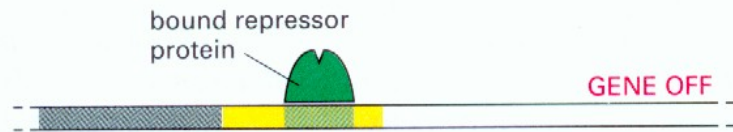


Control of gene expression

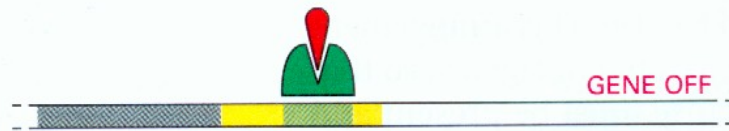
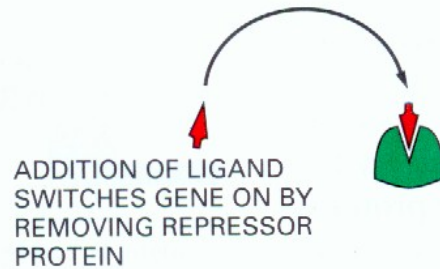
2

(A)

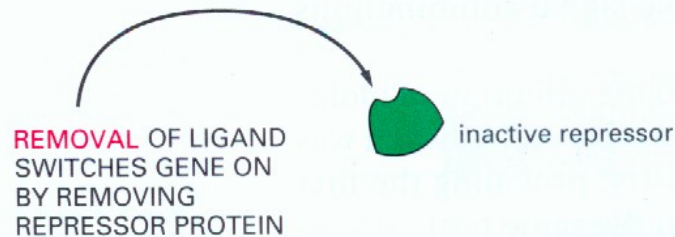
NEGATIVE REGULATION
bound repressor protein prevents transcription



LIGAND BINDS TO REMOVE REGULATORY PROTEIN FROM DNA

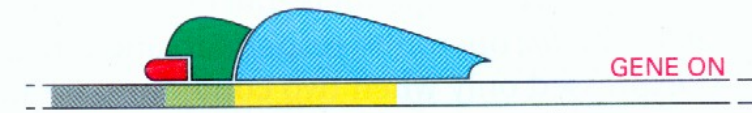
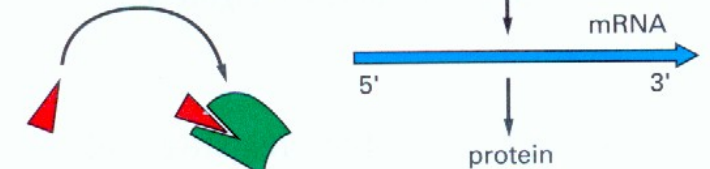
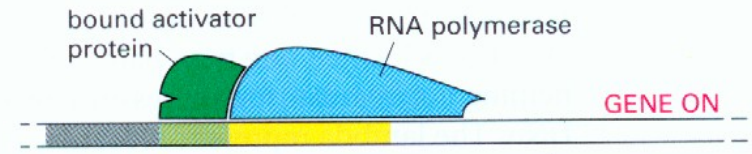


LIGAND BINDS TO ALLOW REGULATORY PROTEIN TO BIND TO DNA



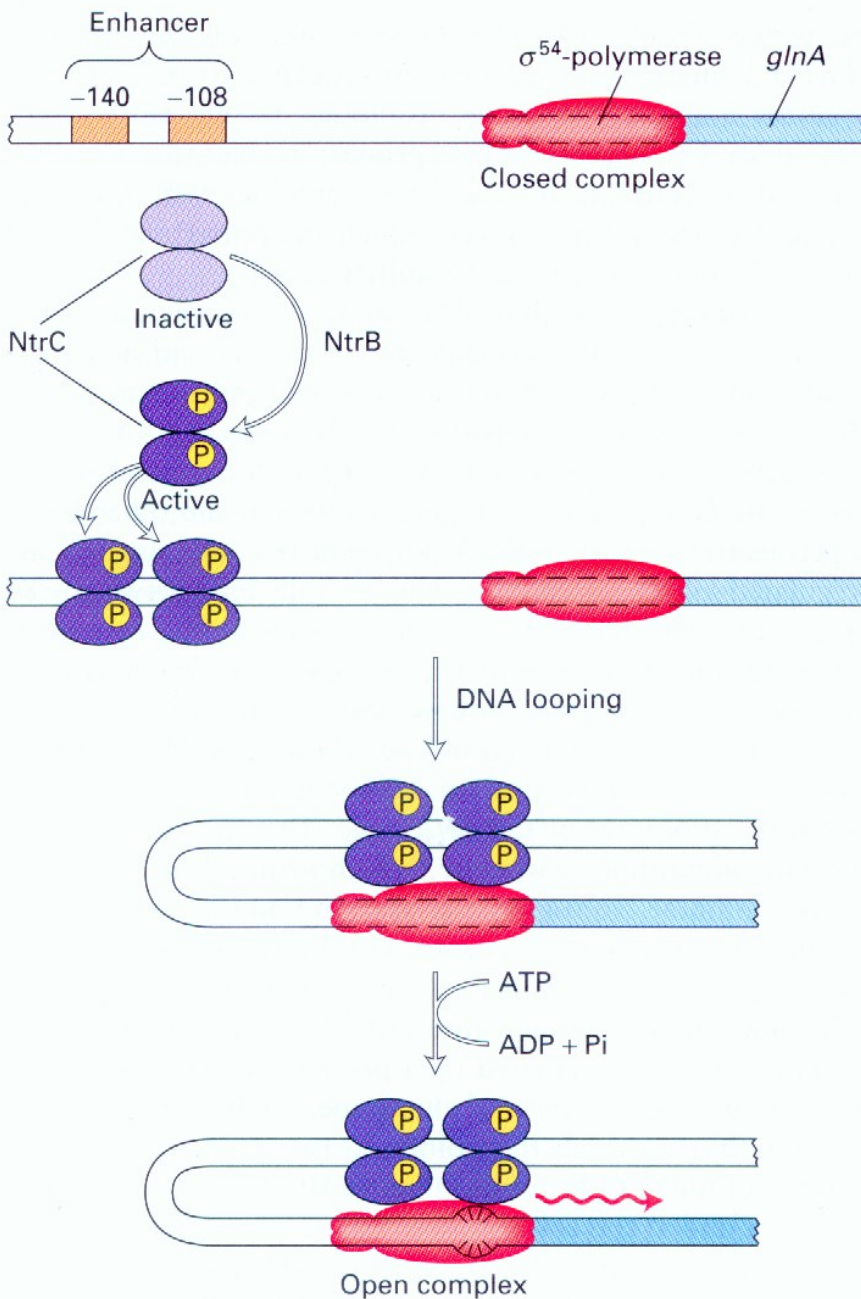
(B)

POSITIVE REGULATION
bound activator protein promotes transcription



REMOVAL OF LIGAND SWITCHES GENE OFF BY REMOVING ACTIVATOR PROTEIN

Bakteerin geeniregulaation perusmahdollisuudet (nelikenttä, joka voi olla tenttikysymyksenä)



Toisenlainen regulaatio *E. colilta*:
glutamiinisyntetaasin operoni

Muistutus: tämä muistuttaa
eukaryoottia sikäli, että kaukana
sijaitseva DNA-sekvenssi
(enhancer) sitoo polymeraasia
aktivoivan tekijän

▲ FIGURE 10-19 Activation of σ^{54} -containing RNA polymerase at *glnA* promoter by NtrC. The polymerase binds

Eukaryoottien geeniregulaation eroja verrattuna bakteereihin

Päähuomio on solun erikoislaadussa ja asemassa, ei ympäristössä

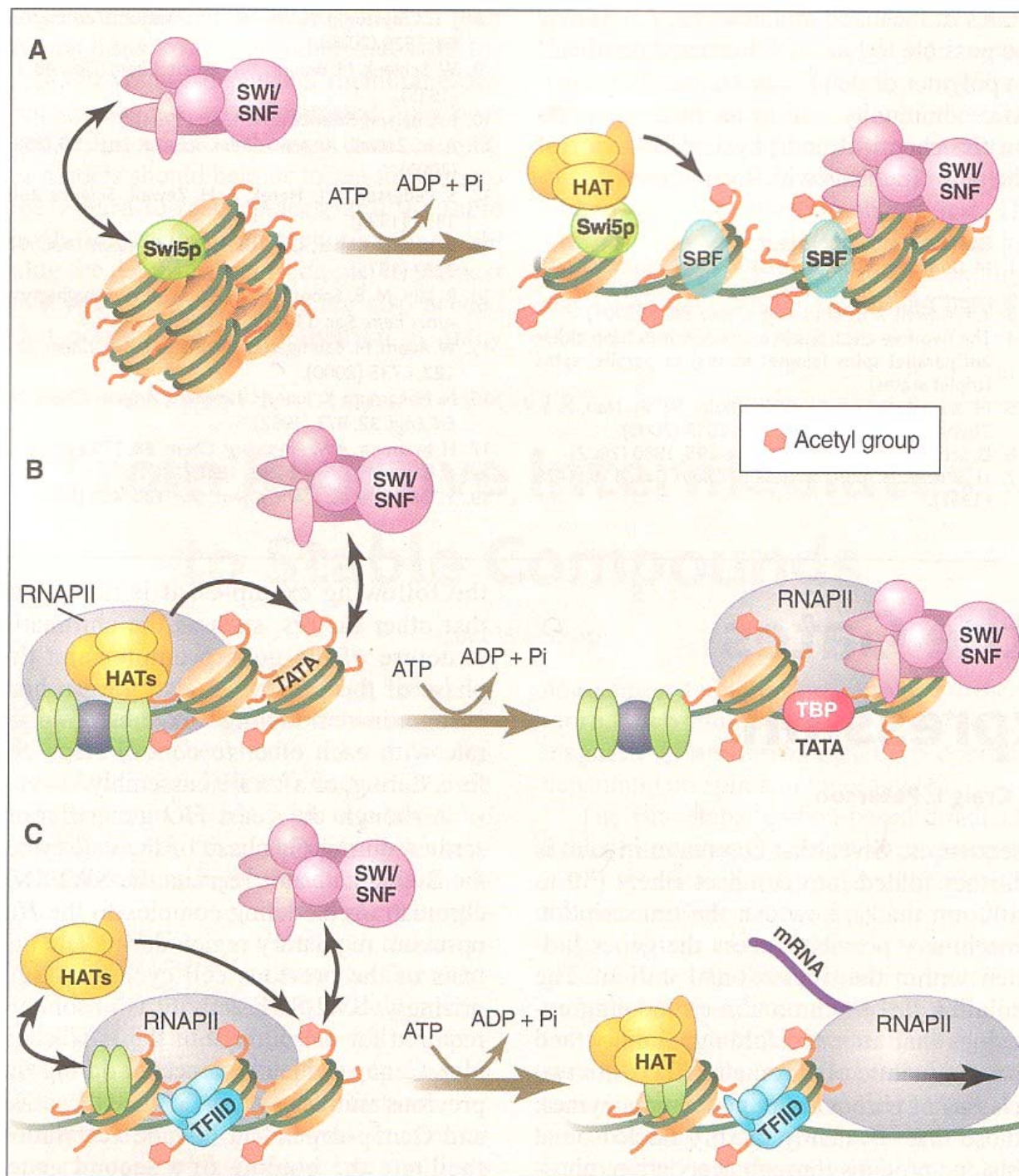
Viestintä solujen välillä on siis keskeistä (signaalit - reseptorit - regulaatio)

Jokaista transkriptiotapahtumaa voidaan aktivoida ja repressoida, kiihdyttää ja jarruttaa, ja nämä prosessit tapahtuvat keskenään “kommunikoivien” proteiinien kautta, jotka sitoutuvat DNA:han määrättyyn järjestykseen

DNA-sekvenssit, jotka sitovat erilaisia säätelymolekyylejä, vaikuttavat *cis*, vaikka eivät voikaan sijaita ihan promootterin vieressä; niiden koodeja on vaikea tulkita

Säätelyyn kuuluu myös mahdollisuus vaientaa geenejä metyloimalla DNA:ta tai asetiloimalla histoneja, nukleosomit (= histonit + DNA) ovat osa järjestelmää

Genomic imprinting CELL 223--



Jotta geenin transkriptiota voidaan säädellä, sen säätelysekvenssejä on voitava “lukea”.

Suuri luokka proteiineja, DNA:han sitoutuvat proteiinit (**DNA binding**) tunnistetaan nimenomaan **sitoutumismotiiveista**; niiden arvataan olevan transkription regulaattoreita, vaikkei (vielä) tiedettäisi, mitä ne oikein säätelevät.

Sinkkisormet Zn -ioni yhdistää joitakin aminohappoja (esim 4 kysteiiniä tai 2 kysteiiniä ja 2 histidiiniä) erityiseksi aiheeksi, joka sitoutuu DNA:han.

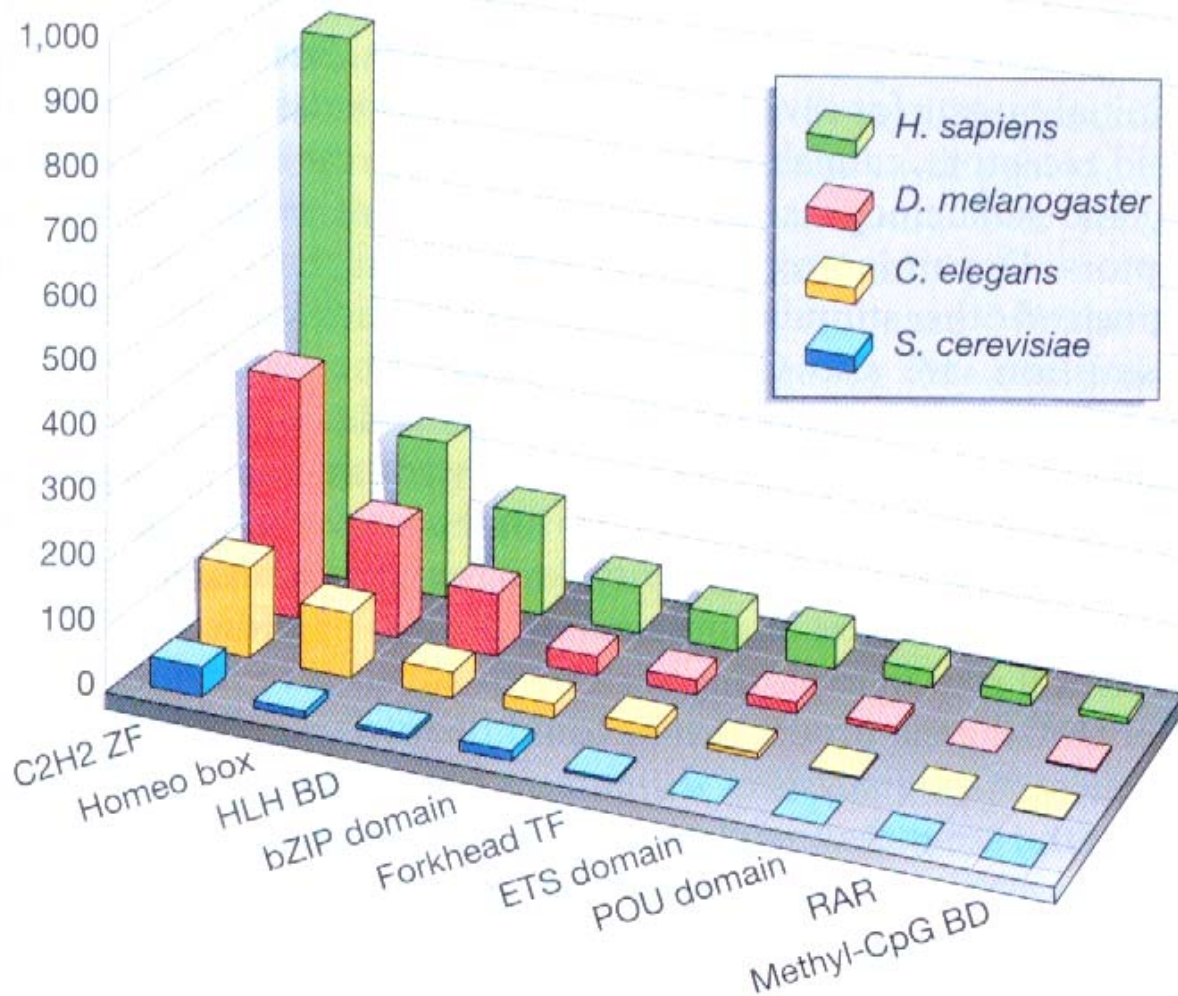
Homeodomain 60 aminohapon mittainen konservatiivinen aihe, jotka liittyvät eläinten kehitysbiologisiin säätelysteemeihin!

Winged helix (forkhead)

Leusiinivetoketju (Leucine zipper)

Helix-loop-helix

Helix-turn-helix



Kun ihmisgenomi oli
luettu, etsittiin ja
tulkittiin
transkriptiofaktorit ja
verrattiin
geeniperheitä
muiden
sekvensoitujen
eukaryoottien kanssa

Figure 1 Genome-wide comparison of transcriptional activator families in eukaryotes. The relative sizes of transcriptional activator families among *Homo sapiens*, *D. melanogaster*, *C. elegans* and *S. cerevisiae* are indicated, derived from an analysis of eukaryotic proteomes using the INTERPRO database, which incorporates Pfam, PRINTS and Prosite. The transcription factors families shown are the largest of their category out of the 1,502 human protein families listed by the IPI.

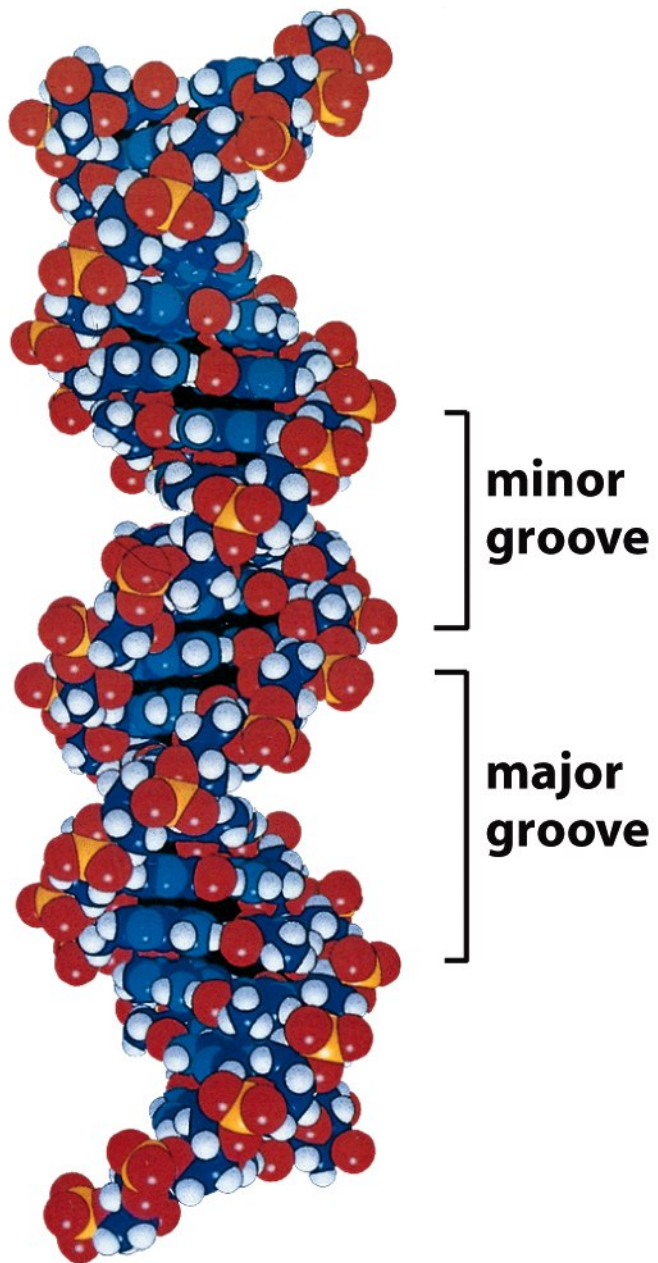
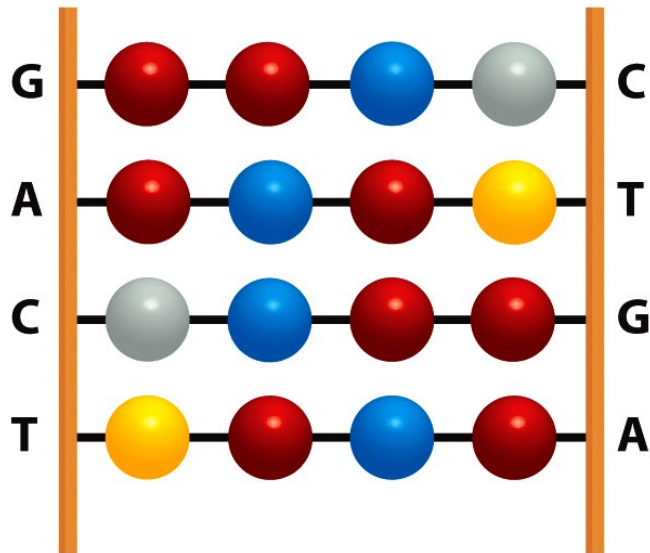
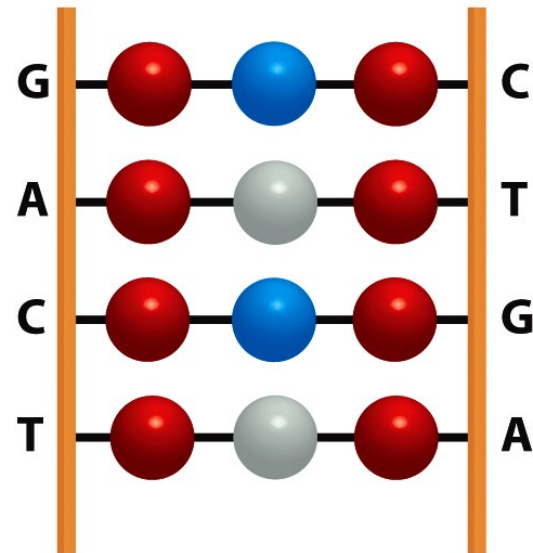


Figure 7-6 Molecular Biology of the Cell 5/e (© Garland Science 2008)

major groove



minor groove

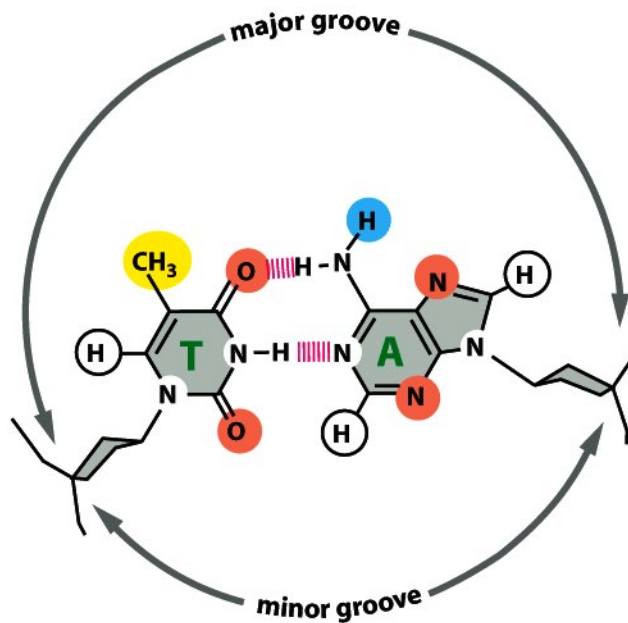
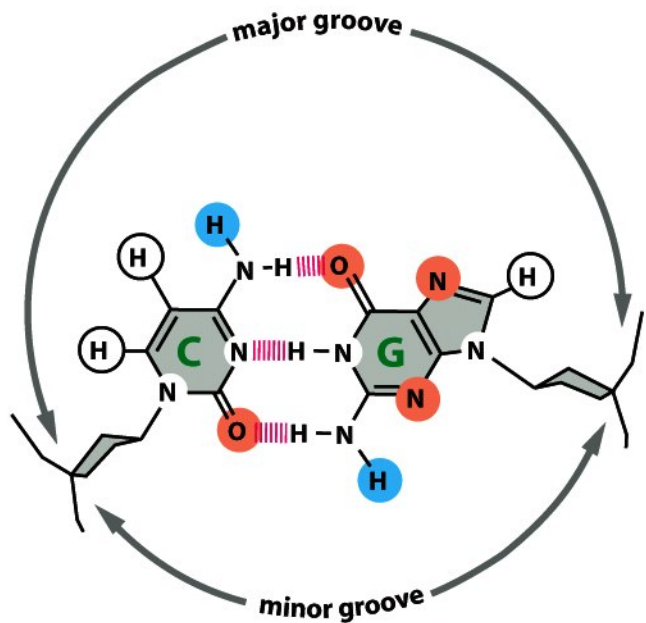
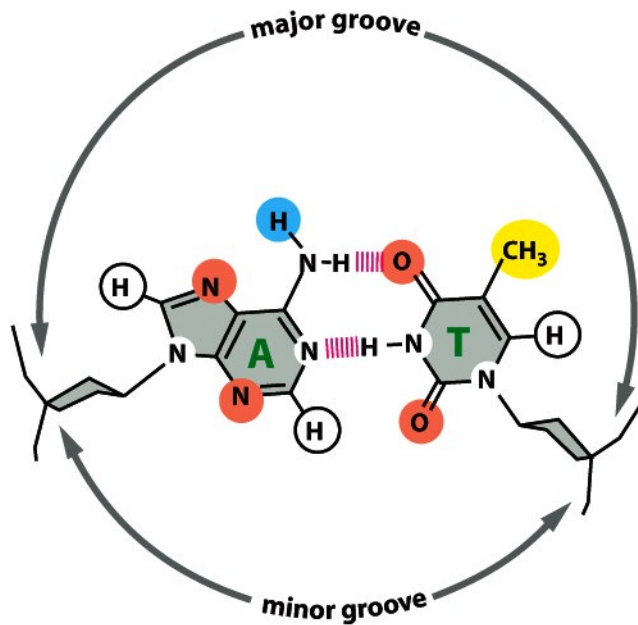
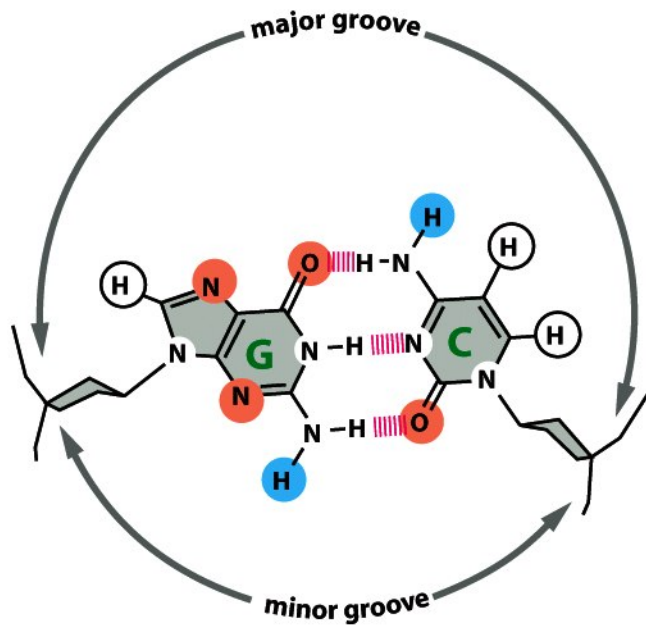


KEY:

- = H-bond acceptor
- = H-bond donor
- = hydrogen atom
- = methyl group

DNA:n koodi säätely- ja tulkinta lukijoiden *silmin* on monipuolisempi kuin pelkät neljä kirjainta

Siksi tätä koodia on vaikea selvittää. Koodisanoja on yhtä monta (tai enemmän?) kuin on säätelyproteiinejakin ja niitä on tosi paljon



Sitoutuminen
on aina
kemiallista;
tässä asteikossa
ei ole tunto-
eikä näköaistia

Figure 7-7 Molecular Biology of the Cell 5/e (© Garland Science 2008)

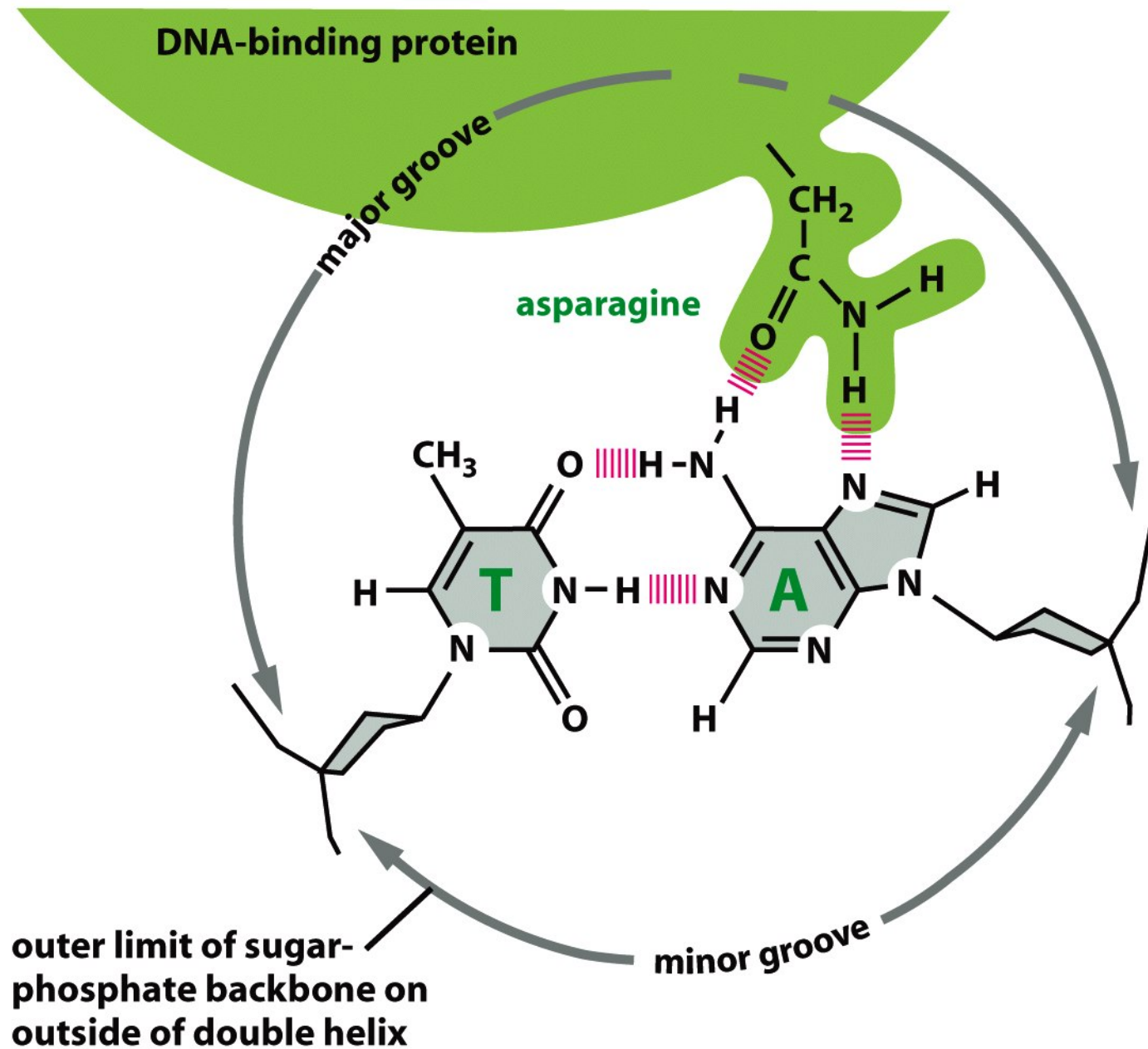


Figure 7-9 Molecular Biology of the Cell 5/e (© Garland Science 2008)

Table 7–1 Some Gene Regulatory Proteins and the DNA Sequences That They Recognize

	NAME	DNA SEQUENCE RECOGNIZED*
Bacteria	Lac repressor	5' AATTGTGAGCGGATAACAATT 3' TTAACACTCGCCTATTGTTAA
	CAP	TGTGAGTTAGCTCACT ACACTCAATCGAGTGA
	Lambda repressor	TATCACCGCCAGAGGT ATAGTGGCGGTCTCCAT
Yeast	Gal4	CGGAGGACTGTCCTCCG GCCTCCTGACAGGAGGC
	Matα2	CATGTAATT GTACATTAA
	Gcn4	ATGACTCAT TACTGAGTA
	Kruppel	AACGGGTAA TTGCCCAATT
Drosophila	Bicoid	GGGATTAGA CCCTAATCT
	Sp1	GGGCGG CCCGCC
Mammals	Oct1 Pou domain	ATGCAAAT TACGTTTA
	GATA1	TGATAG ACTATC
	MyoD	CAAATG GTTTAC
	p53	GGGCAAGTCT CCCGTTCAGA

*For convenience, only one recognition sequence, rather than a consensus sequence (see Figure 6–12), is given for each protein.

Pieni valikoima

"sanoja"

säätelyteksteistä, jotka
koskevat hyvin suppeaa
transkriptiosäätelijöiden
joukkoa

CELL 418

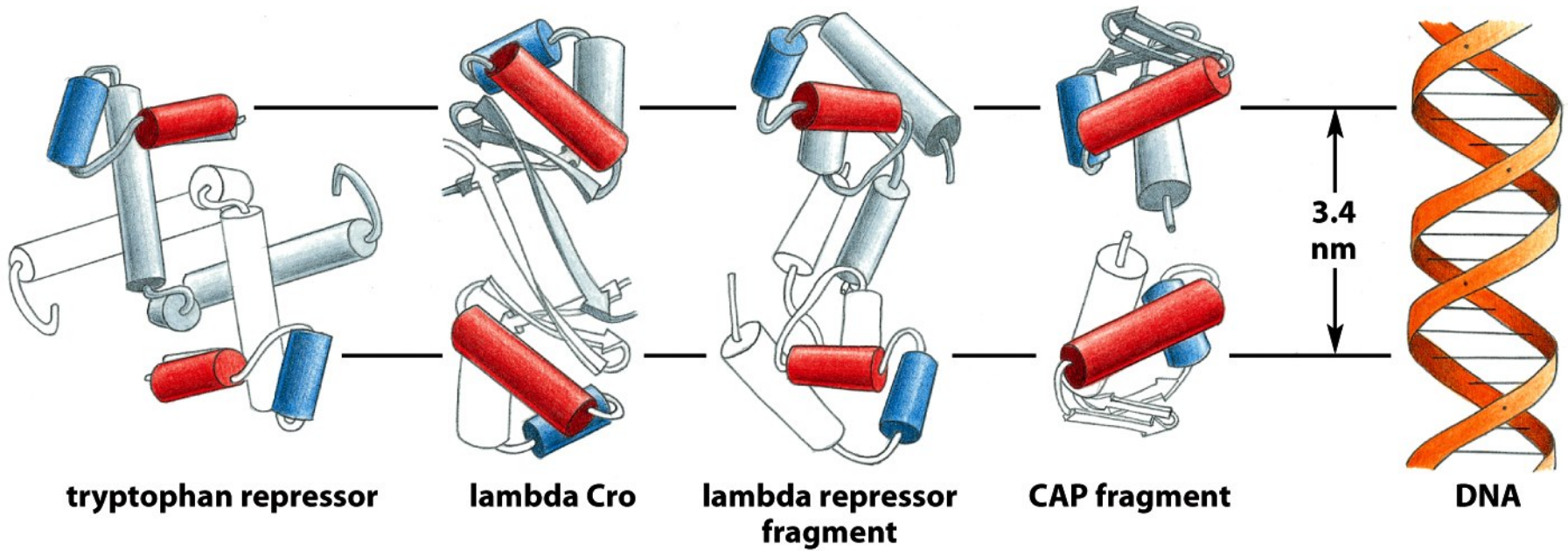


Figure 7-11 Molecular Biology of the Cell 5/e (© Garland Science 2008)

CELL 420

helix-turn-helix säätelijöitä

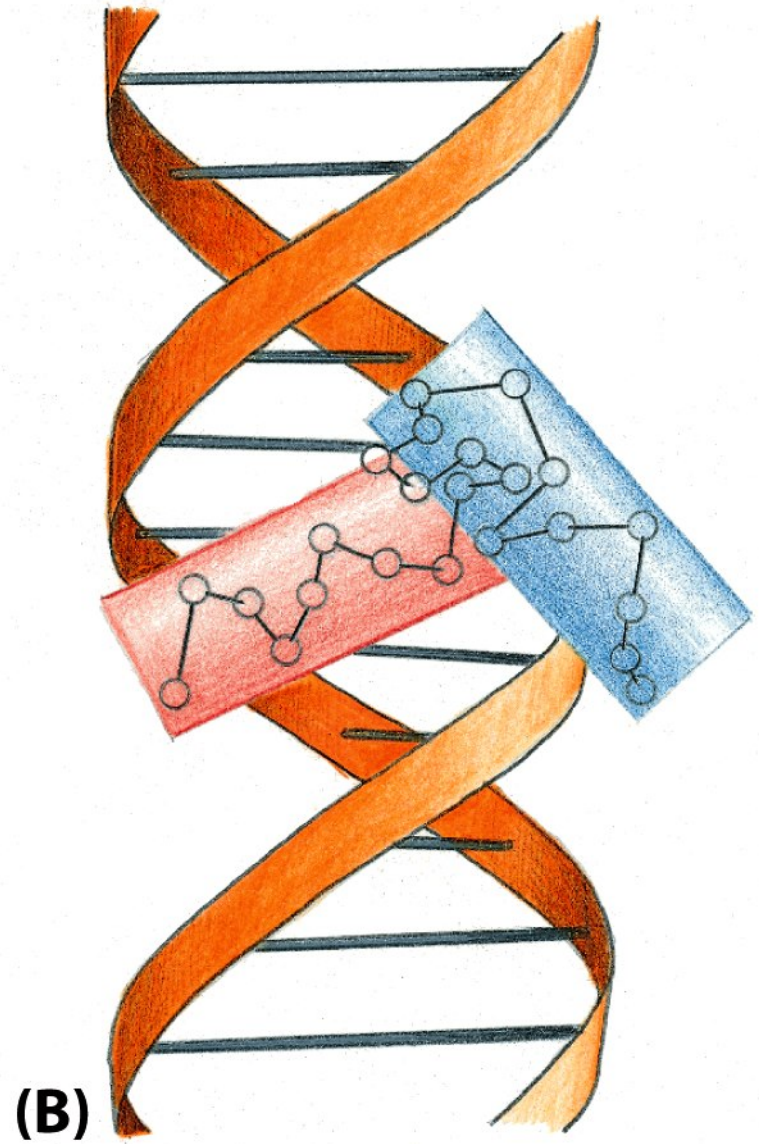
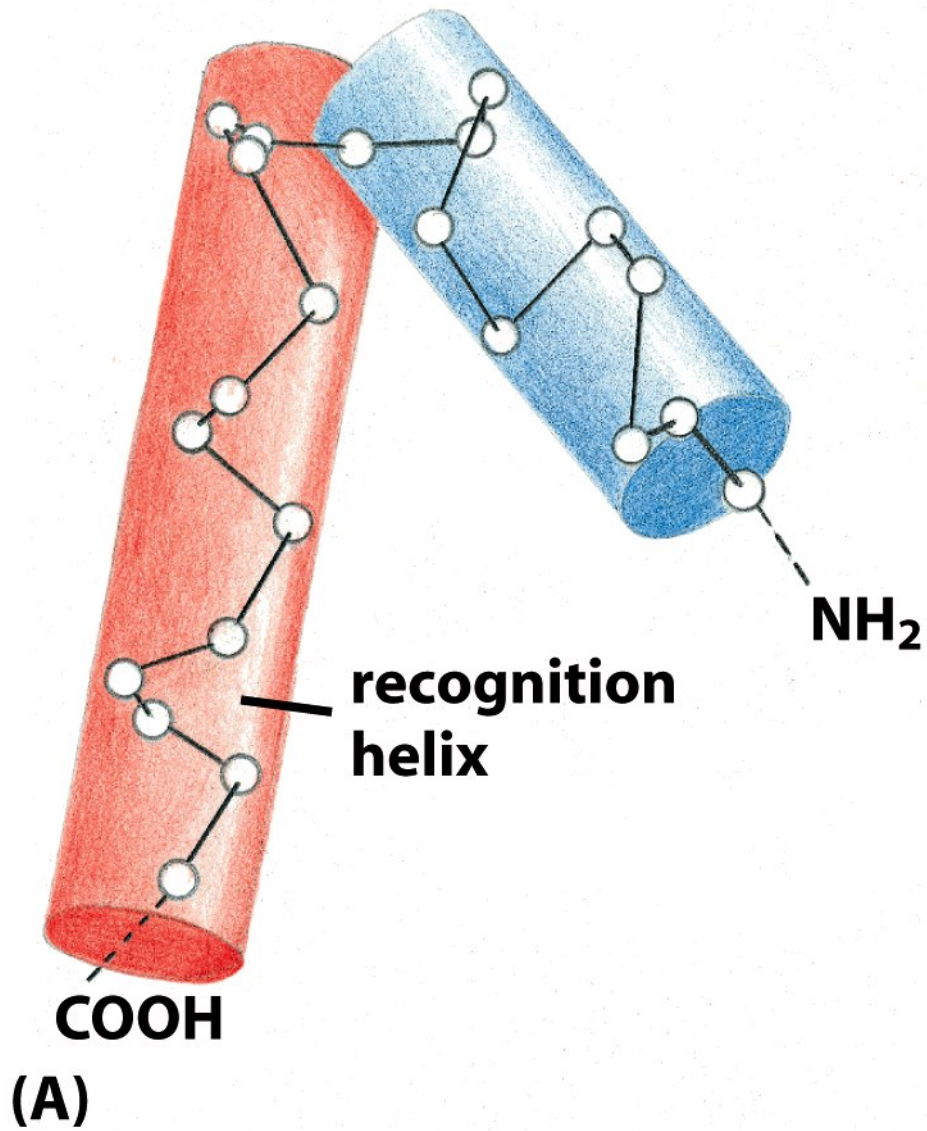
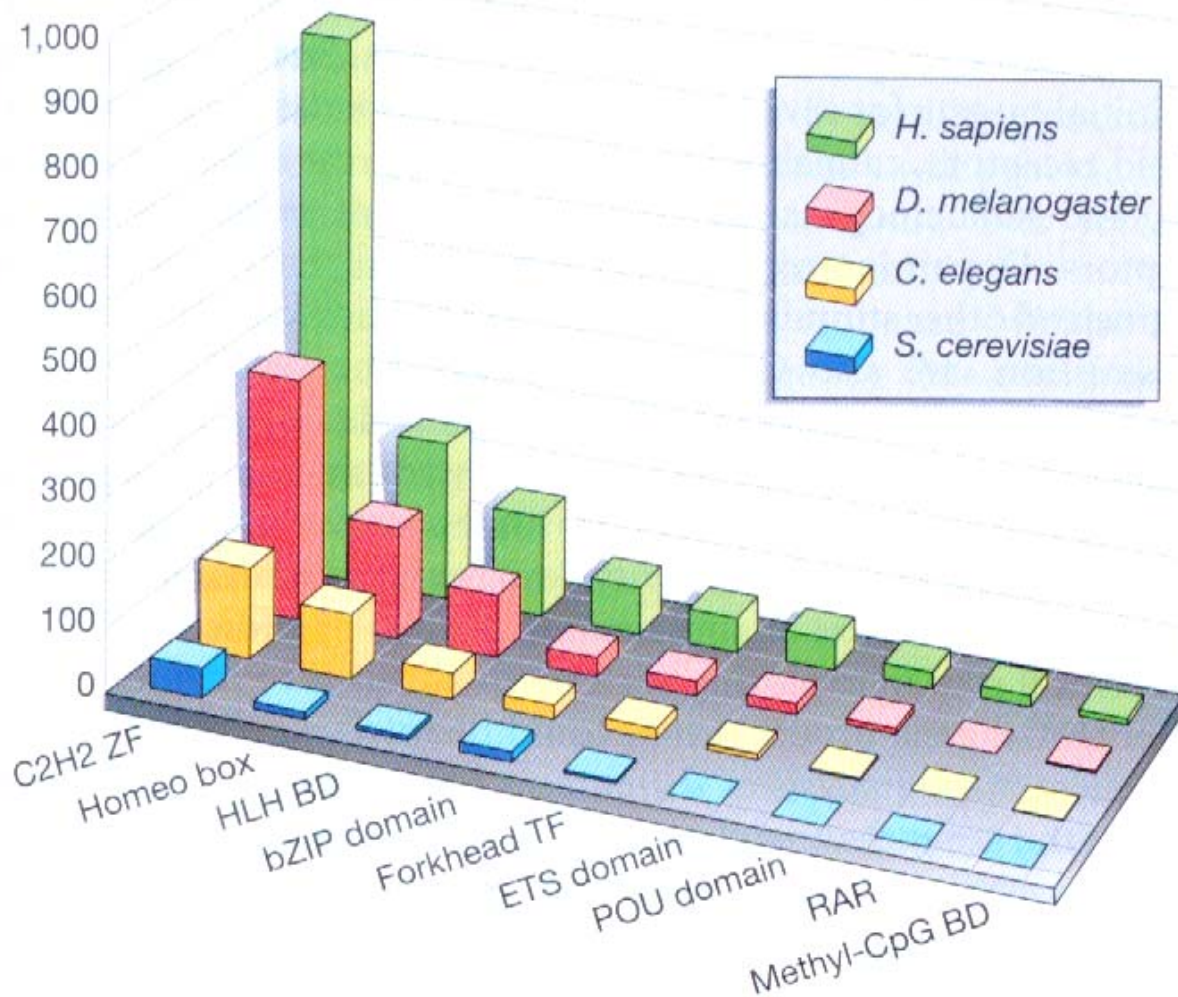


Figure 7-10 Molecular Biology of the Cell 5/e (© Garland Science 2008)



Figure 7-12 Molecular Biology of the Cell 5/e (© Garland Science 2008)

Faagi lambdan Cro-proteiinin kohdesekvenssi



C2H2 ZF

sinkkisormet

ylivoimaisesti yleisin
luokka meillä
ihmisillä

Figure 1 Genome-wide comparison of transcriptional activator families in eukaryotes. The relative sizes of transcriptional activator families among *Homo sapiens*, *D. melanogaster*, *C. elegans* and *S. cerevisiae* are indicated, derived from an analysis of eukaryotic proteomes using the INTERPRO database, which incorporates Pfam, PRINTS and Prosite. The transcription factors families shown are the largest of their category out of the 1,502 human protein families listed by the IPI.

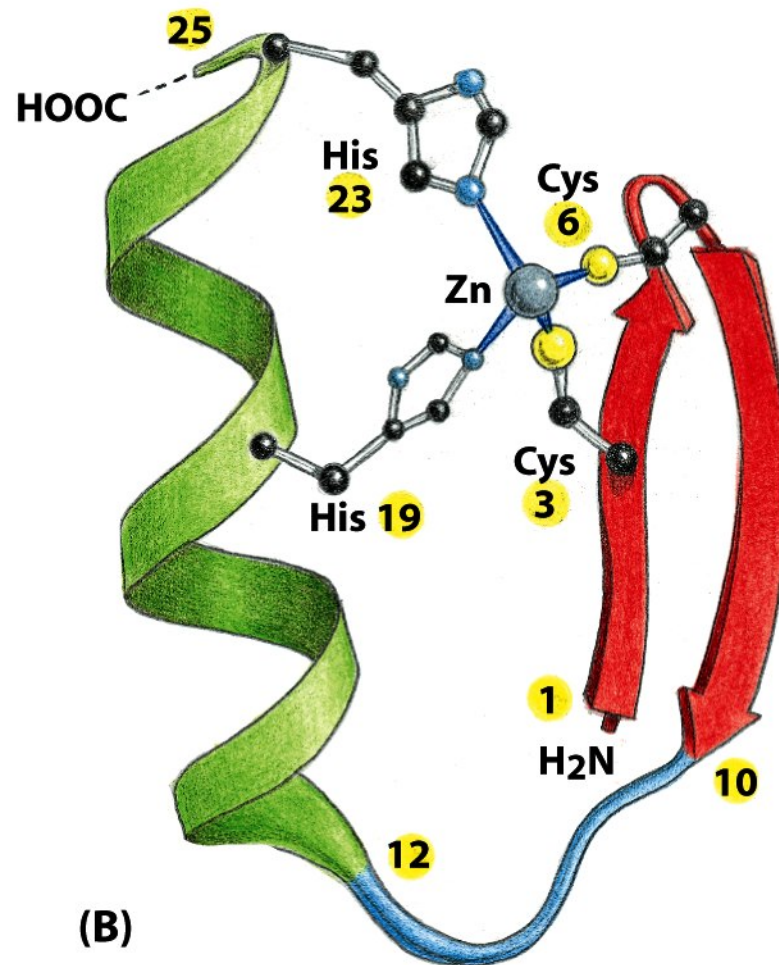
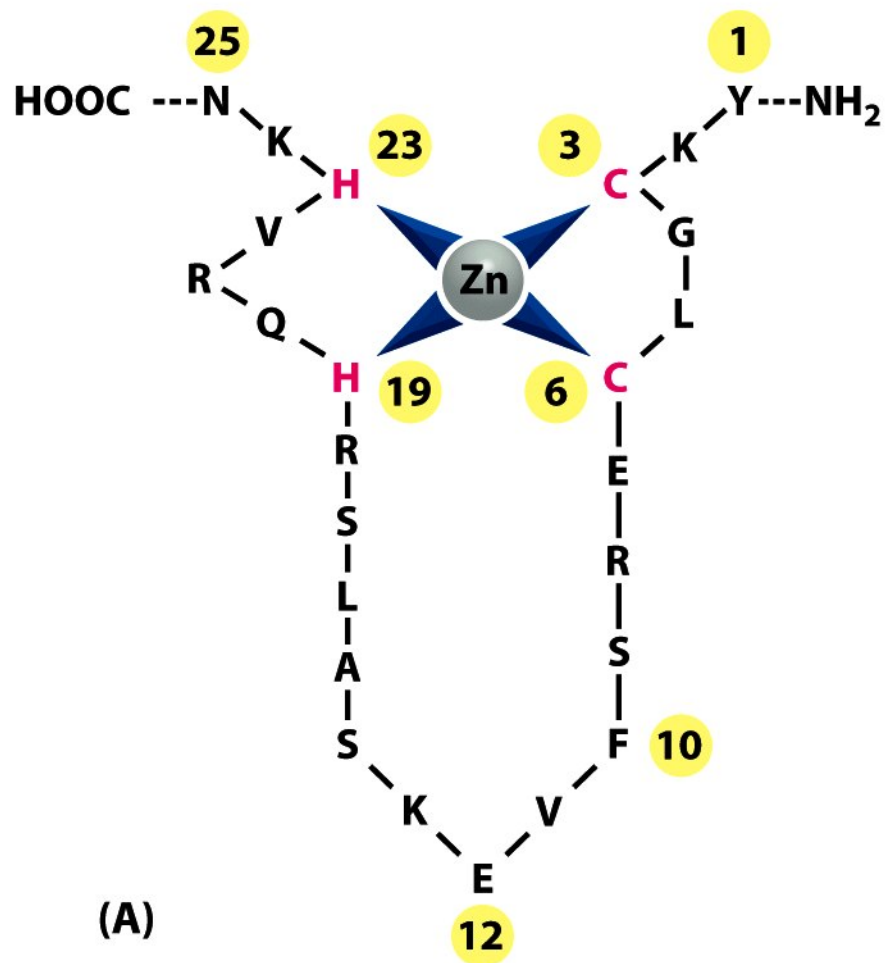
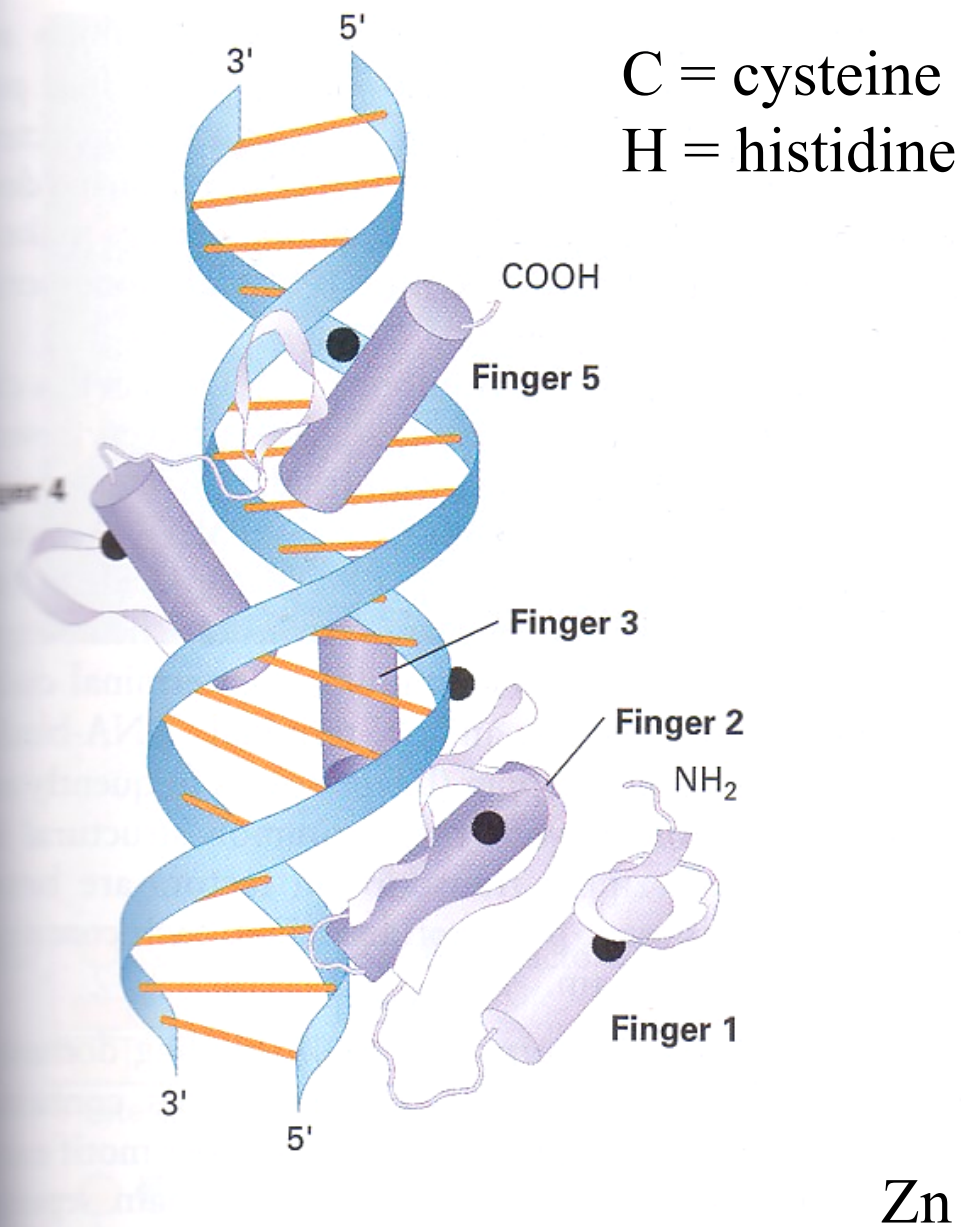
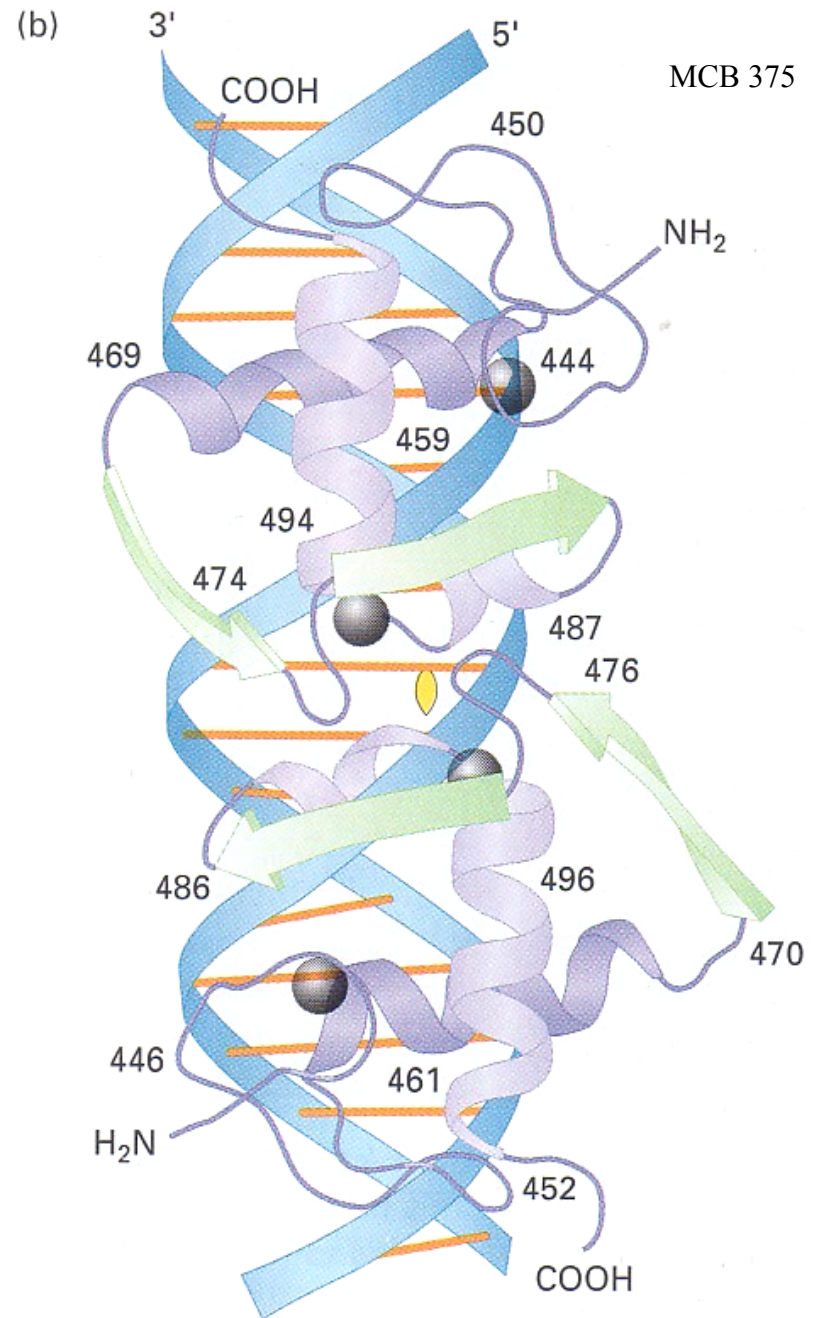


Figure 7-14 Molecular Biology of the Cell 5/e (© Garland Science 2008)

C2H2 -sinkkisormen idea. Sopivin välein toistuvista *his* ja *cys* aminohapoista voidaan tällainen motiivi aavistaa geeniä lueskeltaessa



Viisisorminen **C2H2** monomeeri GL1



C4 -sinkisormi

C6 - sinkkisormi (homodimeeri)



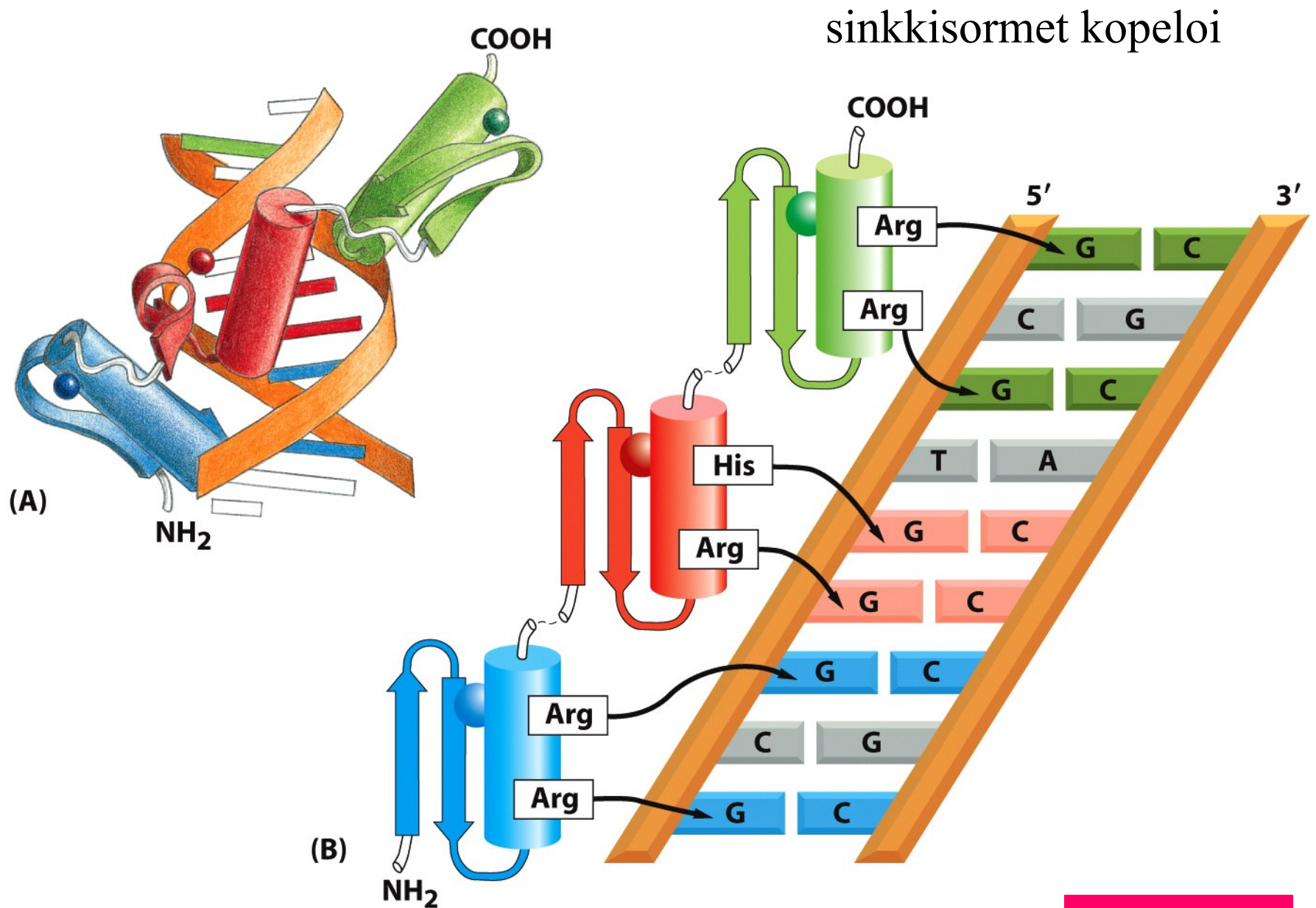


Figure 7-15 Molecular Biology of the Cell 5/e (© Garland Science 2008)

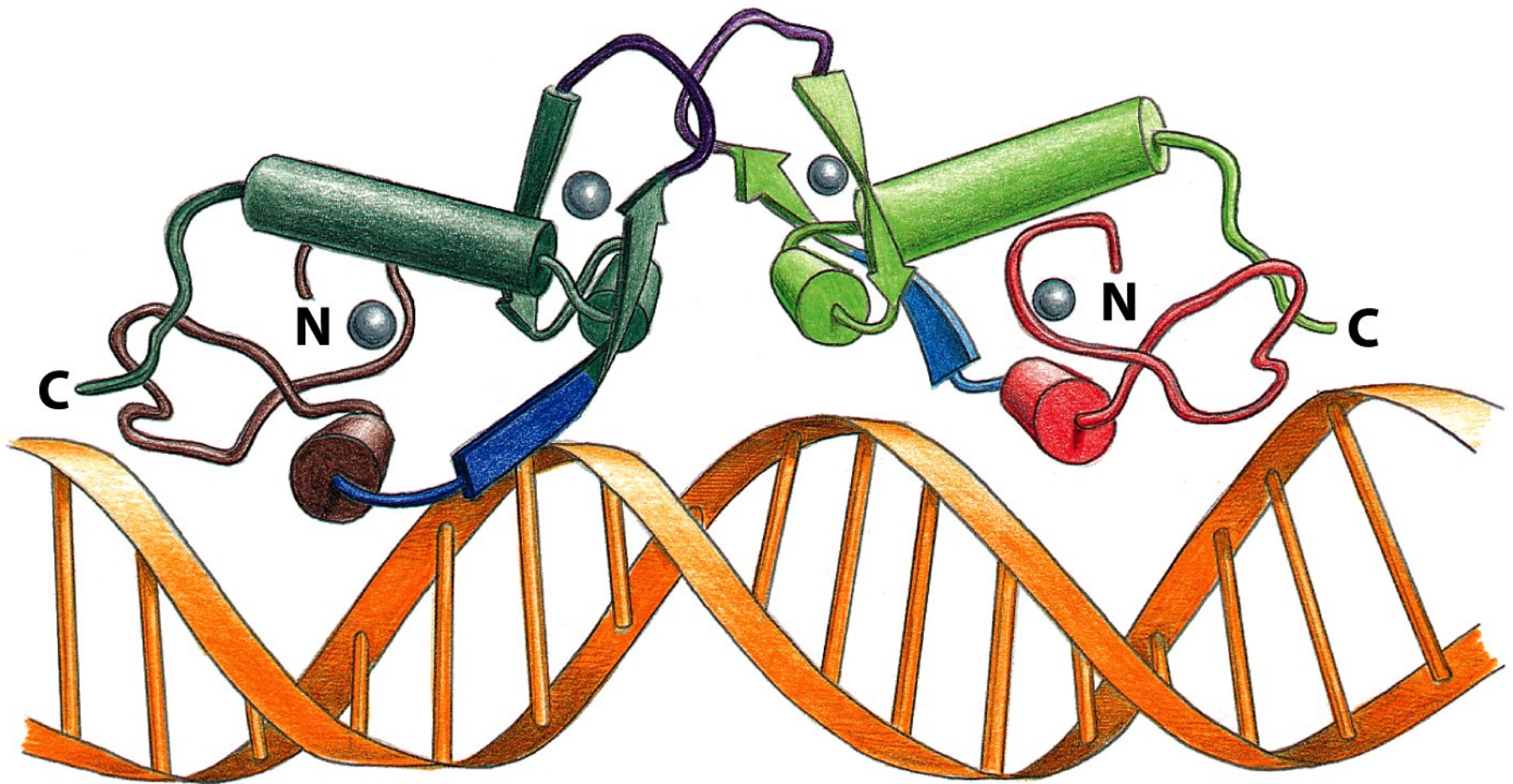
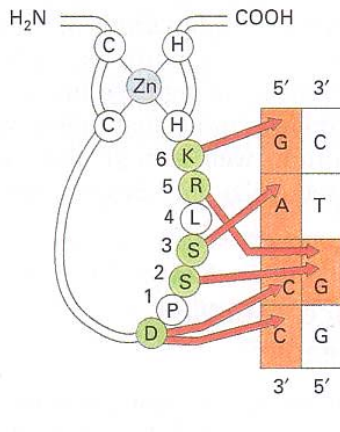
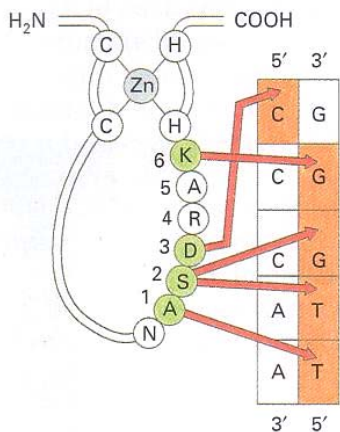
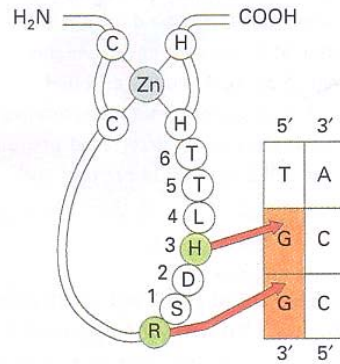
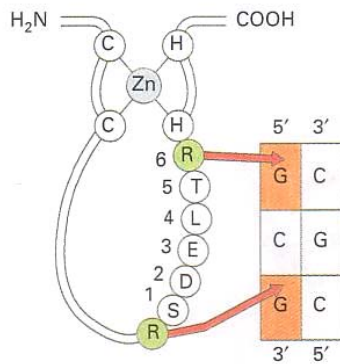
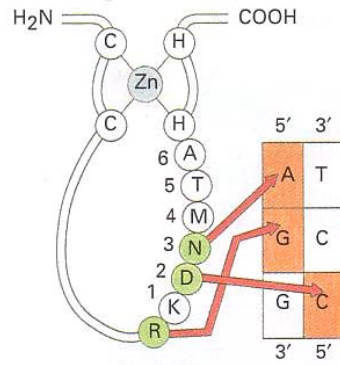
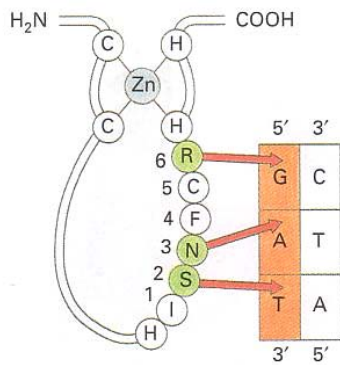


Figure 7-16 Molecular Biology of the Cell 5/e (© Garland Science 2008)



Sinkkisormien sekvenssispesifiset interaktiot

Aminohappokoodin tärkeät
'kirjaimet' vihreällä

Nukleotidikoodin tärkeät
'kirjaimet' oranssilla

C = kysteini

H = histidiini

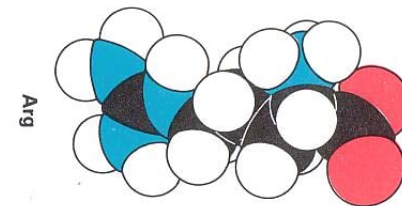
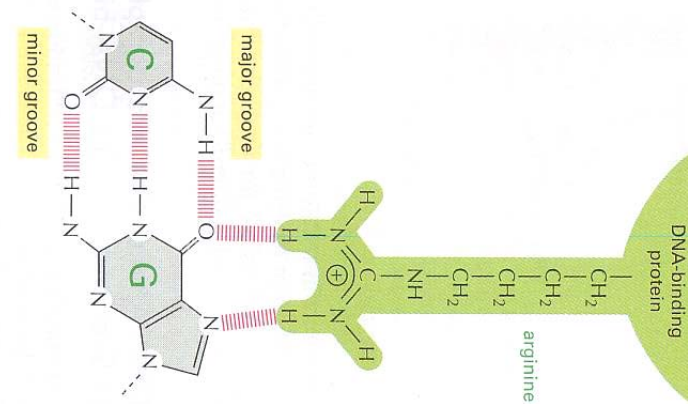
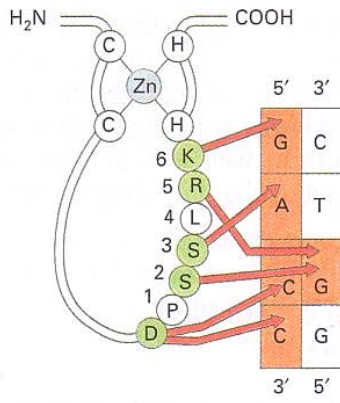
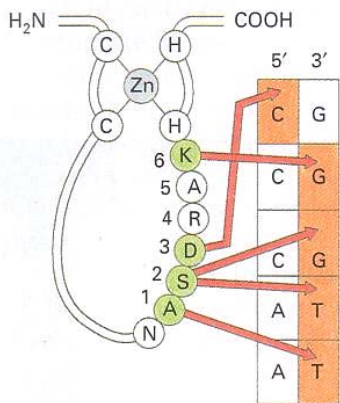
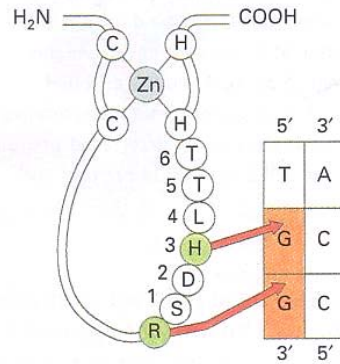
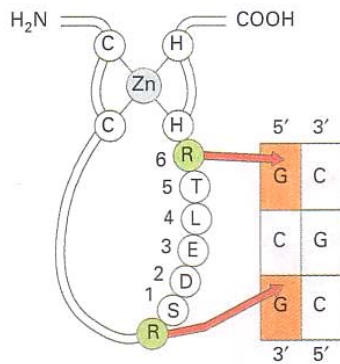
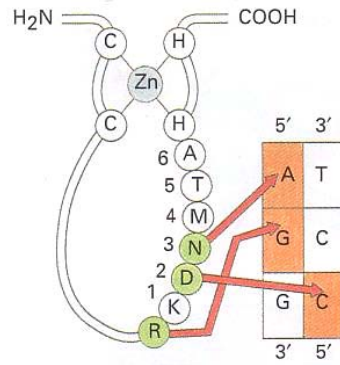
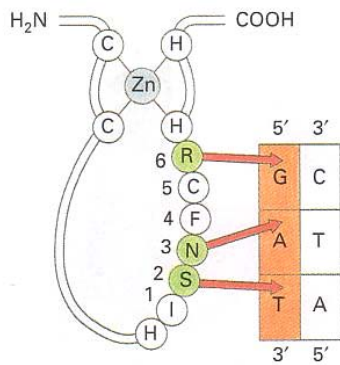
R = arginiini

N = asparagiini

S = seriini

D = aspartaattihappo

K = lyysiini



R = arginiinin sivuketju on erikoisen sopiva sitoutumaan guaniiniin ja on usein tunnistusavaimen tärkeä osa



Leusiinivetoketju (zipper)

CELL 424

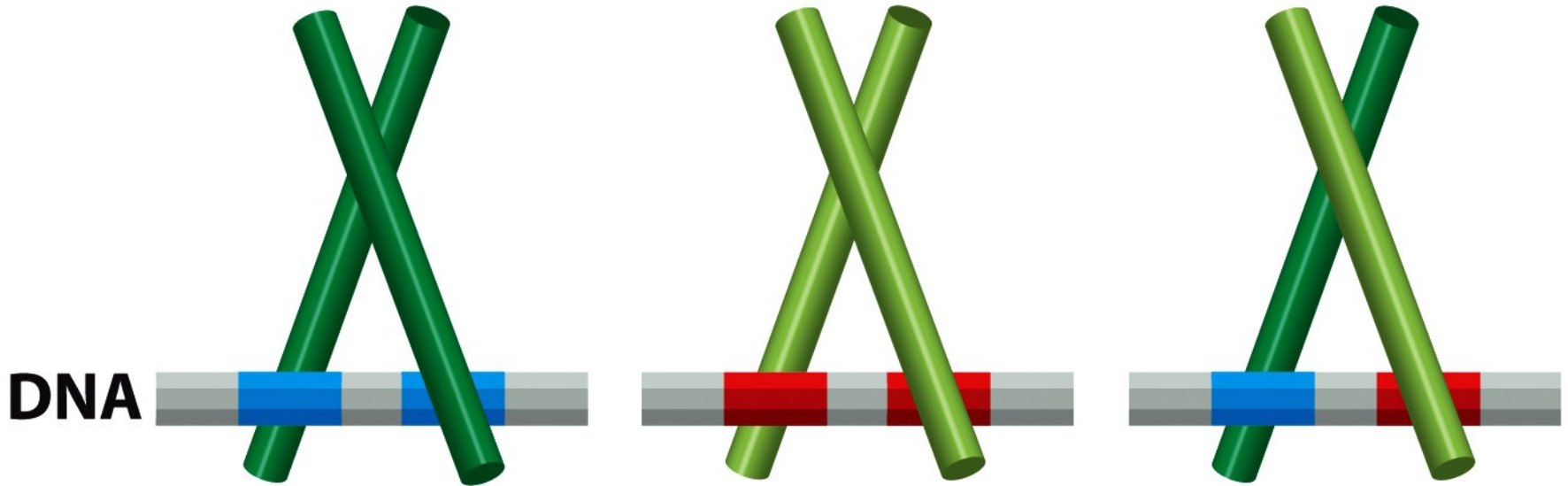
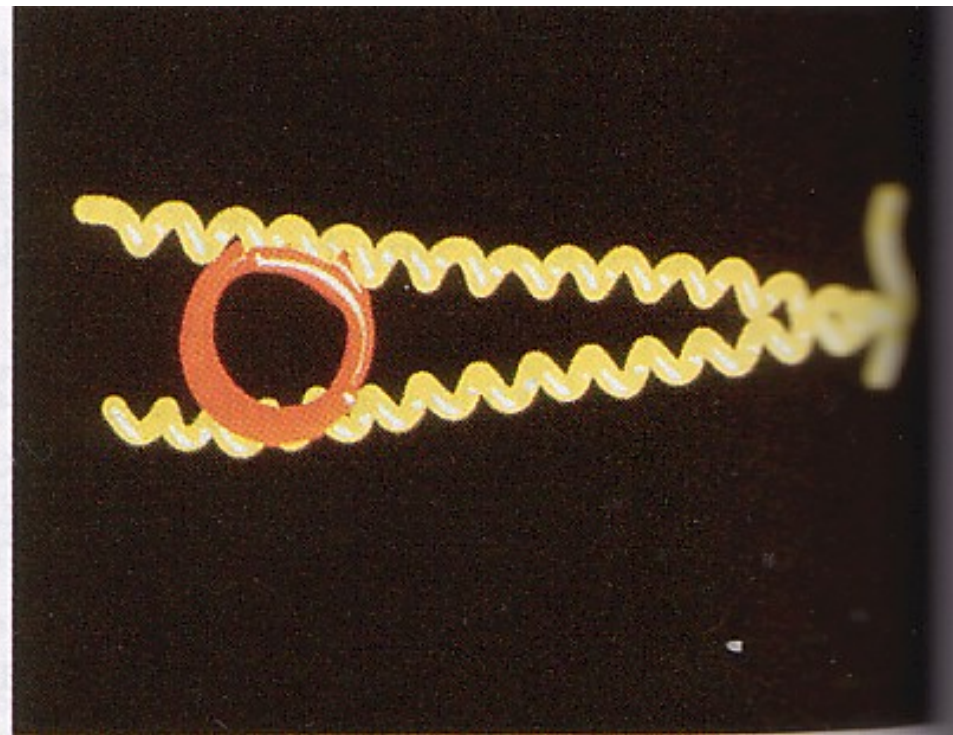
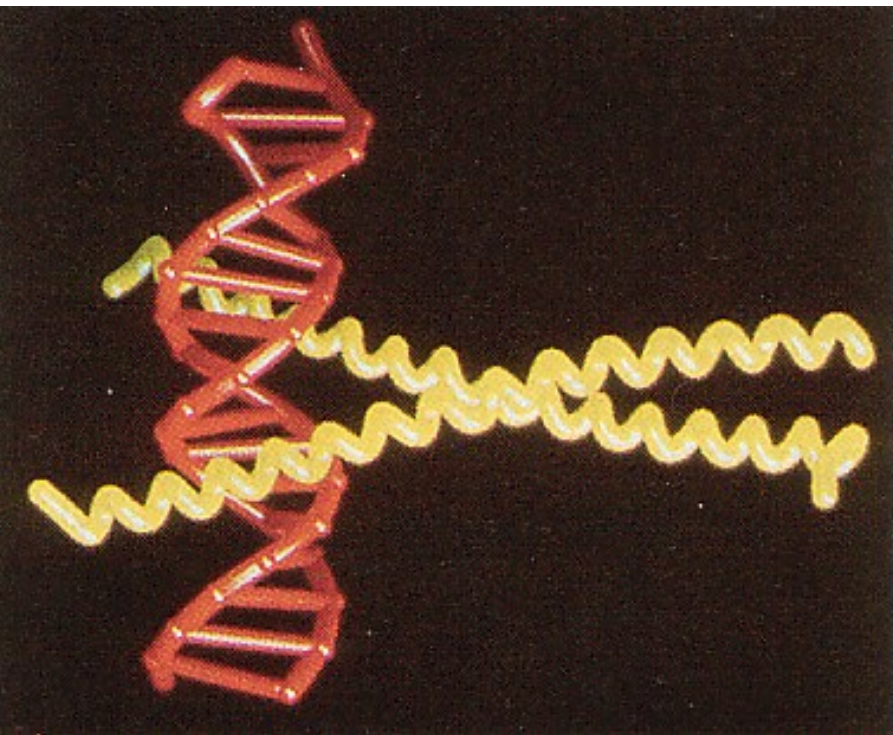
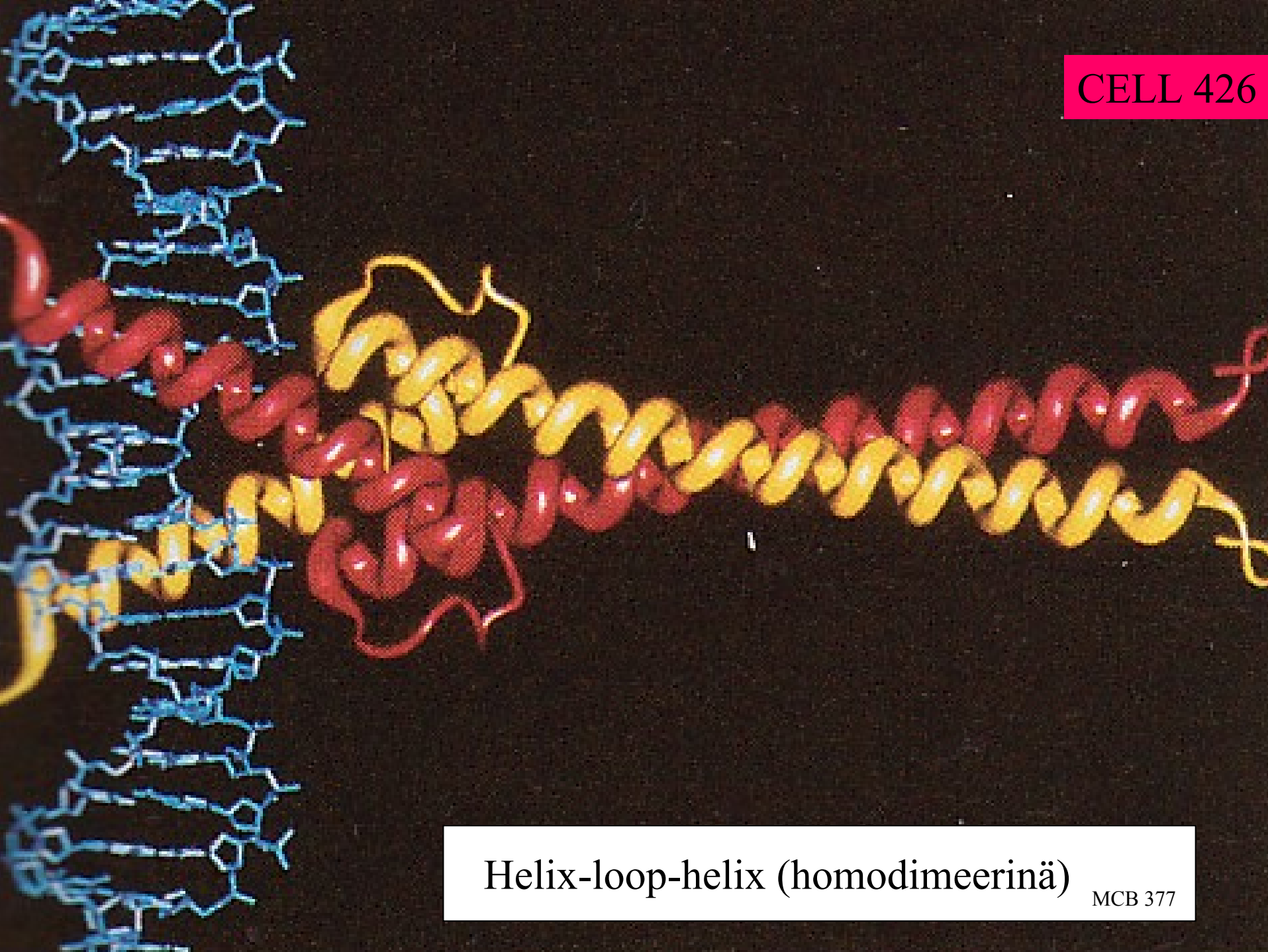


Figure 7-20 Molecular Biology of the Cell 5/e (© Garland Science 2008)

Homo- tai heterodimeerejä, tunnistussekvenssit
sinisiä tai punaisia



Leusiinivetoketju (leucine zipper) homodimeeri



Helix-loop-helix (homodimeerinä)

helix-loop-helix

CELL 426

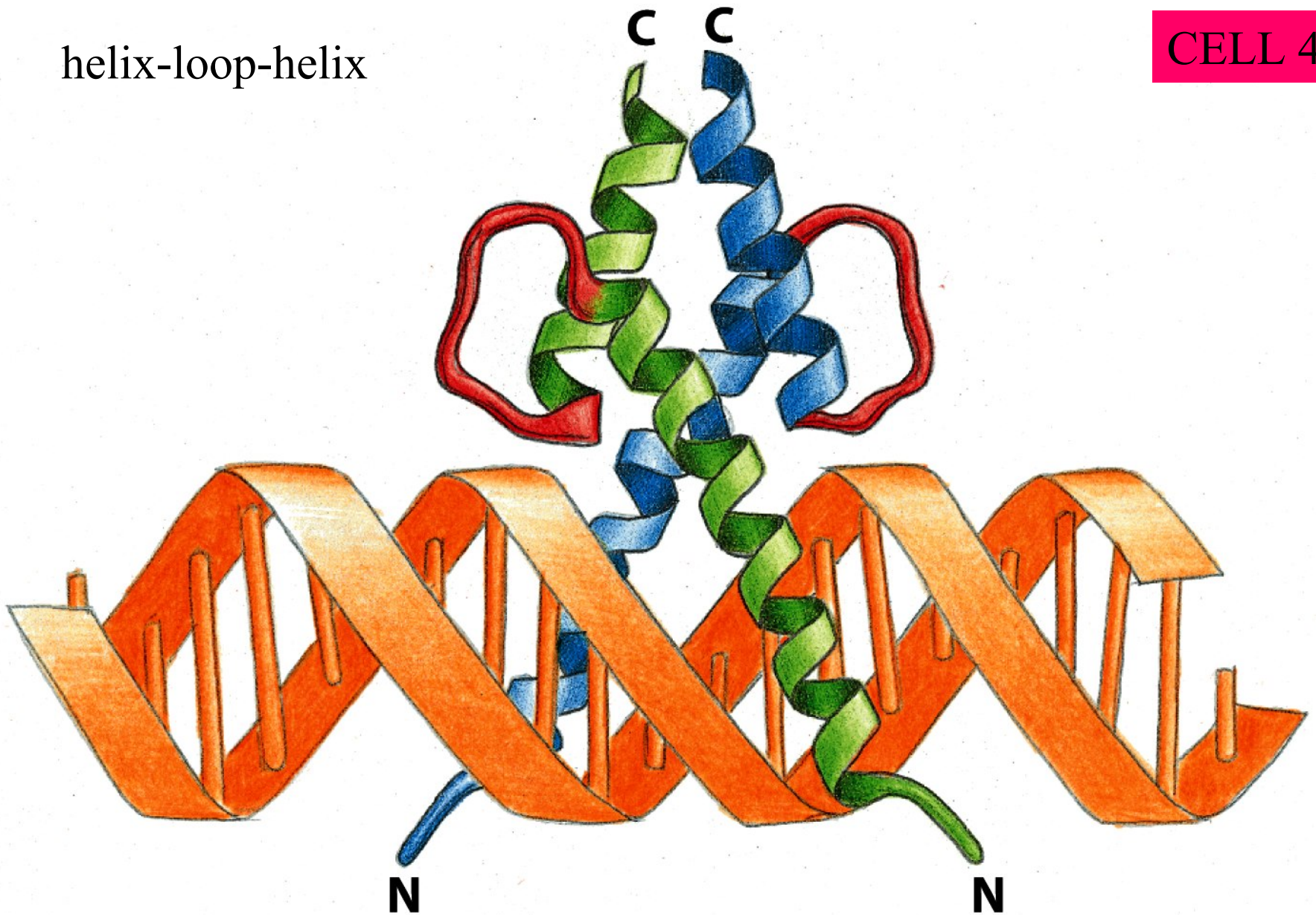
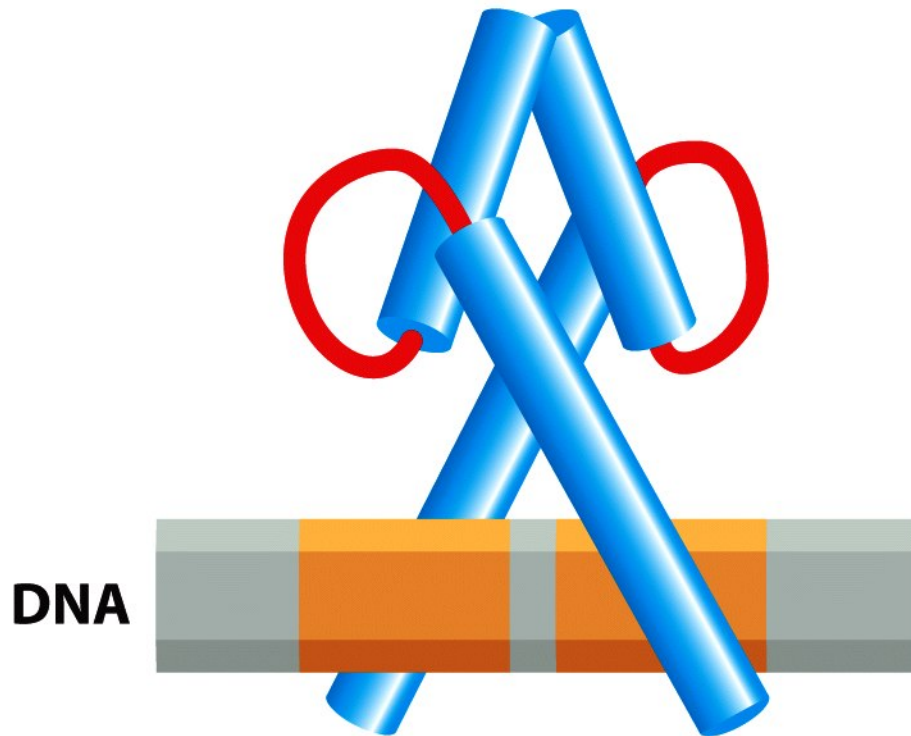


Figure 7-23 Molecular Biology of the Cell 5/e (© Garland Science 2008)

active HLH homodimer



inactive HLH heterodimer

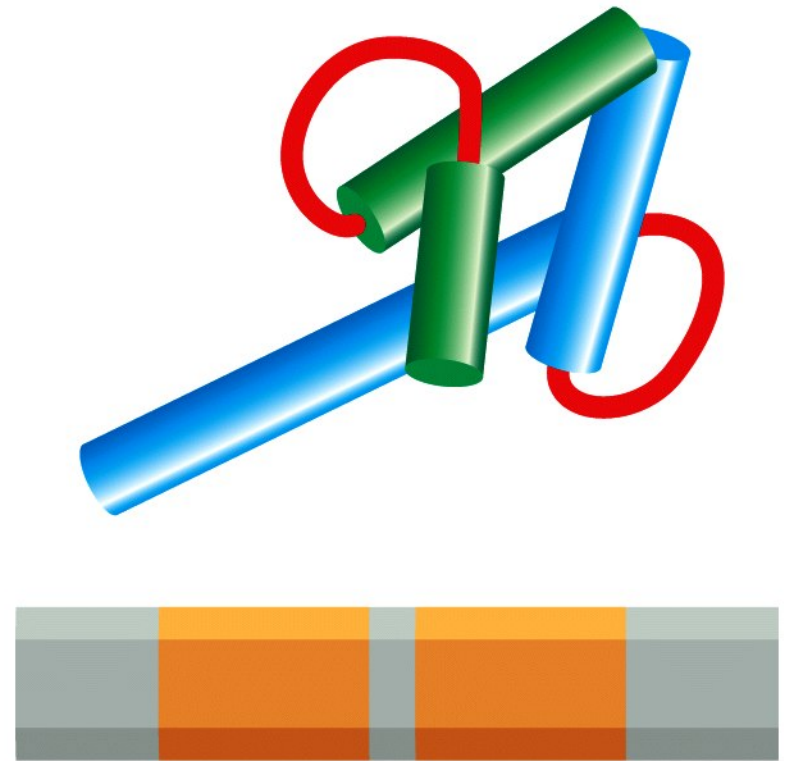
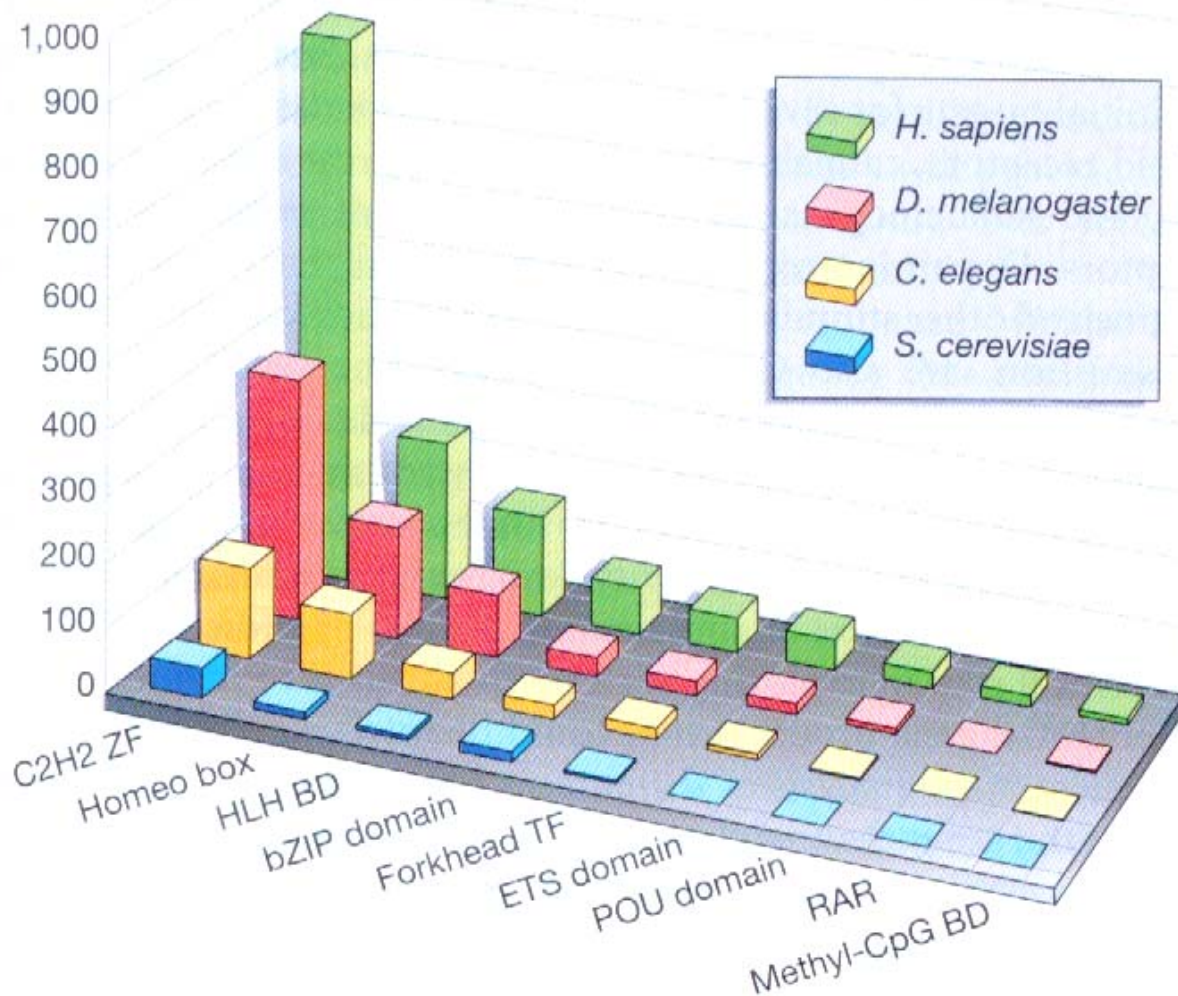


Figure 7-24 Molecular Biology of the Cell 5/e (© Garland Science 2008)

helix-loop-helix: dimeeri ei toimi, jos toinen komponentti on viallinen, esim liian lyhyt



Homeoboksin
sisältävät geenit
ovat
sinkkisormien
jälkeen
yleisimmät
transkription
säätelijät kaikilla
eläimillä

Figure 1 Genome-wide comparison of transcriptional activator families in eukaryotes. The relative sizes of transcriptional activator families among *Homo sapiens*, *D. melanogaster*, *C. elegans* and *S. cerevisiae* are indicated, derived from an analysis of eukaryotic proteomes using the INTERPRO database, which incorporates Pfam, PRINTS and Prosite. The transcription factors families shown are the largest of their category out of the 1,502 human protein families listed by the IPI.

regulaatio3 >>>

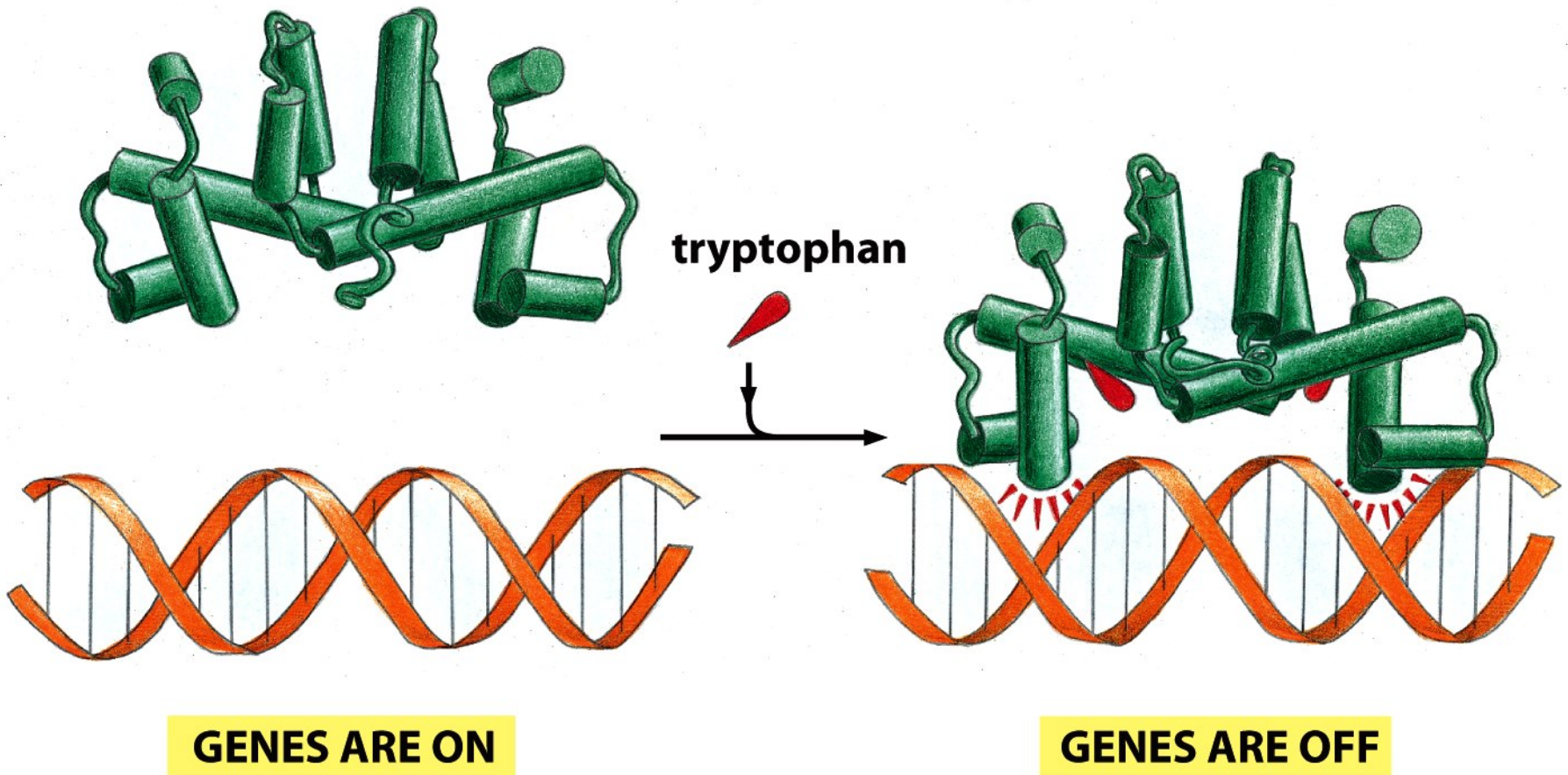
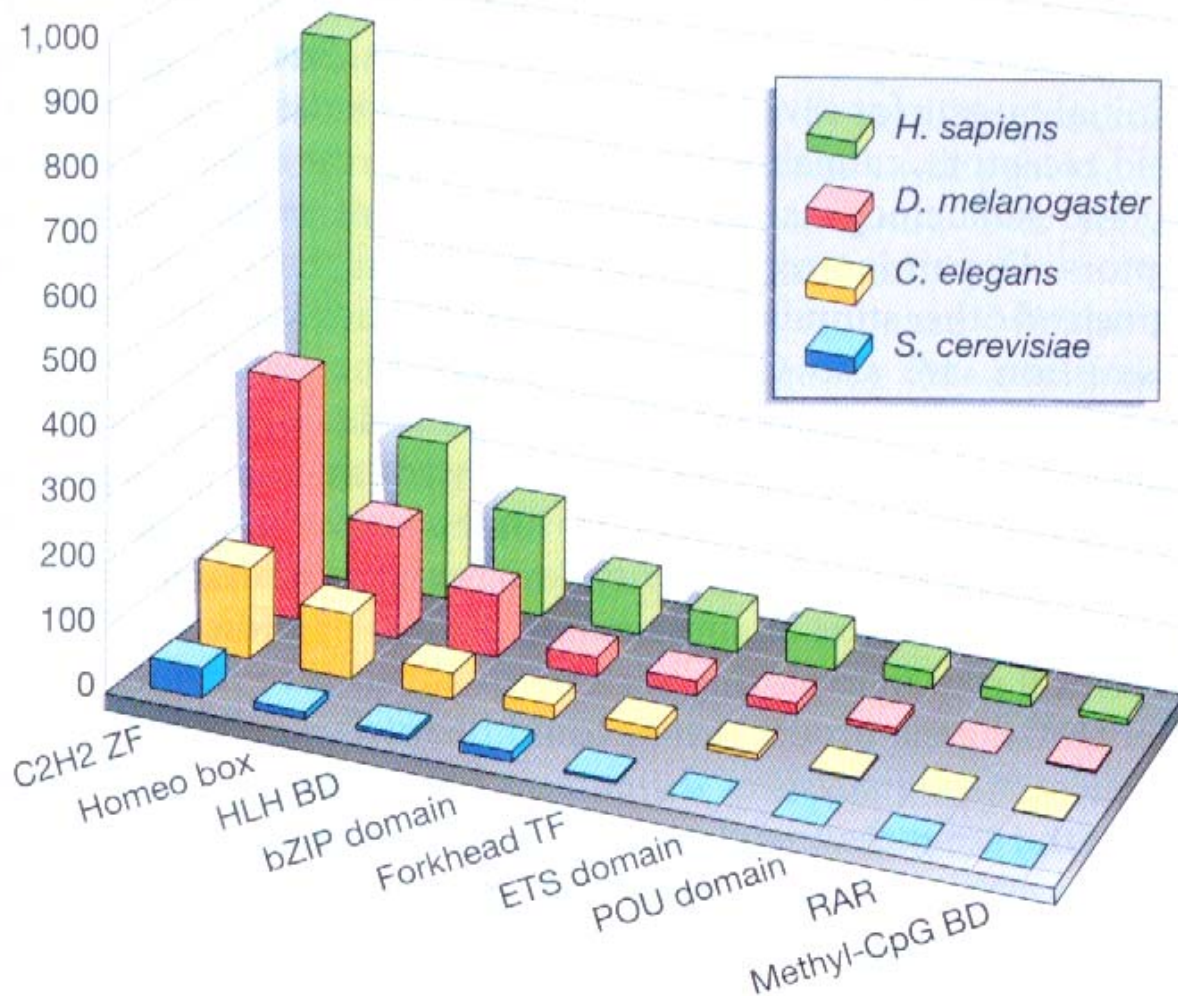


Figure 7-36 Molecular Biology of the Cell 5/e (© Garland Science 2008)

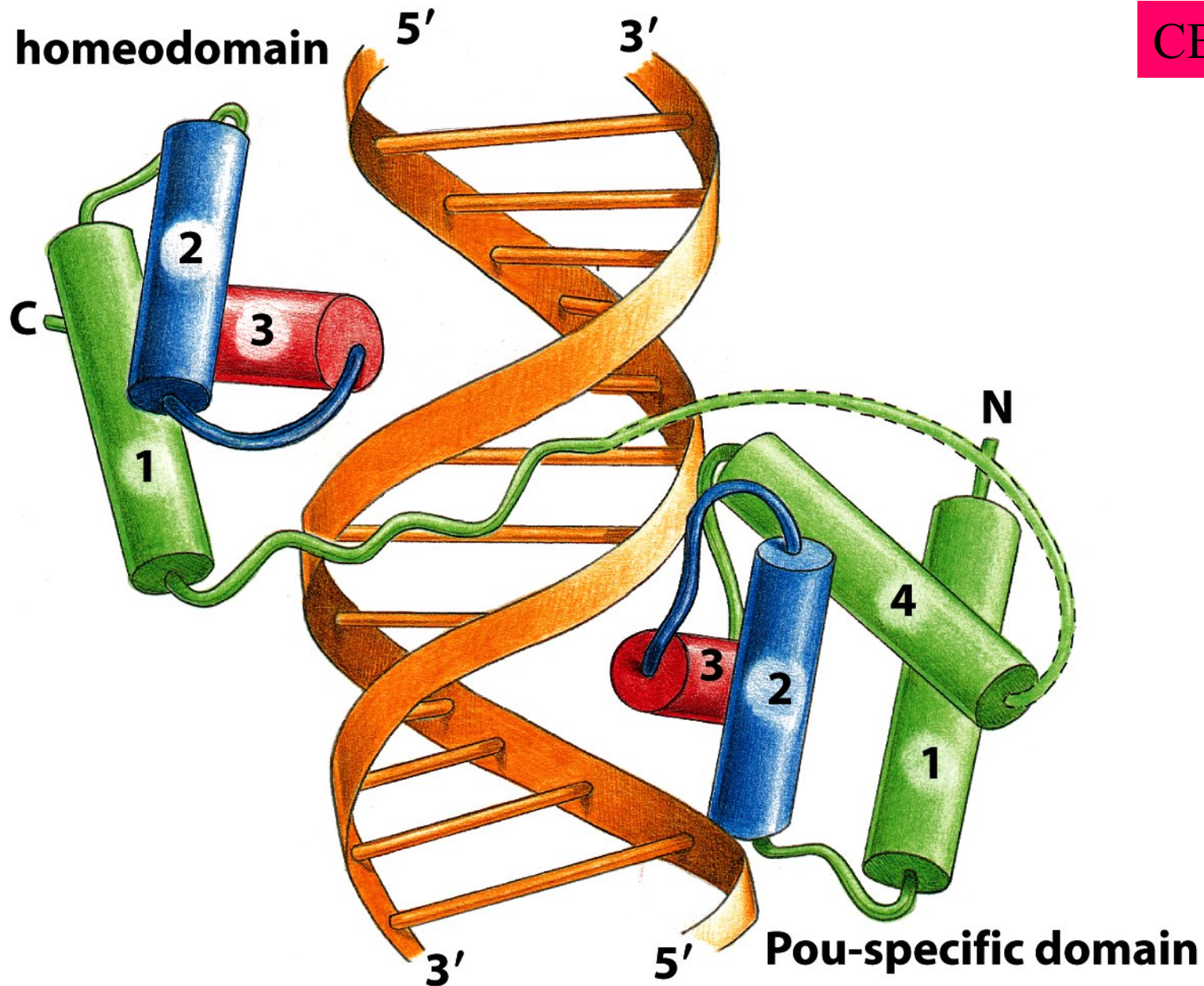


Homeoboksit

toiseksi yleisin luokka
meillä ihmisillä;

niistä lisää
kehitysgenetiikan
puolella

Figure 1 Genome-wide comparison of transcriptional activator families in eukaryotes. The relative sizes of transcriptional activator families among *Homo sapiens*, *D. melanogaster*, *C. elegans* and *S. cerevisiae* are indicated, derived from an analysis of eukaryotic proteomes using the INTERPRO database, which incorporates Pfam, PRINTS and Prosite. The transcription factors families shown are the largest of their category out of the 1,502 human protein families listed by the IPI.



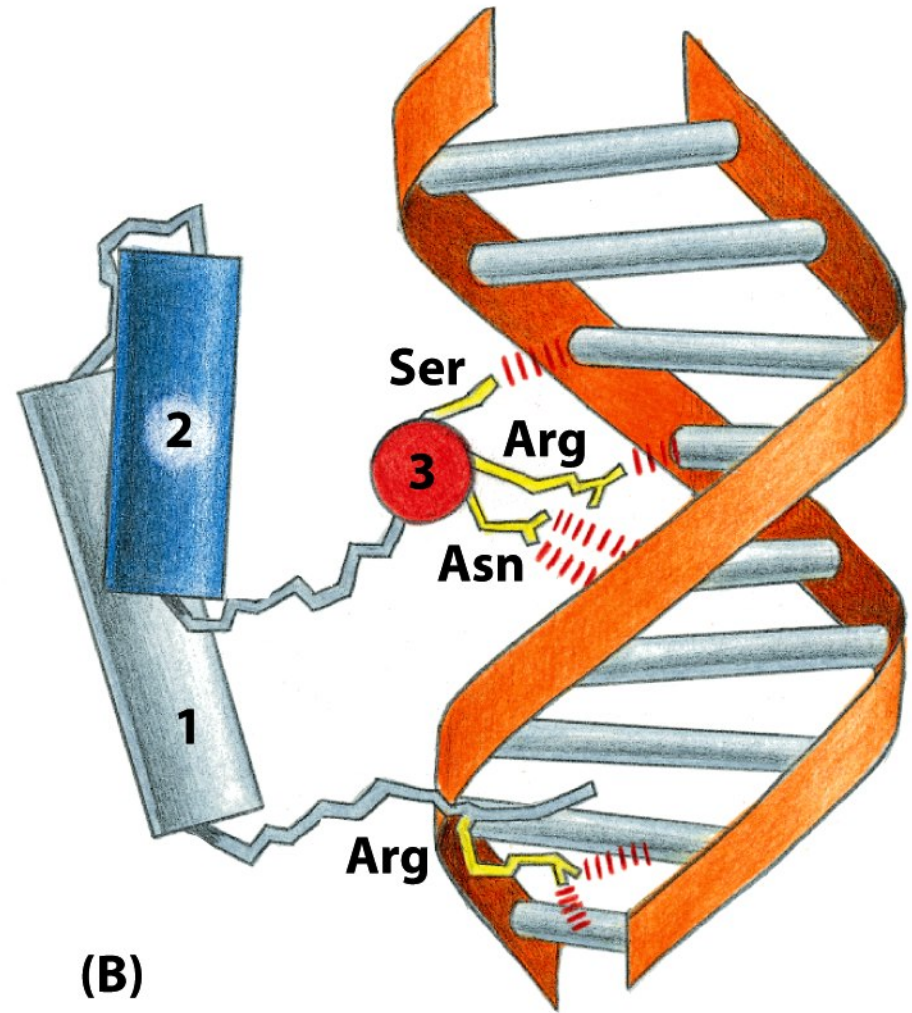
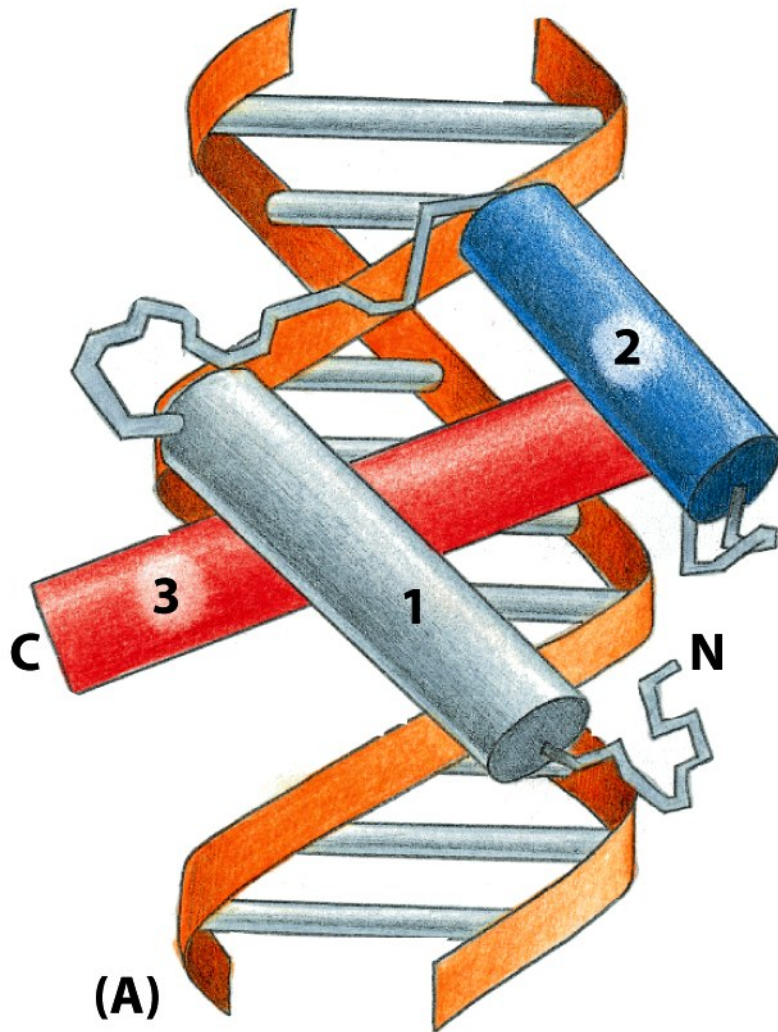


Figure 7-13 Molecular Biology of the Cell 5/e (© Garland Science 2008)

homeodomain sitoutuu spesifiseen sekvenssiin

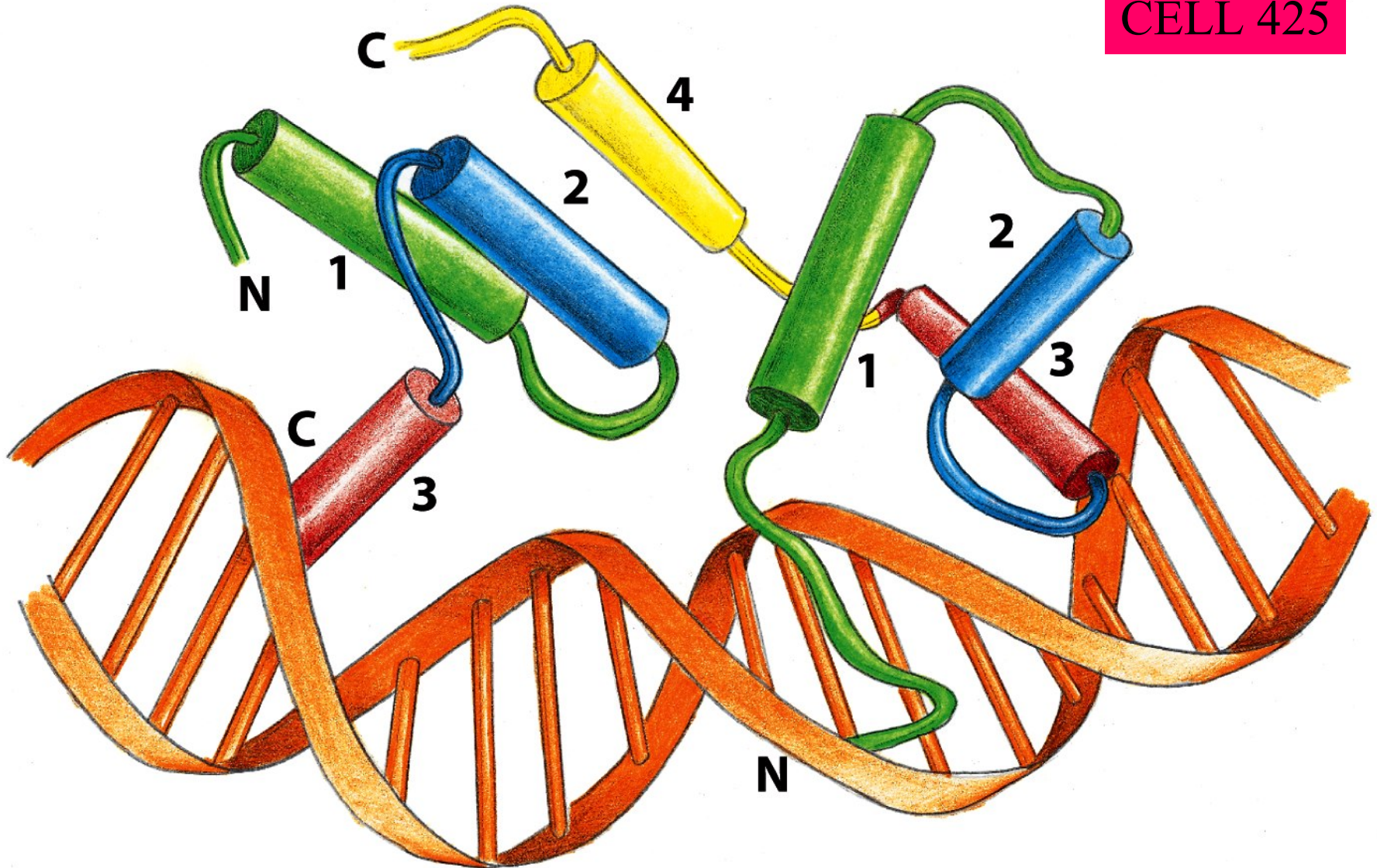


Figure 7-21 Molecular Biology of the Cell 5/e (© Garland Science 2008)

2 homeodomainia heterodimeerinä

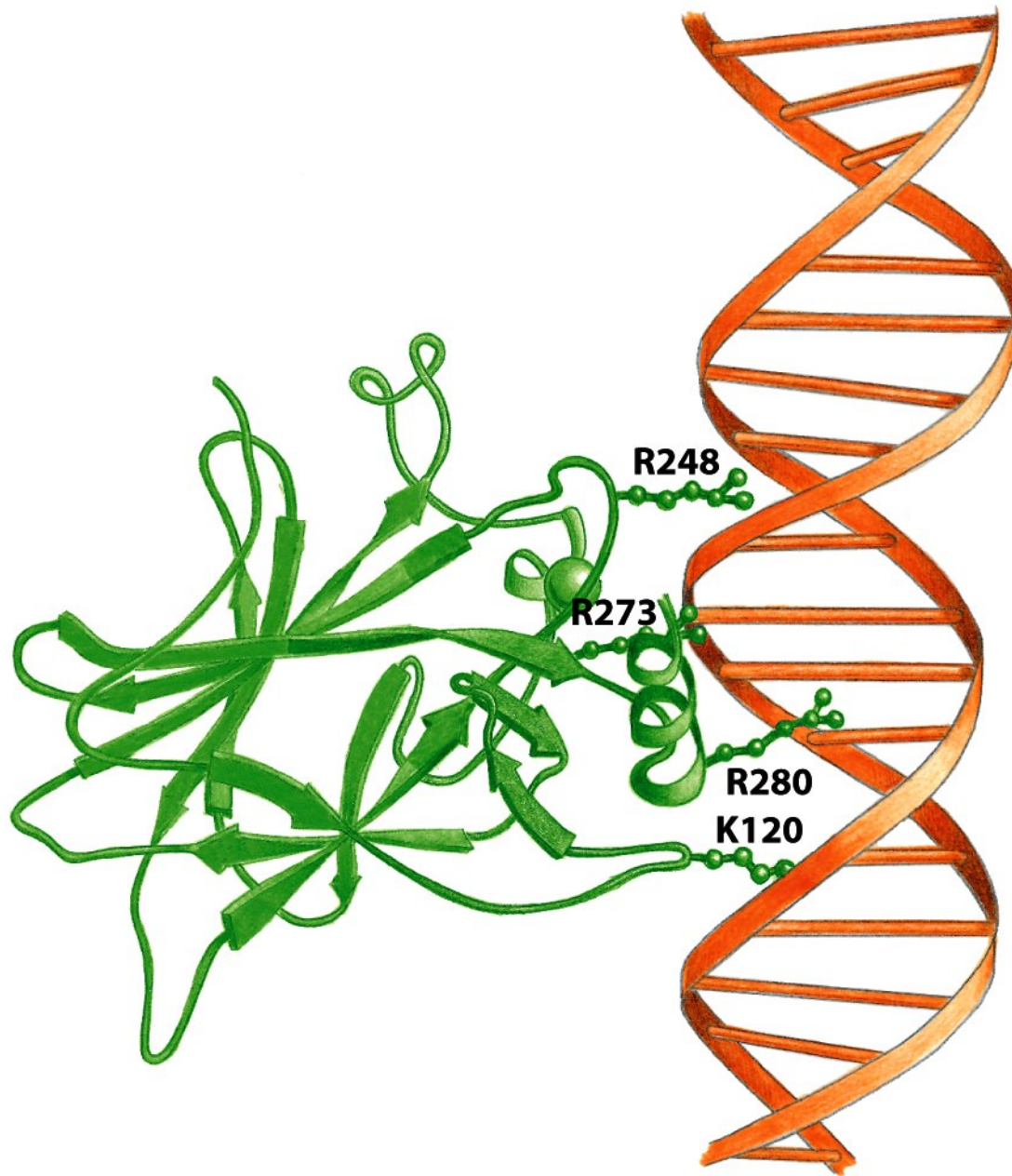
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knotted

[illegible]

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Tärkein solusyklin
jarru ja tarkastaja
p53 on sekin
transkriptiofaktori



GGGCAAGTCT
CCCGTTCAGA

Figure 7-18 Molecular Biology of the Cell 5/e (© Garland Science 2008)

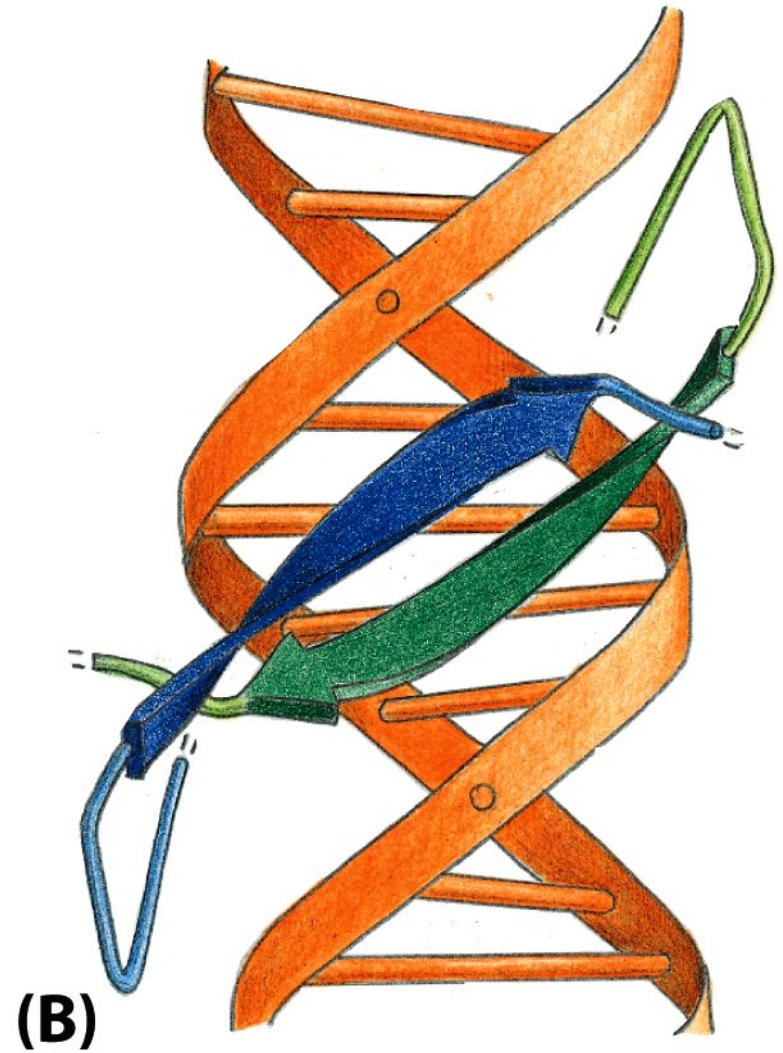
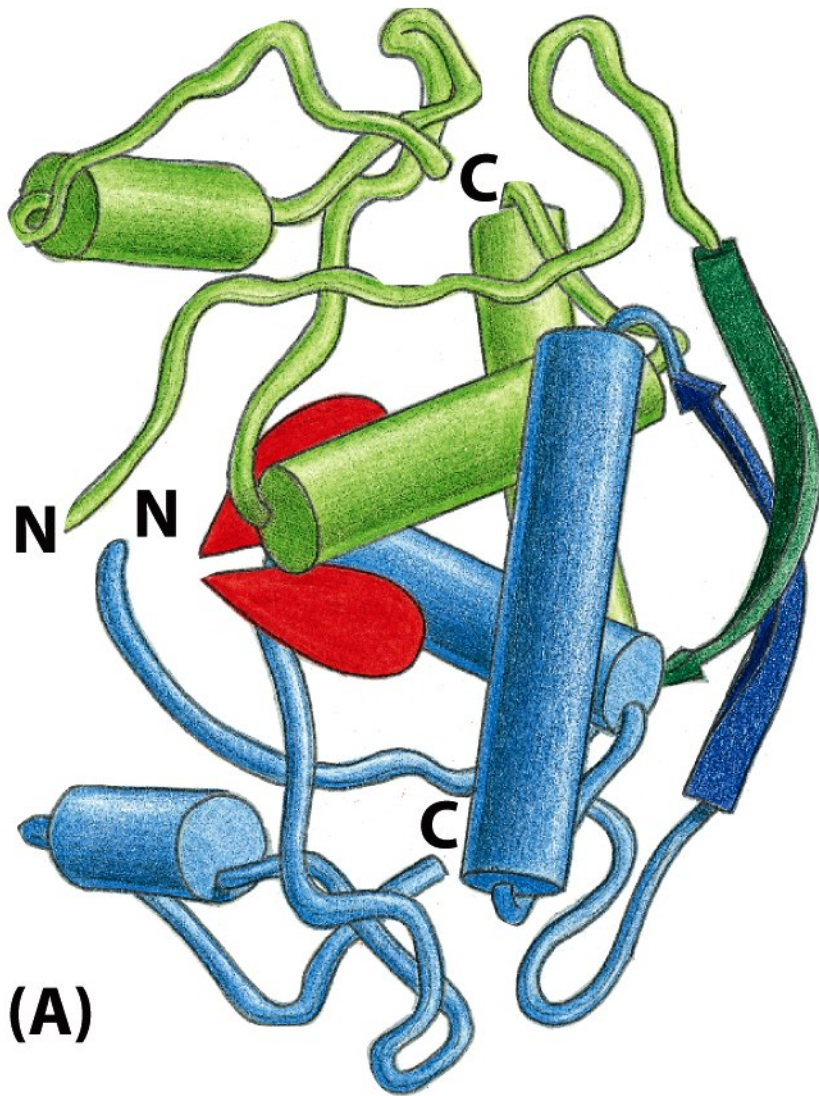
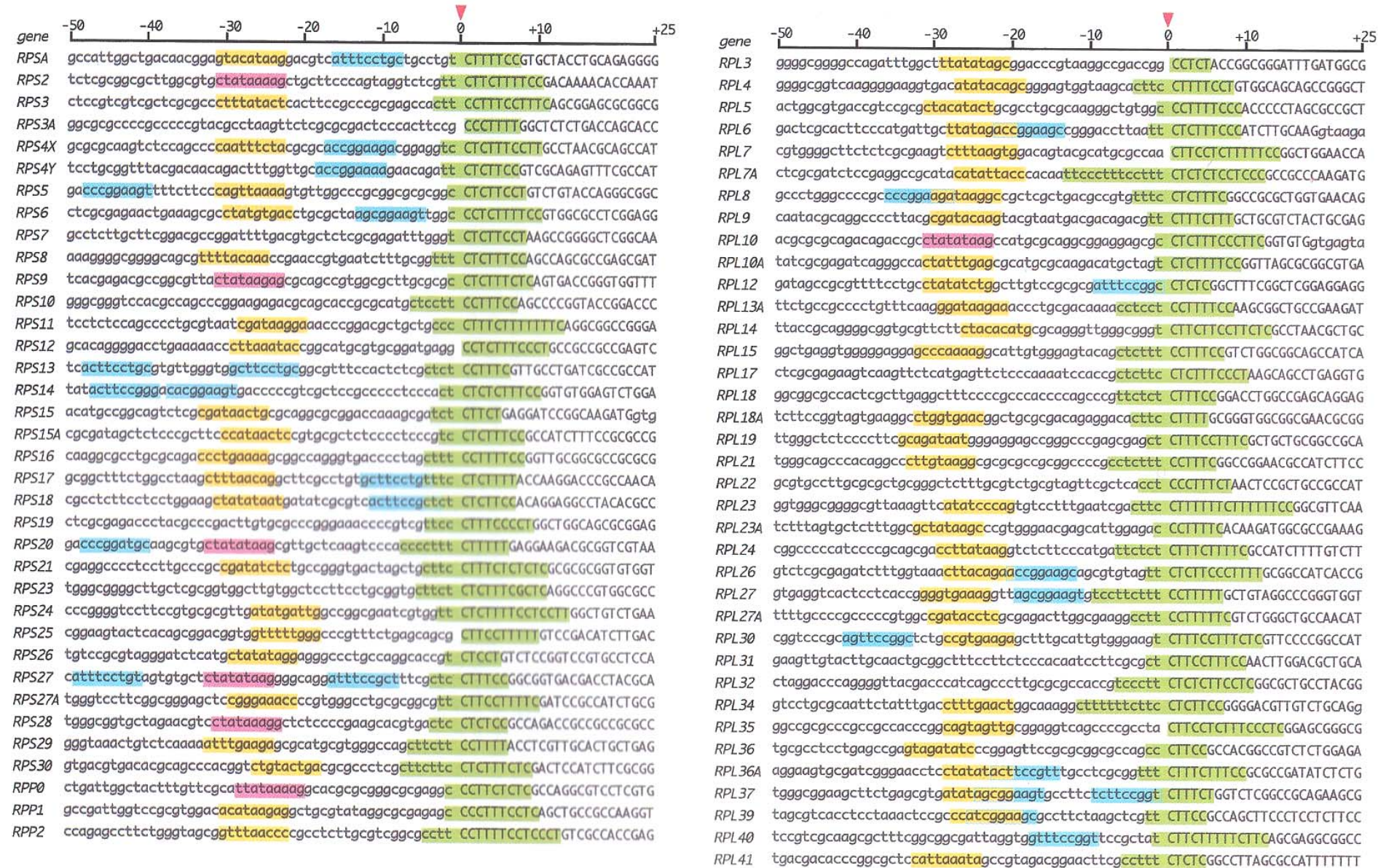


Figure 7-17 Molecular Biology of the Cell 5/e (© Garland Science 2008)

Table 7–1 Some Gene Regulatory Proteins and the DNA Sequences That They Recognize

	NAME	DNA SEQUENCE RECOGNIZED*
Bacteria	Lac repressor	5' AATTGTGAGCGGATAACAATT 3' TTAACACTCGCCTATTGTTAA
	CAP	TGTGAGTTAGCTCACT ACACTCAATCGAGTGA
	Lambda repressor	TATCACCGCCAGAGGT ATAGTGGCGGTCTCCAT
Yeast	Gal4	CGGAGGACTGTCCTCCG GCCTCCTGACAGGAGGC
	Mat α 2	CATGTAATT GTACATTAA
	Gcn4	ATGACTCAT TACTGAGTA
<i>Drosophila</i>	Kruppel	AACGGGTAA TTGCCCAATT
	Bicoid	GGGATTAGA CCCTAATCT
Mammals	Sp1	GGGCGG CCCGCC
	Oct1 Pou domain	ATGCAAAT TACGTTTA
	GATA1	TGATAG ACTATC
	MyoD	CAAATG GTTTAC
	p53	GGGCAAGTCT CCCGTTCAGA

*For convenience, only one recognition sequence, rather than a consensus sequence (see Figure 6–12), is given for each protein.



Ihmisen ribosomiproteiinien promoottorit.

Kaikkia pitää tuottaa samanaikaisesti, kaikissa soluissa

Genome Research, March 2002

www.genome.org

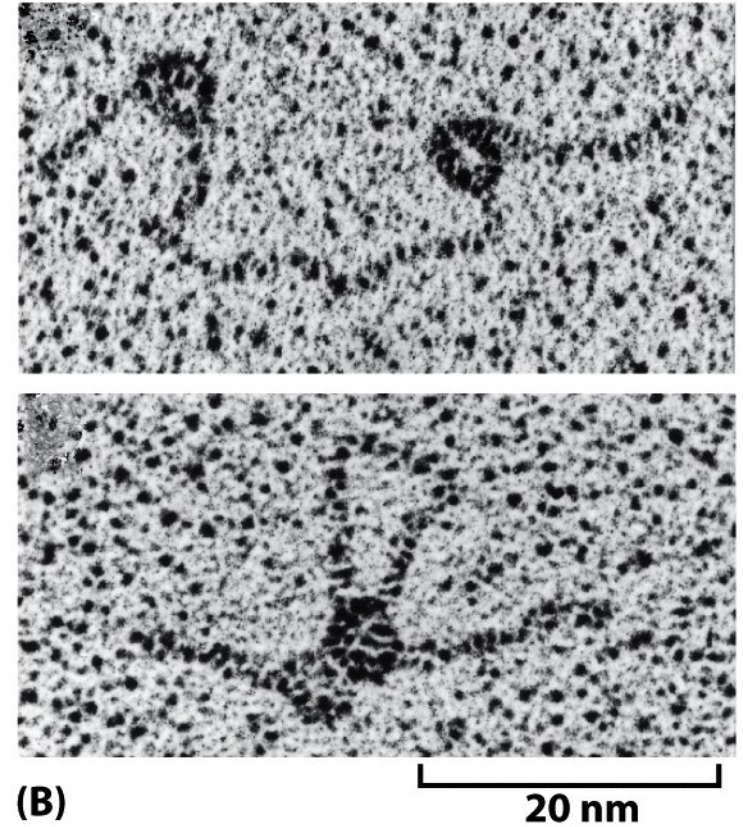
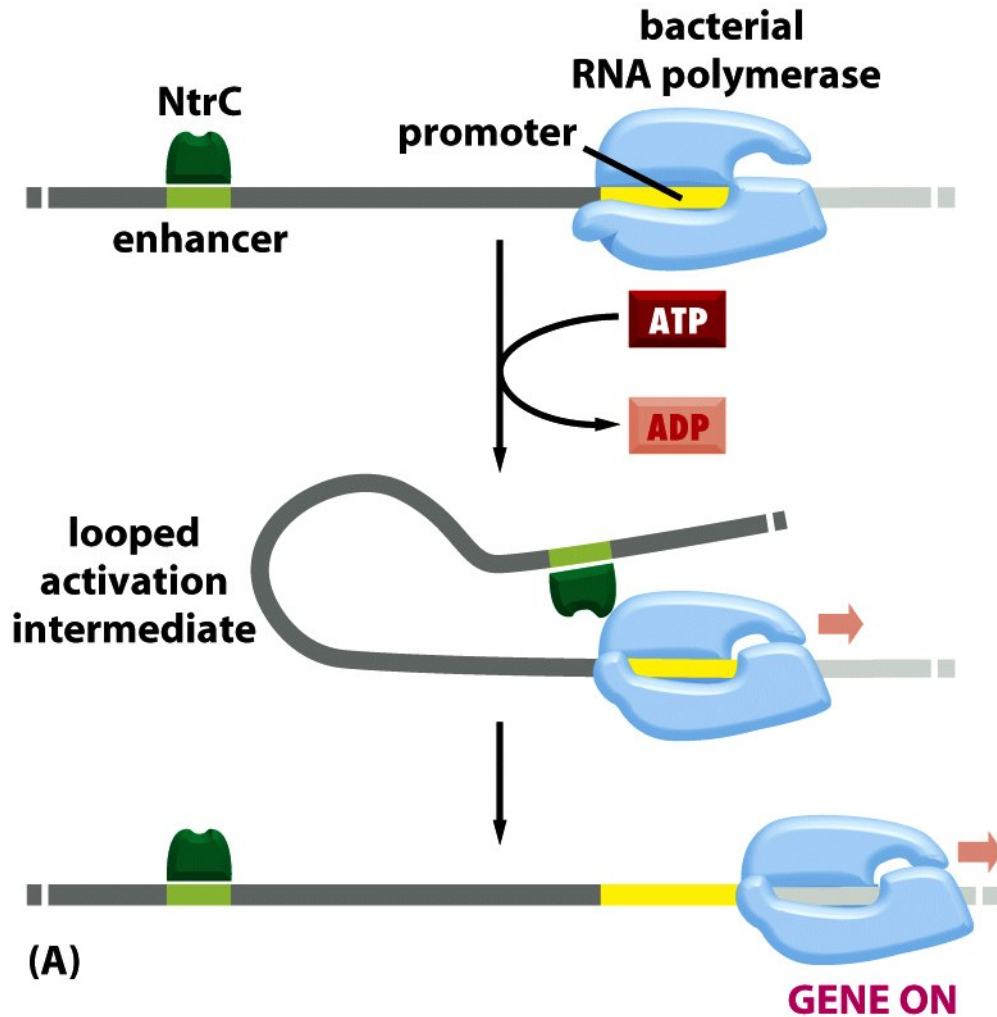


Figure 7-42 Molecular Biology of the Cell 5/e (© Garland Science 2008)

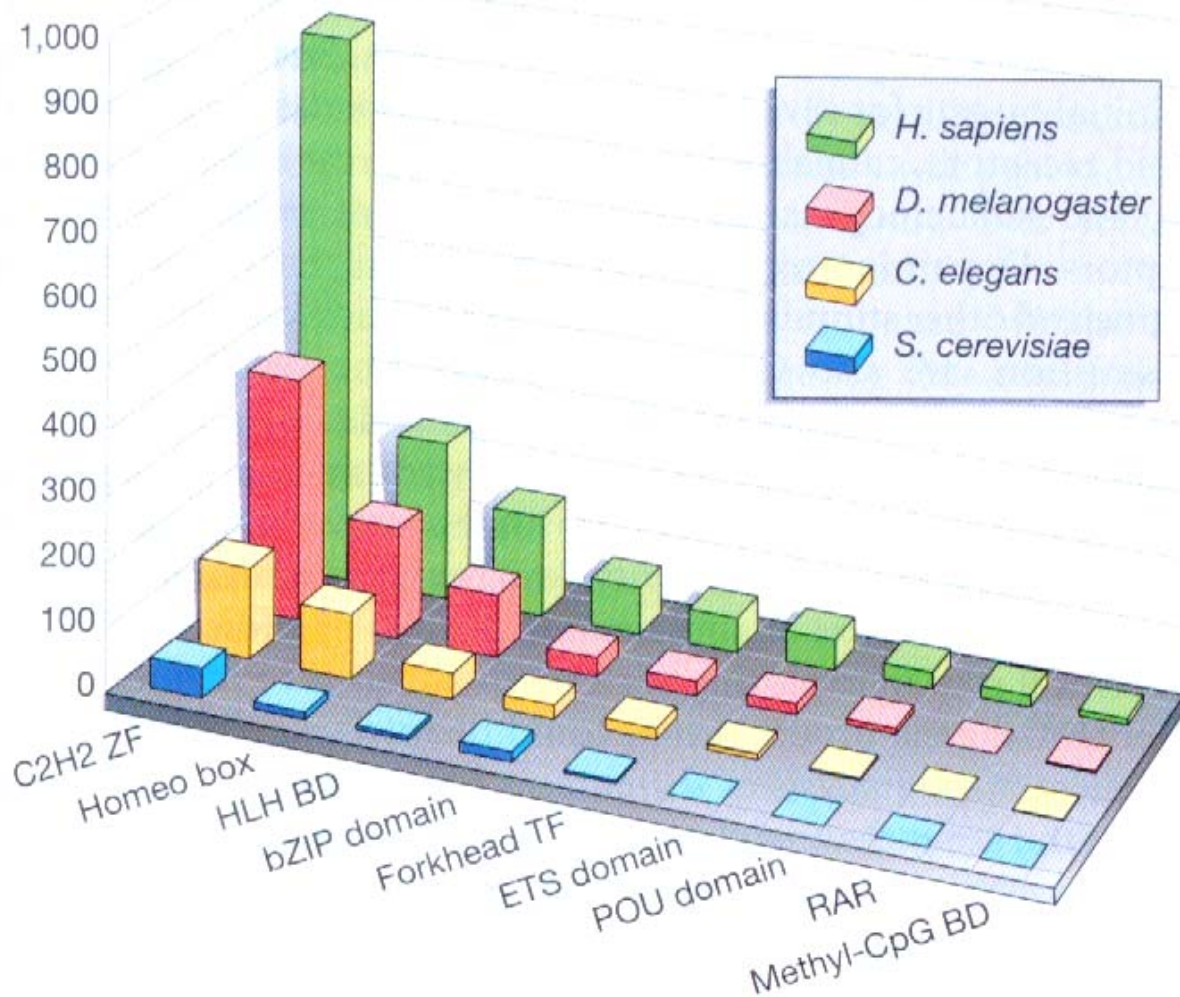


Figure 1 Genome-wide comparison of transcriptional activator families in eukaryotes. The relative sizes of transcriptional activator families among *Homo sapiens*, *D. melanogaster*, *C. elegans* and *S. cerevisiae* are indicated, derived from an analysis of eukaryotic proteomes using the INTERPRO database, which incorporates Pfam, PRINTS and Prosite. The transcription factors families shown are the largest of their category out of the 1,502 human protein families listed by the IPI.

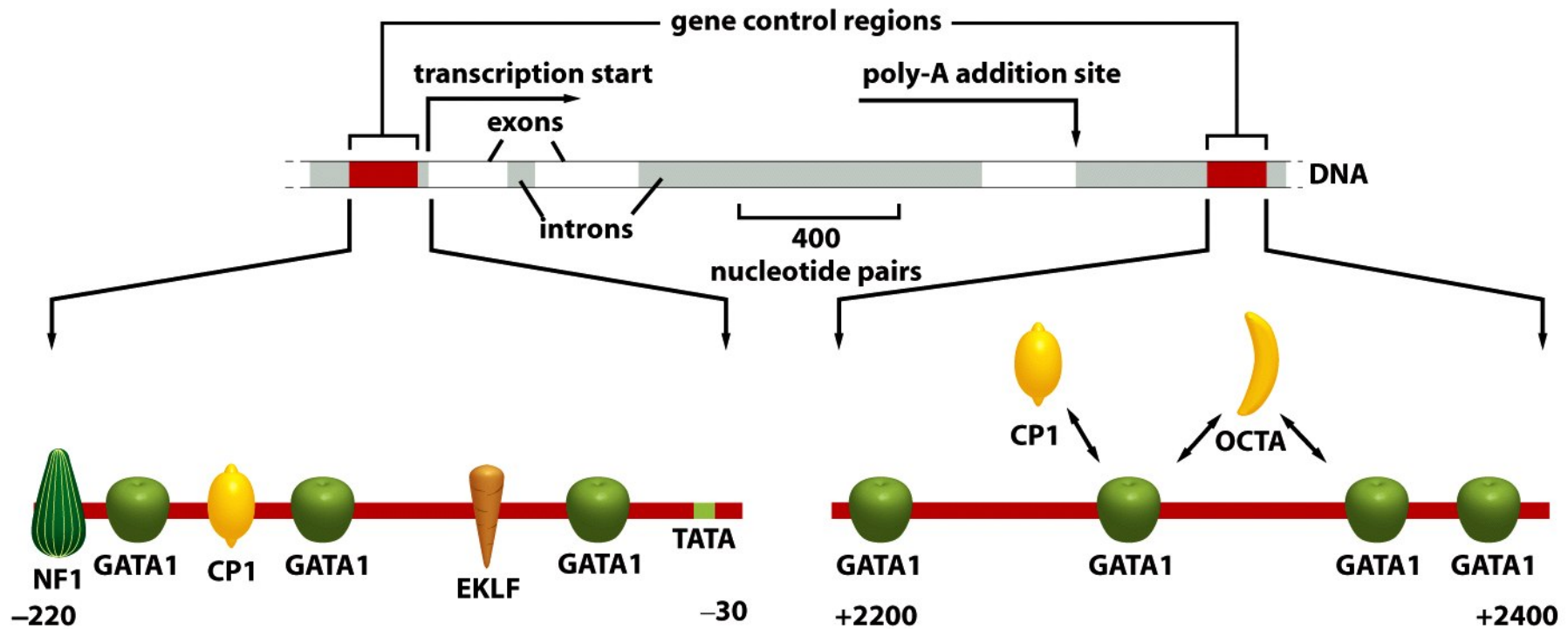


Figure 7-60 Molecular Biology of the Cell 5/e (© Garland Science 2008)

Ihmisen beta-globiinigeenin säätelyn malli. *Sitruunat* ja *omenat* ja *banaanikin* kilpailevat paikoista, toiset estävät ja toiset edistävät polymeraasin toimintaa.

kombinatorinen säätely

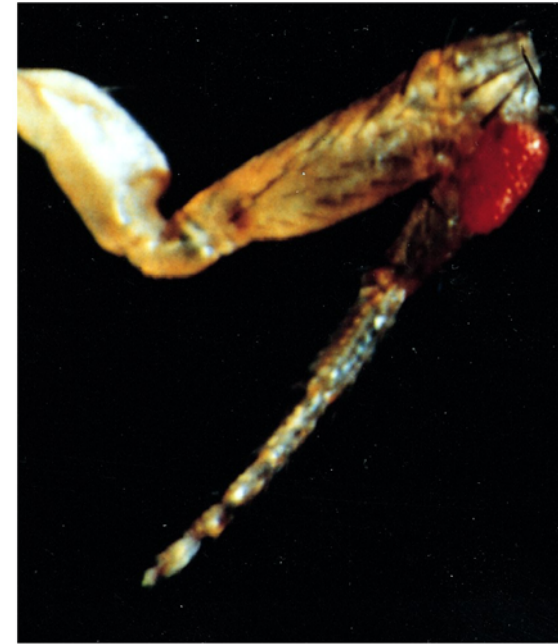
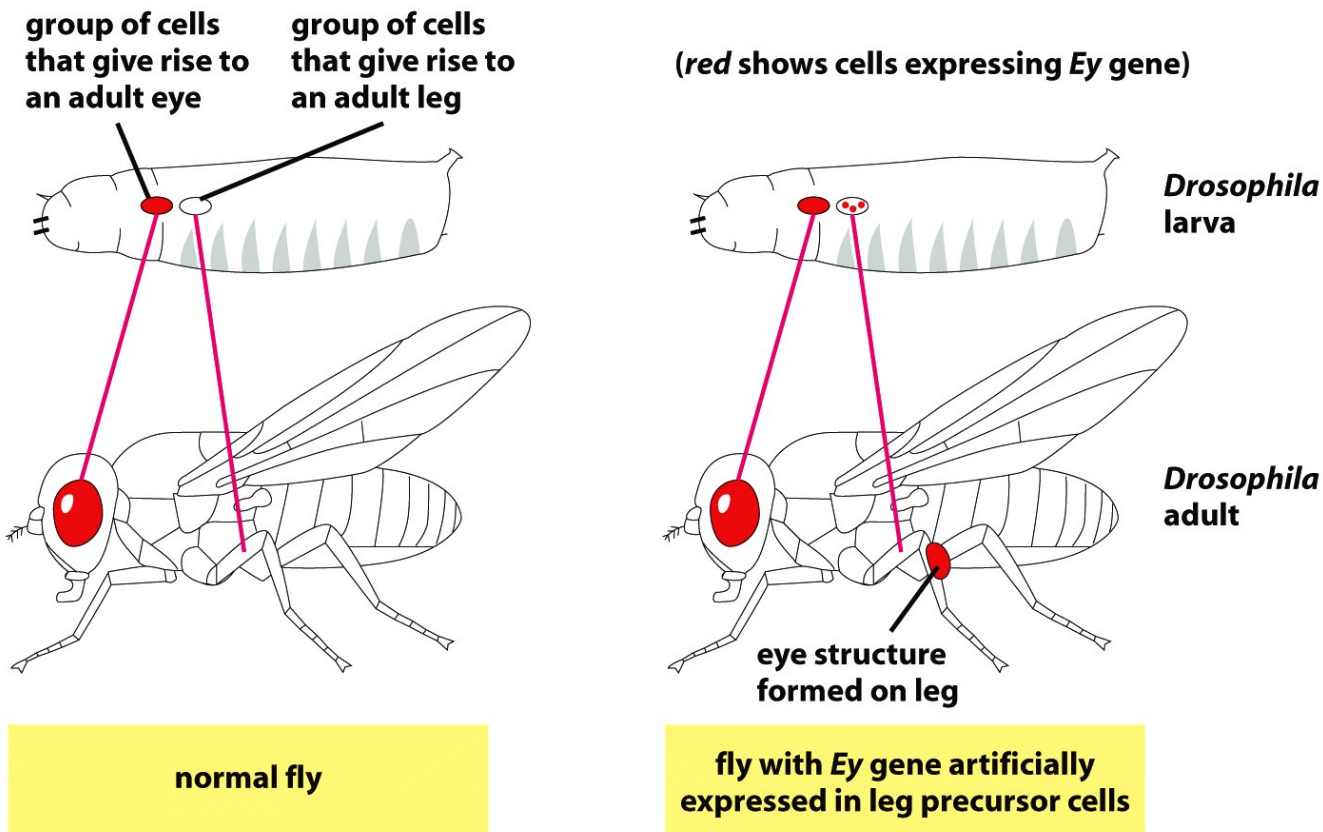


Figure 7-77b Molecular Biology of the Cell 5/e (© Garland Science 2008)

pax6 (*Ey*) indusoi silmän mihin tahansa, jos se aktivoituu

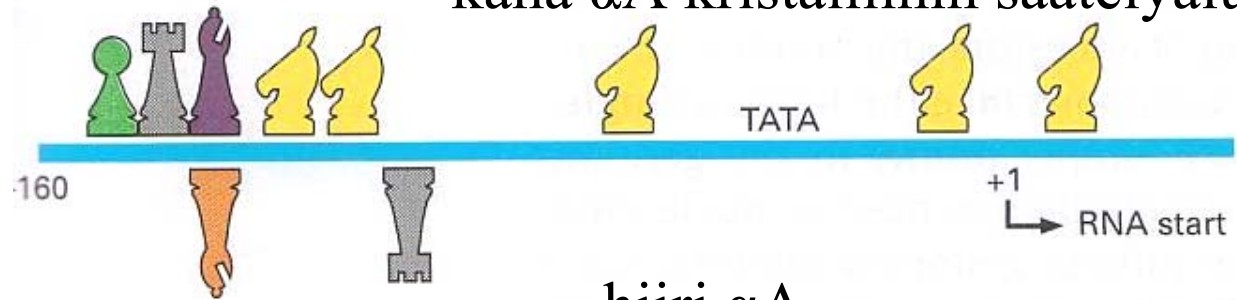
Vieläpä minkä tahansa silmän: etanalle etanan silmän, mustekalalle linssillisen.

Silmän linssin *kristalliini*-geenien säätelyalueet hiirellä ja kanalla

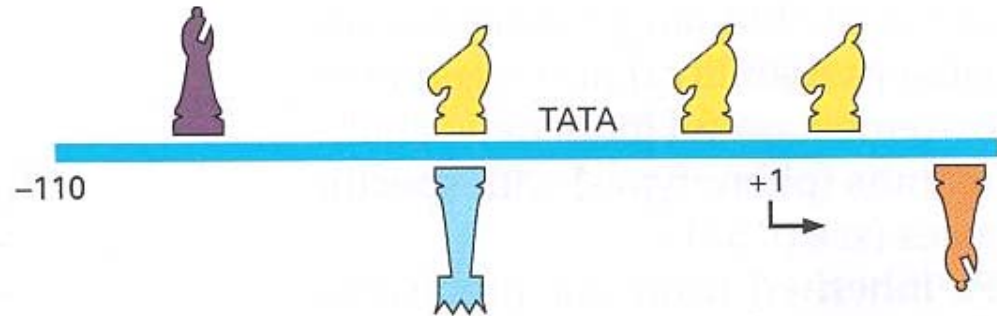
Monet proteiinit soveltuvat silmän linssin rakennusaineeksi. Oleellista on, että niitä tuotetaan juuri siellä. Alpha-kristalliini (kaksi ylintä) löytyy kaikilta selkärangaisilta, mutta alin on ihan erilainen proteiini, jota on lintujen ja matelijoiden linssissä

Pax6 on erikoisen keskeinen säätelygeeni, jonka väärä-aikainen toiminta saa aikaan vaikka silmän *Drosophila*n jalkaan (CELL 466)

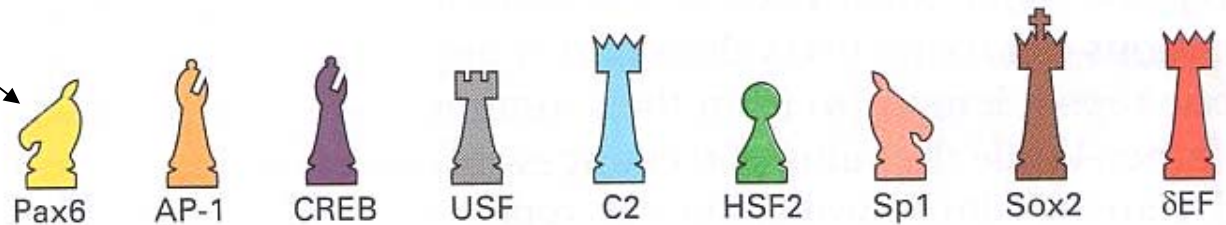
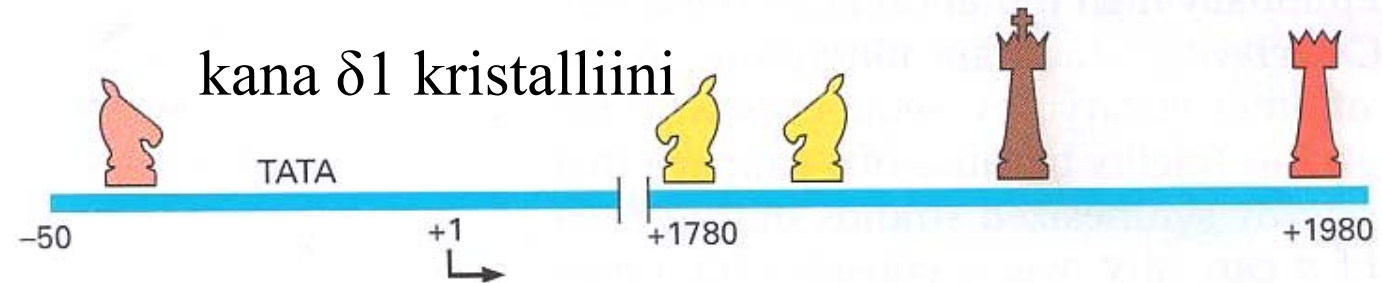
kana αA kristalliinin säätelyalue



hiiri αA



kana $\delta 1$ kristalliini



CELL 466