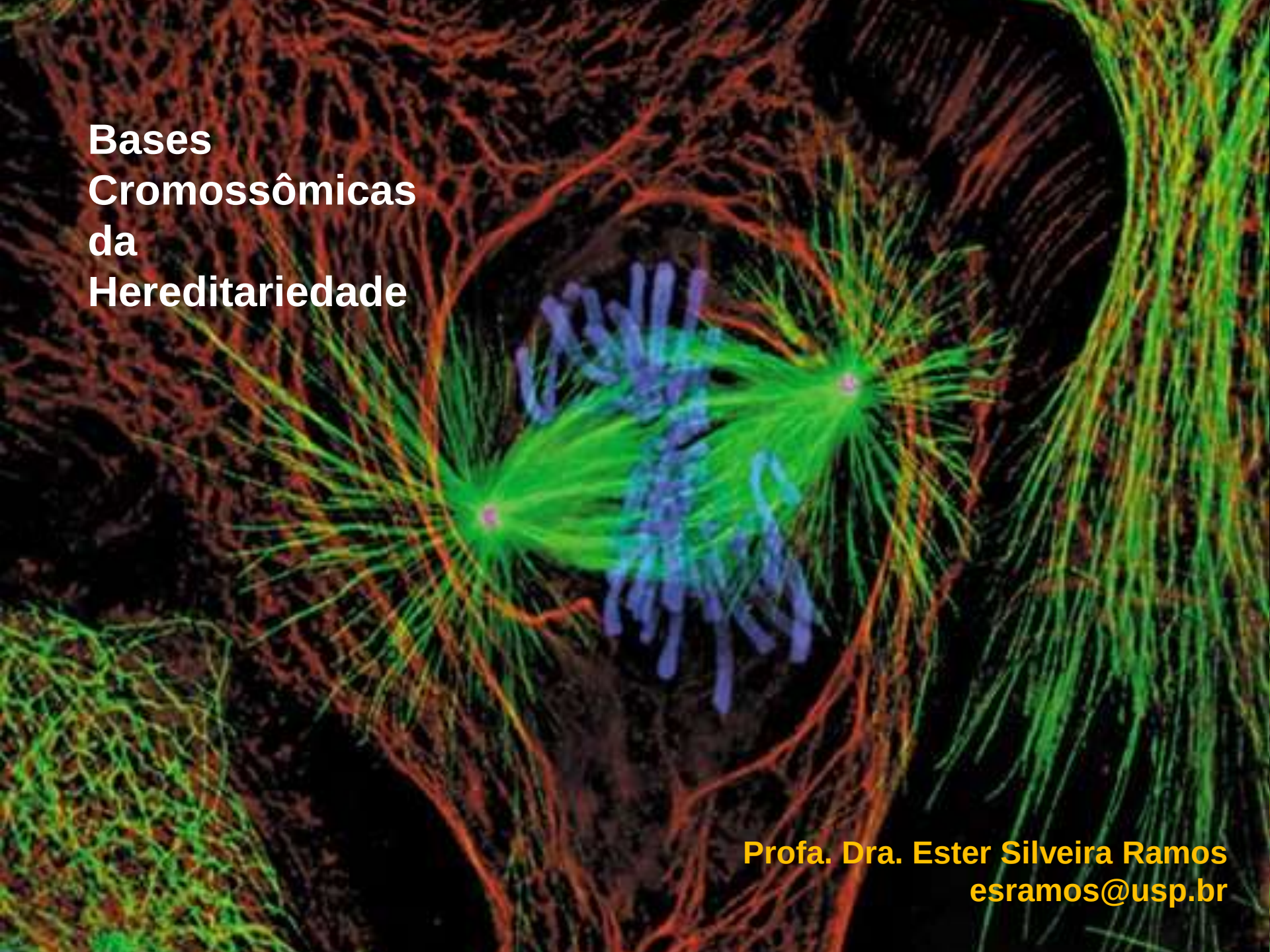
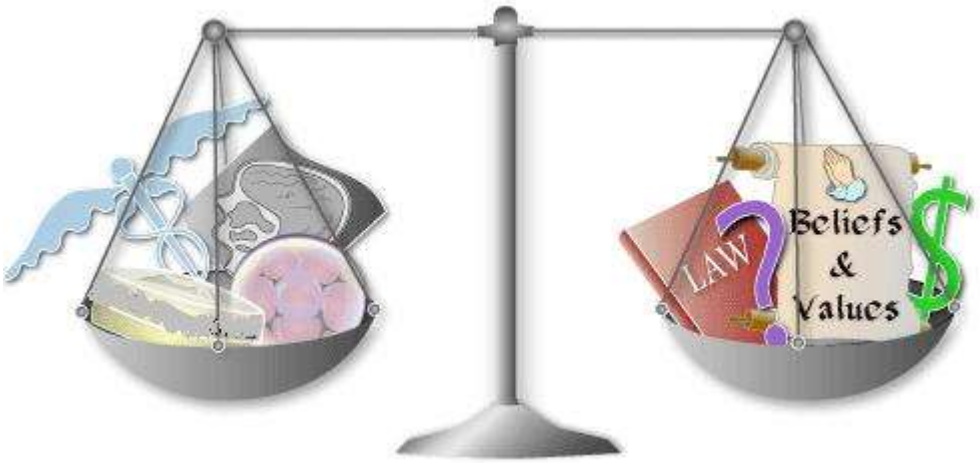


Bases Cromossômicas da Hereditariedade

Profa. Dra. Ester Silveira Ramos
esramos@usp.br

Ética e Genética



ACONSELHAMENTO GENÉTICO

“Processo de comunicação que trata dos problemas humanos relacionados à ocorrência ou ao risco de ocorrência (ou de recorrência) de uma doença genética em uma família”.

Comitê de AG da ASHG, 1975

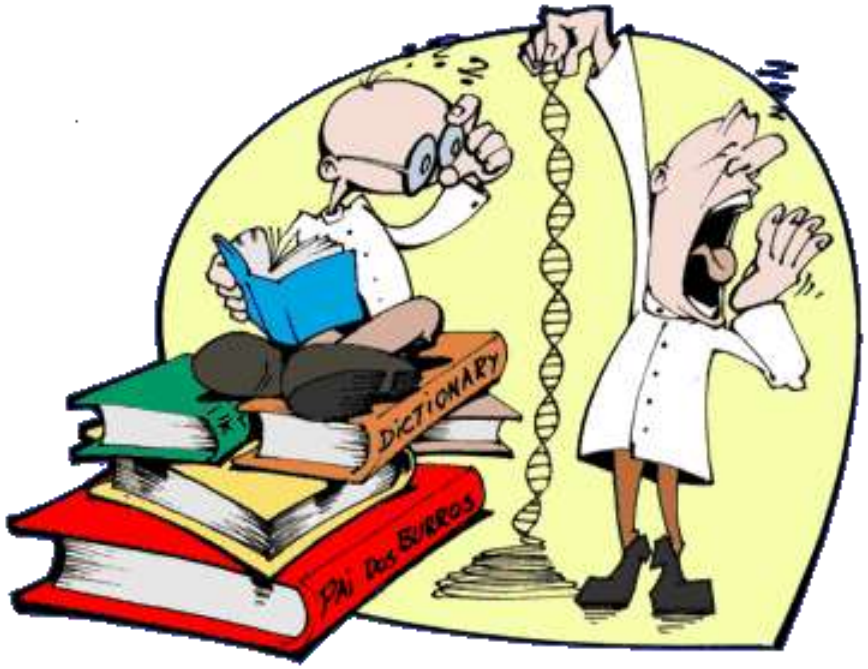
ACONSELHAMENTO GENÉTICO
TESTES GENÉTICOS

- Perspectivas de prevenção, diagnóstico e/ou tratamento precoce
- Idade
- Escolhas reprodutivas
- Confiabilidade e limitações do teste
- Impacto psicológico
- Privacidade e a confidencialidade dos resultados
- Consequências da divulgação a terceiros
- Direitos do paciente: Direito de não saber

Limitações da prática clínica

- Validade clínica e a utilidade das novas variantes;
- Crescimento de testes genéticos *direct to consumer;*
- Falta de formação adequada→ Solicitar, interpretar e utilizar os dados.

Para a prova – capítulo 2
Thompson e Thompson, 8ª Edição
Páginas 11-20

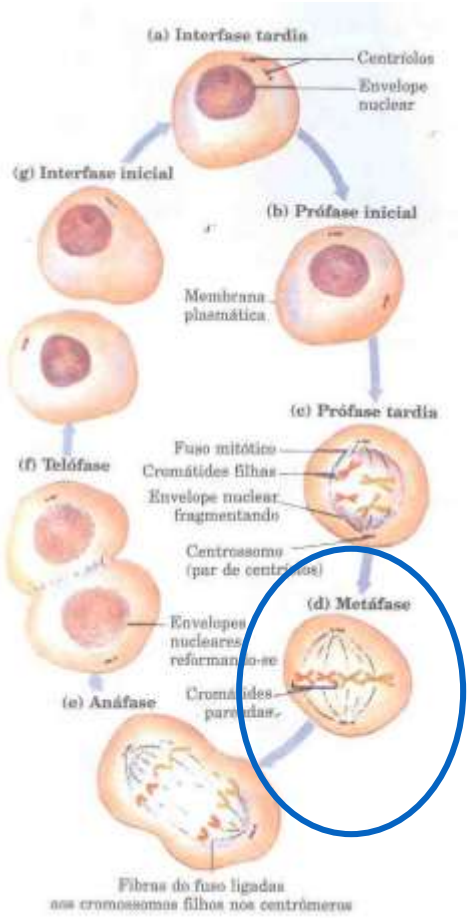


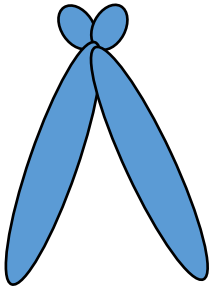
A
T
C
G

.....AATCGTATTCGA.....

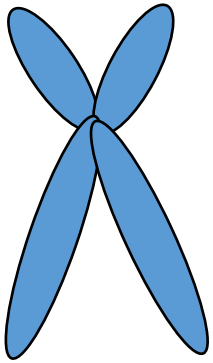
.....GCTATTAGCTA.....

Cromossomopatias
Análise Citogenética (cariótipo)

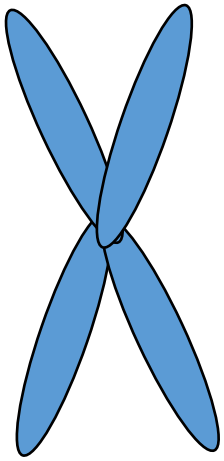




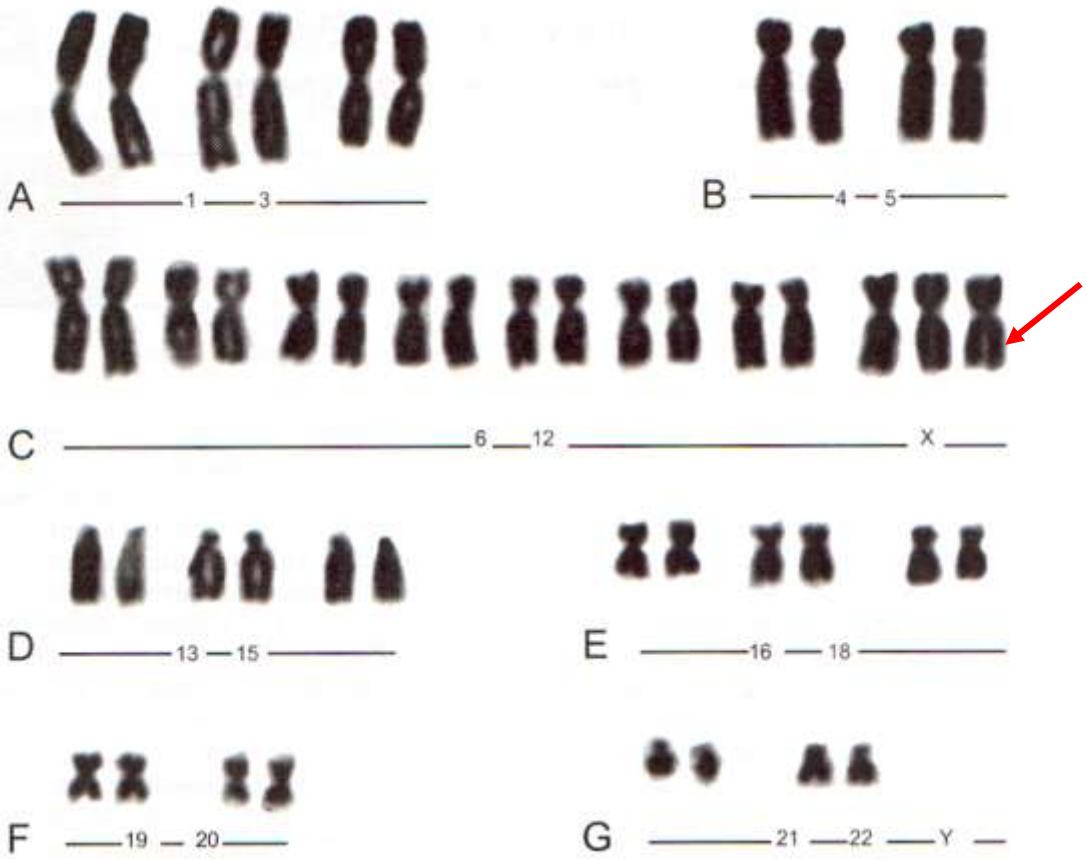
Acrocêntrico



Submetacêntrico



Metacêntrico


A
1
3
B
4
5
C
6
12
X
D
13
15
E
16
18
F
19
20
G
21
22
Y

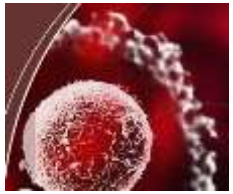
Bandamento GTG

- Giemsa

Setor de Genética Médica HCFMRP-USP

- Laboratório de Citogenética

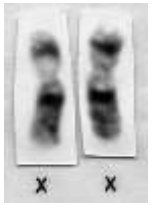
XX e XY

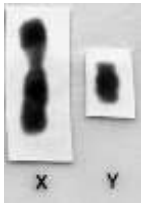


X/X

X/Y

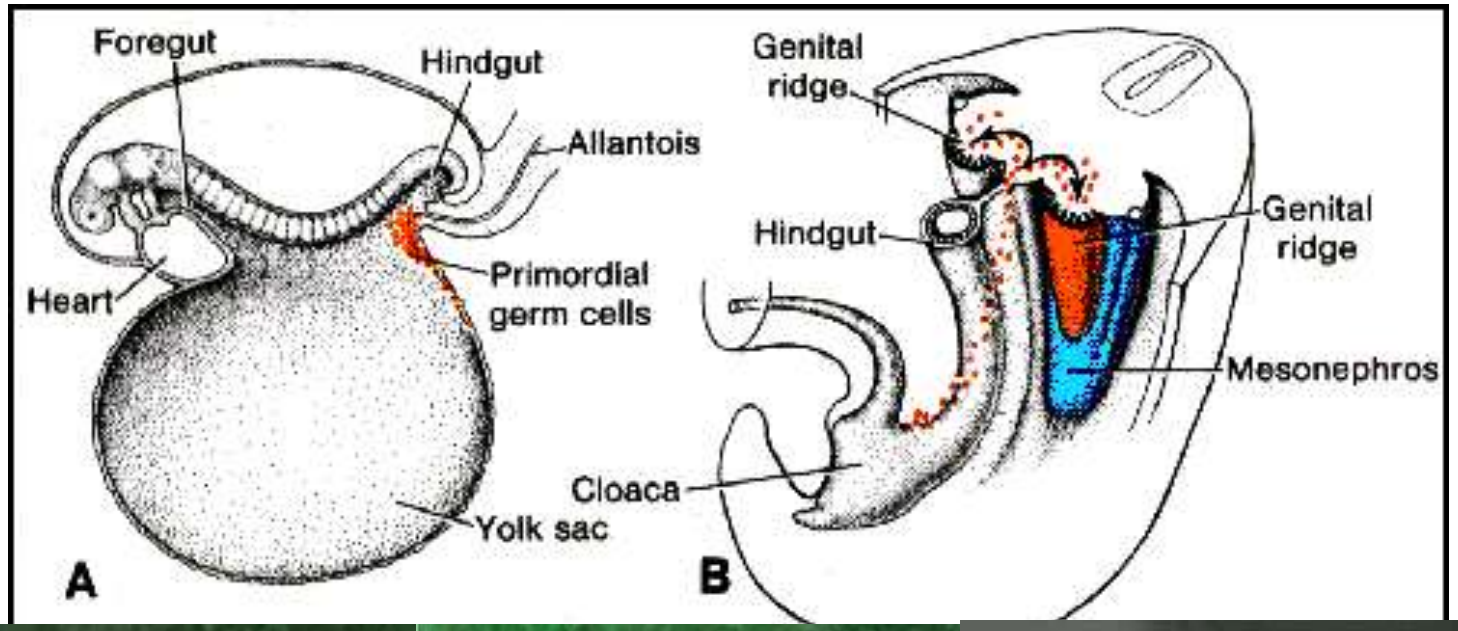
Sexo Genético
46,XX ou 46,XY

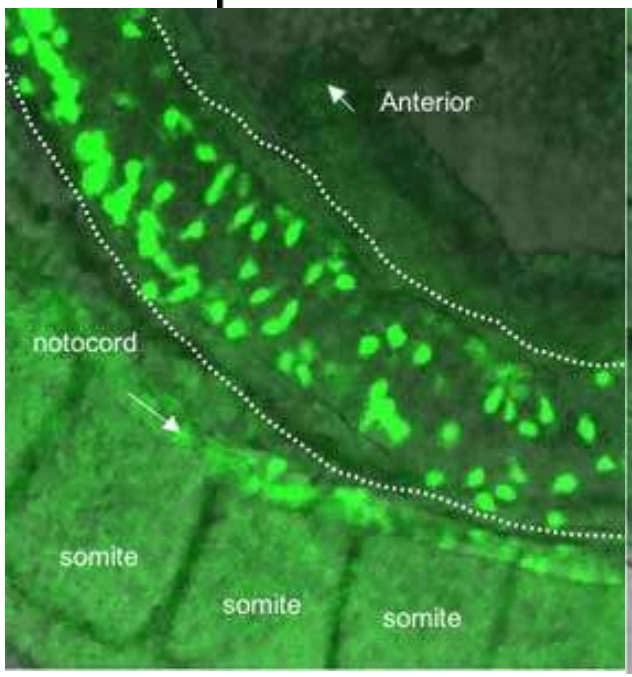


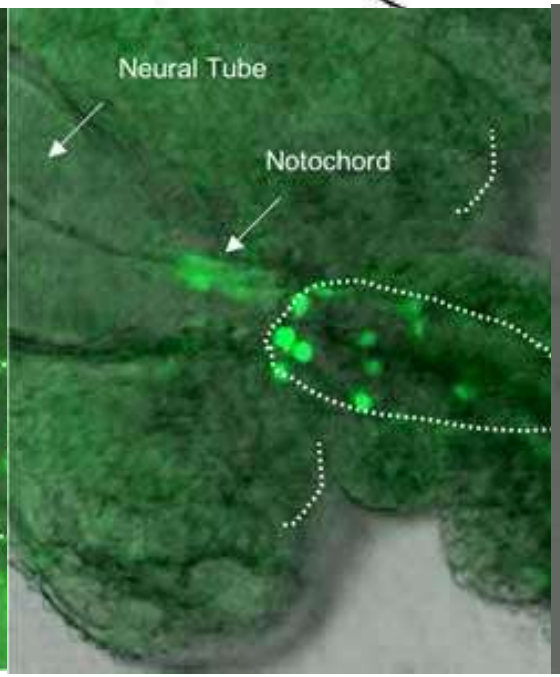


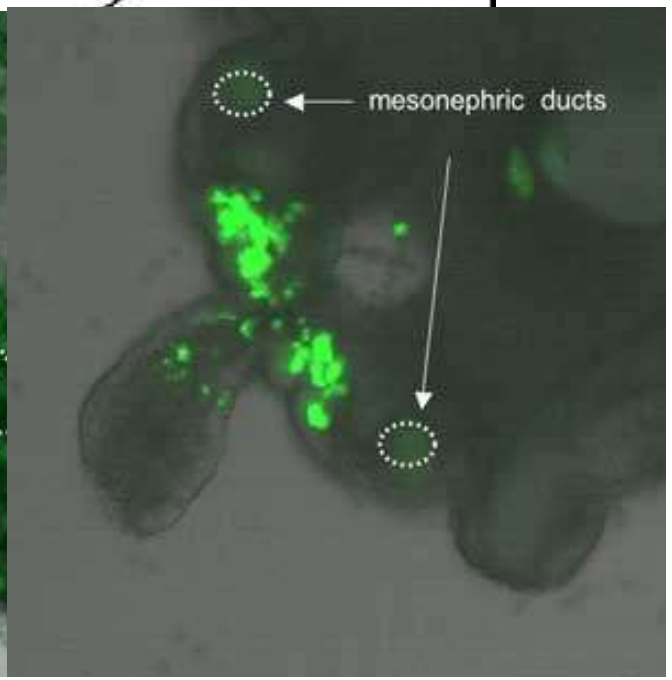
- S. Klinefelter
- S. Turner

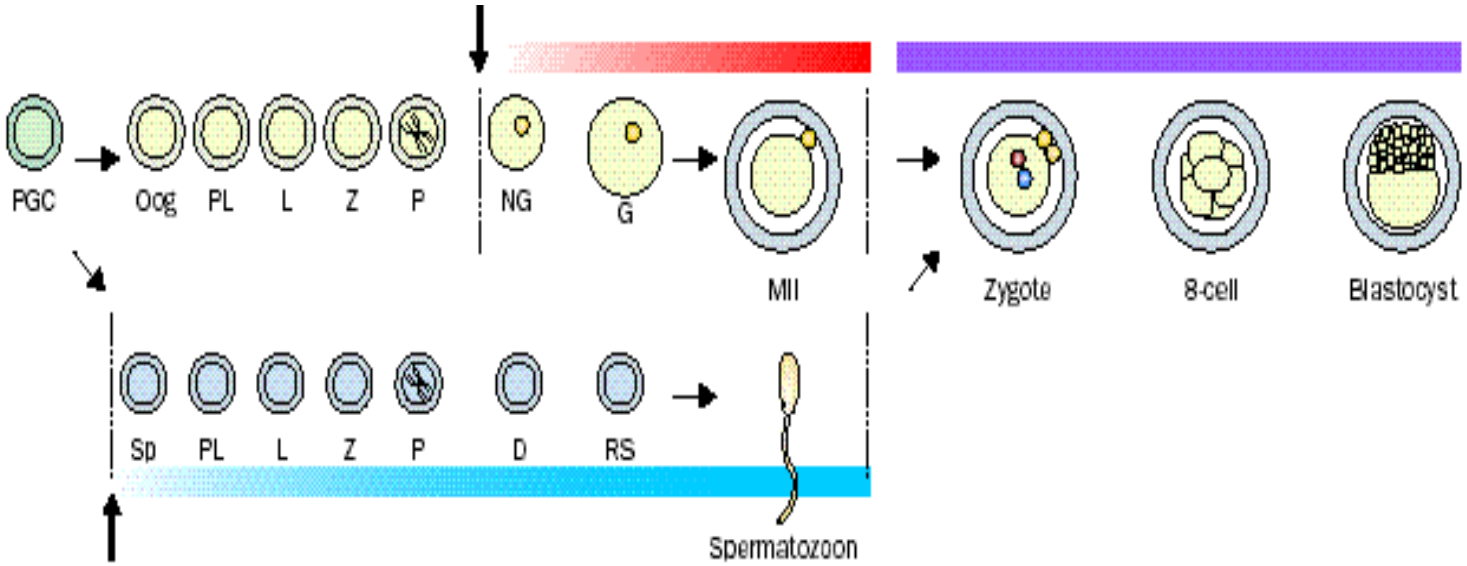
Células germinativas primordiais – Saco vitelino – Migração até a crista gonadal











Gosden et al, 2003

Quimera x Mosaico

Hermafroditismo Verdadeiro
DDS ovotesticular

- Diagnóstico Histopatológico

  Tecido Feminino + Tecido Masculino

  Testículo - Ovário

  Ovoteste - Ovário

  Testículo - Ovoteste

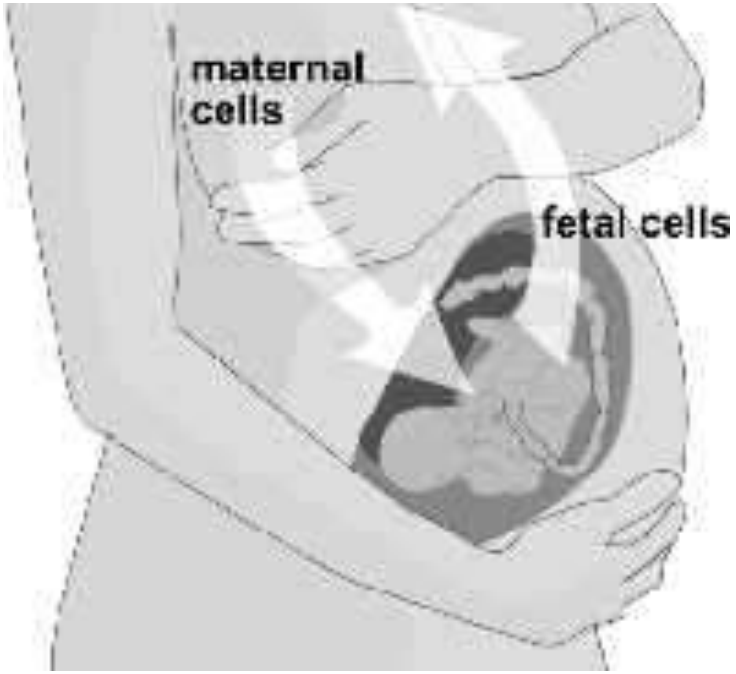
  Ovoteste - Ovoteste

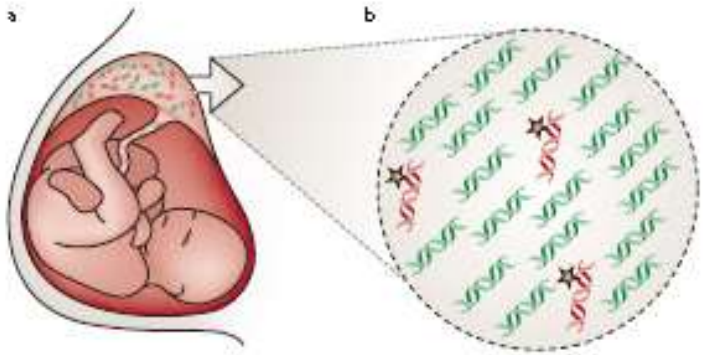
- Cariótipo (alguns casos) – 46,XX/46XY

ZZ/ZW

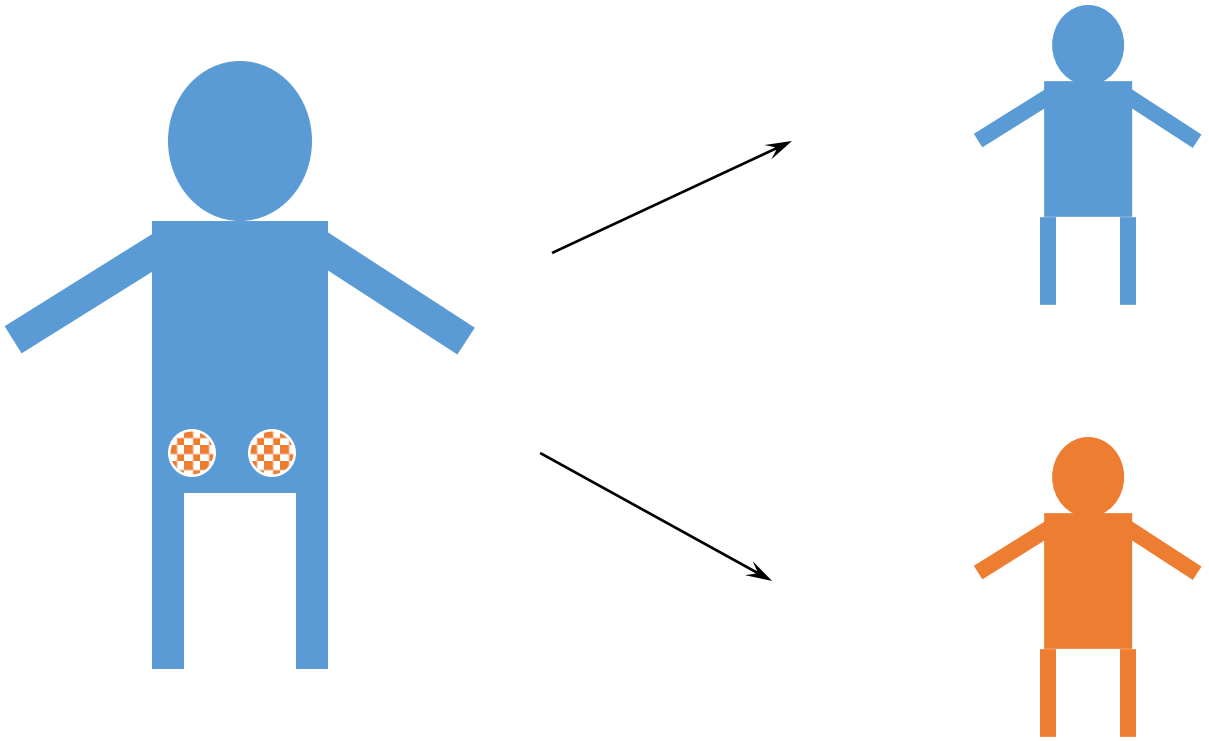
Zhao et al., 2010

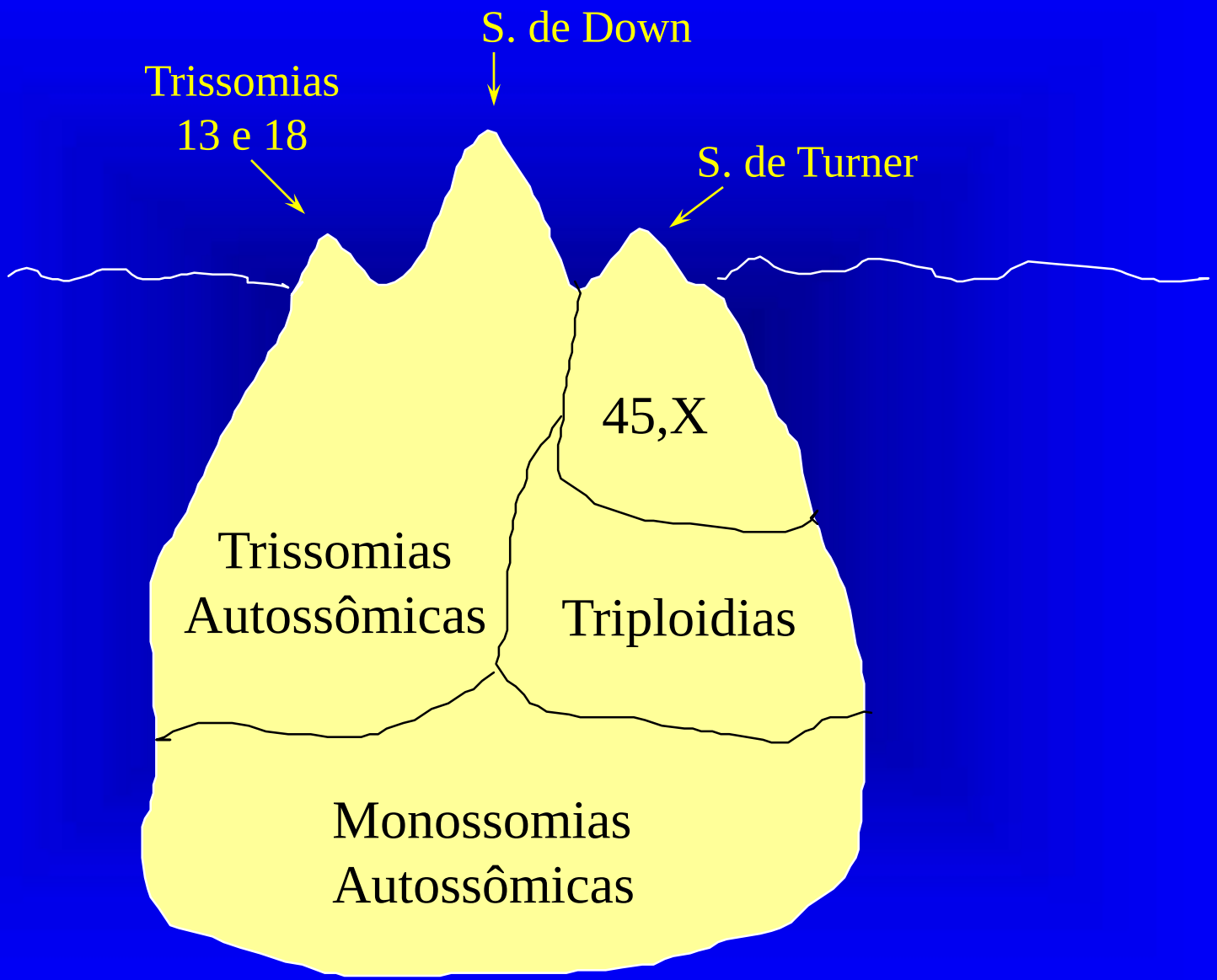
Quimera

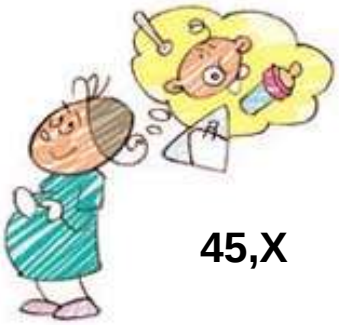




MOSAICISMO (gonadal)




S. de Down
Trissomias
13 e 18
S. de Turner
45,X
Trissomias
Autossômicas
Triploidias
Monossomias
Autossômicas



45,X

99%

45,X Puros

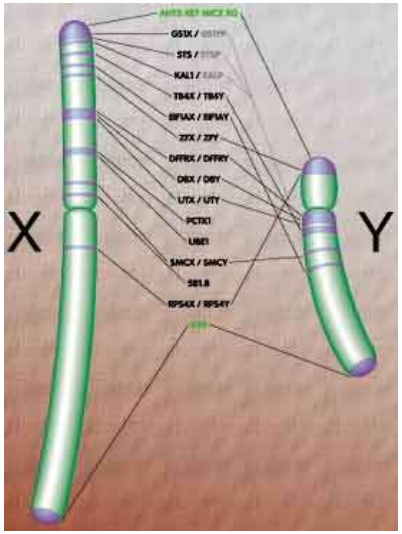
1%

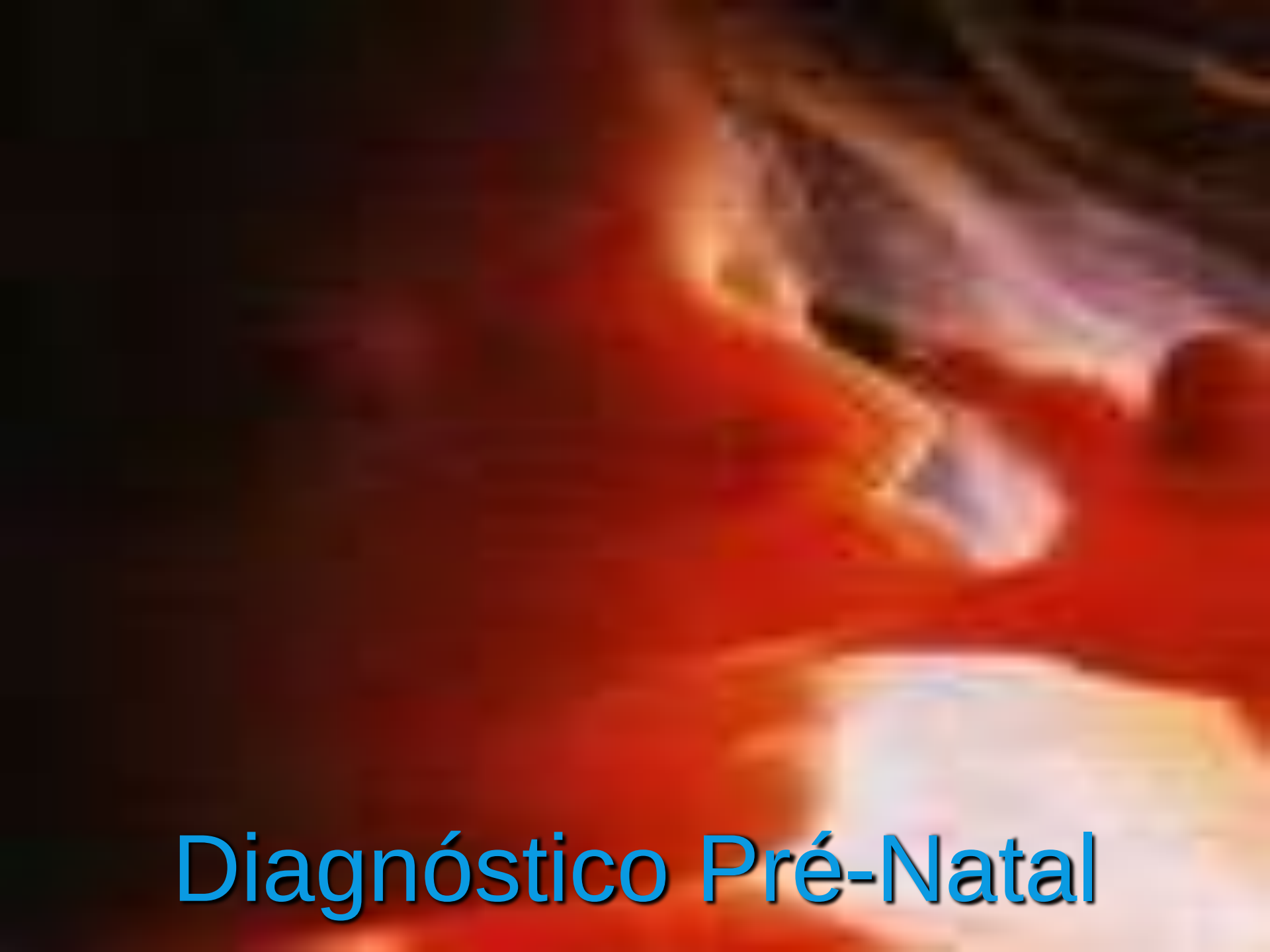
Mosaicos
45,X/46,XX

Inativação do Cromossomo X (humanos)

X X

X X

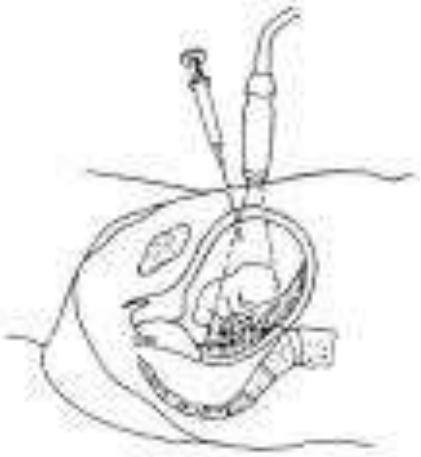


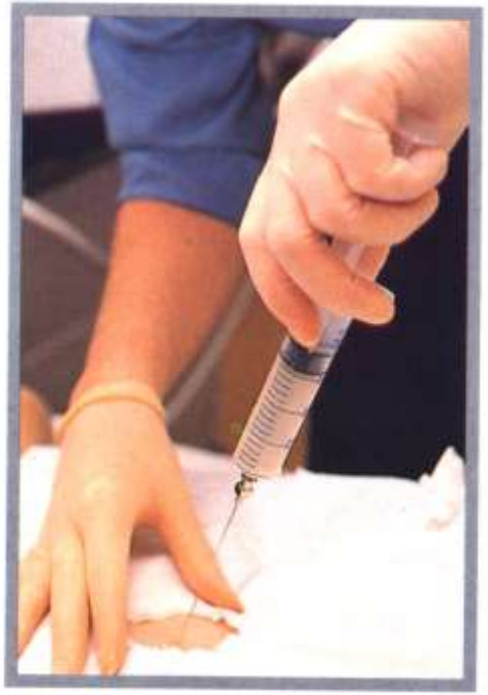

Diagnóstico Pré-Natal

Biópsia de Vilosidade Coriônica

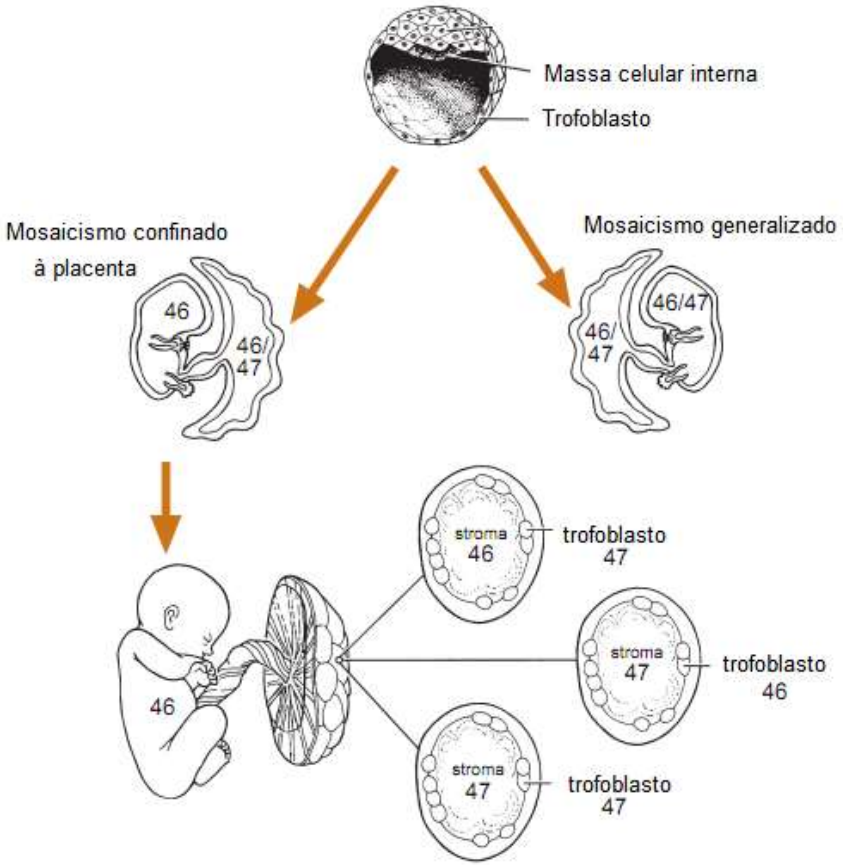
Via Transvaginal
Via Transabdominal

Amniocentese

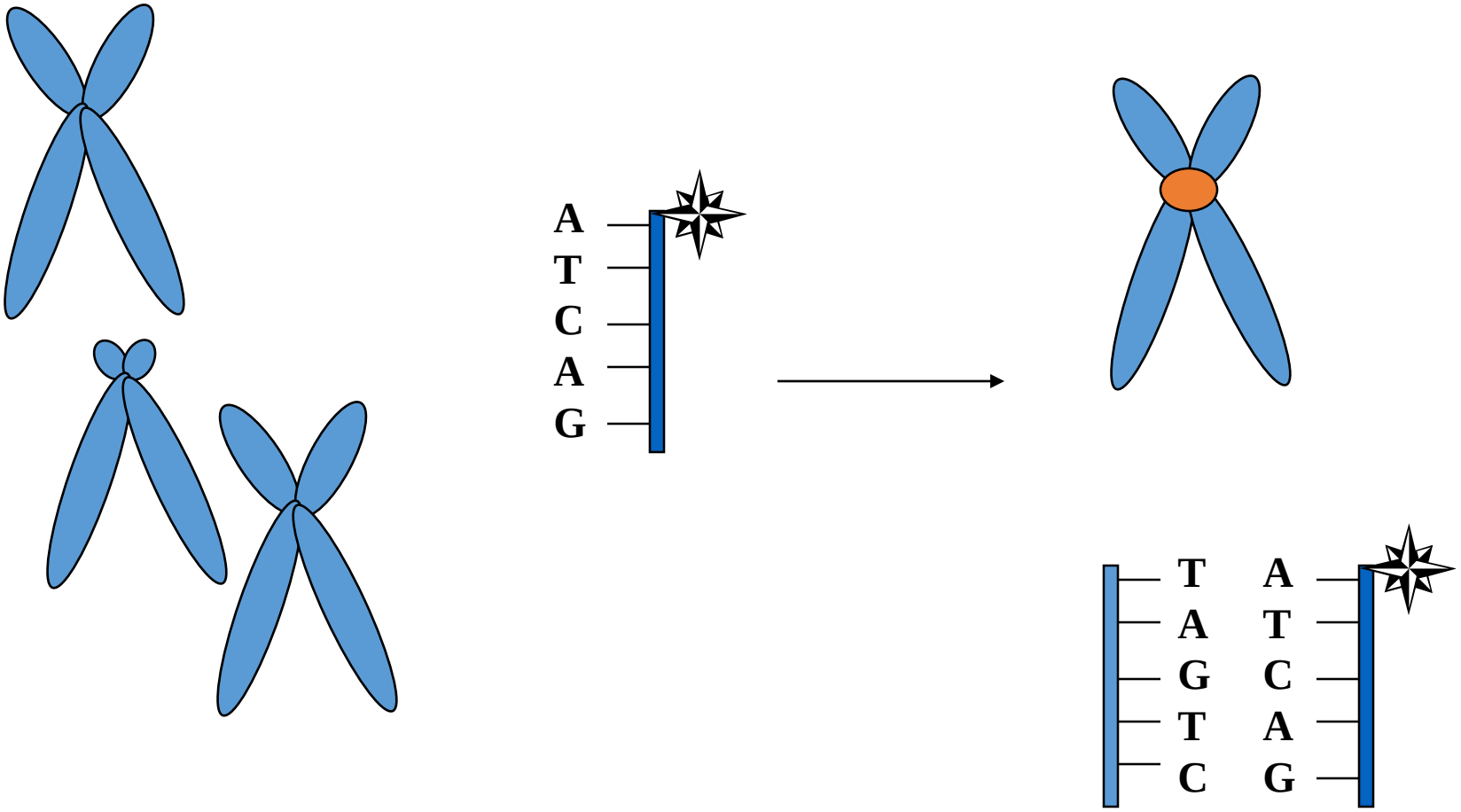




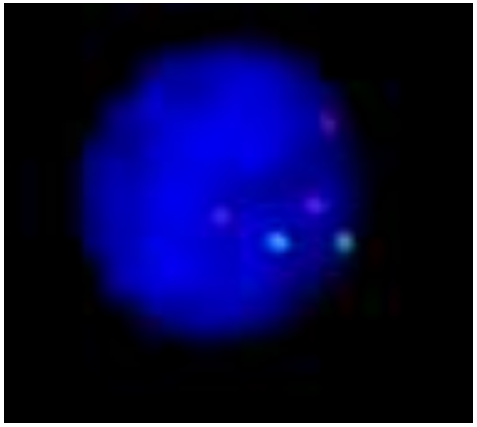
Mosaico

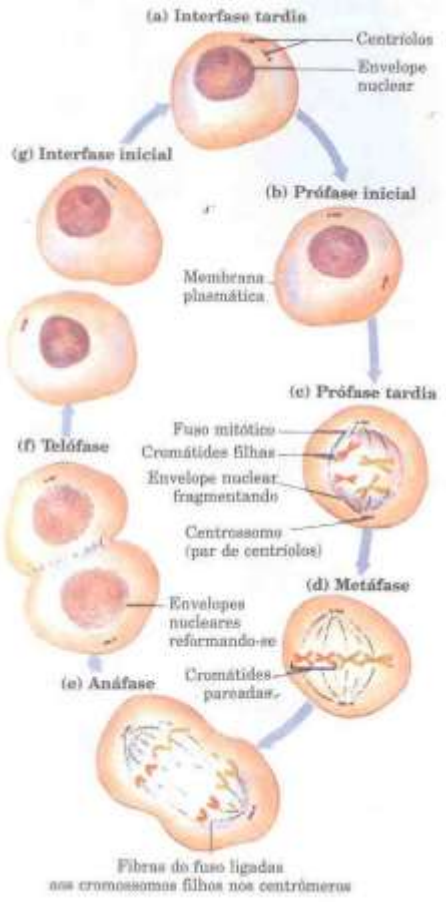

Massa celular interna
Trofoblasto
Mosaicismo confinado
à placenta
46
46/
47
Mosaicismo generalizado
46/47
46/
47
stroma
46
trofoblasto
47
stroma
47
trofoblasto
46
46
stroma
47
trofoblasto
47

FISH (Hibridação *in situ* fluorescente)

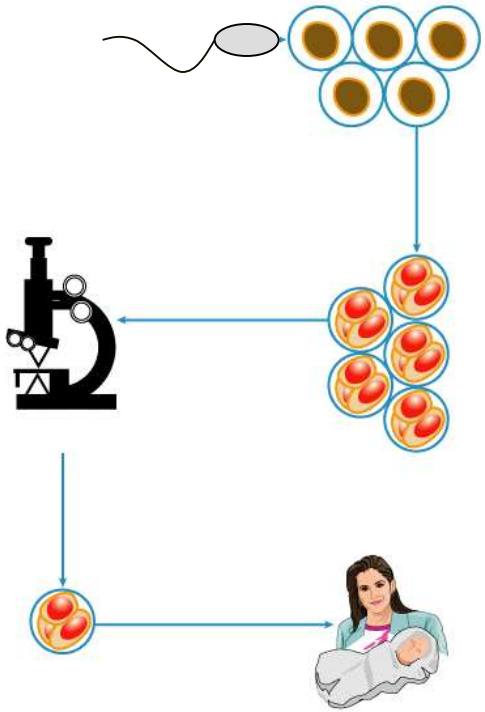


FISH – núcleo interfásico

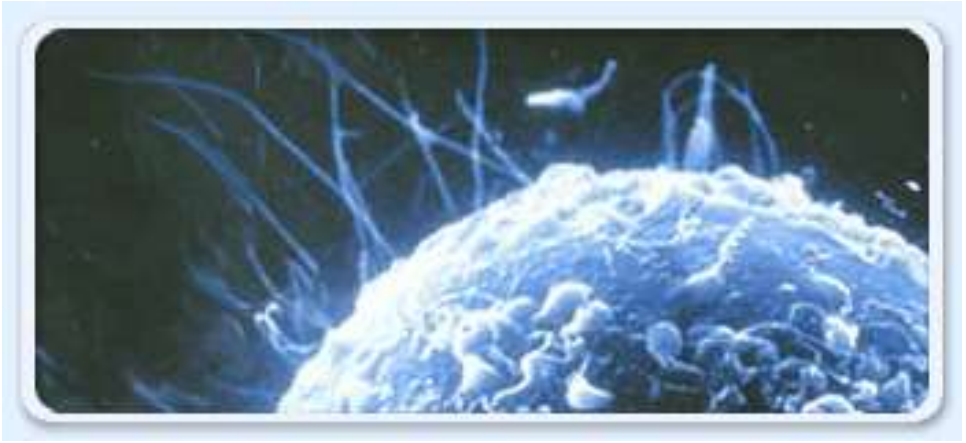


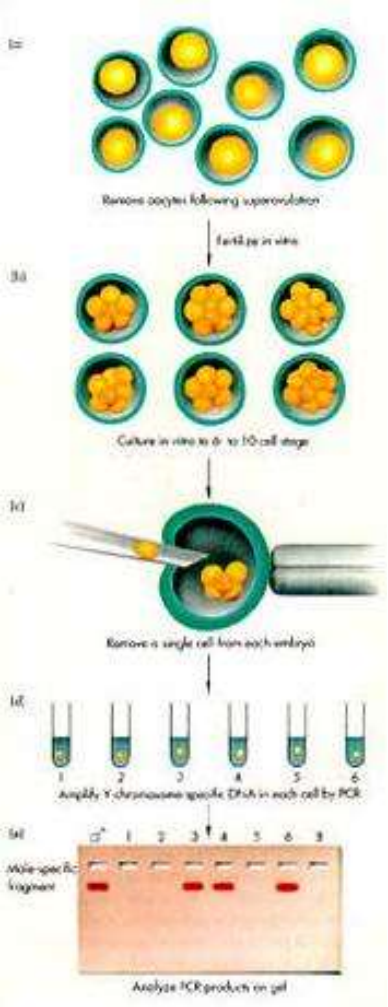


Diagnóstico Genético Pré-Implantação

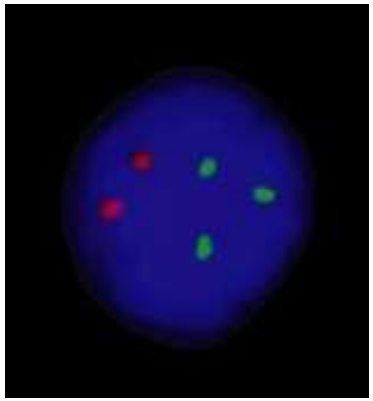


Fertilização *in vitro*

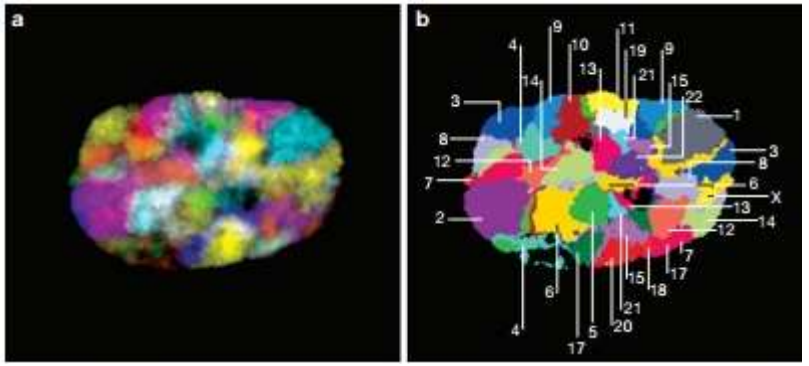




Monogênica



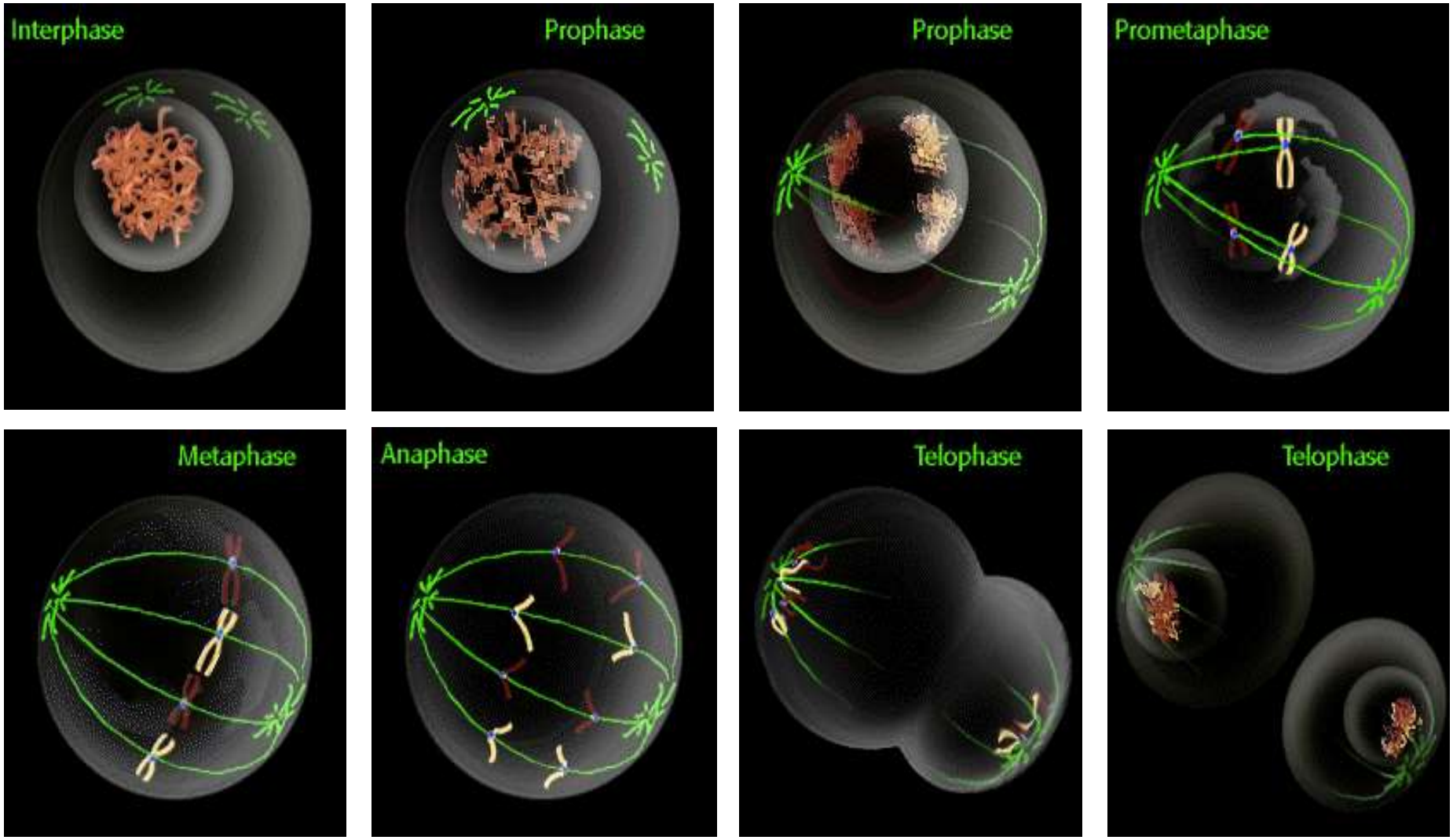
PGD

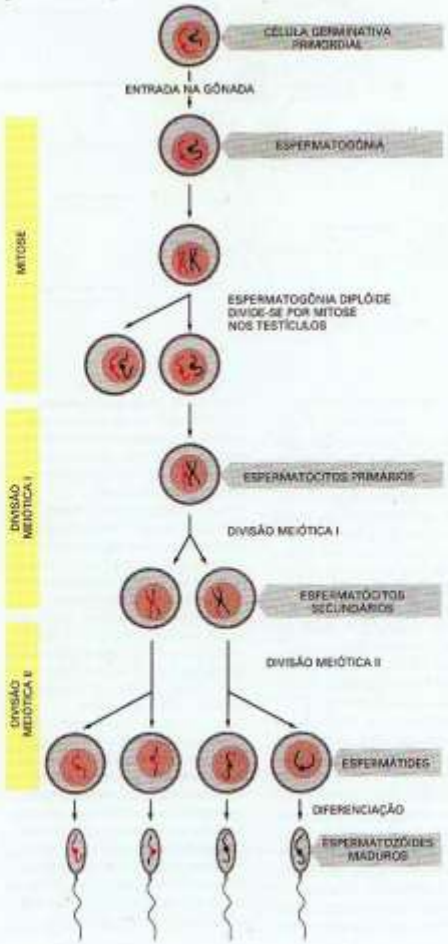


PGS

Cromossômica

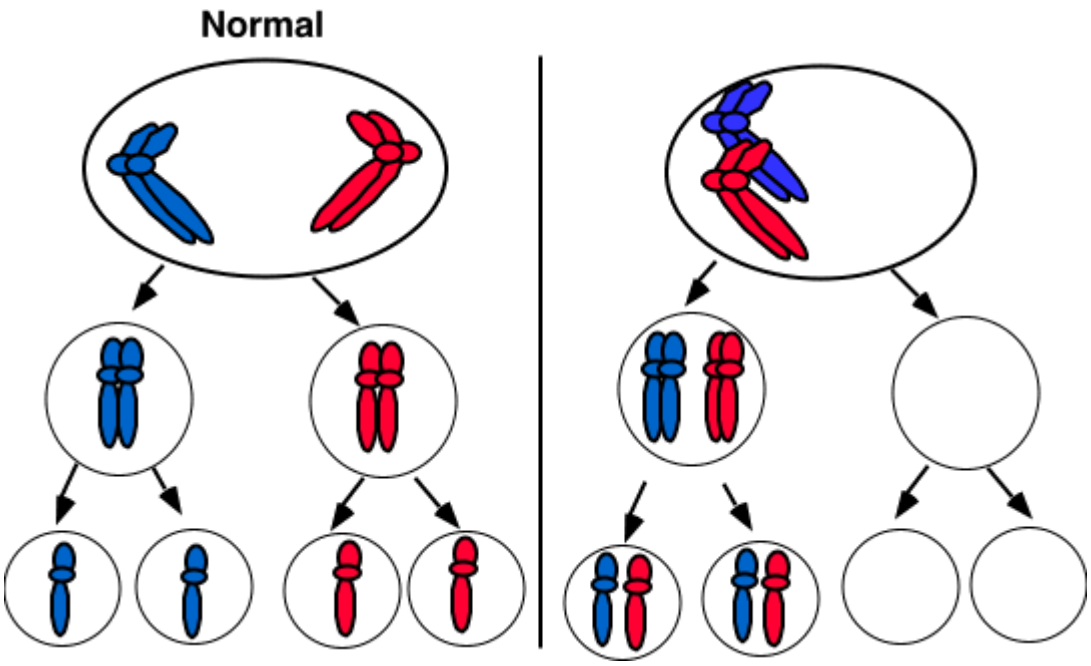
Divisão Celular

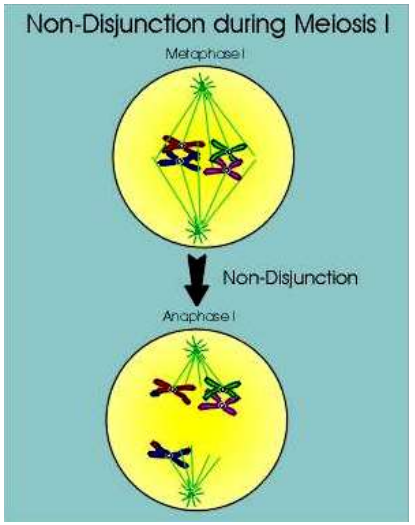




Gametogênese Feminina

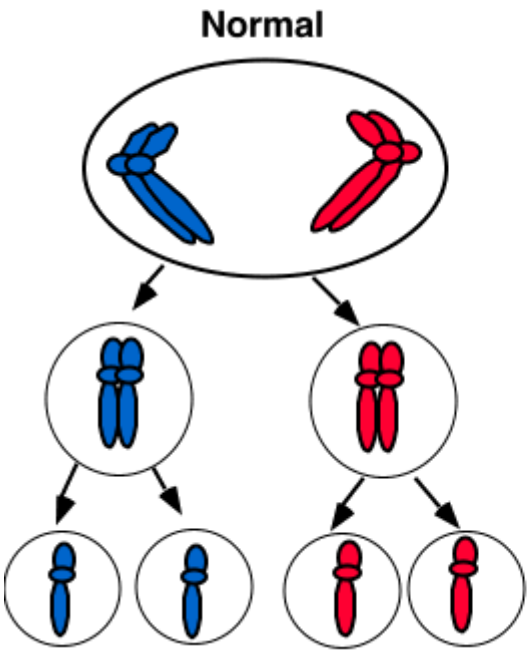
Meiose

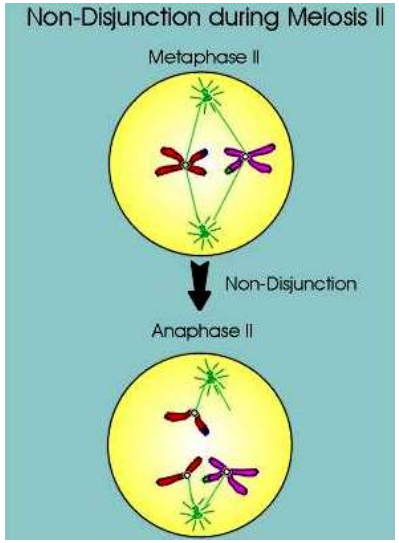




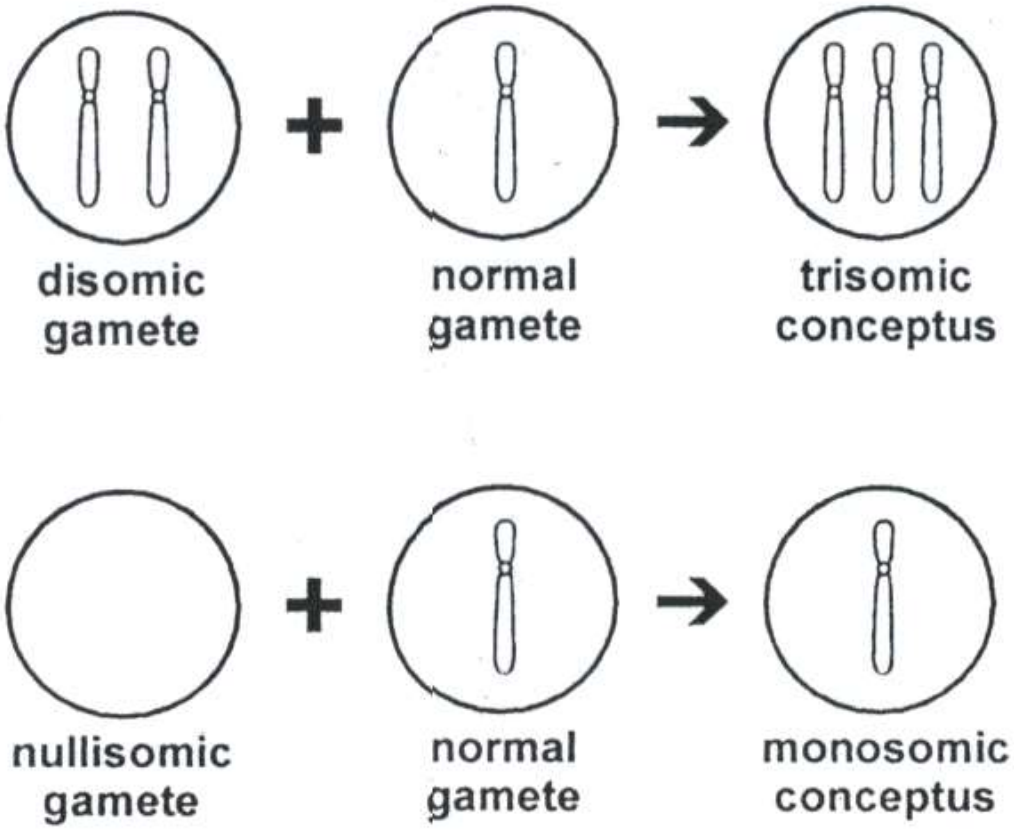
Não disjunção na meiose I

Meiose


Normal

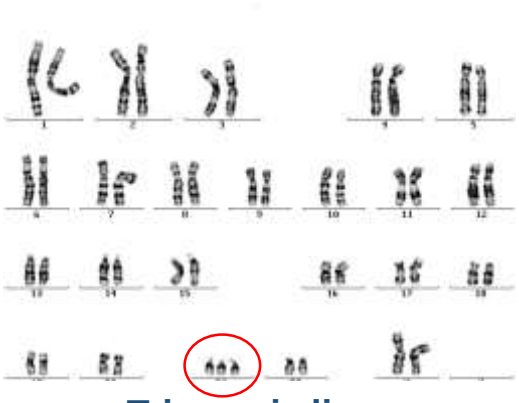

Non-Disjunction during Meiosis II
Metaphase II
Non-Disjunction
Anaphase II

Alterações Cromossômicas Numéricas



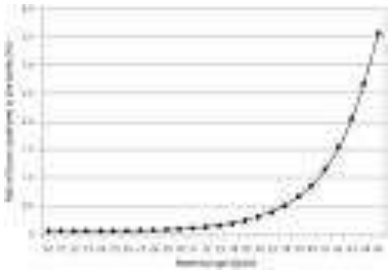
Cálculo de Risco (síndrome de Down)

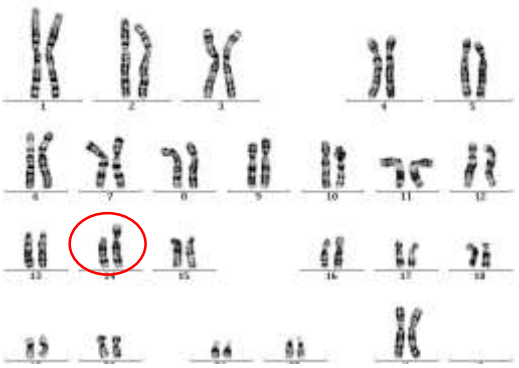
Cariótipo da criança – com a síndrome



Trissomia livre

~~Cariótipo dos pais sem a síndrome~~

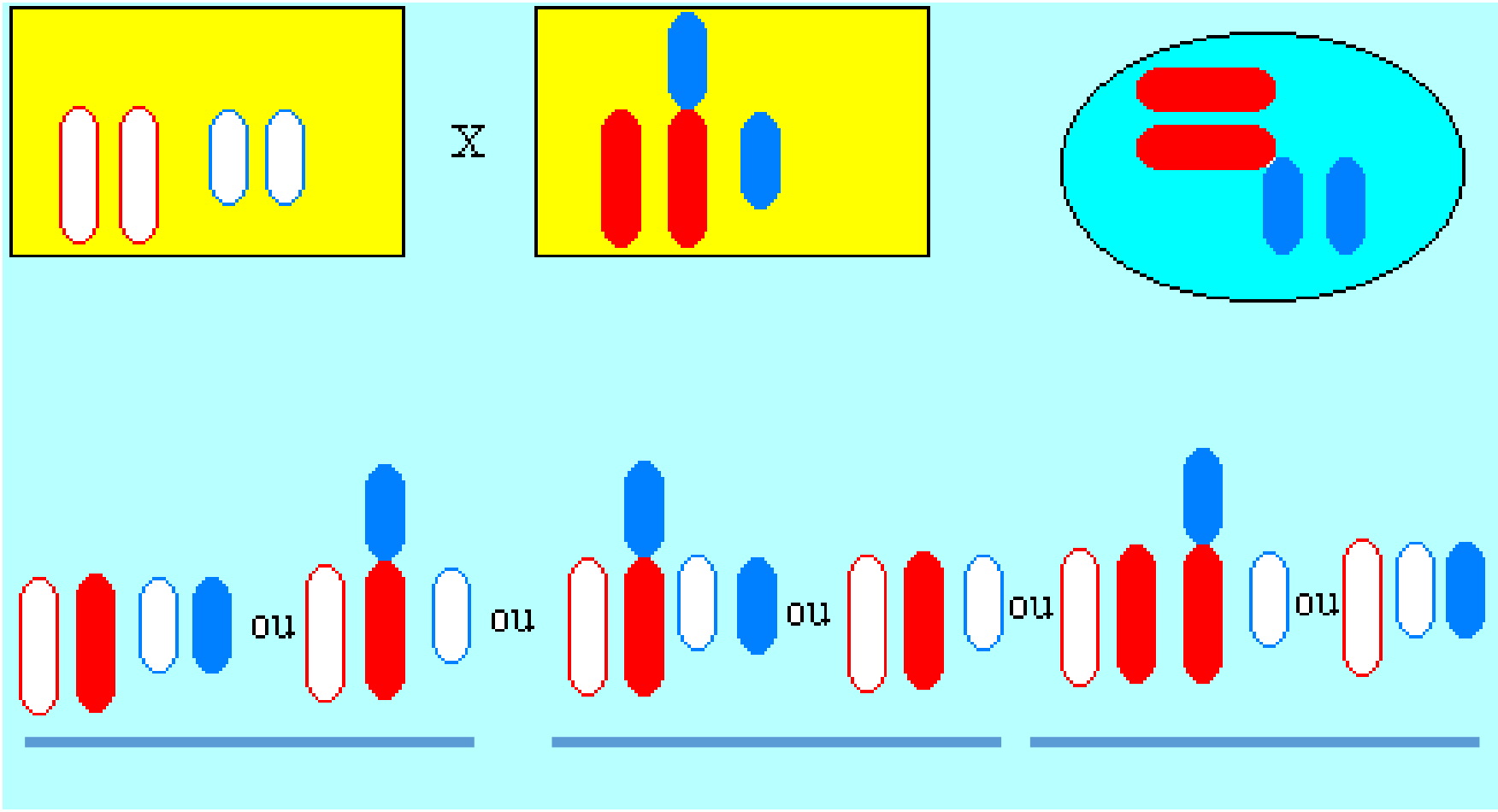


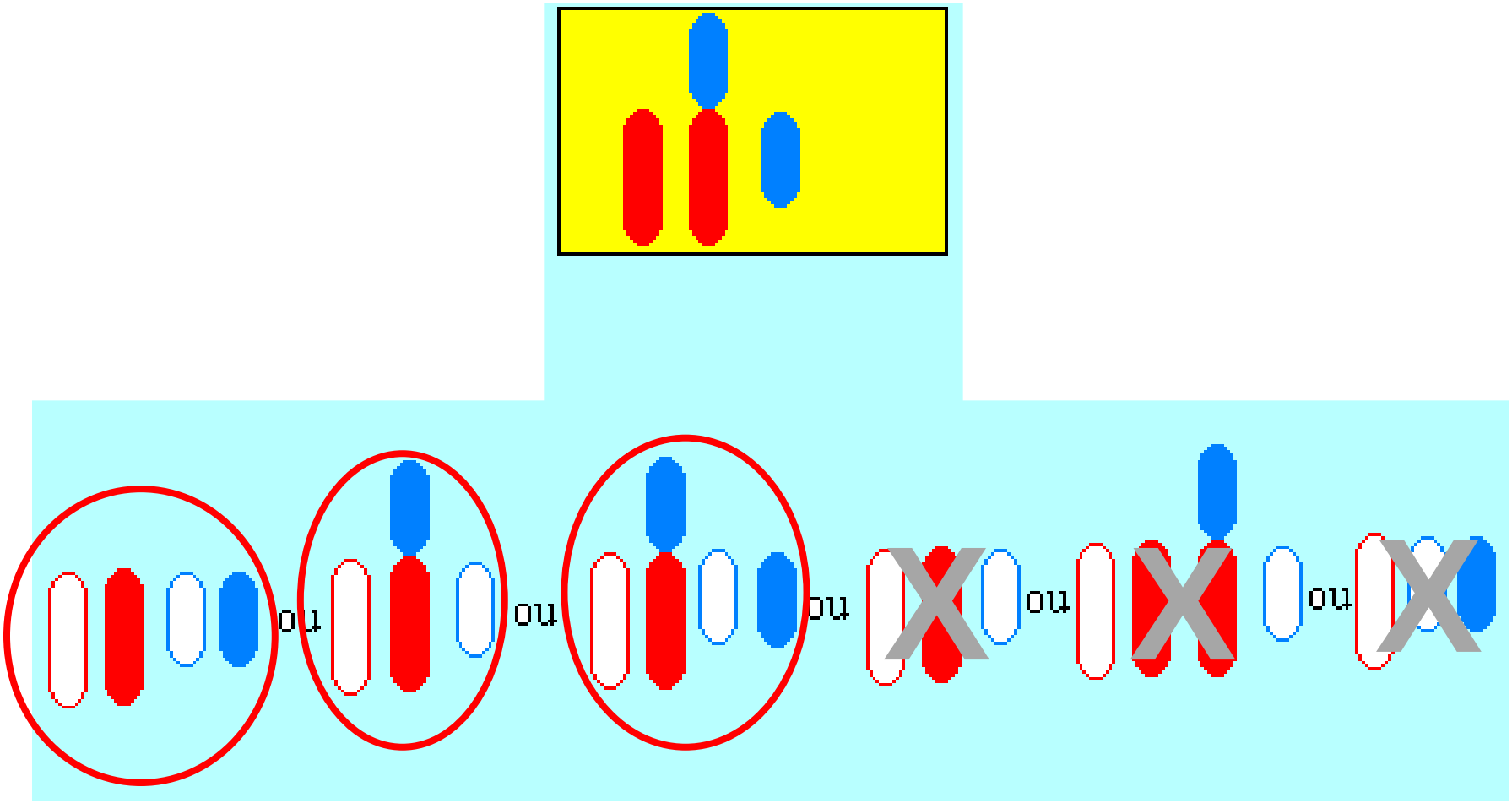


Translocação

Cariótipo dos pais sem a síndrome

SEGREGAÇÃO (meiose)





Normal

Translocado equilibrado igual ao pai

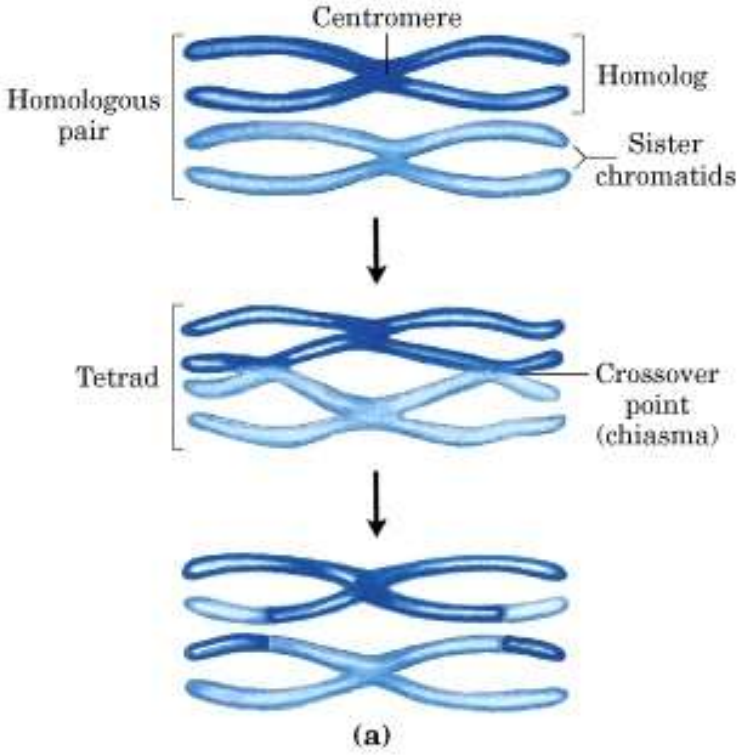
Síndrome de Down

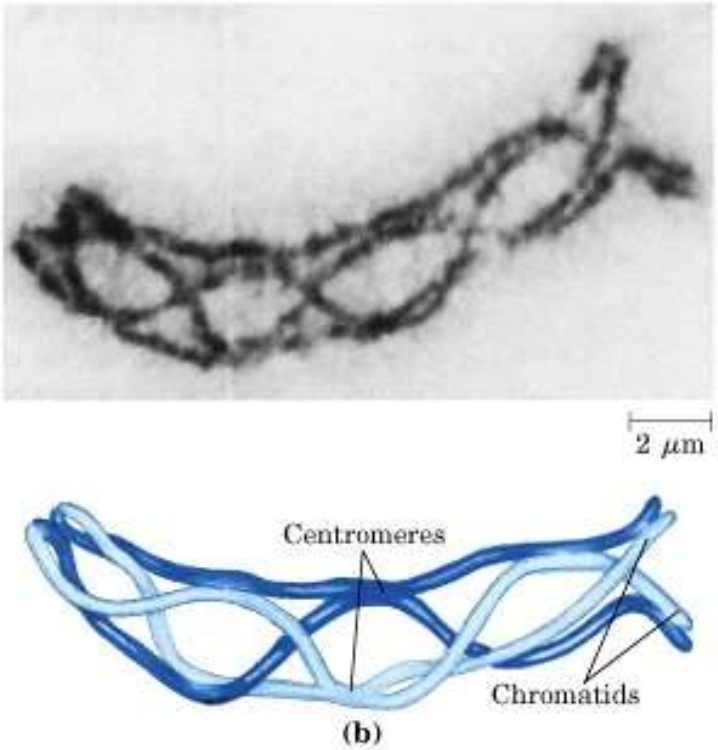
Risco Teórico

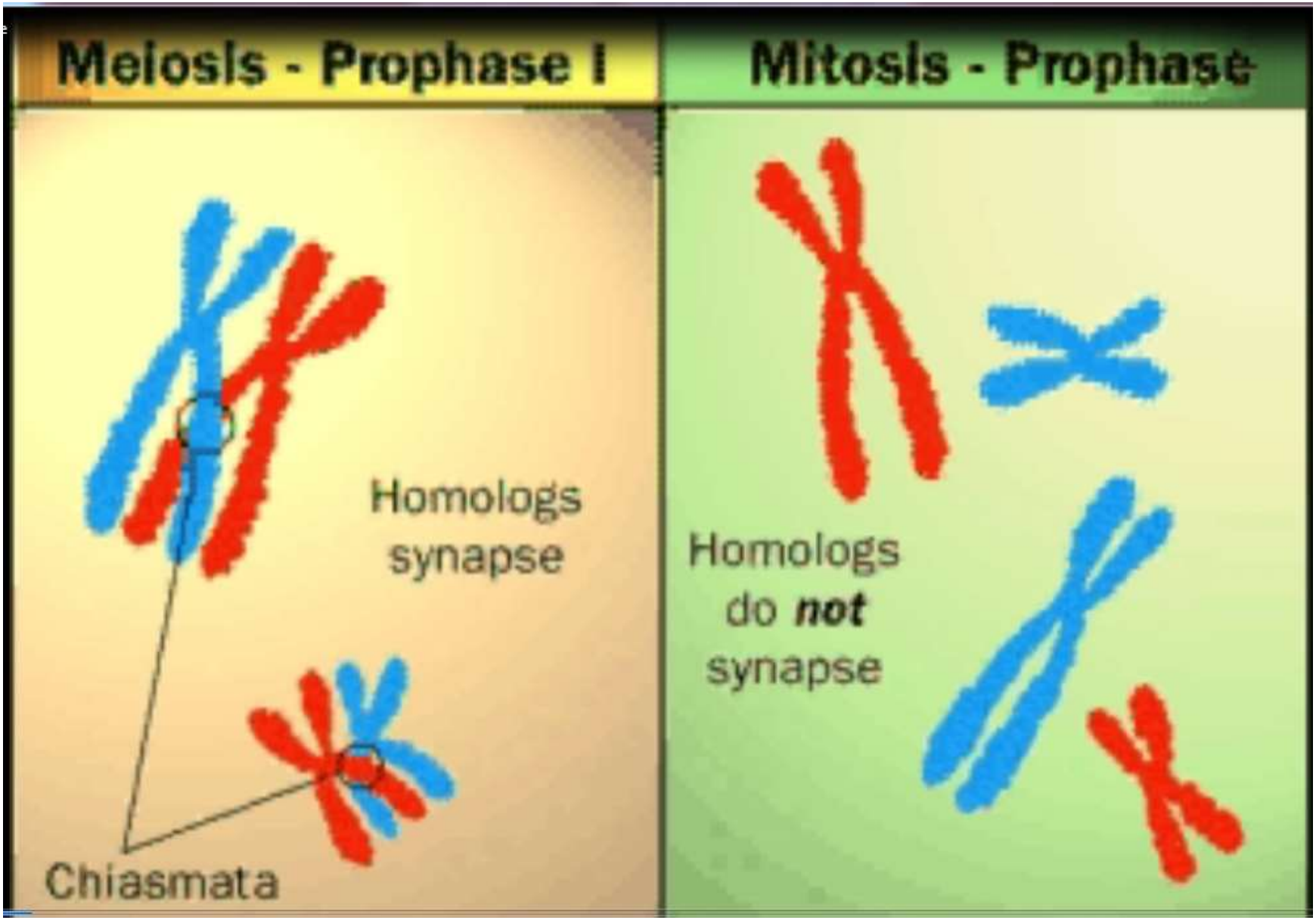
X

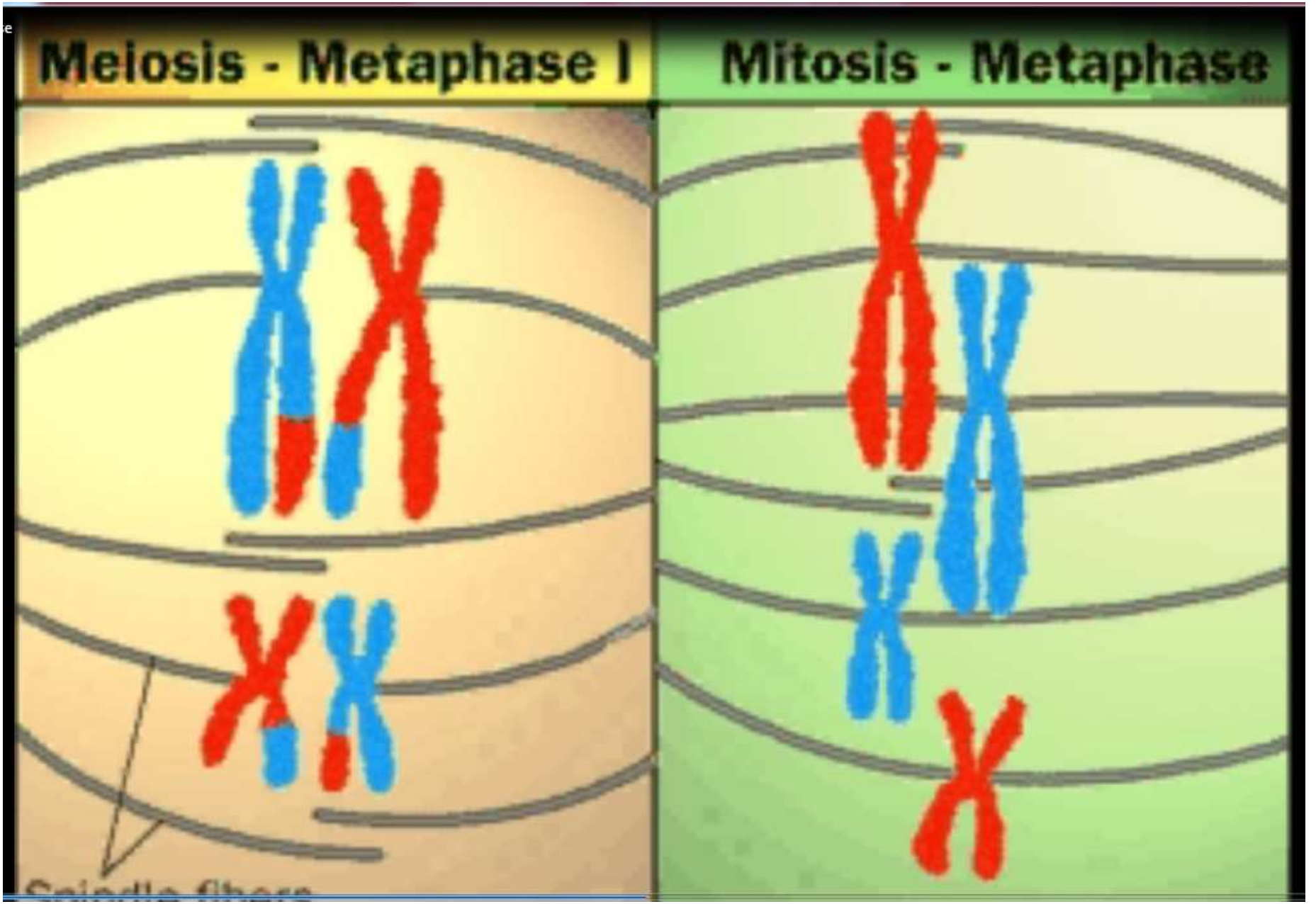
Risco Empírico

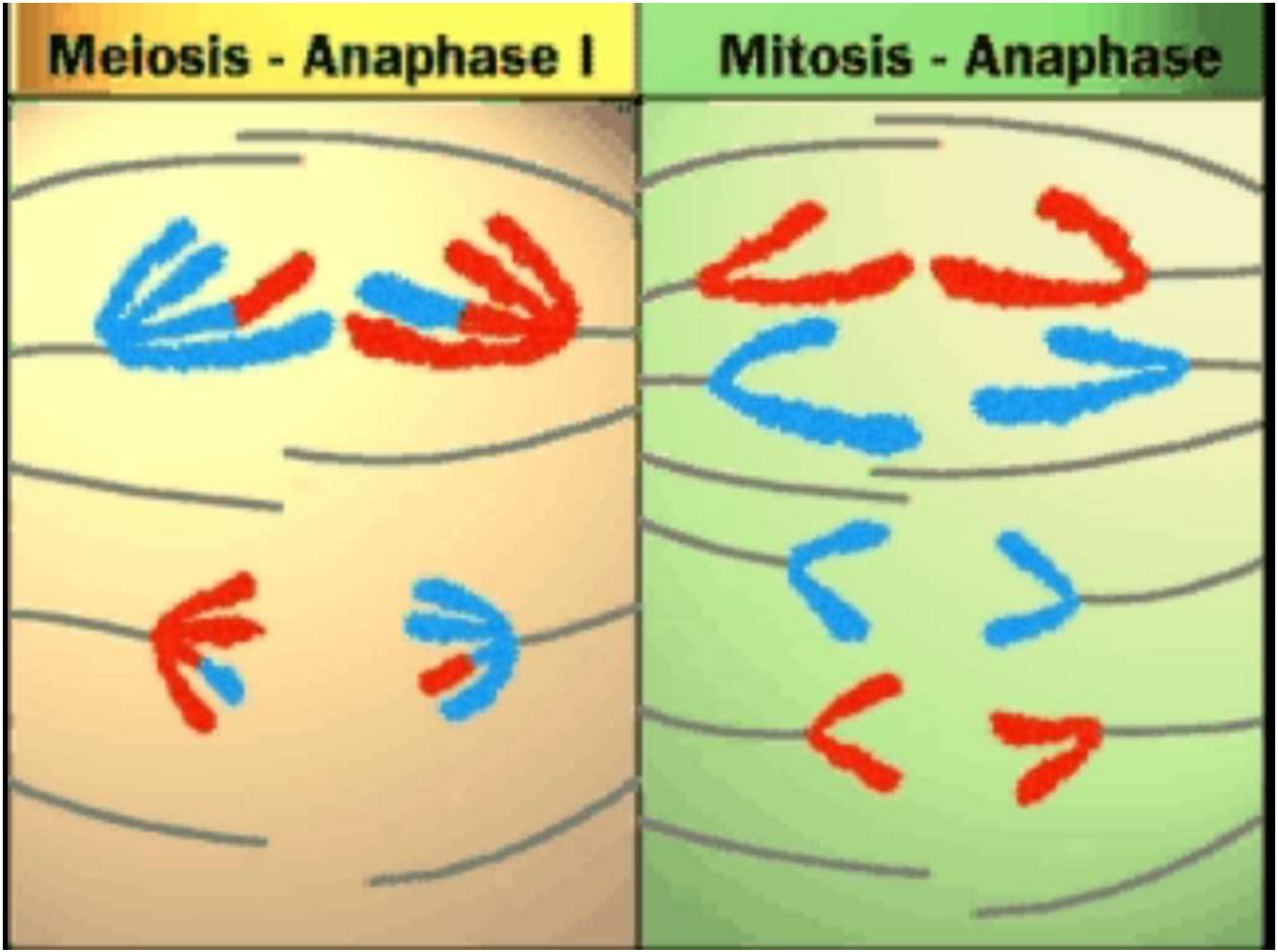
Crossing over

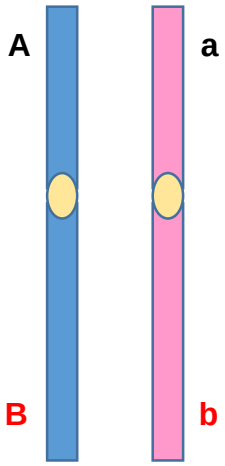


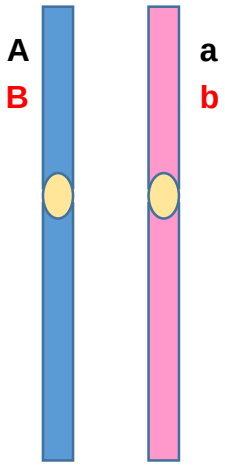


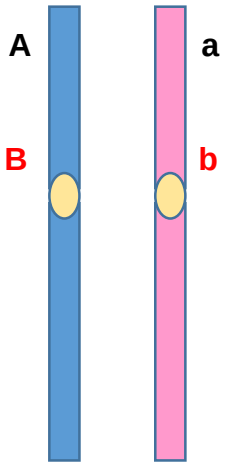

Meiosis - Prophase I
Mitosis - Prophase
Homologs synapse
Chiasmata
Homologs do not synapse

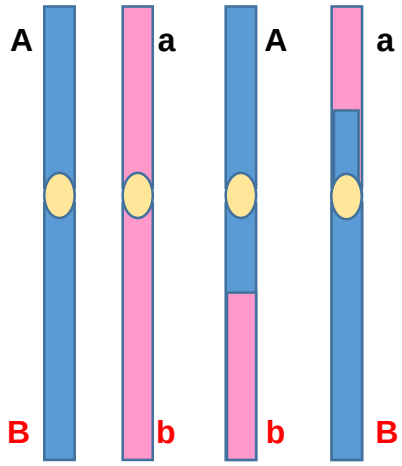

Meiosis - Metaphase I
Mitosis - Metaphase

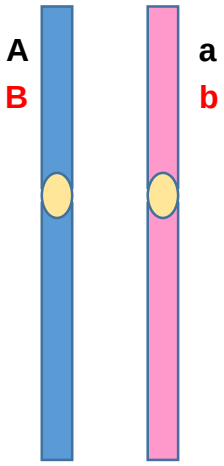

Meiosis - Anaphase I
Mitosis - Anaphase

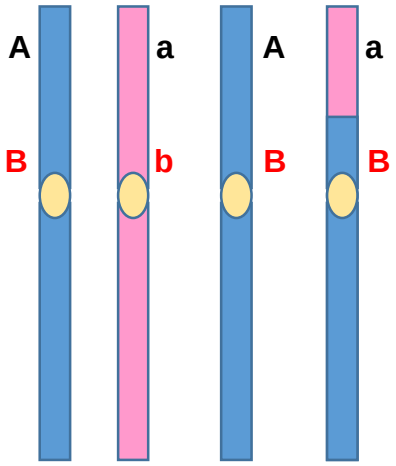










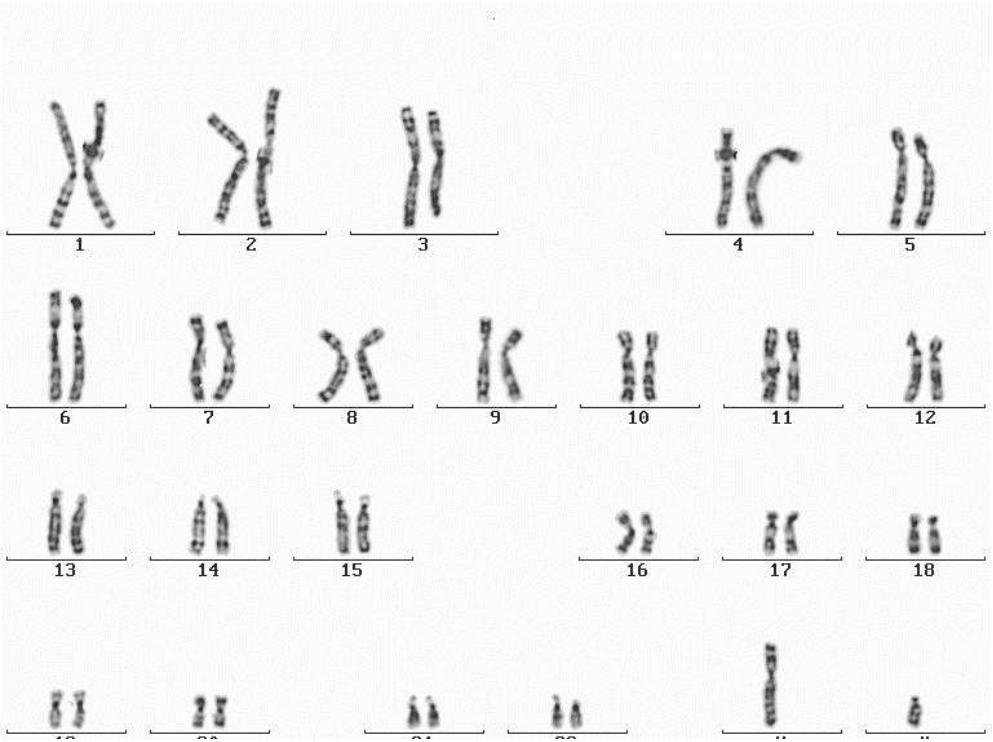


Não recombinante = Recombinante

Não recombinante

Não recombinante > Recombinante

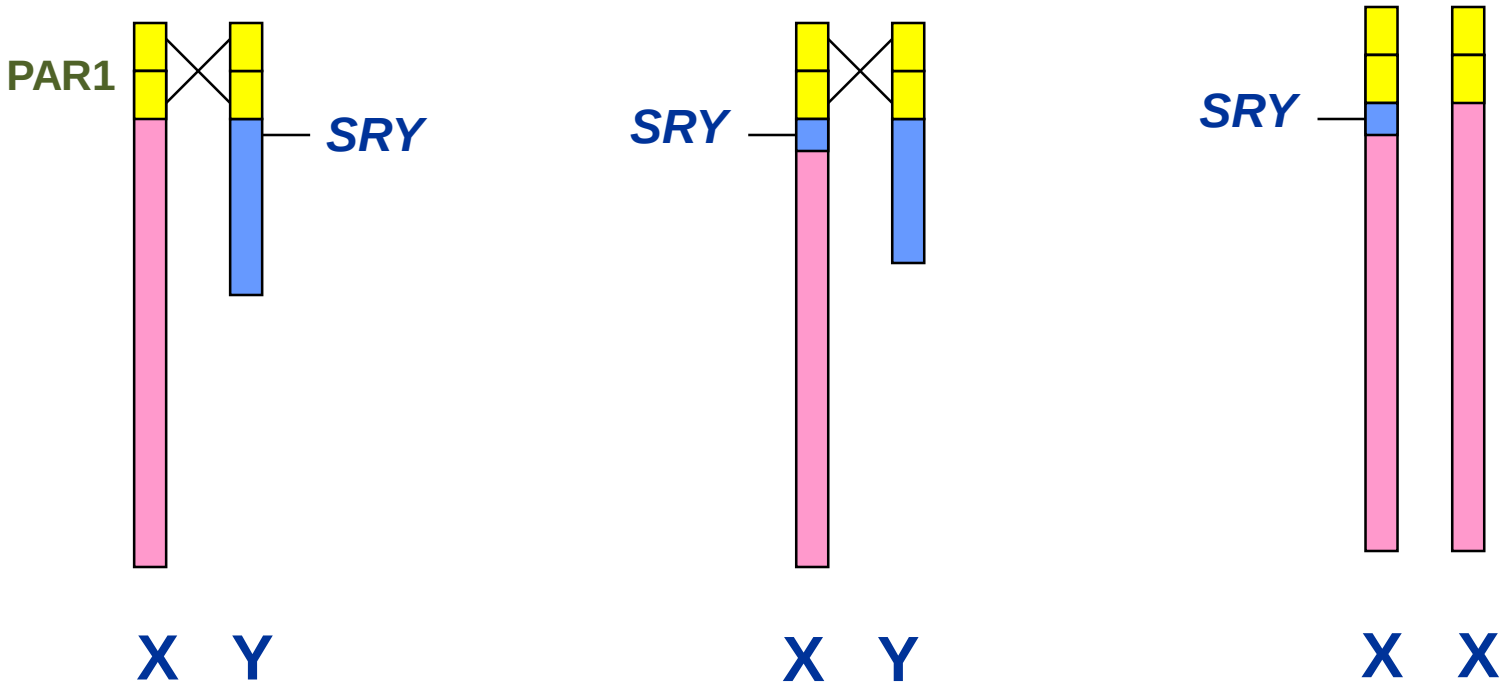
Os seres humanos possuem 46 cromossomos (23 do pai e 23 da mãe)



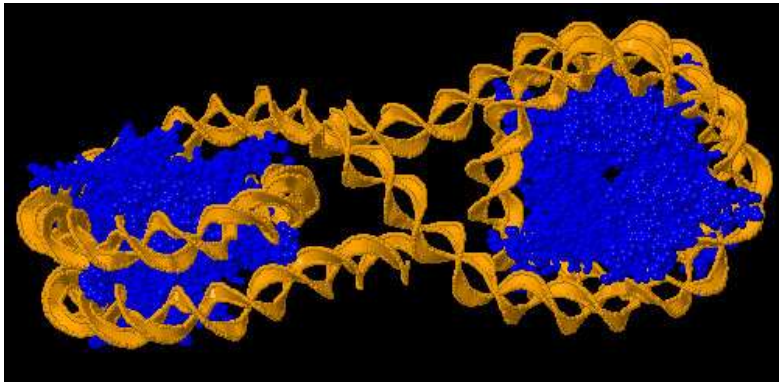
Homem XX
DDS testicular 46,XX

- Fenótipo: altura, genitália
*Testículos

- Cariótipo: 46,XX

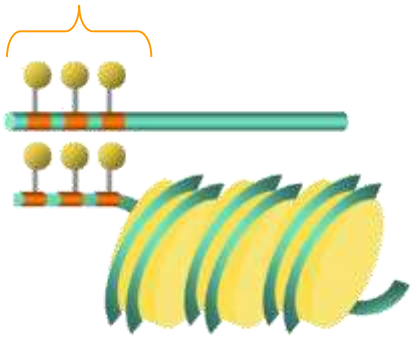

PAR1
SRY
X Y
SRY
X Y
SRY
X X

DNA

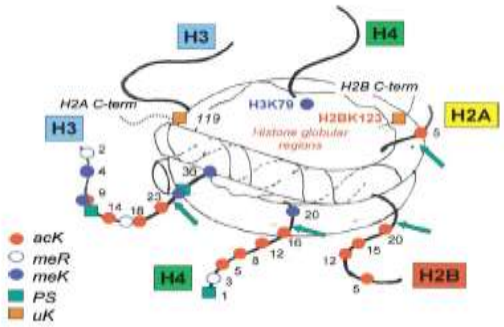


Nucleossomo/
Cromatina

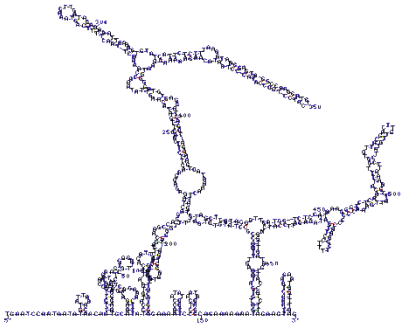
Epigenética – outro módulo da disciplina



Metilação do DNA



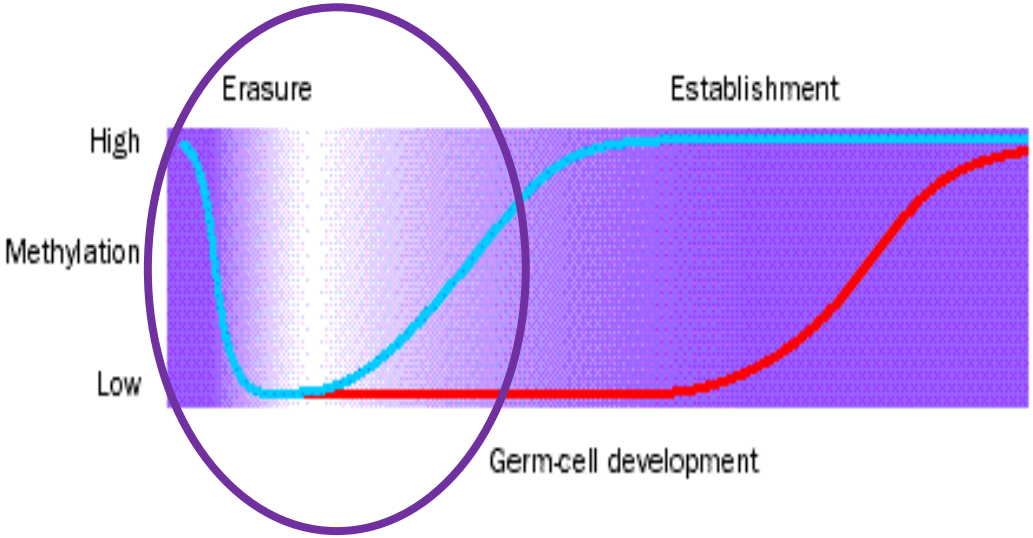
Modificação de histonas

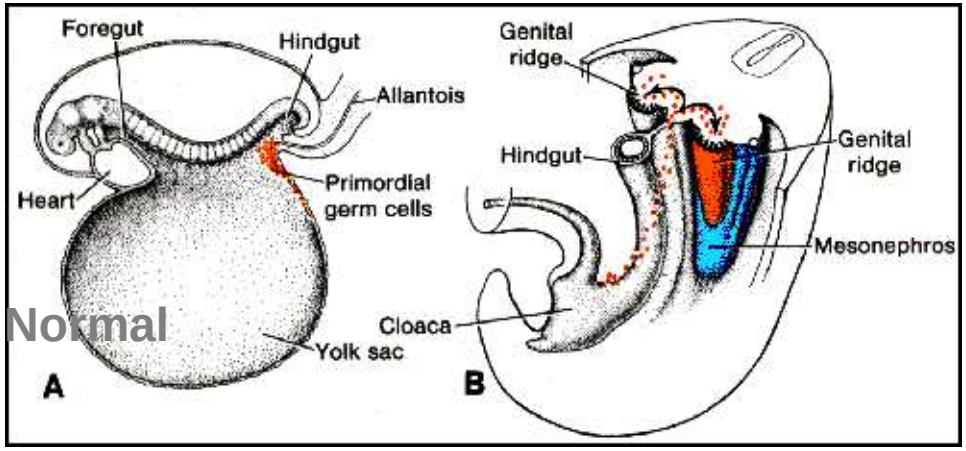


ncRNAs

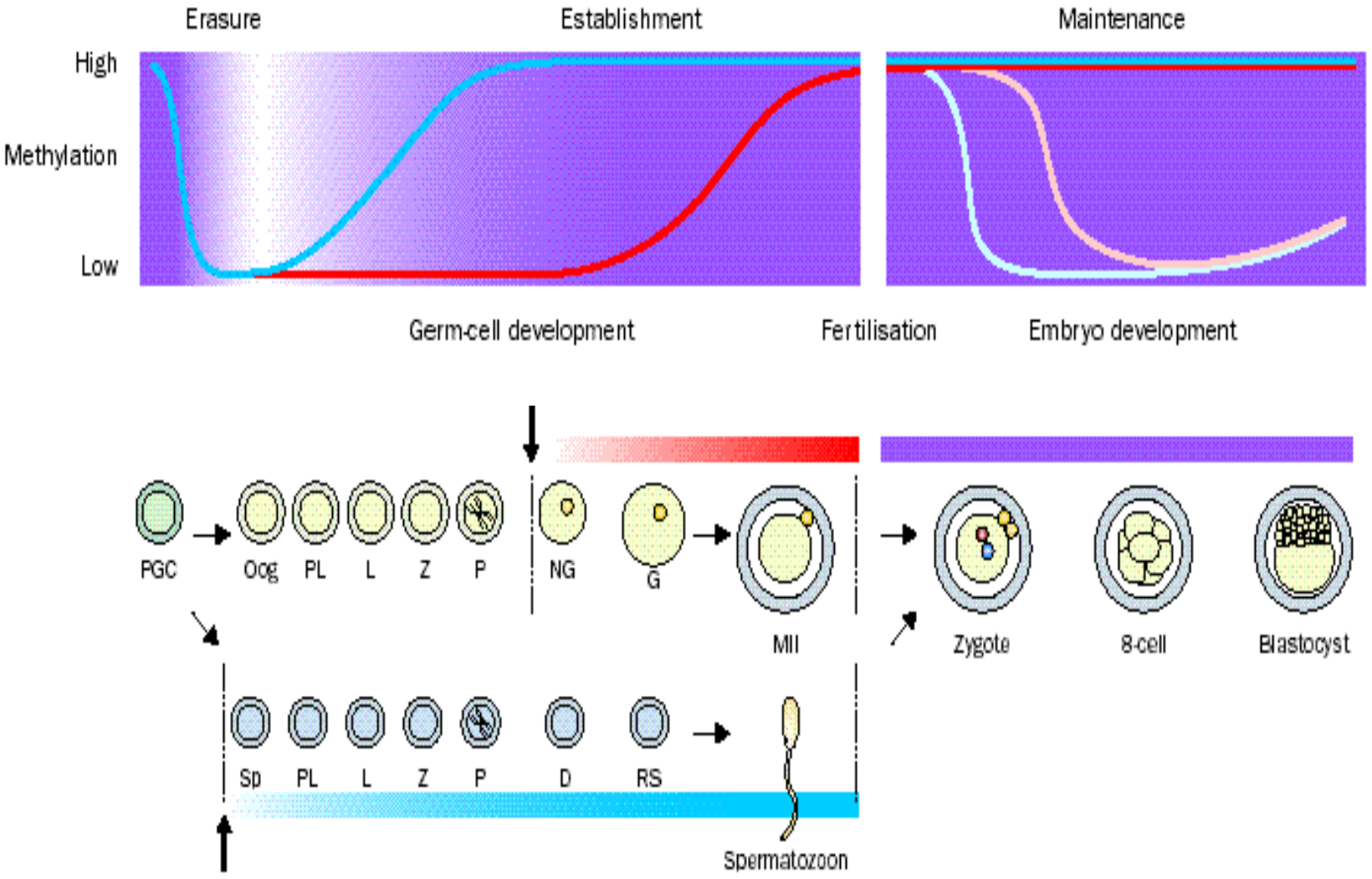
(short, long)

Metilação do DNA





Normal



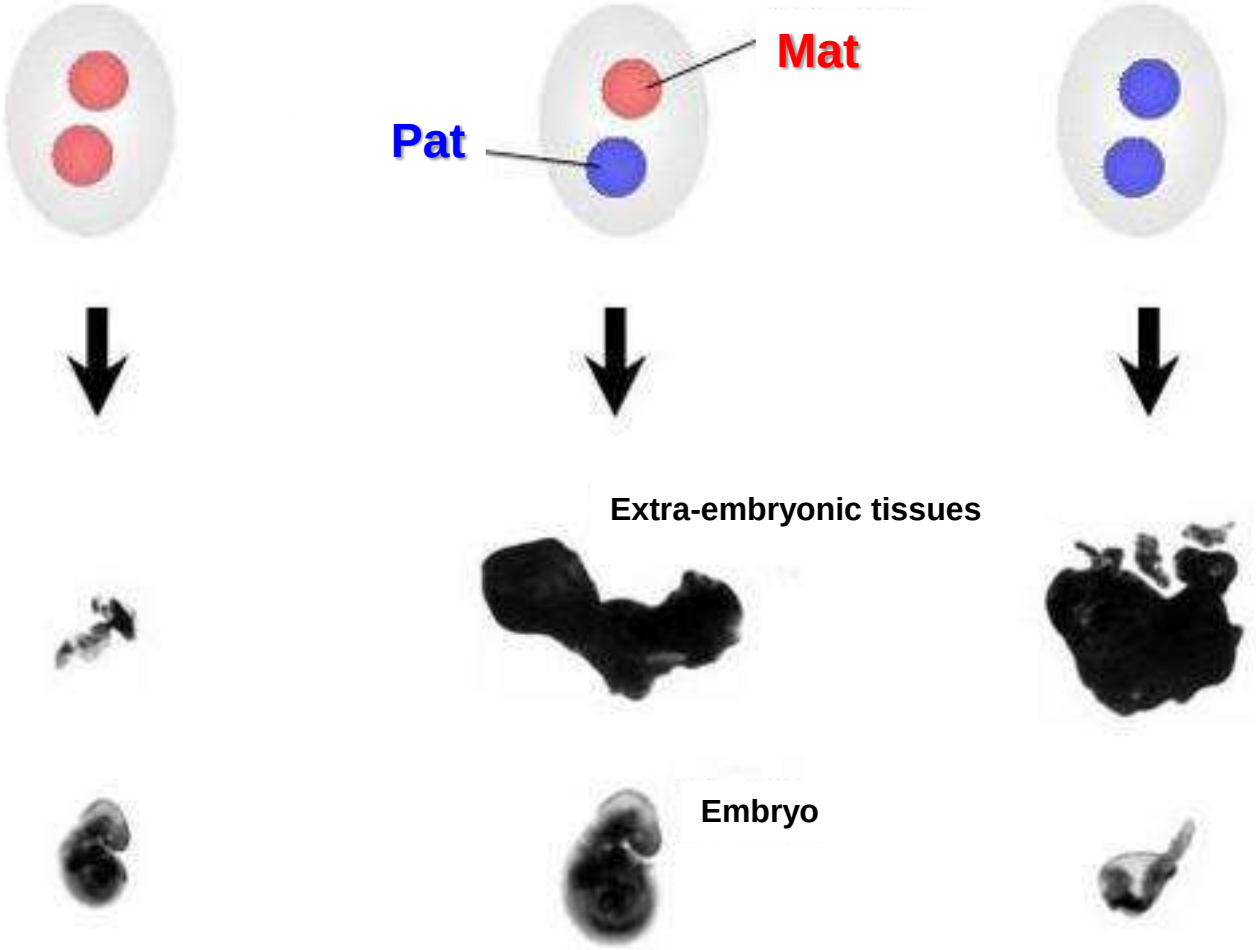
Gosden et al, 2003

	donkey 	horse 
donkey 	donkey 	hinny 
horse 	mule 	horse 

Images credit: http://www.imeha.org/

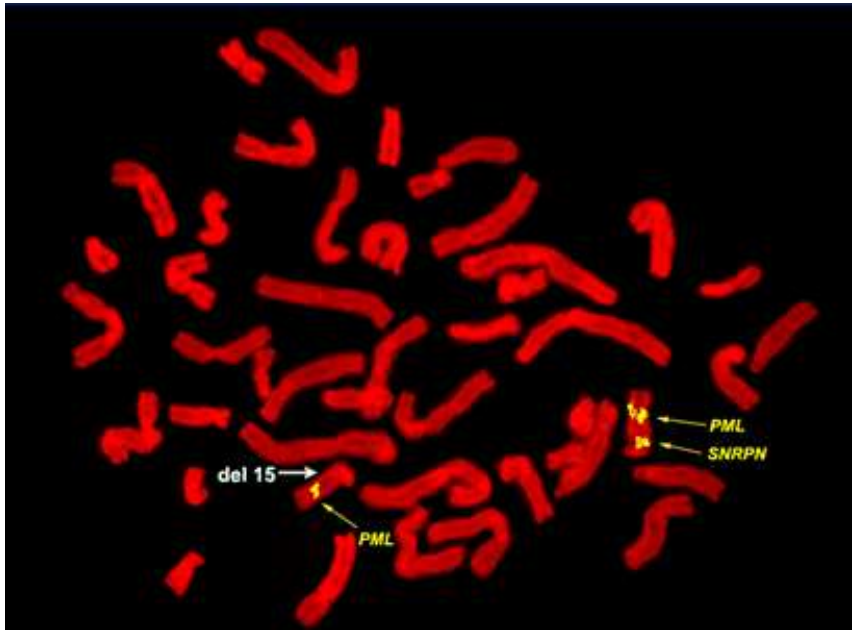
Mula e Bardoto

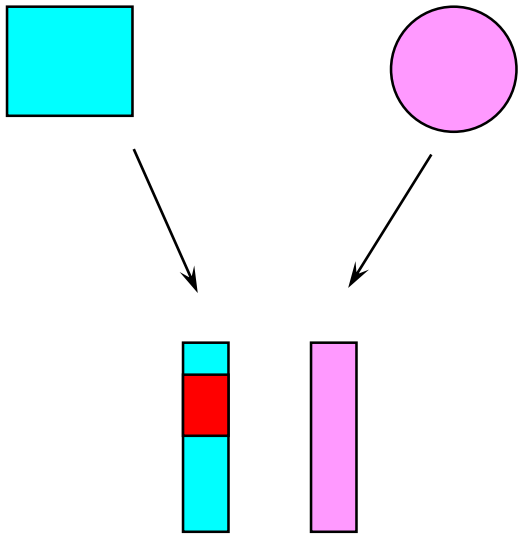
Embriões



Surani et al., 1984; McGrath & Solter, 1984

Síndrome de Prader-Willi

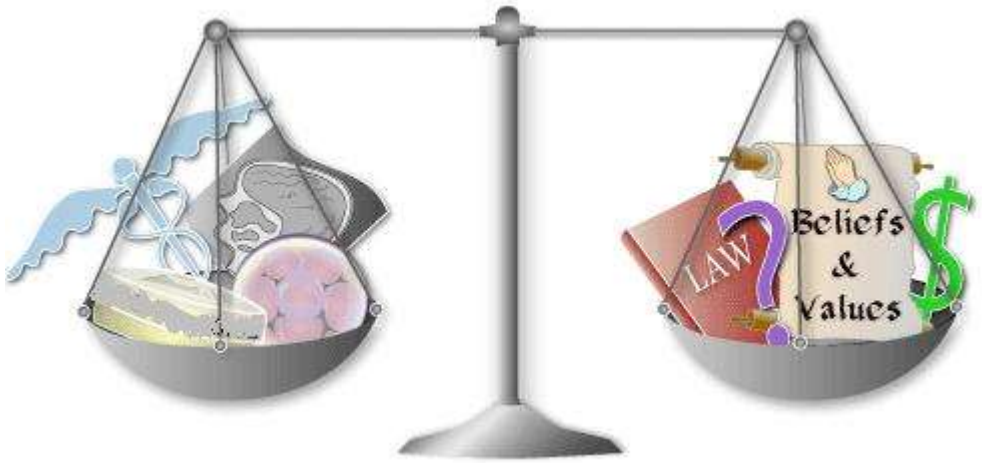




PWS

Chromosome 15
15q11-15q13

Ética e Genética



Bolsa CREMESP – alunos de Medicina