

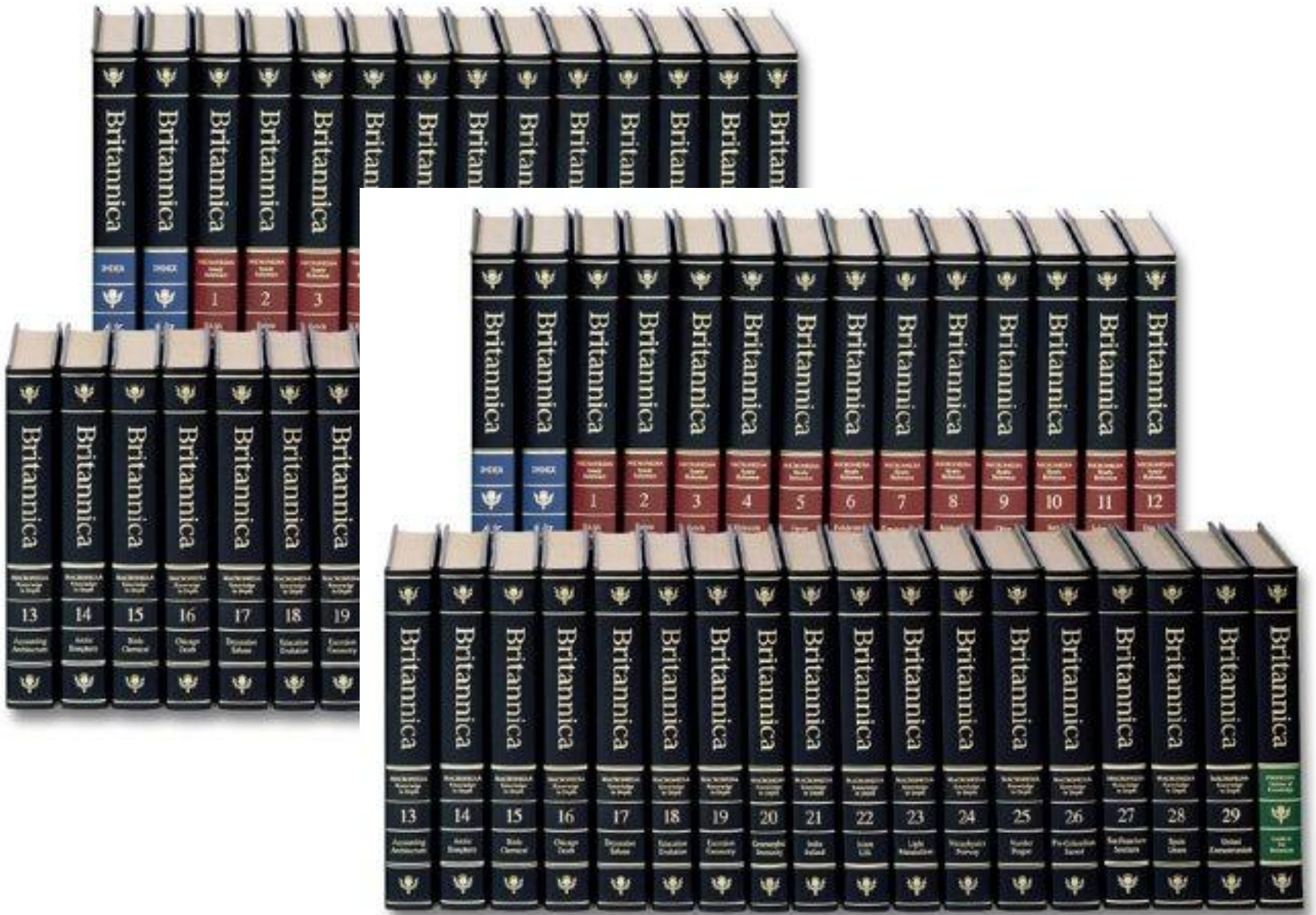
Cromossomos, divisao celular e bases da citogenetica

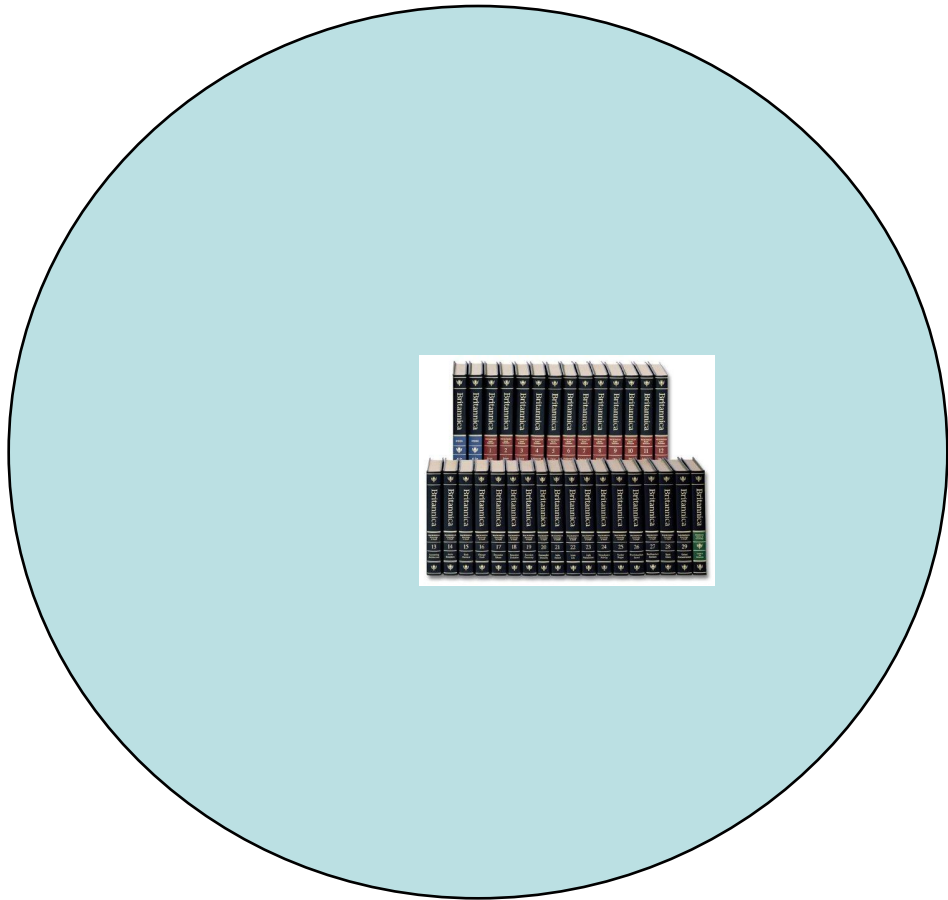
Dr. Jose Claudio Casali
joseclaudior@uol.com.br

Hospital Erasto Gaertner

PUC-PR

Laboratorio Mantis - Curitiba





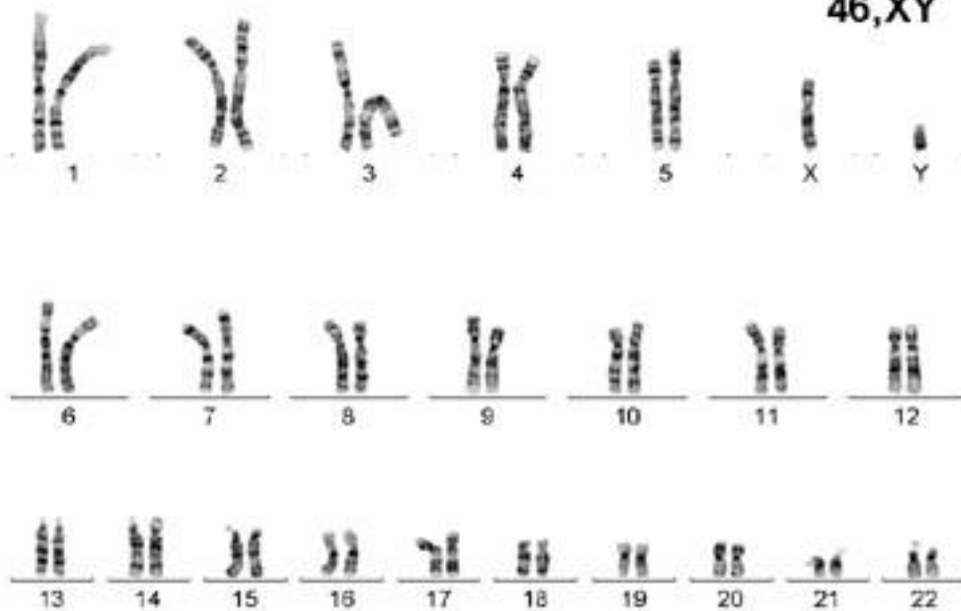
© Les Futurs Québec Amérique inc., 1998.

Chromosomes



Normal male

46,XY

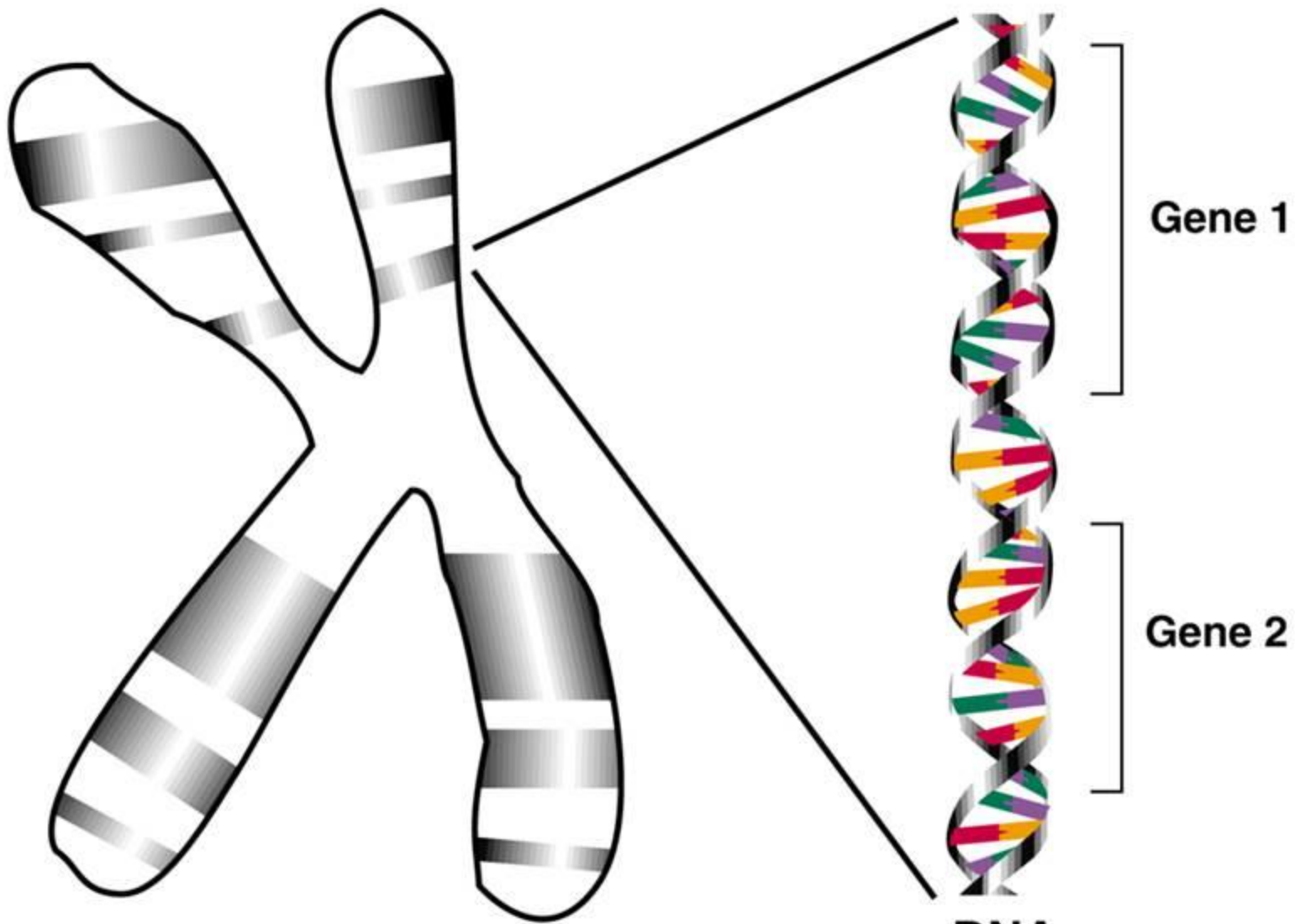




Cada Capitulo
Um GENE

Cada GENE
Uma "receita"

Cada produto
Uma PROTEINA



Chromosome

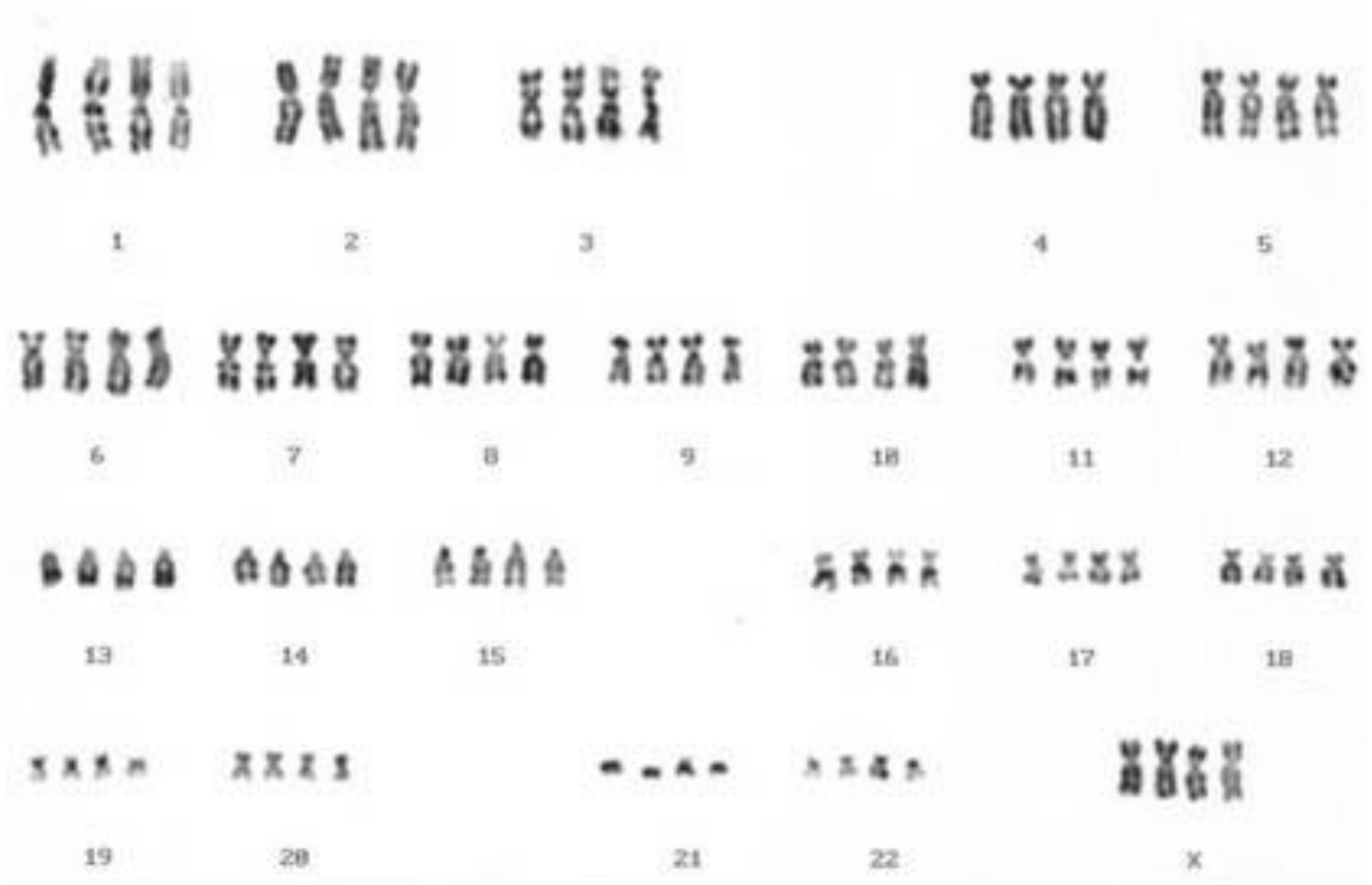
DNA

Genes

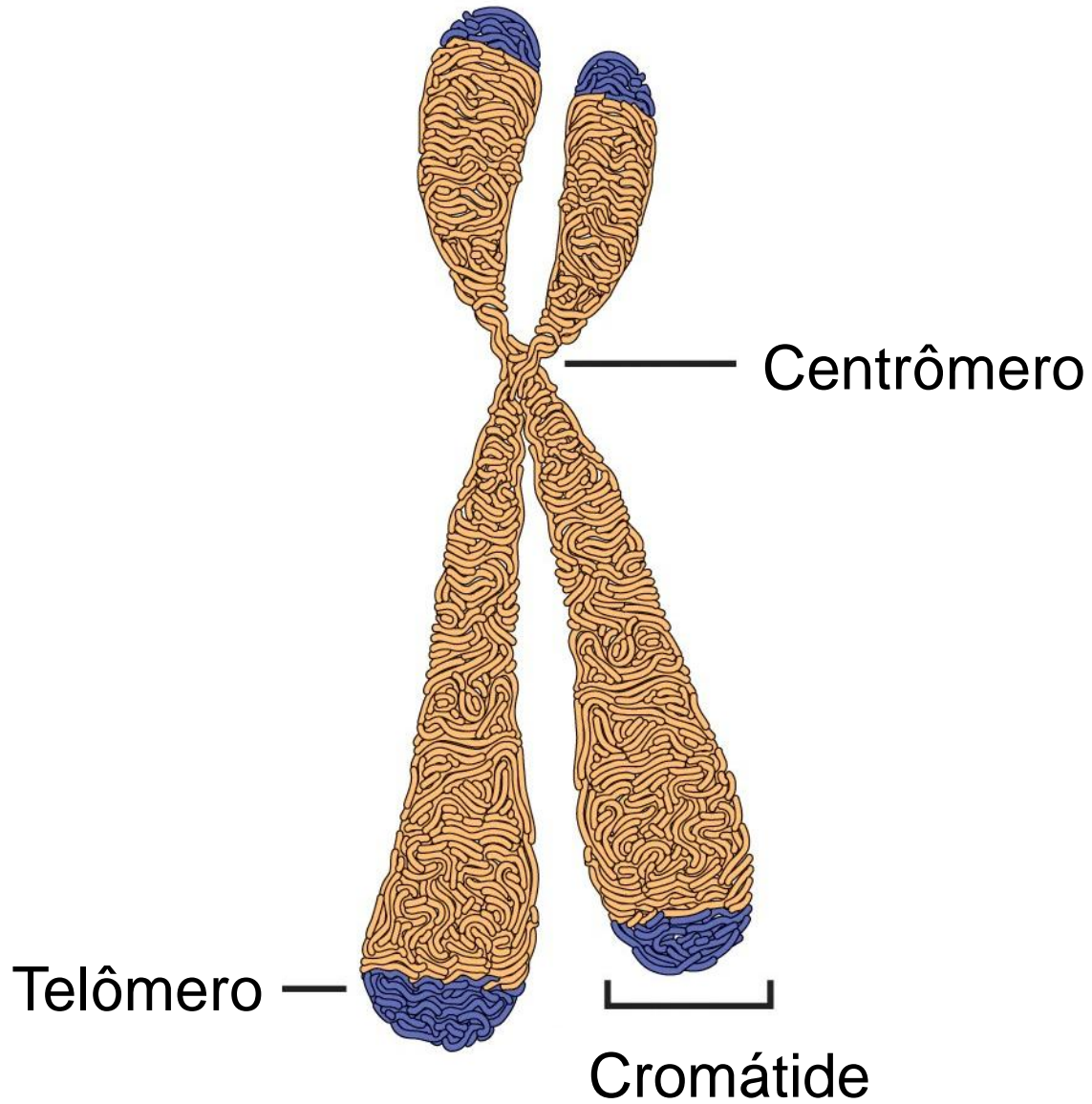
Gene 1

Gene 2

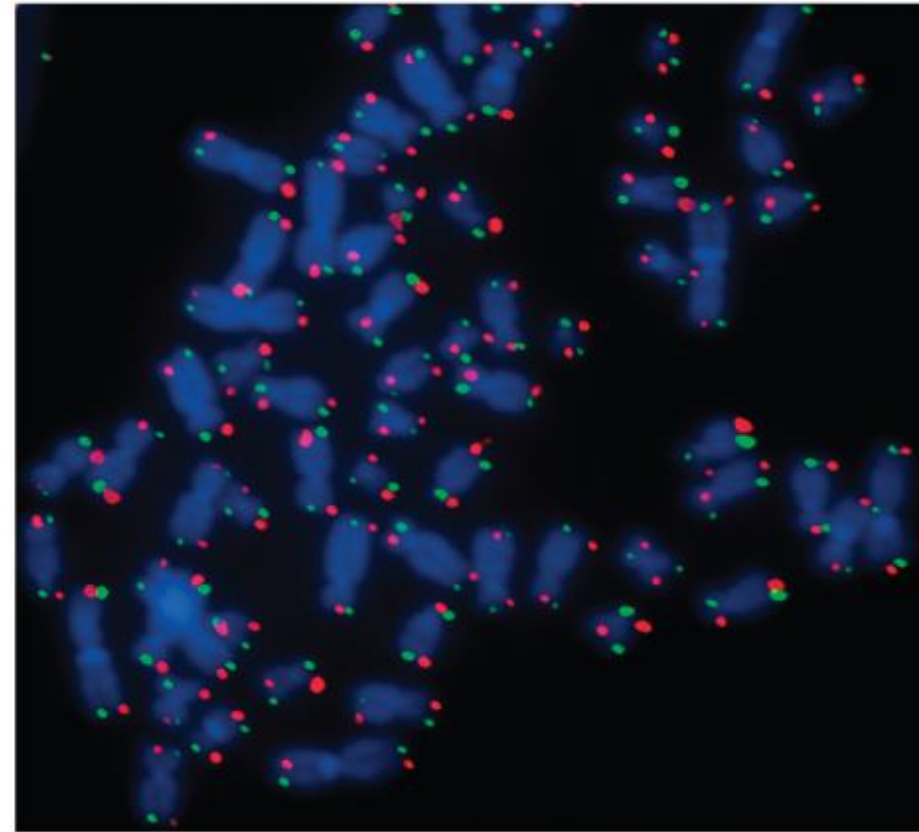
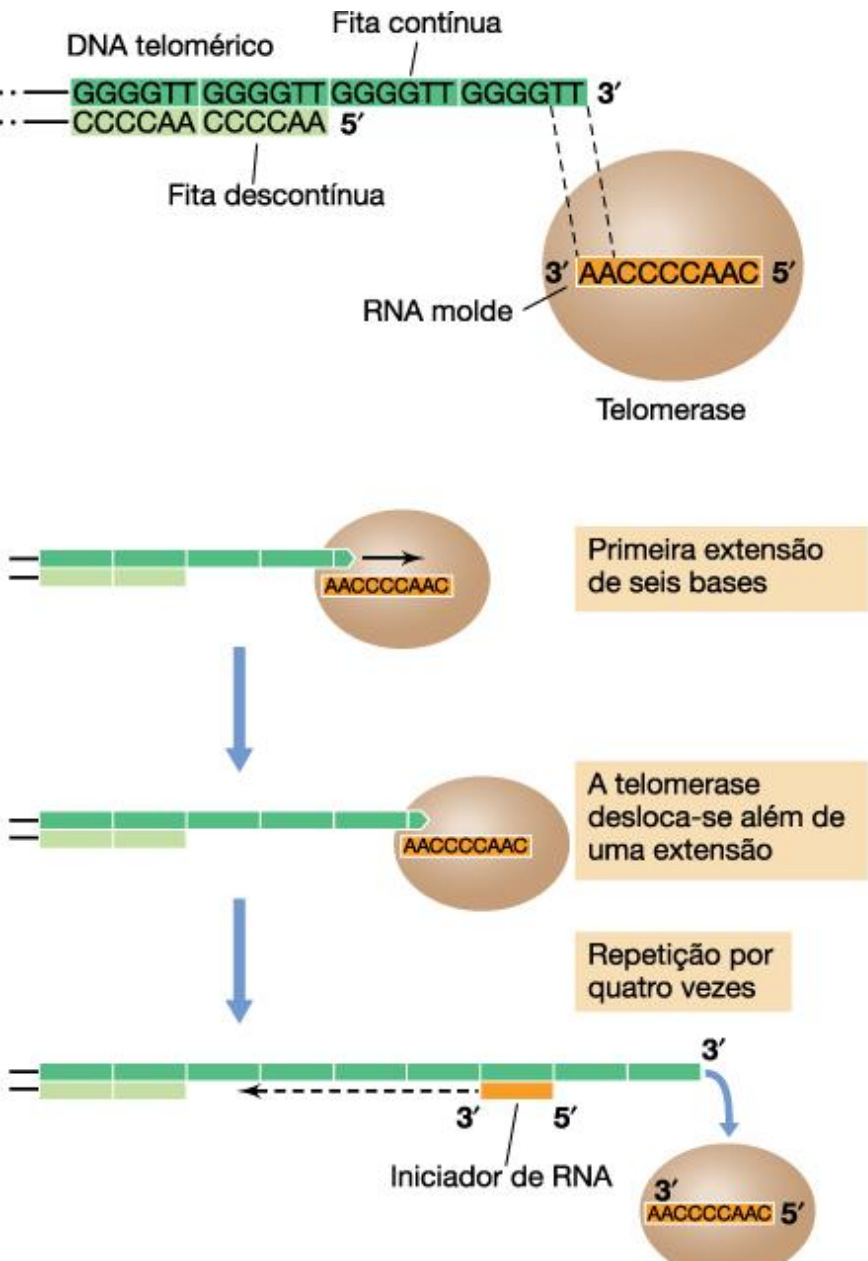
Organização do genoma DNA nuclear – poliplóide (4n)



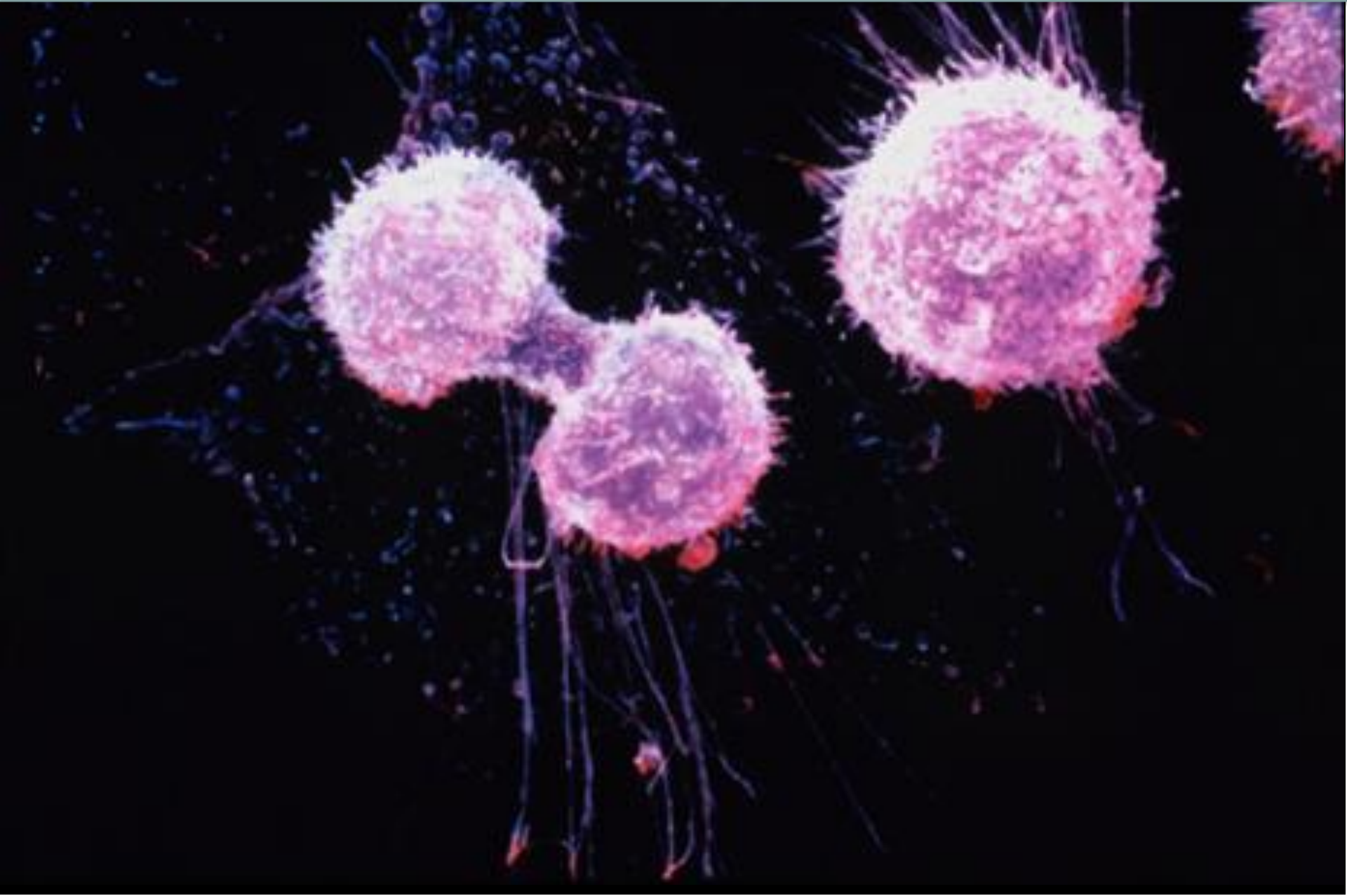
Cromossomo metafásico



Organização do genoma cromossomos lineares - telômeros



ESTÁDIOS DA MITOSE



Citocinese

A célula que não está replicando DNA super-enovelado, com atividade nuclear baixa

Mitose

M

G₀

Cromossomas

G₁

Preparação da célula para a multiplicação, com a produção de constituintes celulares que serão essenciais para a nova célula

G₂

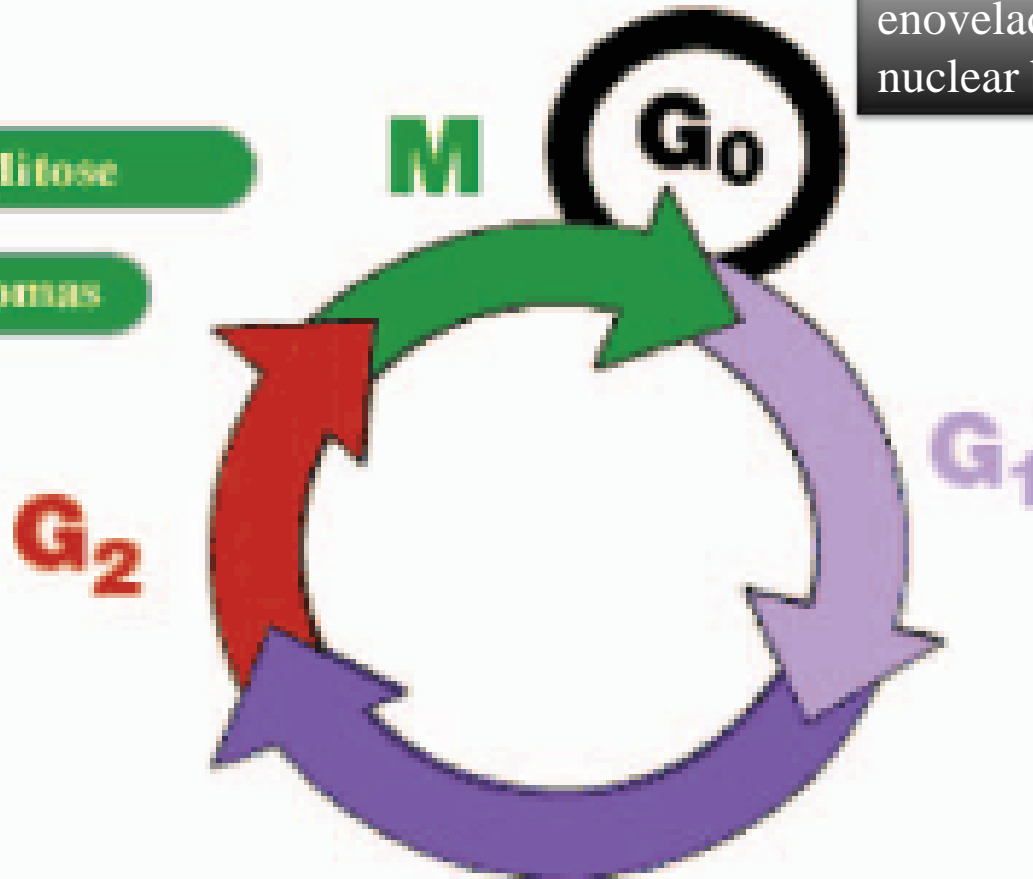
Reparo DNA

S

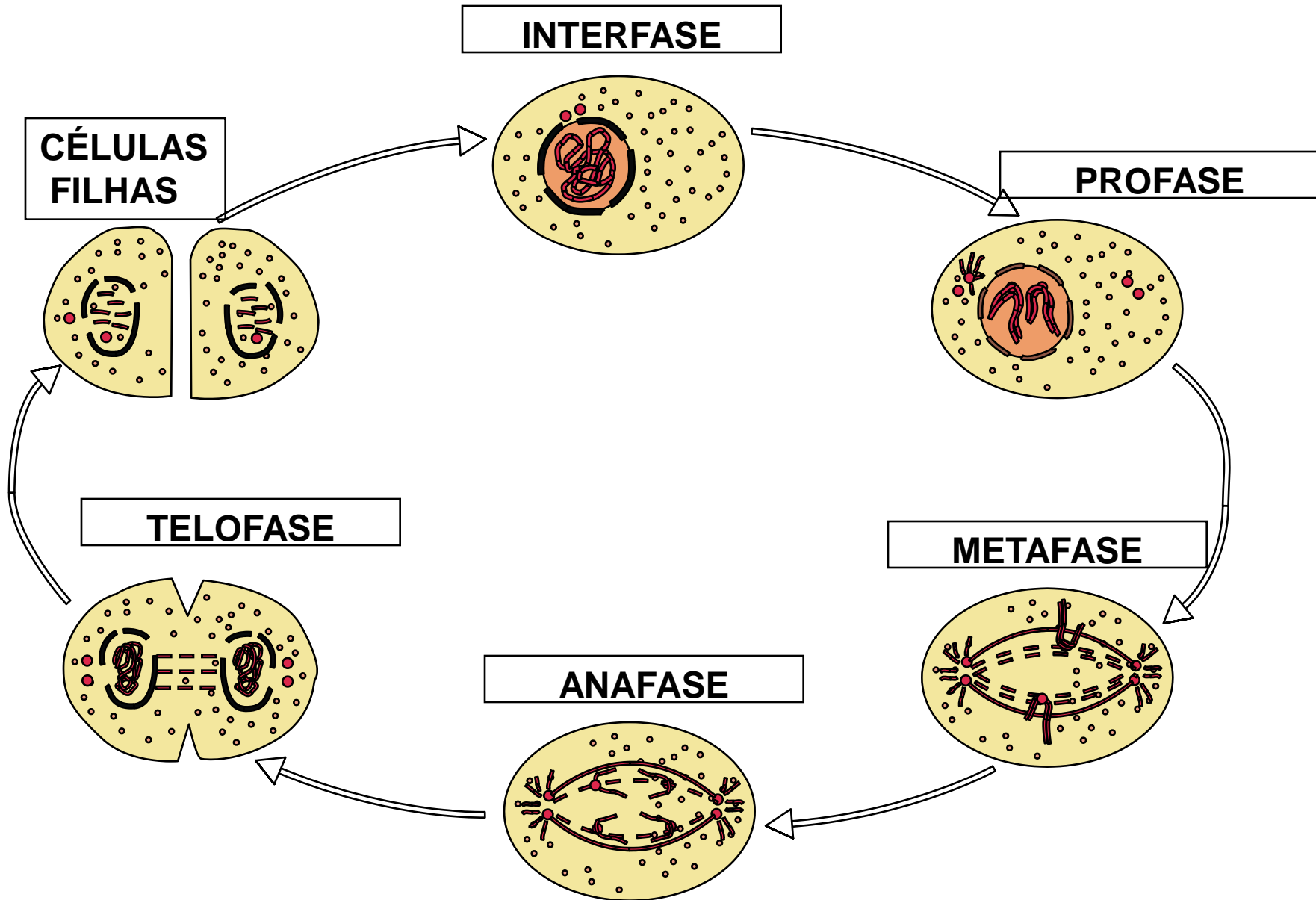
Replicação DNA

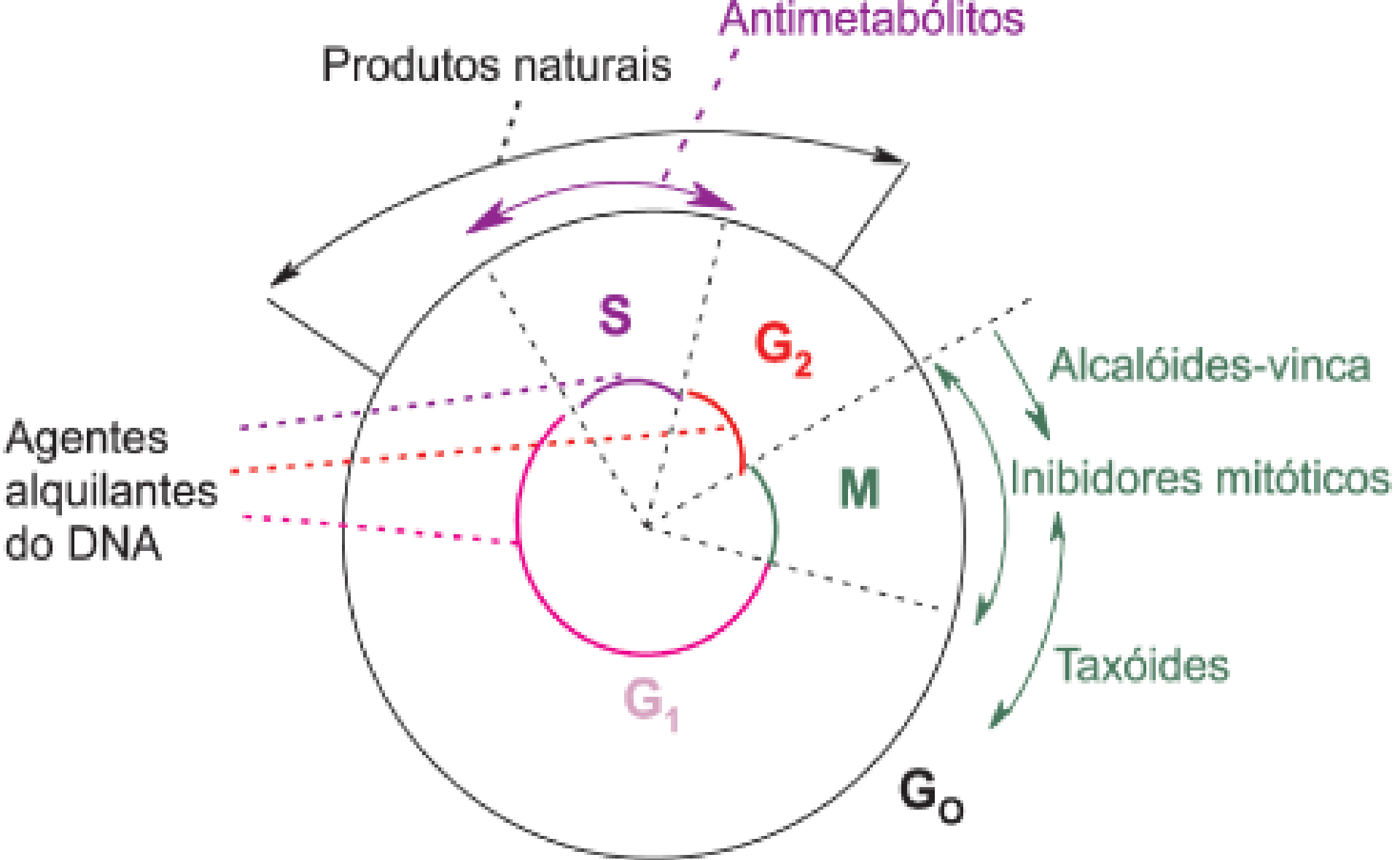
Preparação para a síntese de DNA

1) Há a síntese de componentes para a mitose (divisão celular com manutenção do número de cromossomos específico da espécie).
2) A produção do fuso mitótico (fase M).

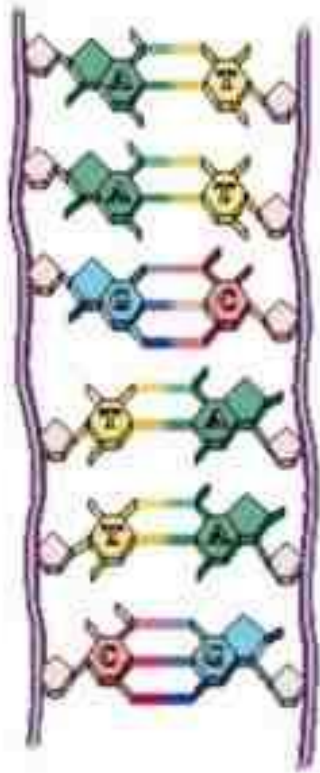


ESTÁDIOS DA MITOSE

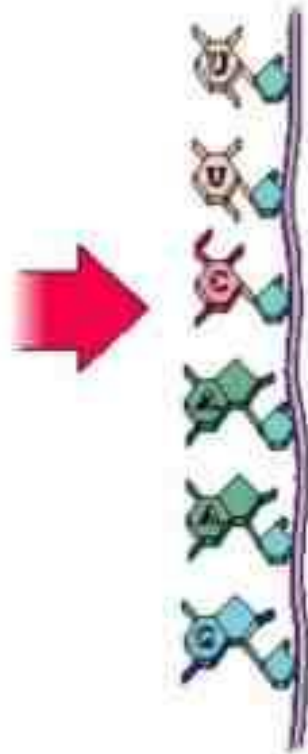




DNA → RNA → PROTEÍNA
COMO NASCEMOS O QUE PODEMOS SER O QUE SOMOS



DNA
genoma



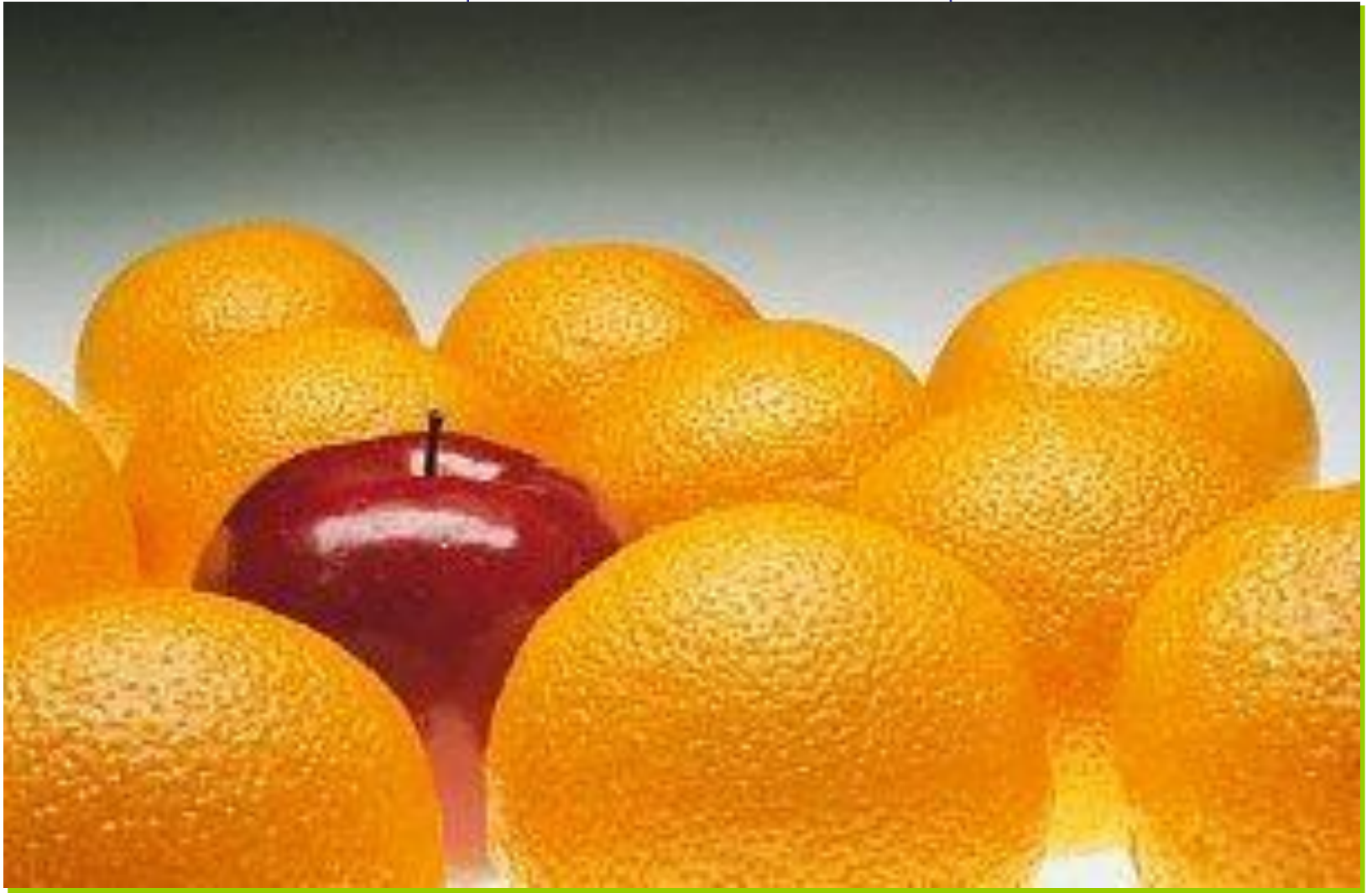
RNA
transcritoma

Met Tir Gli

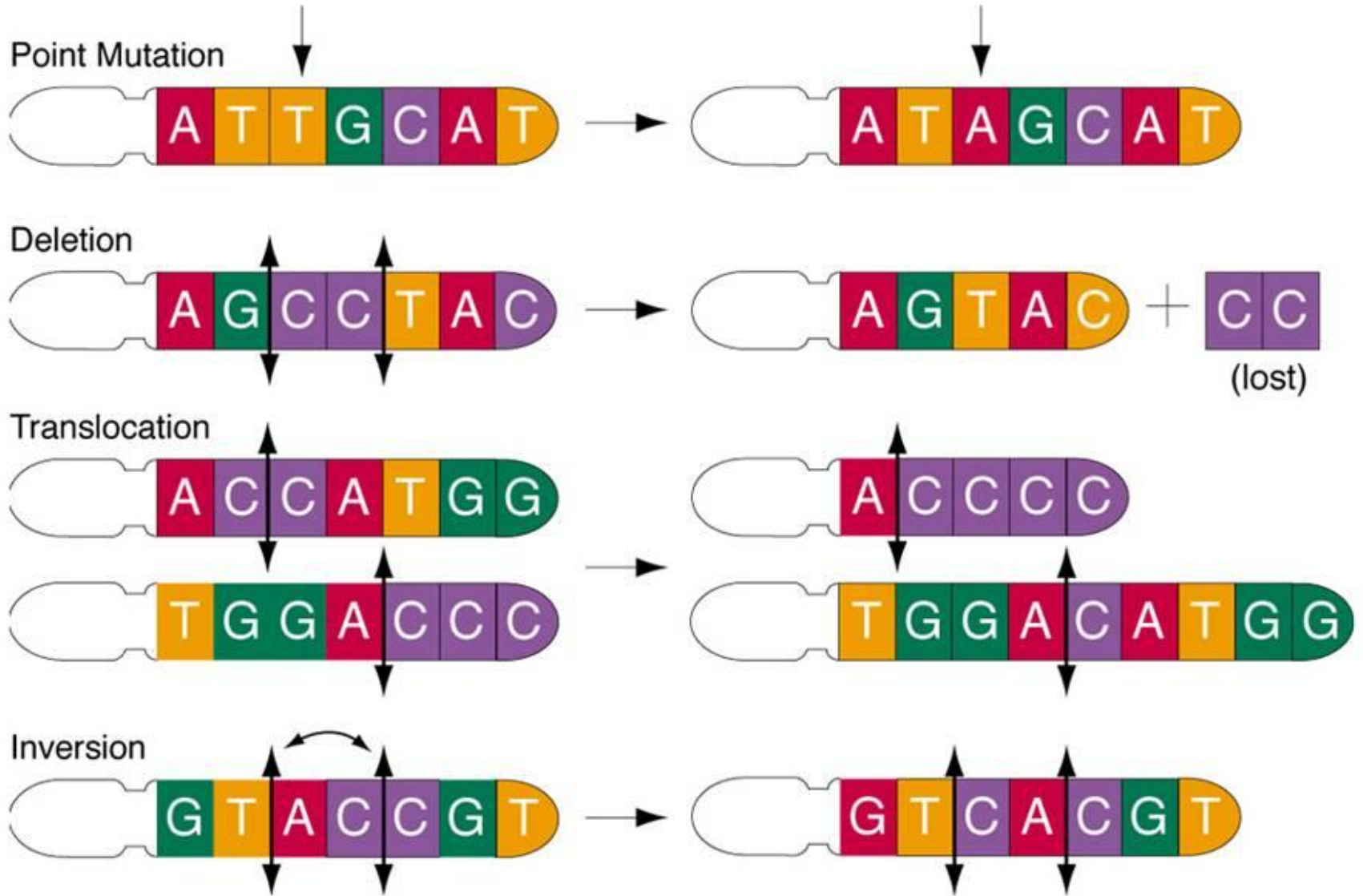


Proteína
Proteoma

MUTACAO



Mutations of Chromosomes

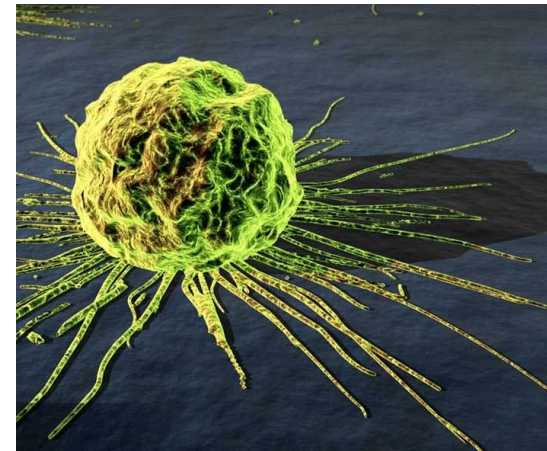


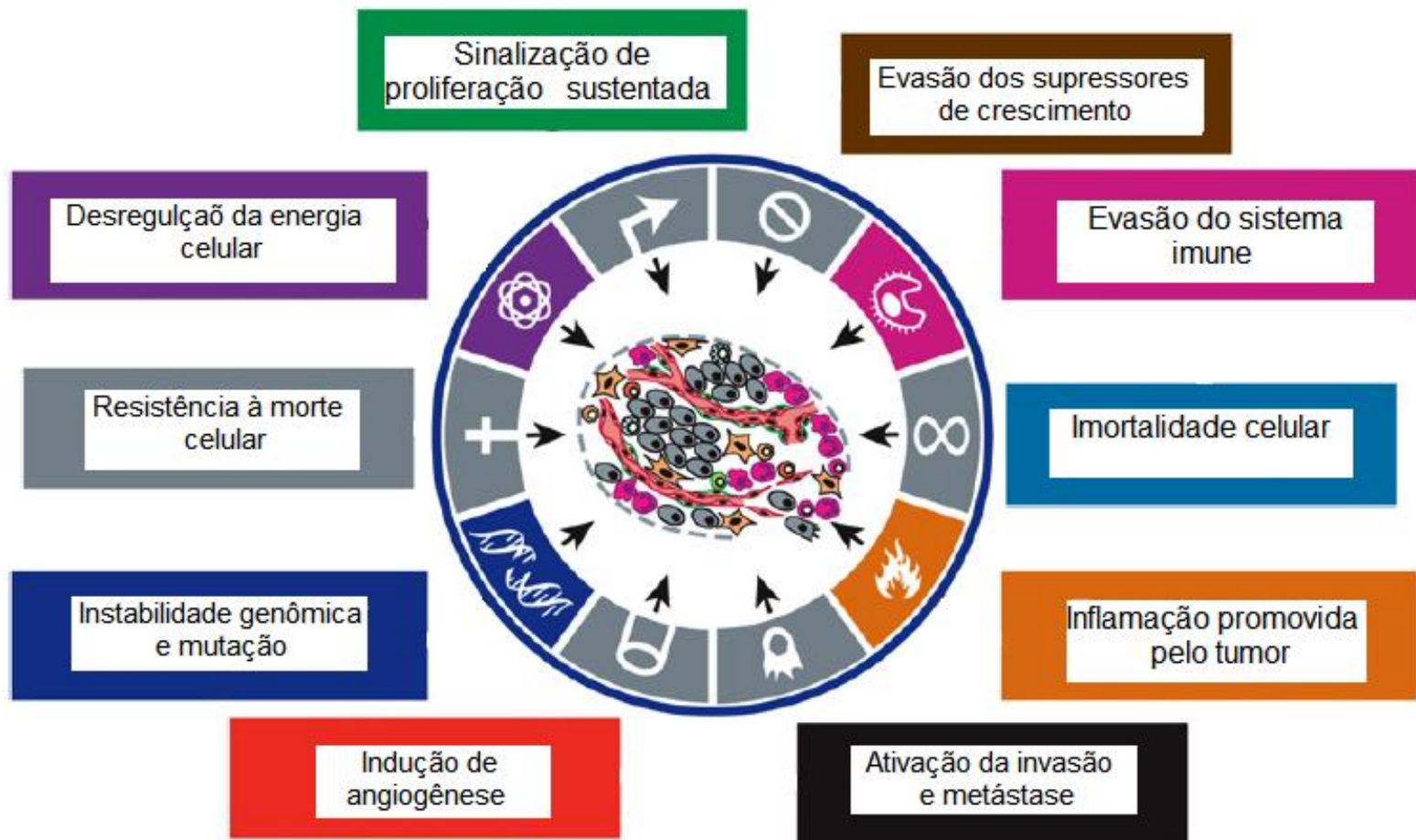
Cancer

um diagnostico...muitas doencas...diferentes respostas

Problema Biologico

Celula normal → Lesao pre-maligna → Cancer → metastase





Pontos chaves para o aparecimento tumoral. Representação de mecanismos necessários para a transformação tumoral: proliferação sem controle; não resposta aos fatores anti-crescimento; escape do sistema imune; imortalização e resistência à morte celular; indução de metástase; produção de vasos sanguíneos; e desregulação do fornecimento energético celular. Todas essas alterações são geradas através da instabilidade genômica e mutação, além da promoção de inflamação pelo tumor.

Câncer Esporádico

Mutação,
amplificação
rearranjos,
LOH,
metilação,
...

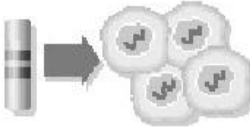
Principais Tipos de Genes Envolvidos no Desenvolvimento de Tumores



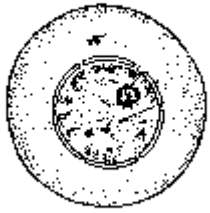
Oncogenes



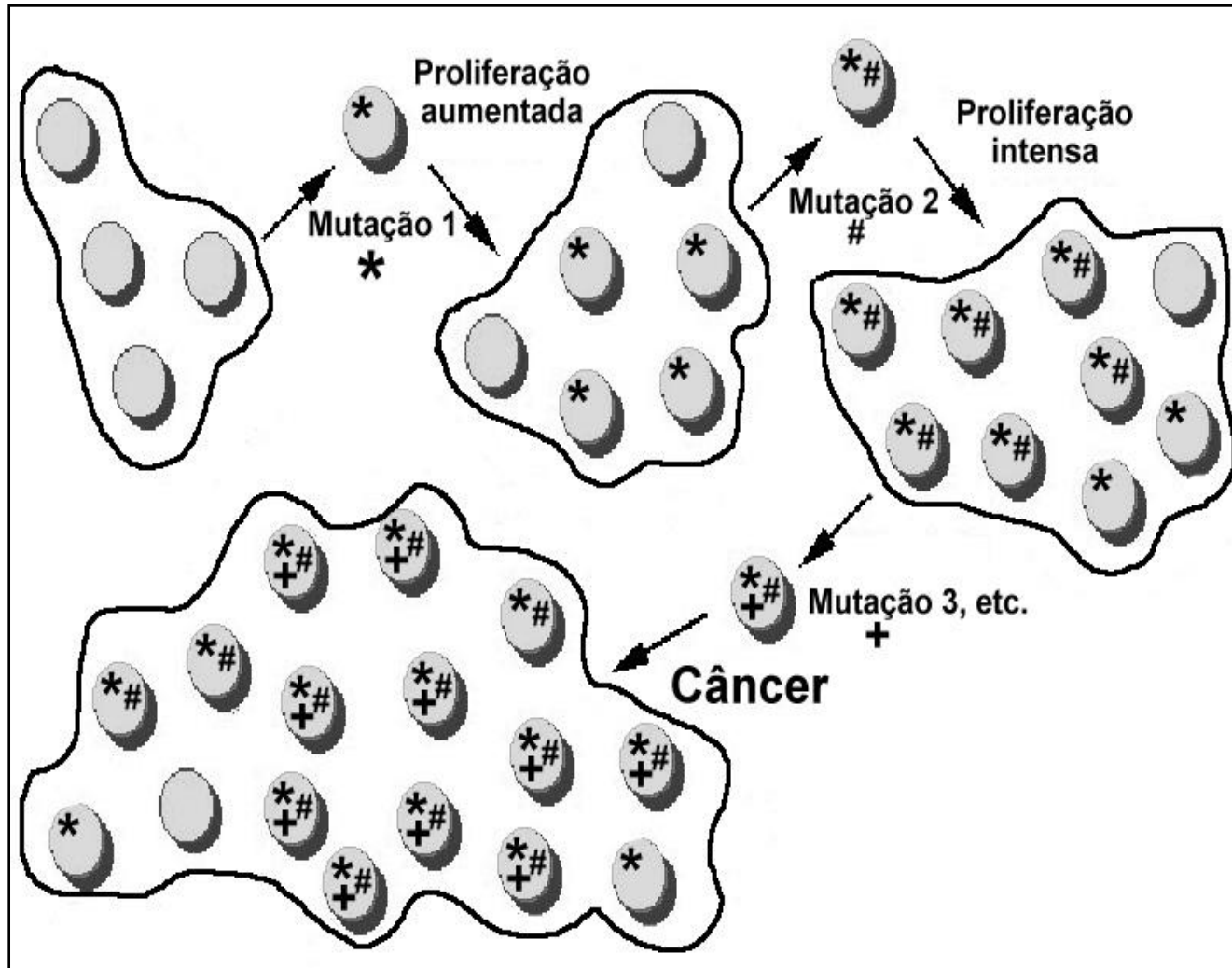
Supressores de tumores



Genes de reparo de
erros de replicação

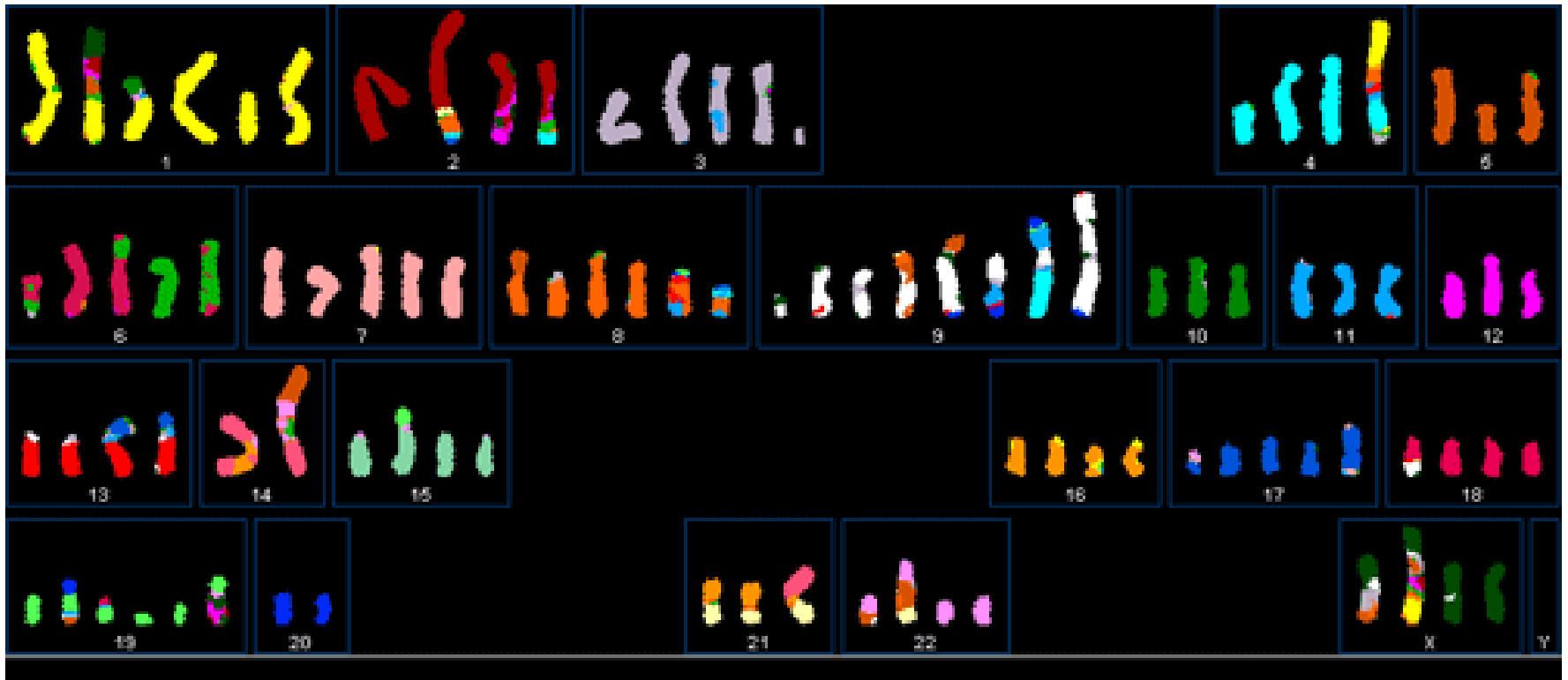


Câncer - expansão clonal

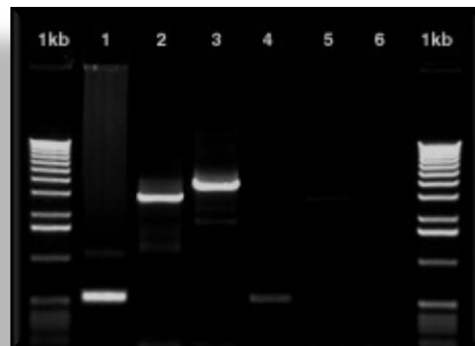
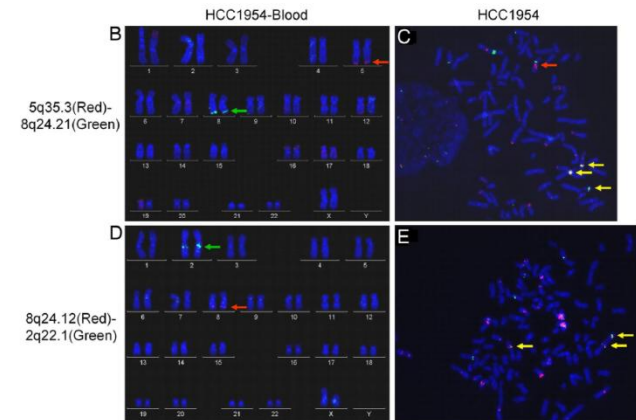
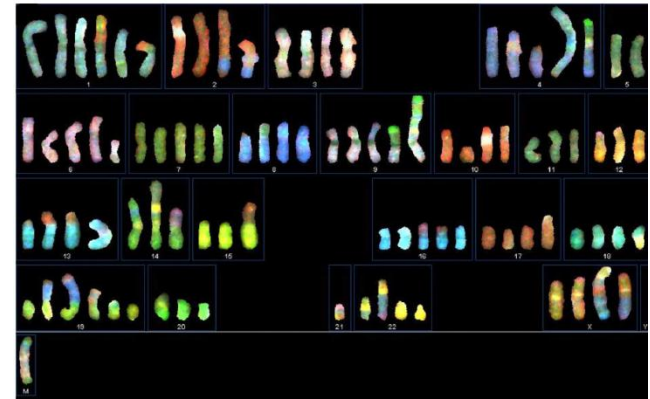
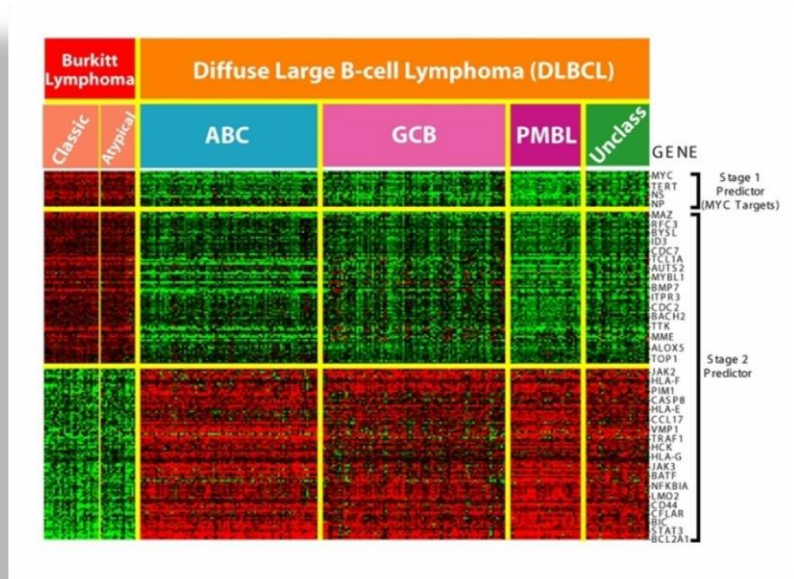


Celula de linhagem de um cancer de mama (HCC1954)

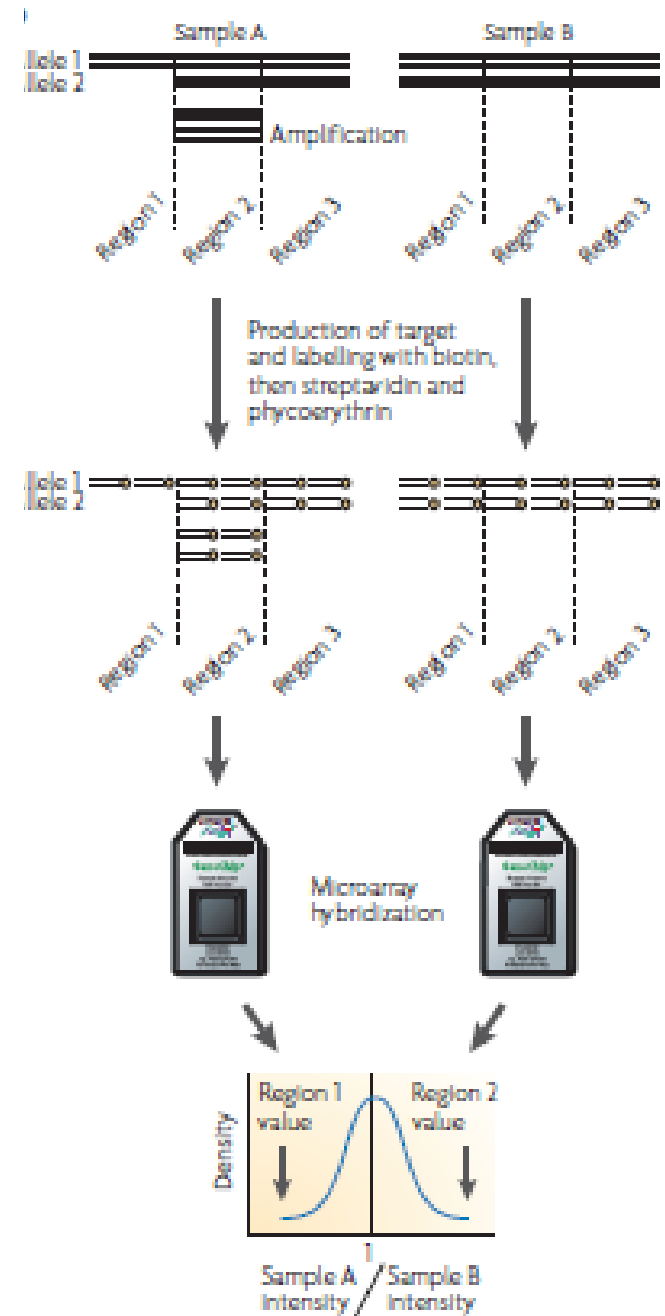
SKY – cariotipo espectral



A complexidade biológica...

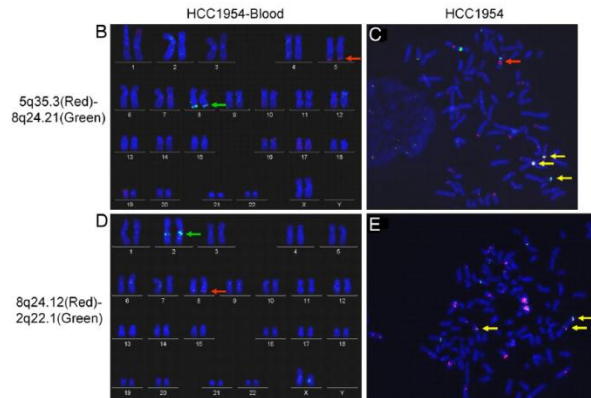
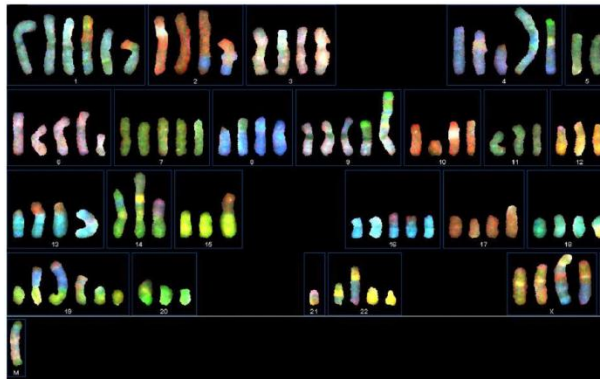


CNV array por SNP (SNP-array)

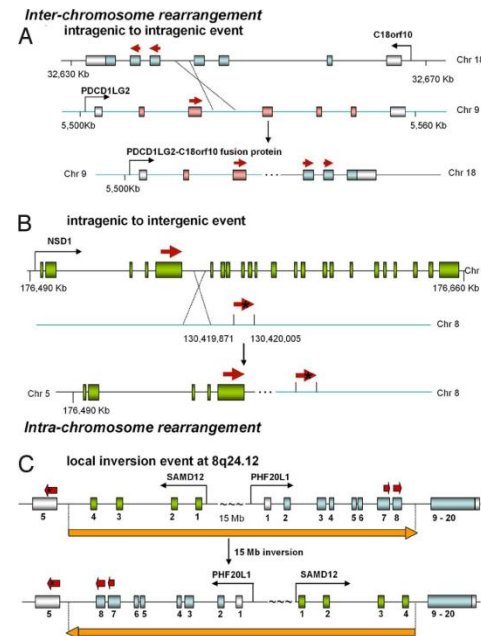


HCC1954: célula de cancer de mama

SKY analysis e FISH



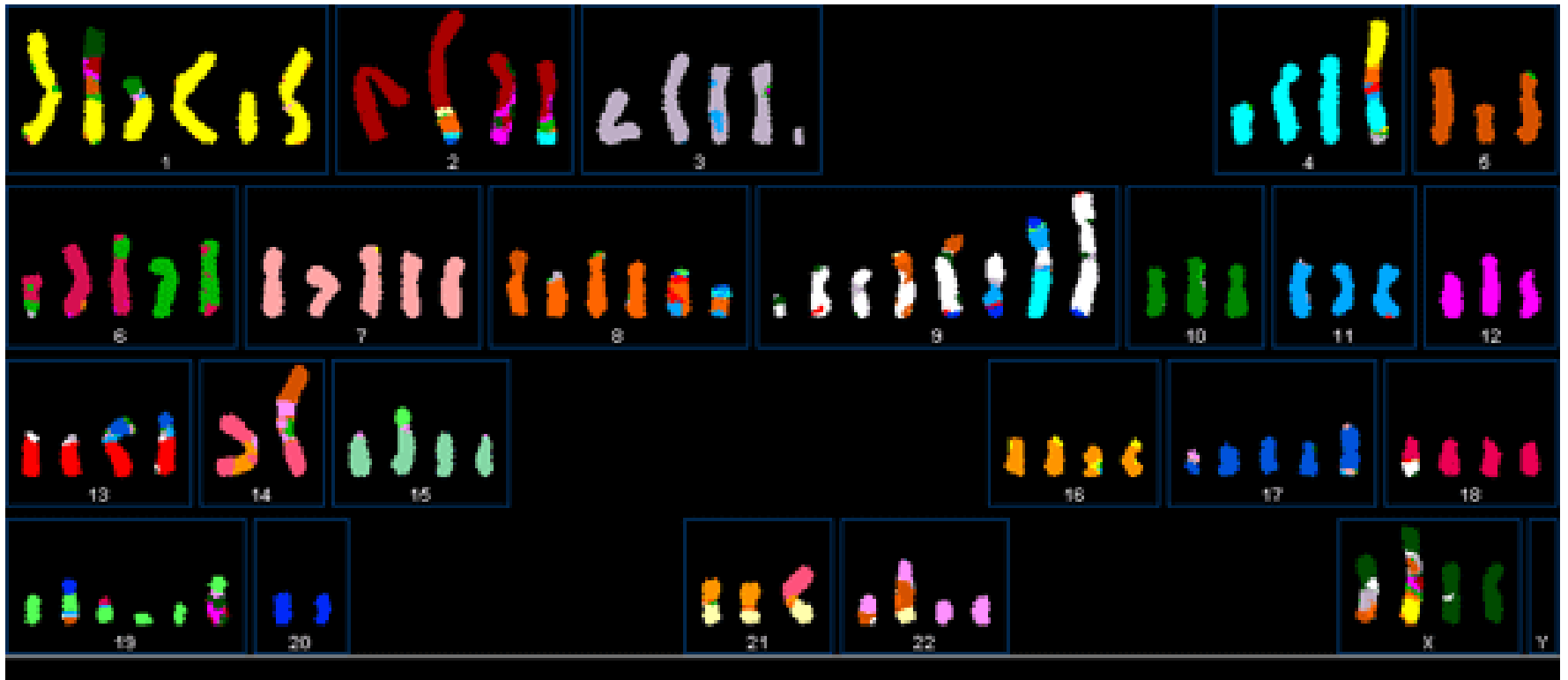
Sequenciamento do transcriptoma
identificação de fusões gênicas
(rearranjos)



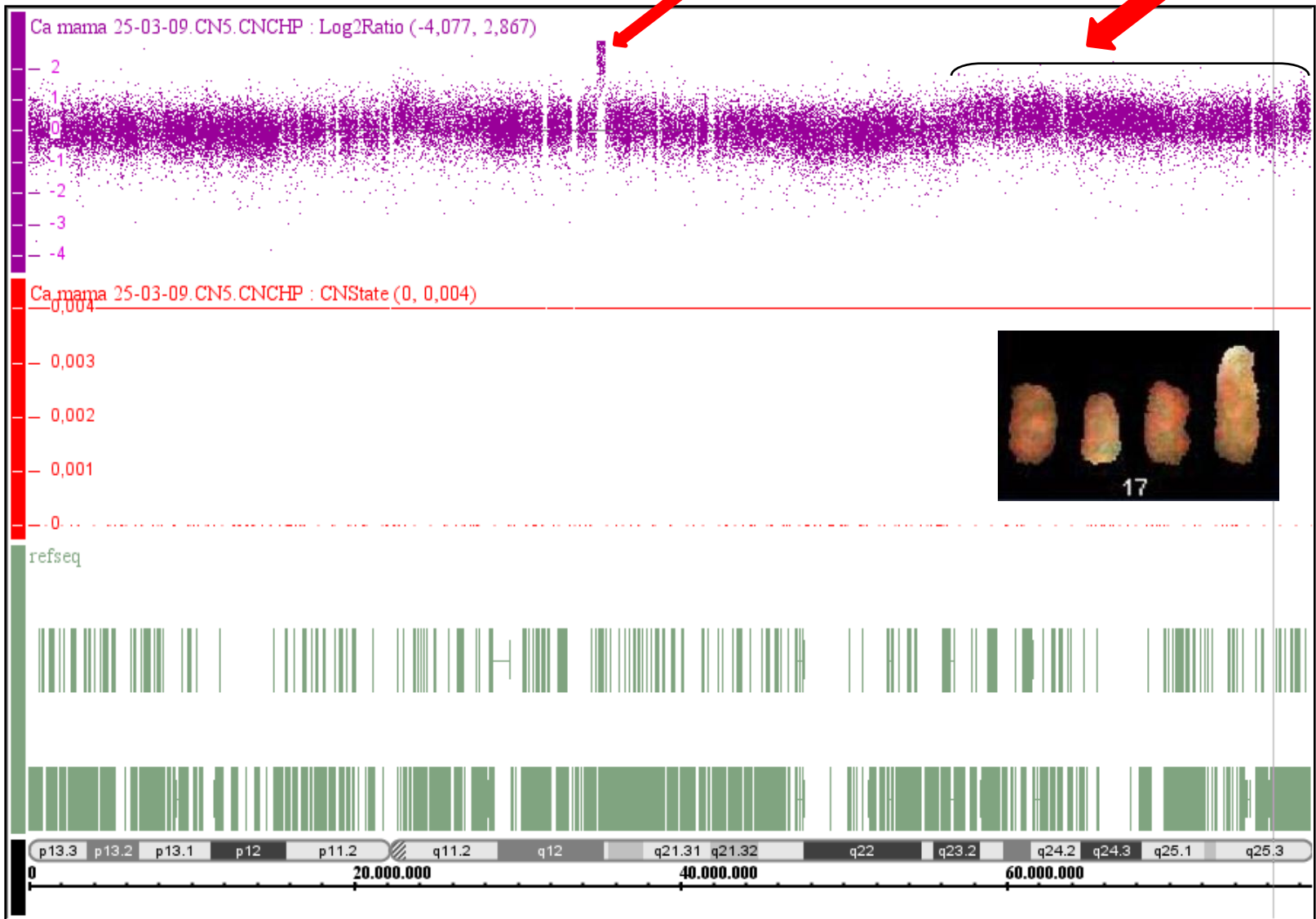
(Zhao, Caballero et al. PNAS 2008)

Celula de linhagem de um cancer de mama (HCC1954)

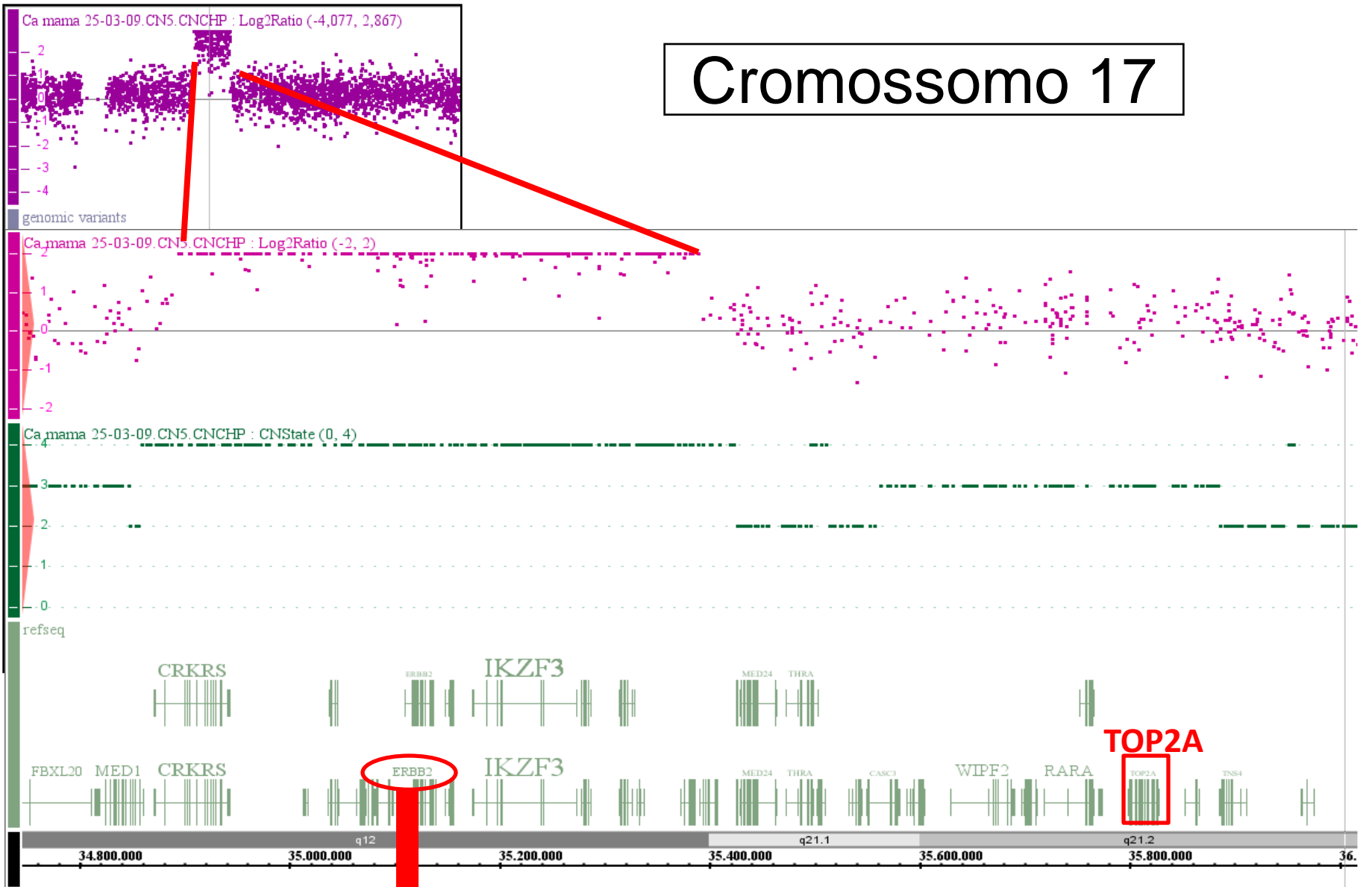
SKY – cariotipo espectral



Cromossomo 17



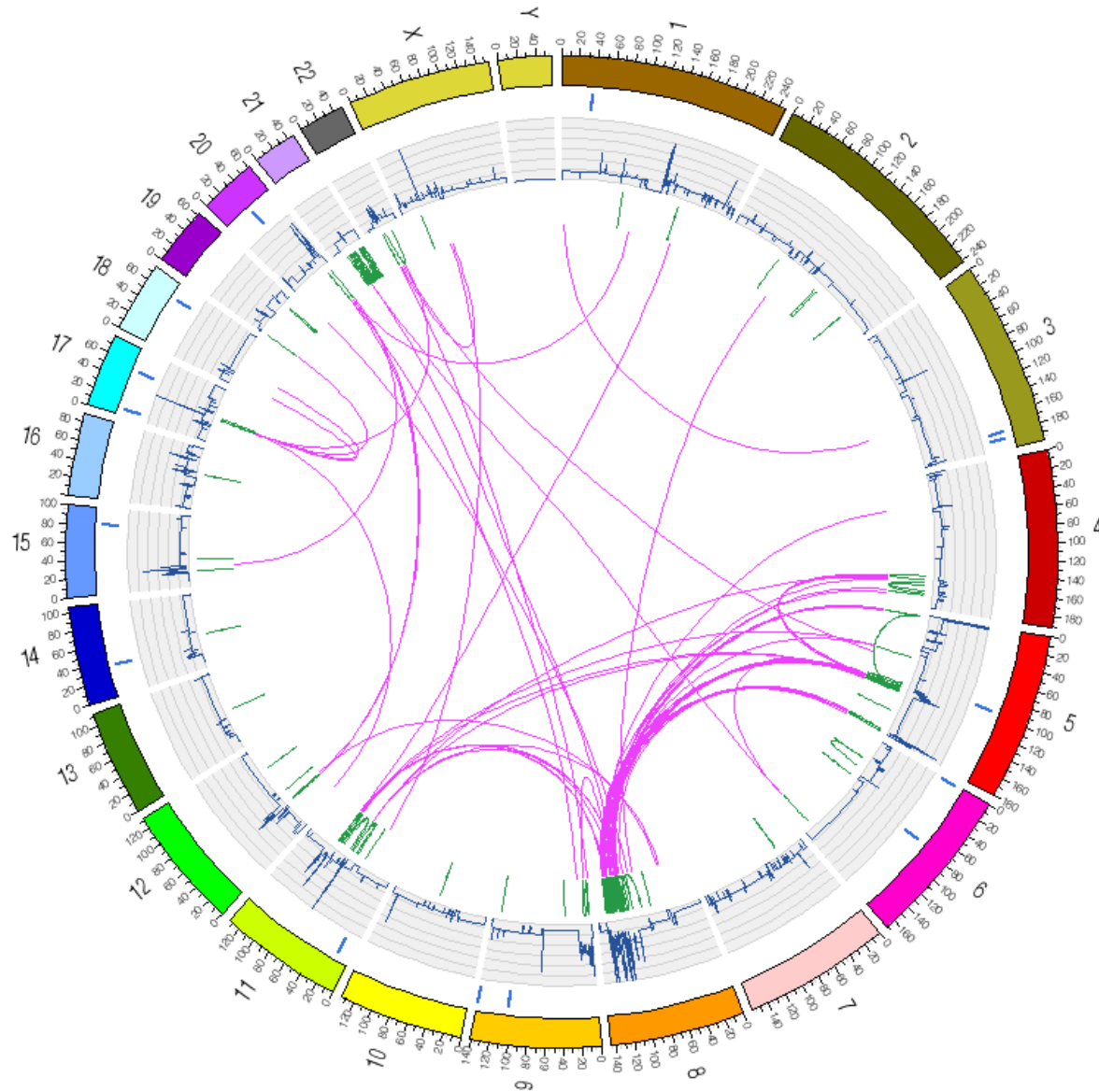
Cromossomo 17



ERBB2

TOP2A

Sequenciamento do transcriptoma da HCC1954





OBRIGADO

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ONCOGENETICISTA

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