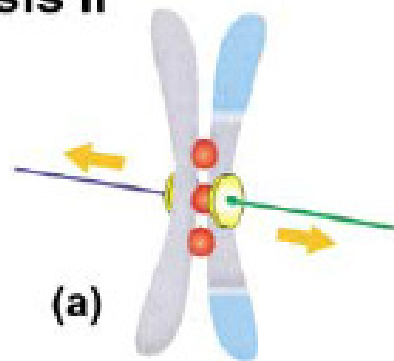


Adapted from Székvölgyi and Nicolas 2010

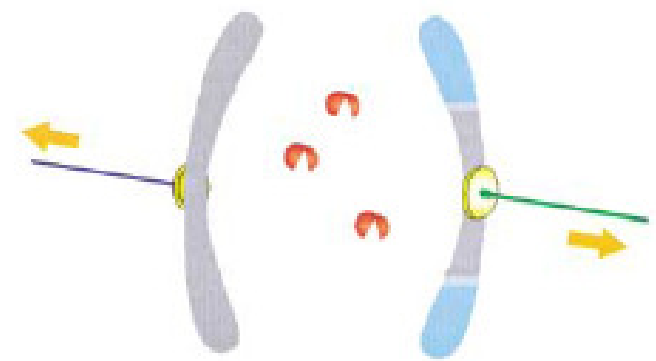
The way to segregation

Second division: Persisting cohesion at pericentromeric regions is essential for correct segregation in meiosis II

Meiosis II



Metaphase II



Anaphase II

Amphitelic attachment of kinetochores
Cohesion
Spindle microtubule tension

Mechanism responsible for
protecting centromeric cohesion
cleavage until Anaphase II ?

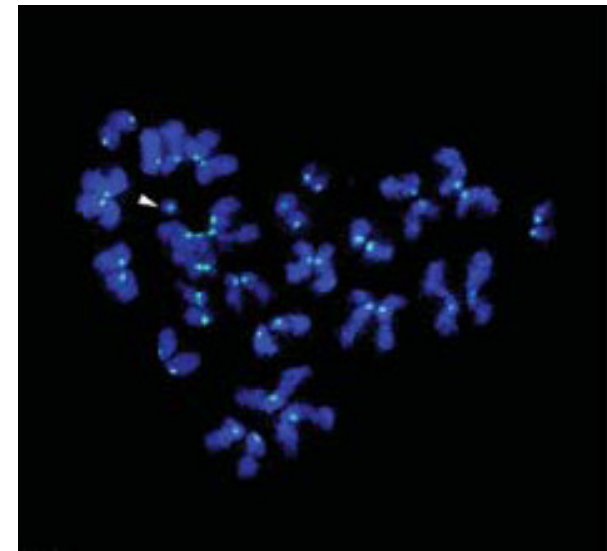
3. The way to segregation

Second division: Persisting cohesion at pericentromeric regions is essential for correct segregation in meiosis II

If not ...

Precocious chromatid separation
Predivision of chromatids

No proper spindle position
Erratic chromatids
Gains/losses chromatids

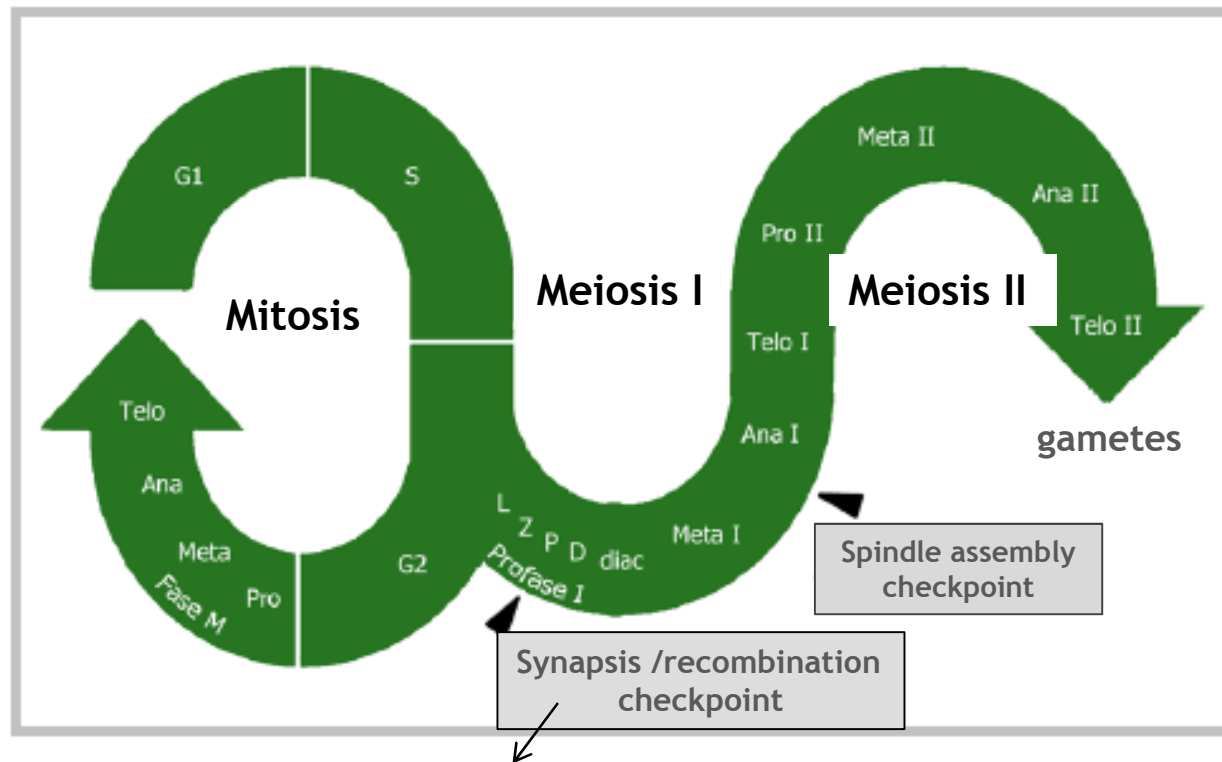


Human oocyte MII showing a single chromatid (arrowhead). Garcia-Cruz et al. 2010

4. Quality control

Meiotic cell cycle checkpoints

Proposed meiotic checkpoints



Persistence of DSBs /Asynapsed chromosome segments

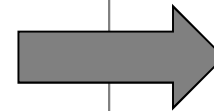
Adapted from Morelli and Cohen, 2005

5. Consequences when things go wrong ...

•Checkpoint activation



Meiotic arrest
Apoptosis

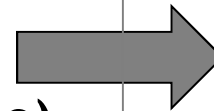


Compromised
gamete production

•Checkpoint escape (attenuated)

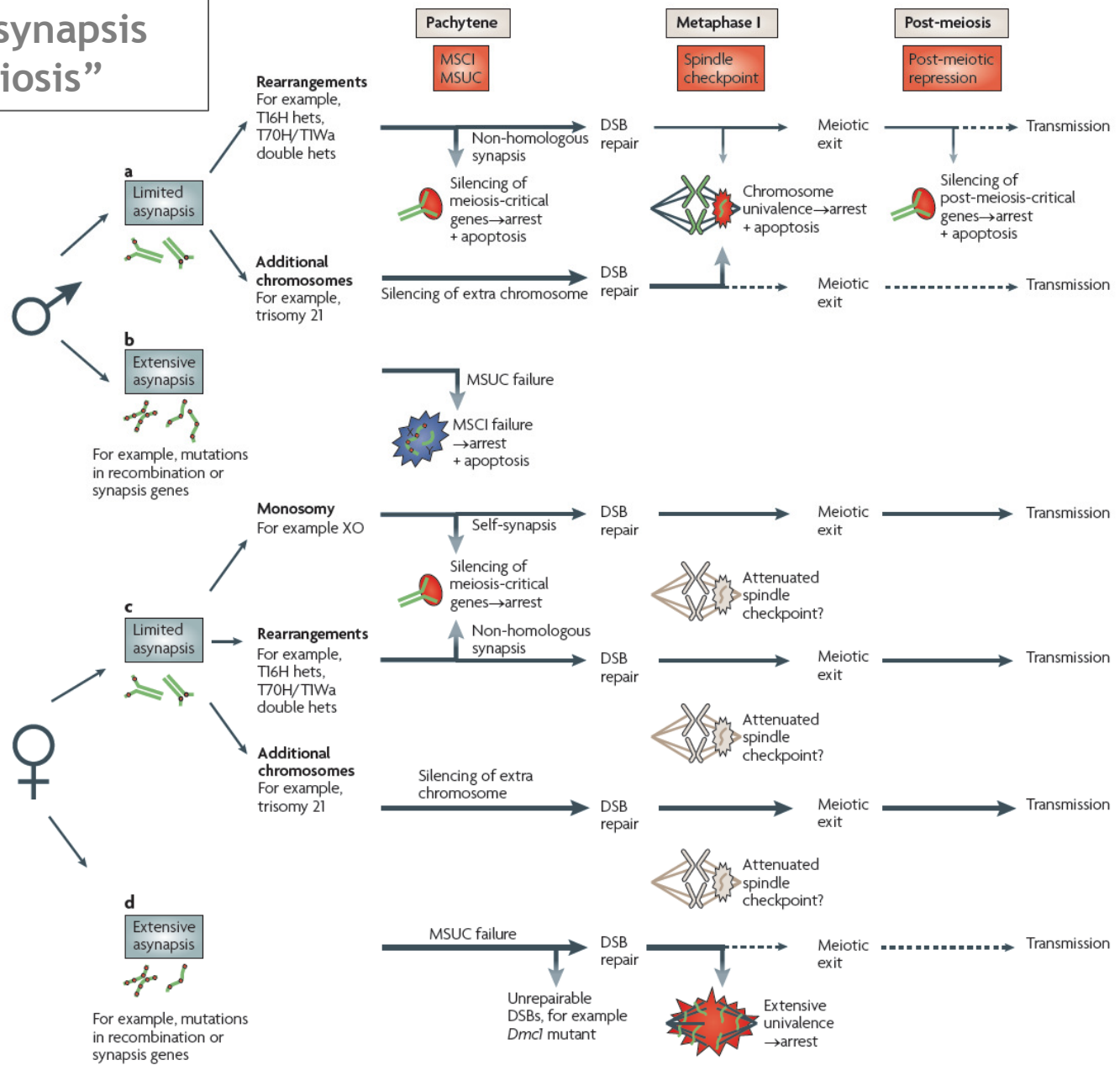


Chromosome abnormalities
Mutations (integrity of the genome)



Transmission

Burgoyne et al., 2009 “The consequences of asynapsis for mammalian meiosis”



6. Gender specific differences

- Temporal aspects
- Progression of meiosis
- Recombination events
- Check-points efficiency
- Cell division, final result
- Age effect

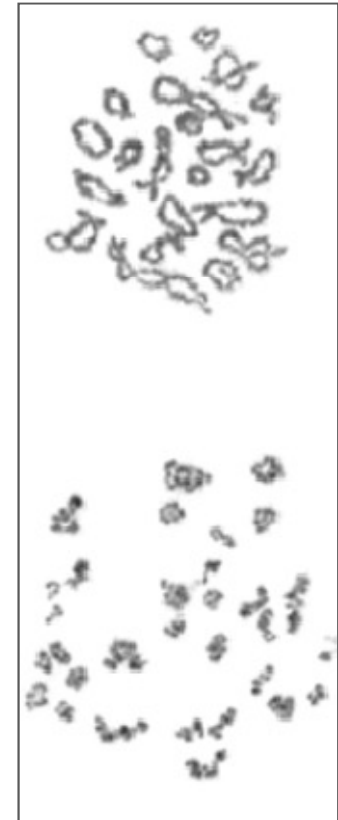
7. Issues still in the *dark side*

- Onset of meiosis
- Complexity of the meiotic machinery
- Uncover roles of specific proteins
- Meiotic silencing
- Novel meiotic mutations
- Interindividual variations
- Impact on fertility, ... and ART

7. Issues still in the *dark side*

- Onset of meiosis
- Complexity of the meiotic machinery
- Uncover roles of specific proteins
- Meiotic silencing
- Novel meiotic mutations
- Interindividual variations
- Impact on fertility, ... and ART

Meiotic disorders are present in about 8% of infertile male patients and this percentage may grow to the 17.5% in severe OA patients (Egozcue et al., 2005)





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Thank you very much

