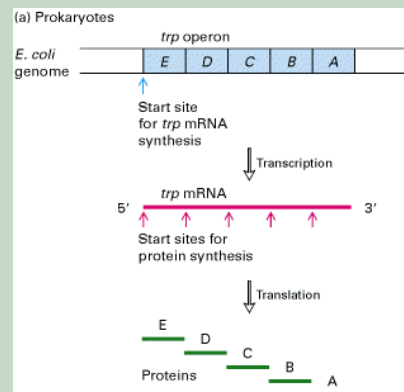
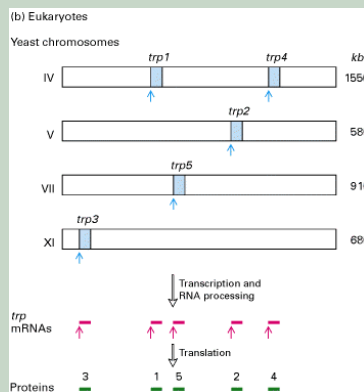


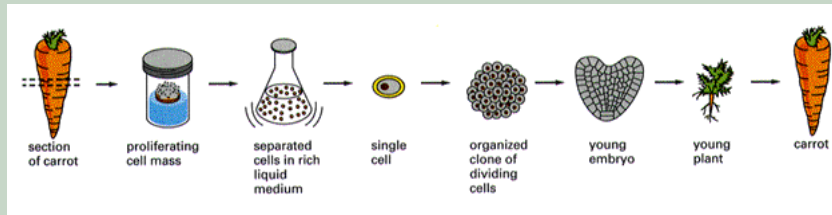
Introducción a la Biología Molecular y Celular

- Regulación de la Actividad Génica -

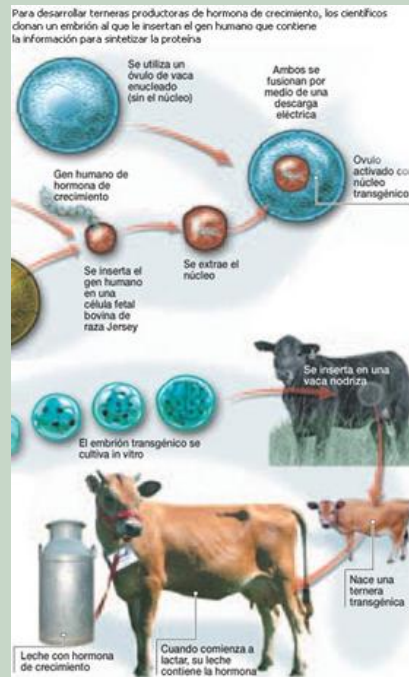
Organización genética



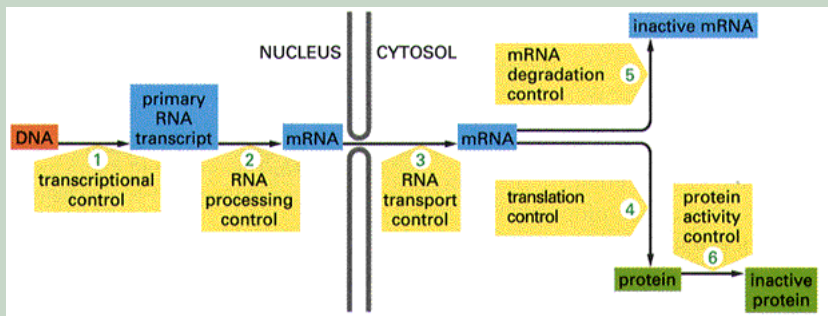
Diferenciación celular y totipotencialidad



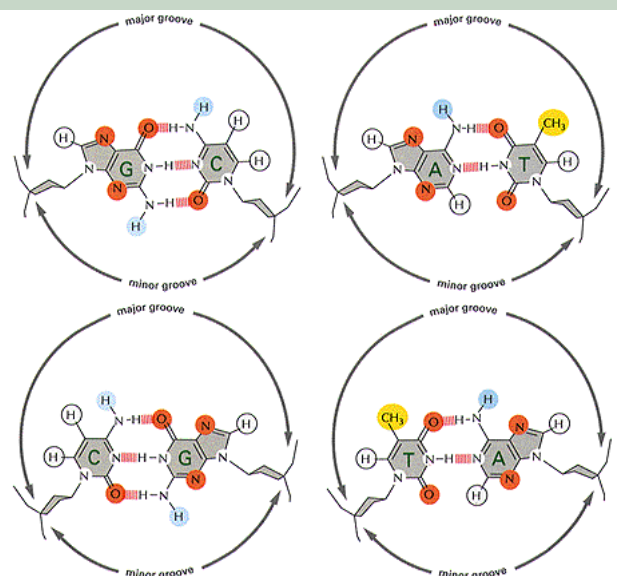
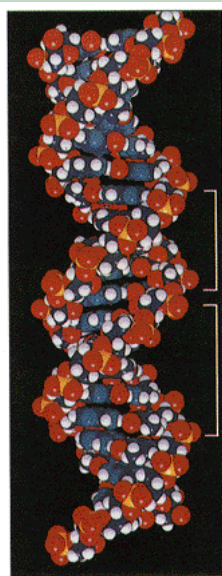
Pampita



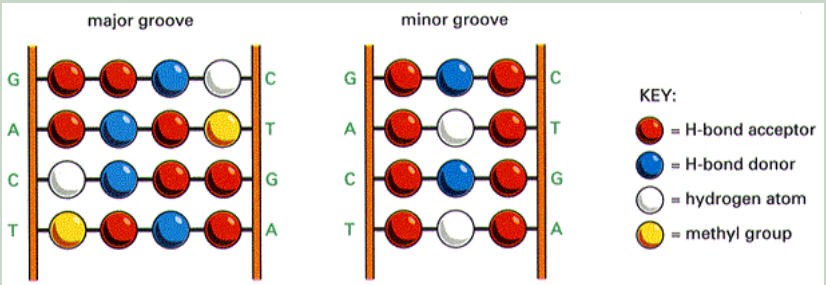
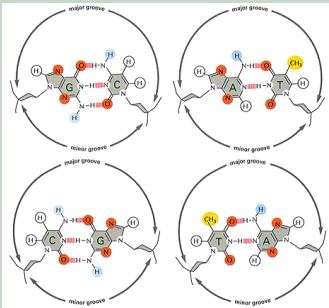
Niveles de control de la expresión génica



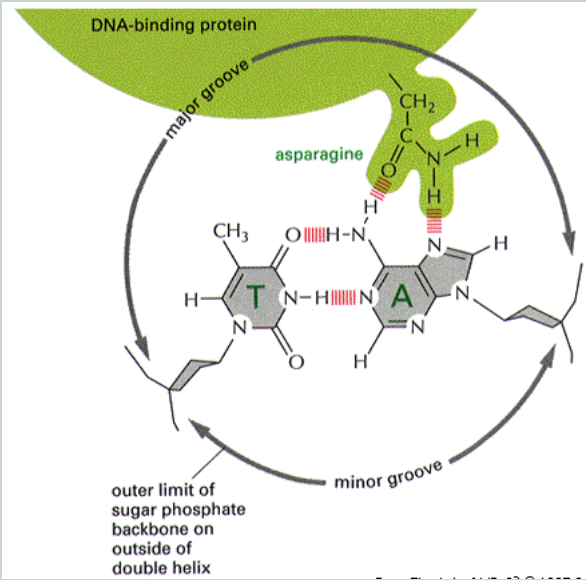
Estructura de la hélice de DNA



Código “conformacional”



Interacción DNA - proteína

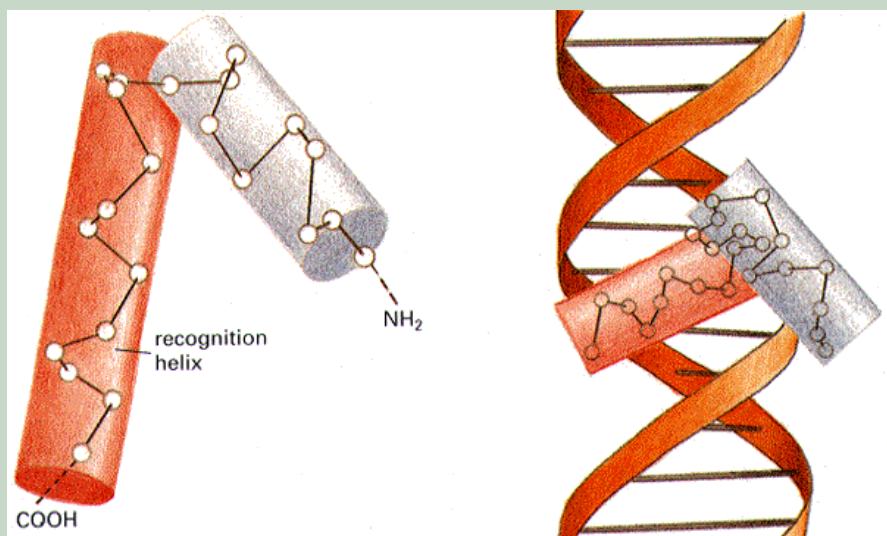


Diferentes motivos preteicos de interacción con DNA

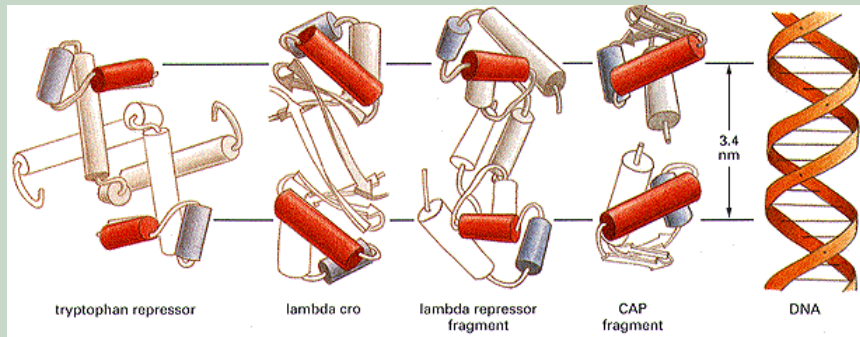
	Nombre	Secuencia de DNA reconocida*
<i>Bacterias</i>	represor lac	AATTGTGAGCGGATAACAATT TTAAGACTCGCCTATTGTAA
	CAP	TGTGAGTTAGCTCACT ACACTCAATCGAGTGA
	represor lambda	TATCACCGCCAGAGGTA ATAGTGGCGGTCTCCAT
		CGGAGGACTGTCTCCG GCCTCCTGACAGGAGGC
<i>Levaduras</i>	GAL4	CATGTAATT GTACATTAA
	MAT α 2	ATGACTCAT TACTGAGTA
	GCN4	AACGGGTAA TTGCCAATT
		GGGATTAGA CCCTAATCT
<i>Drosophila</i>	Krüppel	GGGCGG CCCGCC
	Bicoid	ATGCAAAT TACGTTTA
<i>Mamíferos</i>	Sp1	TGATAG ACTATC
	Oct-1	
	GATA-1	

- Hélice-Giro-Hélice
- Homeodominios
- Dedos de ZINC
- Láminas Beta
- Cremallera de Leucina
- Hélice-Bucle-Hélice

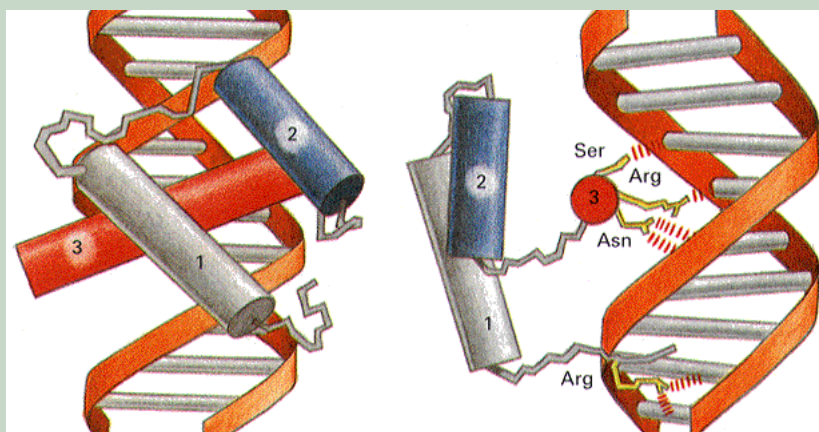
Hélice-Giro-Hélice

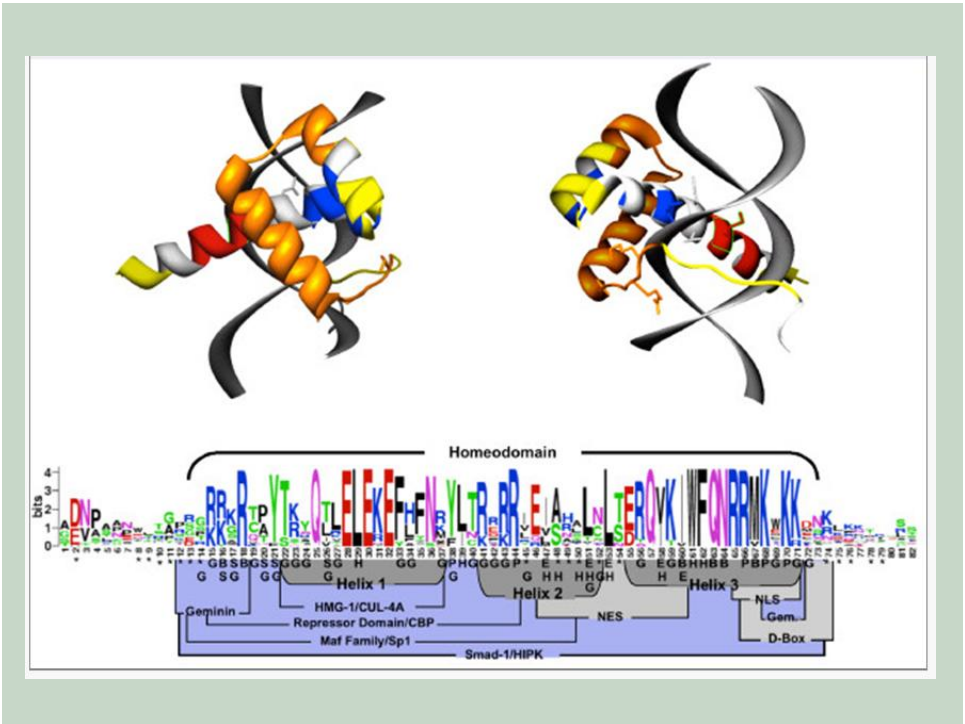


Algunos ejemplos

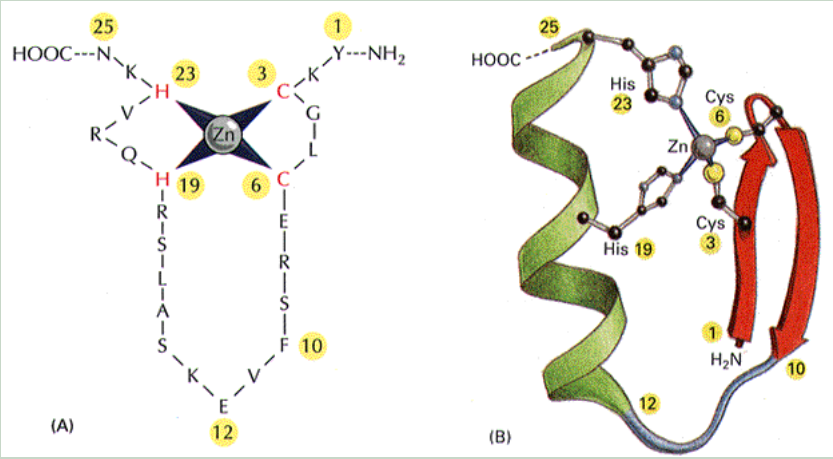


Homeodominios (euca)

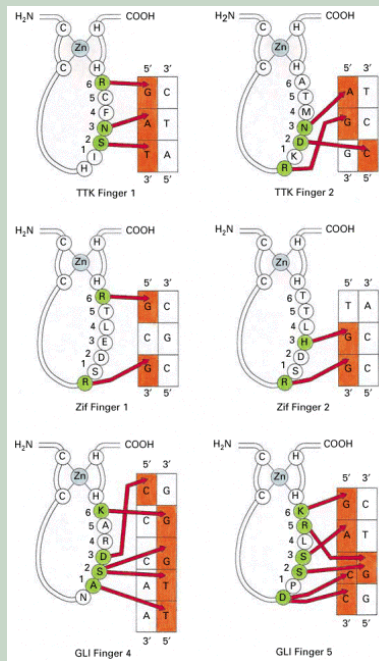




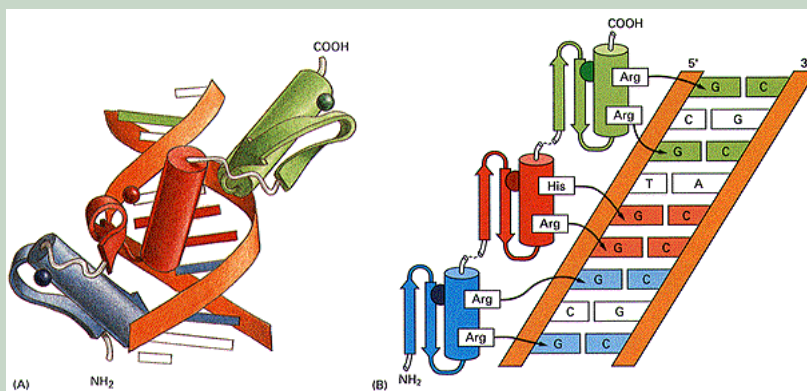
Dedos de ZINC “ZINC FINGERS”



Reconocimiento de dedos de Zink

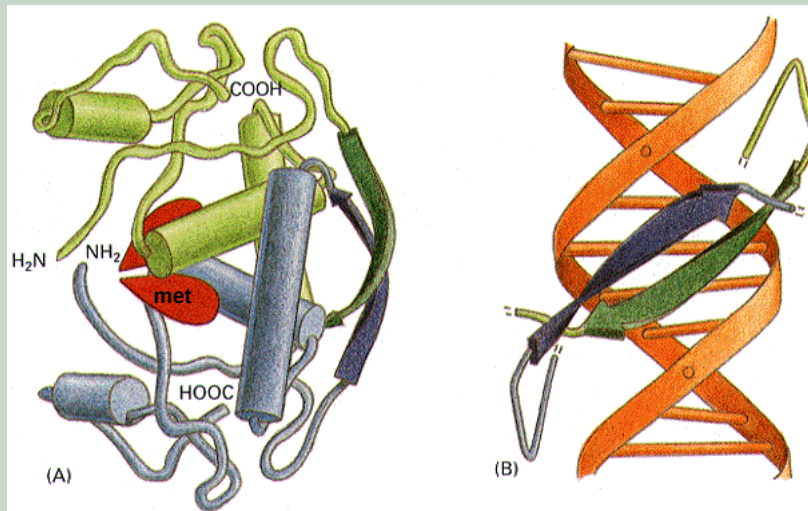


Interacción DNA – Dedos de Zinc



Dedos de Zinc tipo Cys-Cys-His-His

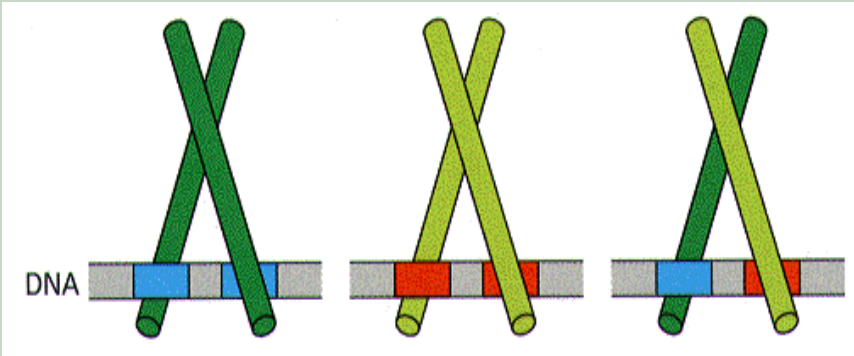
Láminas Beta



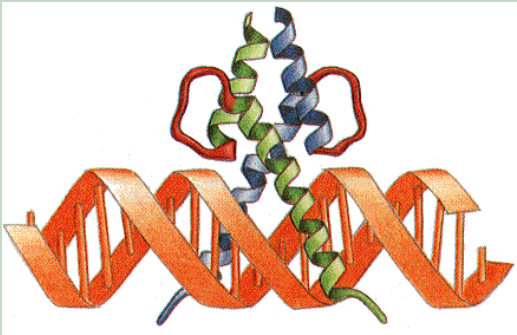
Cremallera de Leucina “LEUCINE ZIPPER”



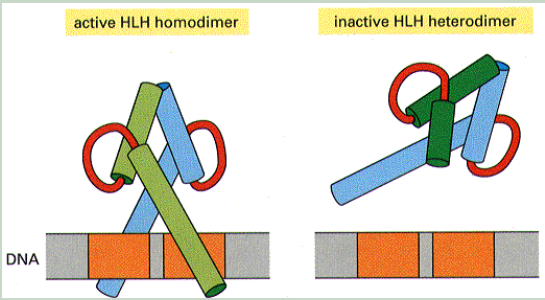
homodímeros y heterodímeros



Hélice – Bucle – Hélice. HLH: helix-loop-helix



homodímeros activos y
heterodímeros inactivos

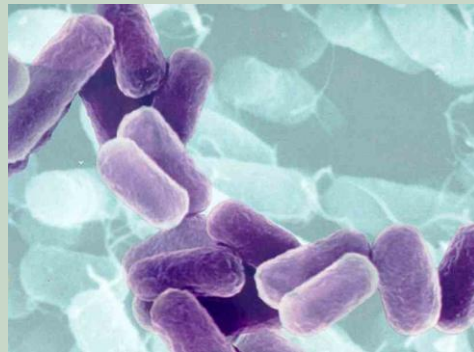
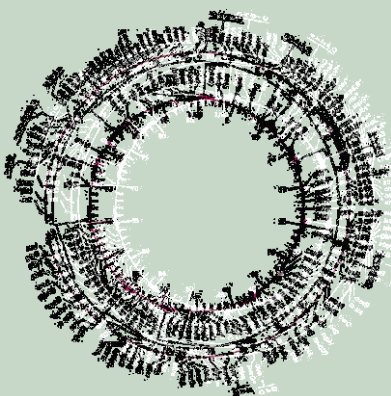


-REGULACIÓN DE LA TRANSCRIPCION EN PROCARIOTAS –

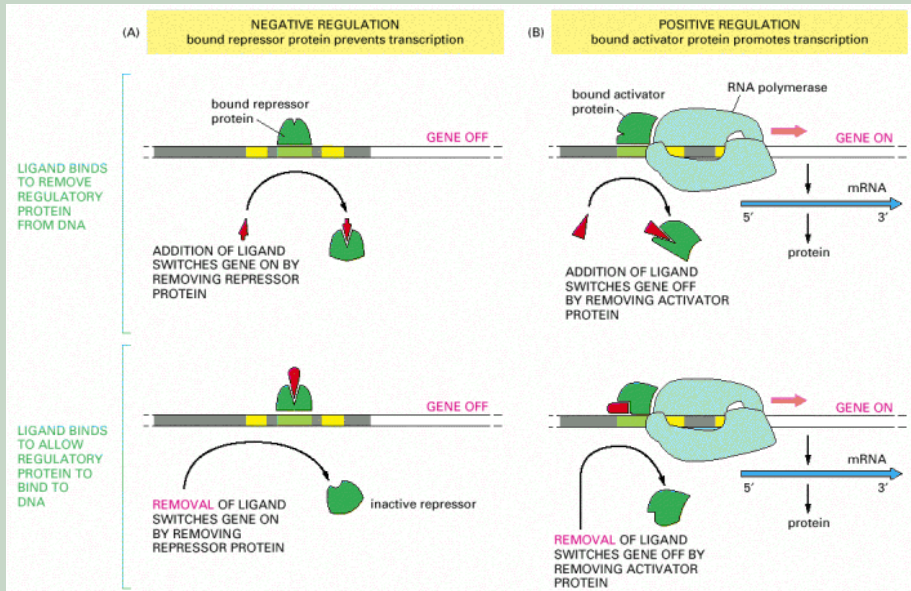
Regulación de la transcripción en procariontes

Escherichia Coli

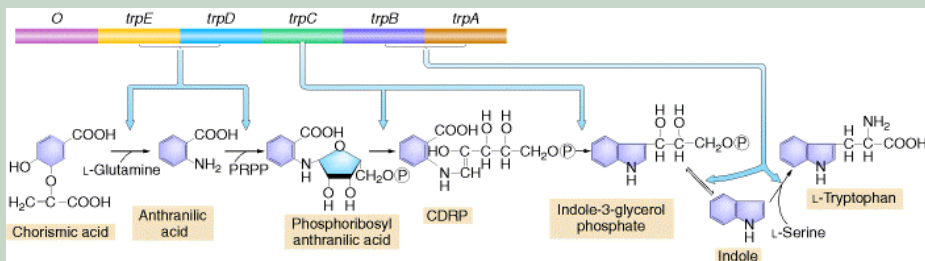
- ADN circular de $4,6 \times 10^6$ pb
- 4300 proteínas



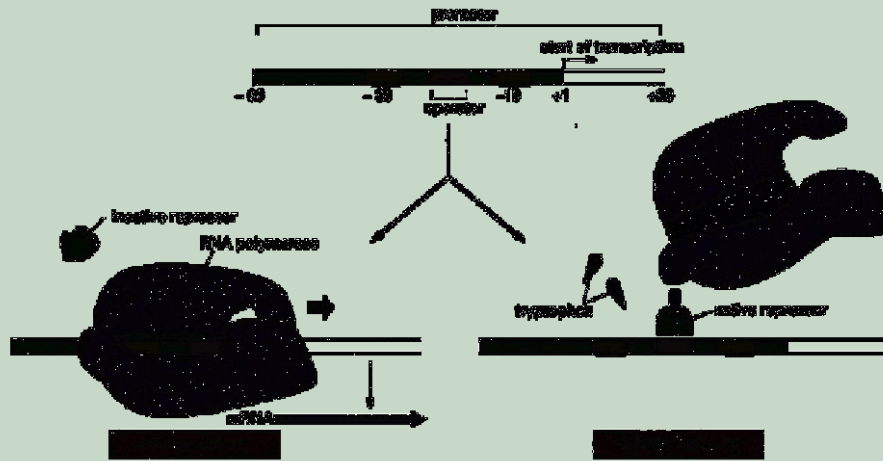
Regulación por ligando



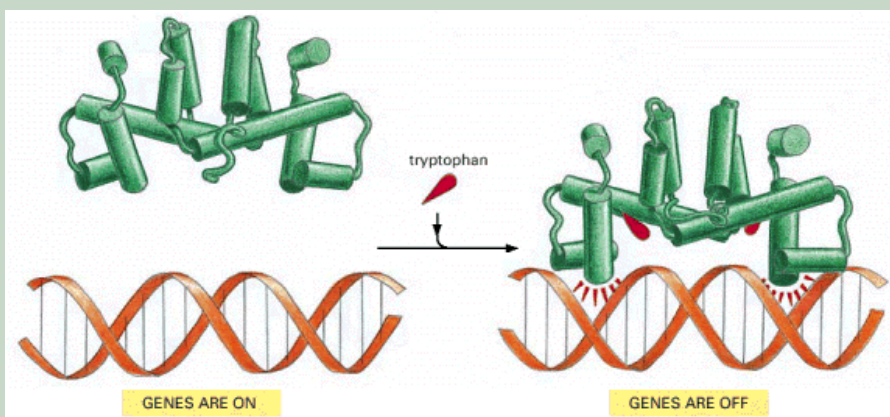
Operón triptofano



Operón triptofano



Operón triptofano



Operón lactosa

Este trabajo es considerado uno de los pioneros en el estudio del control de la expresión génica desde el enfoque de la Biología Molecular.

Fue considerado por las revistas científicas del momento como un trabajo que no cumplía los requisitos de publicación, por lo que los autores fundaron su propia revista (the Journal of Molecular Biology) y el artículo del Operón Lactosa ocupaba 80 páginas del primer número.



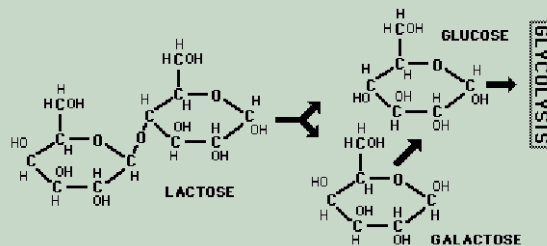
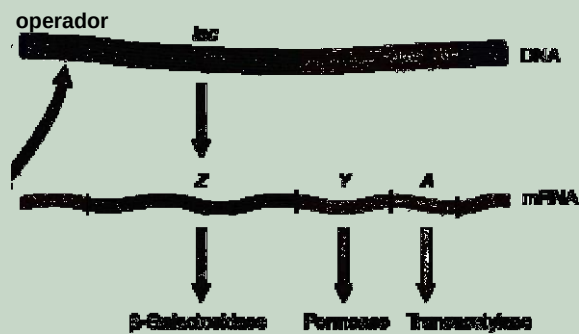
Jacob



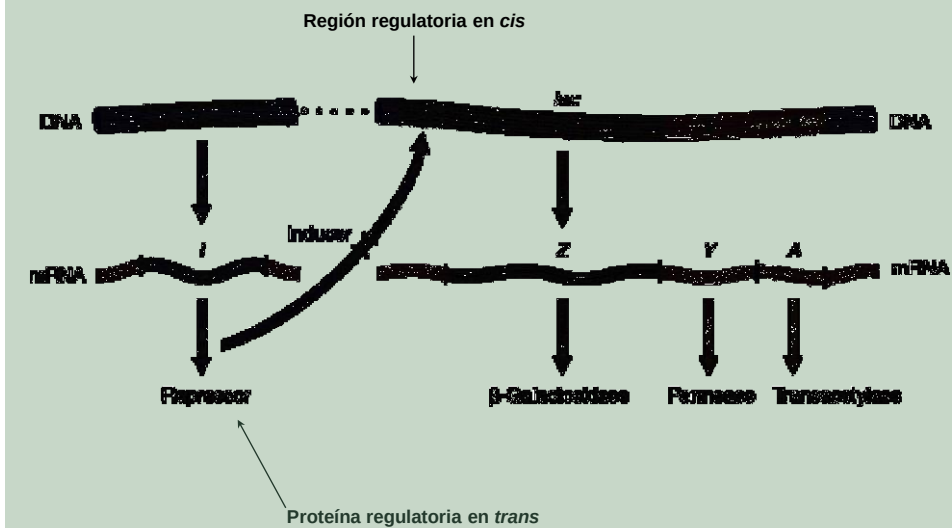
Monod

Premio Nobel
de Química
1965

Operón lactosa



Operón lactosa



Operón lactosa

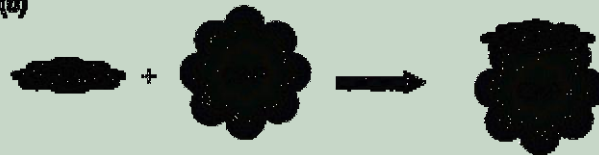
(a) High glucose $\rightarrow$ Inactive adenylate cyclase

ATP $\rightleftharpoons$ No cAMP

(b) Low glucose $\rightarrow$ Active adenylate cyclase

ATP $\rightarrow$ cAMP

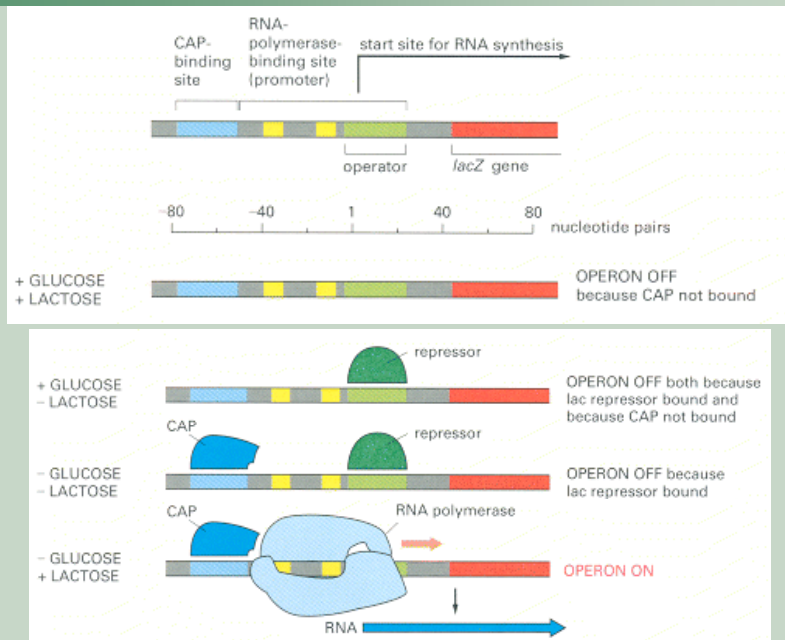
(c)



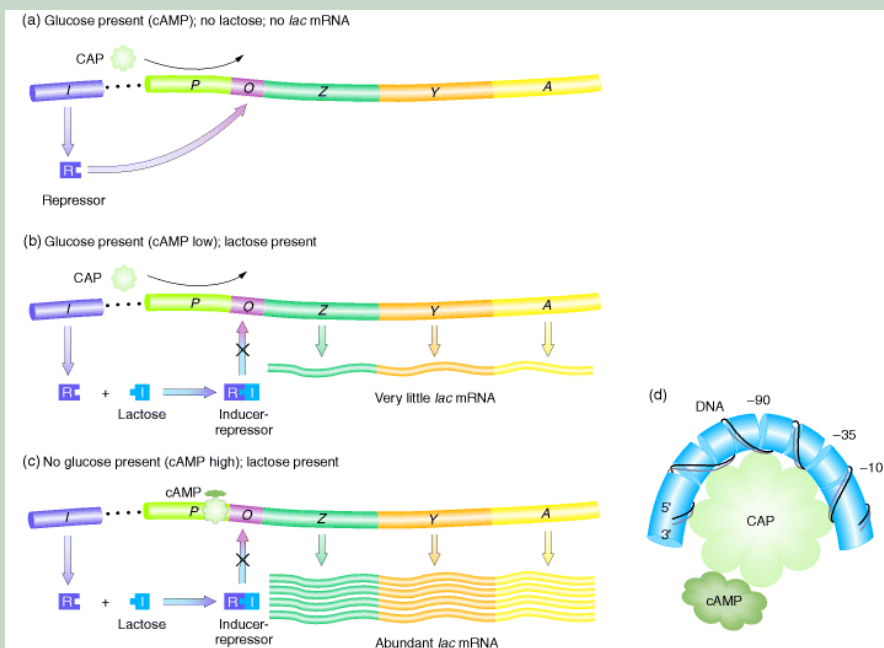
(d)



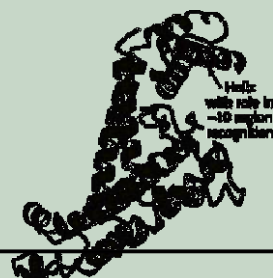
Operón lactosa



Operón lactosa



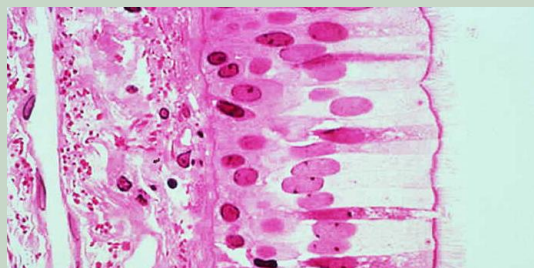
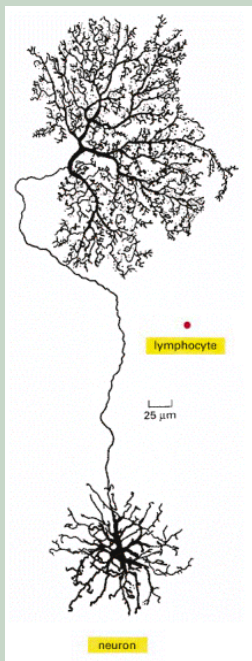
Factores sigma



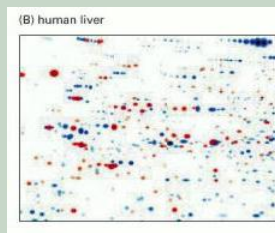
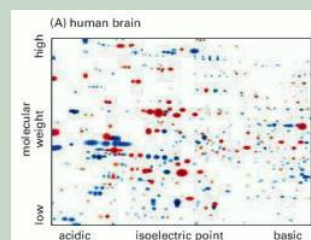
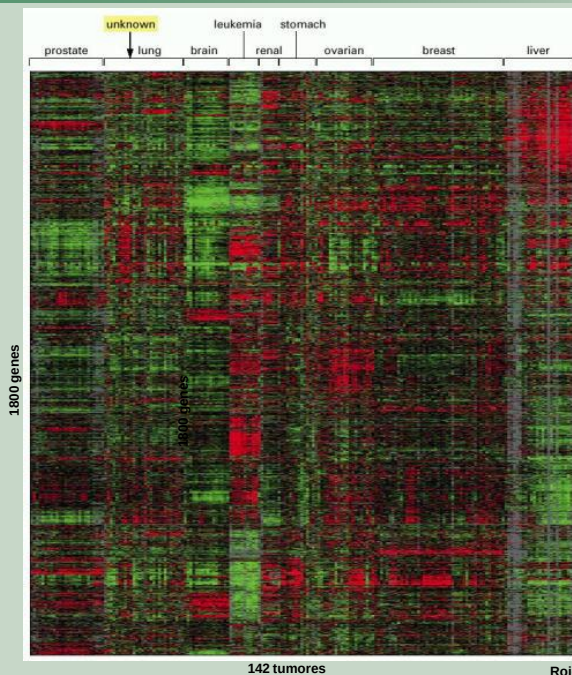
Sigma Factor	Promoters Recognized	Promoter Consensus	
		-35 Region	-10 Region
σ^{70}	Most genes	TTGACAT	TATAAT
σ^{32}	Genes induced by heat shock	TCTCNCCCTTGAA	CCCCATNTA
σ^{28}	Genes for motility and chemotaxis	CTAAA	CCGATAT
σ^{38}	Genes for stationary phase and stress response	?	?
σ^{54}	Genes for nitrogen metabolism and other functions	-24 Region CTGGNA	-12 Region TTGCA

-REGULACIÓN DE LA TRANSCRIPCION
EN EUKARIOTAS –

Expresión diferencial entre células



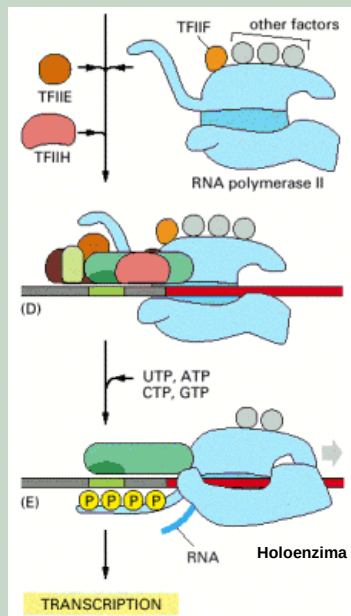
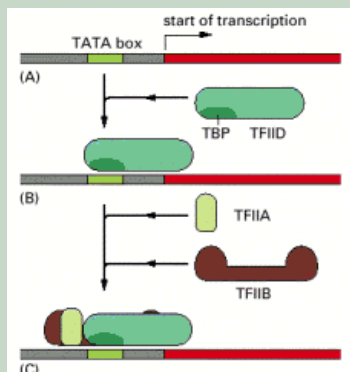
Expresión diferencial entre células



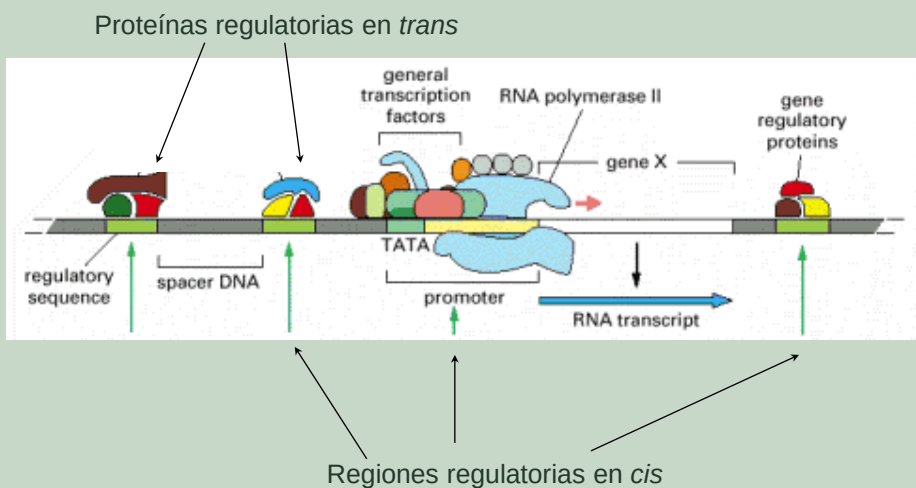
142 tumores

Rojo: Sobreexpresión

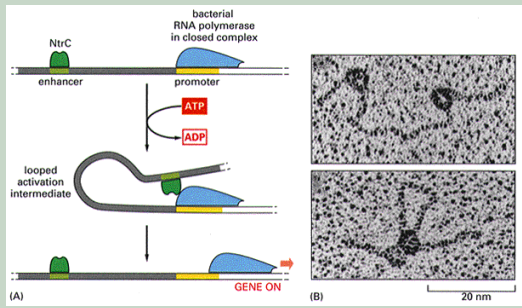
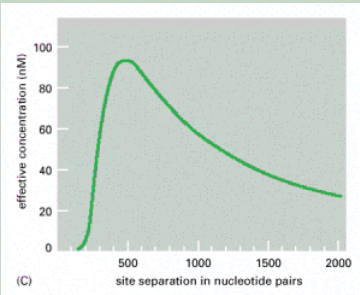
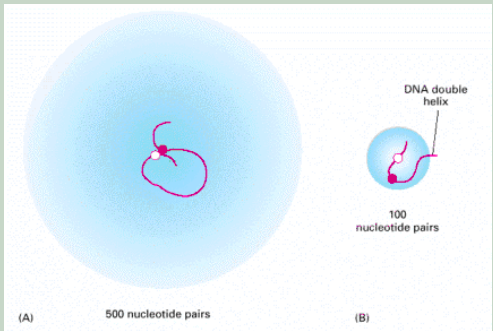
Transcripción Eucariota



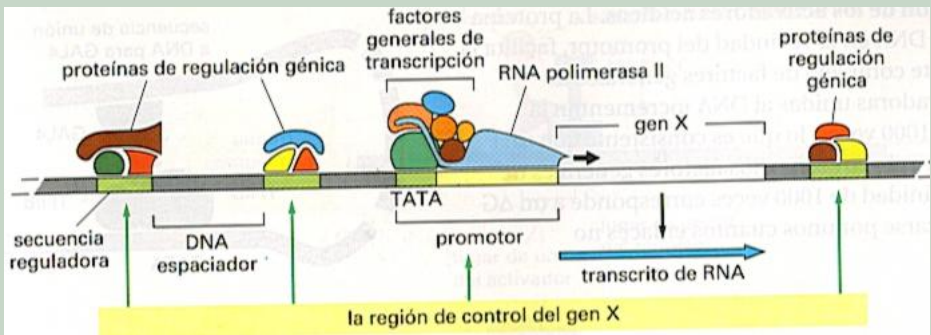
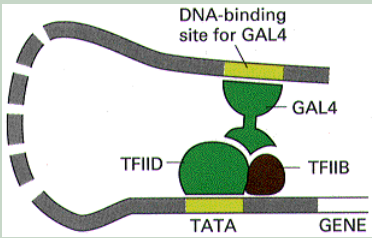
Regulación eucariota



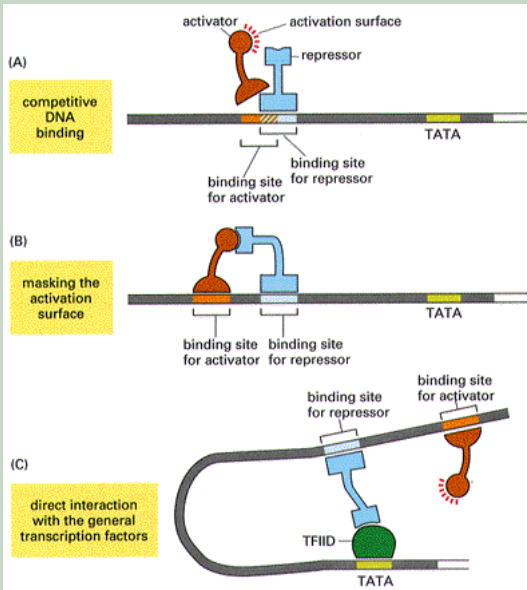
Regulación eucariota



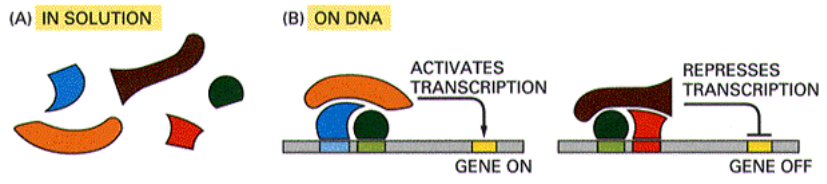
Región de control génico eucariota



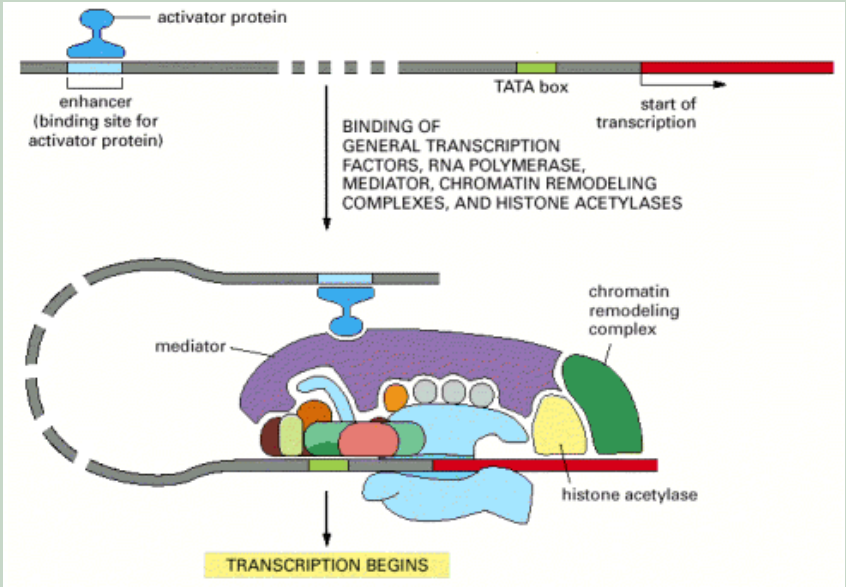
Sistemas de represión



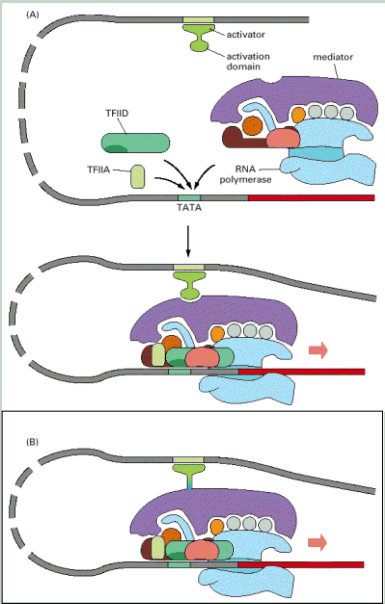
Complejos proteicos



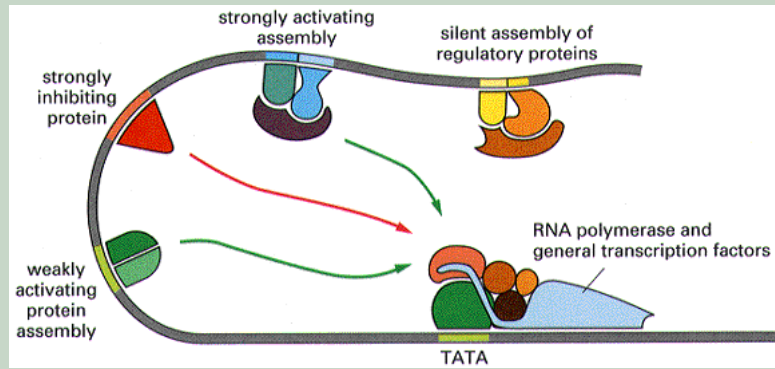
Regulación eucariota



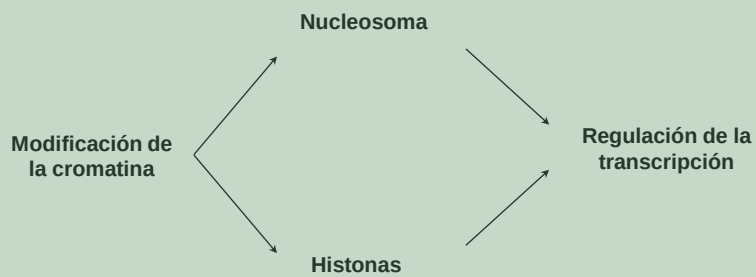
Regulación eucariota



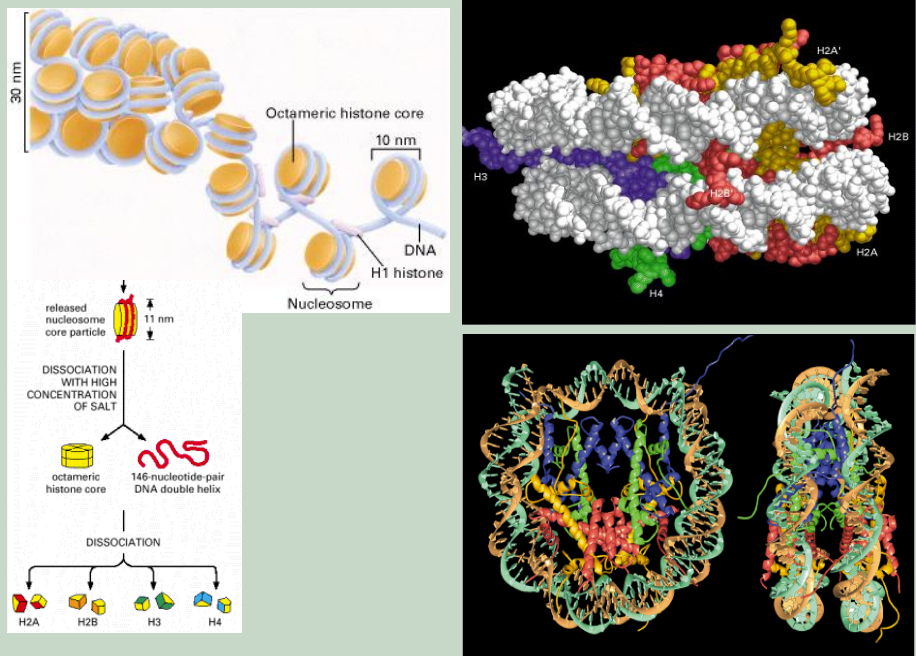
Integración en un promotor



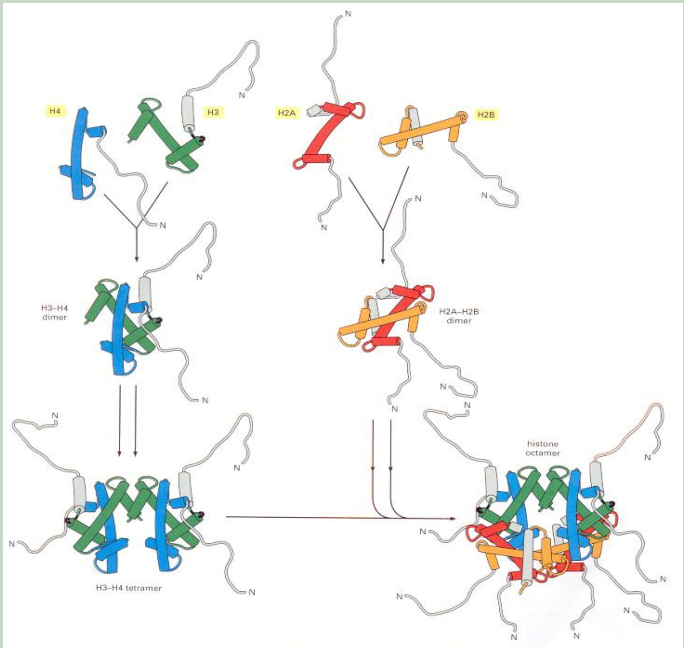
Modificación de la cromatina



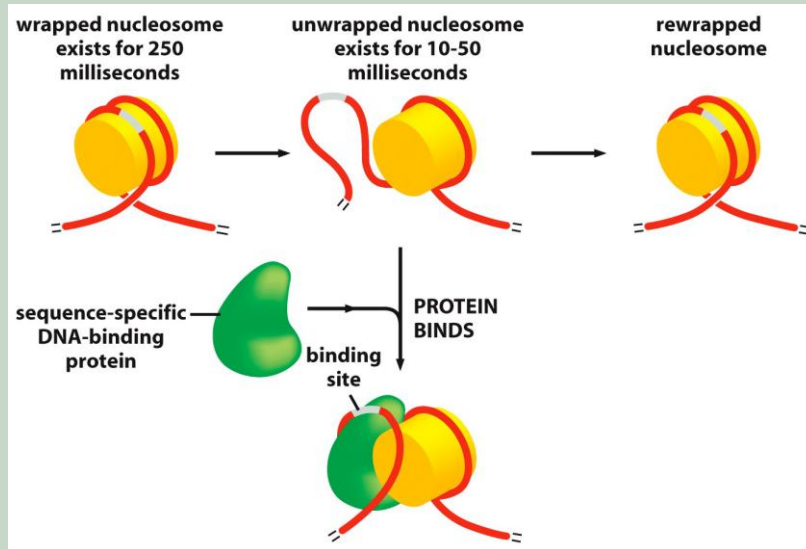
Alteraciones en el nucleosoma



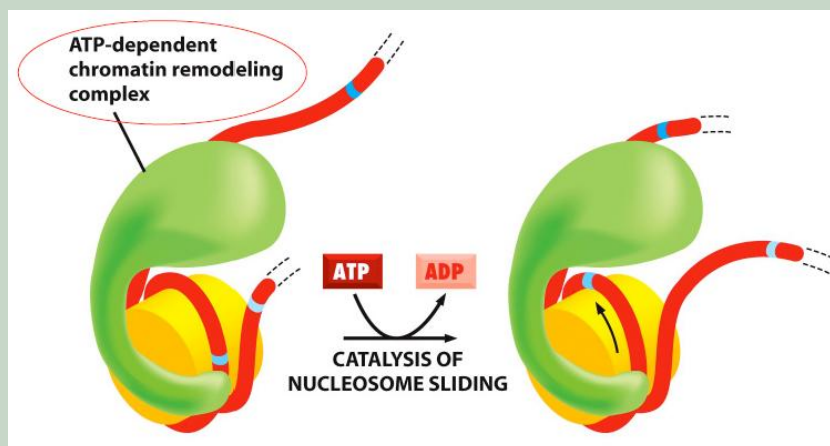
Conformación del nucleosoma



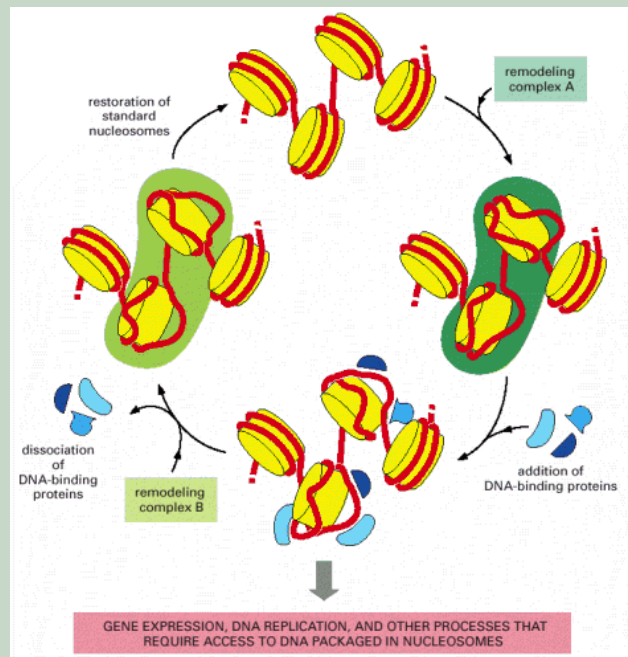
El nucleosoma es una estructura dinámica



Complejo modelador de la cromatina



Modificación del nucleosoma



Variantes de histonas

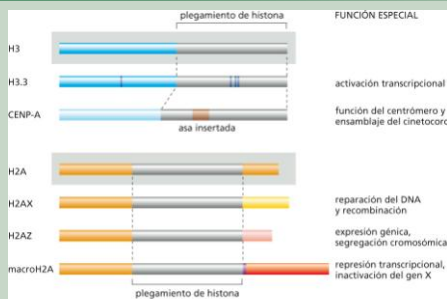


Figura 4-41 Biología molecular de la célula, quinta edición (© Garland Science 2008 y Ediciones Omega 2010)

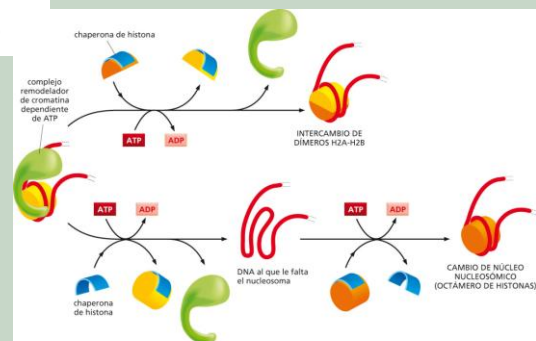


Figura 4-30 Biología molecular de la célula, quinta edición (© Garland Science 2008 y Ediciones Omega 2010)

Código de histonas

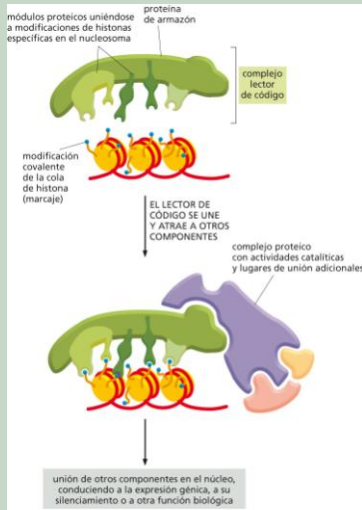


Figura 4-43 Biología molecular de la célula, quinta edición (© Garland Science 2008 y Ediciones Omega 2010)

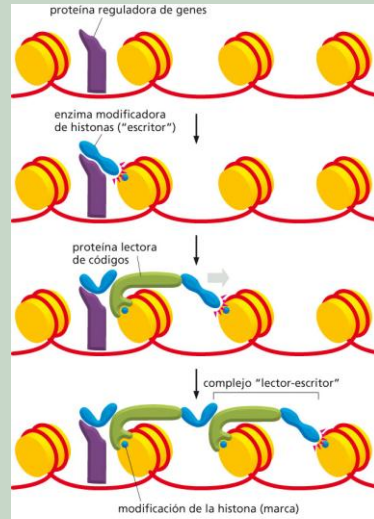


Figura 4-45 Biología molecular de la célula, quinta edición (© Garland Science 2008 y Ediciones Omega 2010)

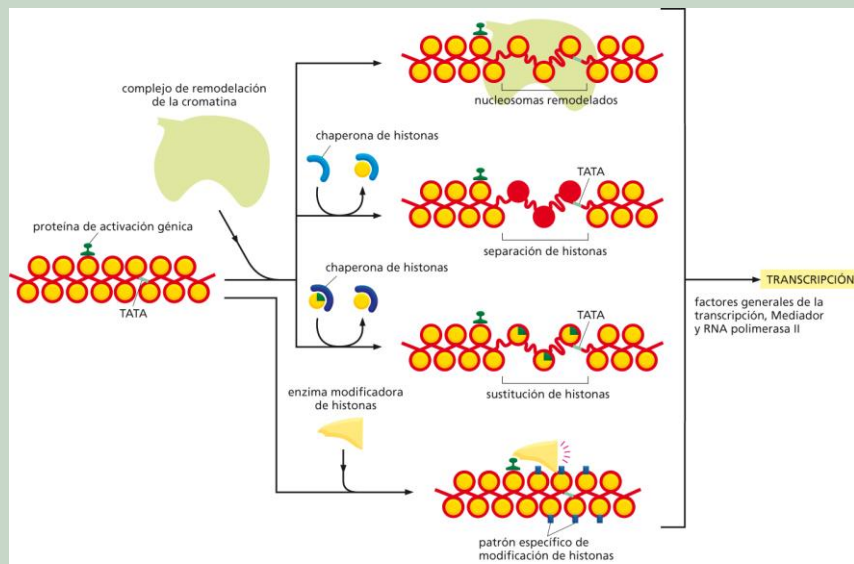
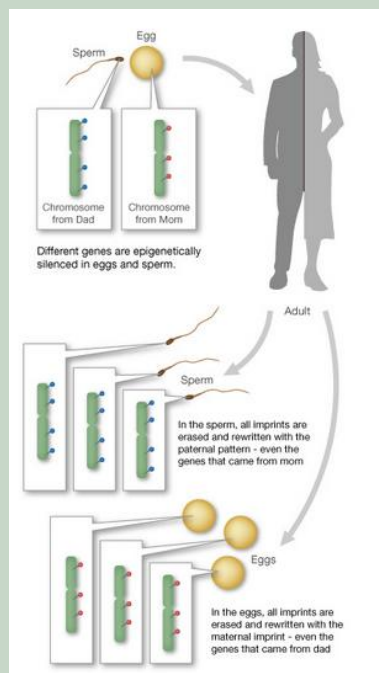
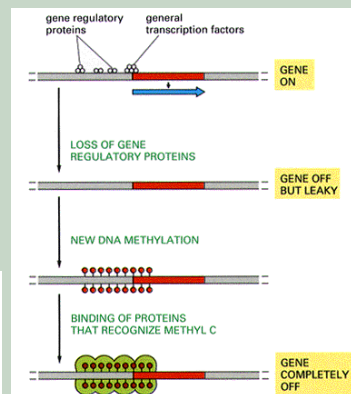
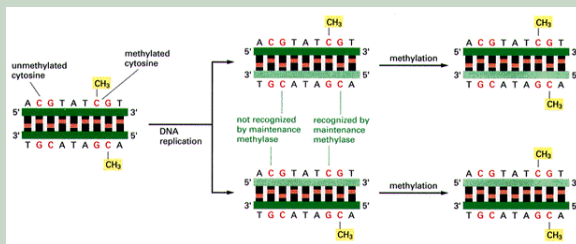
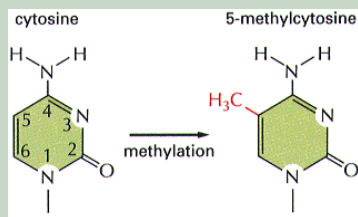
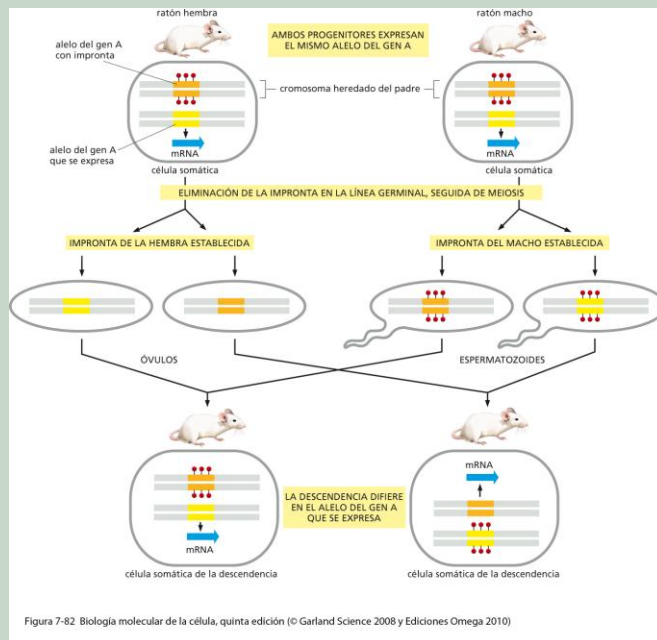


Figura 7-46 Biología molecular de la célula, quinta edición (© Garland Science 2008 y Ediciones Omega 2010)

Metilación del DNA





Genomic imprinting

Prader-Willi syndrome (androgenones)



Chromosome 15



Angelman syndrome (gynogenones)



ARTICLE

Prader–Willi Syndrome and Angelman Syndrome

KARIN BUITING*

INTRODUCTION

The Prader–Willi syndrome (PWS) and Angelman syndrome (AS) are the first known examples of human diseases involving imprinted genes. Each occurs with a frequency of ~1:15,000–1:25,000 live births. De novo interstitial deletions of the same chromosomal region [del(15)(q11q13)] in patients with PWS and AS, were first identified by high-resolution chromosome banding and later confirmed by molecular studies [Ledbetter et al., 1981; Kaplan et al., 1987; Magenis et al., 1987; Donlon, 1988; Knoll et al., 1989; Tantravahi et al., 1989; Nicholls et al., 1989a]. At that time it was hard to explain why indistinguishable deletions of the same chromosomal region could lead to two clinically distinct disorders, each with characteristic cognitive, behavioral, and neurologic phenotypes. The first evidence for a parent-of-origin effect came from a study performed by Butler and Palmer

[1983], who demonstrated, by studying the inheritance of chromosomal polymorphisms, that the deletion always occurs on the chromosome 15 inherited from the father. This finding was confirmed at the molecular level by Knoll et al. [1989], who also demonstrated that chromosome 15q11q13 deletions in AS always occur on the maternal chromosome. Based on the study of polymorphic DNA markers, Nicholls et al. [1989b] provided the first evidence that some PWS individuals inherit both chromosome 15s from the mother. The first patients with AS and a paternal uniparental disomy were identified by Malcolm et al. [1991] indicating that AS results from the absence of the maternal contribution of at least one gene in the chromosomal region 15q11q13. And indeed, further studies revealed that the chromosomal region 15q11–q13 contains a cluster of genes that are expressed from the paternal or maternal chromosome only. It is now known that AS

results from the loss of function of the *UBE3A* gene, which in brain is expressed from the maternal chromosome only [Kishino et al., 1997; Matsura et al., 1997]. In PWS, the situation is less clear, but a deficiency of the paternally expressed *SNORD116* snoRNAs can result in a PWS or PWS-like phenotype [Sahoo et al., 2008;

It is now known that AS results from the loss of function of the UBE3A gene, which in brain is expressed from the maternal chromosome only. In PWS, the situation is less clear, but a deficiency of the paternally expressed SNORD116 snoRNAs can result in a PWS or PWS-like phenotype.

Represión de la transcripción en eucariontes

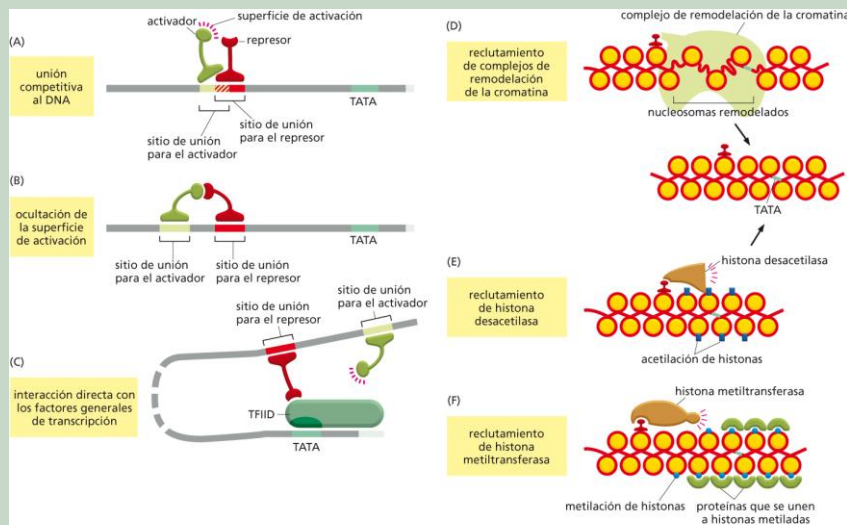
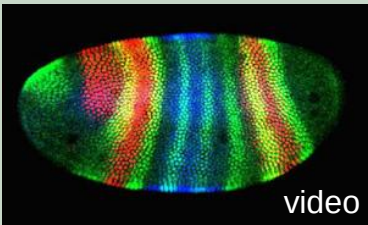
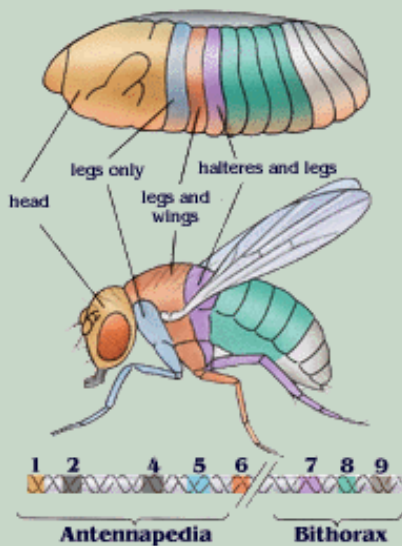


Figura 7-50a Biología molecular de la célula, quinta edición (© Garland Science 2008 y Ediciones Omega 2010)

Regulación por genes homeóticos



Comparten una seq de alrededor de 60 aa (homeodominio)

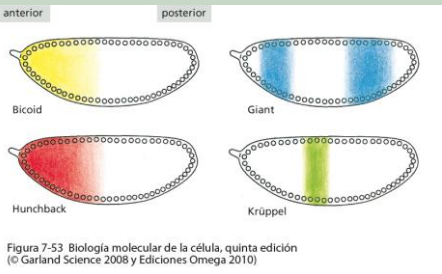


Figura 7-53 Biología molecular de la célula, quinta edición (© Garland Science 2008 y Ediciones Omega 2010)

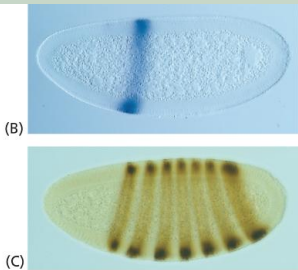
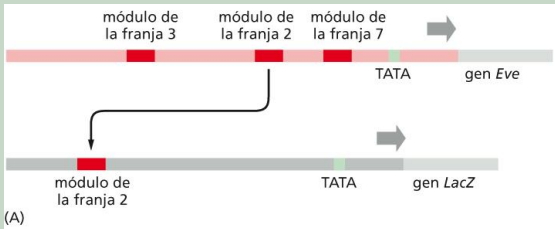
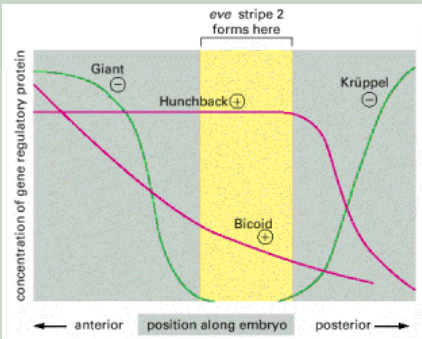
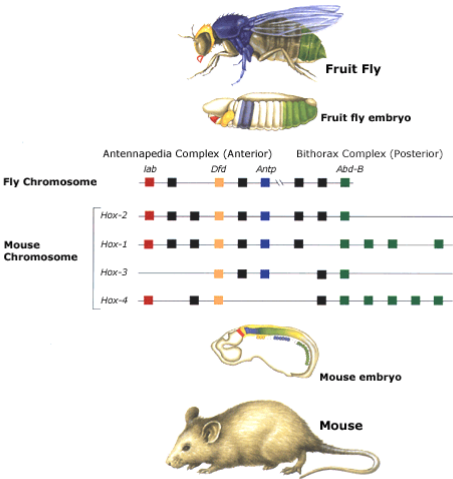


Figura 7-55a Biología molecular de la célula, quinta edición (© Garland Science 2008 y Ediciones Omega 2010)

HEADS OR TAILS? FLIES AND MICE SHARE GENES THAT CONTROL BODY PATTERNS



In insects and mammals, very similar genes—in the same order—control the development of front and back parts of the body.

These homeobox-containing genes lie on a single chromosome in the fly (top row of colored squares). Mammals have four similar gene clusters that lie on four separate chromosomes (lower rows of squares).

The genes are color-coded to match the parts of the body in which they are expressed.

