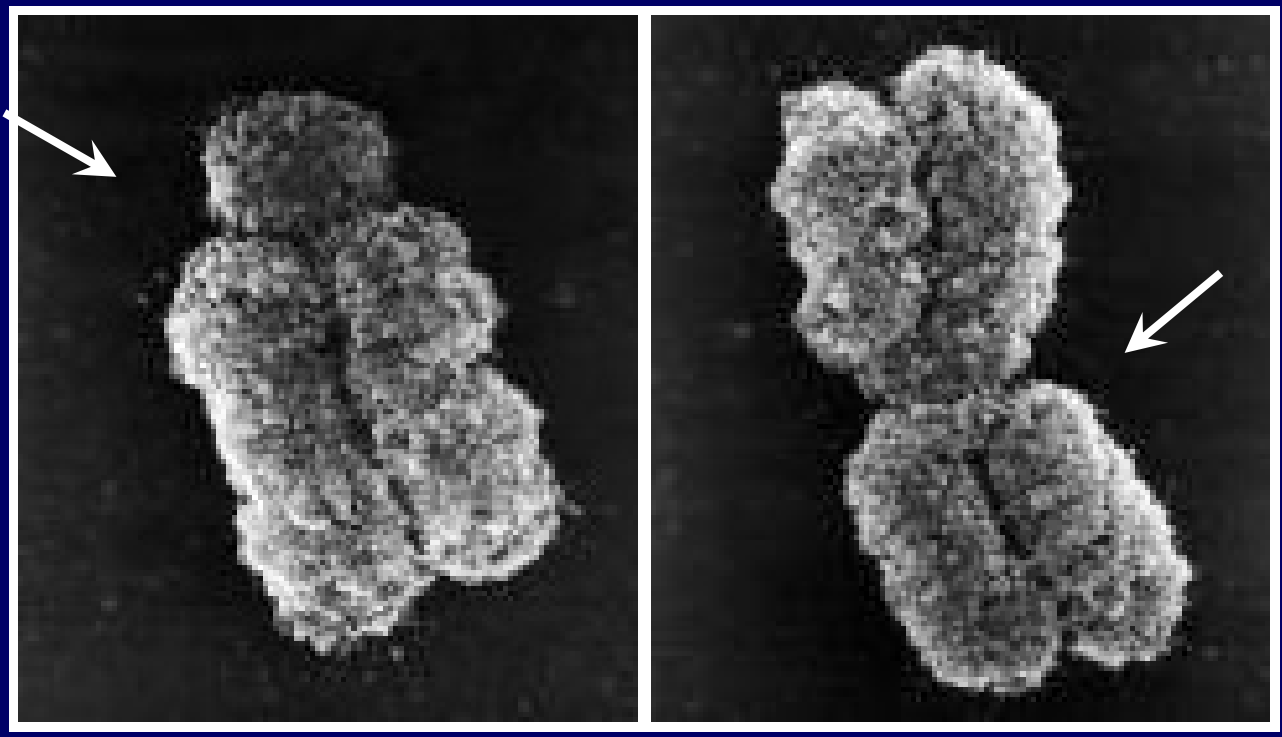
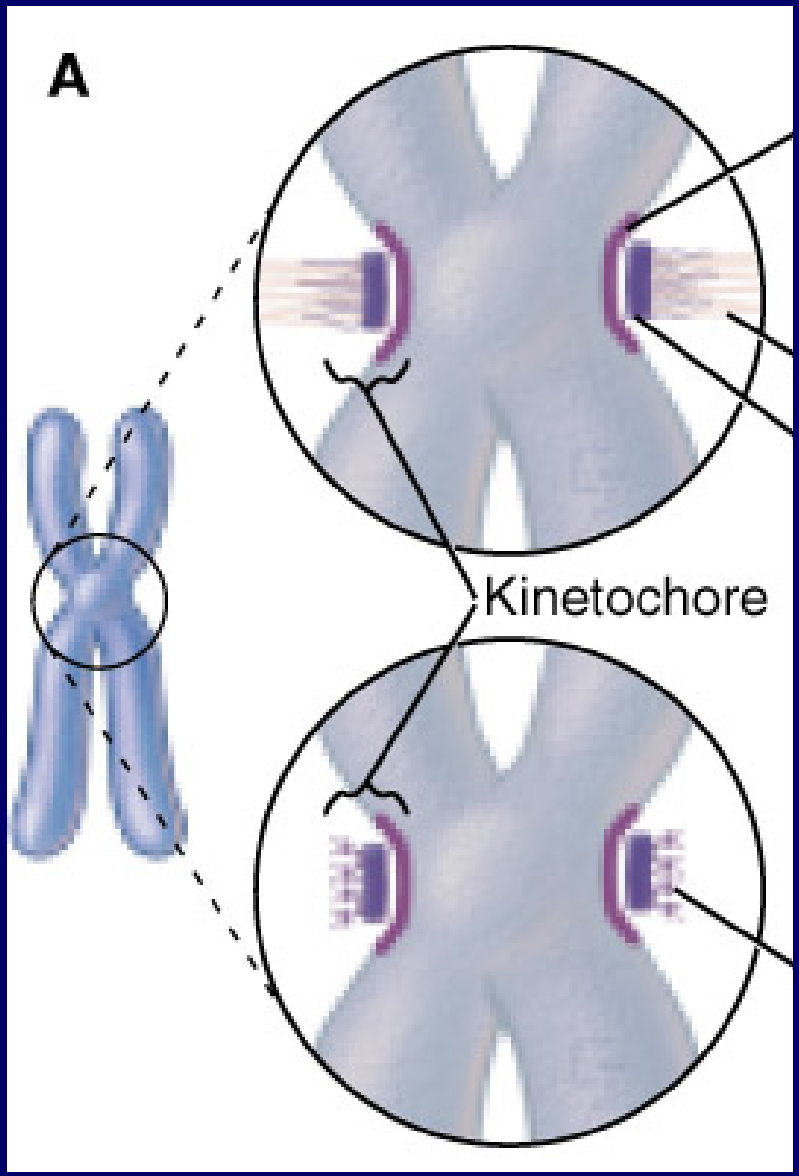
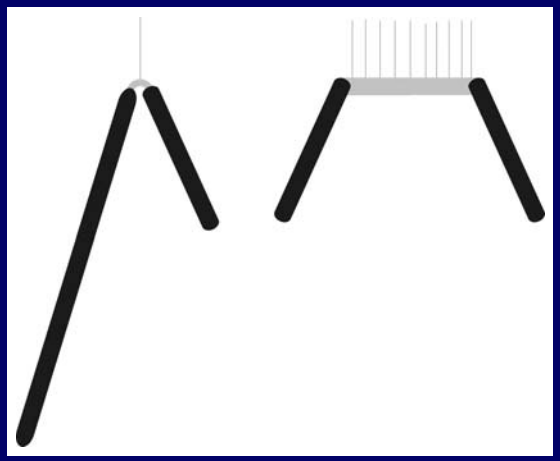
Центромера



Центромера – место формирования кинетохора



Моно- и голо-центрические (полицентрические) хромосомы

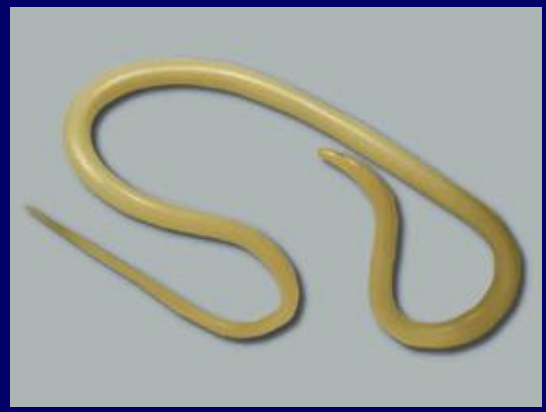


Tetranychus

Luzula

Megoura

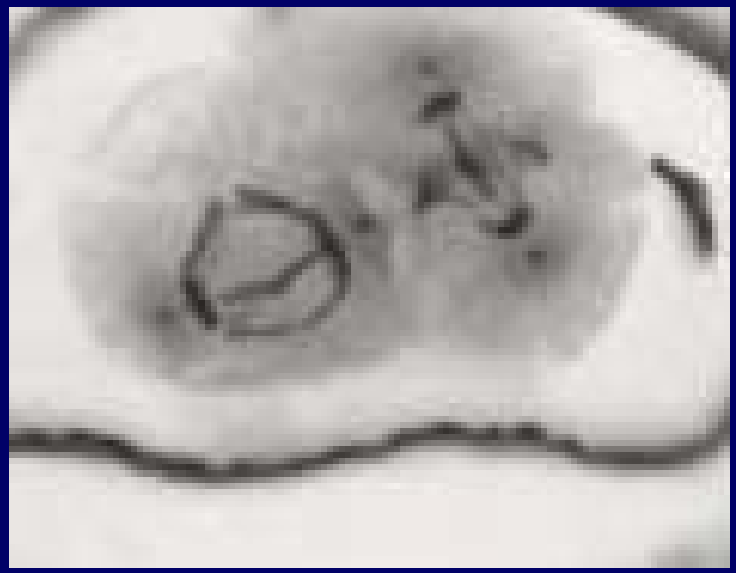
Parascaris

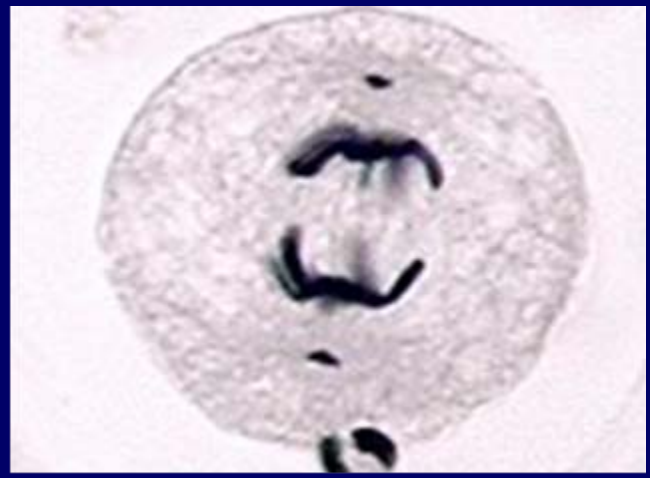


Agallia

Megoura

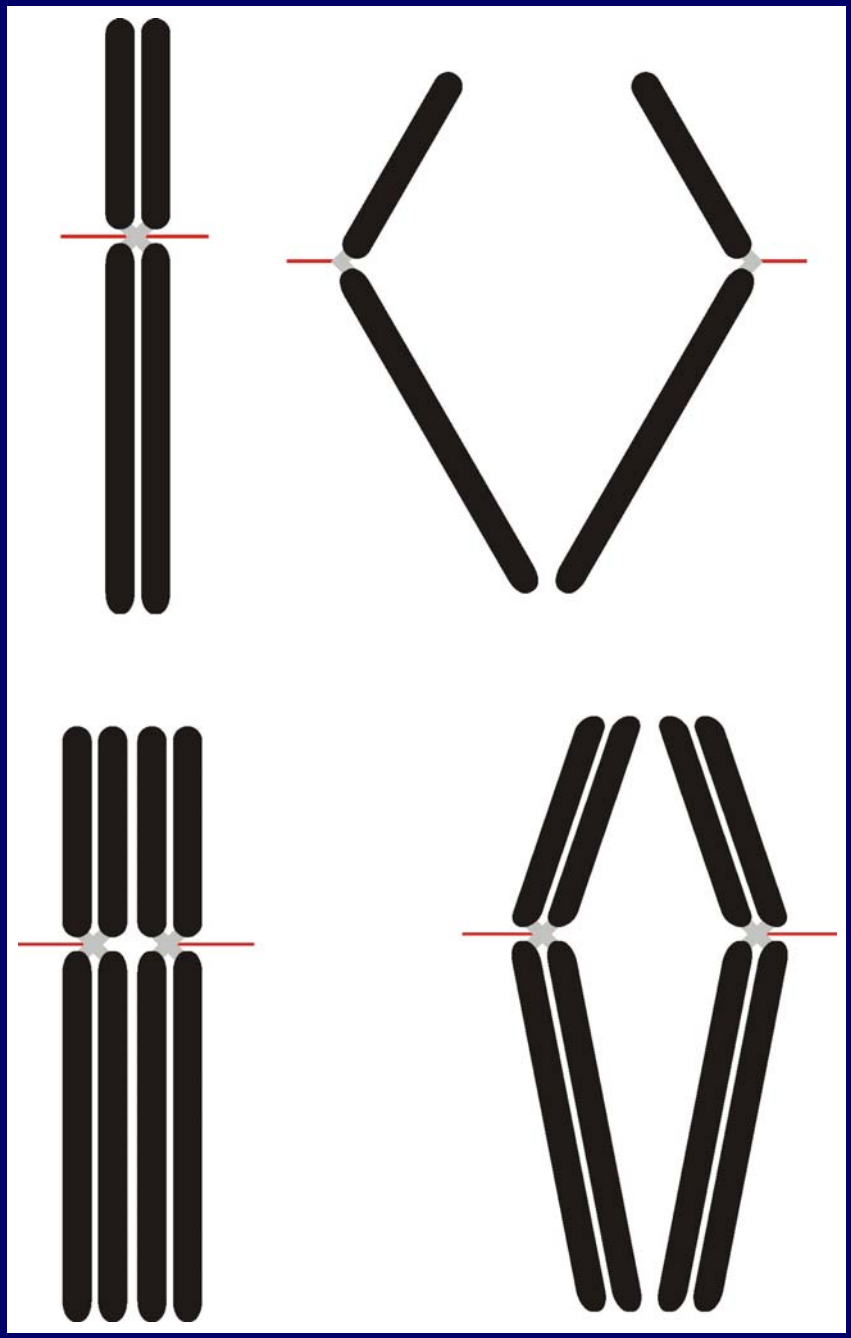
Parascaris





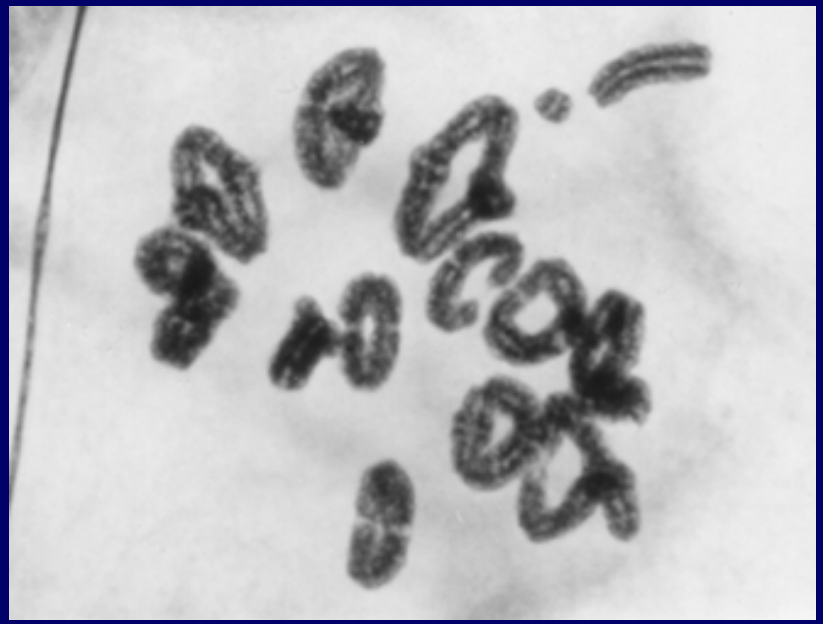
Митоз

Мейоз

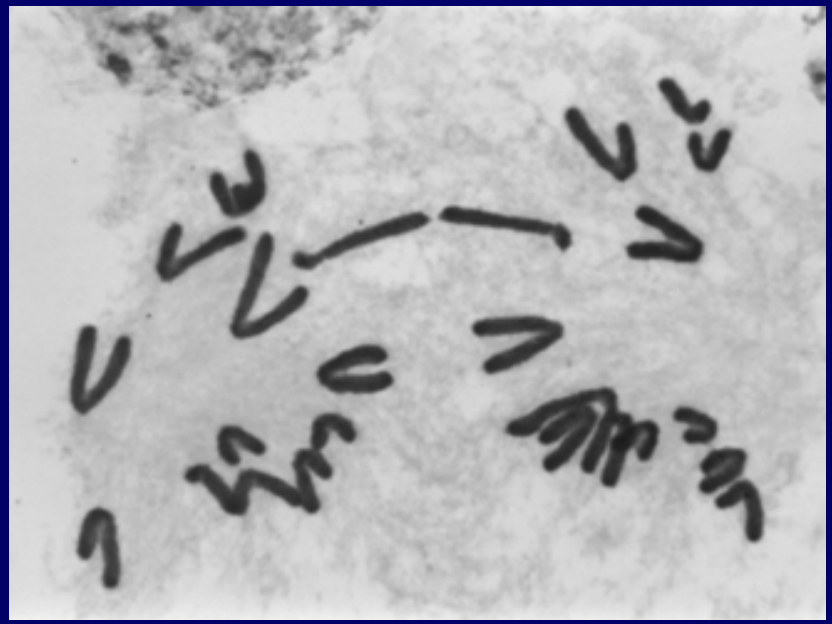


Анафаза митоза

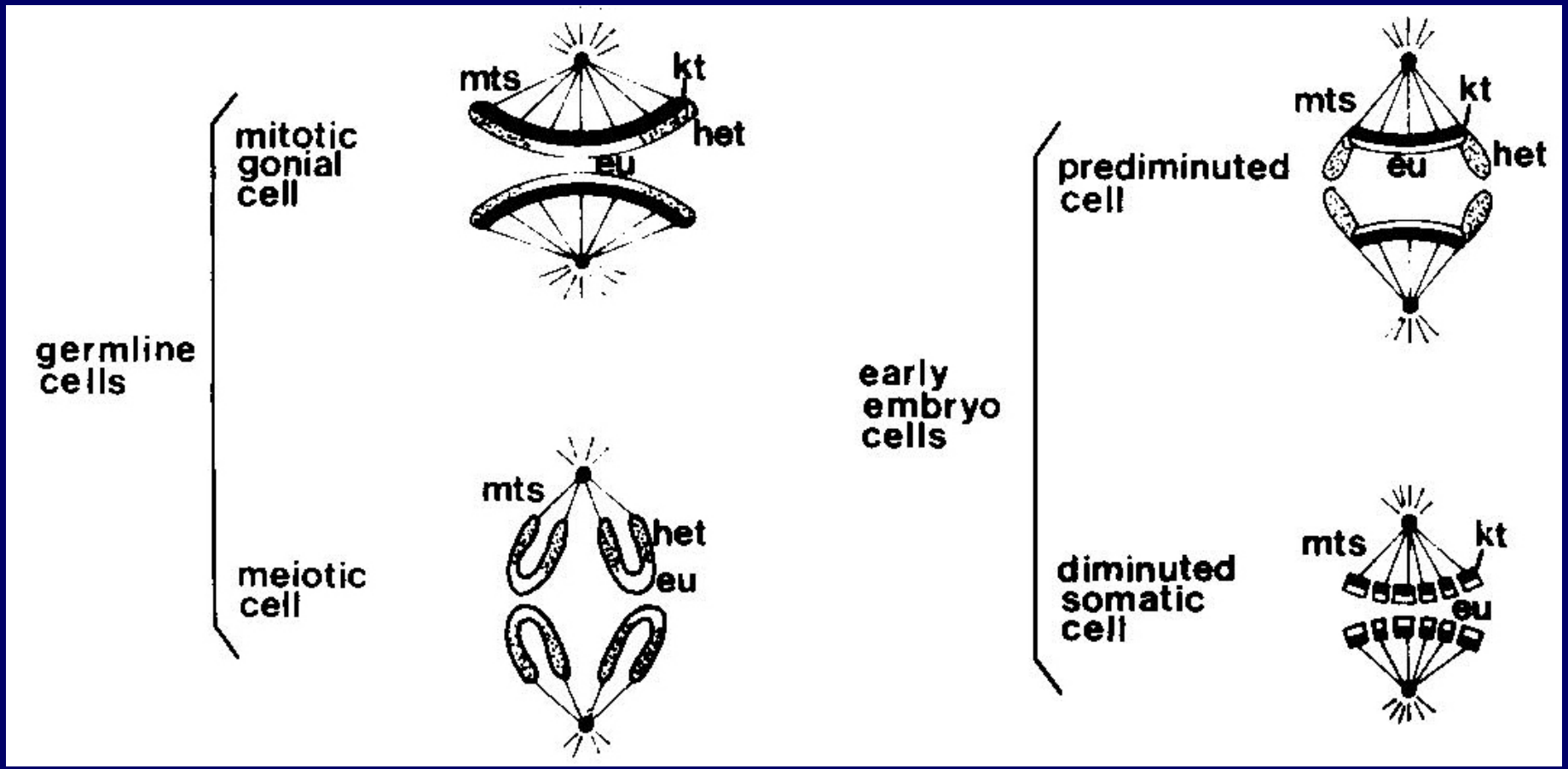
Анафаза I мейоза

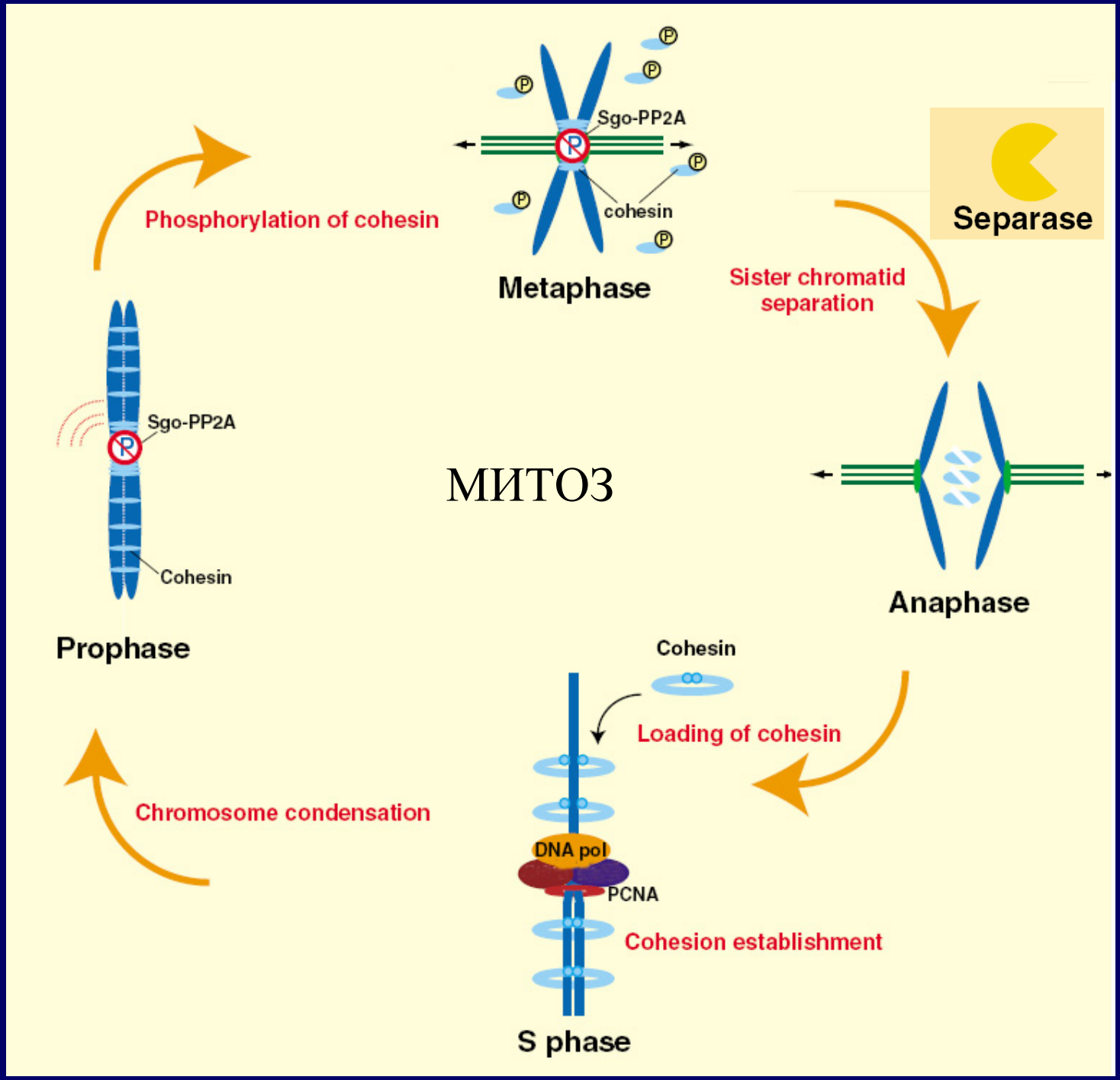


Анафаза II мейоза

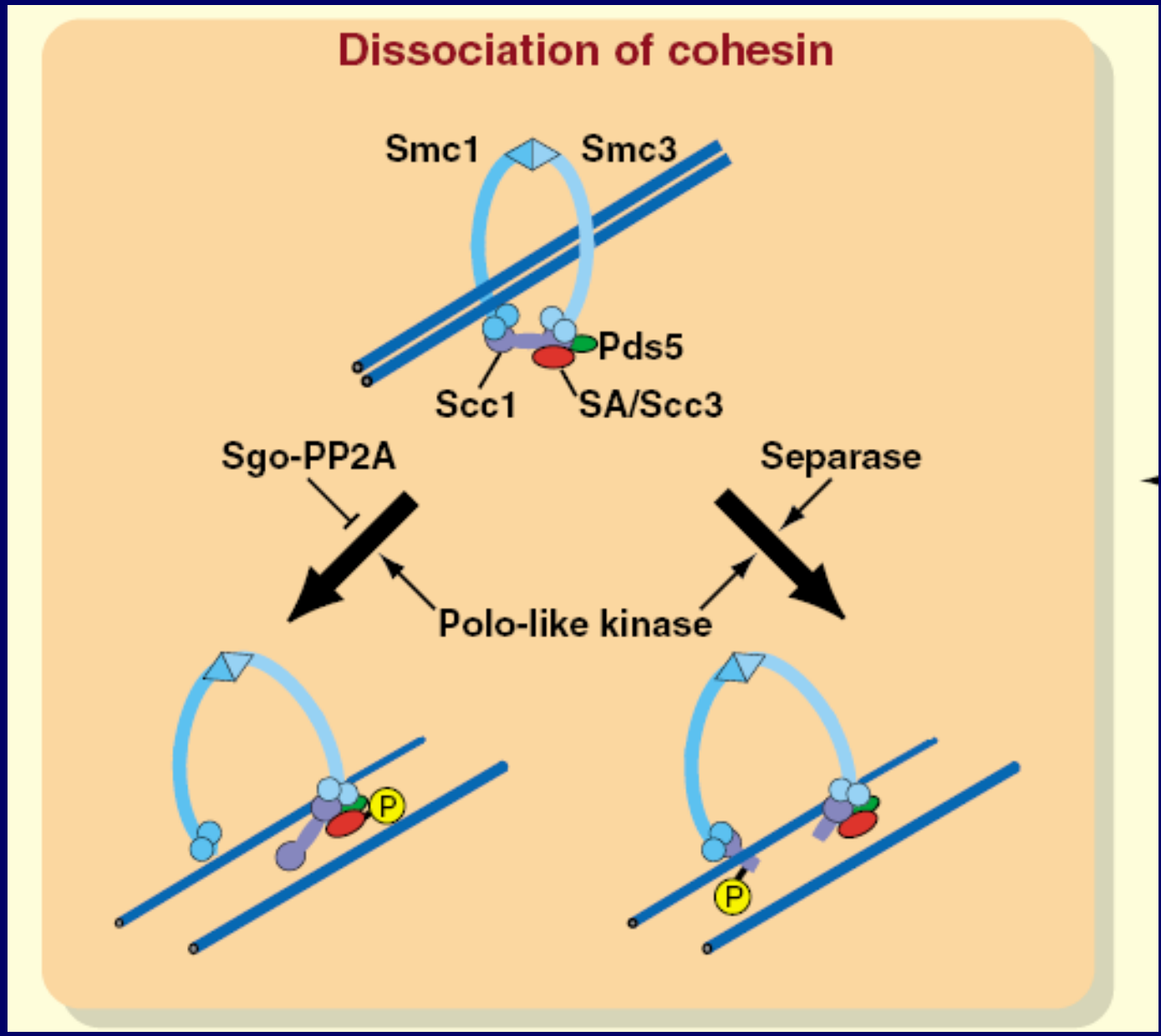


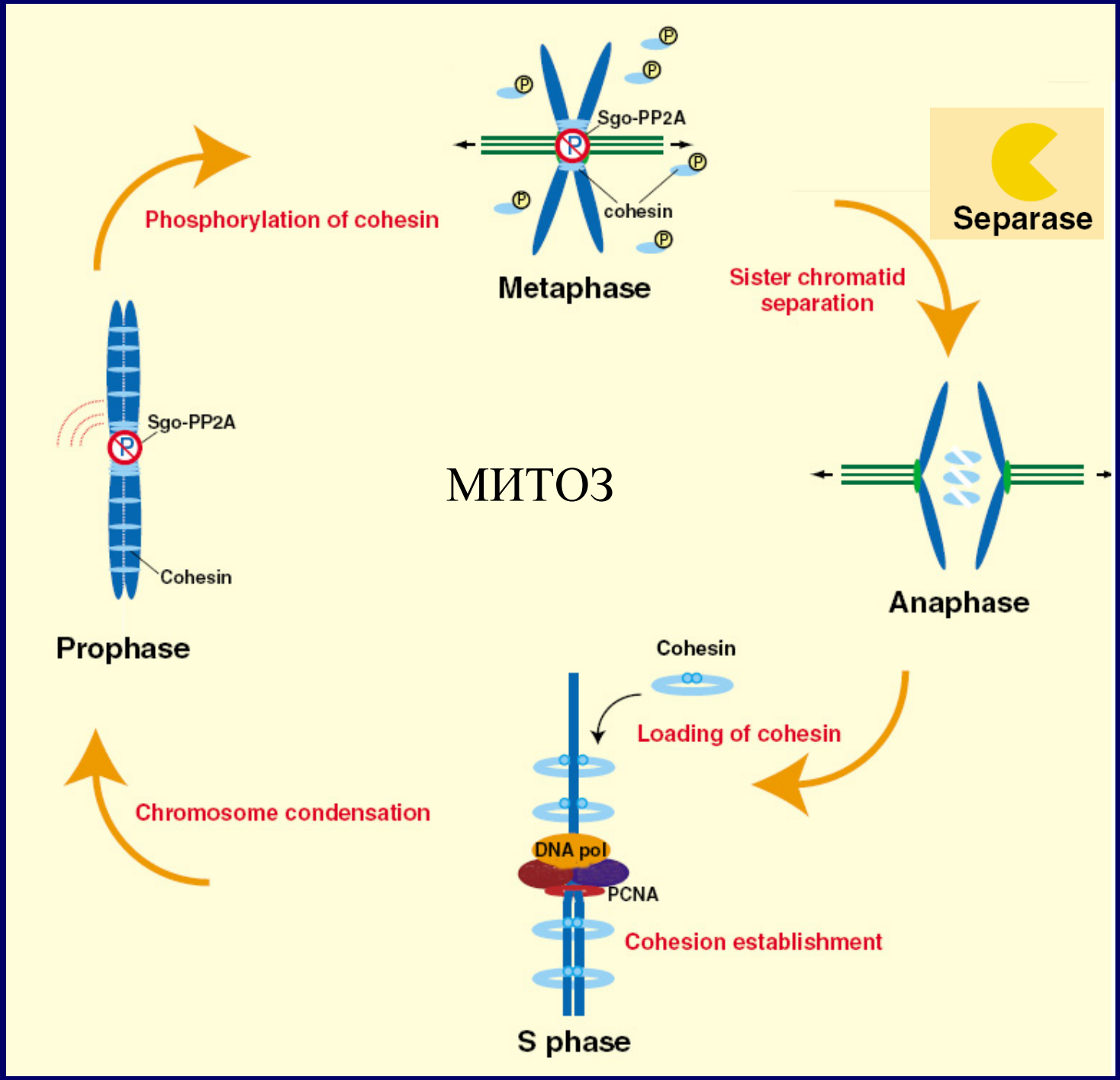
Parascaris univalens



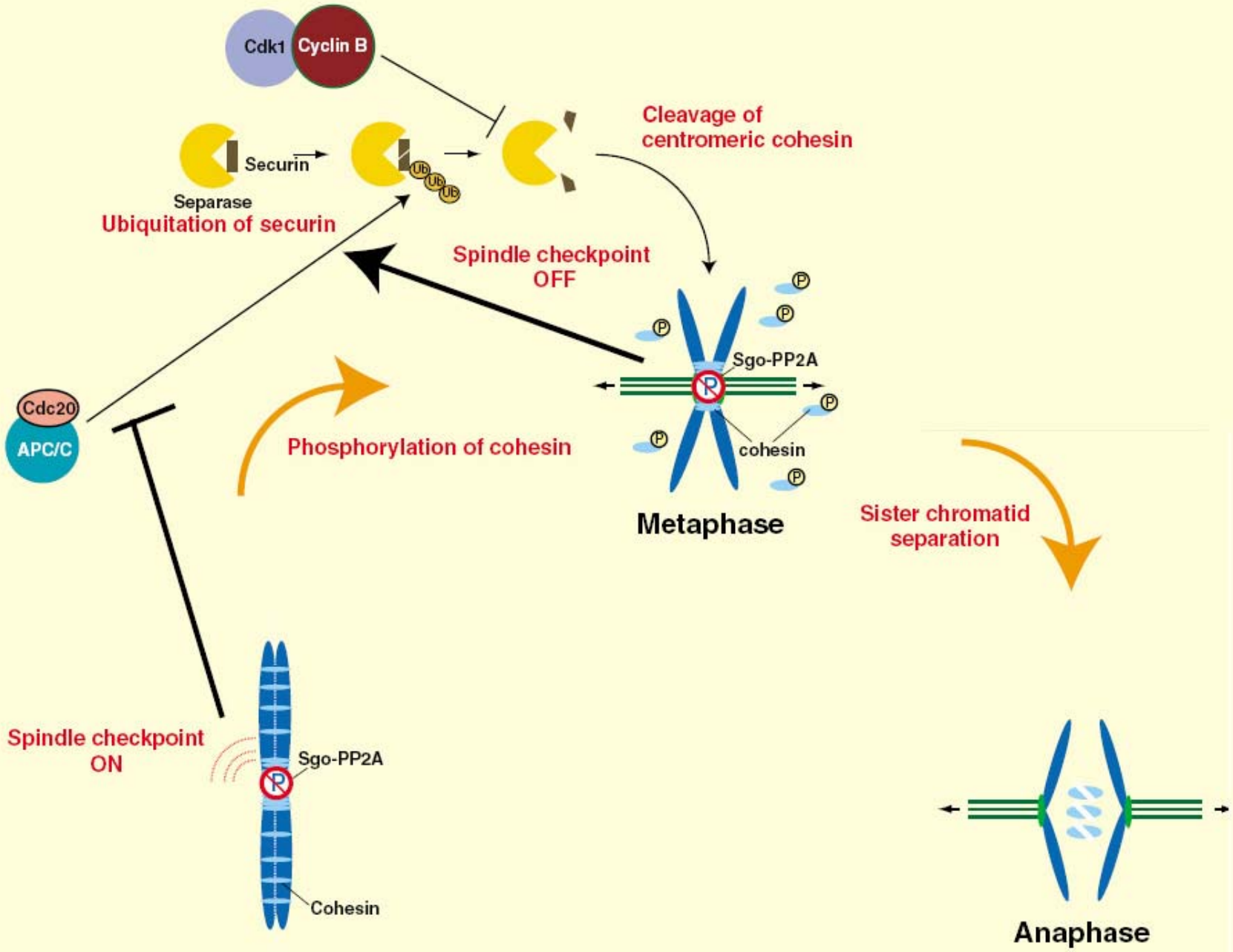

Sgo-PP2A
cohesin
Metaphase
Separase
Sister chromatid separation
Anaphase
Cohesin
Loading of cohesin
DNA pol
PCNA
Cohesion establishment
S phase
Chromosome condensation
Prophase
Sgo-PP2A
Cohesin
Phosphorylation of cohesin

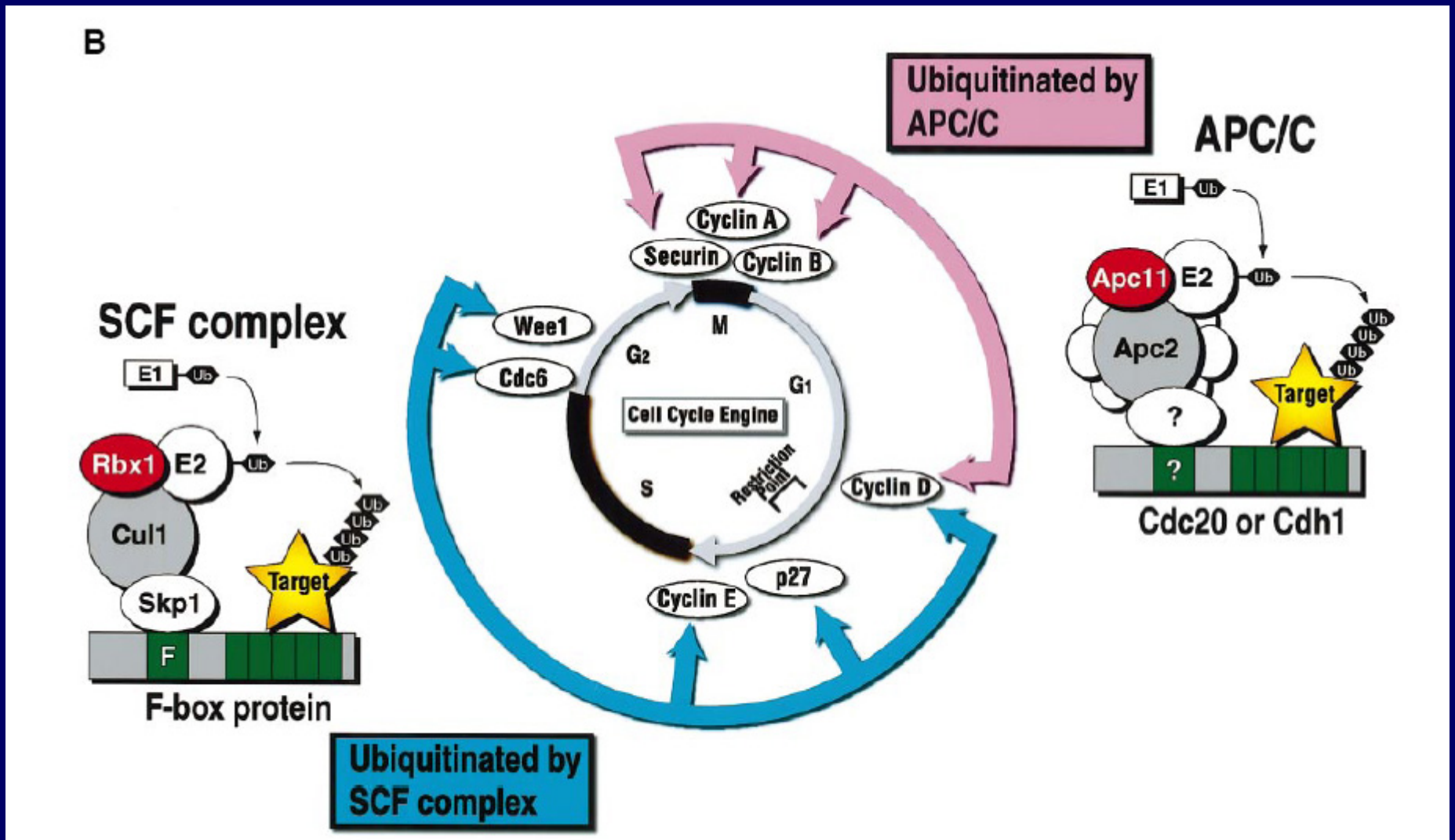
МИТОЗ

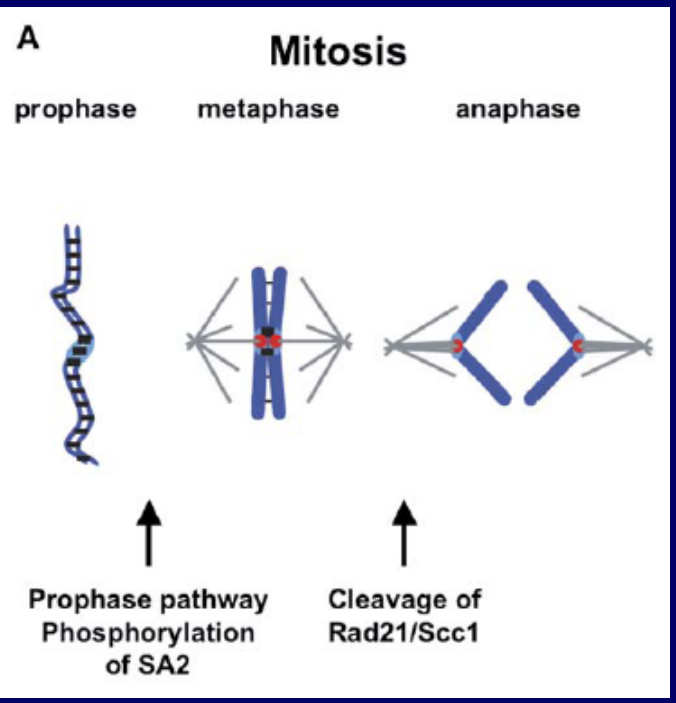

Dissociation of cohesin
Smc1
Smc3
Pds5
Scc1
SA/Scc3
Sgo-PP2A
Separase
Polo-like kinase
P
P

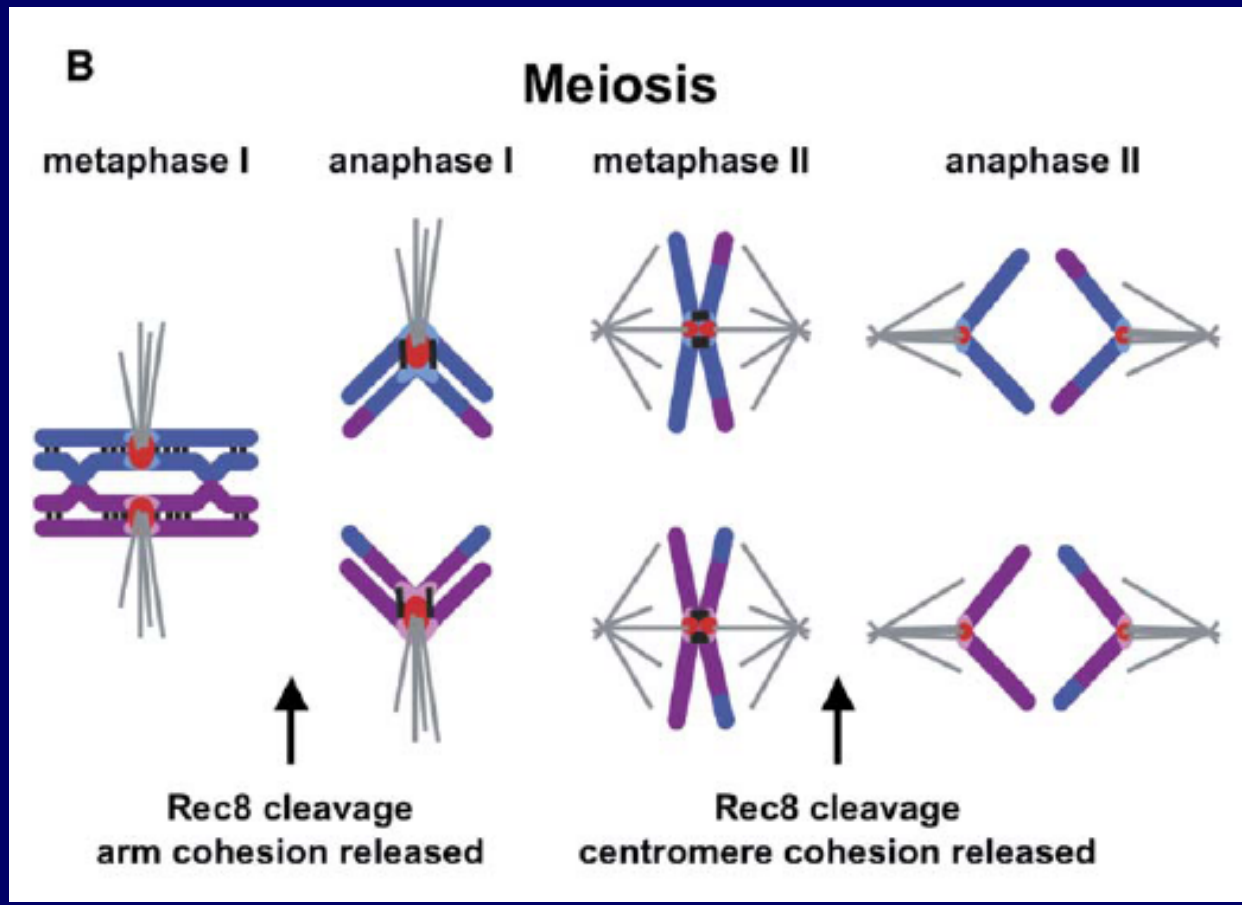

Sgo-PP2A
cohesin
Metaphase
Separase
Sister chromatid separation
Anaphase
Cohesin
Loading of cohesin
DNA pol
PCNA
Cohesion establishment
S phase
Chromosome condensation
Prophase
Sgo-PP2A
Cohesin
Phosphorylation of cohesin

МИТОЗ


Cdk1
Cyclin B
Securin
Separase
Ubiquitation of securin
Cleavage of centromeric cohesin
Spindle checkpoint OFF
Cdc20
APC/C
Phosphorylation of cohesin
Sgo-PP2A
cohesin
Metaphase
Sister chromatid separation
Spindle checkpoint ON
Sgo-PP2A
Cohesin
Anaphase


B
Ubiquitinated by APC/C
APC/C
E1
Ub
Cyclin A
Securin
Cyclin B
Apc11
E2
Apc2
?
Target
Cdc20 or Cdh1
SCF complex
Wee1
Cdc6
M
G2
G1
Cell Cycle Engine
S
Restriction point
Cyclin D
Rbx1
Cul1
Skp1
F
F-box protein
Cyclin E
p27
Ubiquitinated by SCF complex


A
Mitosis
prophase
metaphase
anaphase
Prophase pathway
Phosphorylation
of SA2
Cleavage of
Rad21/Scc1

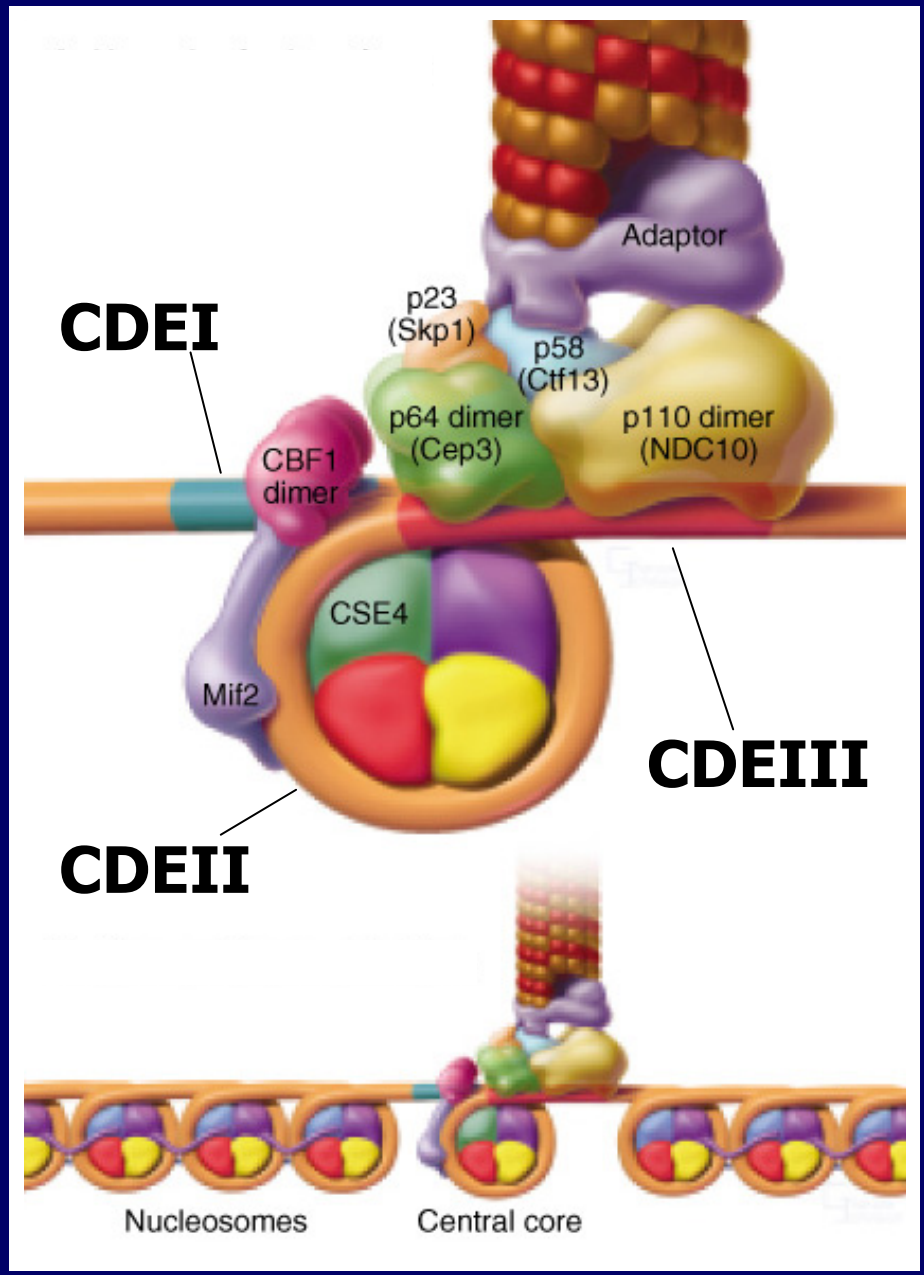

B
Meiosis
metaphase I
anaphase I
metaphase II
anaphase II
Rec8 cleavage
arm cohesion released
Rec8 cleavage
centromere cohesion released

		Vertebrate	*S. cerevisiae*	*S. pombe*	*D. melanogaster*
Cohesin subunits	SMC	SMC1α **SMC1β***	Smc1	Psm1	DmSMC1
		SMC3	Smc3	Psm3	DmSMC3
	Kleisin α	SCC1/RAD21	Scc1/Mcd1	Rad21	DmRAD21
		REC8*	**Rec8***	**Rec8***	**C(2)M***
		SA1, SA2	Scc3	Psc3	DmSA1
		SA3*		**Rec11***	**DmSA2***
		PDS5	Pds5	Pds5	DmPDS5
Securin		PTTG1	Pds1	Cut2	PIM
Separase/separin		Separase	Esp1	Cut1	THR, SSE
Shugoshin		Sgo1, Sgo2	Sgo1	**Sgo1***, Sgo2	Mei-S332
Polo kinase		PLK1	Cdc5	Plo1	Polo

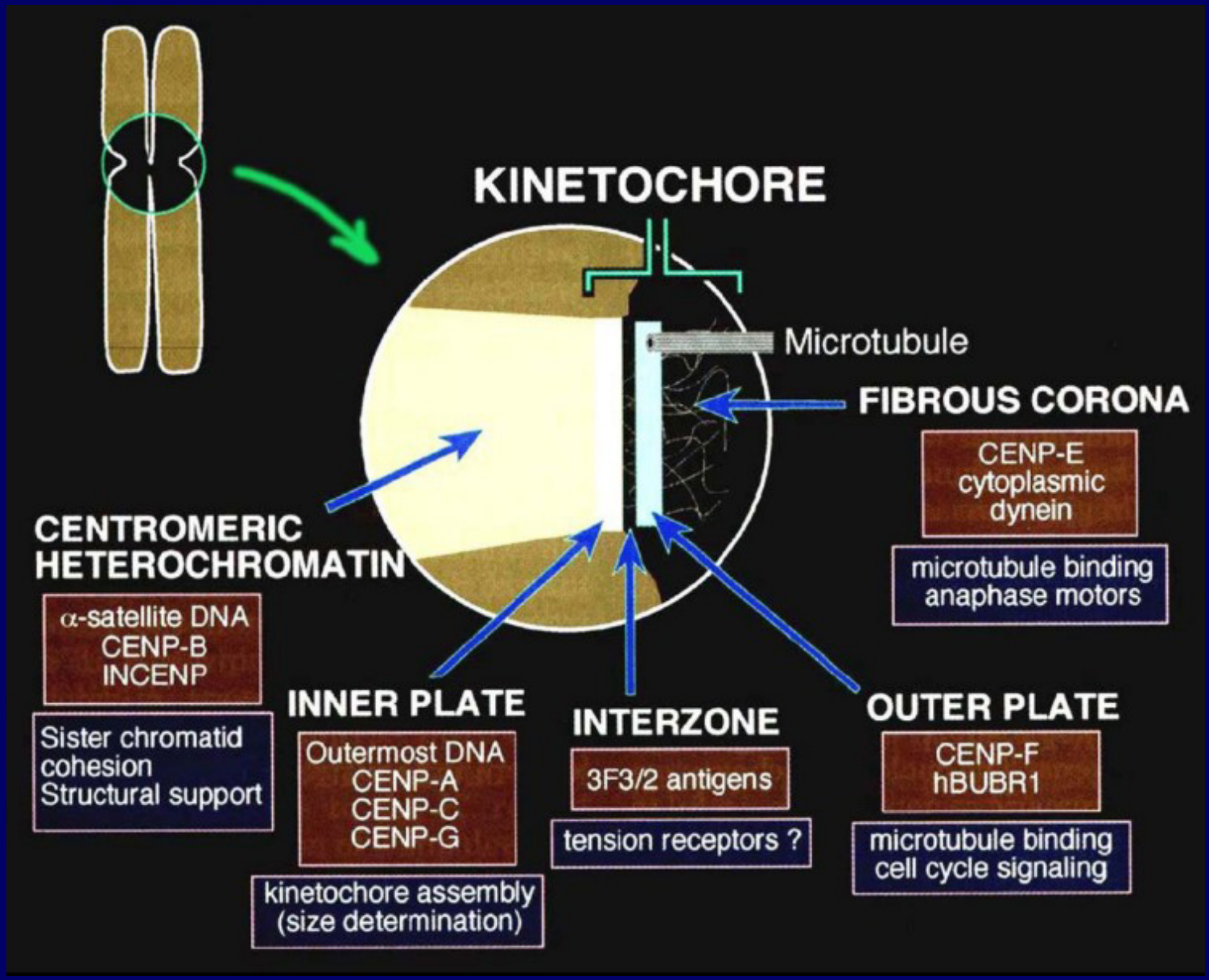
(* **meiosis specific**)

Кинетохор

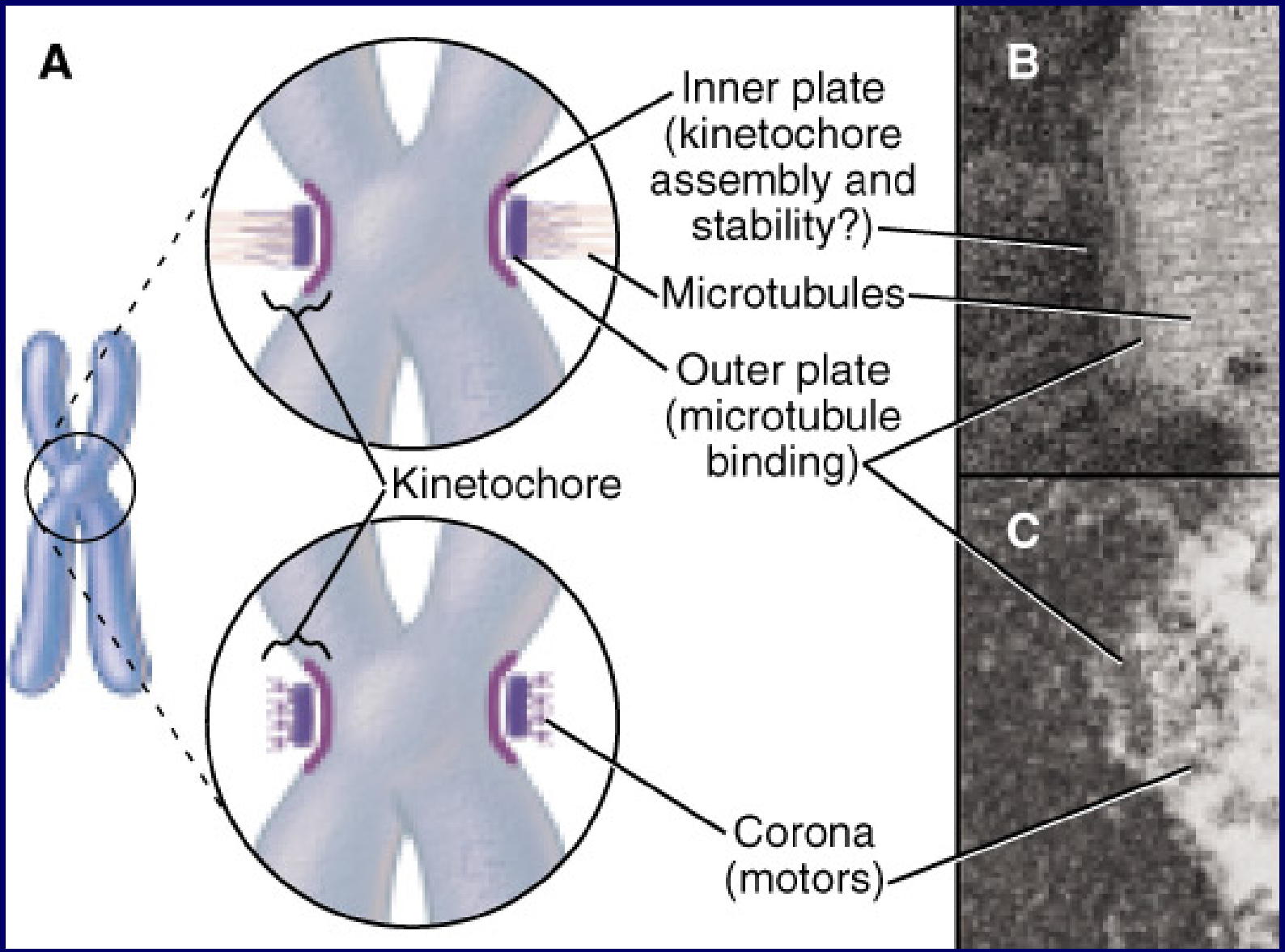
кинетохор в хромосомах S. cerevisiae



Кинетохор в хромосомах человека



Кинетохор в хромосомах человека



Центромерно-Кинетохорные белки

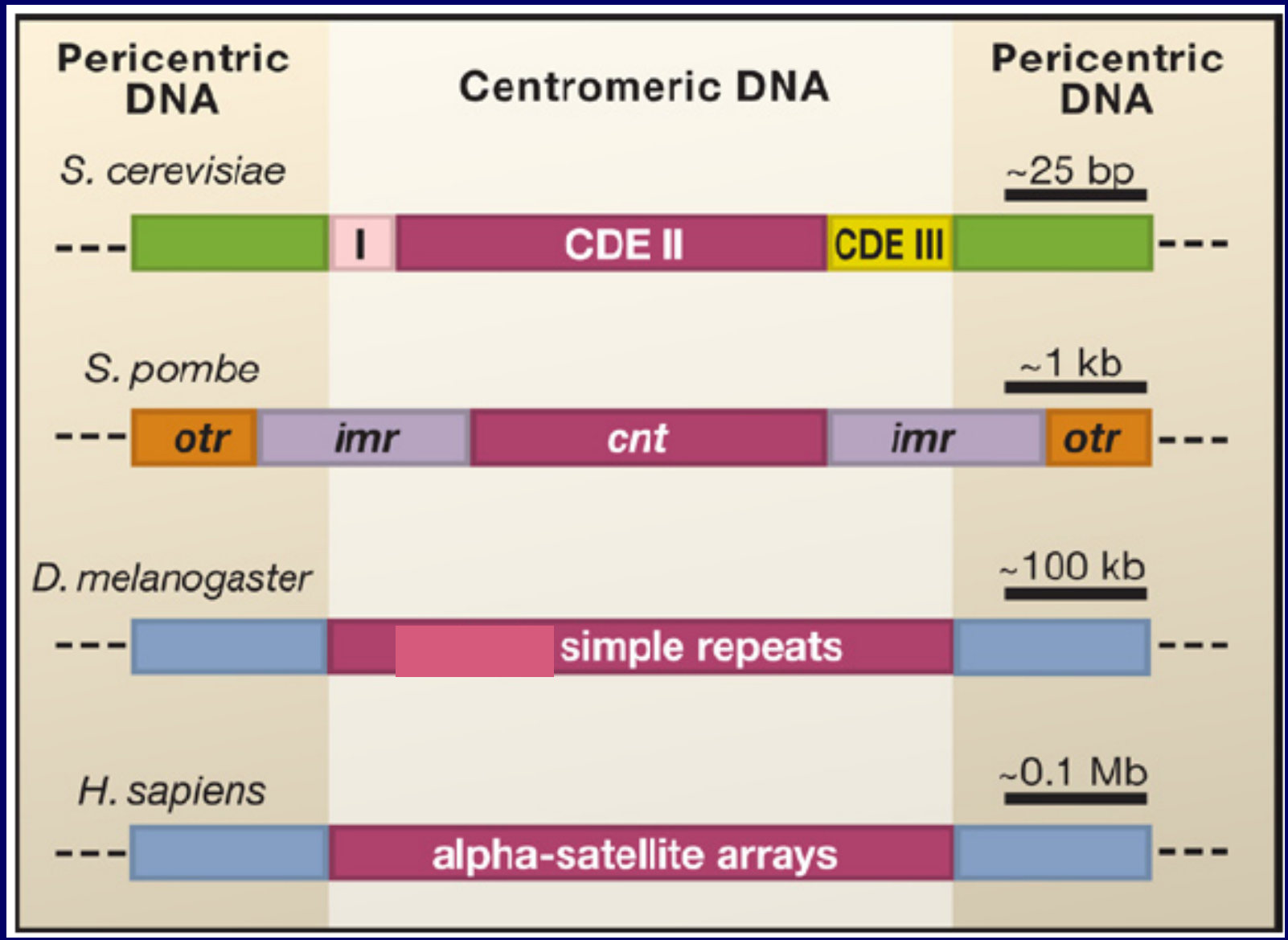
Белки внутреннего слоя кинетохора
Белки среднего слоя кинетохора
Белки внешнего слоя кинетохора
Регуляторные белки

Что нужно для работы центромеры?

Нет консервативности последовательностей ДНК

КОНСЕРВАТИВНЫЕ БЕЛКИ!

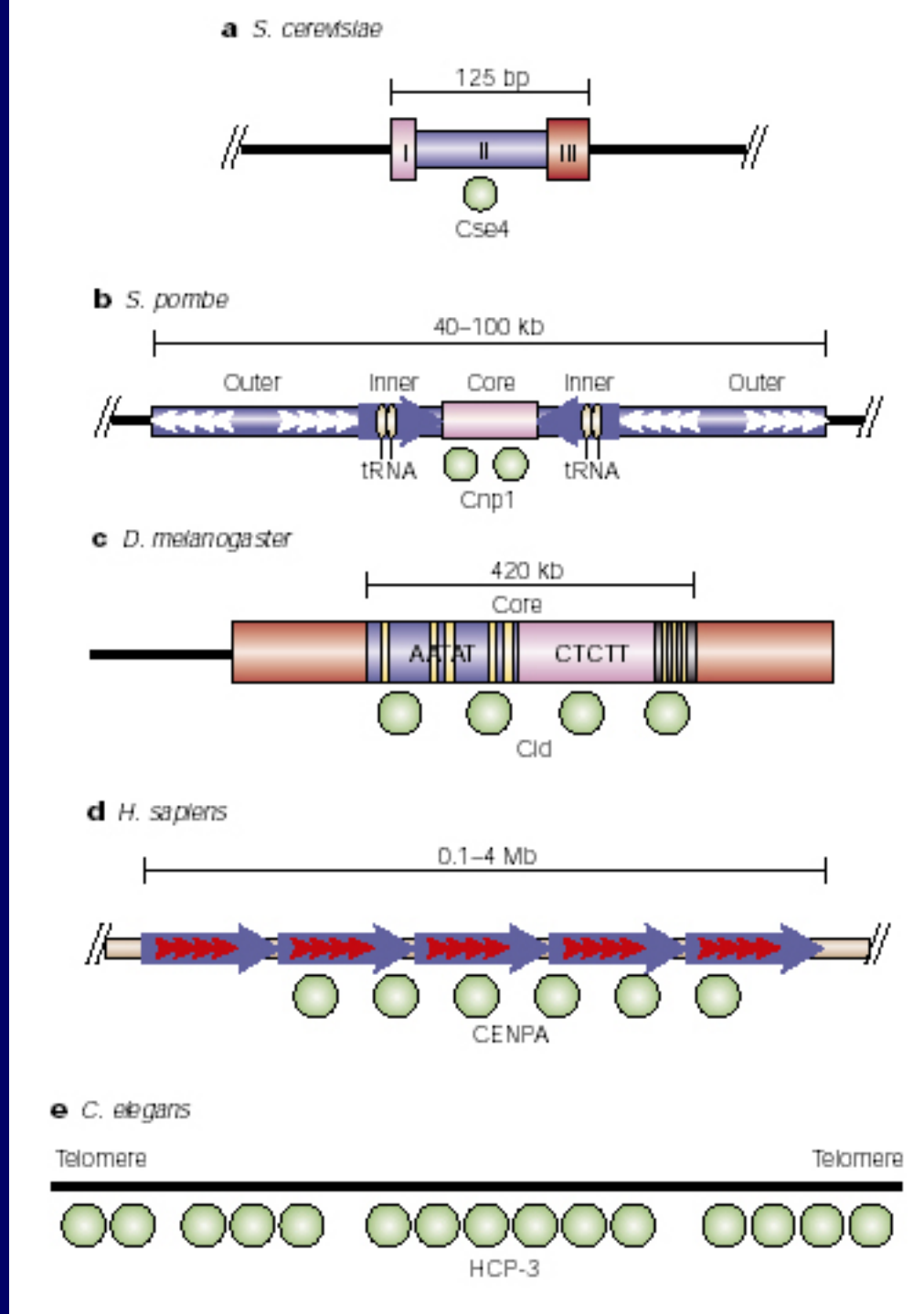
Организация центромеры эукариот

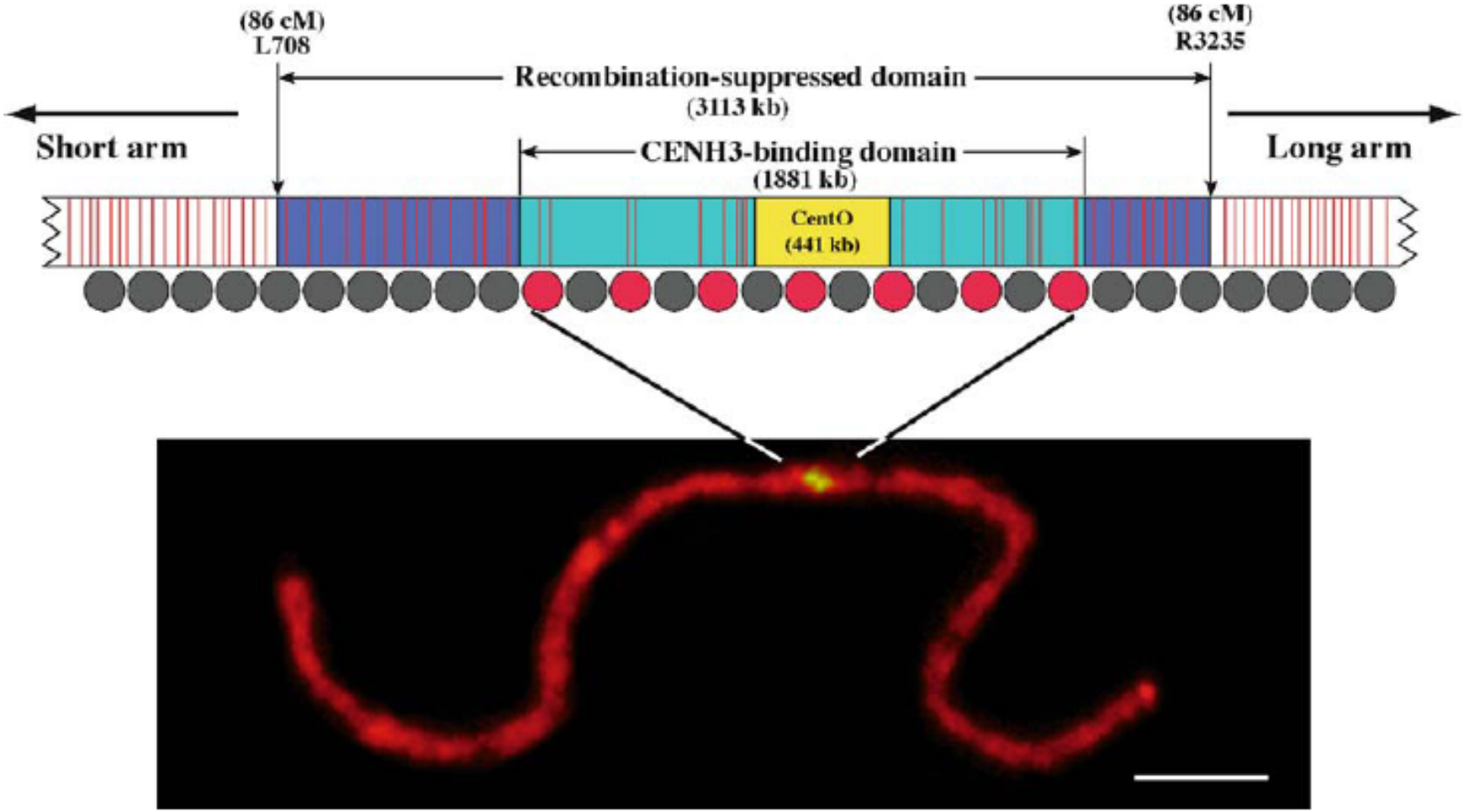


Организация центромеры эукариот

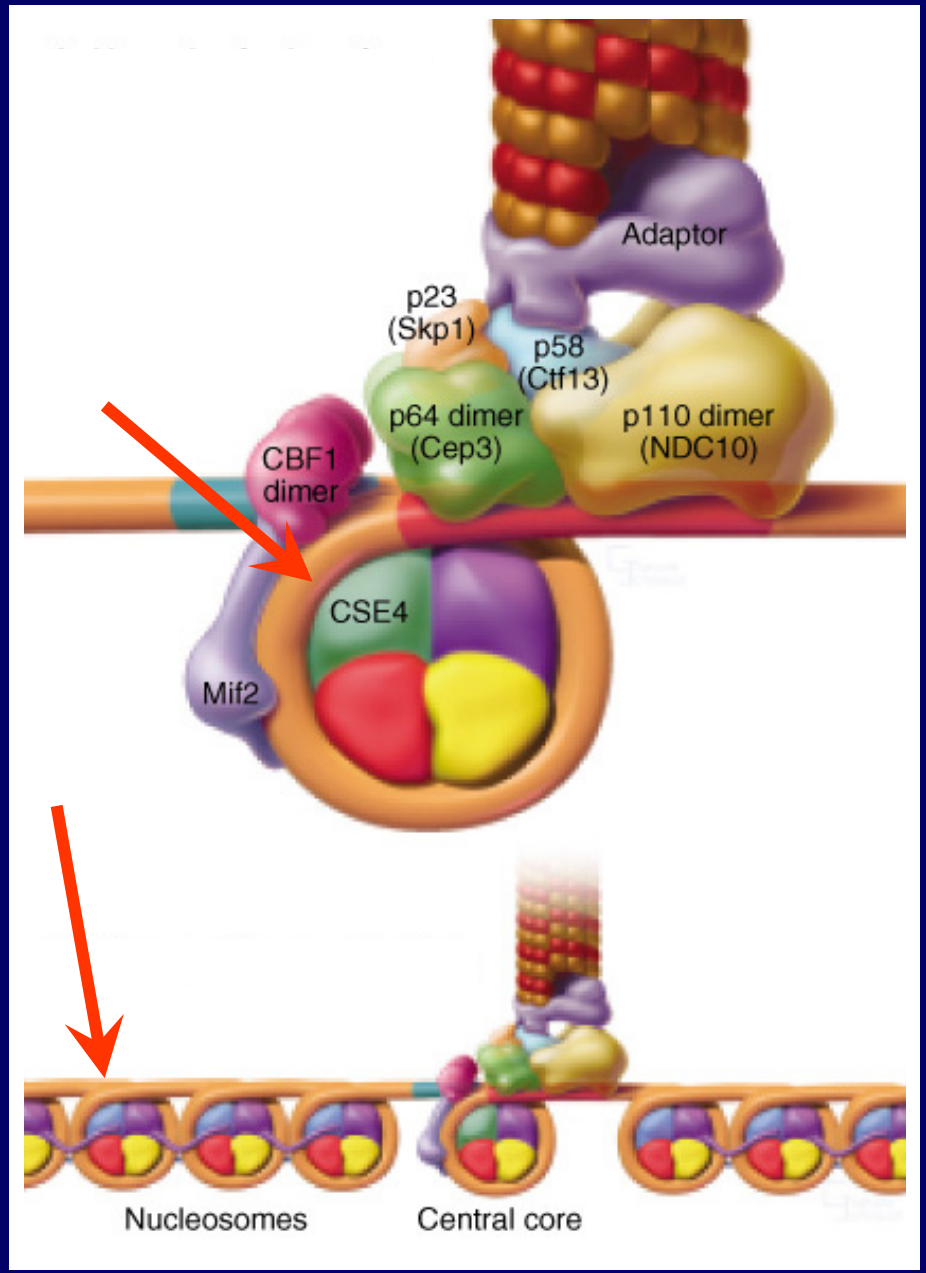
- CENP-A

CENP-A = центромерный белок А, центромерный аналог гистона Н3



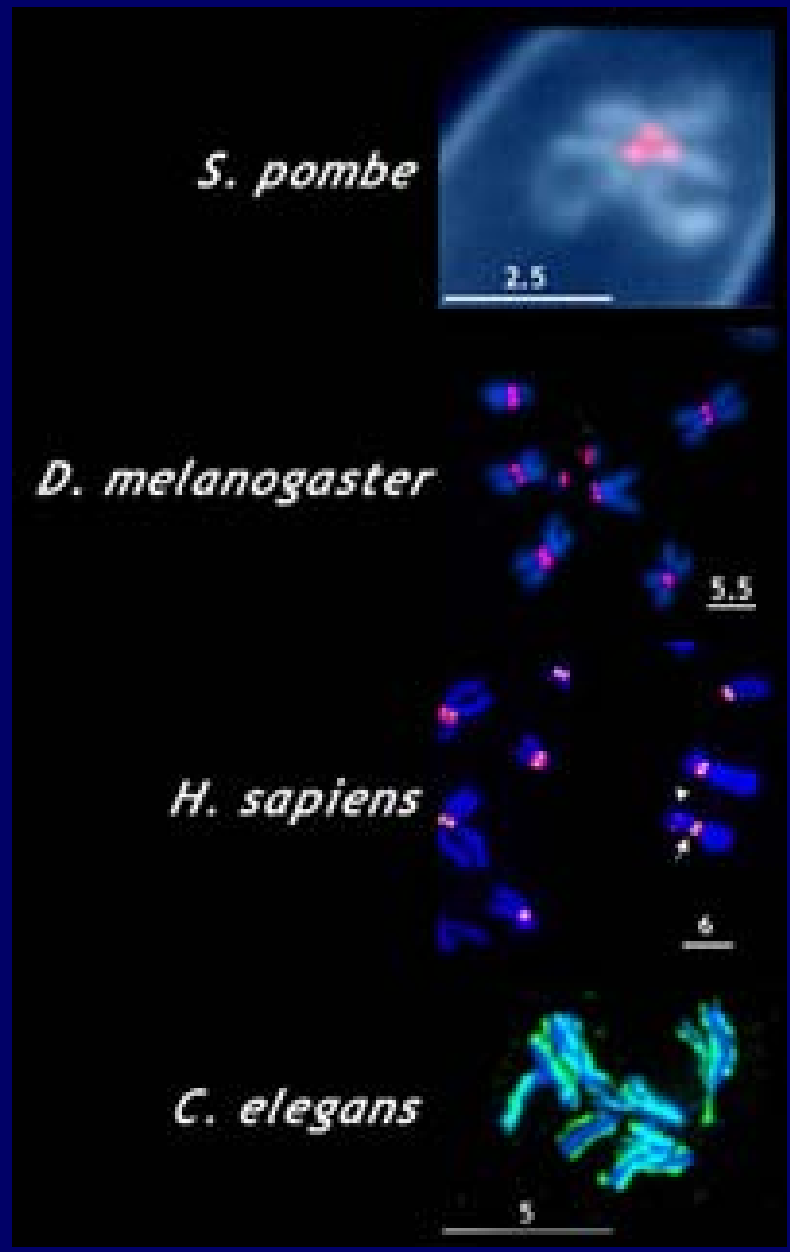


H. Yan and J. Jiang Chromosome Research (2007) 15:77–84



CSE4
белок, заменяющий
гистон H3 в центромере

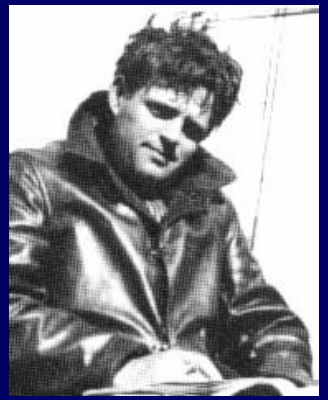
	H. sapiens	CENP-A
	M. musculus	CENP-A
	G. gallus	CENP-A
H3 ⟷	X. laevis	CENP-A
	S. cerevisiae	CSE4
	S. pombe	CND1
	D. melanogaster	CID
	C. elegans	HCP3



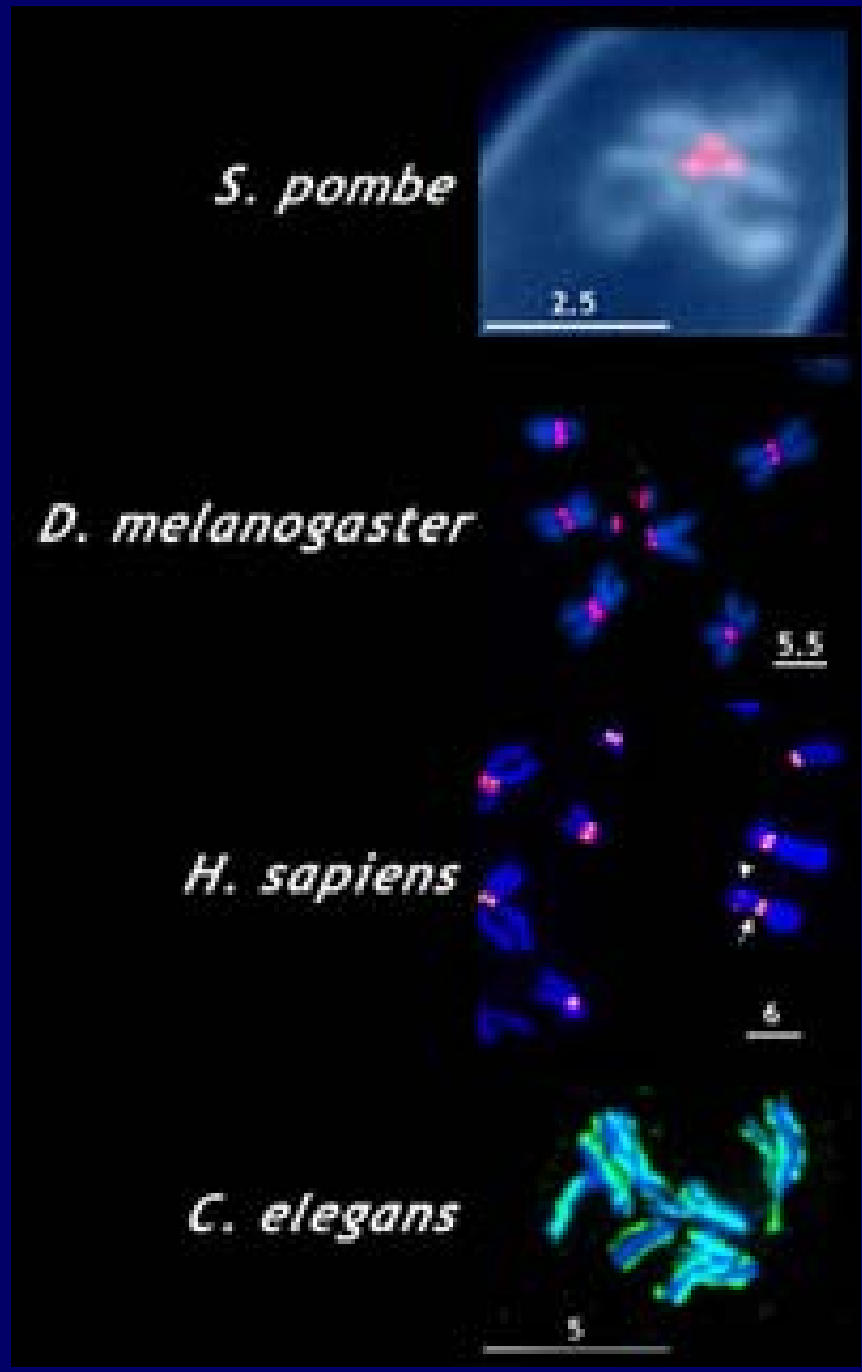
CENP-A = центромерный белок А

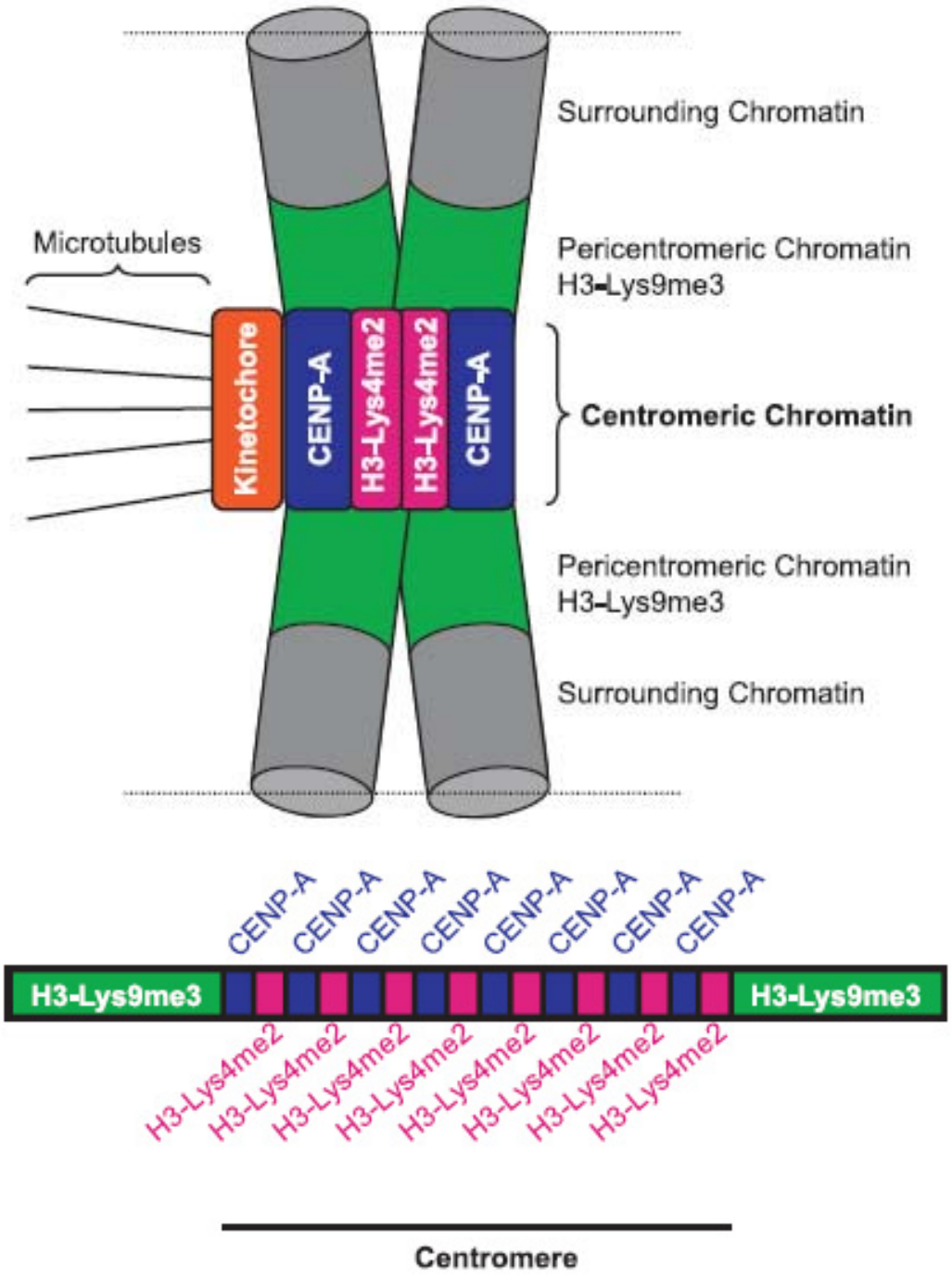
Белок CENP-A менее консервативен, чем основной набор гистонов

```
Hamster    MGPRR---KPRTPRRRPSSPVP--GPSRRSSRPG------KRRKFLWLKEI    40
Mouse      MGPRR---KPQTPRRRPSSPAP--GPSRQSSSVGSQ-TLRRRQKFMWLKEI    45
Human      MGPRRRSRKPEAPRRRSPSPTPTPGPSRRGPSLGASSHQHSRRRQGWLKEI    51

Hamster    KKLQRSTDLLLRKLPFSRVVREICGKFTRGVDLCWQAQALLALQEAAEAFL    91
Mouse      KTLQKSTDLLFRKKPFSMVVREICEKFSRGVDFWWQAQALLALQEAAEAFL    96
Human      RKLQKSTHLLIRKLPFSRLAREICVKFTRGVDFNWQAQALLALQEAAEAFL   102

Hamster    VHLFEDAYLLTLHAGRVTIFPKDIQLTRRIRGIEGGLG                 129
Mouse      IHLFEDAYLLSLHAGRVTLFPKDIQLTRRIRGFEGGLP                 134
Human      VHLFEDAYLLTLHAGRVTLFPKDVQLARRIRGLEEGLG                 140
```

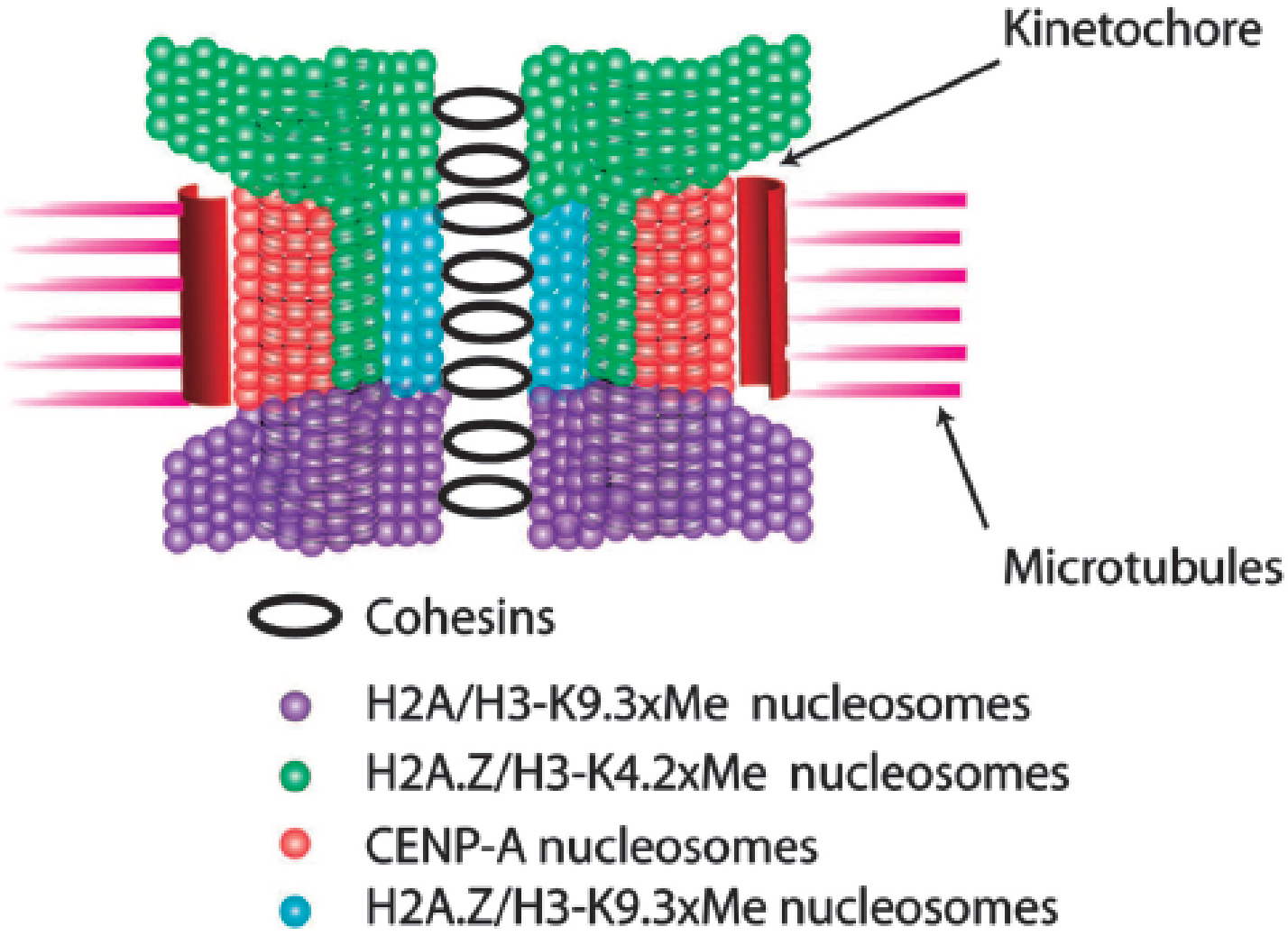


= CENP-A дрозофилы


S. pombe
2.5
D. melanogaster
5.5
H. sapiens
4
C. elegans
5

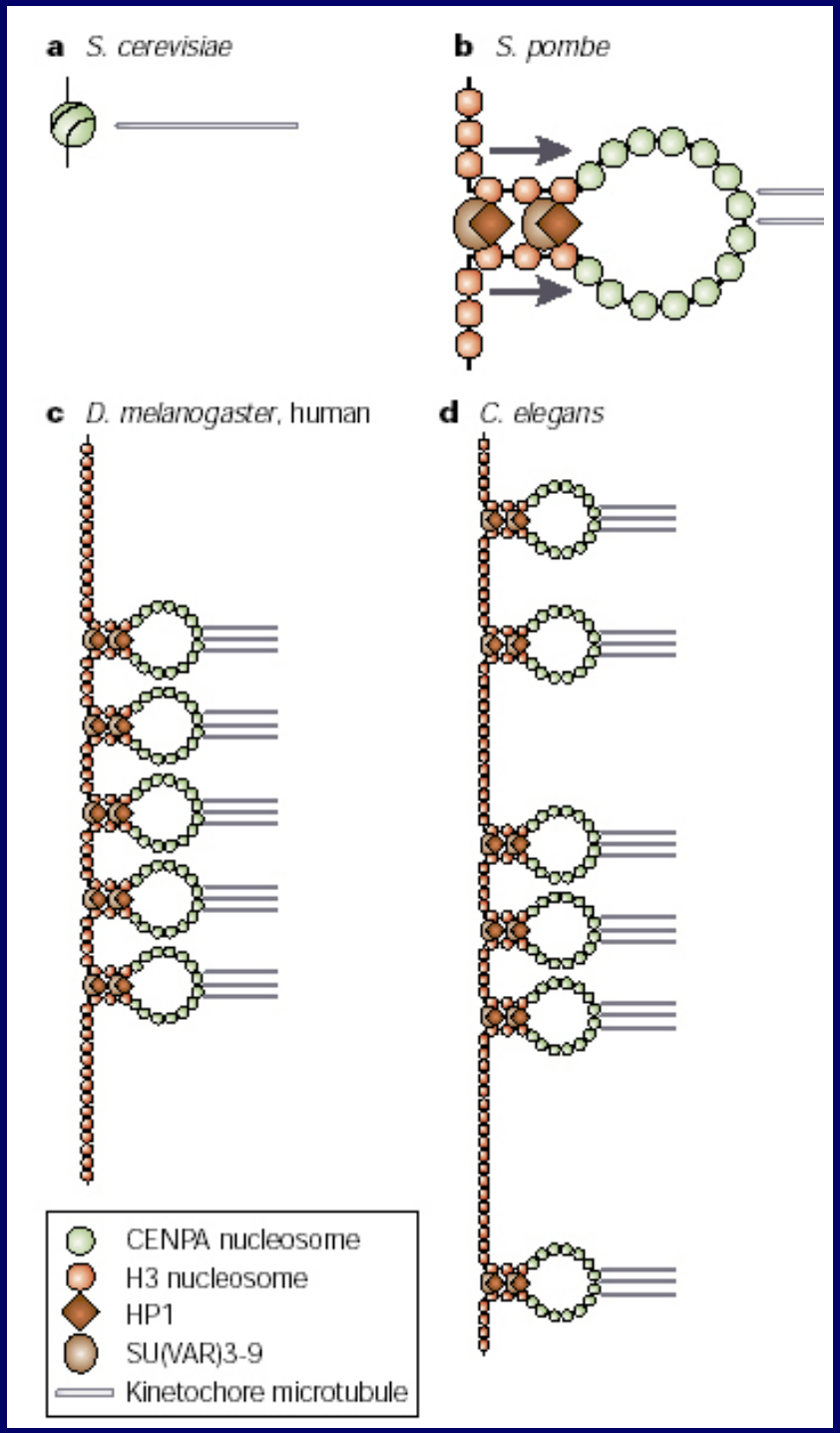


Vos et al., 2006



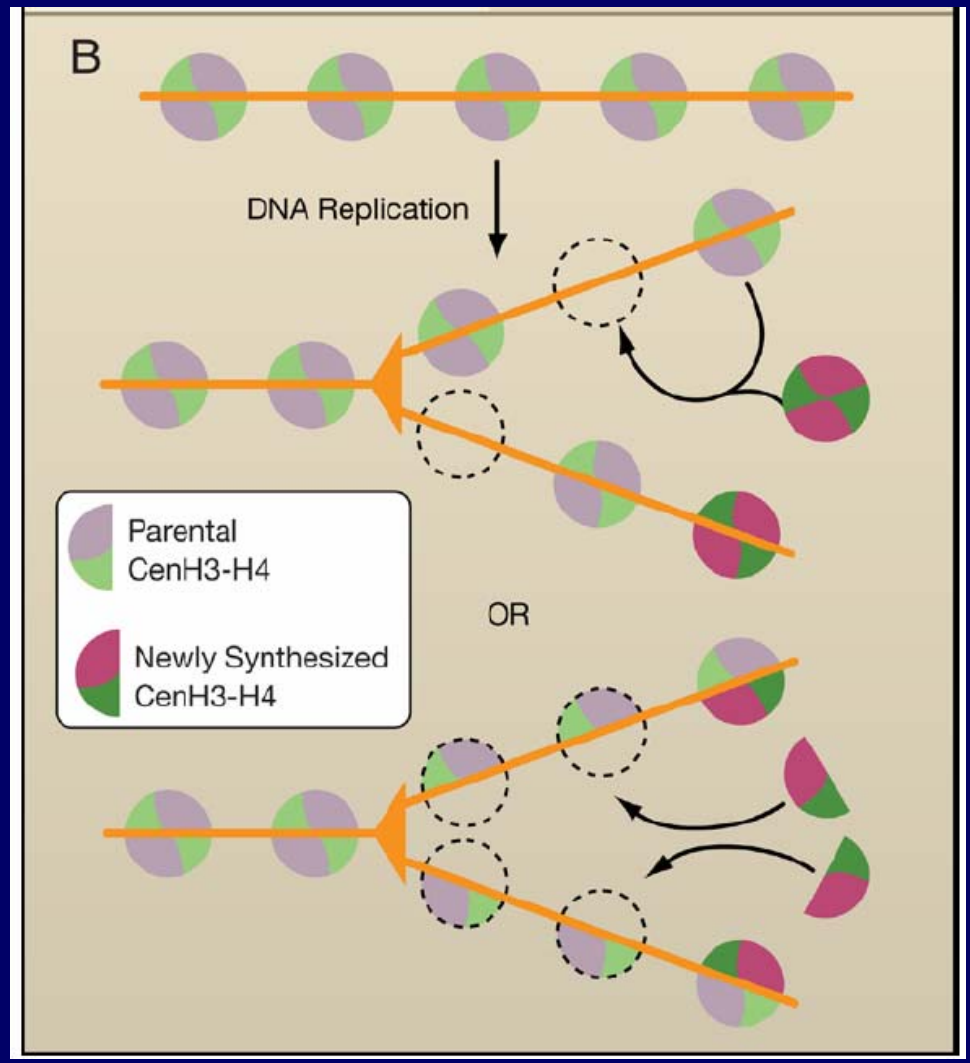
Greaves *et al*.
PNAS **January 9, 2007**

Одна из современных моделей организации центромеры



Эпигенетическое поддержание центромеры

Воспроизведение центромерного хроматина во время репликации



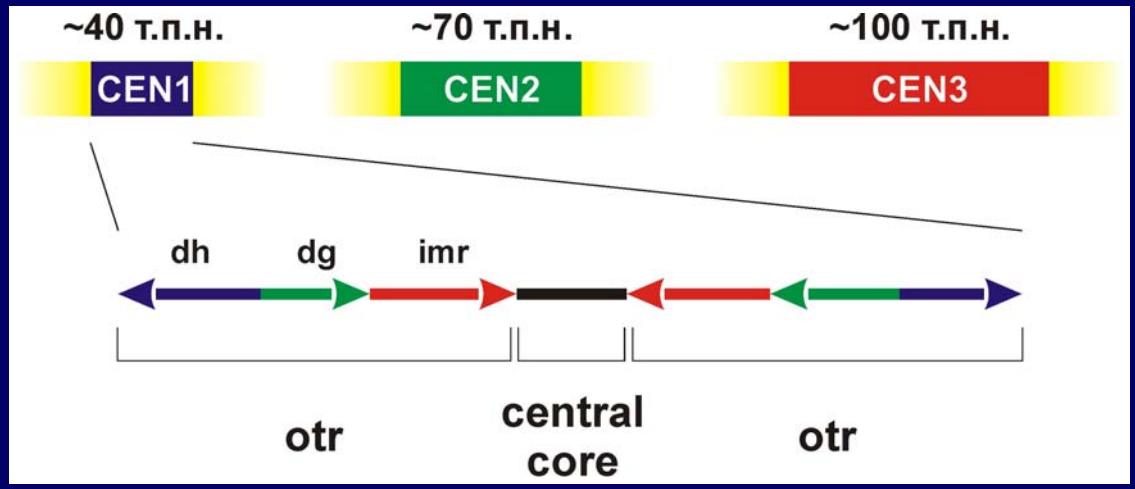
У всех исследованных эукариот за исключением *S. cerevisiae* последовательности ДНК в центромерах отличаются даже между хромосомами одного набора хромосом

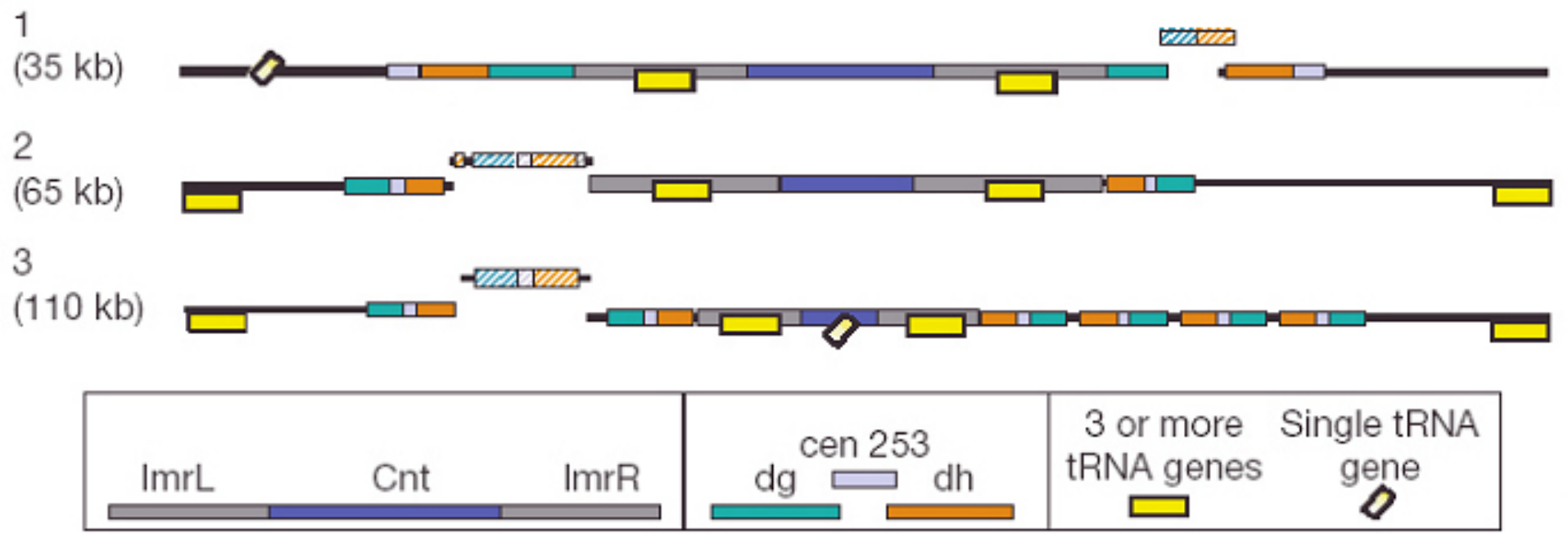
Saccharomyces cerevisiae

111-120 п.н.

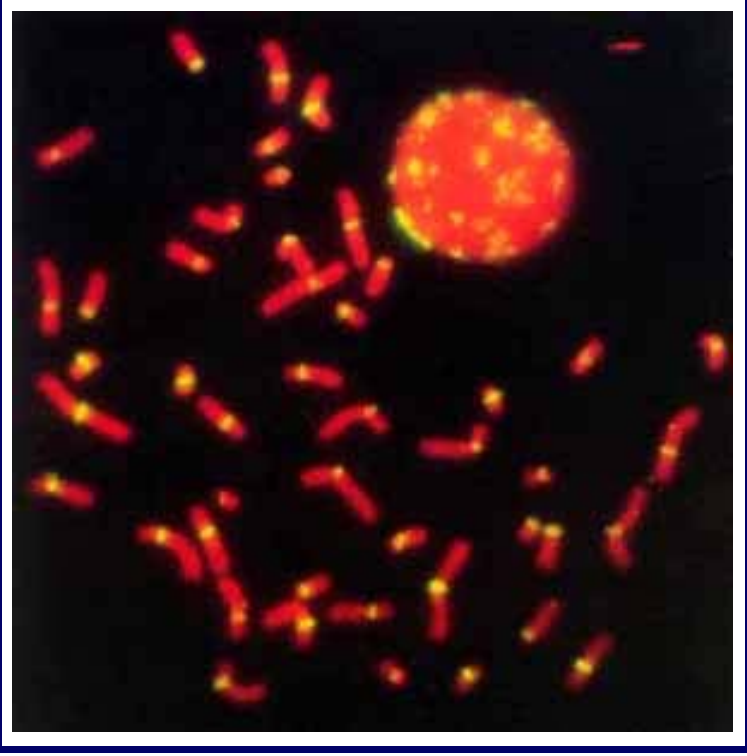
```
                         *        20         *        40         *        60
                TCA  TG
Cen6     :  ATCACGTGCT-ATAAAAATAATTATAATTTAAATTTTTAATATAAATATATAAATTAAA  :  59
Cen11    :  GTCACATGAT-AAAAACATATTTAAAATTTTAAAAAAATTAATTTCAAAATAAATTTAT  :  59
Cen10    :  ATCACGTGTT-AAATAATTAATTTACTTTAAAATTTATTTTTTAATATAAAATATTTATT  :  59
Cen8     :  ATCACATGAC-TAATAATTCTTTTAATTTTAATTAATTTAATAAAATTAAAATAATATAT  :  59
Cen5     :  ATCACGTGCT-TTTTAAAAAATATAAATTTAATTTCATTT-TCTATTTCAATATTTATTA  :  58
Cen7     :  ATCACGTGTTATATTTACTATATAAAAATTCAAT-AAATAAAAAGTTAGAAGATAAAAAT  :  59
Cen12    :  ATCACGTGTAATAAATATTATTAAAAAGTTTATTAAAATAAAATAATAATTTAAATTACT  :  60
Cen1     :  GTCACATGACATAATAATAAATAATTTTAAAAATATAAAATATTTTTAATAGTTTTT--A  :  58
Cen2     :  ATCATGTGACTTATTTATTTAATTATTATTAAGTAAAAAAGATTTTCTATTTAAATT--T  :  58
Cen3     :  GTCACATGATGATATTTG--ATTTTATTATATTTTTAAAAAAAGTAAAAAATAAAAAGTA  :  58
Cen16    :  ATCACATGATATATTTTT--TATTTTTAATTTTTTTTAATTATAAAAATAATTTTTTTCT  :  58
Cen4     :  GTCACATGCTTATAATCA--ACTTTTTTAAAAATTTAAAATACTTTTTTATTTTTTATTT  :  58
Cen9     :  TTCACGTGAAAAT-TTTTATATTTTTAATTAAATTTTTATAATATTATAAATTATTATAA  :  59
Cen14    :  GTCACGTGCAGCT-TTTTAAAAATATTTTAAAACATTTTAAAAAATATACATTTTTTTAT  :  59
Cen15    :  ATCACGTGAACTTATTTTGCATTTAAAAAAAAGTAAAAACTATTTGCTAAAATATATTTT  :  60
Cen13    :  ATCACATGACTACCTAACAAAATATTTATTTTTCTTTTTTAATATTTGAAAATACTAAAA  :  60
            <-CDEI-><---------------------CDEII---(>90% AT-rich)------>
                         *        80         *       100         *       120
                                                     G     G     CCGAA
Cen6     :  AATAGAAAGTAAAAAAAGAAATTAAAGAAAAA-ATAGTTTTTGTTTTCCGAAGATGTAAA  :  118
Cen11    :  TATATTTTTTTAATTACATAATCATAAAAATA-AATGTTCATGATTTCCGAACGTATAAA  :  118
Cen10    :  CTTTTTATTTAAAAATAAAAAACACAAAAAAACAATGTTTATGATTTCCGAACCTAAATA  :  119
Cen8     :  ATACTAAATTGTTTATTAAAAATGATTAAACATTGGGTTT-TGTGTTCCGAACTTAGAAA  :  118
Cen5     :  AATAAAAAATTTGAAAAATATATAAAAATTGTAGCAGTATTAGATTTCCGAAAAGAAAAA  :  118
Cen7     :  TATATTATACATATTTTTATTTTTATTATAATTTTTGTTTTTGCCTTCCGAAAAGAAAAT  :  119
Cen12    :  ATTTTTAAATAAGTTTTATTTTTTTAATAACACTATTGTATTTGTTATCCGAACAATAAAA  :  120
Cen1     :  AATATTTTACAGTTTATTTTTTTAAATTTATTTATATGTTTTTGTTTTCCGAAGCAGTCAA  :  118
Cen2     :  ATTAATTAATTTTTTTTCTTAAATAATTATTT-TATGTTTTTGTTTTCCGAAAAAGAAAA  :  117
Cen3     :  GTTTATTTTTAAAAAATAAAATTTAAAA-TATTAGTGTATTTGATTTCCGAAAGTTAAAA  :  117
Cen16    :  TTAAATTAAACAAAAATAAAAAATTGTT-TTTTGTTGGTTAAGATTTCCGAAAATAGAAA  :  117
Cen4     :  TTAAACATAAATGAAATAATTTAT-------TTATTGTTTATGATTACCGAAACATAAAA  :  111
Cen9     :  TATTGATATTTAAAATTA-AAAACAAAT-TATTAATGGTTTTGTTTTCCGAAATGTTTTT  :  117
Cen14    :  TATTTTTTTATATATTAATGTTAAAATT-TATTTATGTATTTGTCTTCCGAAAAGTAAAA  :  118
Cen15    :  TTTAATTTTTAAAAATAATGTTTTAATT-ATTTAATGTATATGACTTCCGAAAAATATAT  :  119
Cen13    :  TATTTTTGTTGTTTTTTGAAA-AAAGGATTTTTAATGTGTATGCGTTCCGAACTTTAAAT  :  119
            <------------CDEII---------------><---------CDEIII--------->
```

Schizosaccharomyces pombe





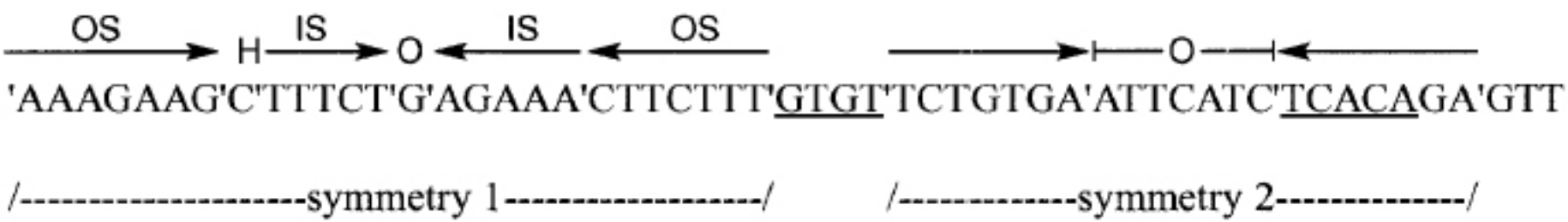
Центромеры в хромосомах человека



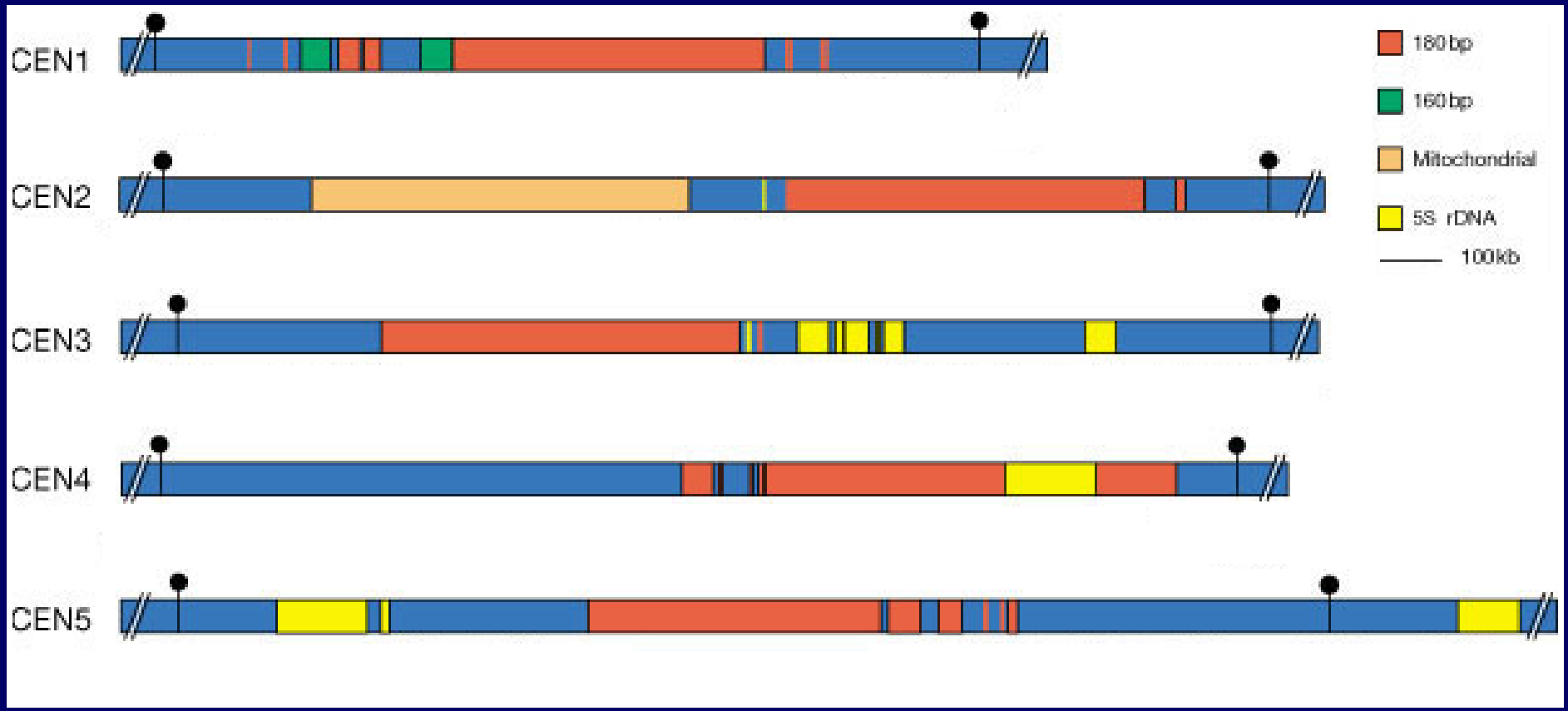
альфа-сателлит
~171 п.н.

консервативная часть - 54 п.н.
вариабельная часть - ~117 п.н.

Primate alpha satellite DNA

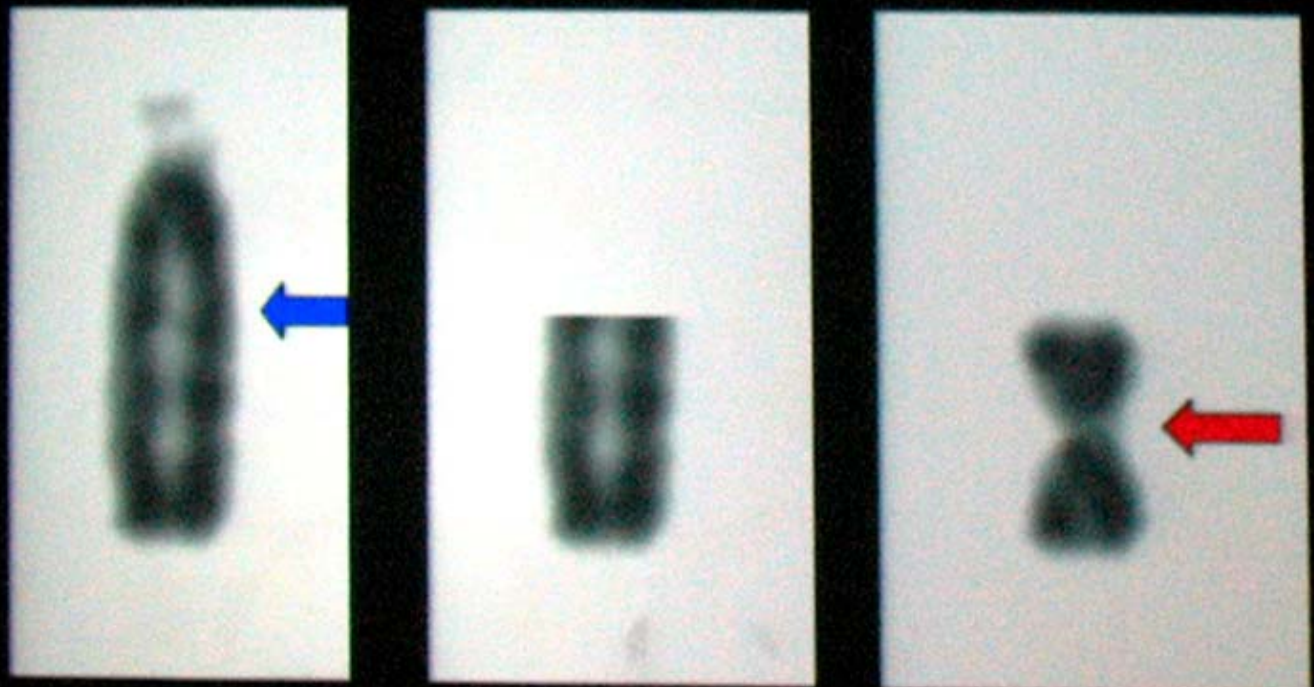


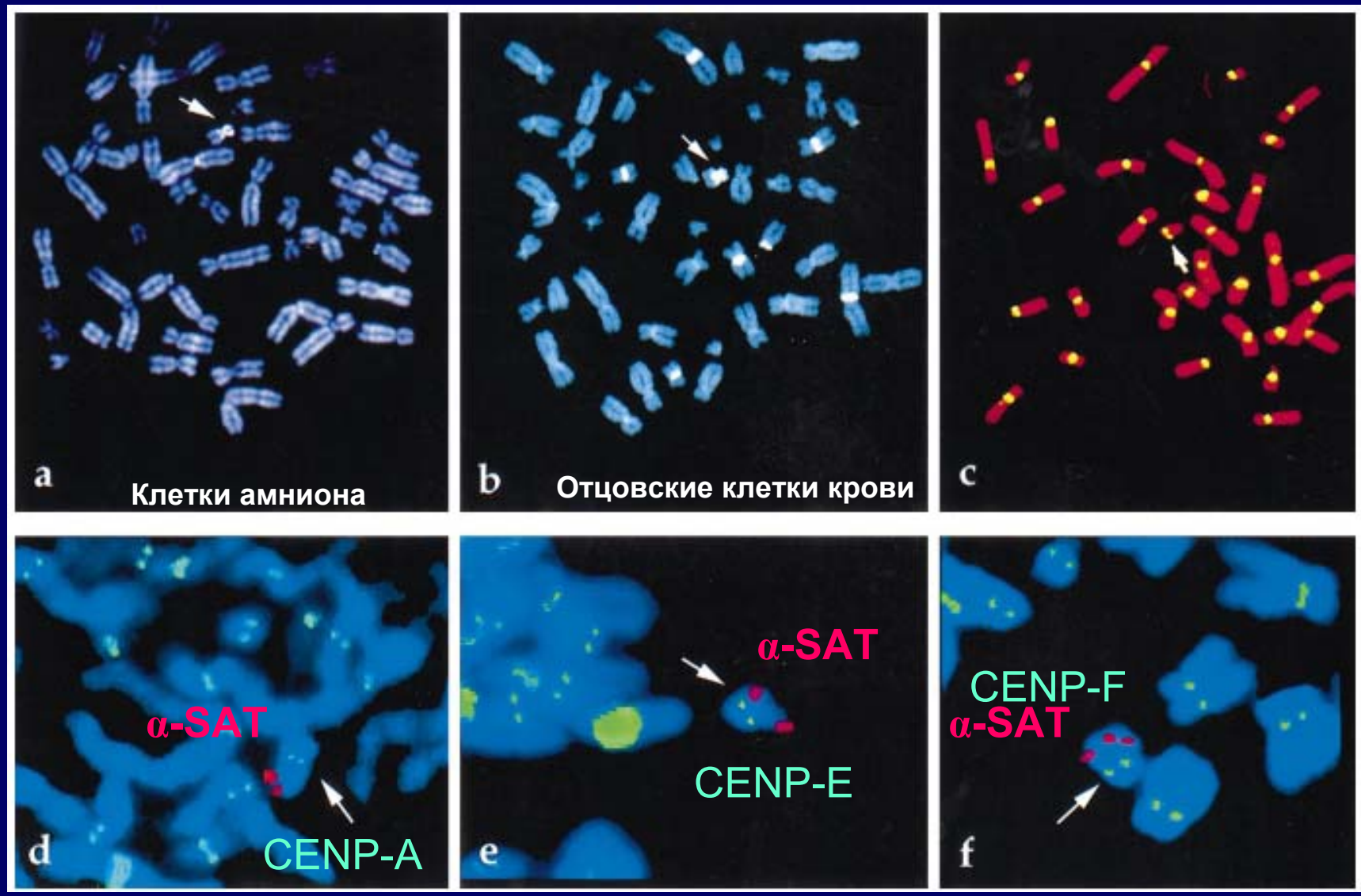
Центромеры в хромосомах арабидопсиса



Неоцентромеры –ключ к пониманию эволюции и устройства центромер

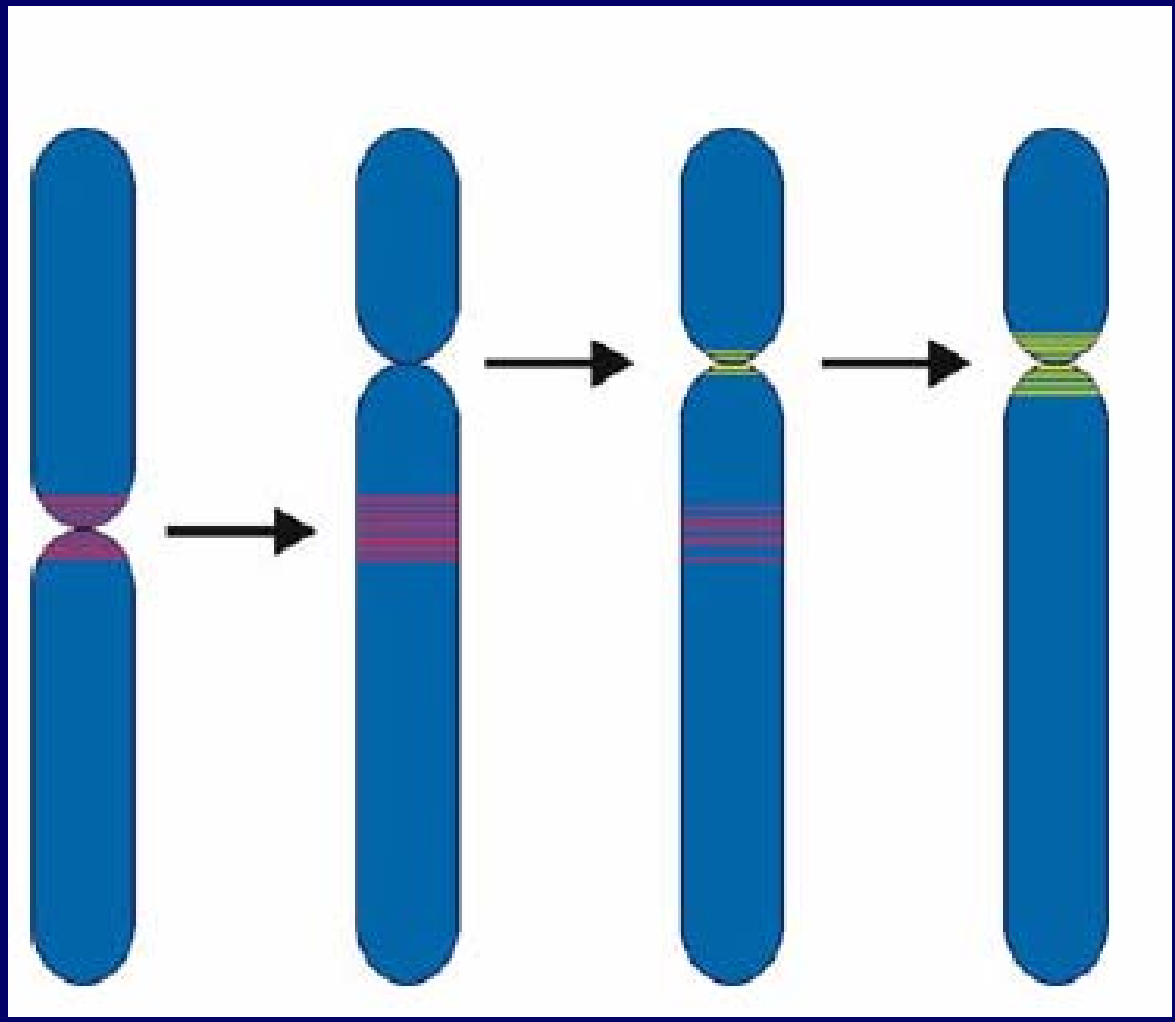
Human clinical neocentromeres

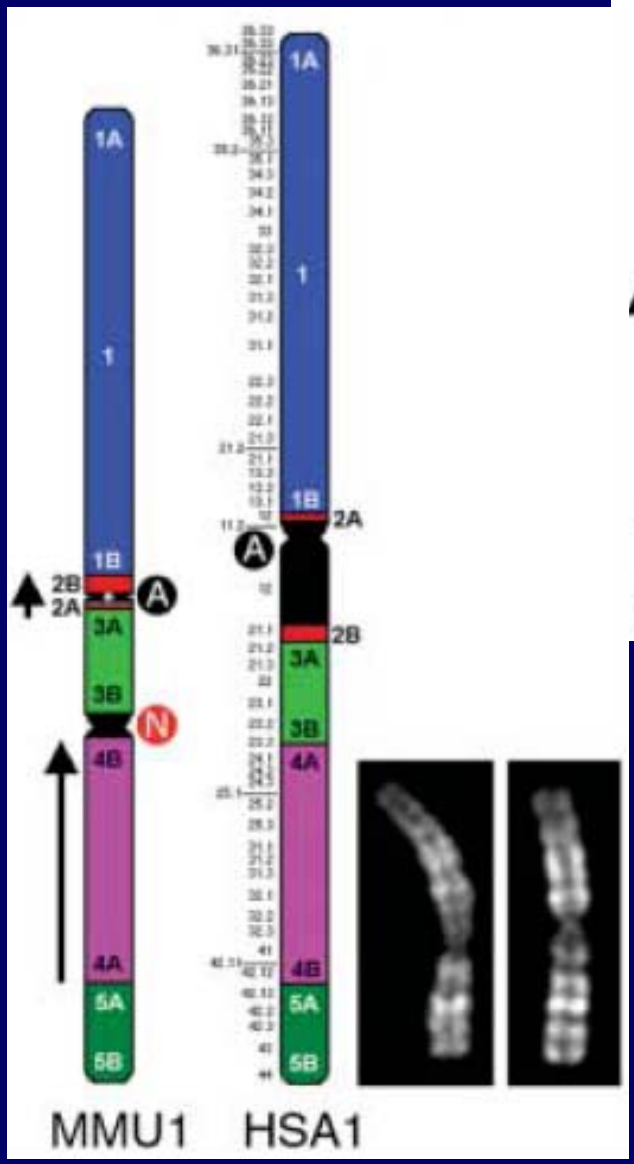


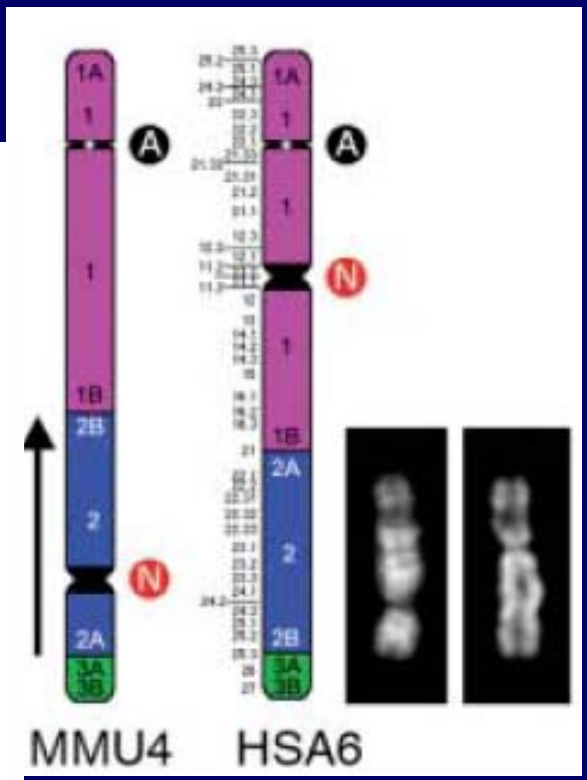


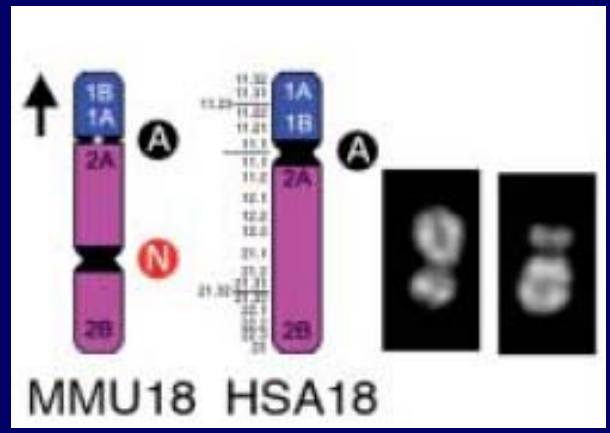
Transmission of a Fully Functional Human Neocentromere through Three Generations
Chris Tyler-Smith et al., 1999

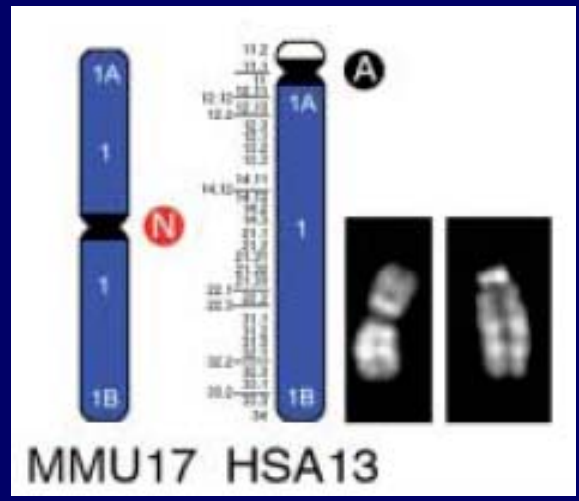
Модель эволюции центромер

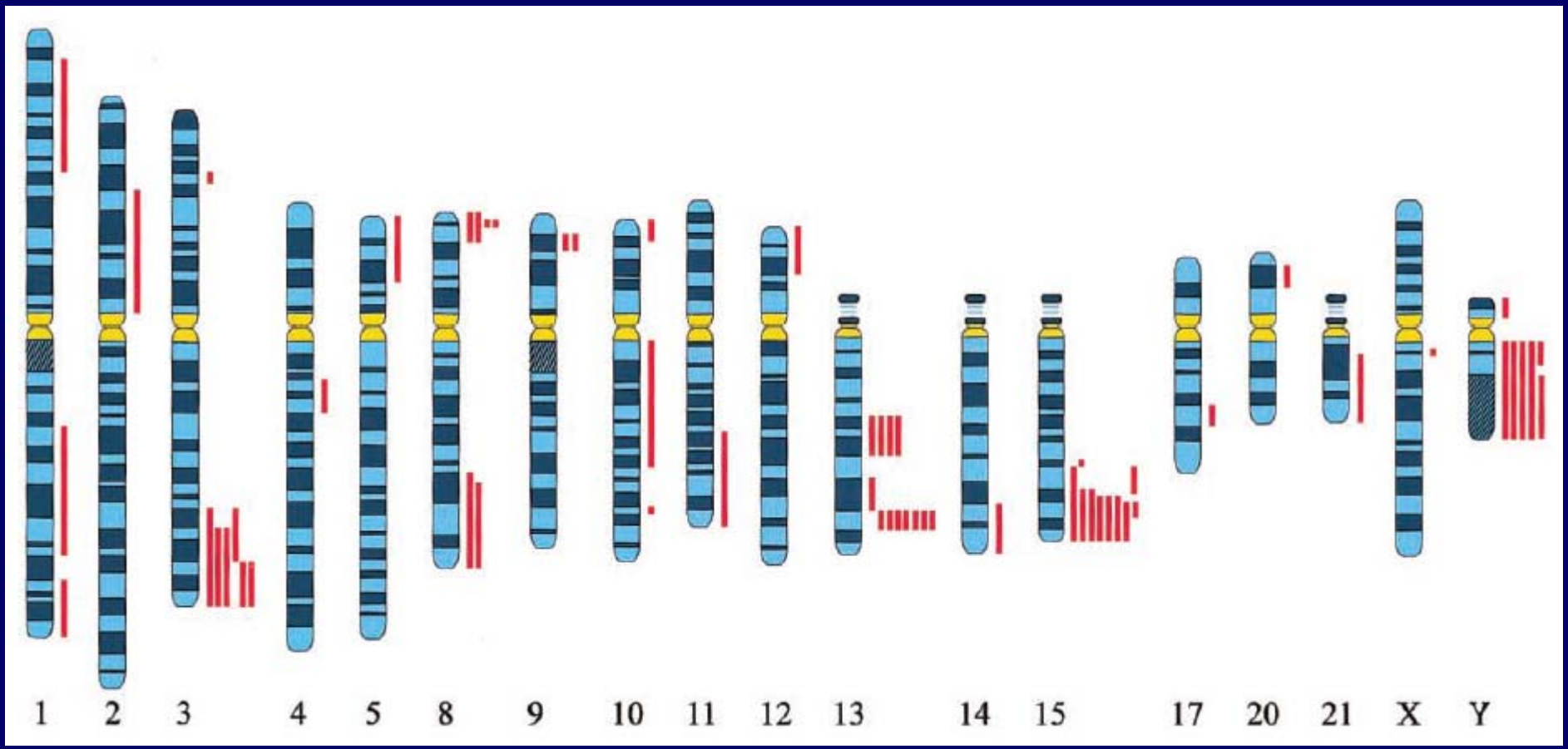



1A
1
1B
2B
2A
A
3A
3B
N
4B
4A
5A
5B
MMU1
HSA1


1A
1
A
1B
2B
2
N
2A
3A
3B
MMU4
HSA6


1B
1A
2A
A
N
2B
MMU18
HSA18


1A
1
N
1B
A
MMU17
HSA13



1. Неоцентромеры возникают случайно,
   а последующий отбор оставляет лишь некоторые?

2. Есть «горячие точки» возникновения неоцентромер?