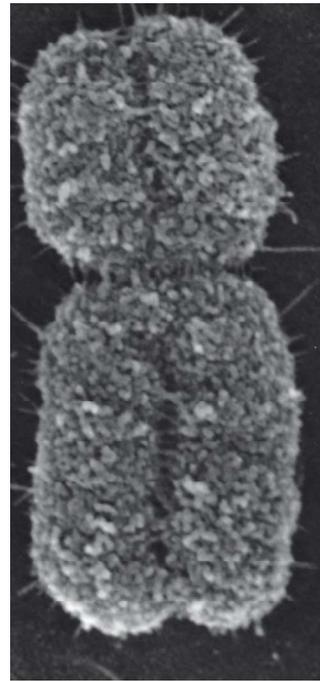
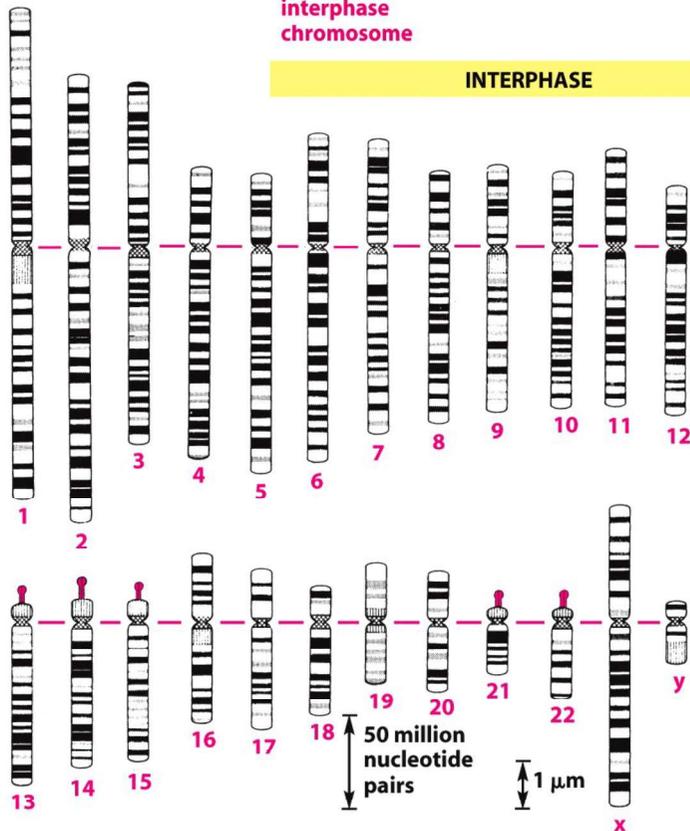
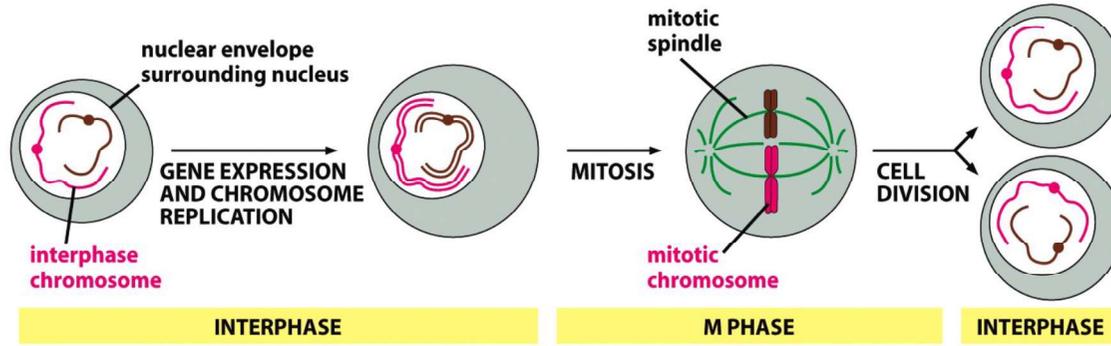


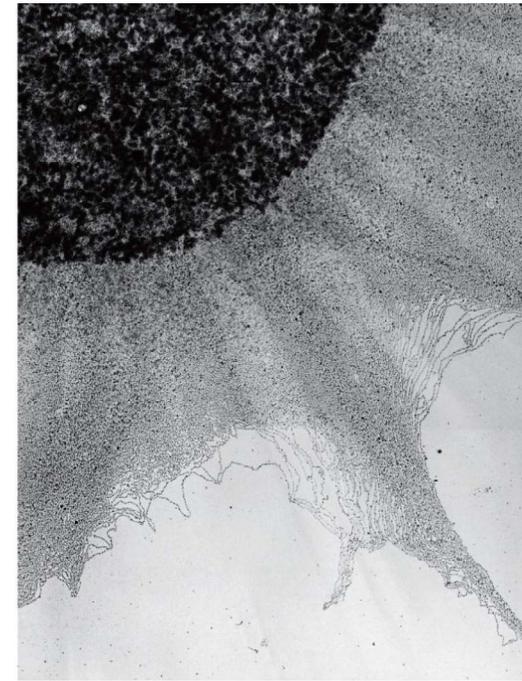
Genoma y su organización intranuclear,
cromosomas y cromatina

Territorios cromosómicos.

Cromosomas



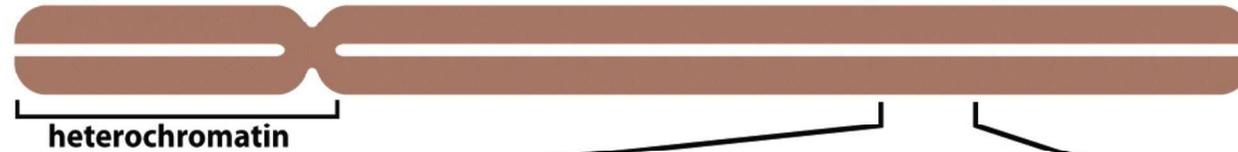
A)



B)

Cromosomas y genes

(A) human chromosome 22 in its mitotic conformation, composed of two DNA molecules, each 48×10^6 nucleotide pairs long



$\times 10$

10% of chromosome arm ~ 40 genes



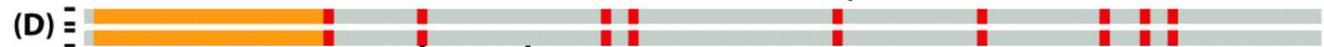
$\times 10$

1% of chromosome containing 4 genes



$\times 10$

one gene of 3.4×10^4 np



regulatory DNA sequences

exon

intron

gene expression

protein

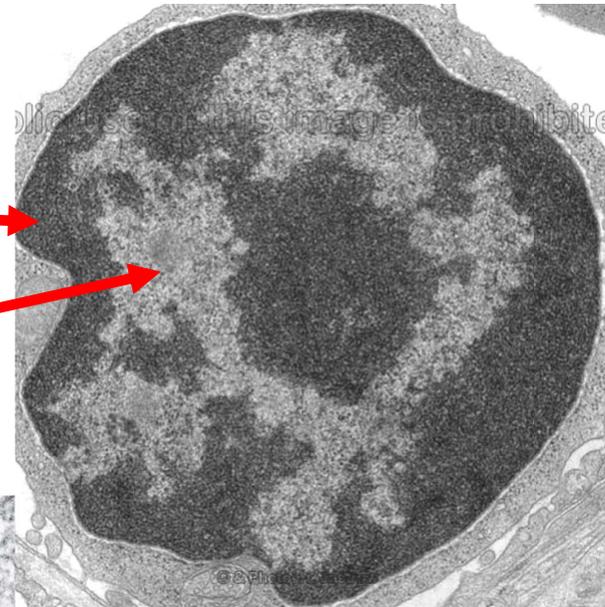


folded protein

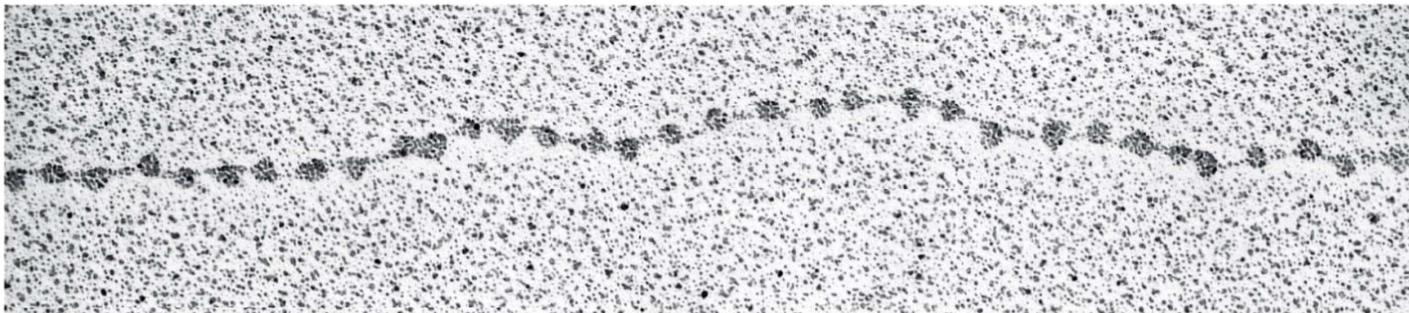
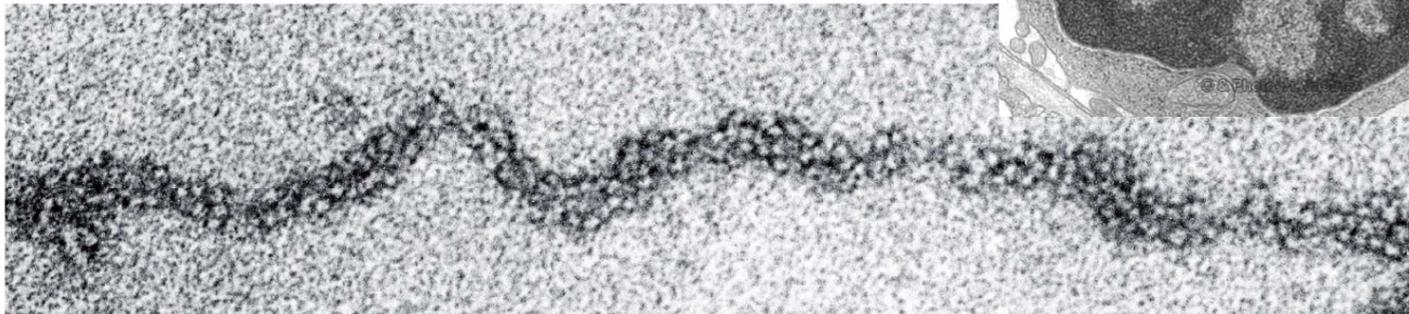
La cromatina

Heterocromatina

Euromatina



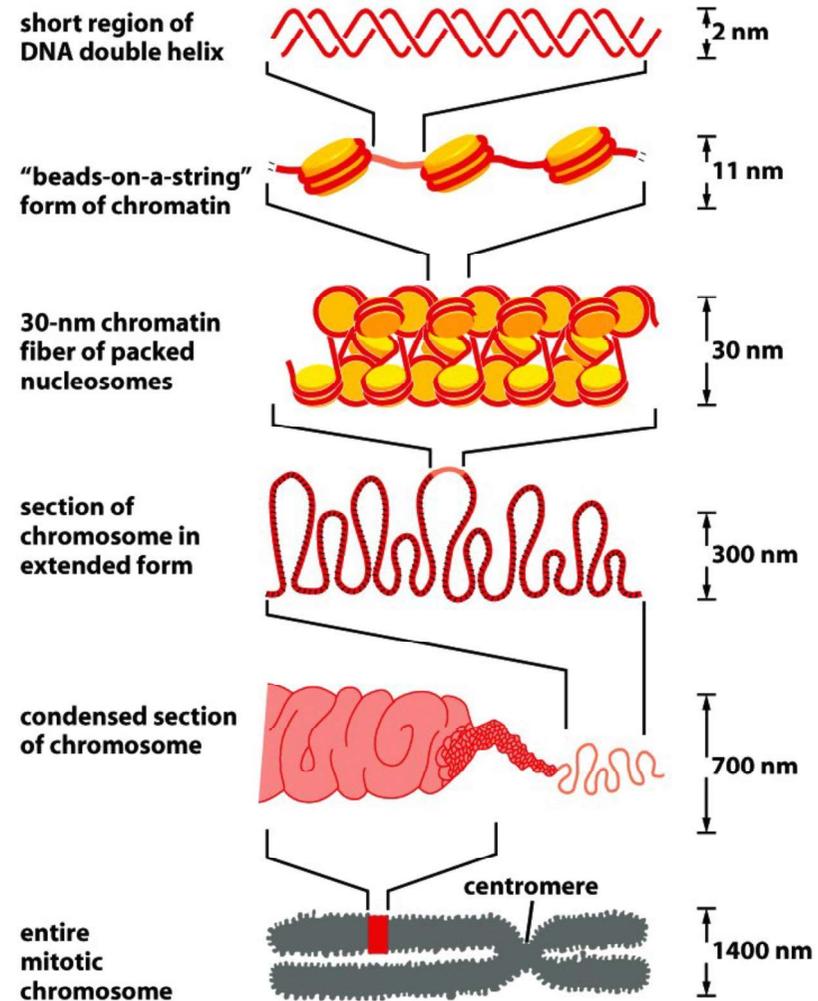
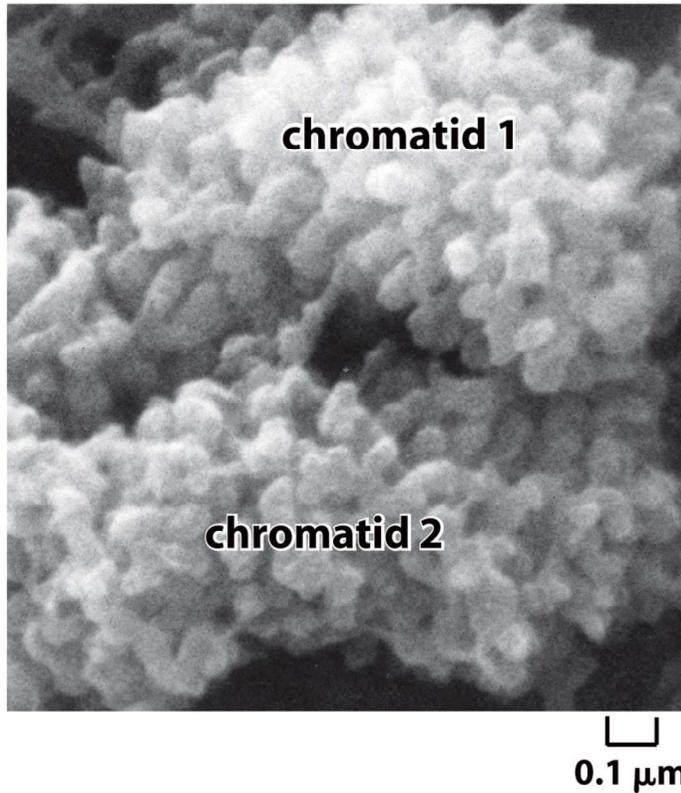
Fibra de cromatina de 30 nm



Fibra de cromatina de 11 nm

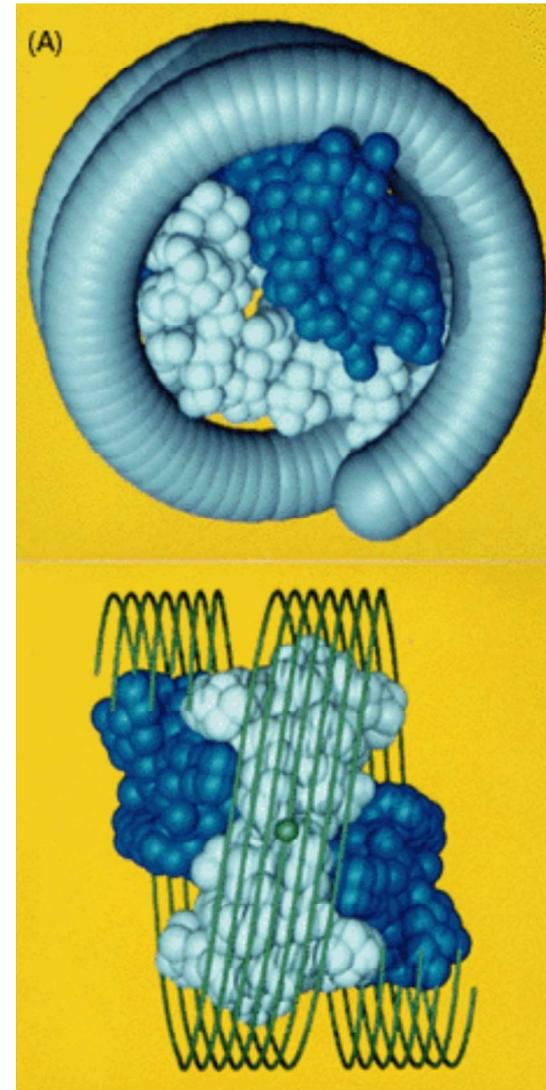
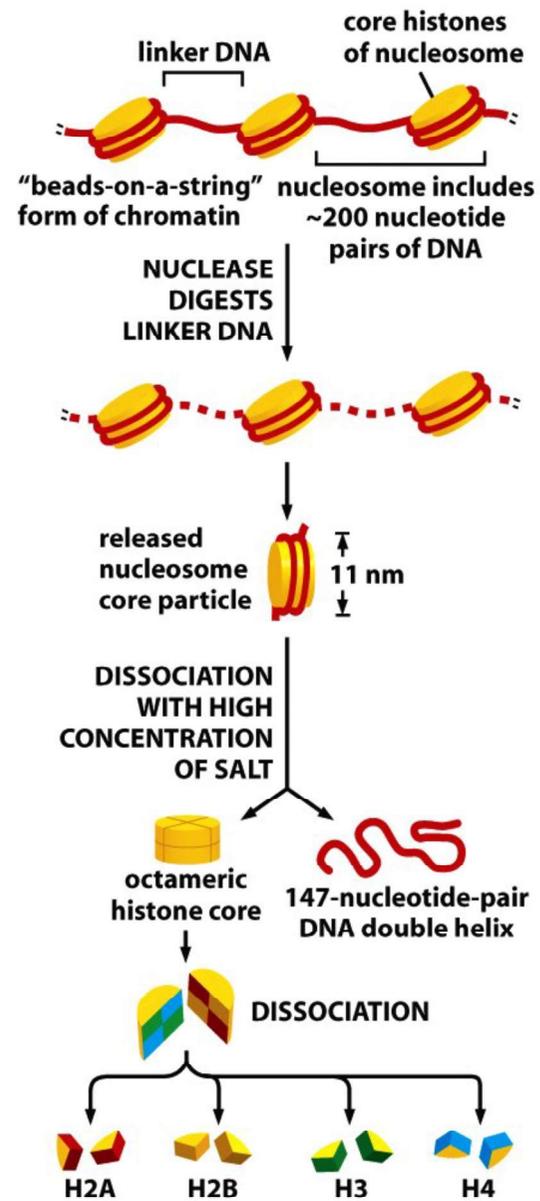
50 nm

La cromatina en cromosomas mitóticos

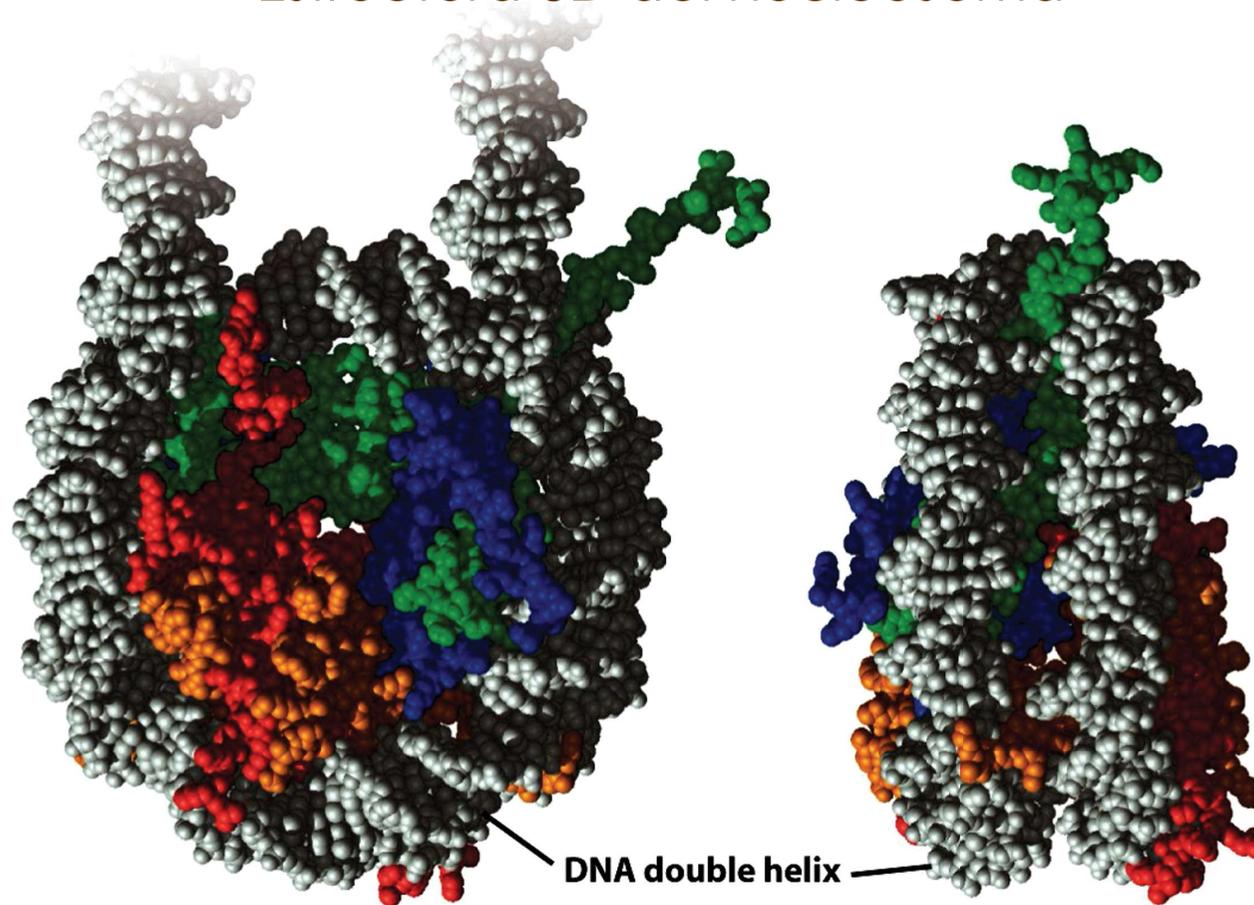


NET RESULT: EACH DNA MOLECULE HAS BEEN PACKAGED INTO A MITOTIC CHROMOSOME THAT IS 10,000-FOLD SHORTER THAN ITS EXTENDED LENGTH

Cromatina y nucleosomas



Estructura 3D del nucleosoma

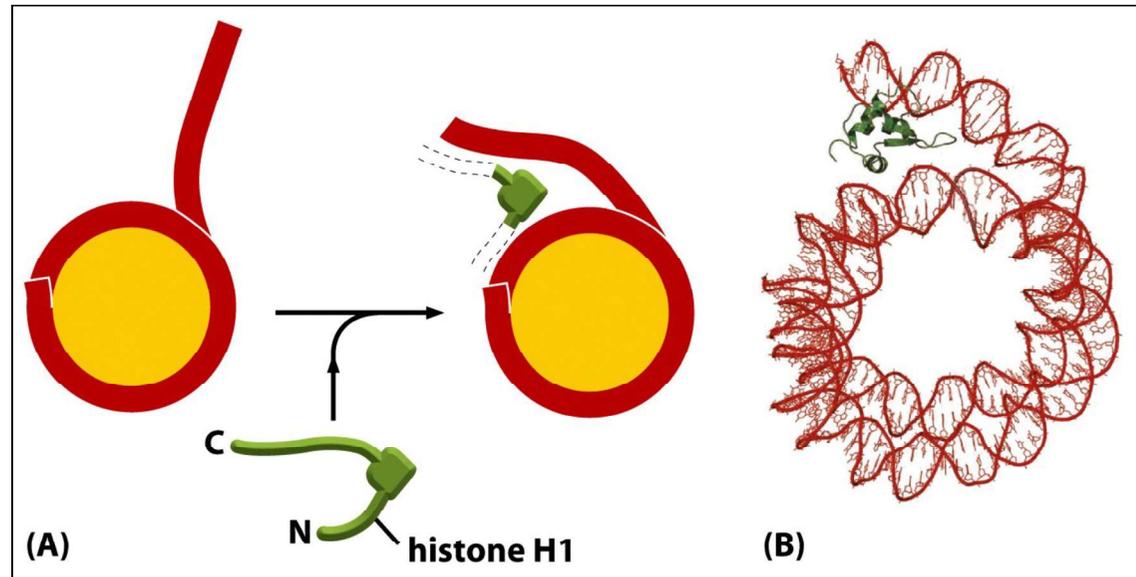
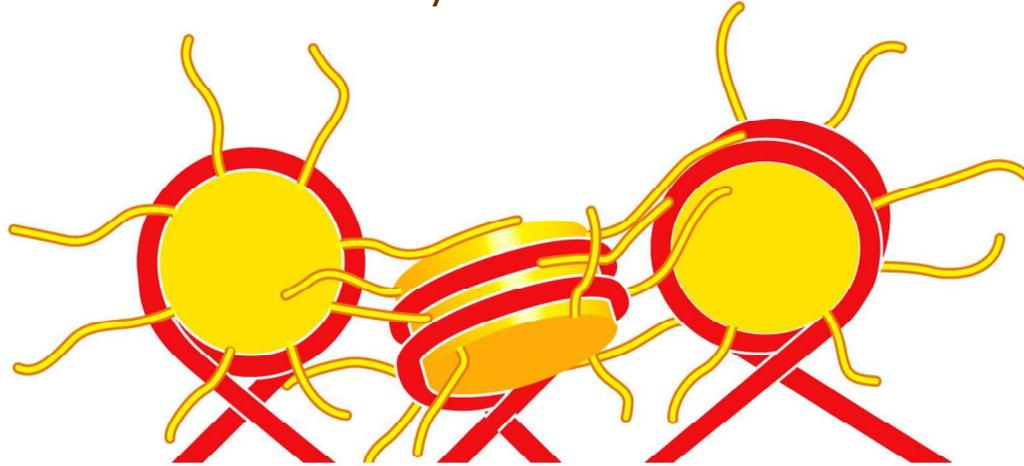


side view

bottom view

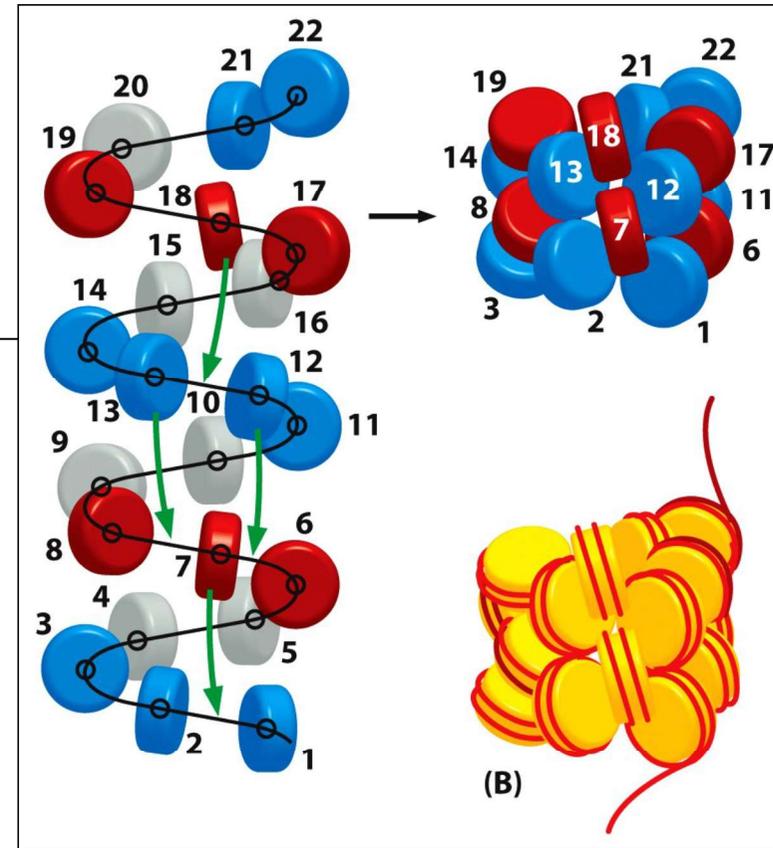
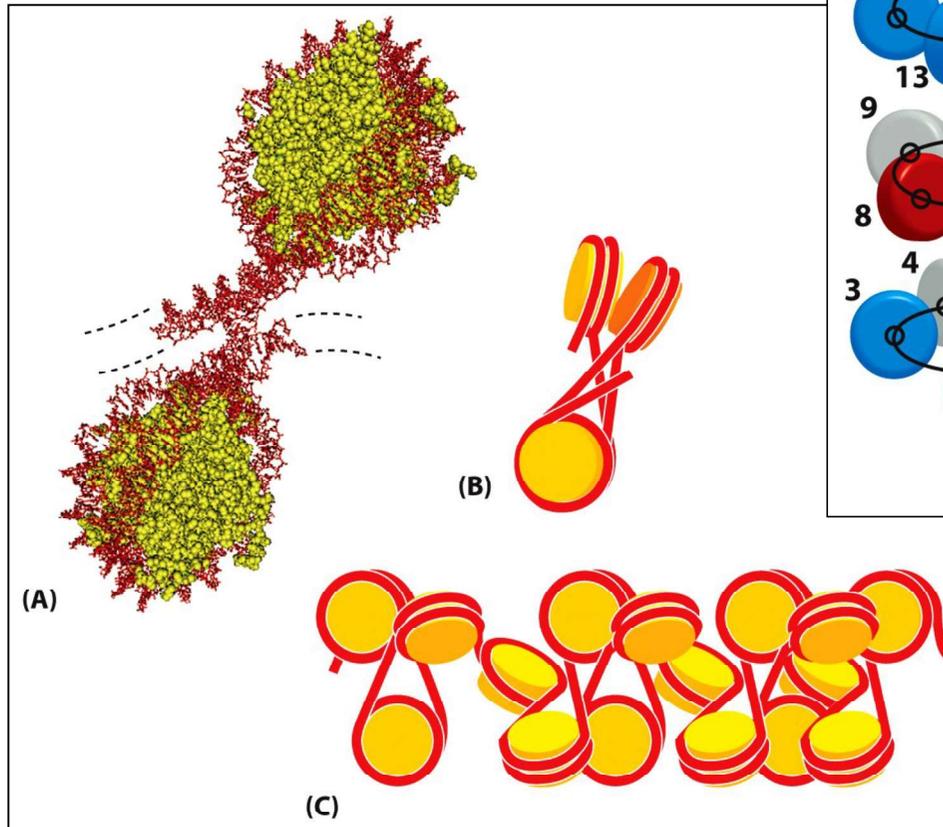
● histone H2A ● histone H2B ● histone H3 ● histone H4

Histonas y estructura de la cromatina

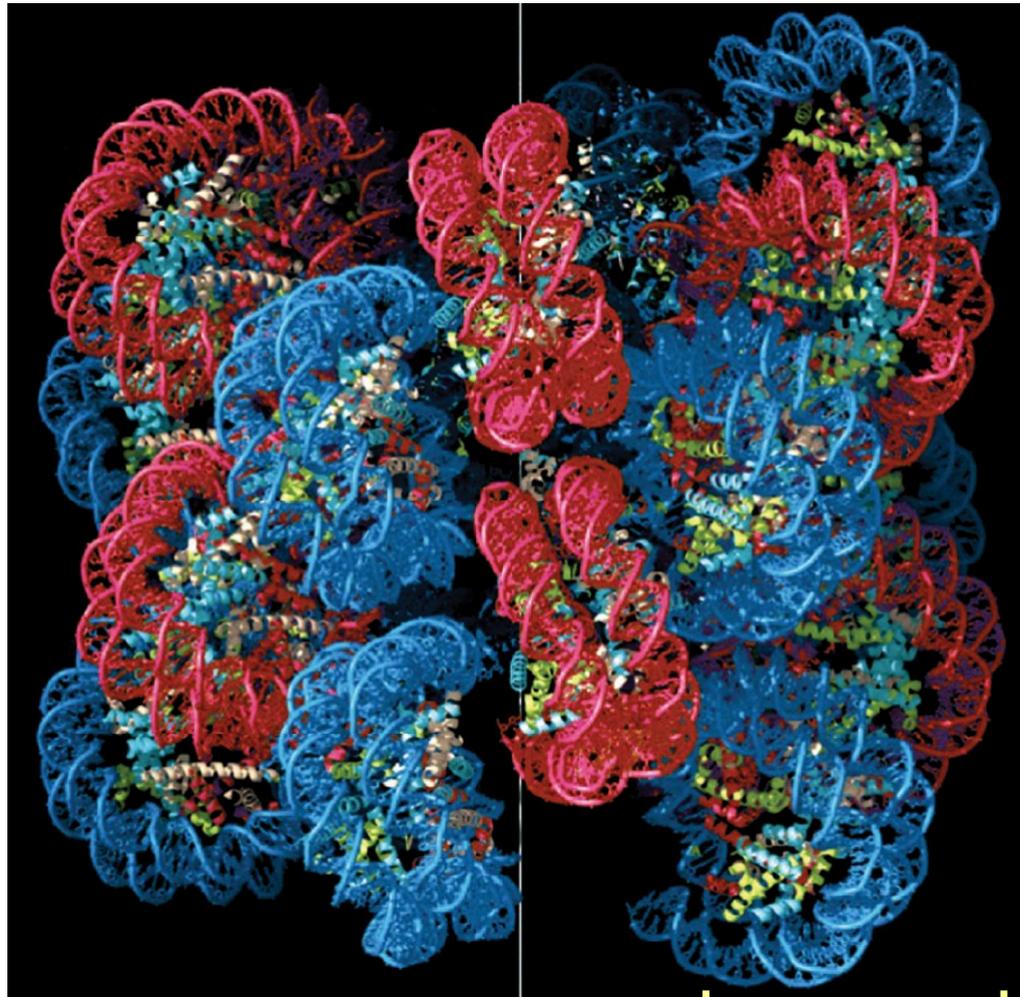


Modelos de estructura de la cromatina

“Zig-zag”



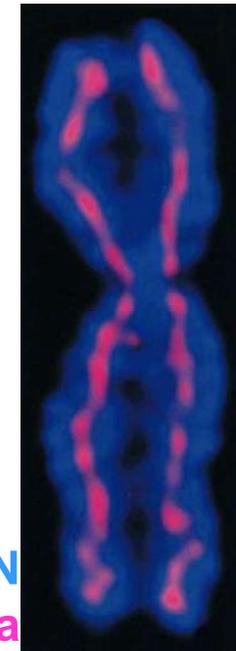
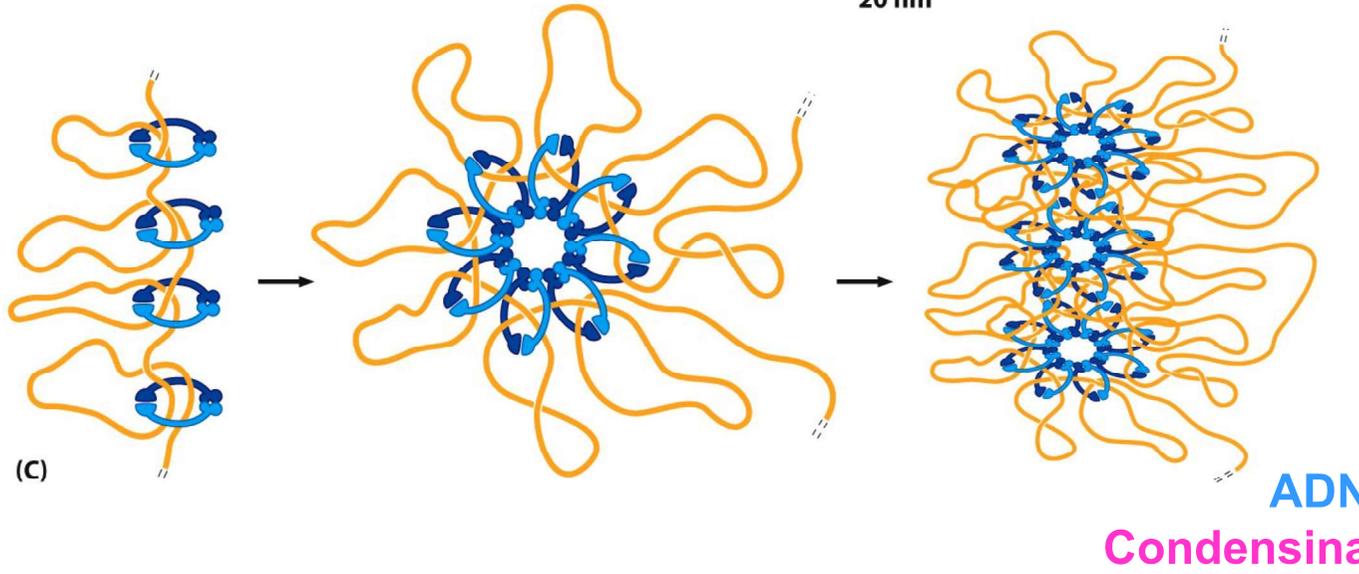
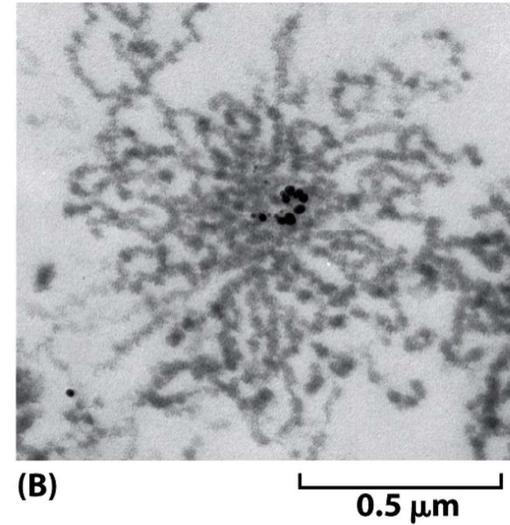
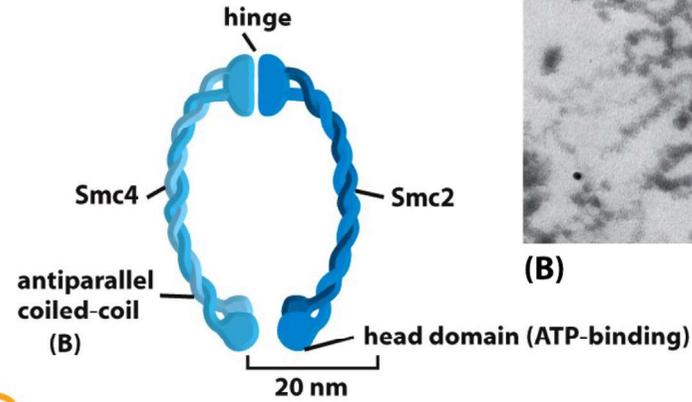
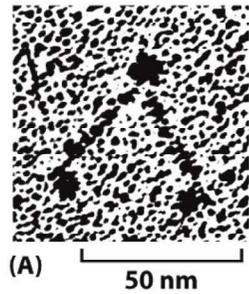
“Solenoid”



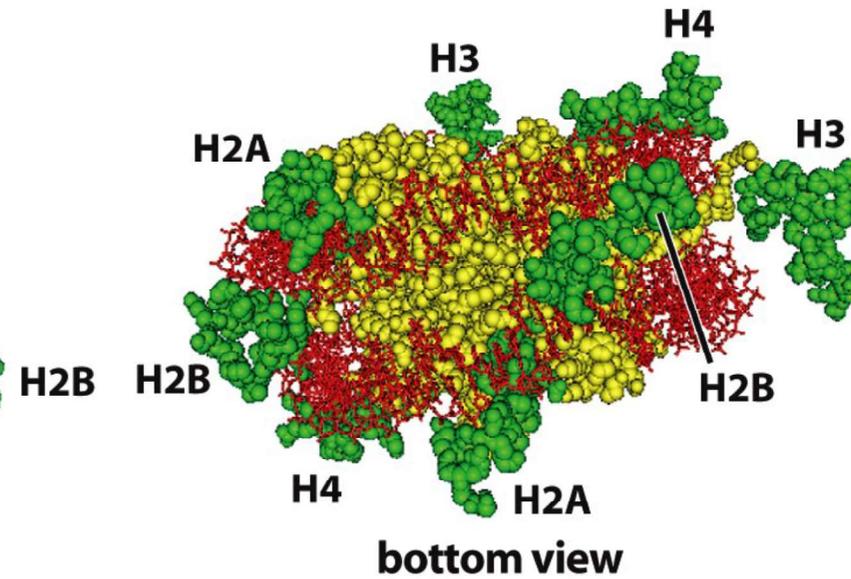
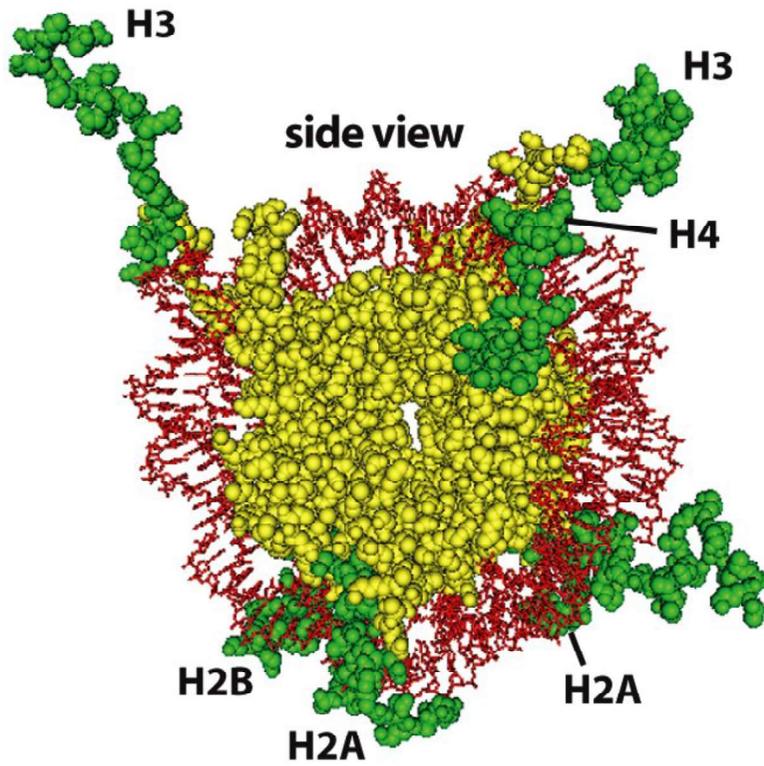
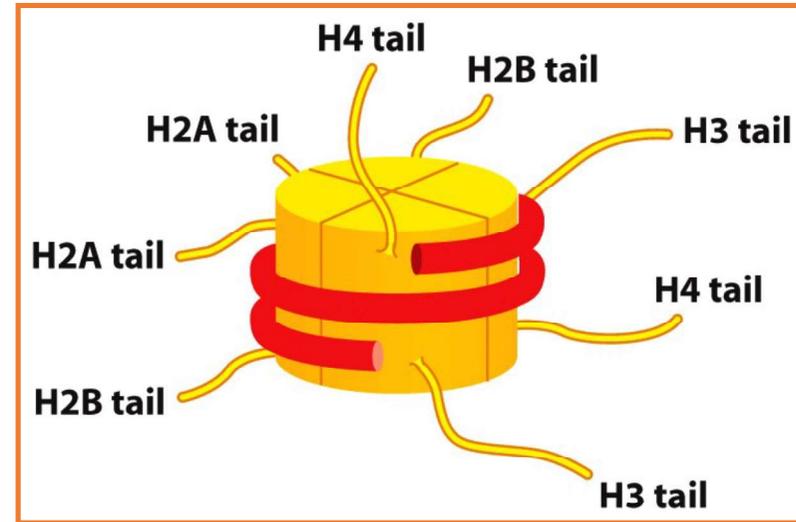
30 nm

10 nm

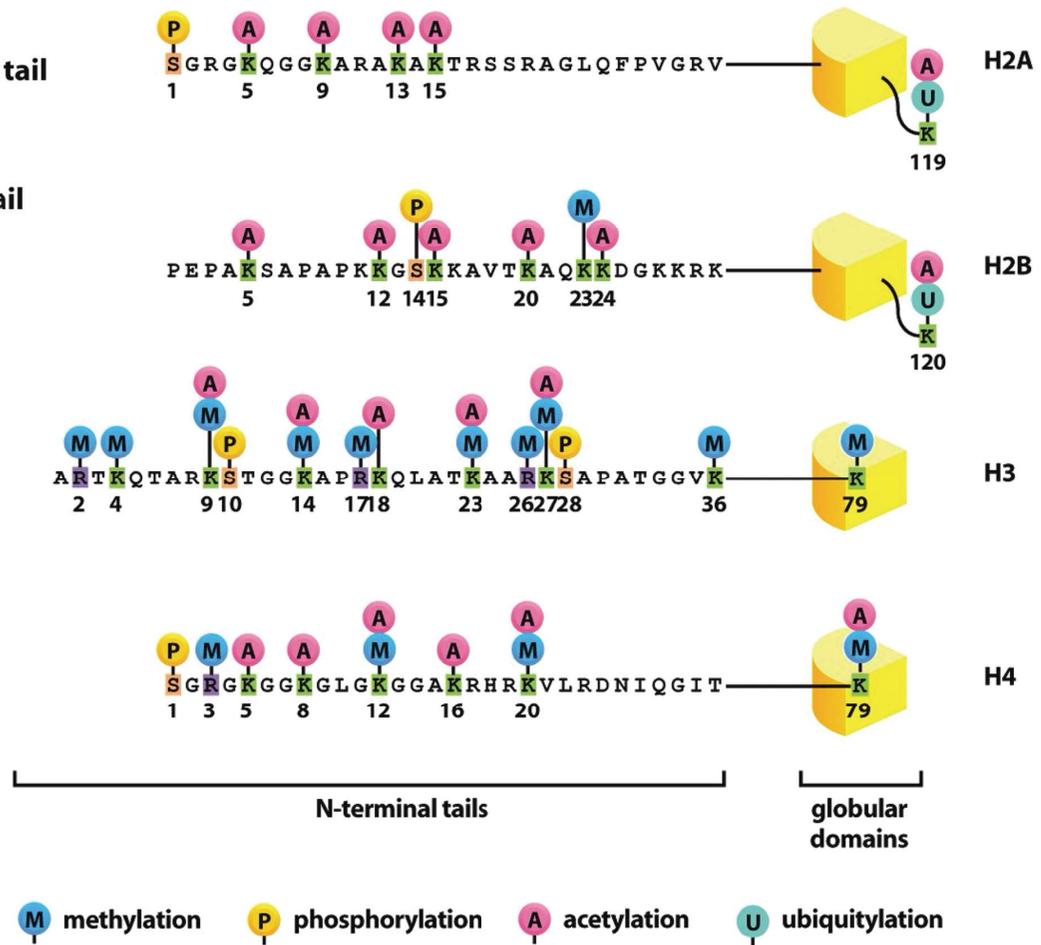
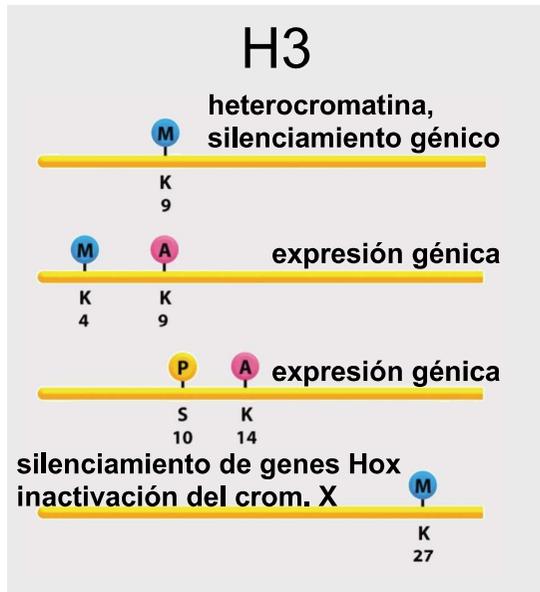
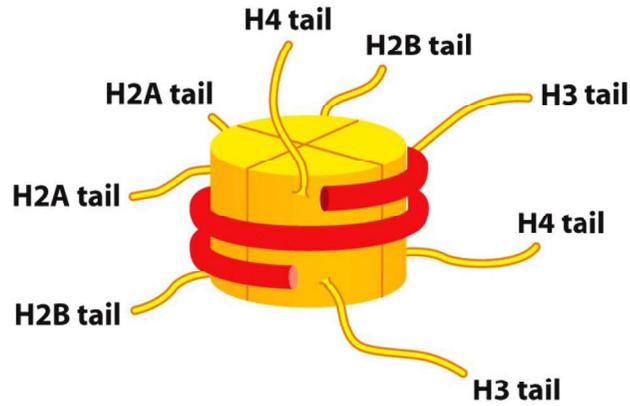
Cohesinas y ensamblado del cromosoma mitótico



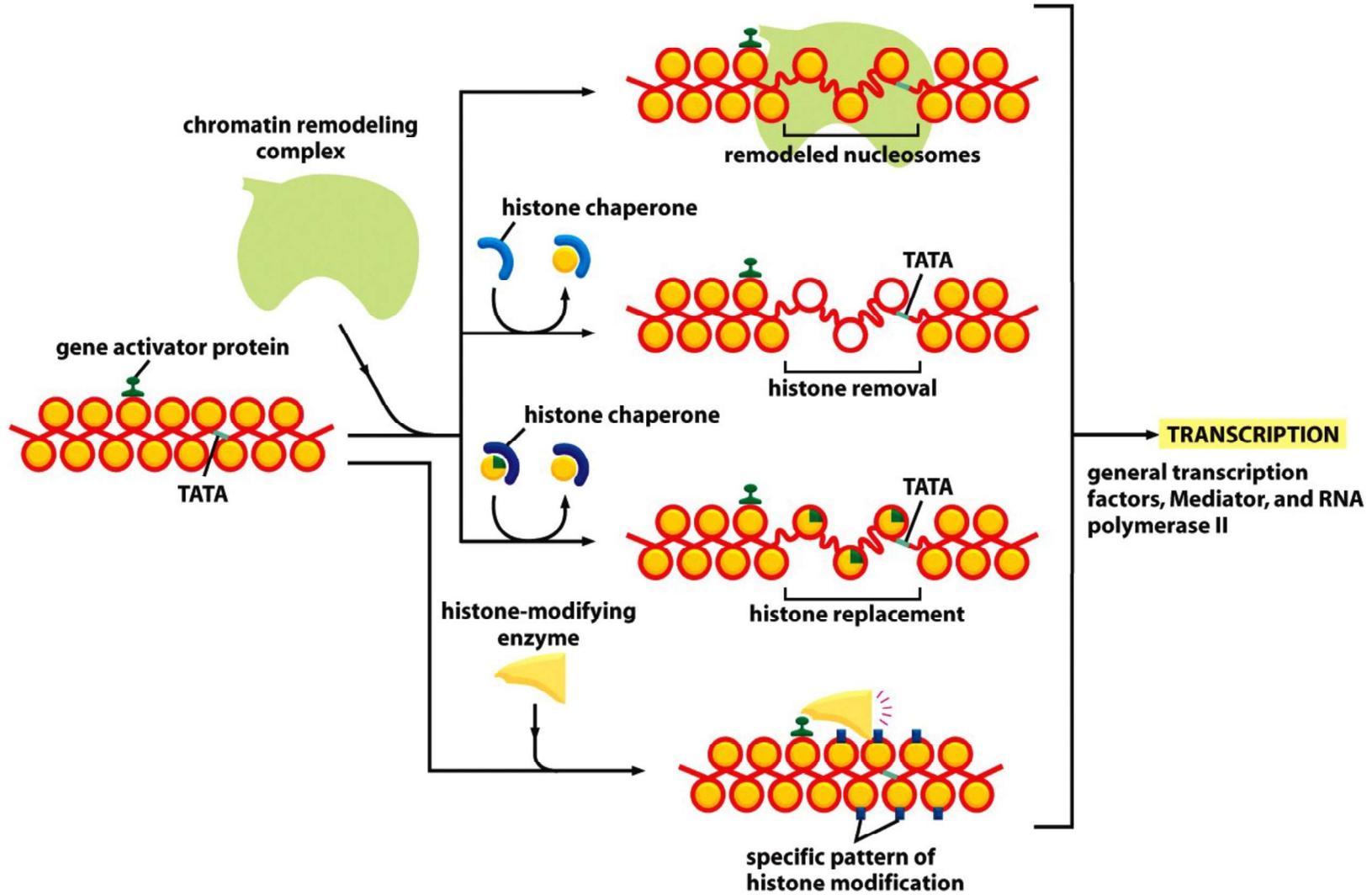
Histonas y ensamblado del nucleosoma



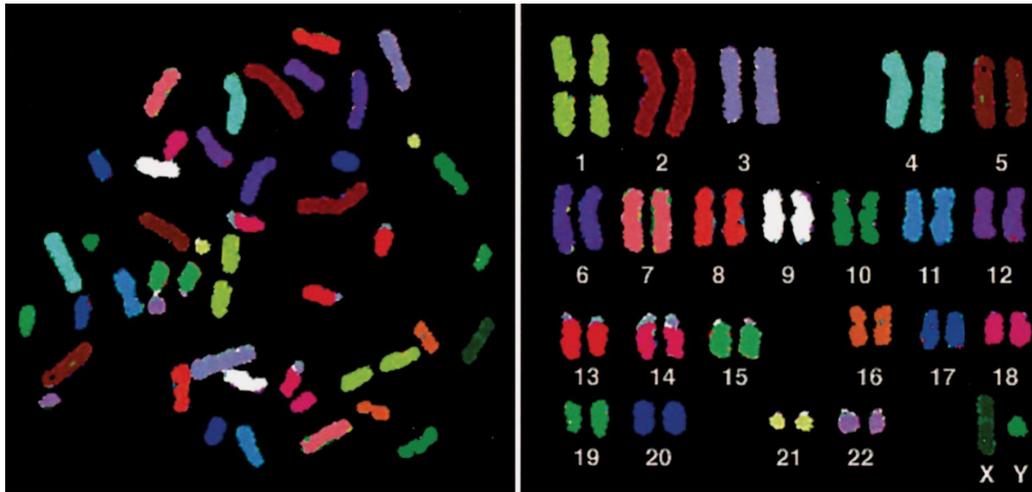
Modificaciones post-traduccionales de histonas



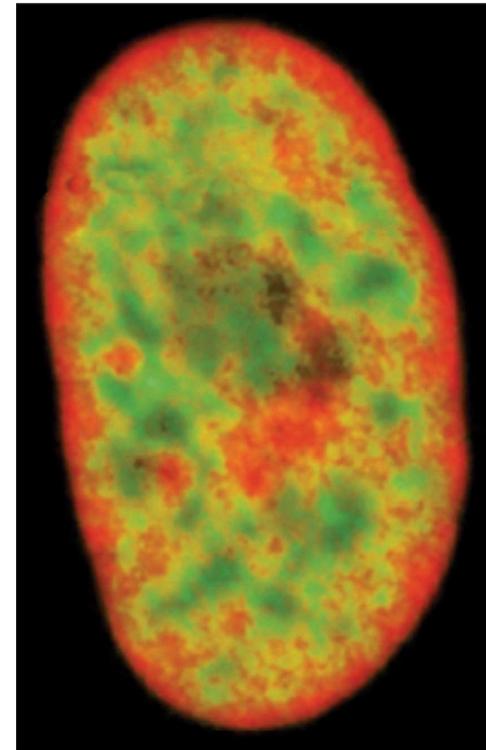
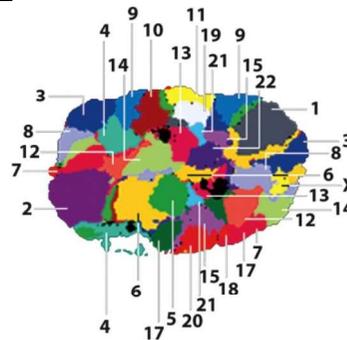
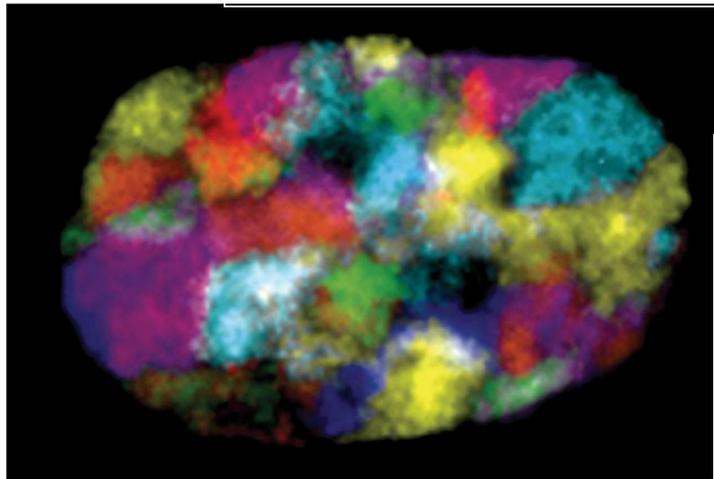
Cromatina y expresión génica



Organización del núcleo



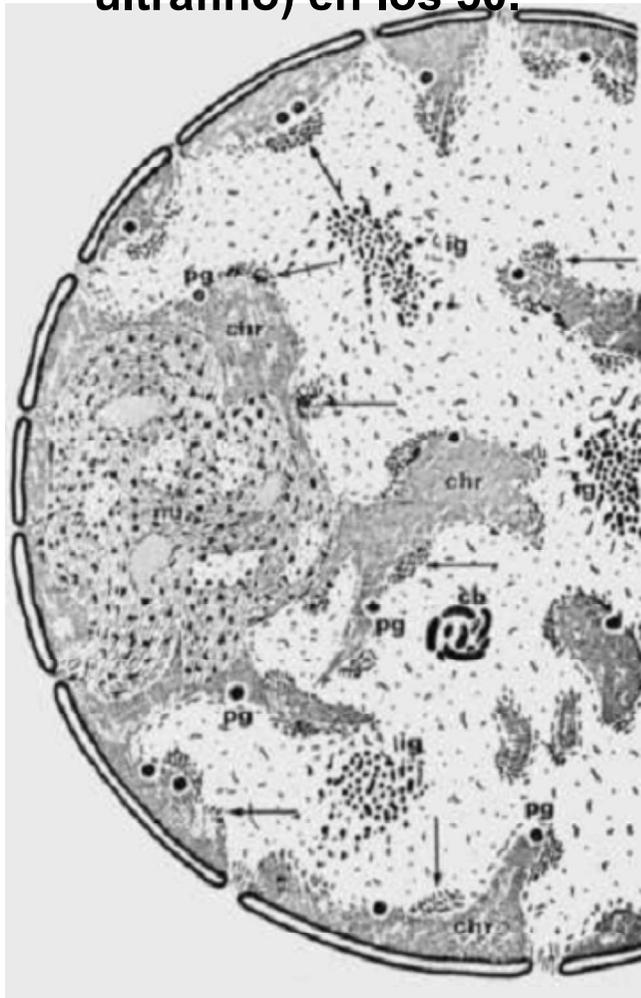
Chromosome painting”



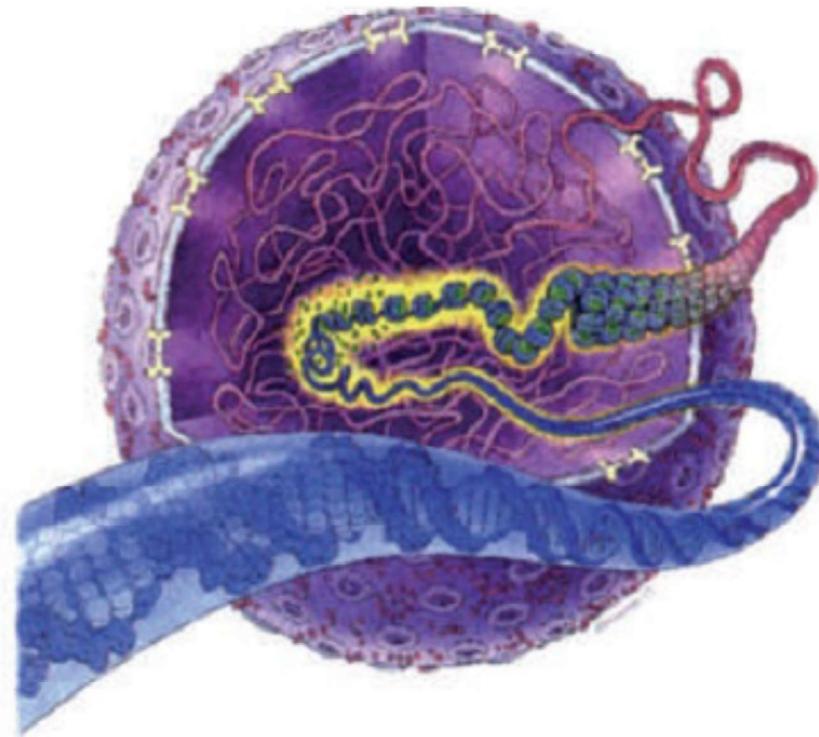
Muchos genes
Algunos genes
Pocos genes

Territorios cromosómicos.

**Microscopía electrónica de
transmisión
del núcleo celular (corte
ultrafino) en los 50.**



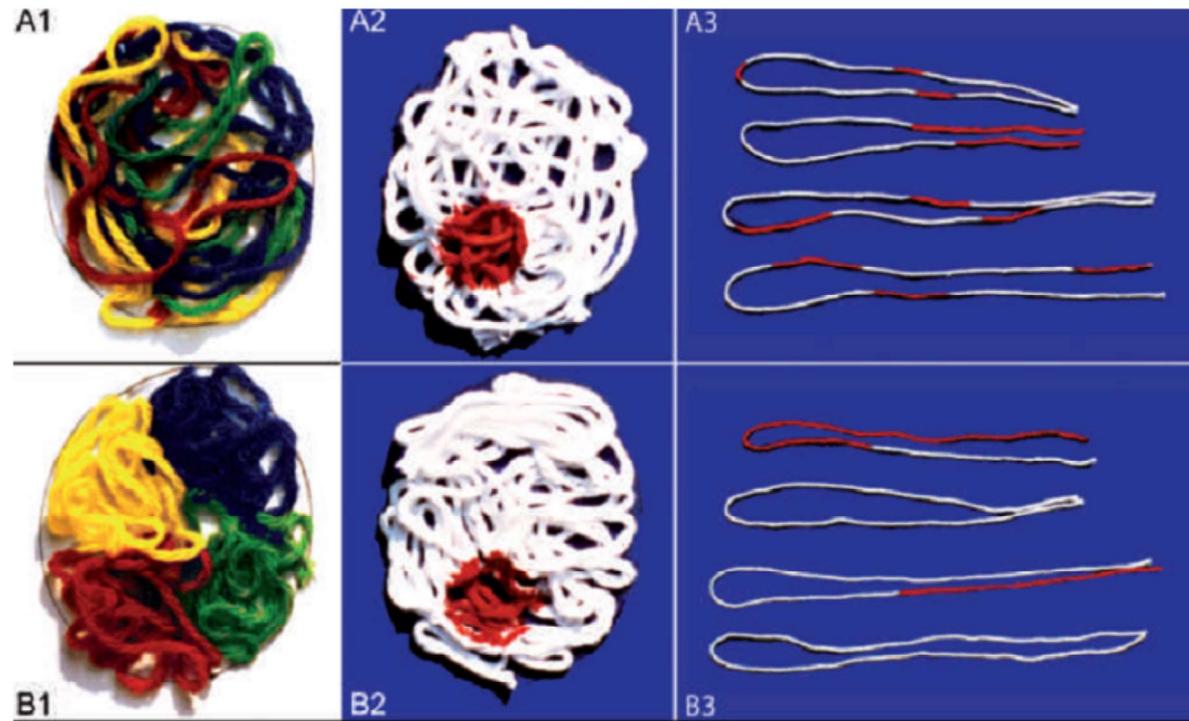
**Esquema de organización
nuclear (década del 90')**



“During the 1970s and 80ies most researchers seemed to be content with the assumption that the nucleus is filled with intermingling chromatin fibers and loops like a dish of spaghetti, an assumption widely reflected by textbooks of cell biology”.
Extraído de Cremer y Cremer (Cold Spring Harb Perspect Biol 2010; doi: 10.1101/cshperspect.a003889)

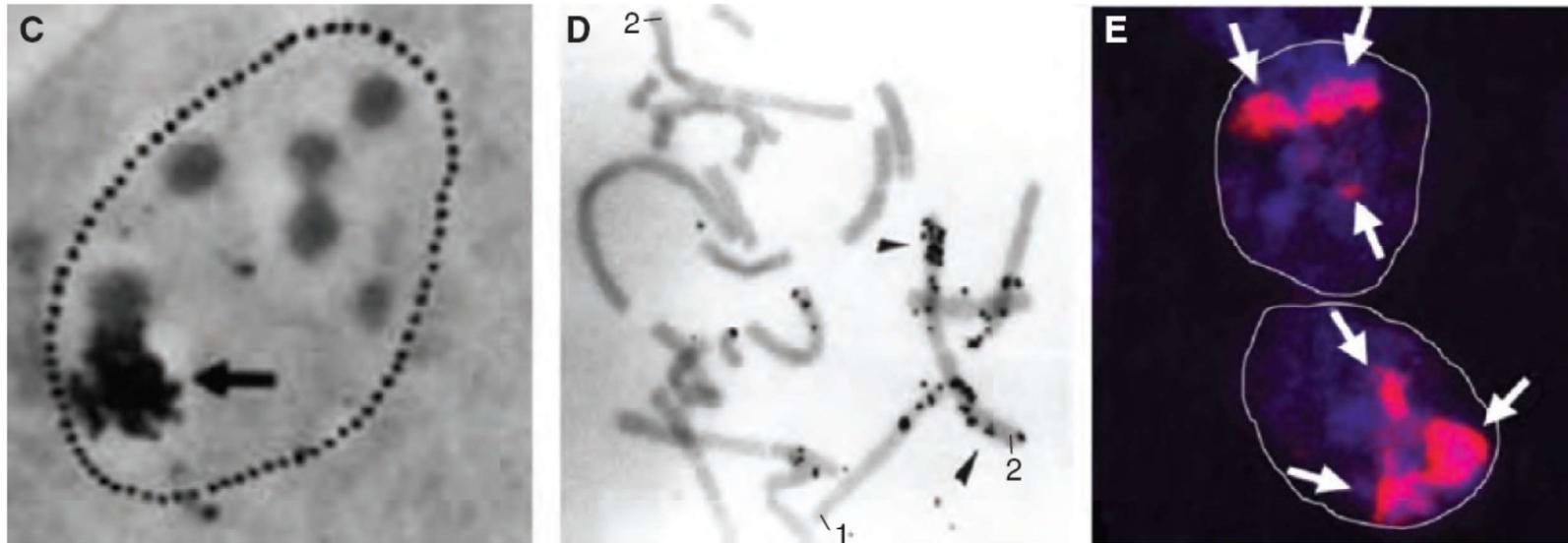


Experimentos de microirradiación de núcleos (Cremer, 1983)



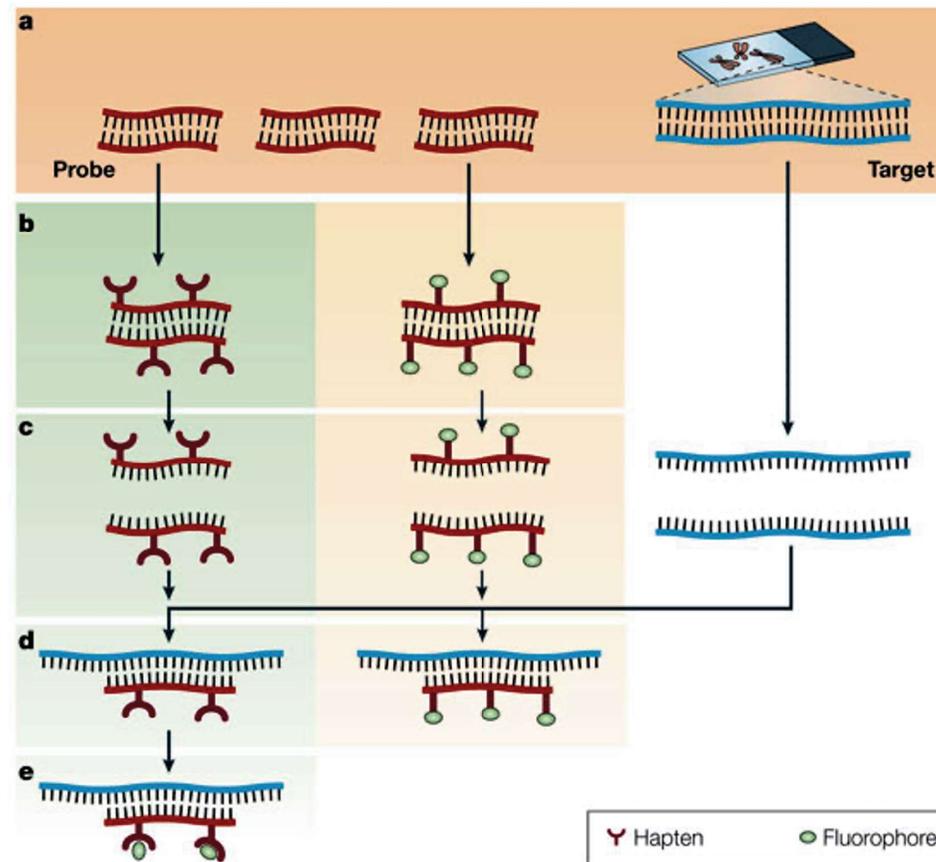
Extraído de Cremer y Cremer 2010

Experimentos de microirradiación de núcleos (Cremer, 1983)



Primeras evidencias experimentales de la existencia de territorios cromosómicos en el núcleo interfásico

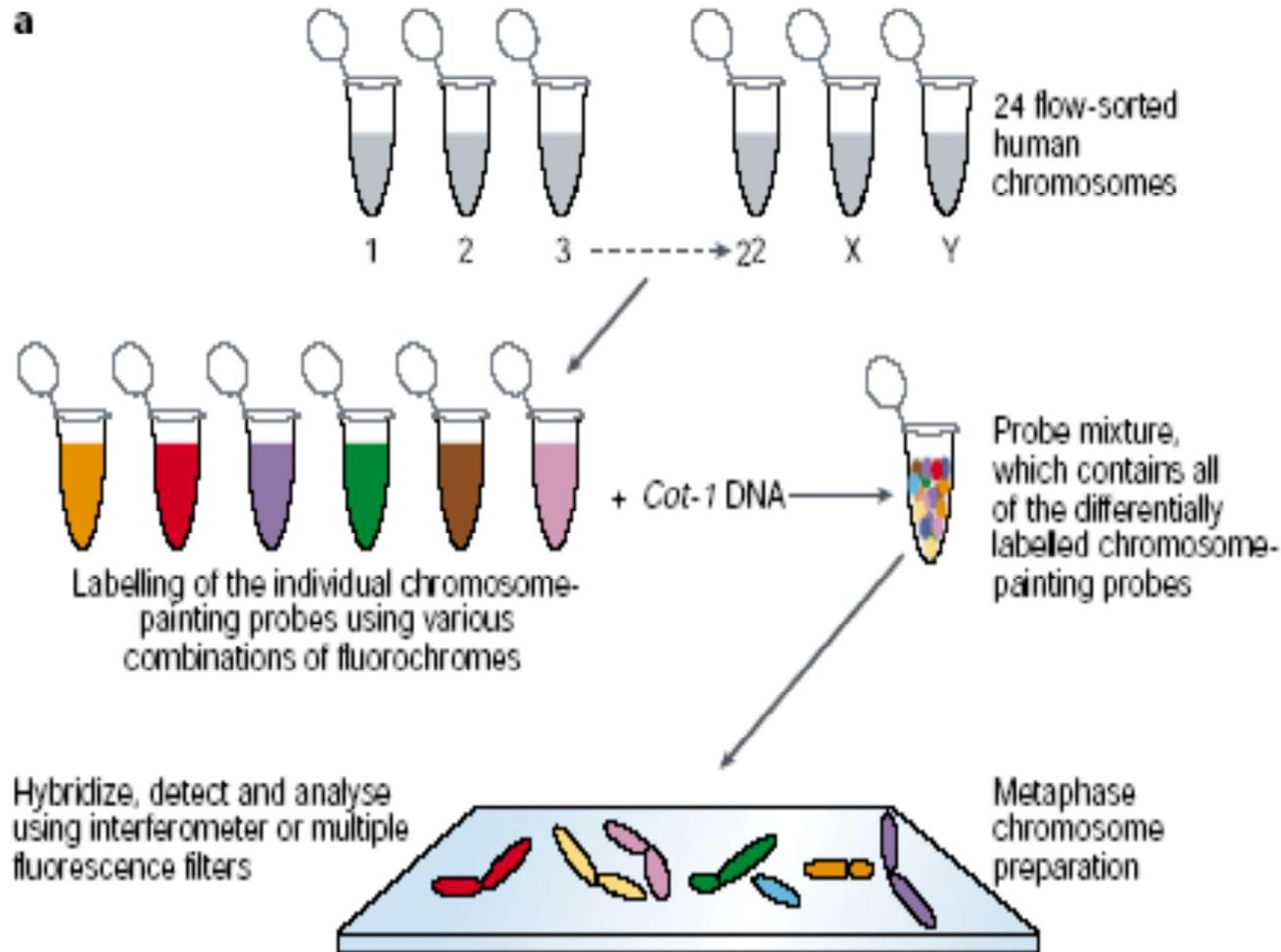
Hibridización in situ fluorescente (Fluorescence in situ hybridization, FISH)



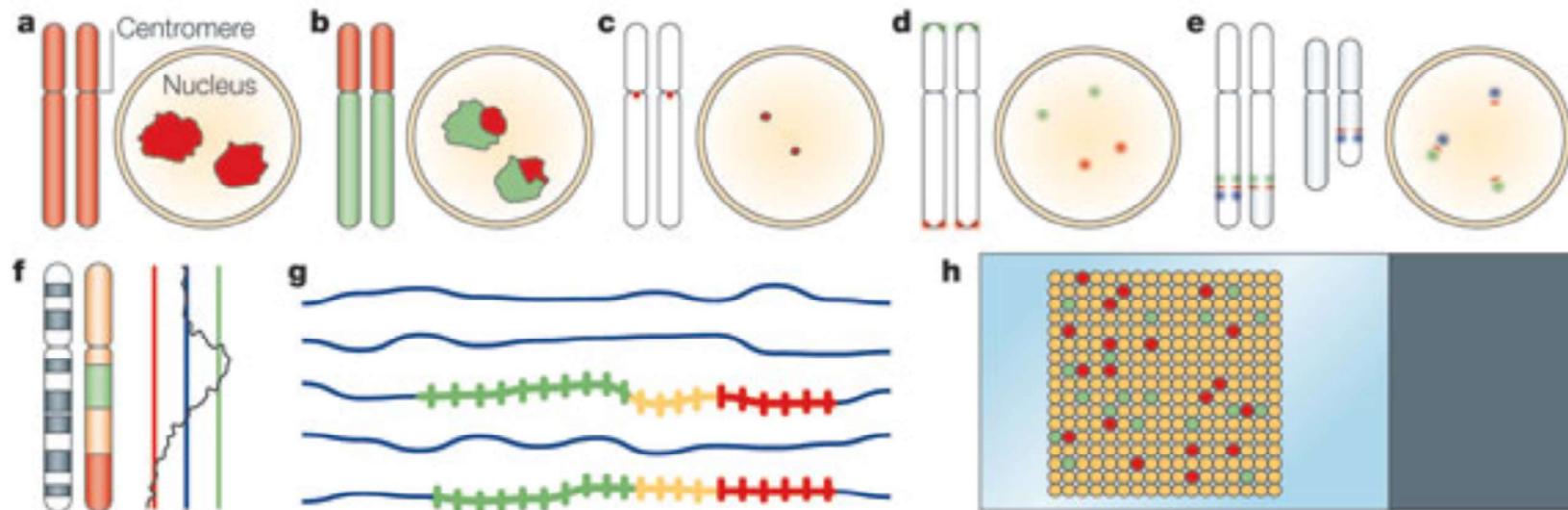
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Nature Reviews | Genetics

Speicher & Carter (2005) Nature Rev Genet 6:782]

Pintura de cromosomas específicos (Chromosome-specific paints) for FISH



Pintura de cromosomas específicos (Chromosome-specific paints) for FISH



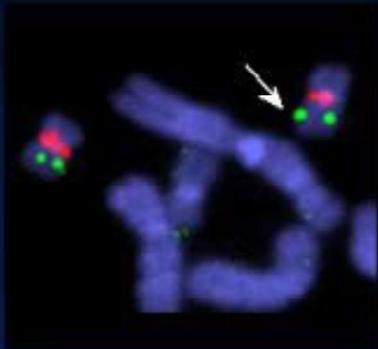
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Nature Reviews | **Genetics**

Microscopia de Barrido Laser Confocal y tratamiento de imágenes logran una visión y localización tridimensional de alta precisión

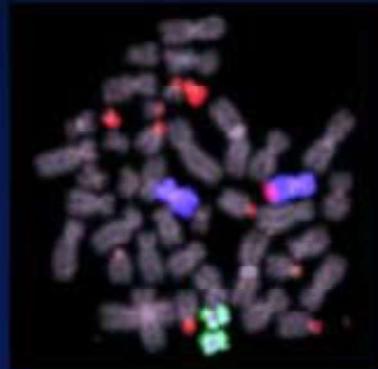
Speicher & Carter (2005) Nature Rev Genet 6:782

Fluorescence *In Situ* Hybridisation (FISH)

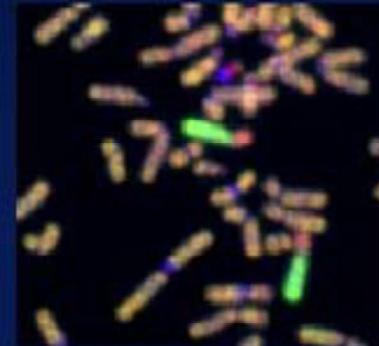
Small DNA clones



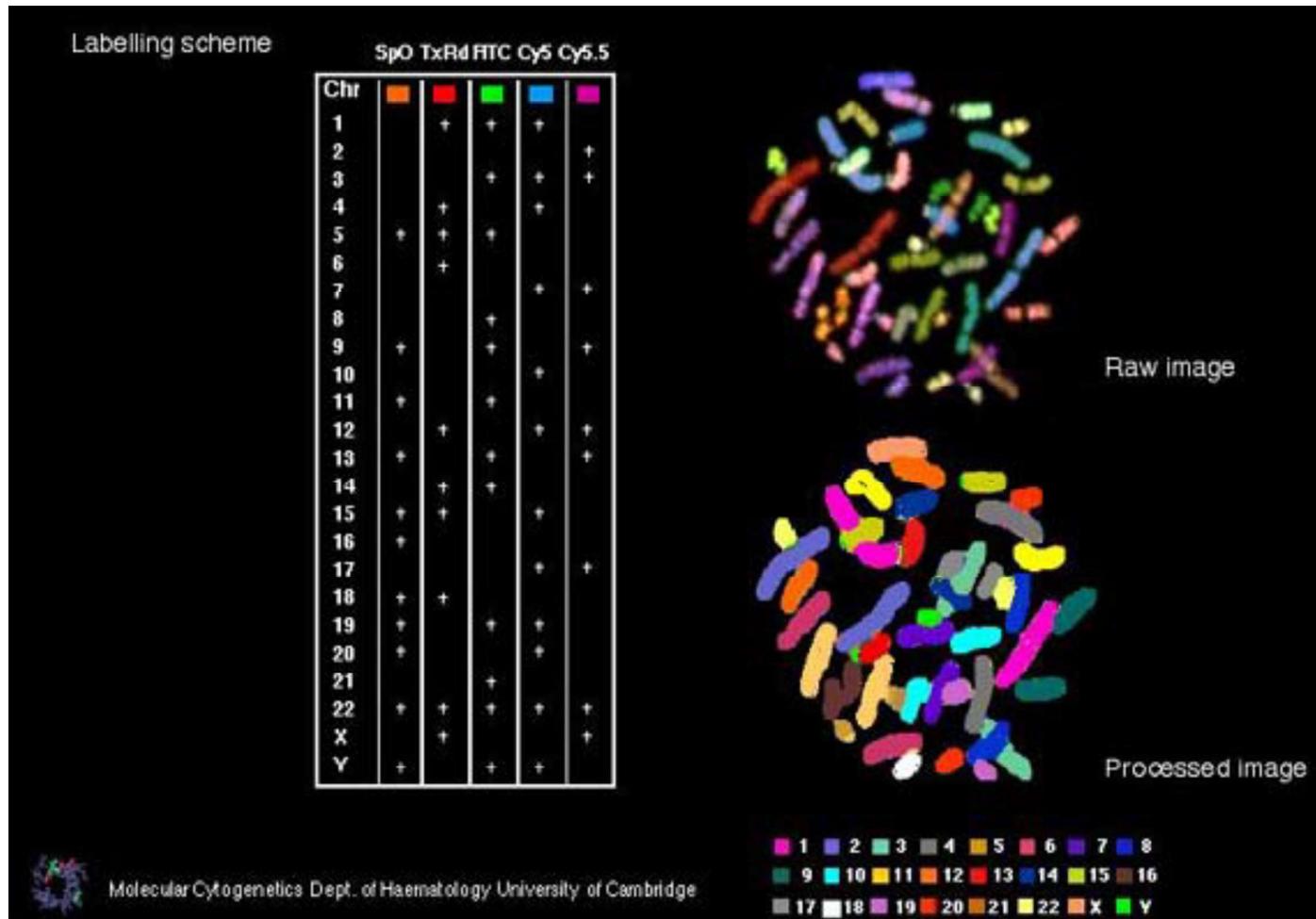
Repetitive sequences



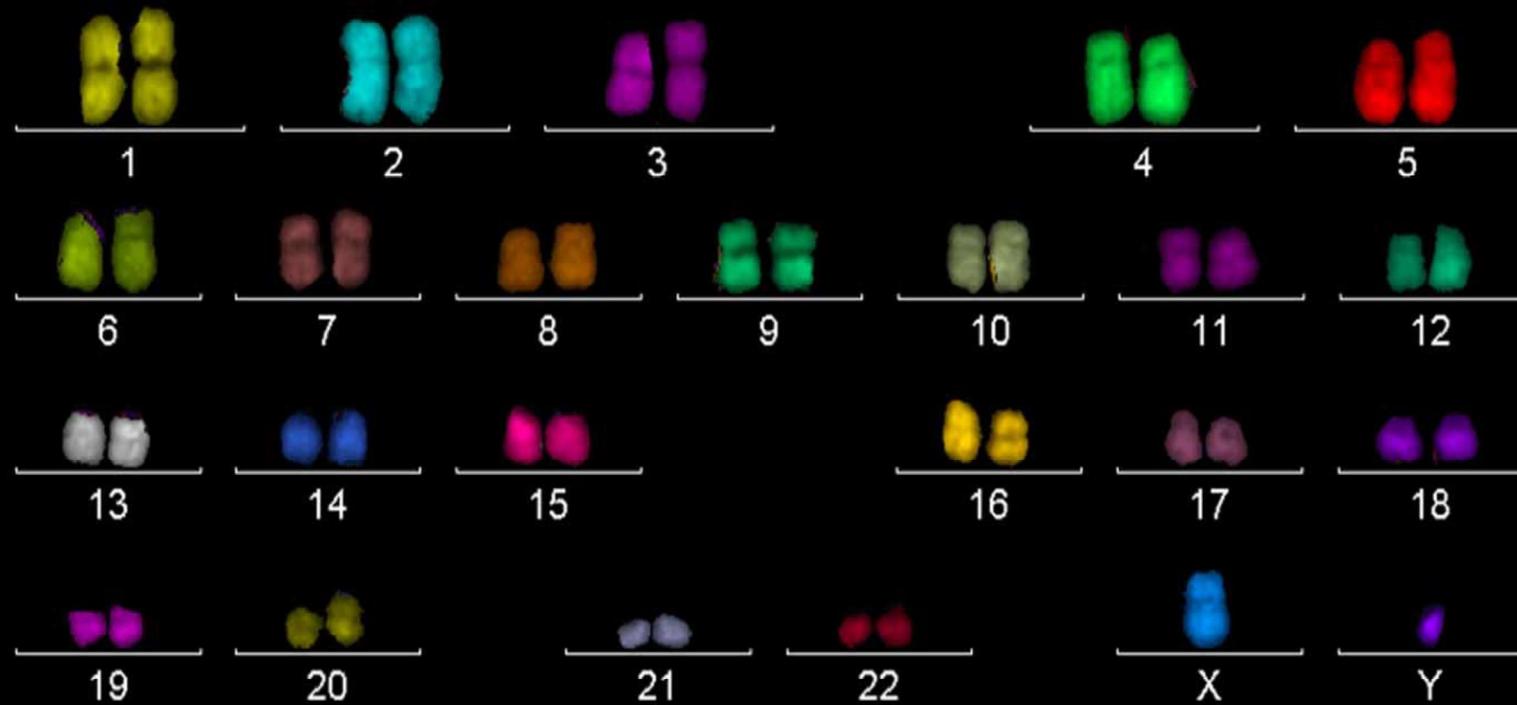
Total genomic DNA



(FISH) – Metaphase chromosome painting

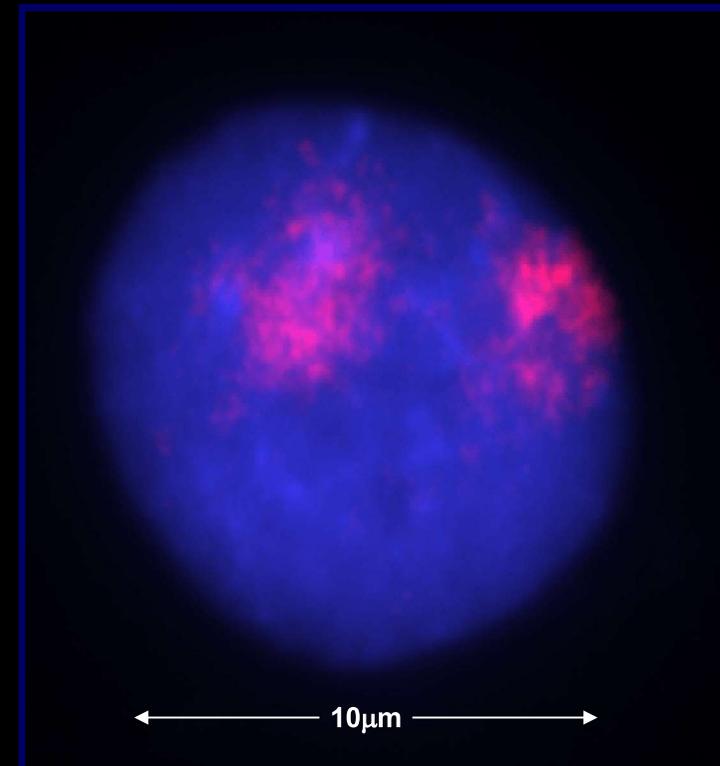


Cromosomas humanos: FISH multicolor

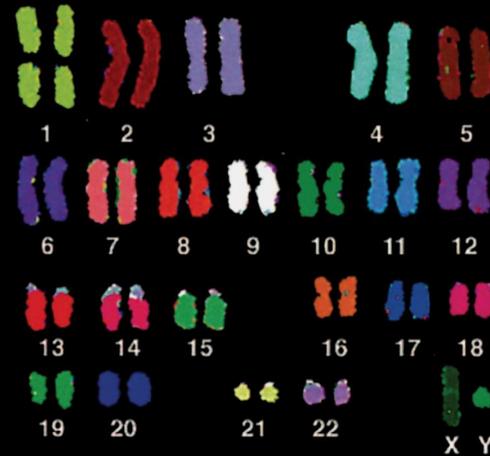


Territorios Cromosómicos (TCs)

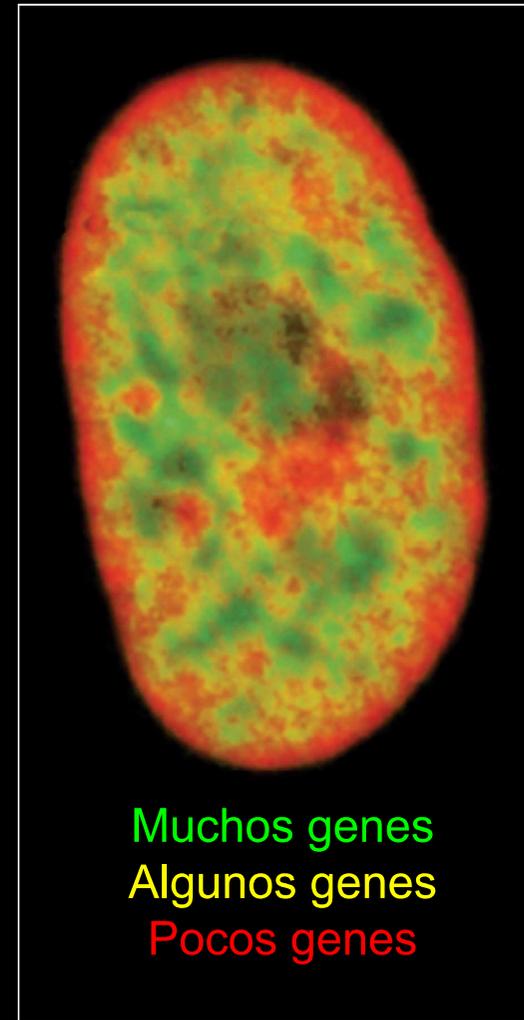
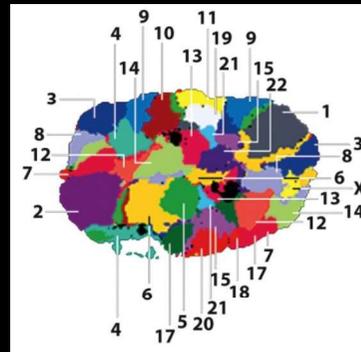
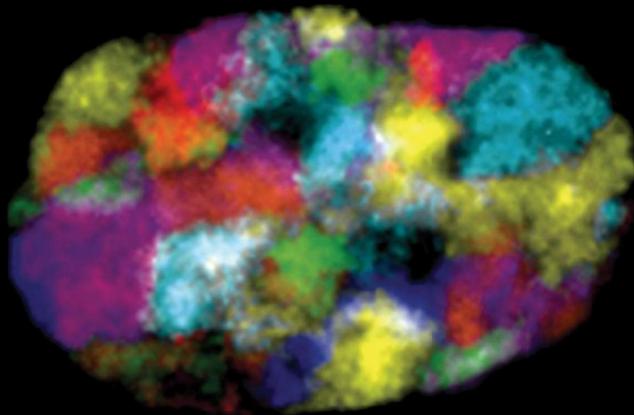
La técnica de FISH utilizando sondas para detectar todo el cromosoma (WCP) revelaron que el núcleo eucariótico posee un elevado nivel de organización. El volumen nuclear se halla compartimentado en territorios cromosómicos (TCs) tridimensionales discretos y no superpuestos.



Organización del núcleo

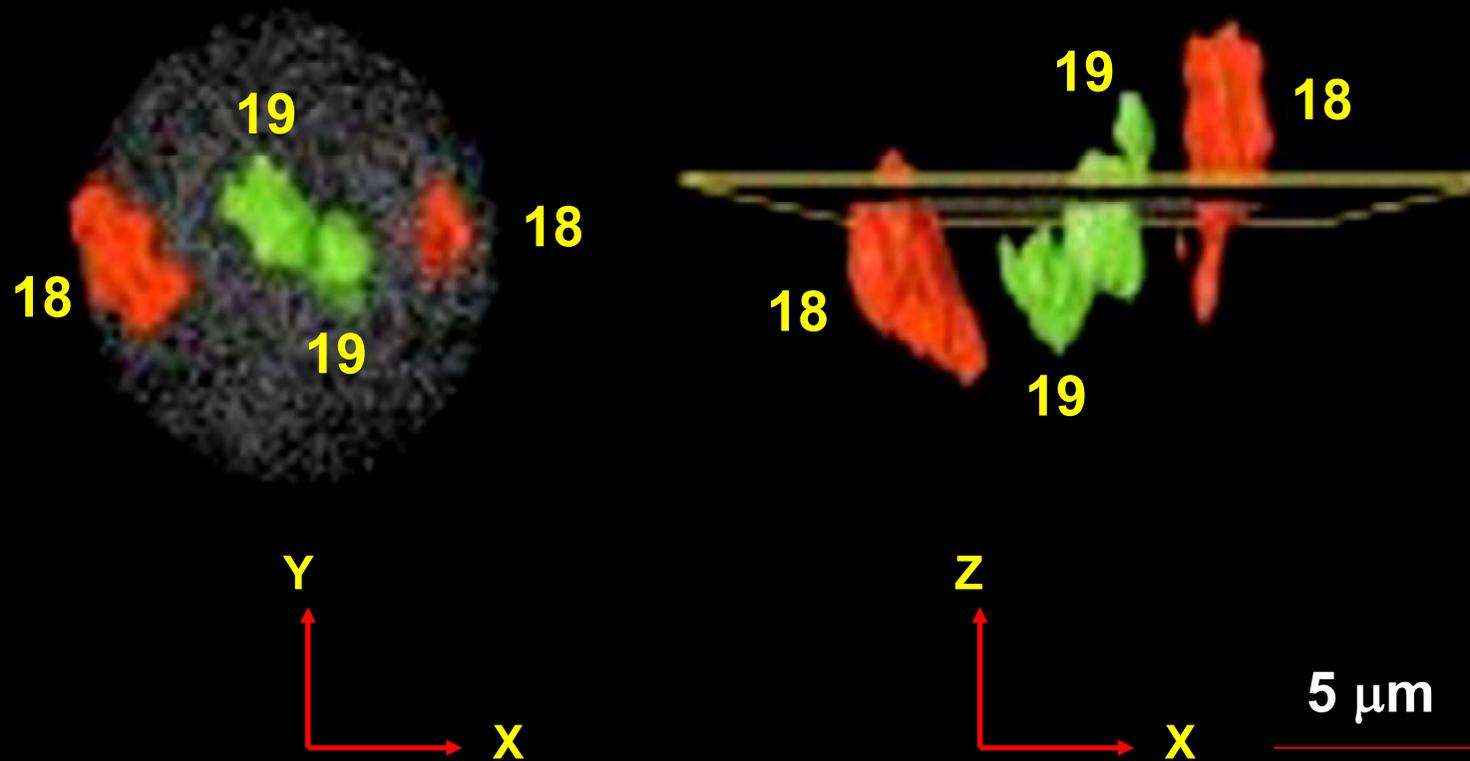


“Chromosome painting”

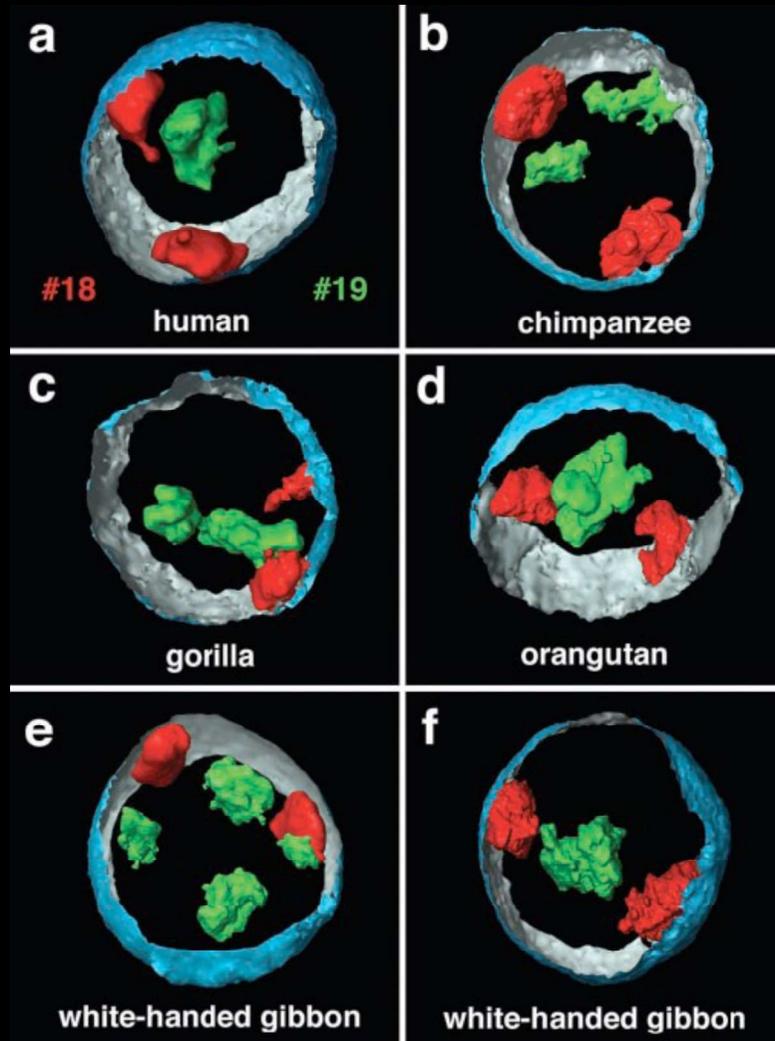


Muchos genes
Algunos genes
Pocos genes

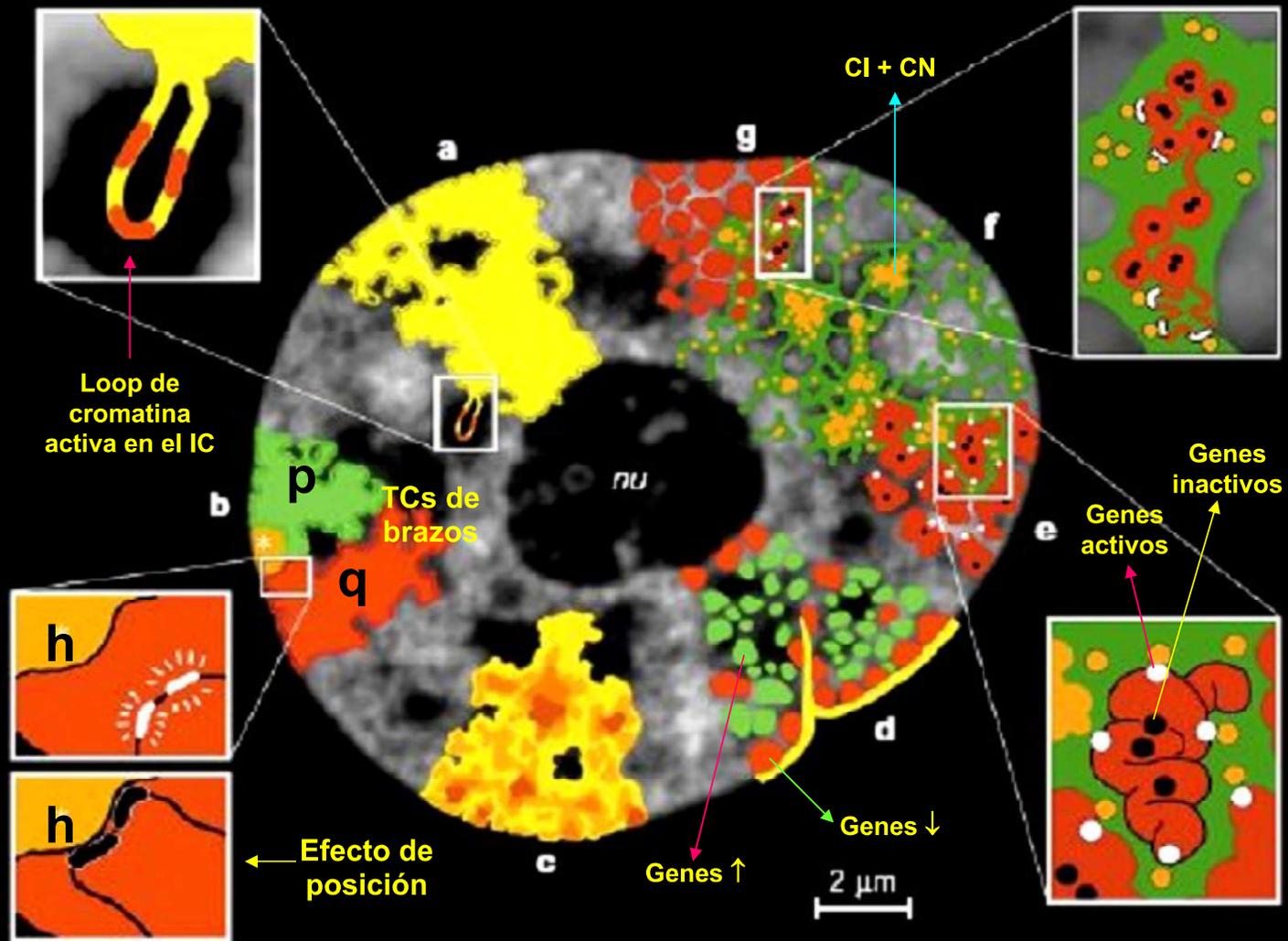
Topología nuclear de cromosomas ricos (19) y pobres (18) en genes



Territorios cromosómicos y evolución

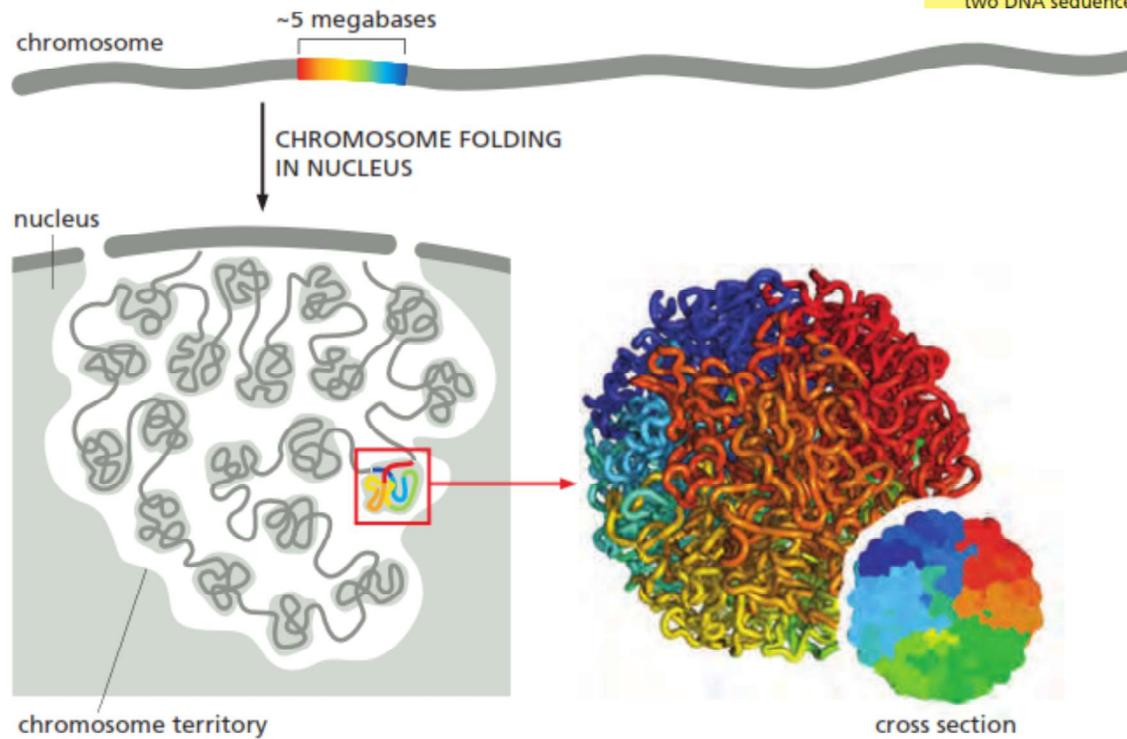
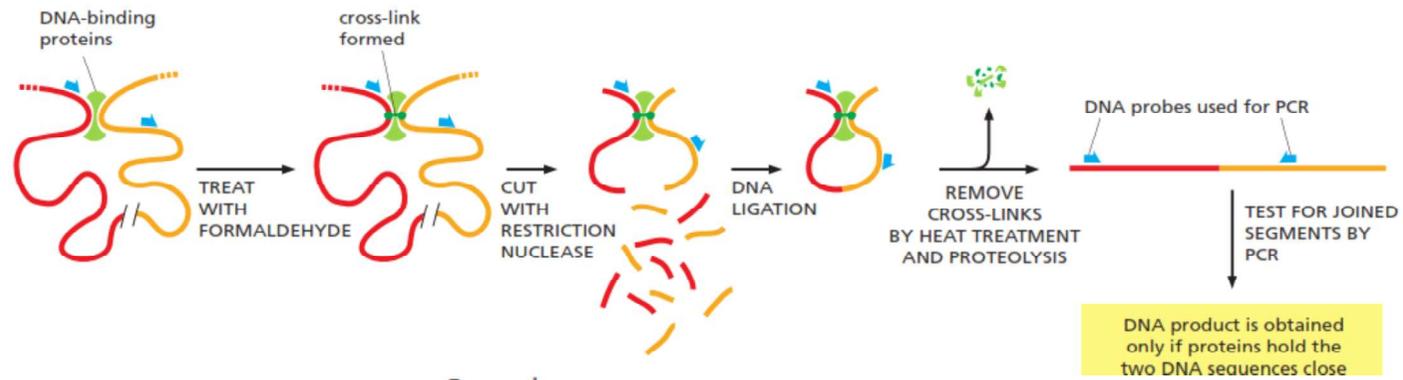


Modelo TC/IC

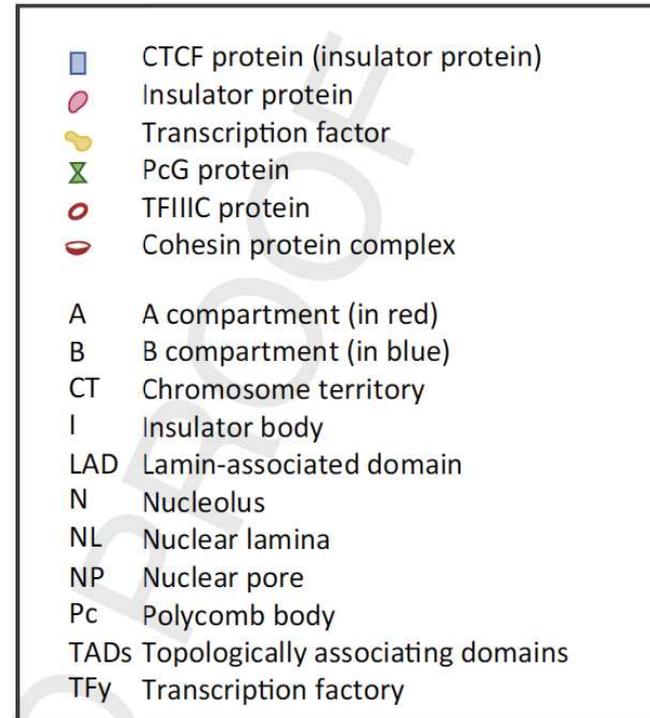
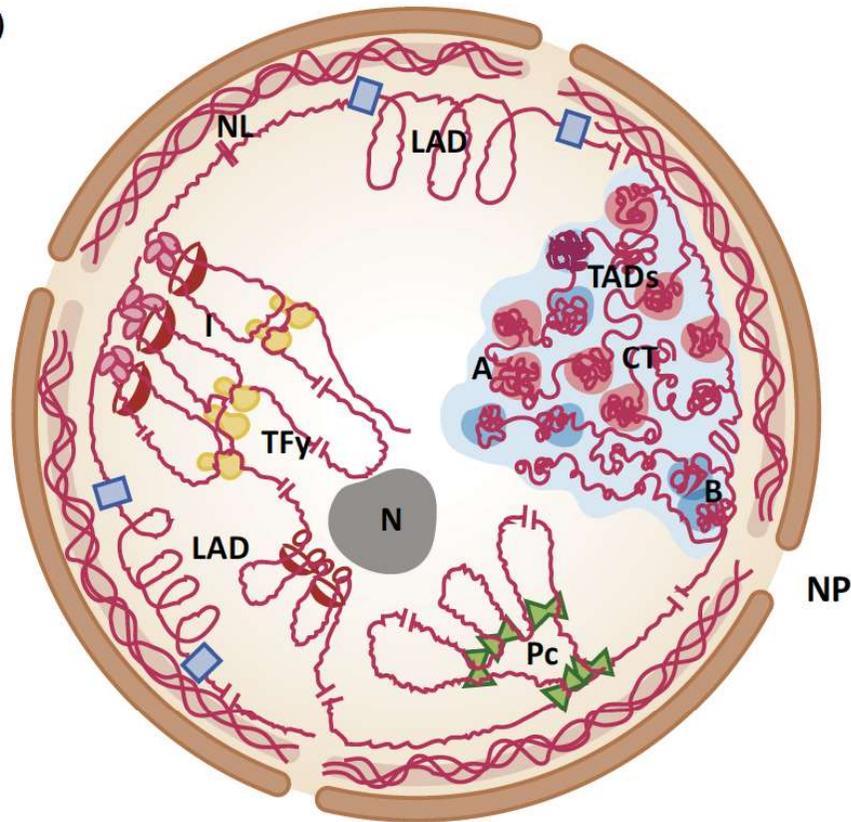


Cremer y Cremer (2001) *Nat Rev Genet* 2: 292-301 (modificado)

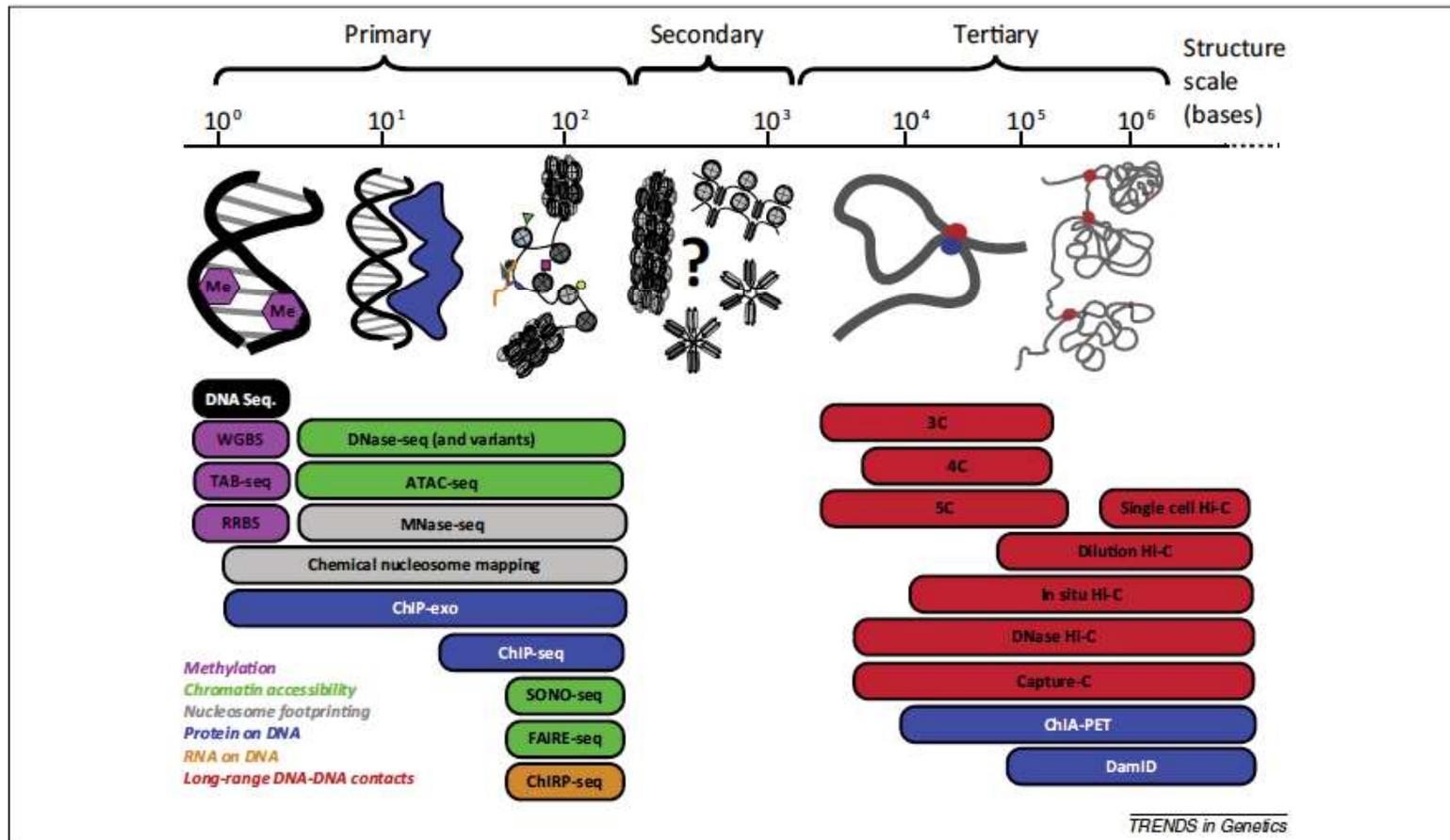
Captura de la conformación de la cromatina: secuenciando para comprender estructura

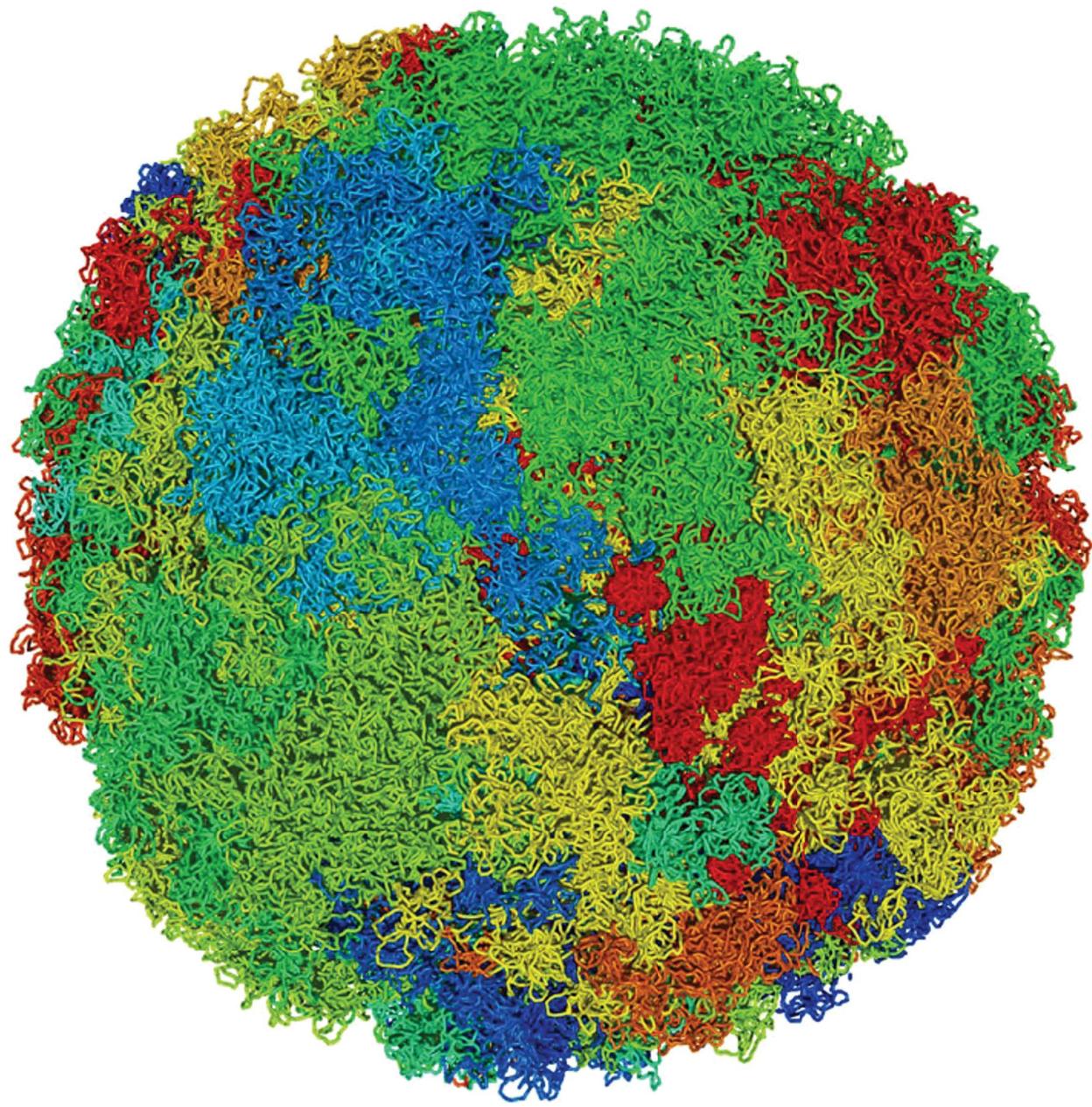


(A)



Diferentes escalas estructurales y diferentes métodos de análisis

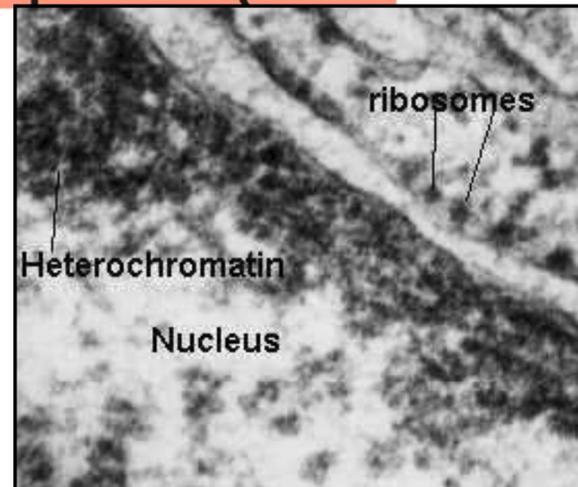
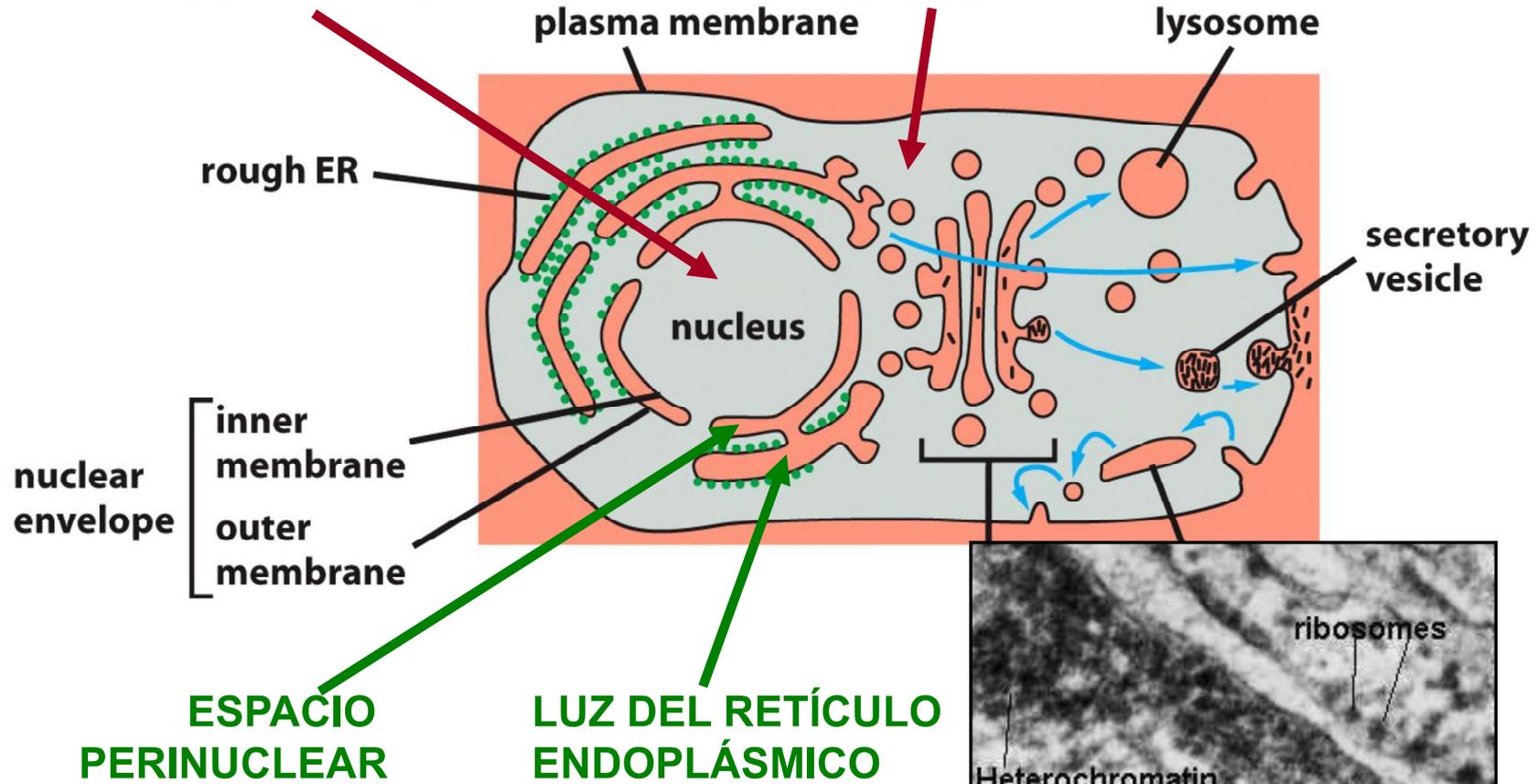




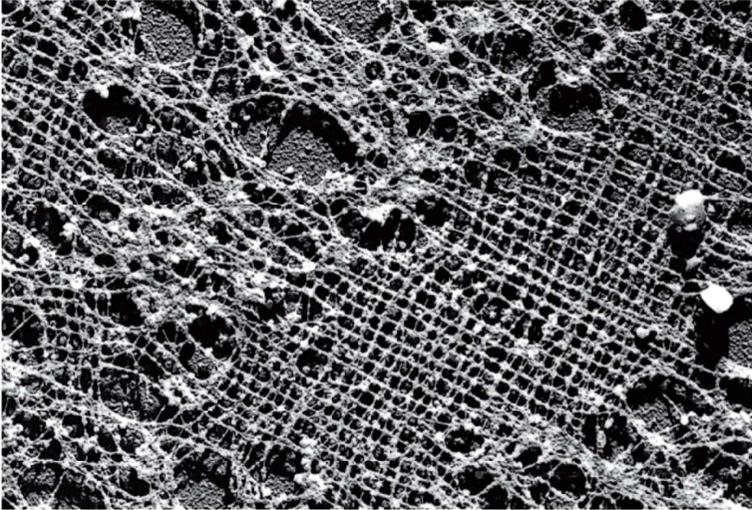
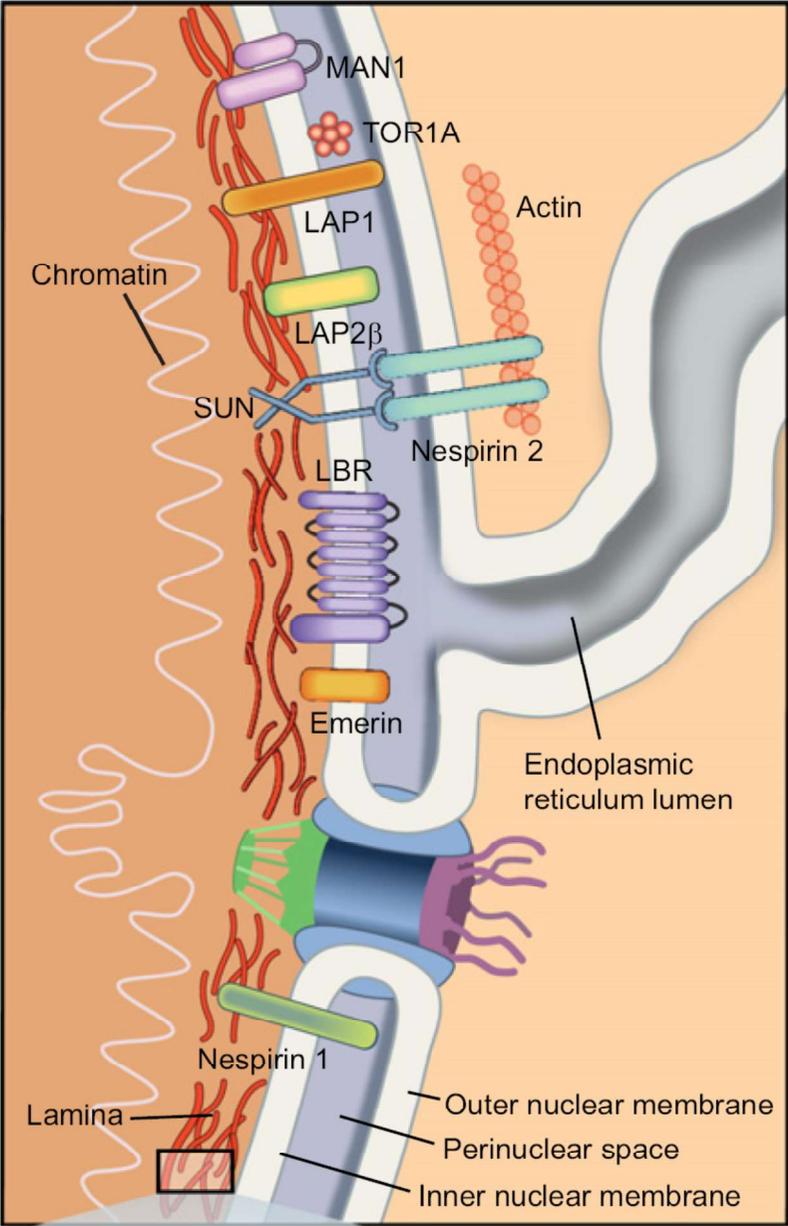
Relaciones entre los compartimientos celulares

NUCLEOPLASMA

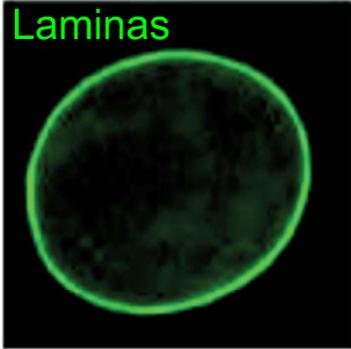
CITOSOL



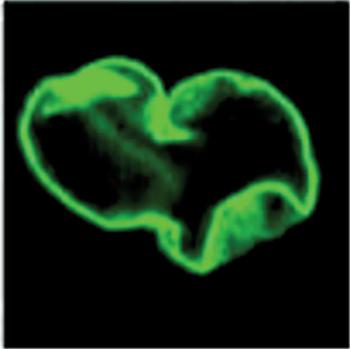
Envoltura y lámina nuclear



1 μ m



Normal

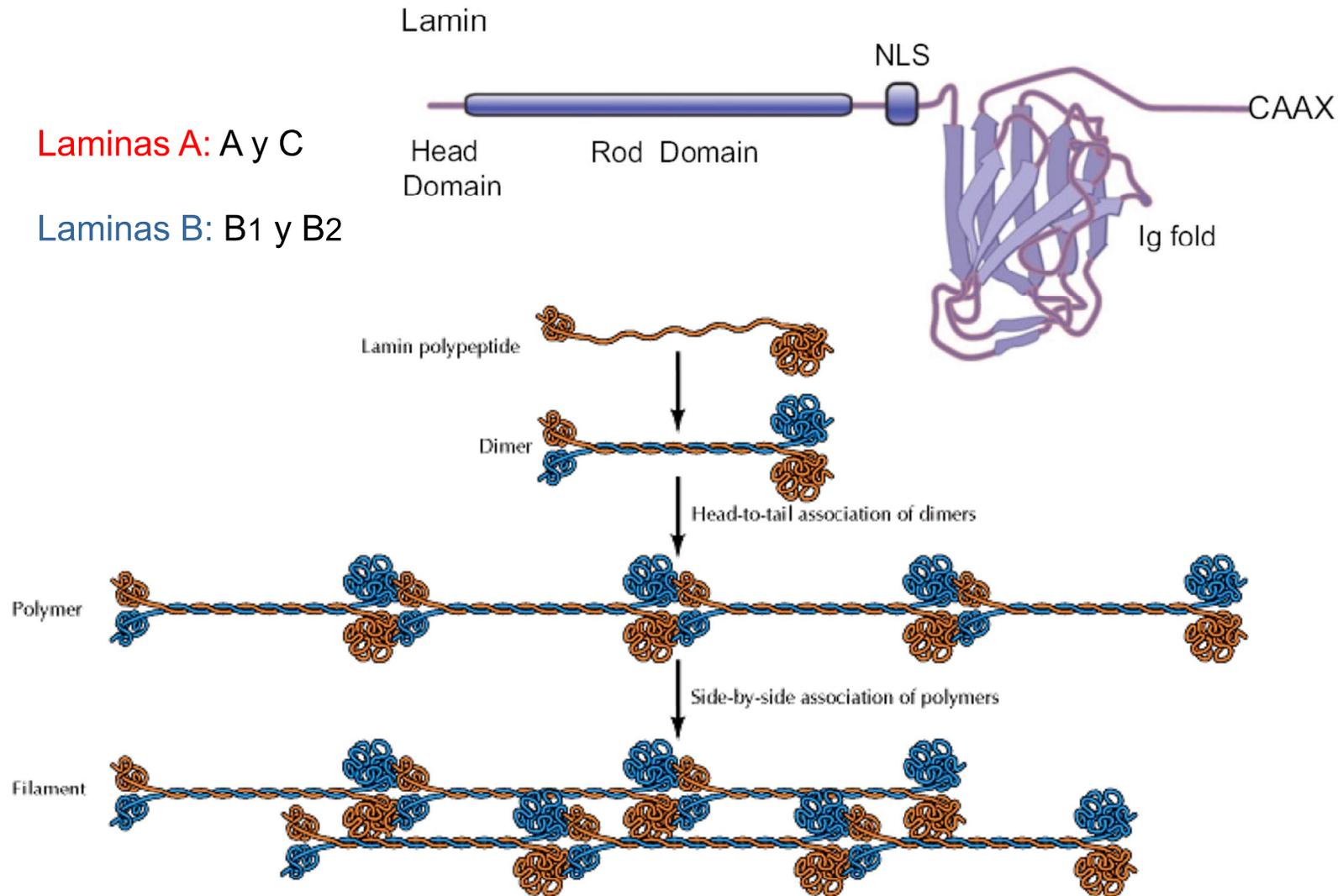


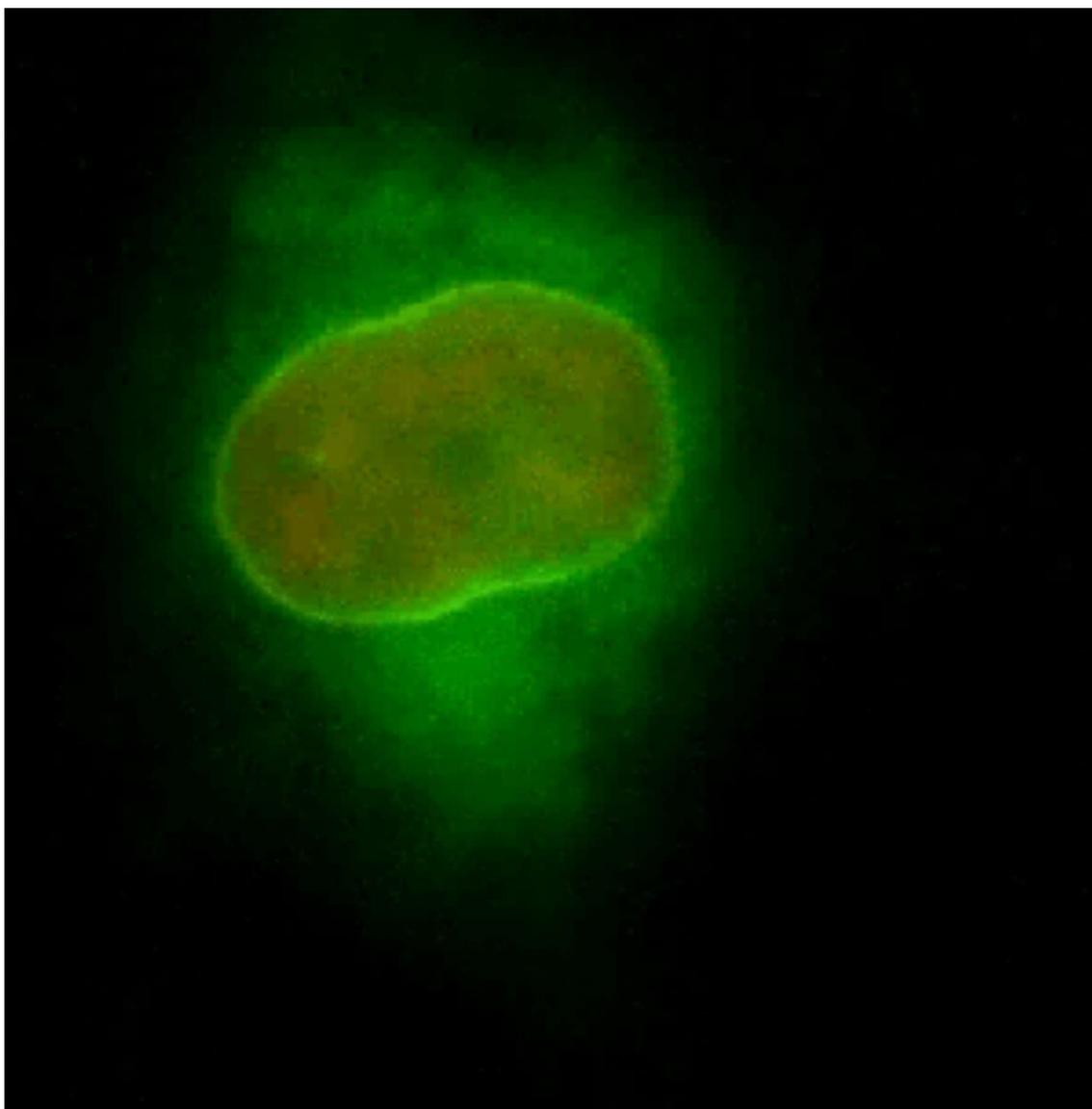
Progeria

Lámina nuclear y "laminas"

Laminas A: A y C

Laminas B: B1 y B2





Envoltura y lámina nuclear en el ciclo celular

