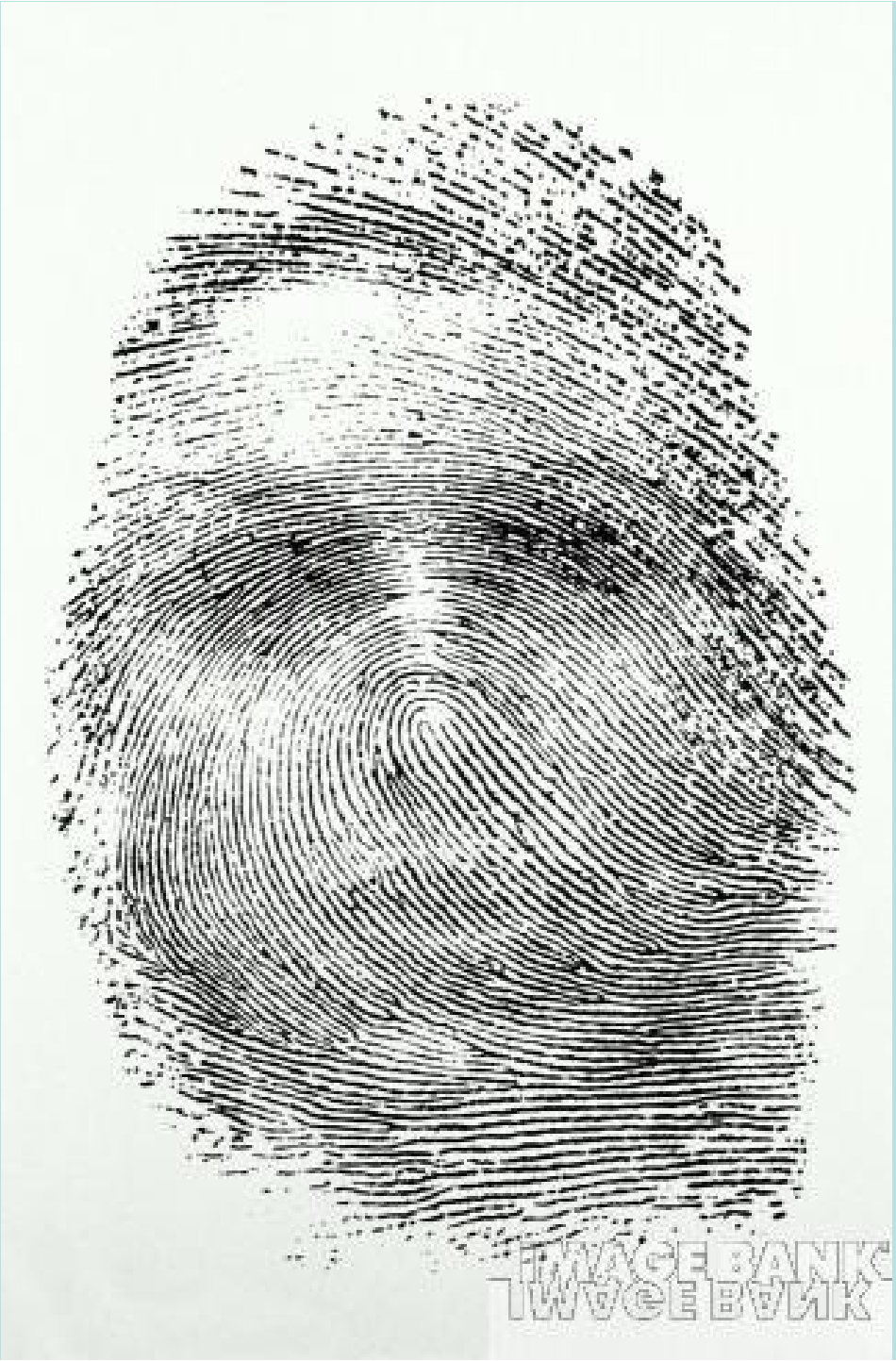
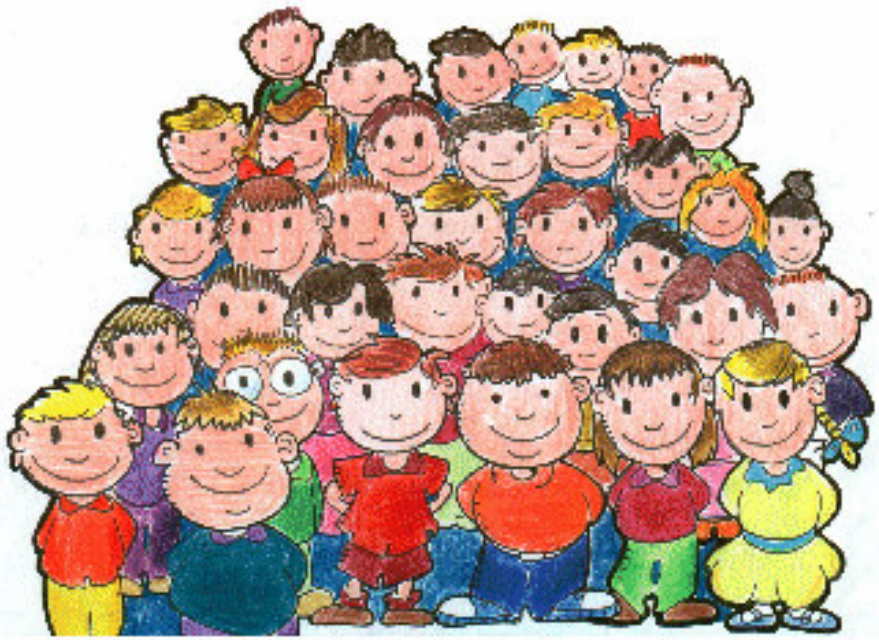


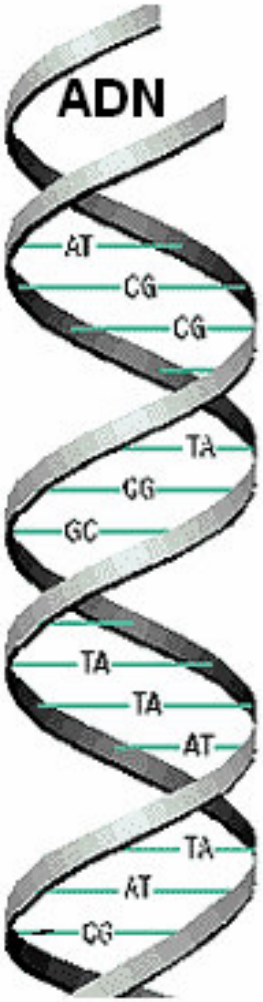
Moléculas codificadas por el Complejo Mayor de Histocompatibilidad " MHC" o "CPH"

I.Pepper



Se ven diferentes. Son diferentes sin embargo

99.9% de la secuencia de bases es igual en todos los individuos



El genoma humano tiene 3164.7 millones de pares de bases (TA o CG)

Sólo el 2% de las pares de bases constituye genes que codifican proteinas (30 a 40 mil genes)

Fig:5

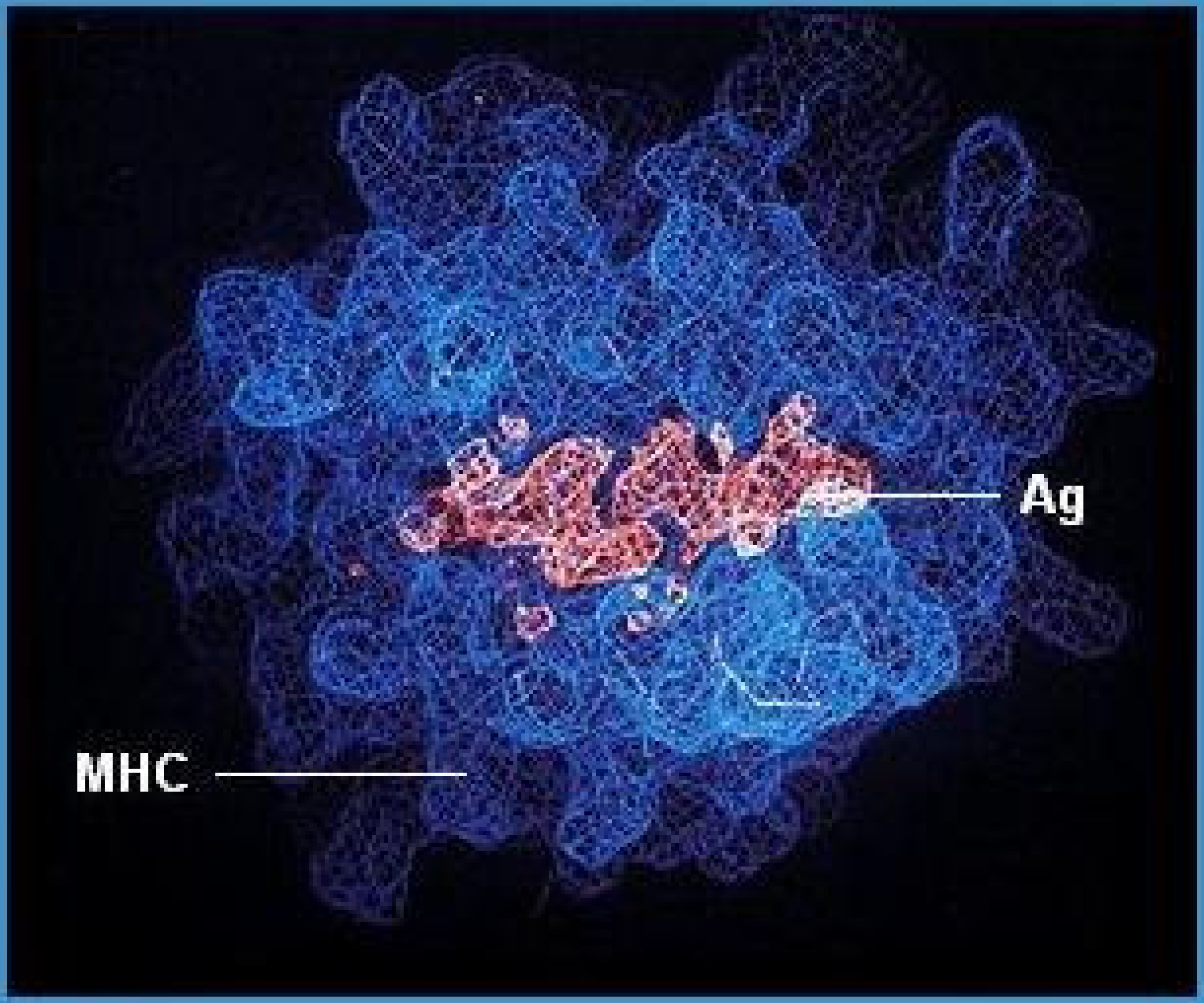


Fig.6

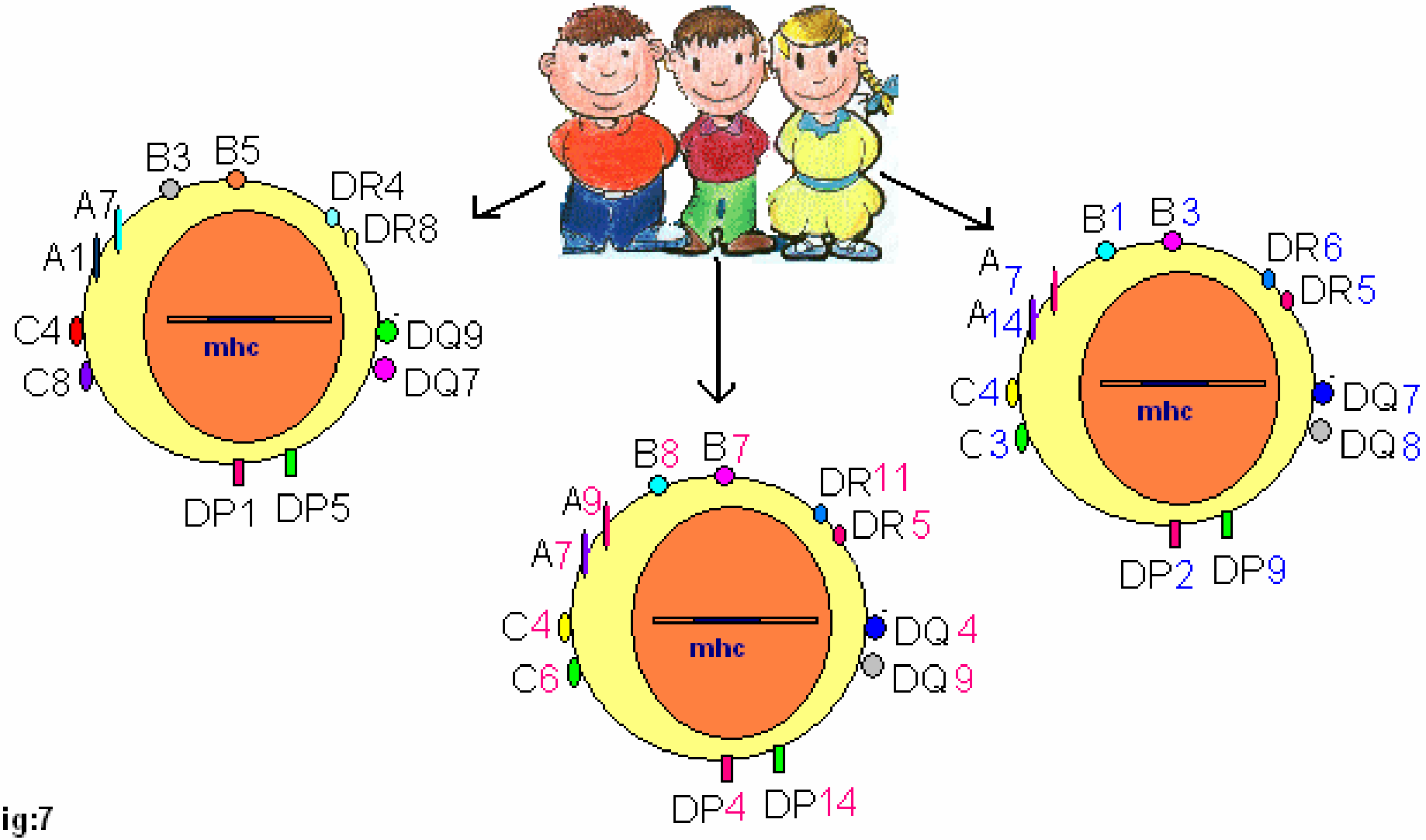
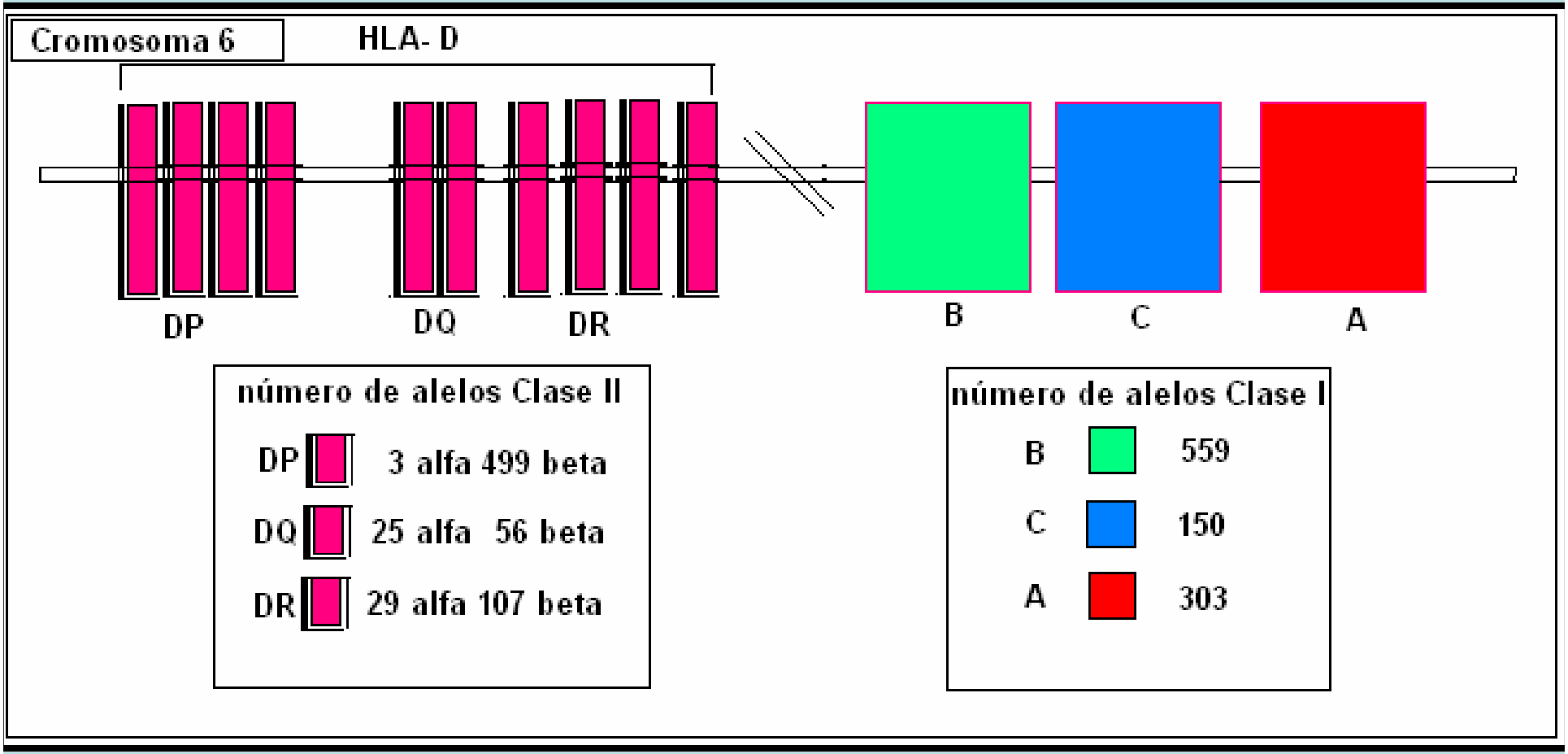

B3
B5
A7
DR4
DR8
A1
C4
mhc
DQ9
C8
DQ7
DP1
DP5
B1
B3
DR6
A7
DR5
A14
C4
mhc
DQ7
C3
DQ8
DP2
DP9
B8
B7
DR11
A9
DR5
A7
C4
mhc
DQ4
C6
DQ9
DP4
DP14

Fig:7


Cromosoma 6
HLA- D
DP
DQ
DR
B
C
A
número de alelos Clase II
DP 3 alfa 499 beta
DQ 25 alfa 56 beta
DR 29 alfa 107 beta
número de alelos Clase I
B 559
C 150
A 303

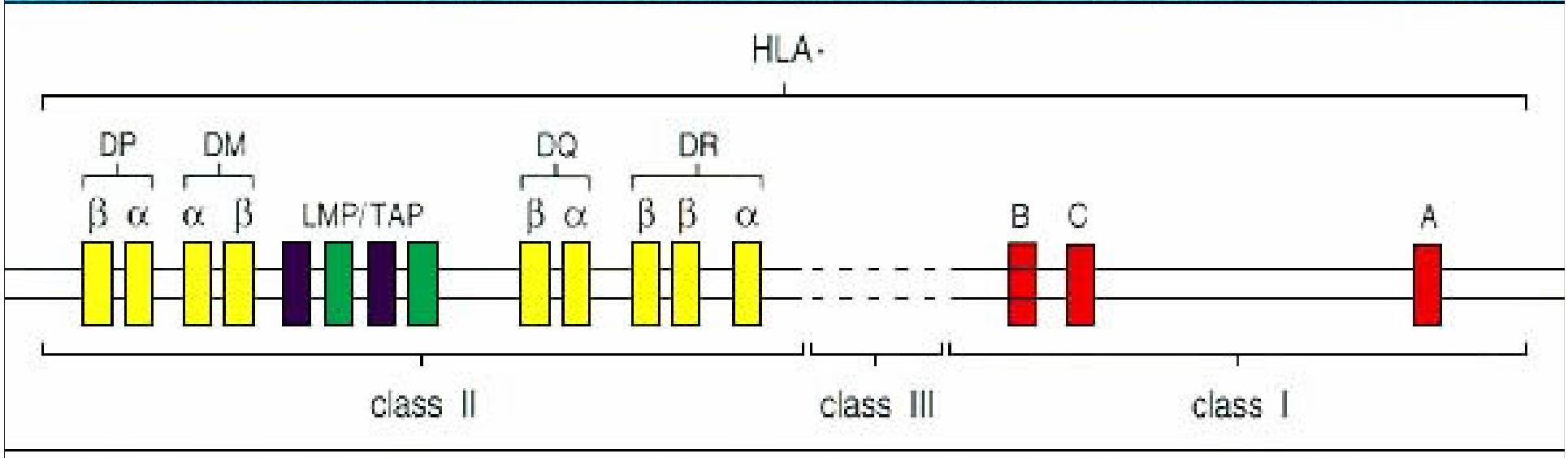
Full List of HLA Class I alleles assigned as of July 2005

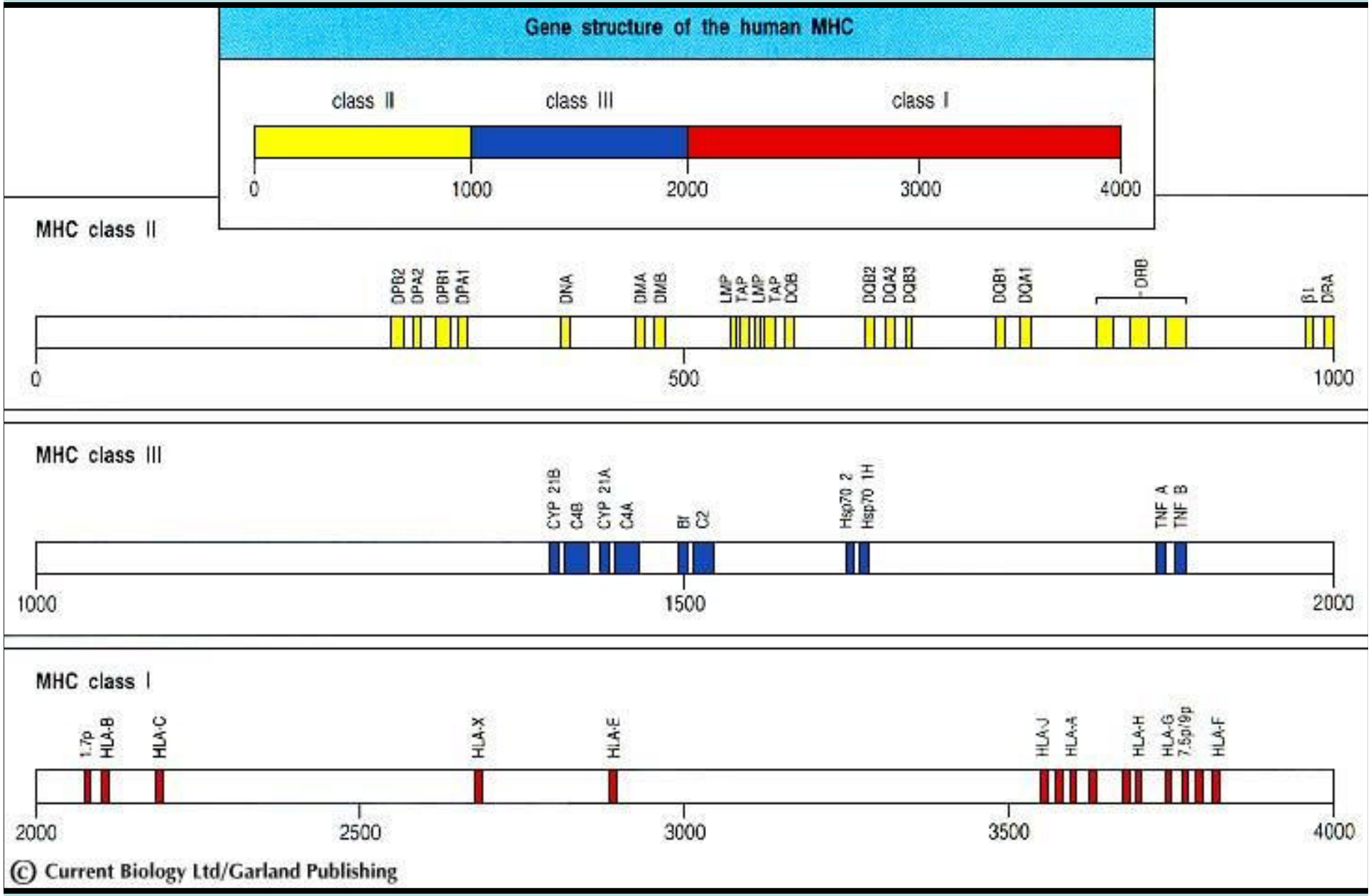
HLA-A	HLA-B	HLA-C
A*01010101	B*070201	Cw*010201
A*01010102N	B*070202	Cw*010202
A*010102	B*070203	Cw*010203
A*010103	B*070204	Cw*0103
A*0102	B*0703	Cw*0104
A*0103	B*0704	Cw*0105
A*0104N	B*0705	Cw*0106
A*0106	B*0706	Cw*0107
A*0107	B*0707	Cw*0108
A*0108	B*0708	Cw*0109
A*0109	B*0709	Cw*0110
A*0110	B*0710	Cw*0111
A*0111N	B*0711	Cw*020201
A*0112	B*0712	Cw*020202
A*0113	B*0713	Cw*020203
A*0114	B*0714	Cw*020204
A*0115N	B*0715	Cw*020205
A*02010101	B*0716	Cw*0203
A*02010102L	B*0717	Cw*0204
A*020102	B*0718	Cw*0205
A*020103	B*0719	Cw*0206
A*020104	B*0720	Cw*0207
A*020105	B*0721	Cw*0208
A*020106	B*0722	Cw*0209
A*020107	B*0723	Cw*0210
A*020108	B*0724	Cw*0211
A*020109	B*0725	Cw*0212
A*020110	B*0726	Cw*030201
A*020111	B*0727	Cw*030202
A*0202	B*0728	Cw*030301
A*020301	B*0729	Cw*030302
A*020302	B*0730	Cw*030303
A*0204	B*0731	Cw*030304
A*0205	B*0732	Cw*030401
A*020601	B*0733	Cw*030402
A*020602	B*0734	Cw*030403
A*020603	B*0735	Cw*0305
A*0207	B*0736	Cw*0306
A*0208	B*0737	Cw*0307
A*0209	B*0738	Cw*0308
A*0210	B*0739	Cw*0309
A*0211	B*0740	Cw*0310
A*0212	B*0741	Cw*0311
A*0214	B*0743	Cw*0313
A*0215N	B*080101	Cw*0314
A*0216	B*080102	Cw*0315
A*021701	B*0802	Cw*0316
A*021702	B*0803	Cw*0317
A*0218	B*0804	Cw*0318

HLA-A	HLA-B	HLA-C
A*022001	B*0806	Cw*04010101
A*022002	B*0807	Cw*04010102
A*0221	B*0808N	Cw*040102
A*0222	B*0809	Cw*040103
A*0224	B*0810	Cw*0403
A*0225	B*0811	Cw*040401
A*0226	B*0812	Cw*040402
A*0227	B*0813	Cw*0405
A*0228	B*0814	Cw*0406
A*0229	B*0815	Cw*0407
A*0230	B*0816	Cw*0408
A*0231	B*0817	Cw*0409N
A*0232N	B*0818	Cw*0410
A*0233	B*0819N	Cw*0411
A*0234	B*0820	Cw*0412
A*023501	B*0821	Cw*0413
A*023502	B*0822	Cw*0414
A*0236	B*0823	Cw*0415
A*0237	B*0824	Cw*0416
A*0238	B*0825	Cw*0417
A*0239	B*1301	Cw*050101
A*0240	B*130201	Cw*050102
A*0241	B*130202	Cw*0502
A*0242	B*1303	Cw*0503
A*0243N	B*1304	Cw*0504
A*0244	B*1306	Cw*0505
A*0245	B*1307N	Cw*0506
A*0246	B*1308	Cw*0507N
A*0247	B*1309	Cw*0508
A*0248	B*1310	Cw*0509
A*0249	B*1311	Cw*0510
A*0250	B*1312	Cw*0511
A*0251	B*1313	Cw*0602
A*0252	B*1401	Cw*0603
A*0253N	B*140201	Cw*0604
A*0254	B*140202	Cw*0605
A*0255	B*1403	Cw*0606
A*0256	B*1404	Cw*0607
A*0257	B*1405	Cw*0608
A*0258	B*140601	Cw*0609
A*0259	B*140602	Cw*0610
A*0260	B*1407N	Cw*0611
A*0261	B*15010101	Cw*0612
A*0262	B*15010102N	Cw*0613
A*0263	B*150102	Cw*070101
A*0264	B*150103	Cw*070102
A*0265	B*150104	Cw*070103
A*0266	B*150105	Cw*07020101
hasta A 801	**hasta B 9504**	**hasta Cw1802**

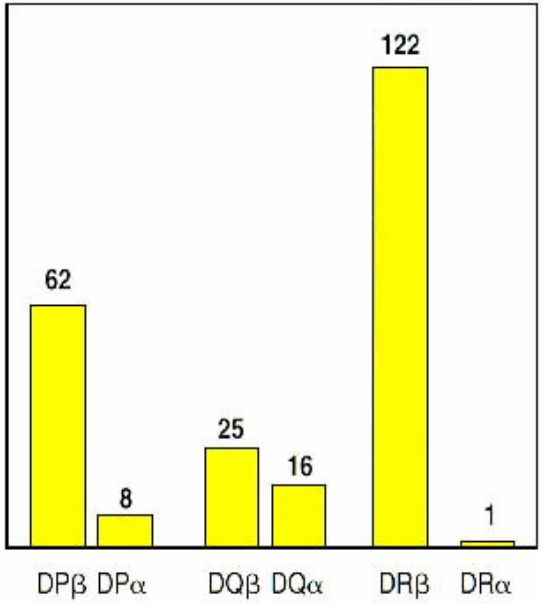
ID	Population Study	Allele	Phenotype Frequency(%)	Allele Frequency (3 places)	IMGT/HLA Sequence Database
213298	Algeria	A*01	23		Click Here
43792	Argentina Buenos Aires	A*01	19.7	0.105	Click Here
21865	Argentina Chiriguanos	A*01	3.8	0.019	Click Here
14832	Argentina La Plata City	A*01	22.0	0.115	Click Here
21605	Argentina Toba Rosario	A*01	16.3	0.081	Click Here
21768	Argentina Wichis	A*01	0	0	Click Here
15620	Australia West	A*01	33.6	0.185	Click Here
211872	Australian Aborigine Cape York Peninsula	A*01		0.053	Click Here
212038	Australian Aborigine Groote Eylandt	A*01		0.027	Click Here
212288	Australian Aborigine Yuendumu	A*01		0.008	Click Here
193289	Azores	A*01		0.109	Click Here
697	Brazil Belo Horizonte	A*01	13.7	0.079	Click Here
208179	Brazil Pernambuco State	A*01		0.084	Click Here
154781	Brazil Sao Paulo	A*01	13	0.067	Click Here
16193	Bulgaria	A*01		0.073	Click Here
5790	Cabo Verde	A*01		0.055	Click Here
212649	China Linqu County Shandong Province	A*01	2.2		Click Here
48790	China Wuhan	A*01	3.3	0.017	Click Here
90274	Colombia African Black	A*01		0.043	Click Here
91948	Colombia Mestizos	A*01		0.000	Click Here
70	Cuban Mulatto	A*01	14.3	0.071	Click Here
1544	Cuban White	A*01	15.7	0.079	Click Here
152924	France South East	A*01	27.7	0.15	Click Here
21983	German Essen	A*01	25.9	0.144	Click Here
193291	Greece Crete	A*01		0.120	Click Here
213884	Israel Moroccan Jews	A*01		0.259	Click Here
5316	Italy	A*01		0.121	Click Here
18331	Italy Bergamo	A*01	14.9	0.075	Click Here
214500	Italy North Pavia	A*01		0.08	Click Here
19891	Italy Rome	A*01	24	0.12	Click Here
86418	Japan Aichi	A*01	4.4	0.022	Click Here
74379	Japan Hyogo	A*01	6.3	0.033	Click Here
193296	Macedonia pop 3	A*01			Click Here
209360	Macedonia pop 4	A*01		0.113	Click Here
14200	Madeira	A*01		0.07	Click Here
1912	Mexico Mestizos	A*01	14.6	0.085	Click Here
215133	Mongolia Khalkh Ulaanbaatar	A*01	etc...	0.085	Click Here
84698	Mongolia Khalkha	A*01		0.080	Click Here

Gene structure of the human MHC

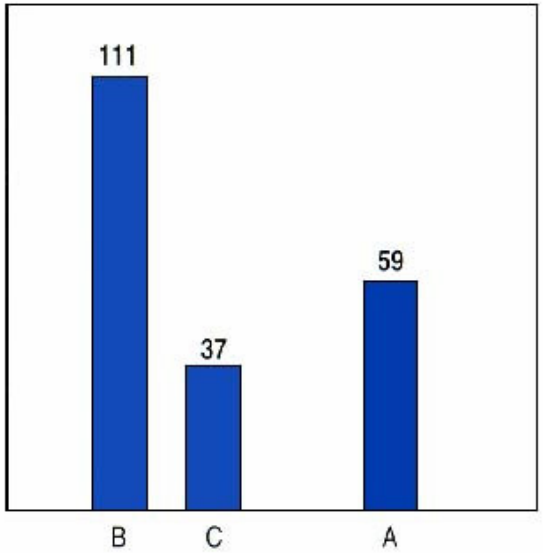



Gene structure of the human MHC
class II
class III
class I
0
1000
2000
3000
4000
MHC class II
DPB2
DPA2
DPB1
DPA1
DNA
DMA
DMB
LMP
TAP
LMP
TAP
DOB
DQB2
DQA2
DQB3
DQB1
DQA1
DRB
β1
DRA
0
500
1000
MHC class III
CYP 21B
C4B
CYP 21A
C4A
Bf
C2
Hsp70 2
Hsp70 1H
TNF A
TNF B
1000
1500
2000
MHC class I
1.7p
HLA-B
HLA-C
HLA-X
HLA-E
HLA-J
HLA-A
HLA-H
HLA-G
7.5p/9p
HLA-F
2000
2500
3000
3500
4000
© Current Biology Ltd/Garland Publishing

MHC class II

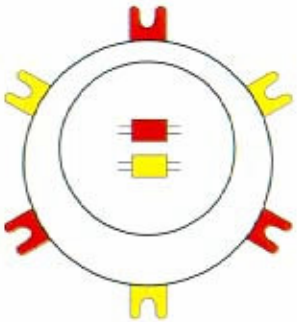


MHC class I

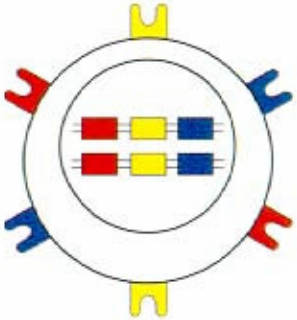


© Current Biology Ltd/Garland Publishing

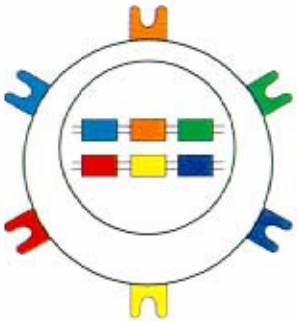
Polymorphism



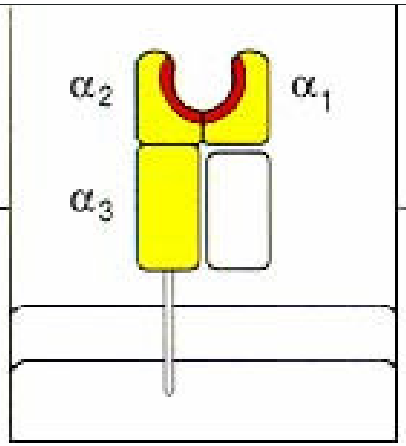
Polygenism

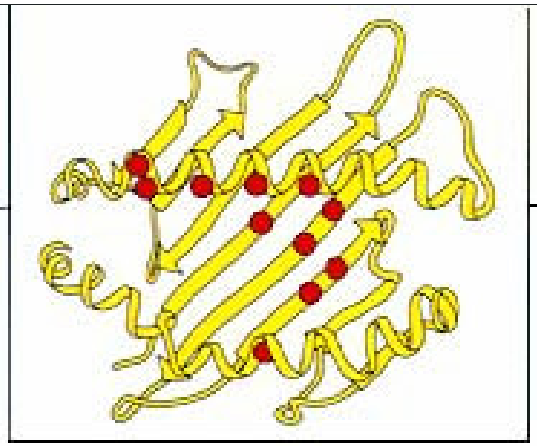


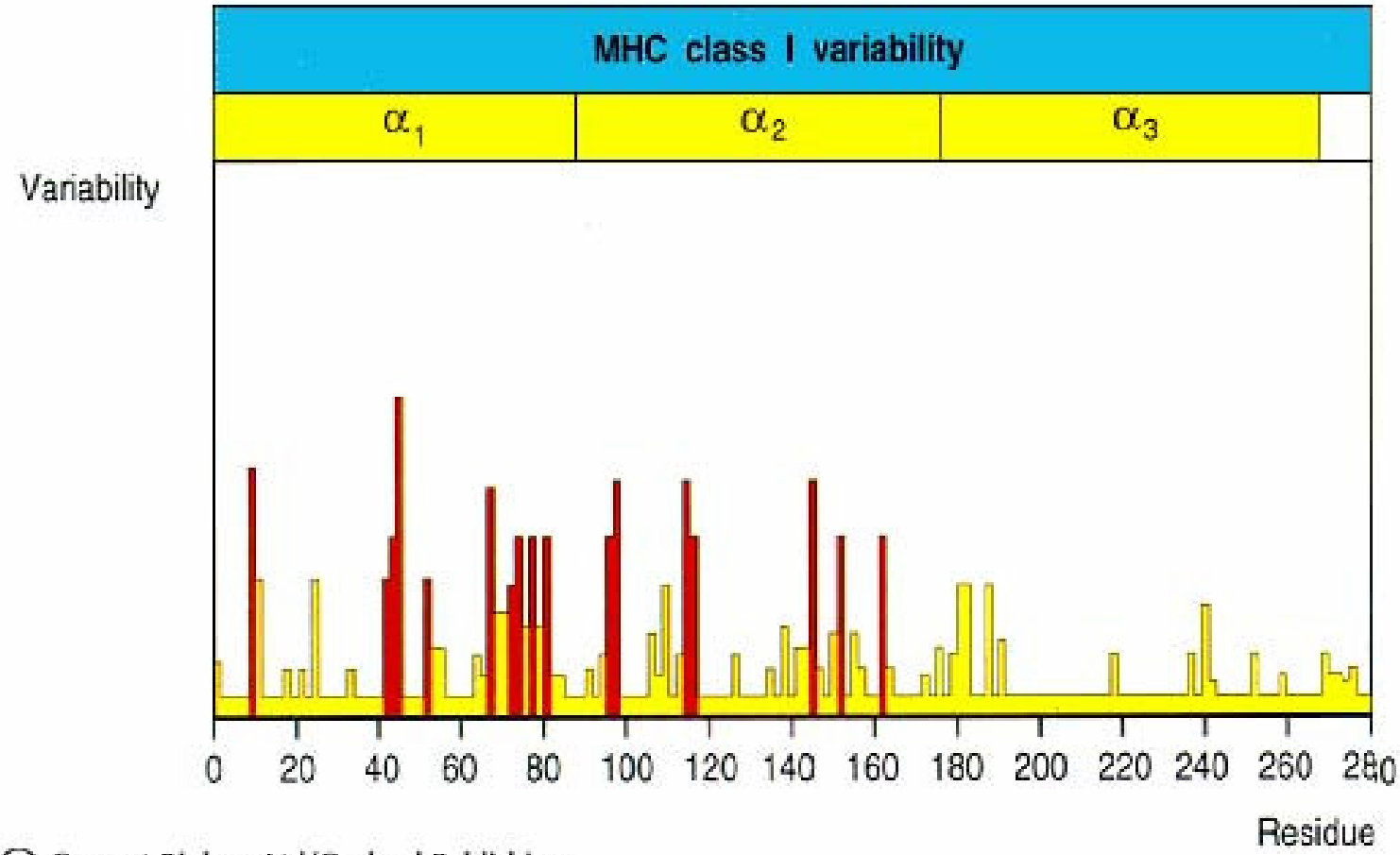
Polymorphism and polygenism



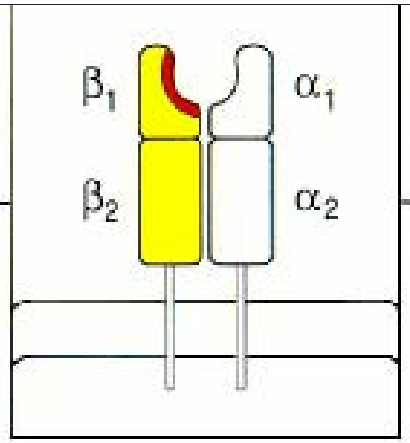
© Current Biology Ltd/Garland Publishing

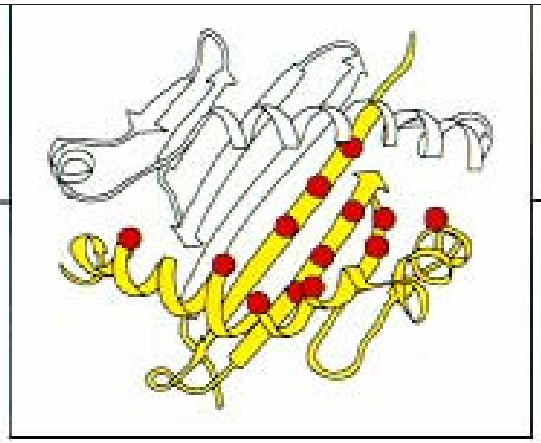


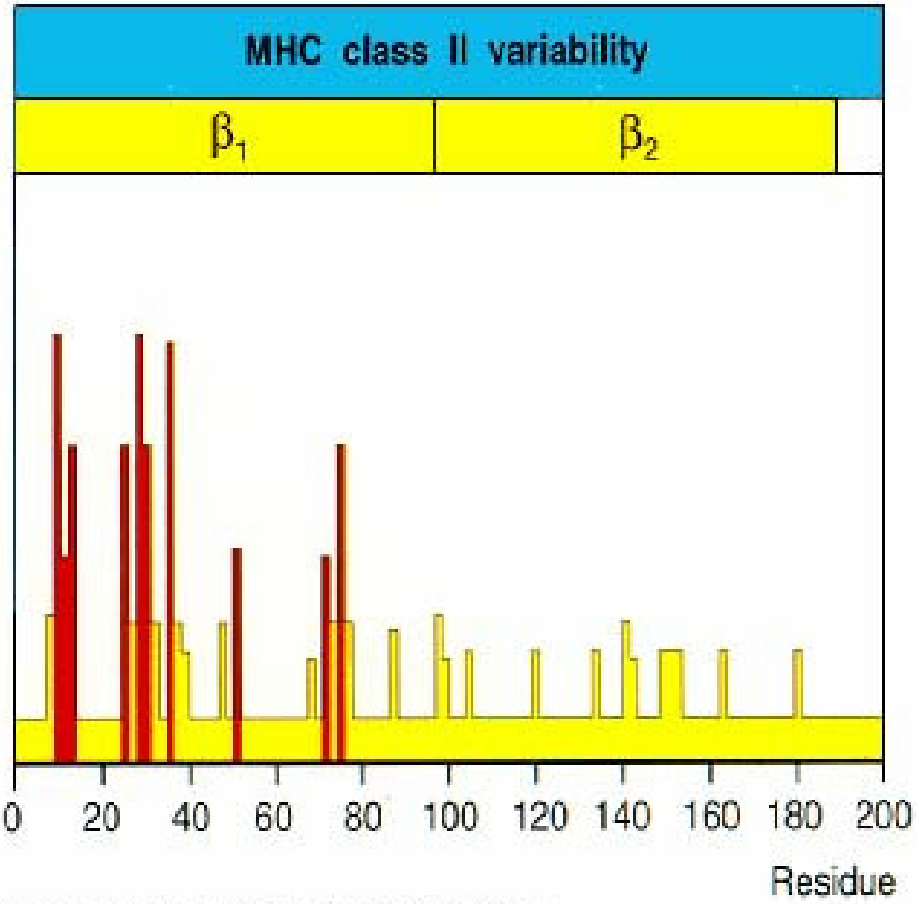




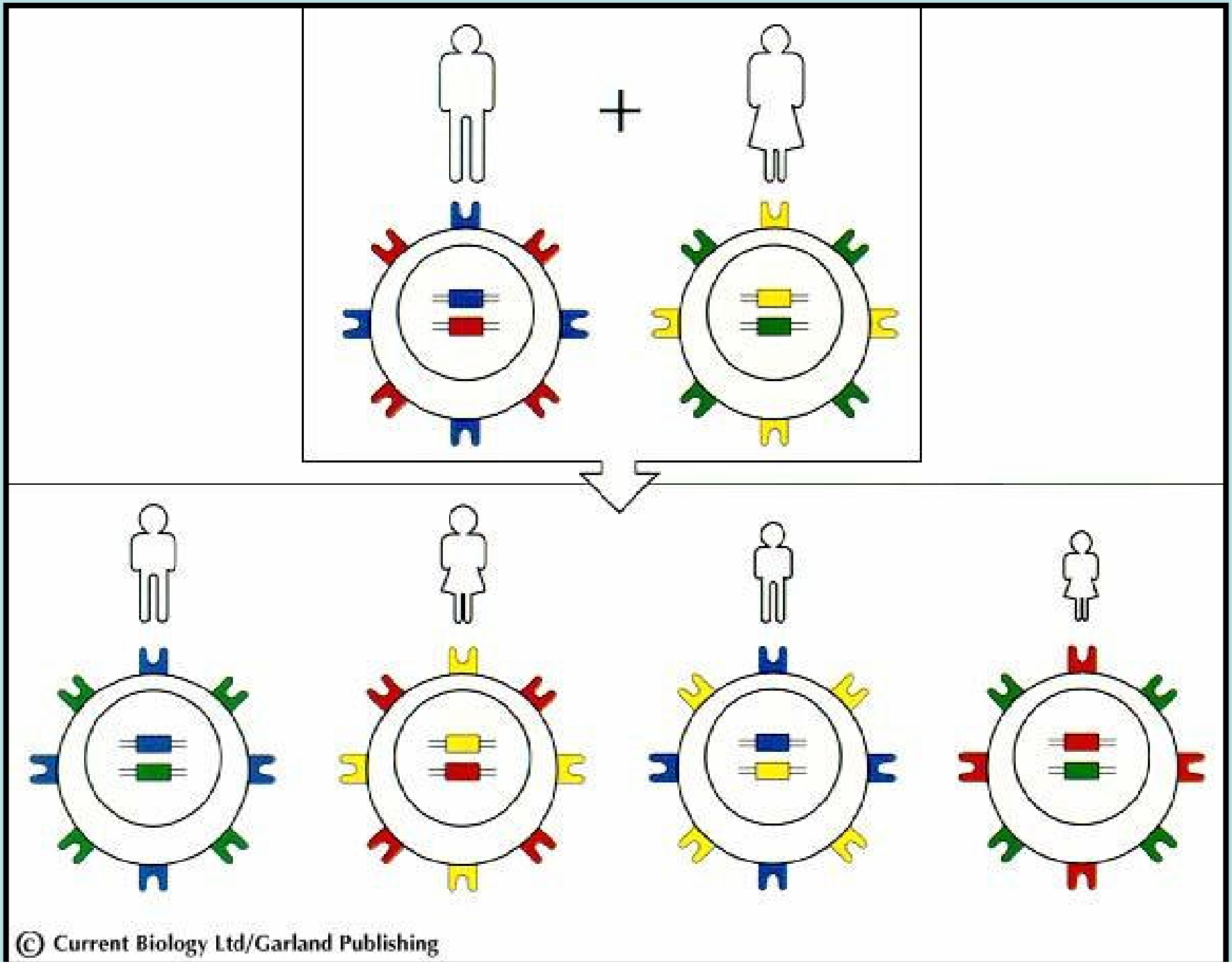
© Current Biology Ltd/Garland Publishing





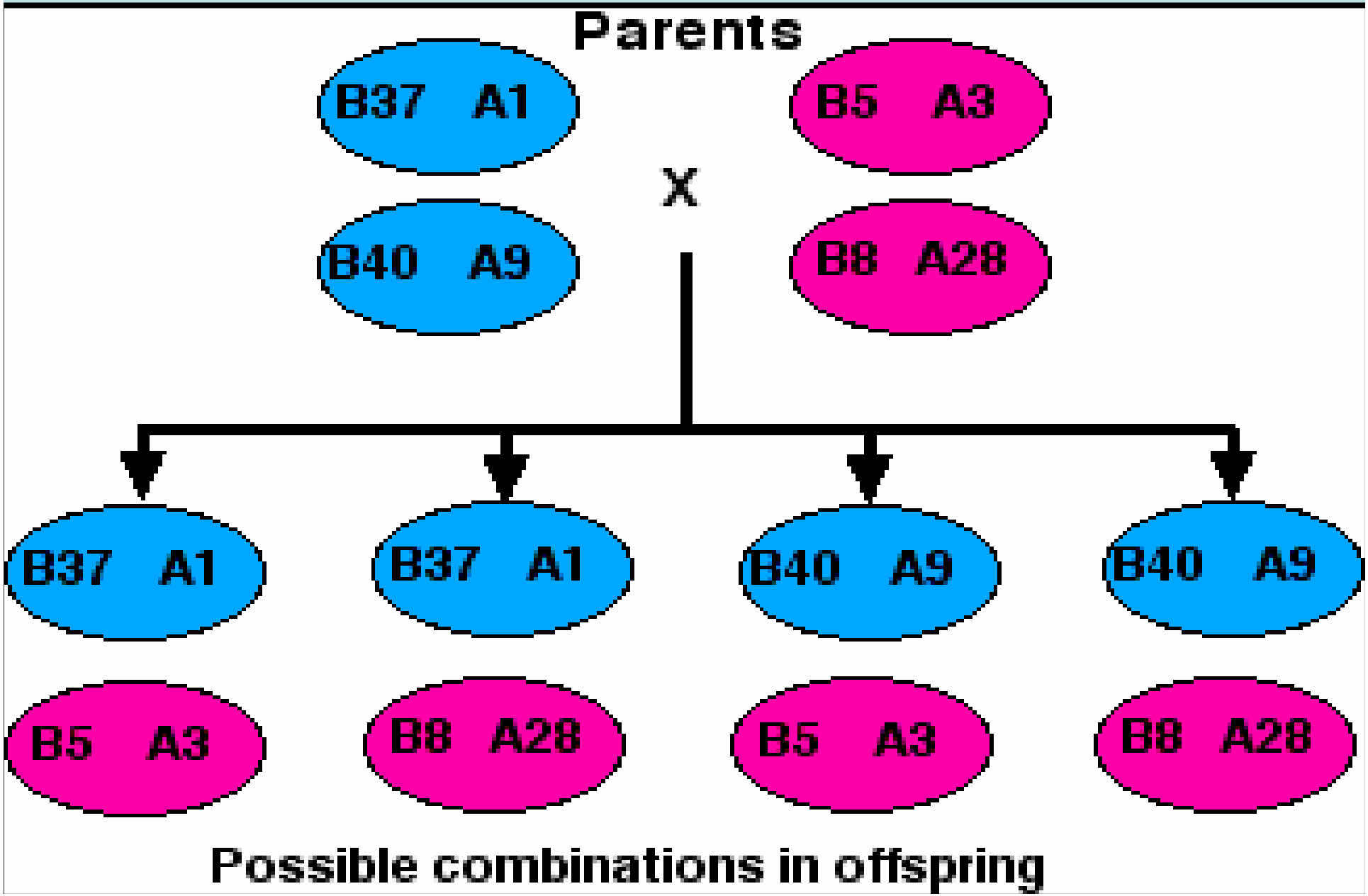


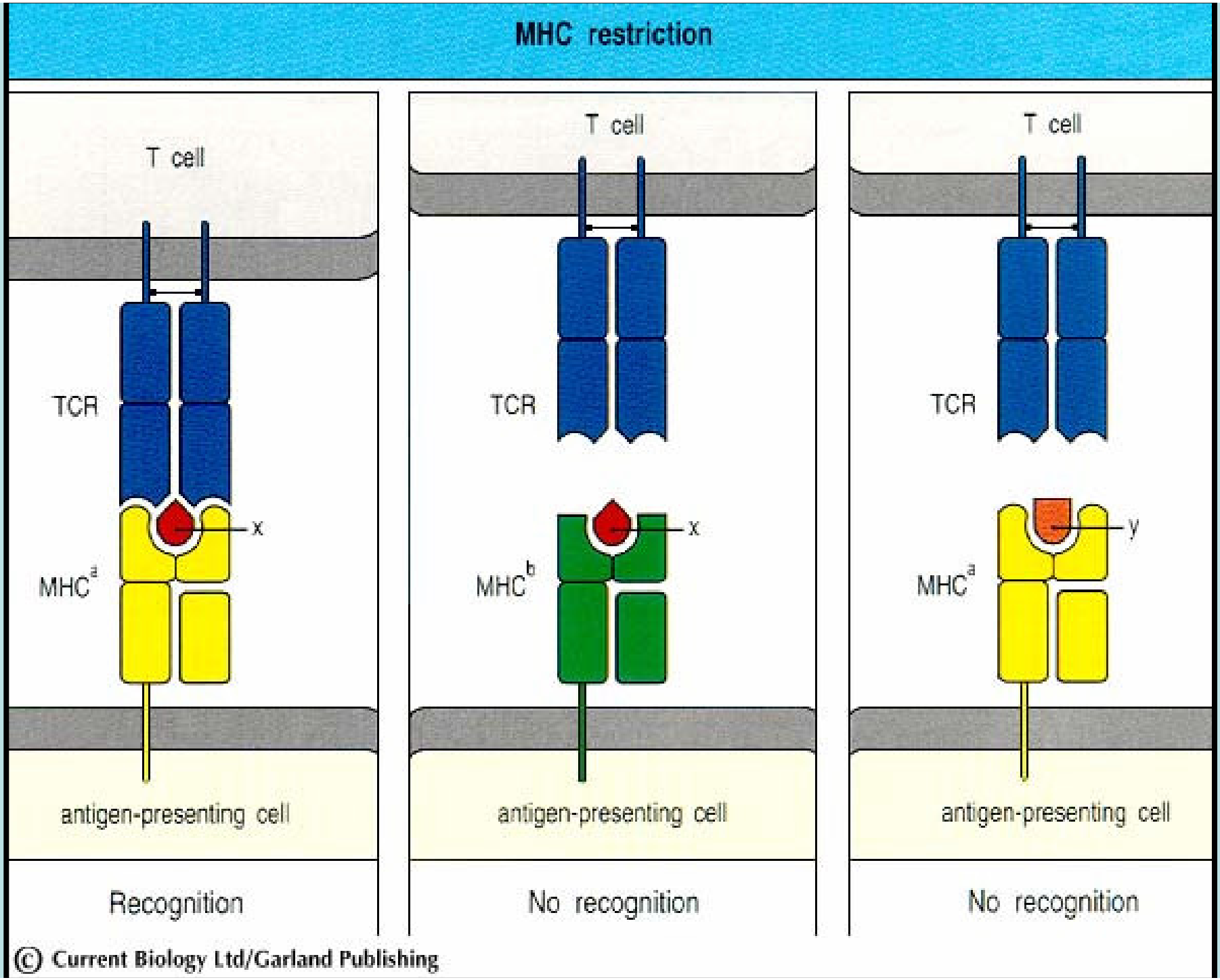
© Current Biology Ltd/Garland Publishing



© Current Biology Ltd/Garland Publishing

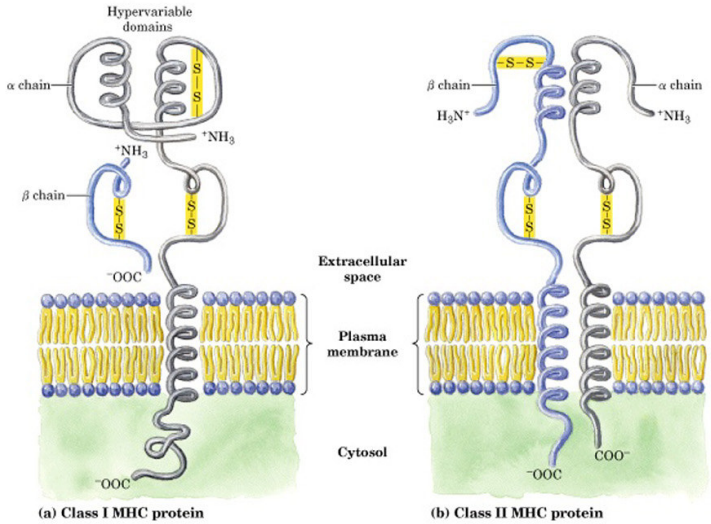
HLA se hereda como haplotipo

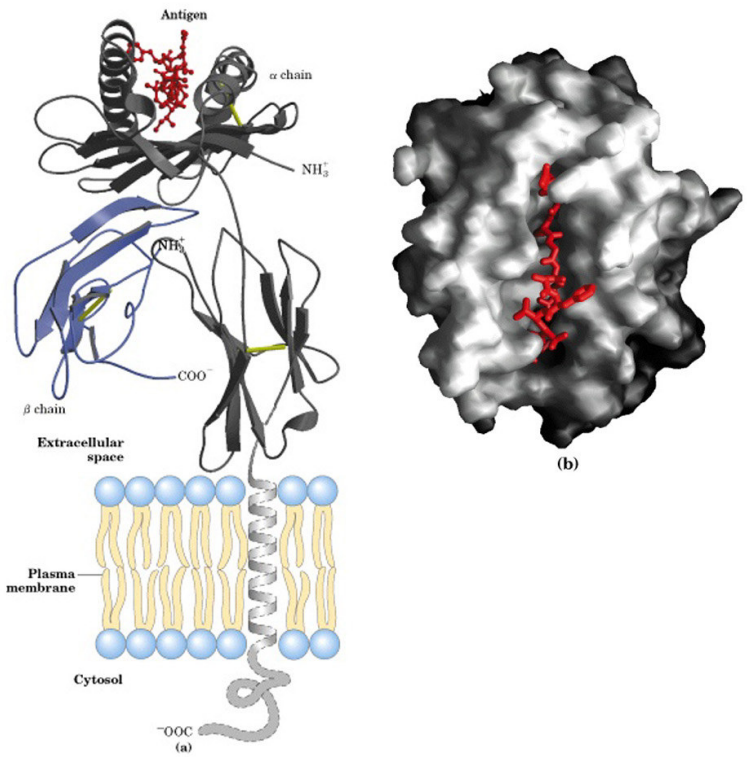




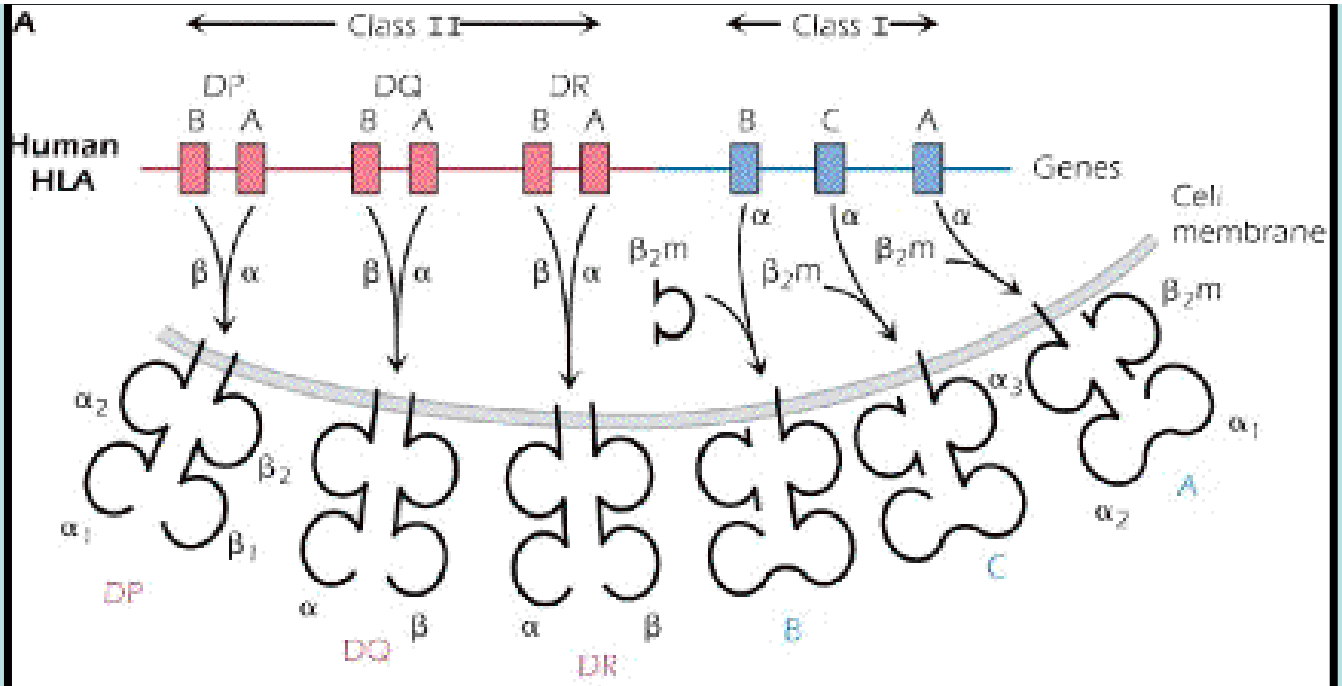
© Current Biology Ltd/Garland Publishing

MHC proteins



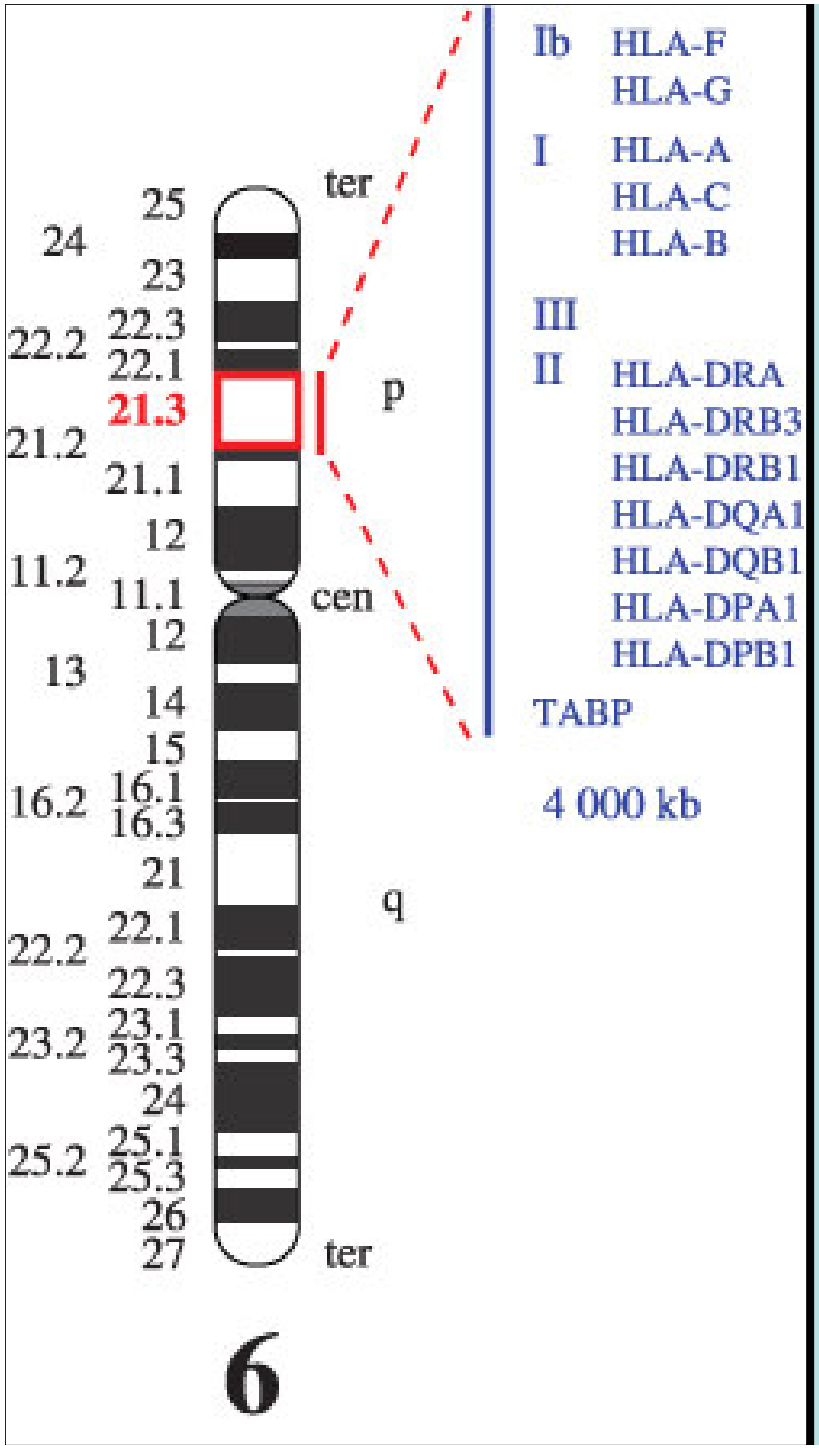


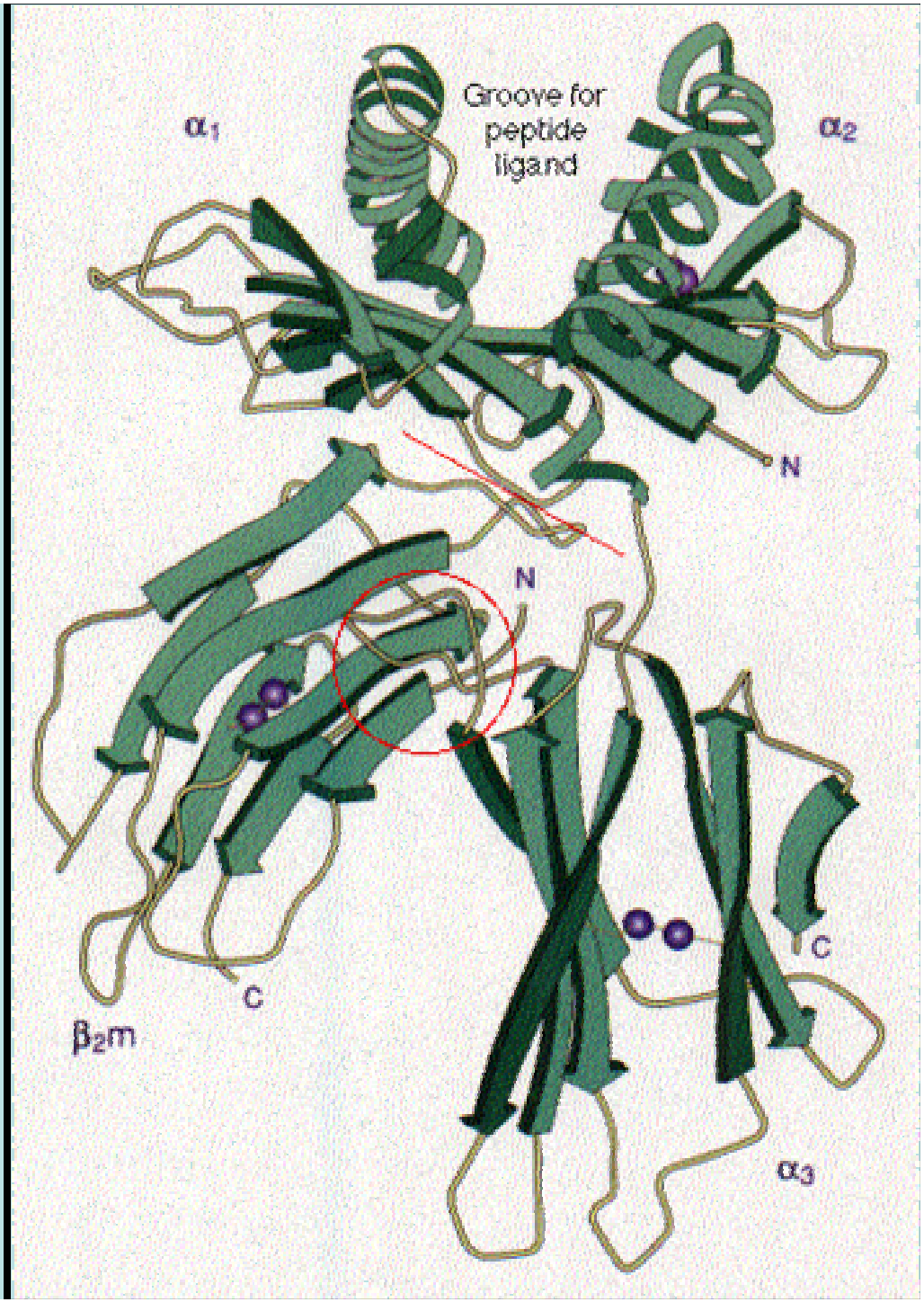
- MHC clase I se expresan en todas las células nucleadas
- MHC clase II se expresa en Células presentadoras de Antígeno (CPA profesionales) celulas endoteliales y epiteliales del timo y su presencia puede aumentar por acción de citoquinas (IFNγ)

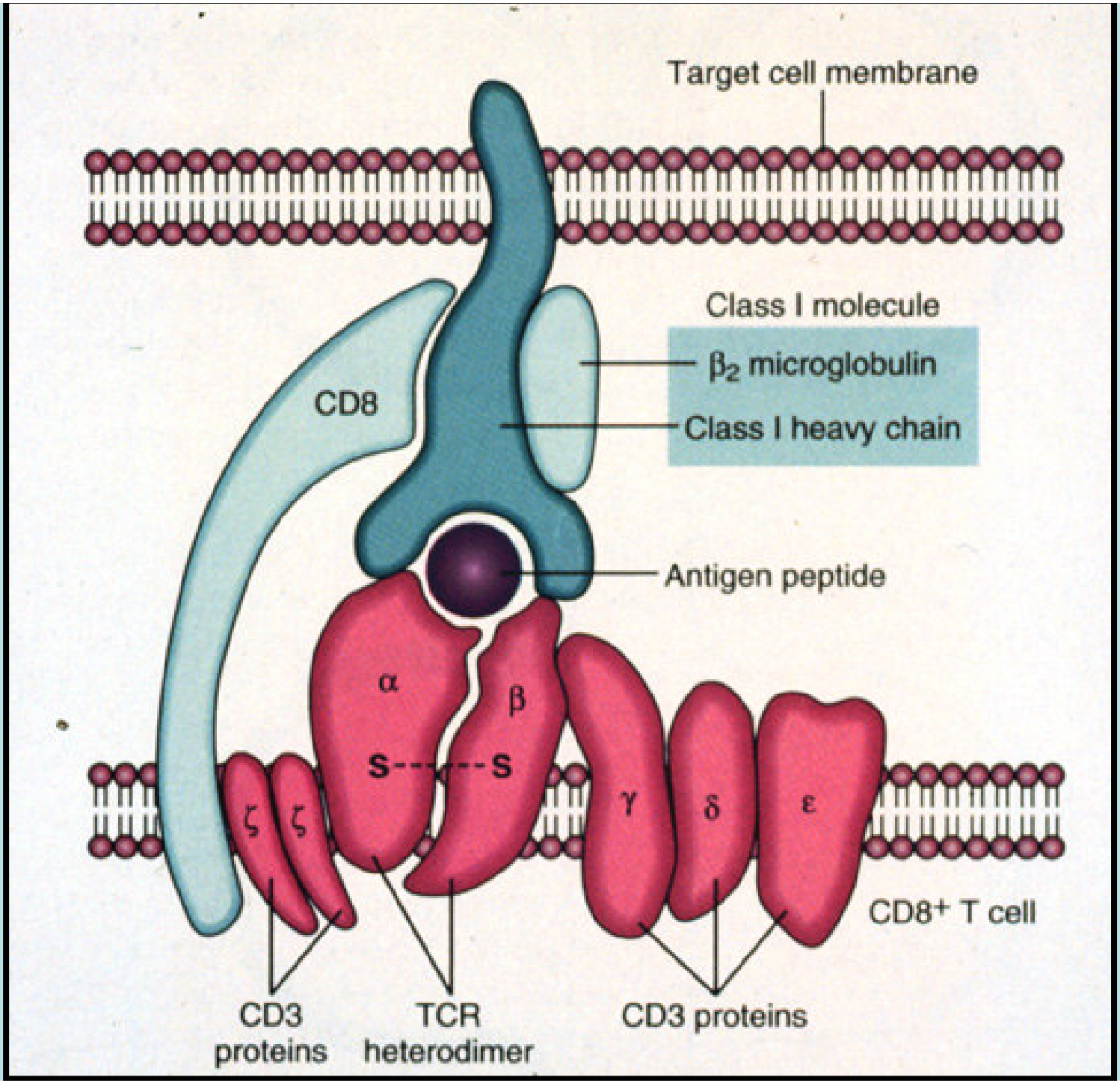


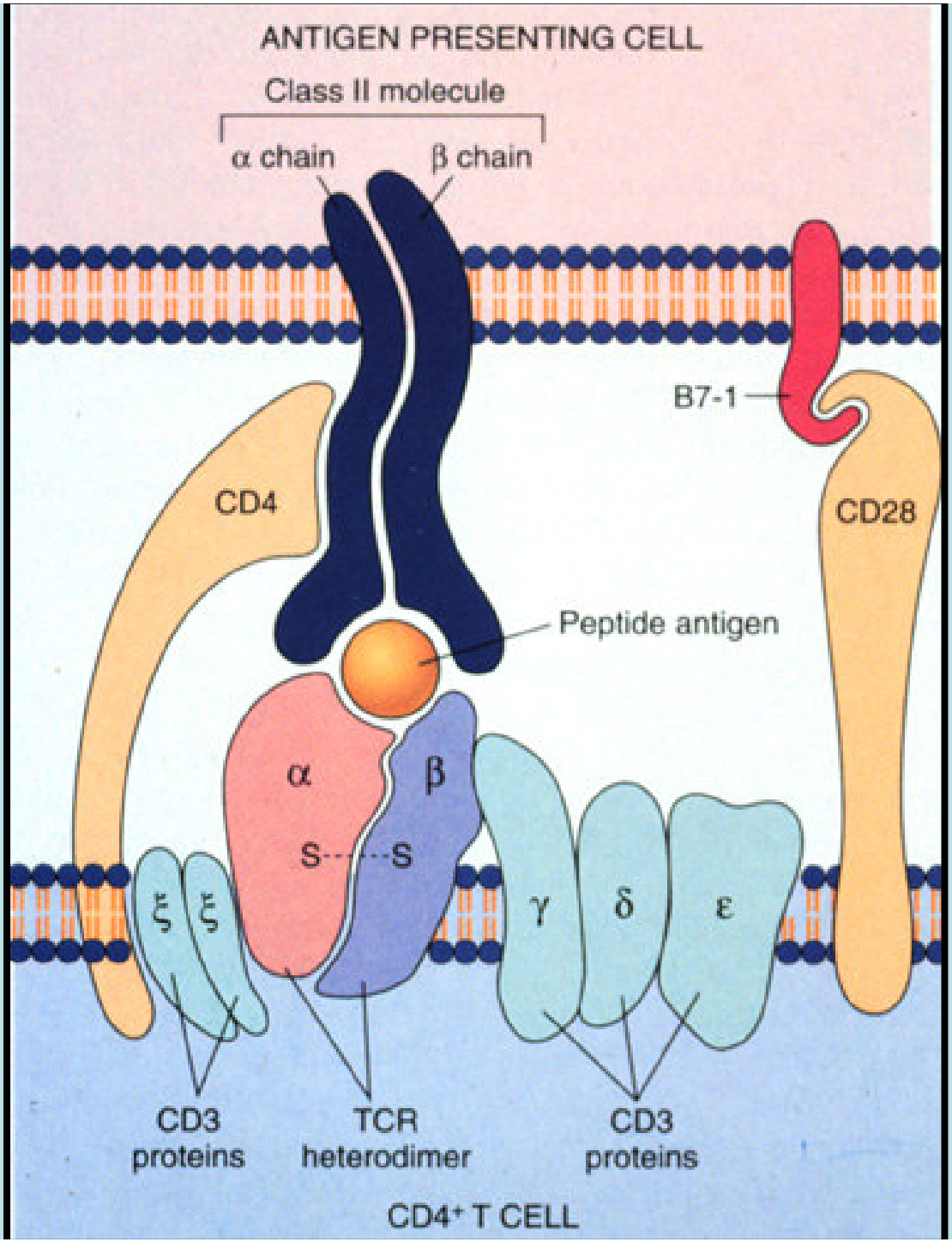
Cada célula nucleada expresa 6 alelos MHC clase I o sea seis cadenas alfa diferentes

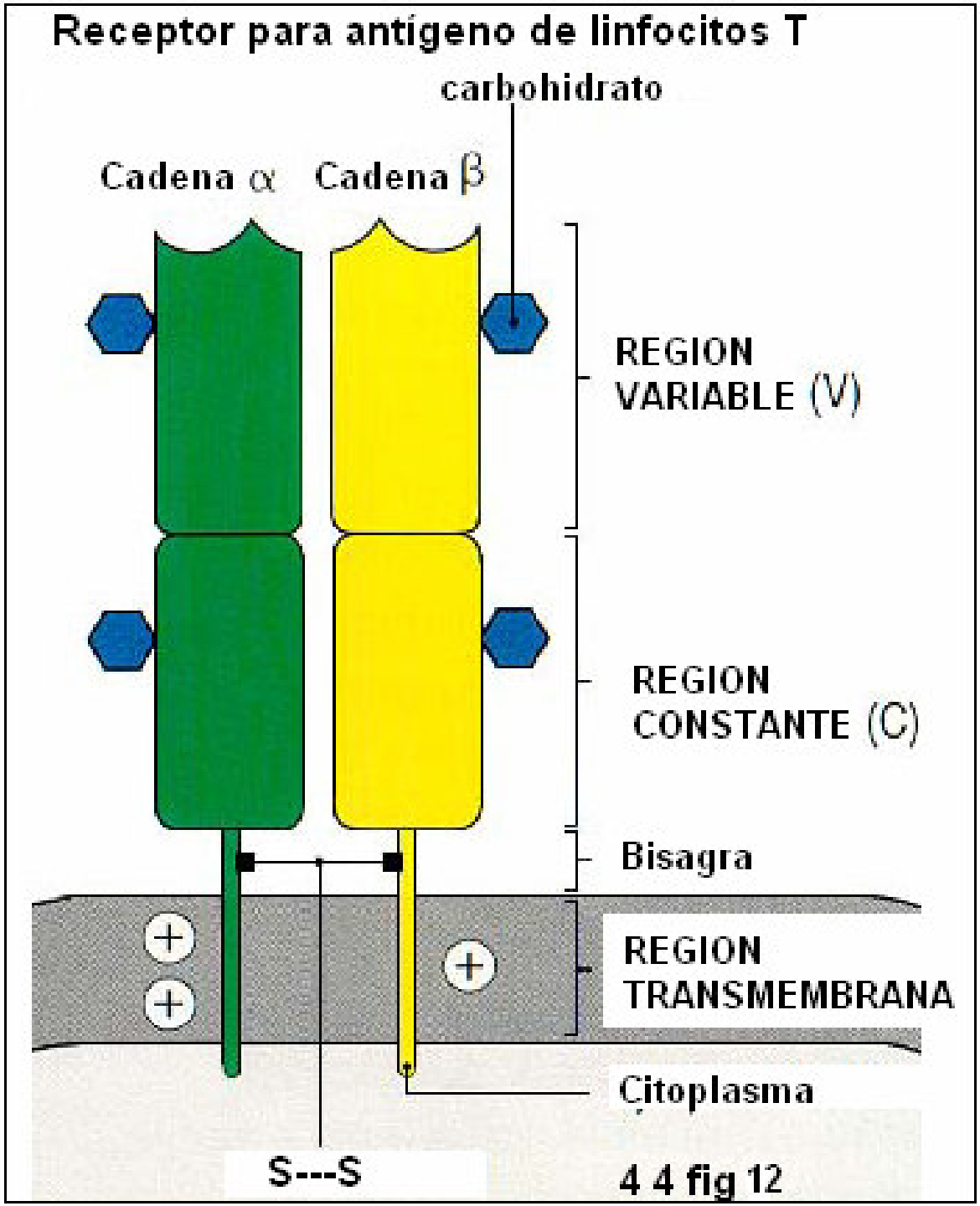
Cada célula presentadora de antígeno expresa un minimo de 6 alelos MHC clase II:
cadena alfa : seis alelos paternos y seis alelos maternos
cadena beta : seis alelos paternos y seis alelos maternos
pero.....puede haber parejas heterólogas:
DQ beta con DQ alfa por lo que una CPA puede expresar hasta 20 moleculas MHC clase II distintas

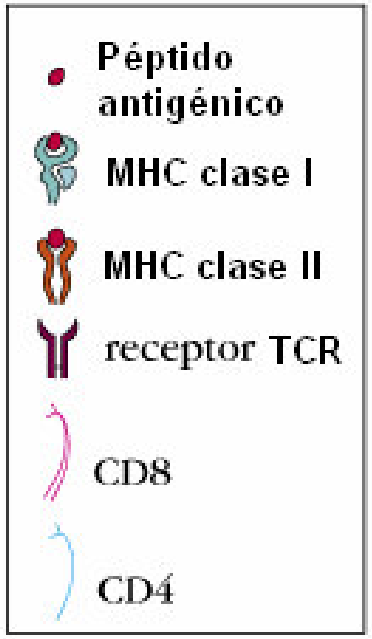

ter
25
24
23
22.3
22.2
22.1
21.3
21.2
21.1
12
11.2
11.1
cen
12
13
14
15
16.2
16.1
16.3
21
22.1
22.2
22.3
23.1
23.2
23.3
24
25.1
25.2
25.3
26
27
ter
p
q
6
Ib HLA-F
HLA-G
I HLA-A
HLA-C
HLA-B
III
II HLA-DRA
HLA-DRB3
HLA-DRB1
HLA-DQA1
HLA-DQB1
HLA-DPA1
HLA-DPB1
TABP
4 000 kb

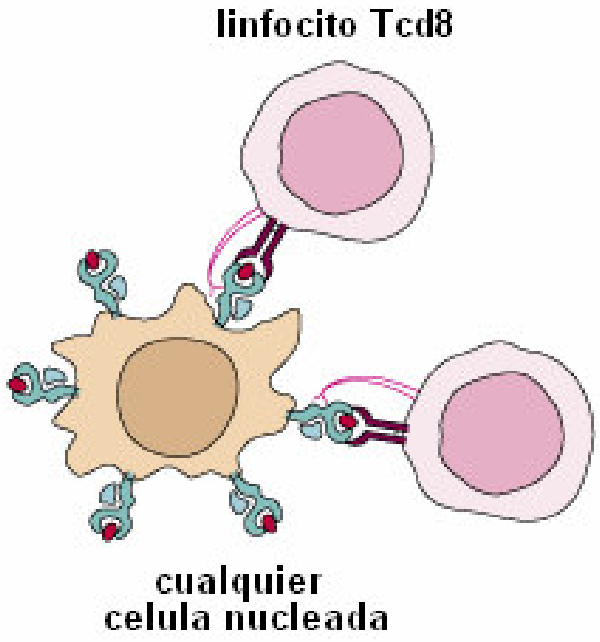

α1
Groove for peptide ligand
α2
N
N
C
C
β2m
α3

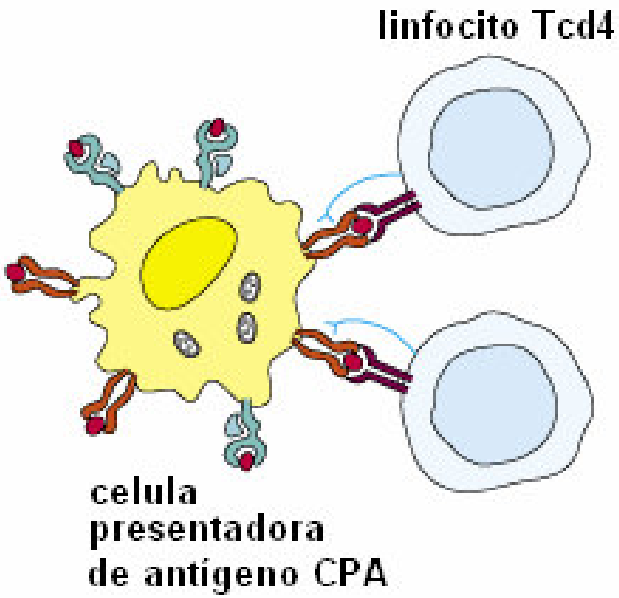

Target cell membrane
Class I molecule
β_2 microglobulin
Class I heavy chain
CD8
Antigen peptide
α
β
S
S
ζ
ζ
γ
δ
ε
CD8+ T cell
CD3 proteins
TCR heterodimer
CD3 proteins


ANTIGEN PRESENTING CELL
Class II molecule
α chain
β chain
B7-1
CD4
CD28
Peptide antigen
α
β
S
S
ξ
ξ
γ
δ
ε
CD3
proteins
TCR
heterodimer
CD3
proteins
CD4+ T CELL

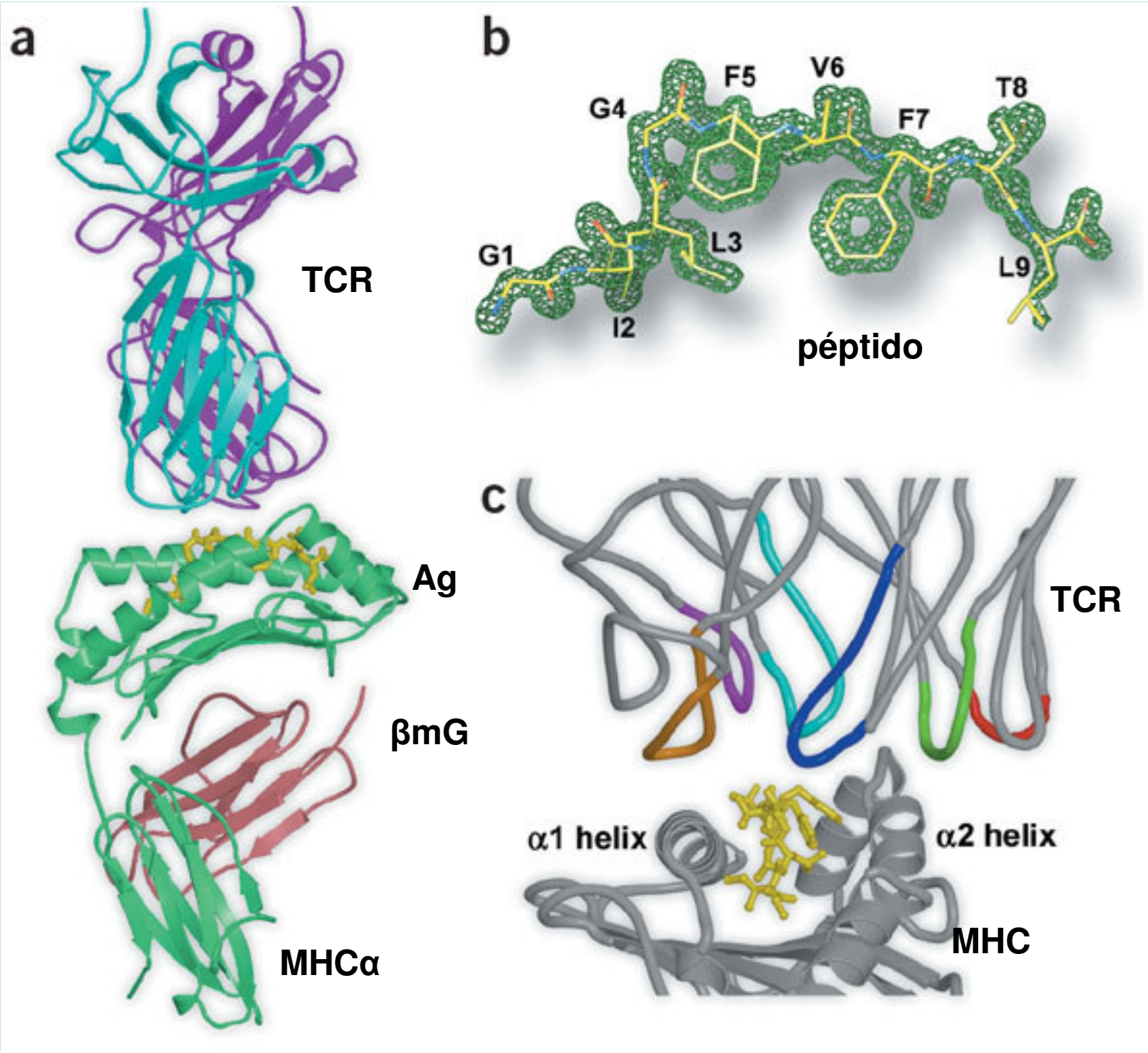

Receptor para antígeno de linfocitos T
carbohidrato
Cadena α
Cadena β
REGION
VARIABLE (V)
REGION
CONSTANTE (C)
Bisagra
REGION
TRANSMEMBRANA
Citoplasma
S---S
4 4 fig 12

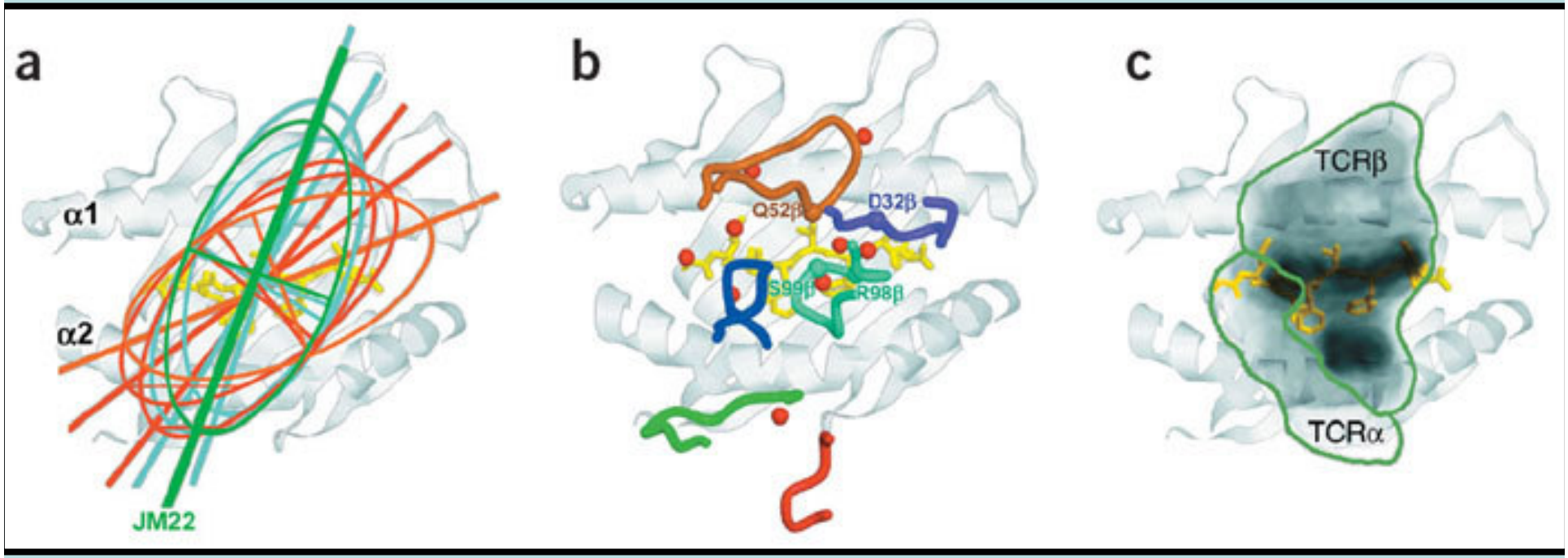

Péptido antigénico
MHC clase I
MHC clase II
receptor TCR
CD8
CD4

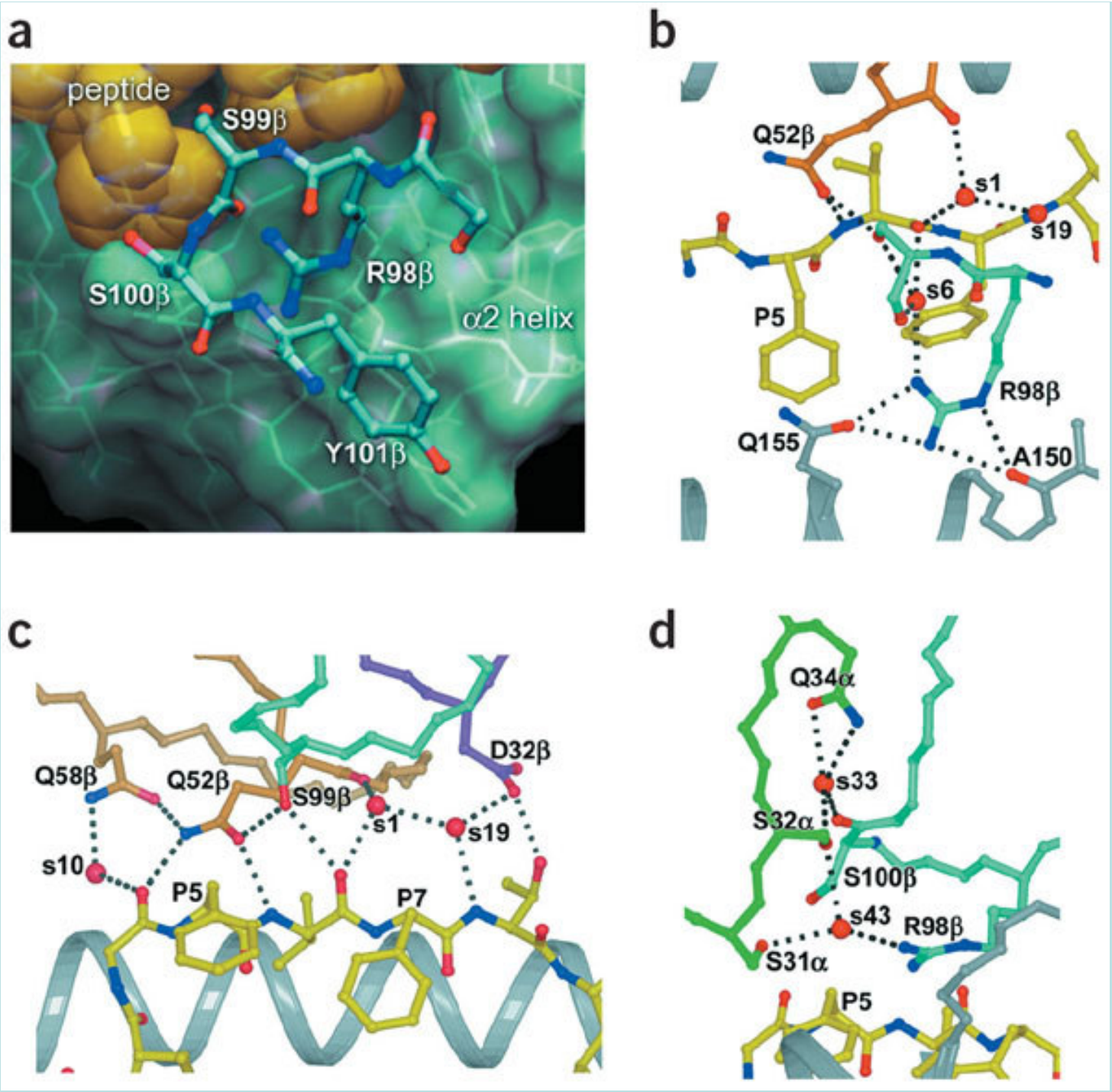

linfocito Tcd8
cualquier celula nucleada


linfocito Tcd4
celula presentadora de antigeno CPA

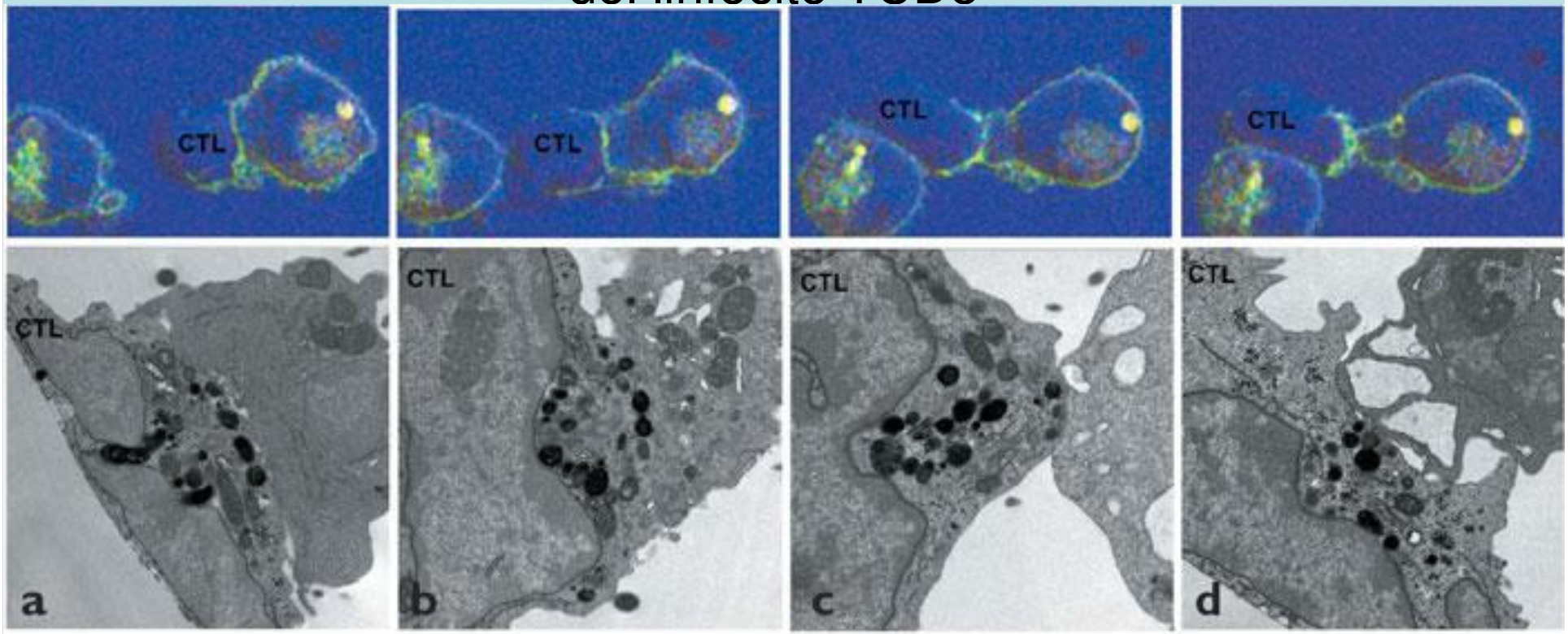
4 4 fig 19

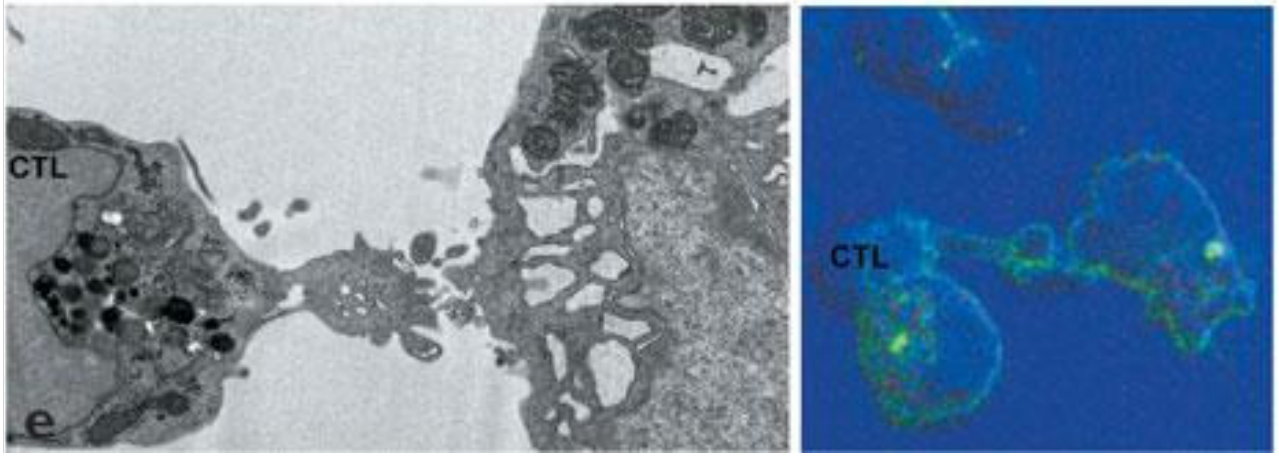

a
TCR
Ag
βmG
MHCα
b
F5
V6
T8
G4
F7
G1
L3
L9
I2
péptido
c
TCR
α1 helix
α2 helix
MHC


a
α1
α2
JM22
b
Q52β
D32β
S99β
R98β
c
TCRβ
TCRα


a
peptide
S99β
S100β
R98β
α2 helix
Y101β
b
Q52β
s1
s19
s6
P5
R98β
Q155
A150
c
Q58β
Q52β
S99β
s1
s19
D32β
s10
P5
P7
d
Q34α
s33
S32α
S100β
s43
R98β
S31α
P5

El MHC clase I es también reconocido en la fase efectora del linfocito TCD8





Citolisis por linfocito T CD8