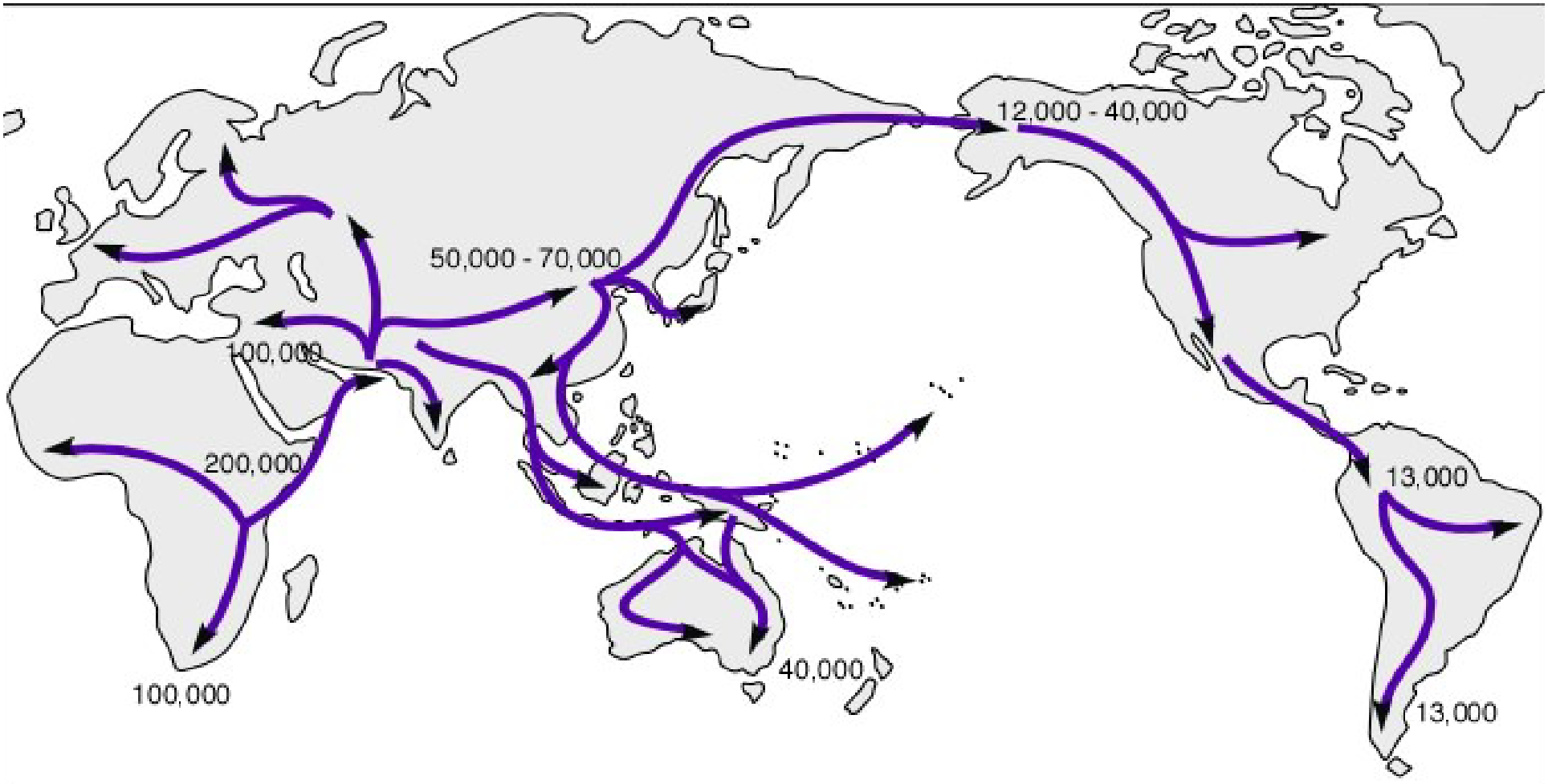
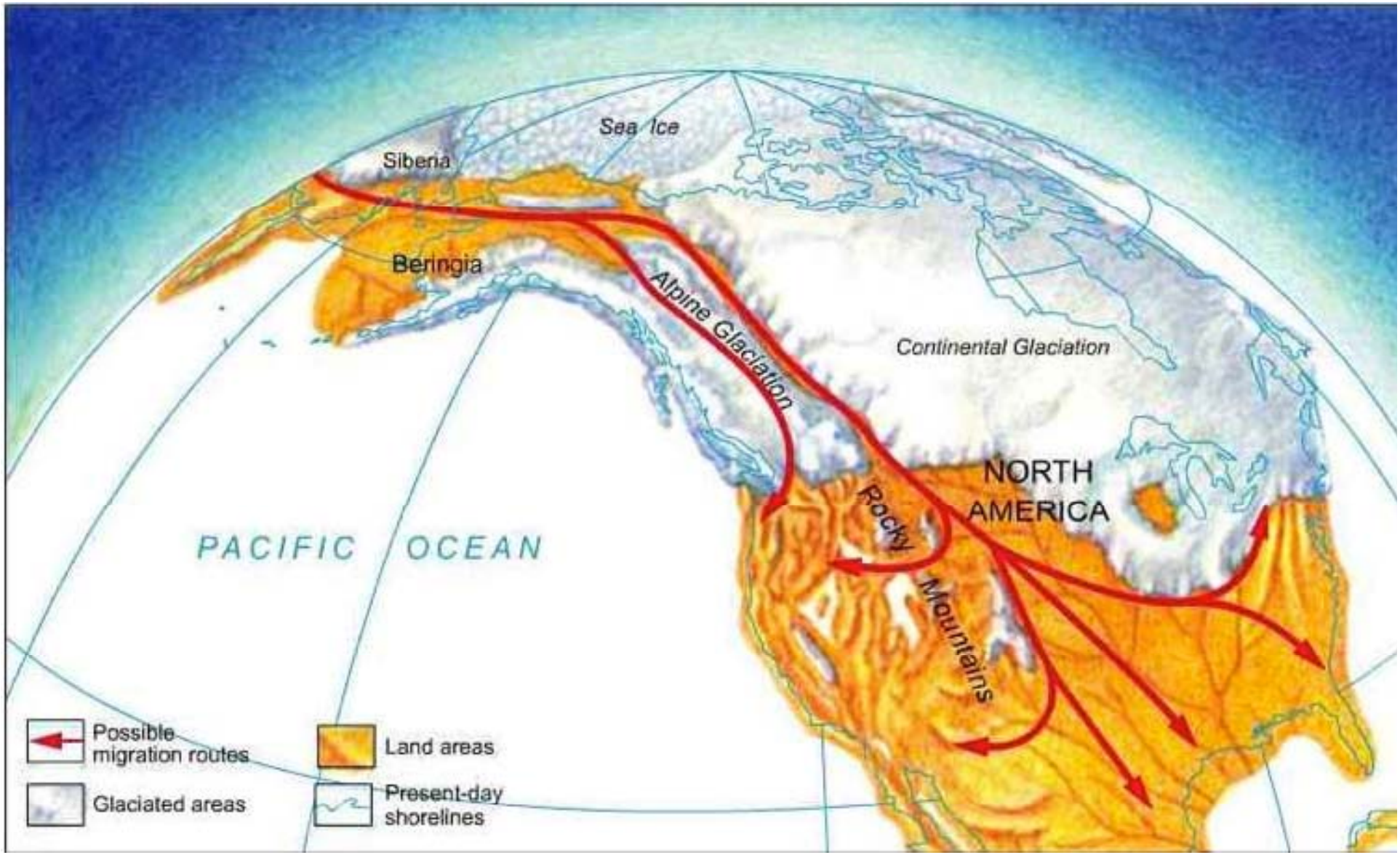
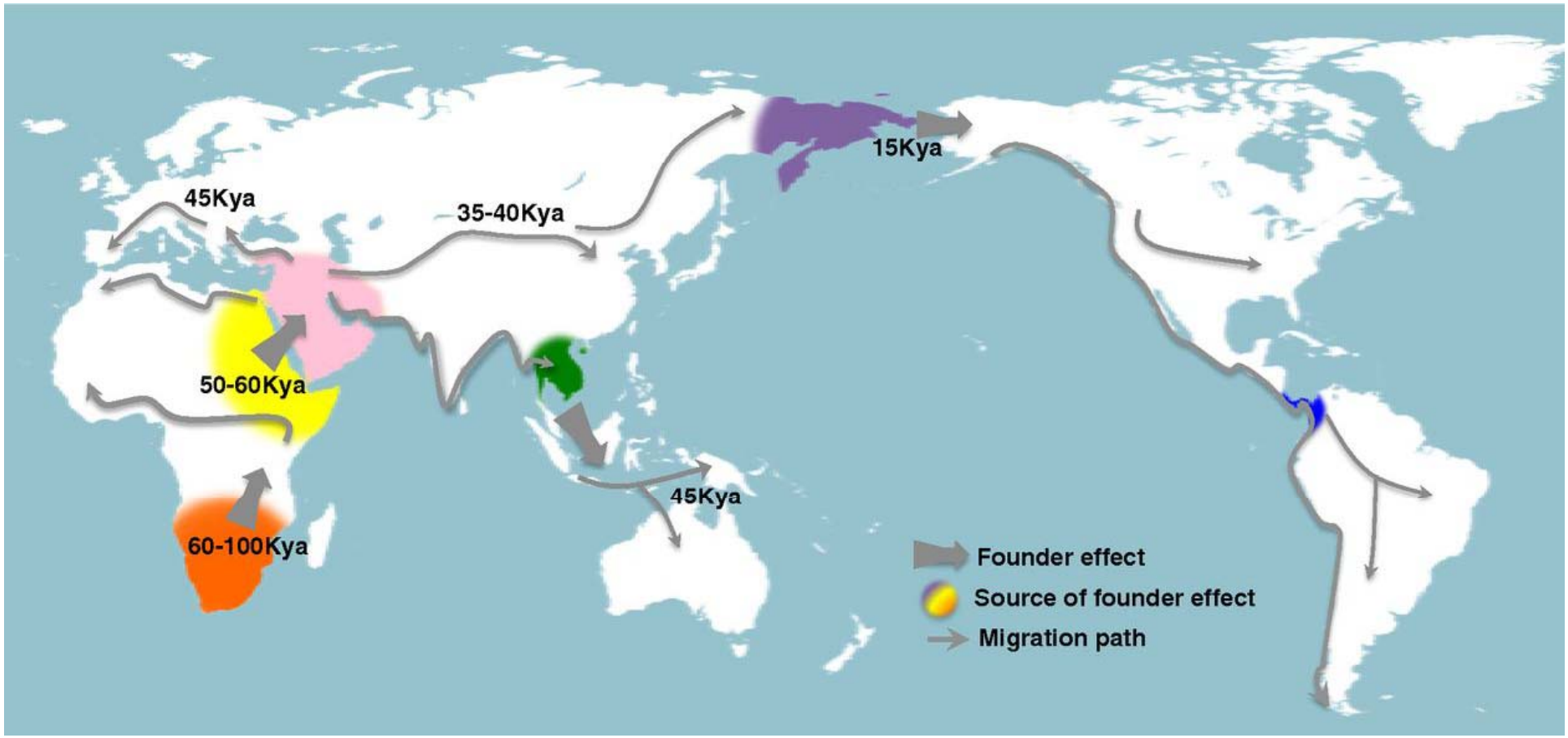
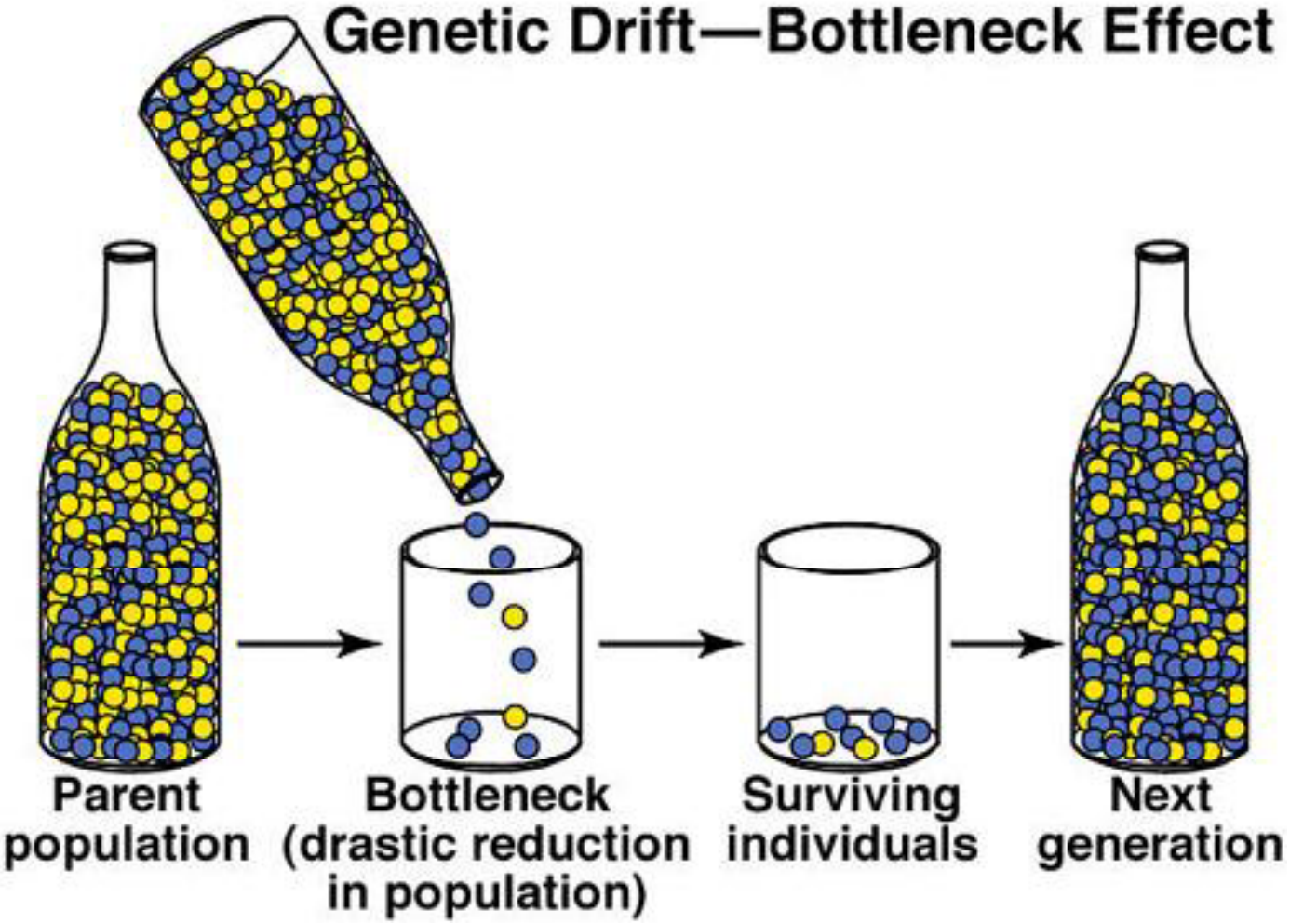
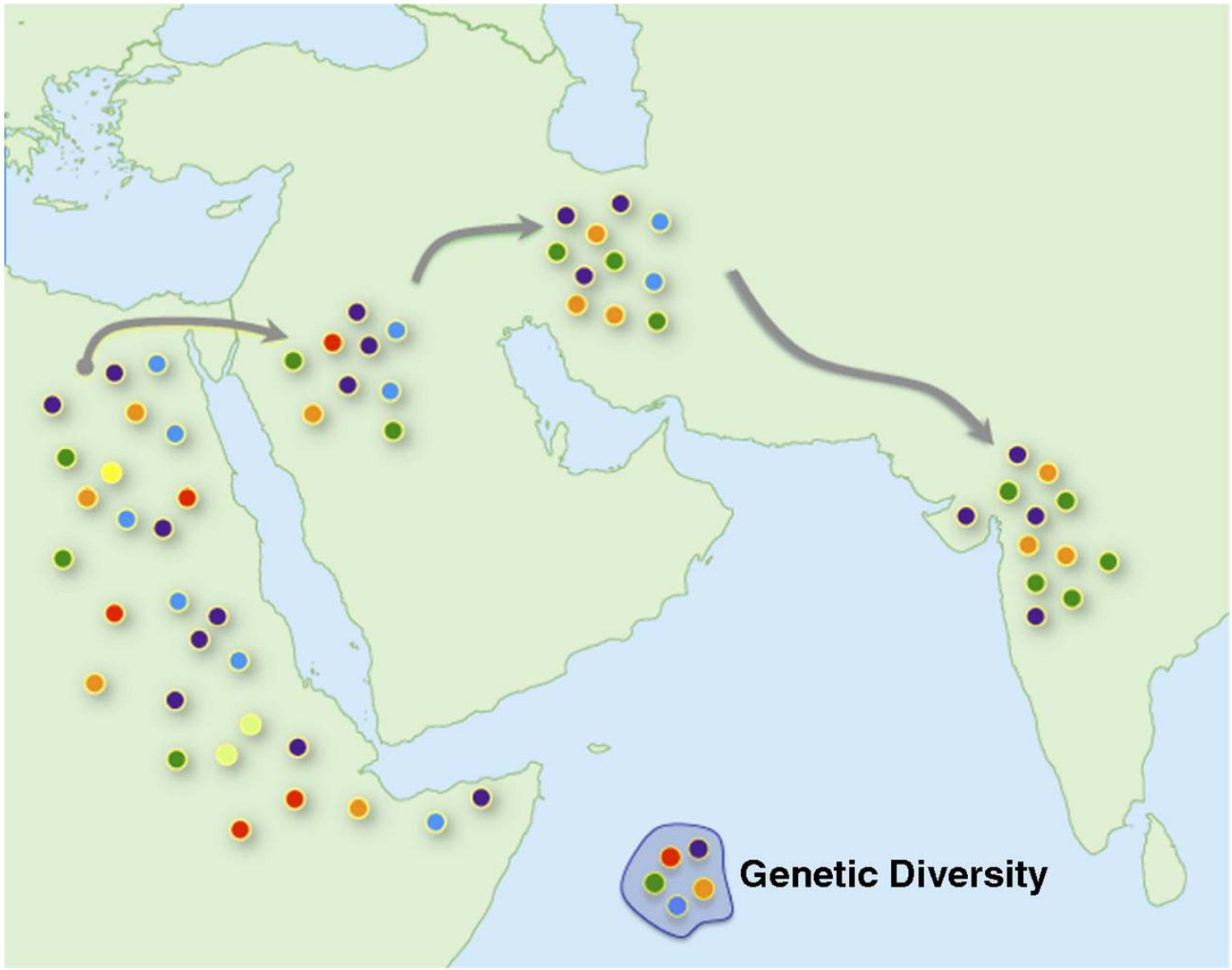

12,000 - 40,000
50,000 - 70,000
100,000
200,000
100,000
40,000
13,000
13,000

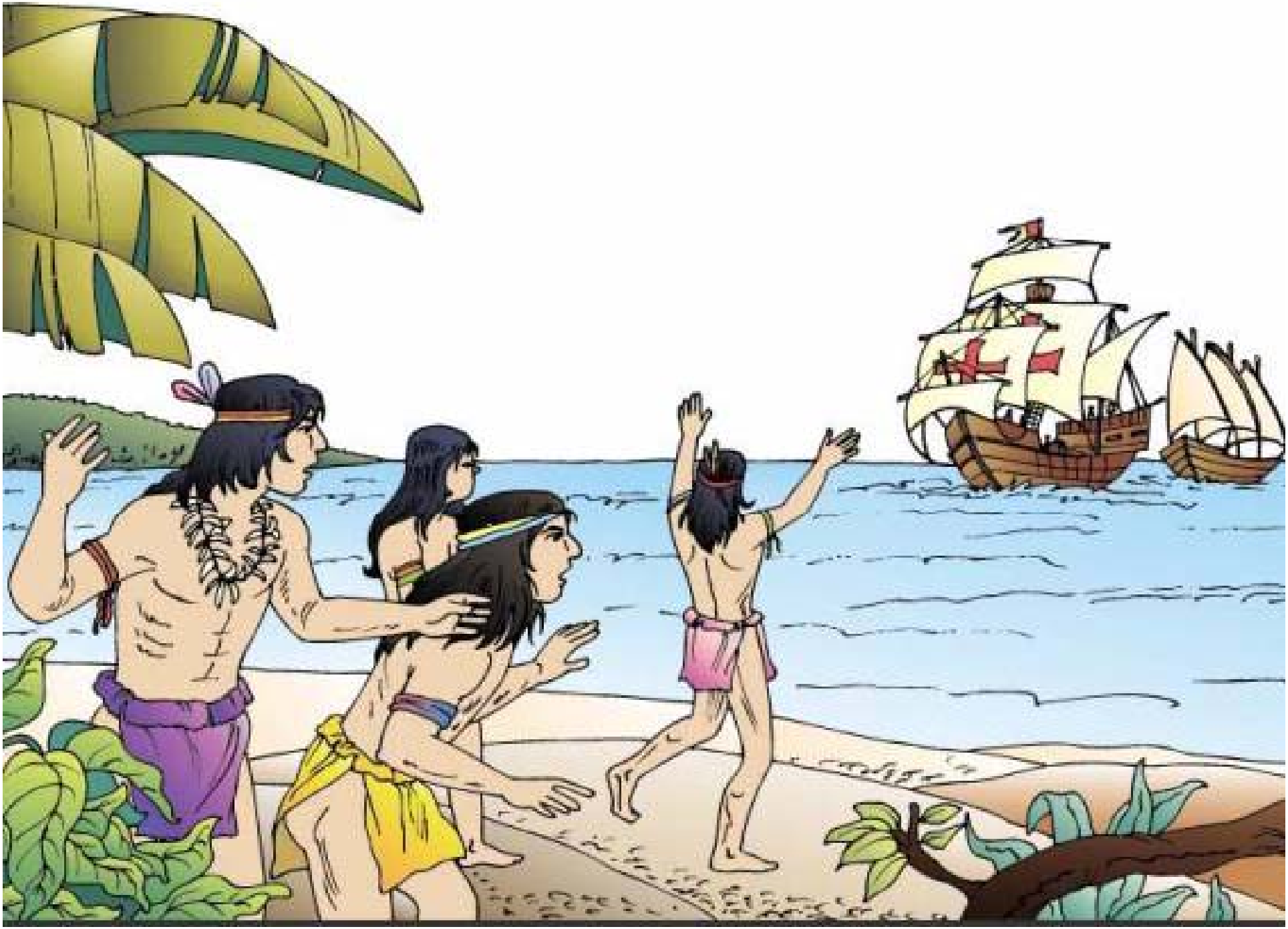

Sea Ice
Siberia
Beringia
Alpine Glaciation
Continental Glaciation
NORTH AMERICA
Rocky Mountains
PACIFIC OCEAN
Possible migration routes
Glaciated areas
Land areas
Present-day shorelines


15Kya
45Kya
35-40Kya
50-60Kya
45Kya
60-100Kya
Founder effect
Source of founder effect
Migration path

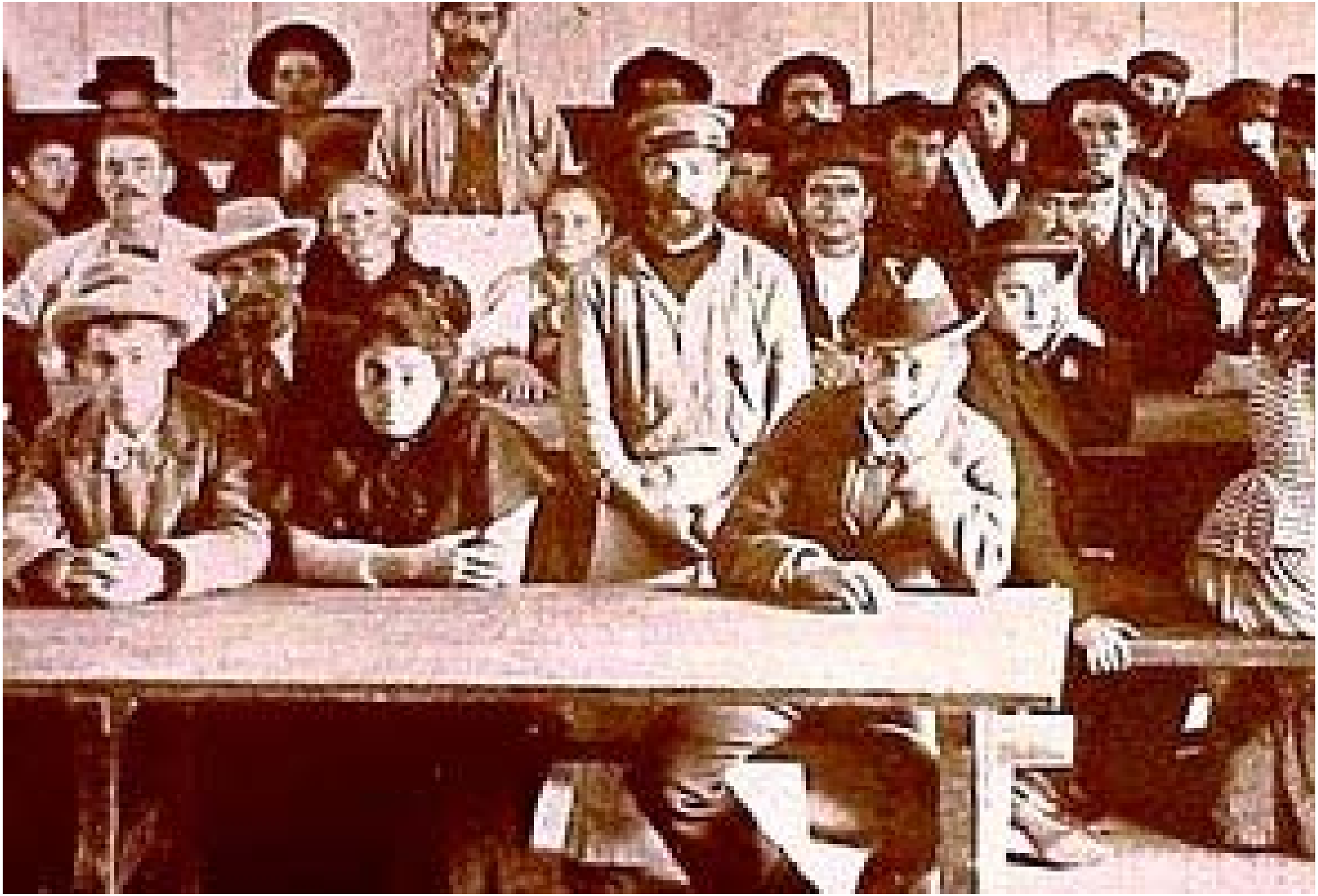

Genetic Drift—Bottleneck Effect
Parent population
Bottleneck (drastic reduction in population)
Surviving individuals
Next generation

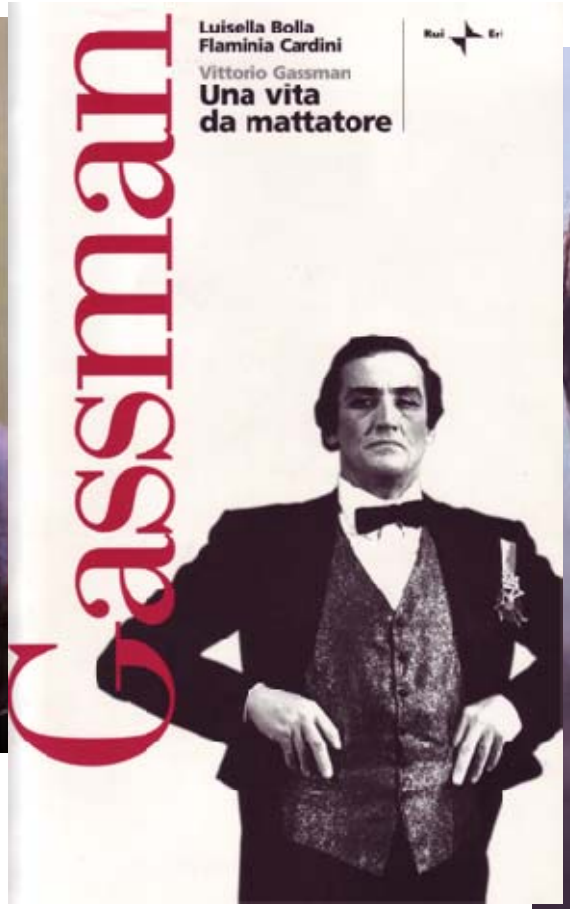
EL EFECTO FUNDADOR SERIAL EN LA REDUCCCIÓN DE LA DIVERSIDAD GENÉTICA



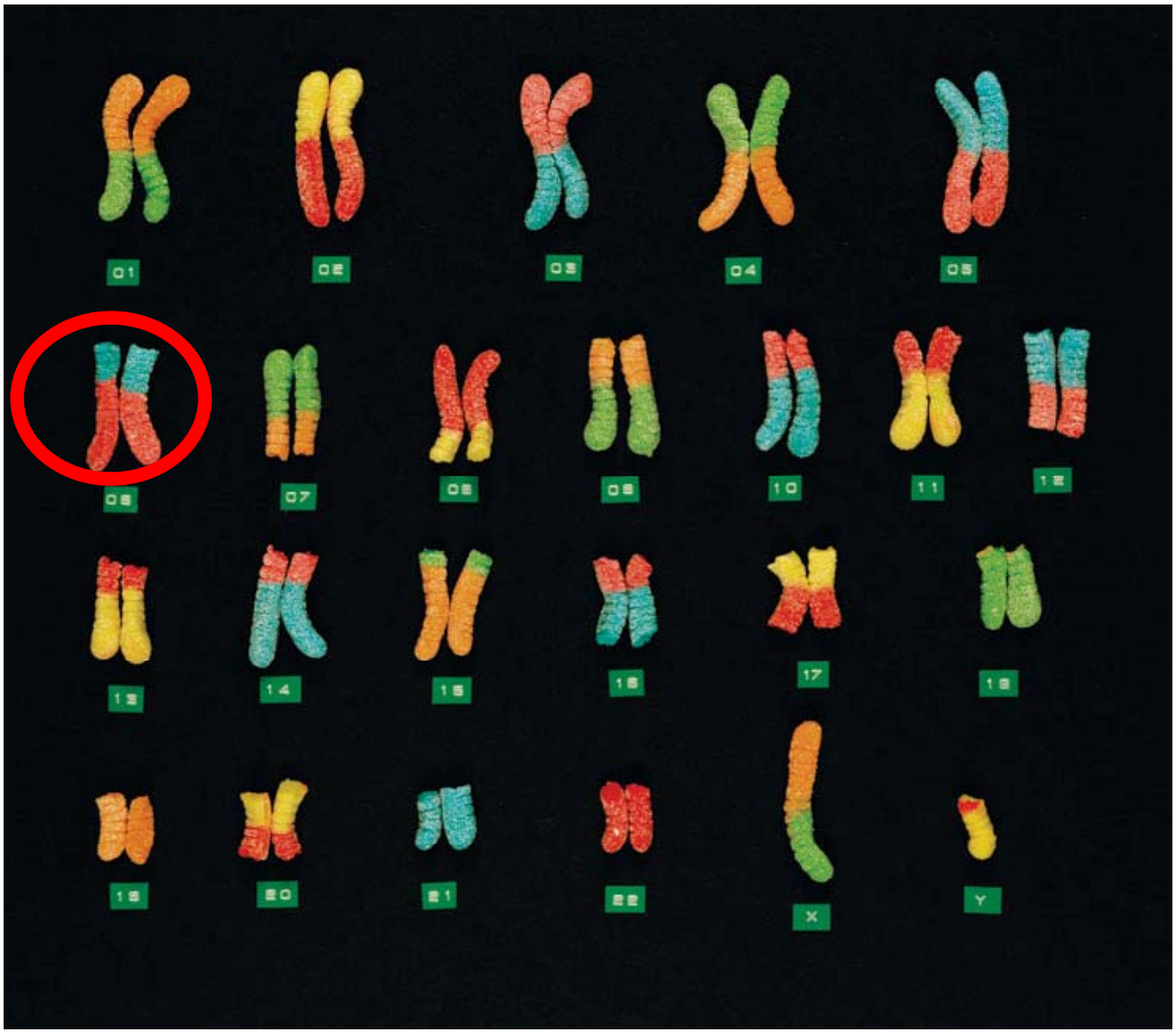


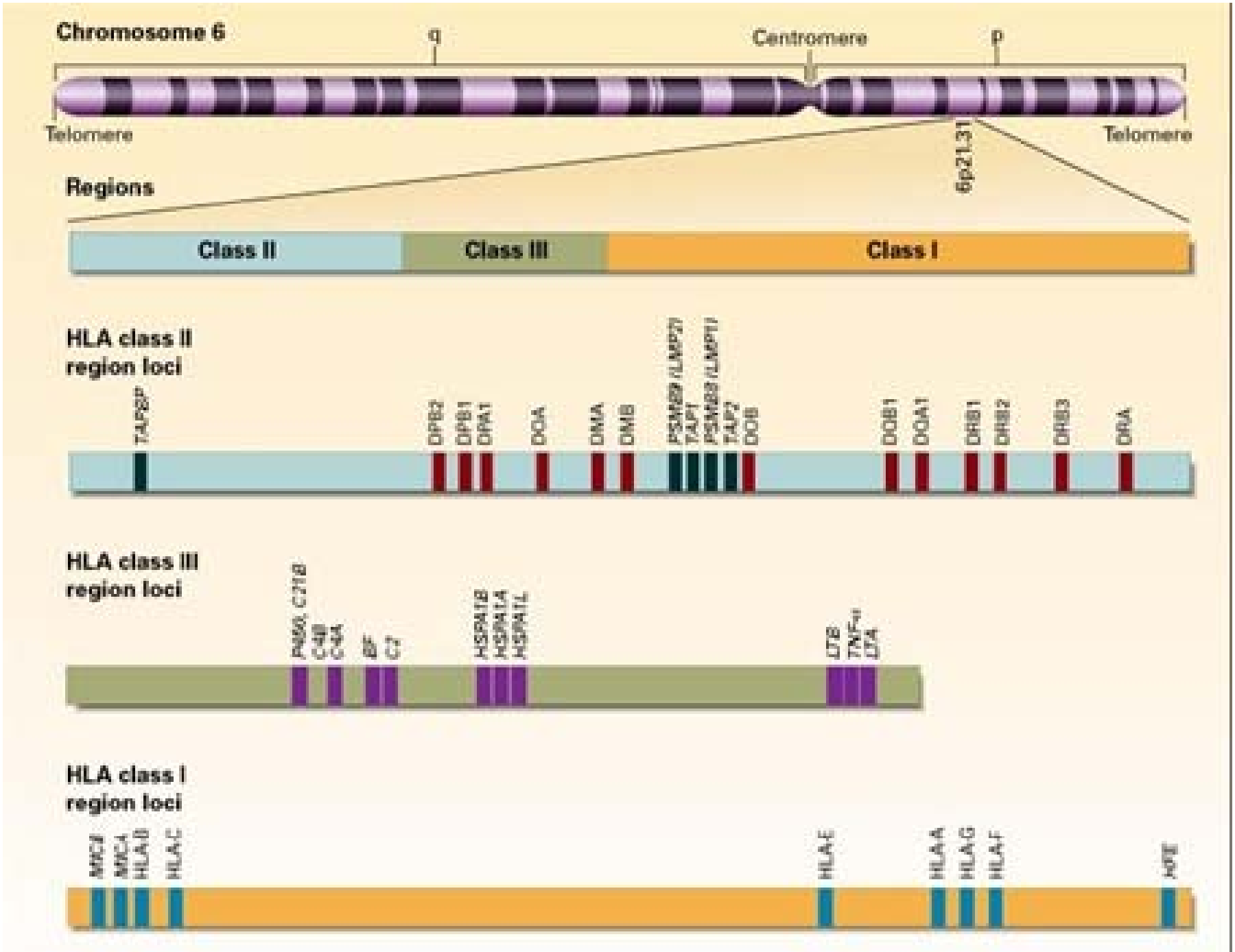

DQ2
DQ8

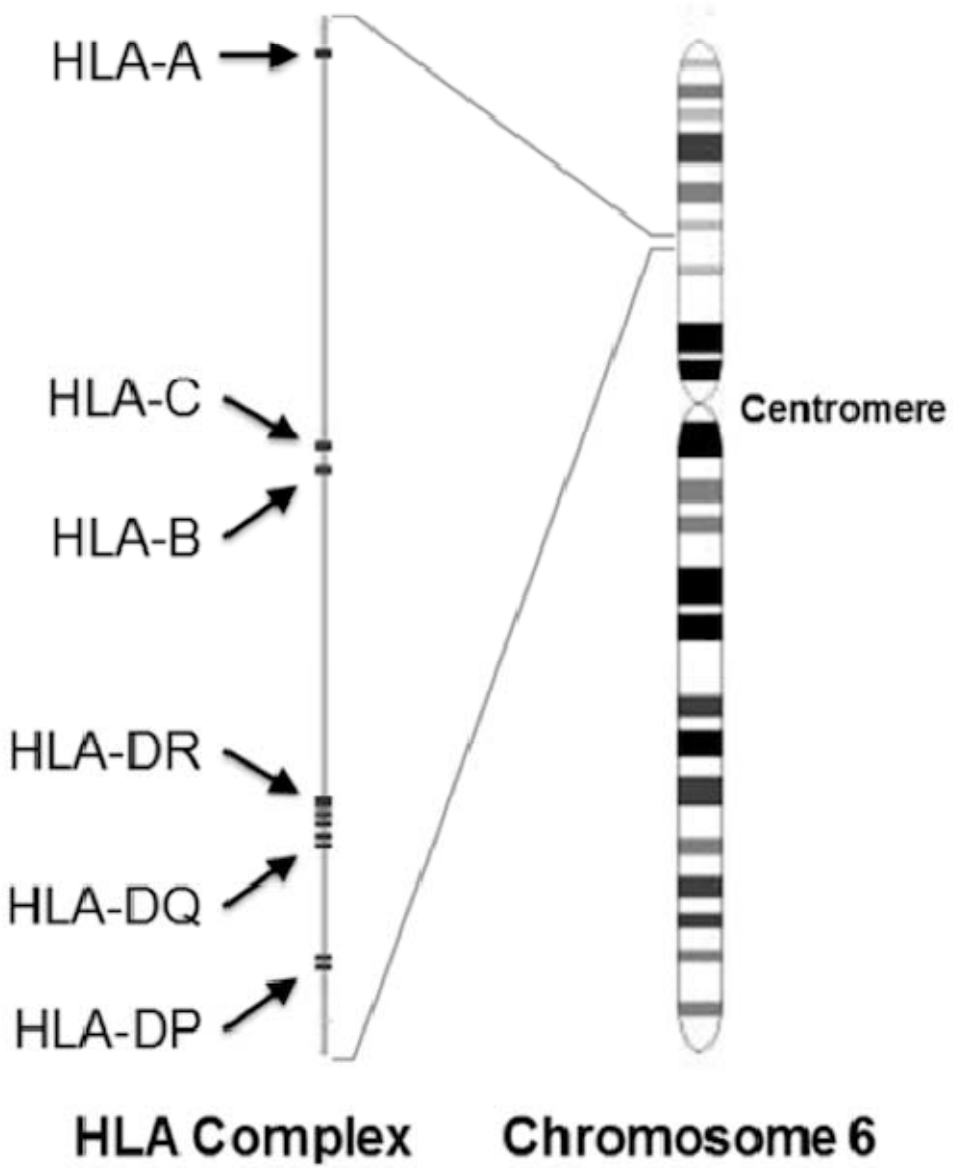


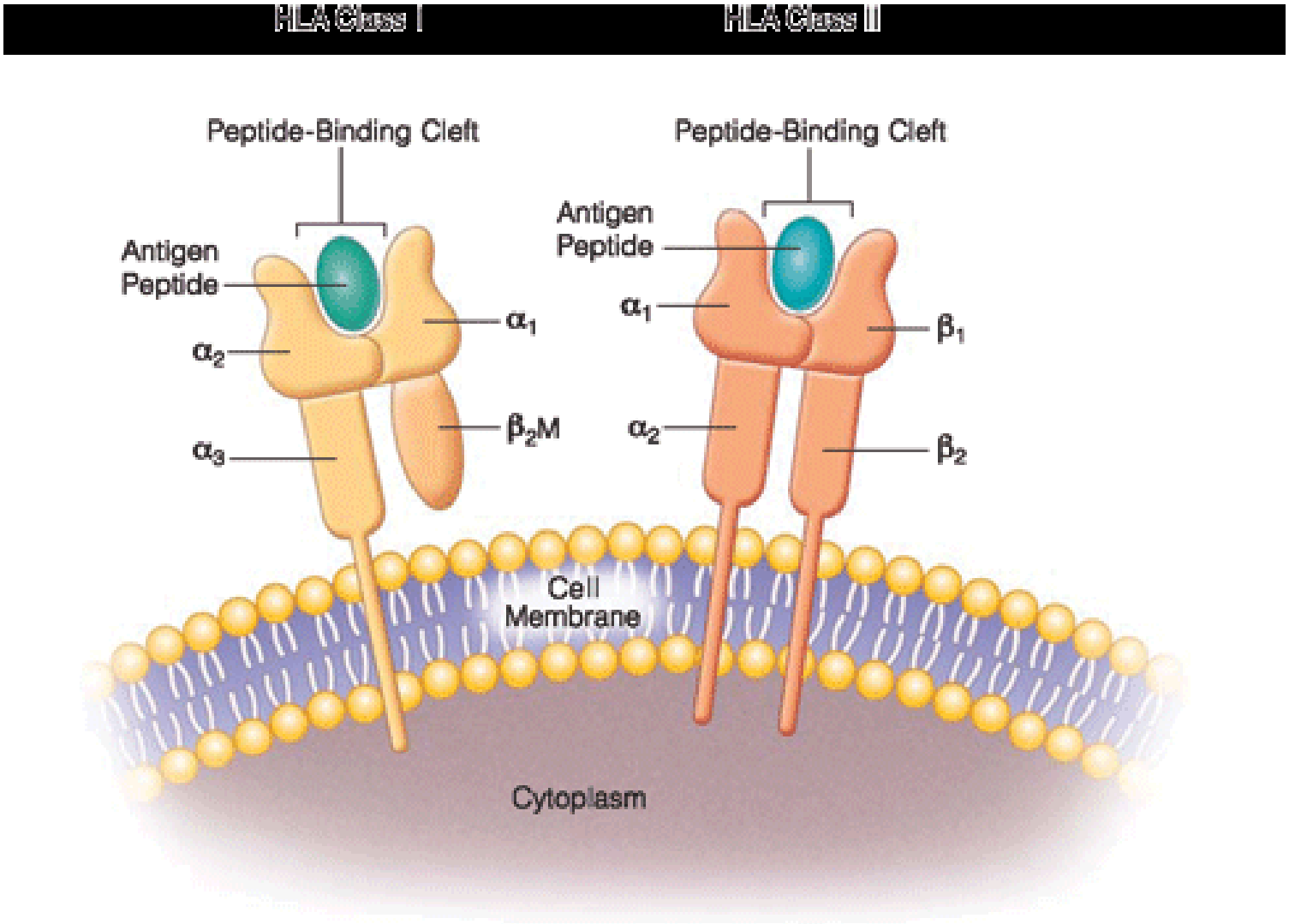

Gassman
Luisella Bolla
Flaminia Cardini
Vittorio Gassman
Una vita
da mattatore
Rai Eri

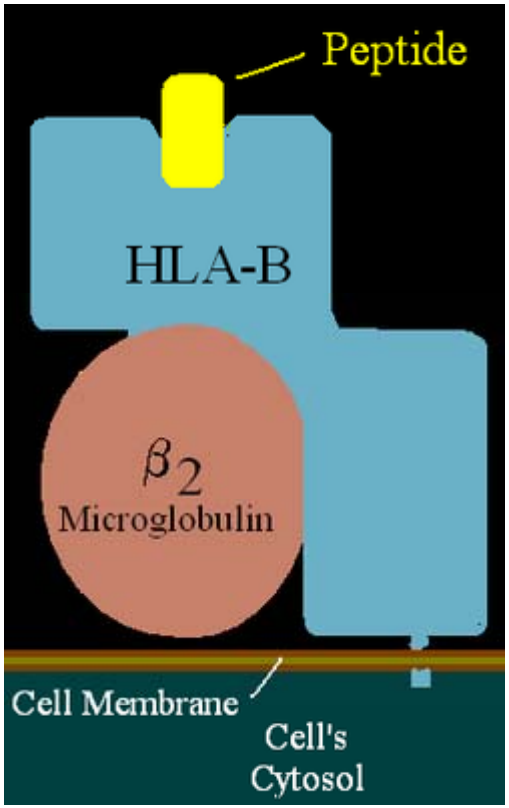
CROMOSOMAS

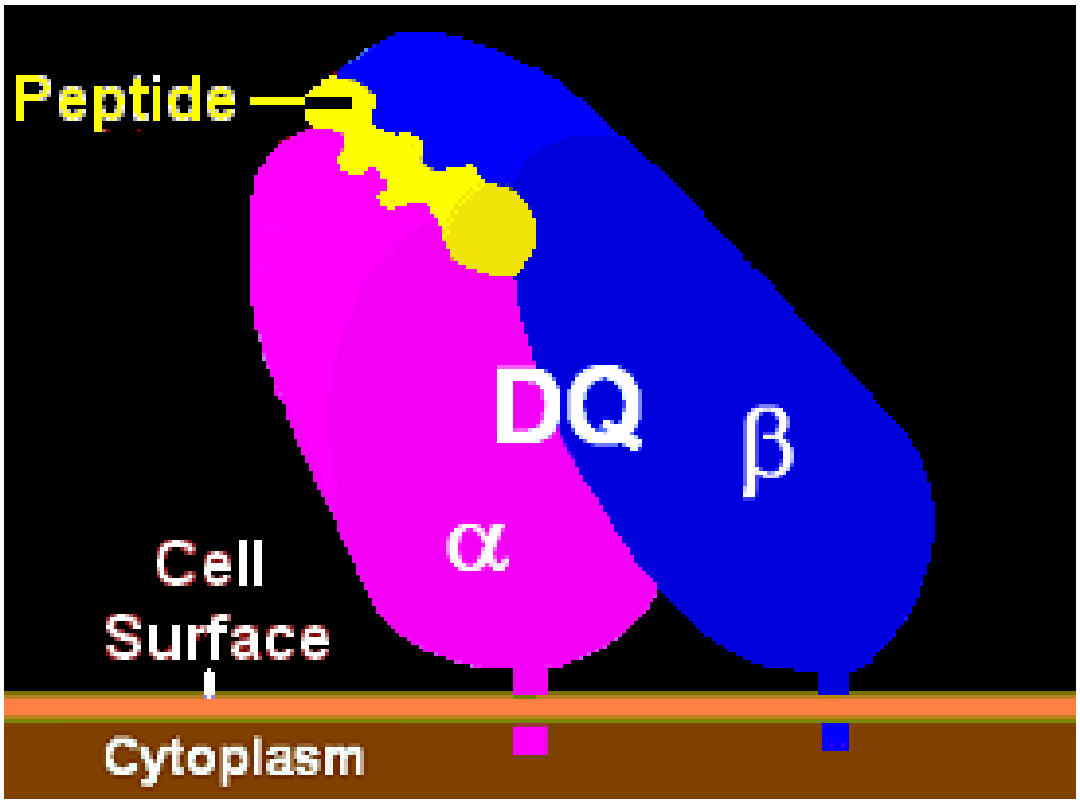



Chromosome 6
q
Centromere
p
Telomere
Telomere
6p21.31
Regions
Class II
Class III
Class I
HLA class II region loci
TAP2P
DPB2
DPB1
DPA1
DOA
DMA
DMB
PSMB9 (LMP2)
TAP1
PSMB8 (LMP7)
TAP2
DOB
DQB1
DQA1
DRB1
DRB2
DRB3
DRA
HLA class III region loci
RING, C2TB
C4B
C4A
BF
C2
HSP70 2B
HSP70 1A
HSP70 1L
LTB
TNF-α
LTA
HLA class I region loci
MICB
MICA
HLA-B
HLA-C
HLA-E
HLA-A
HLA-G
HLA-F
HFE

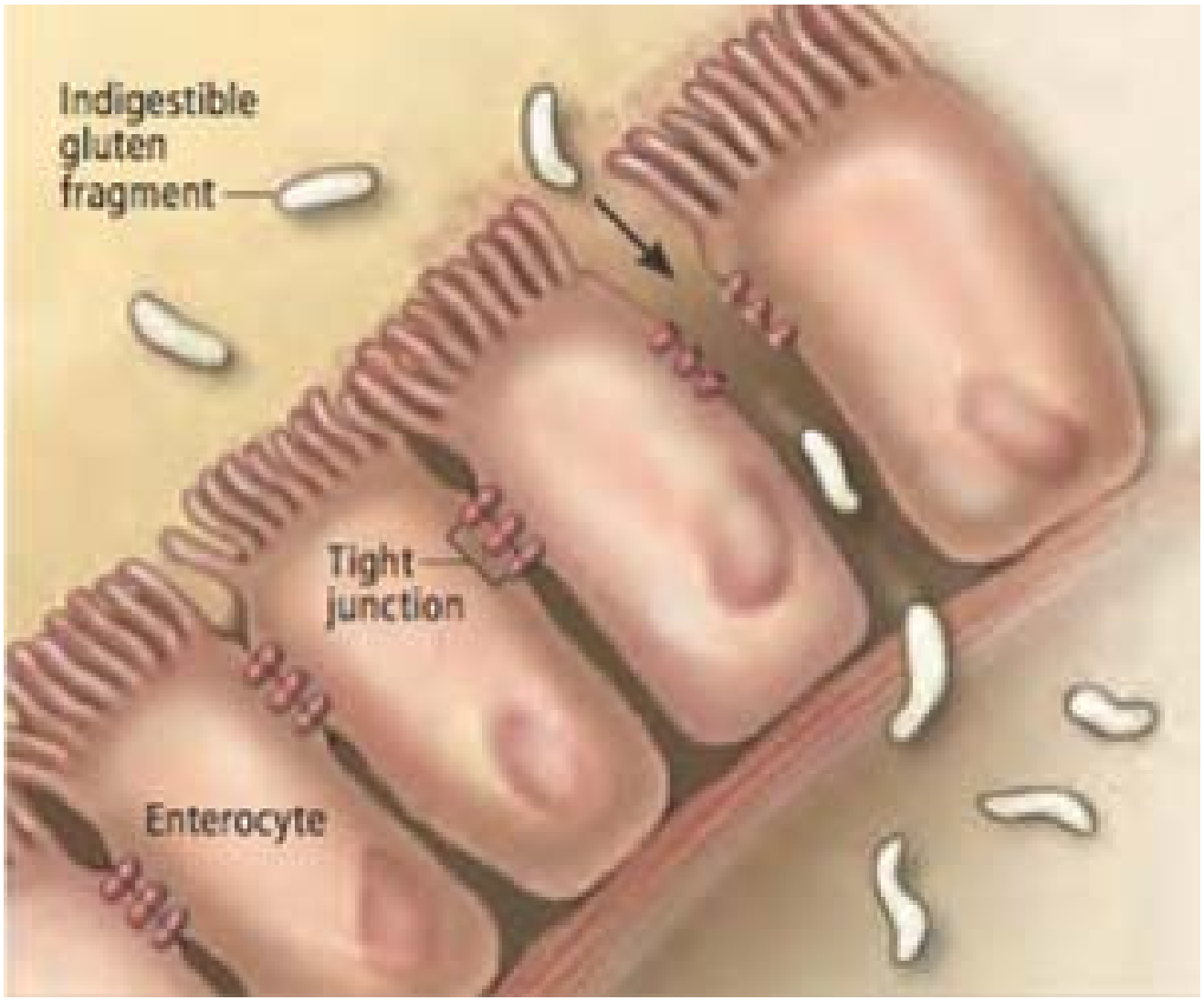

HLA-A
HLA-C
HLA-B
HLA-DR
HLA-DQ
HLA-DP
Centromere
HLA Complex
Chromosome 6

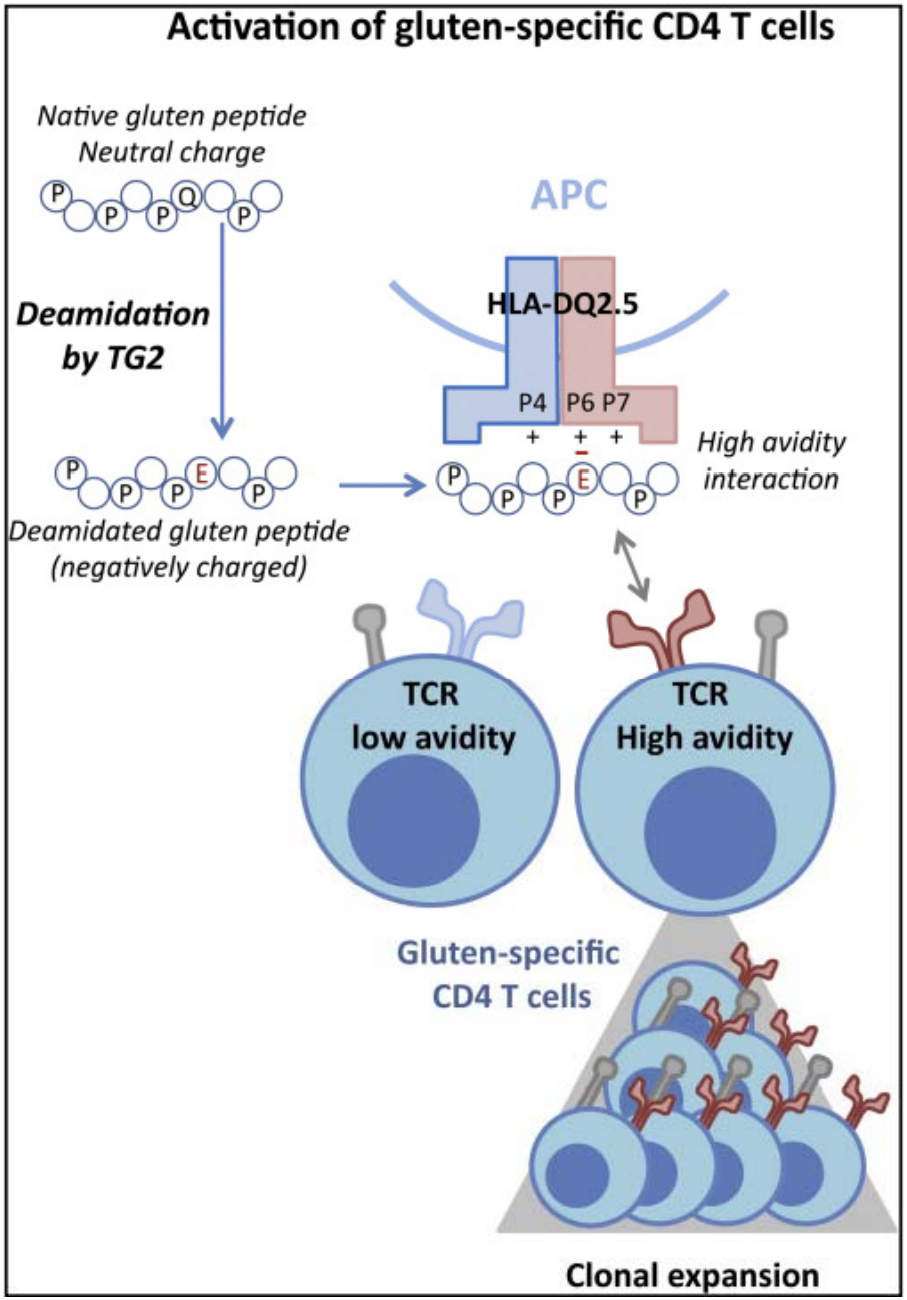

HLA Class I
HLA Class II
Peptide-Binding Cleft
Antigen Peptide
α_1
α_2
α_3
β_2M
Peptide-Binding Cleft
Antigen Peptide
α_1
β_1
α_2
β_2
Cell Membrane
Cytoplasm

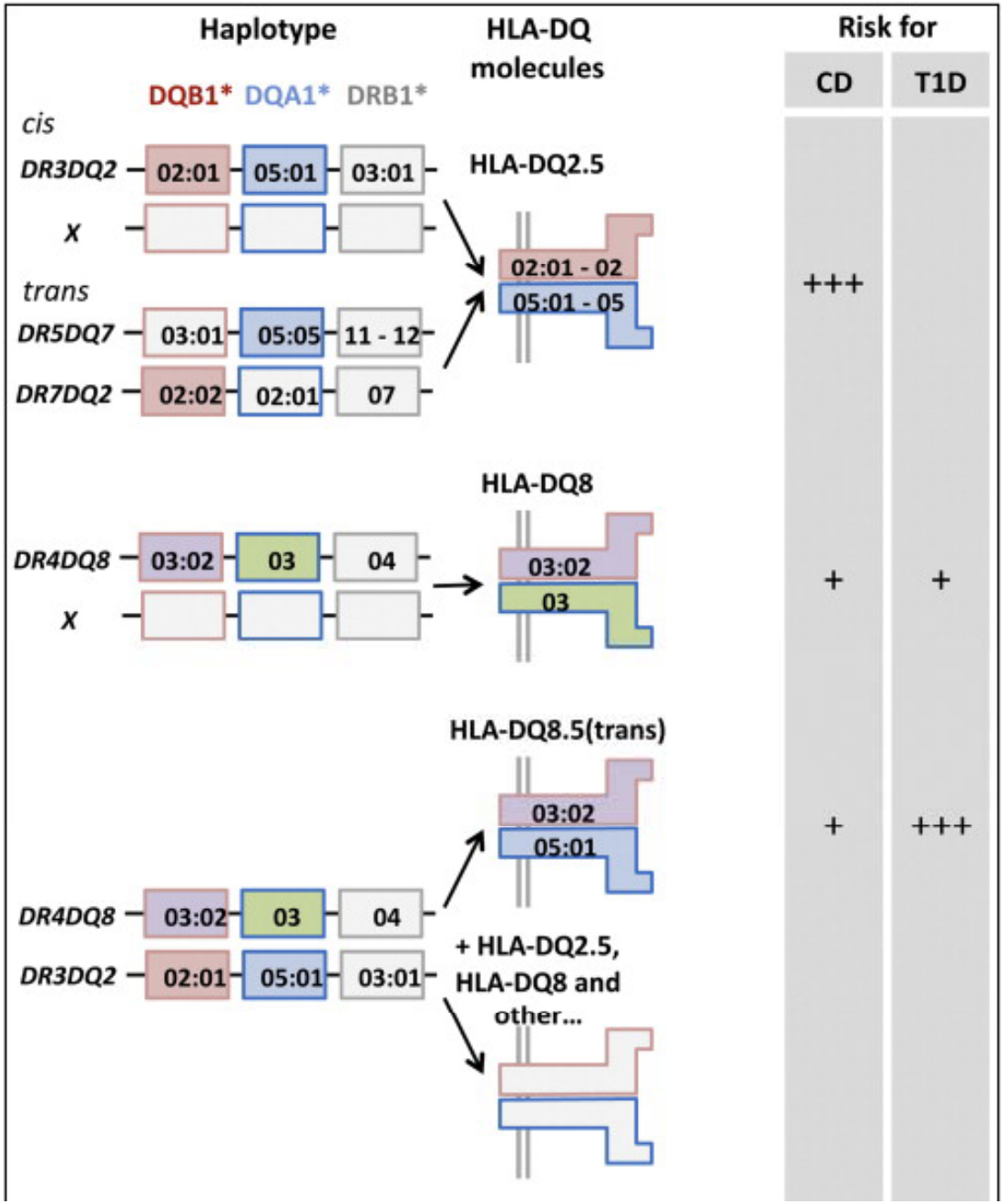

Peptide
HLA-B
β_2
Microglobulin
Cell Membrane
Cell's
Cytosol


Peptide
DQ
β
α
Cell
Surface
Cytoplasm

LOS PÉPTIDOS NO DIGERIDOS DE LA GLIADINA PENETRAN A TRAVÉS DEL EPITELIO




Activation of gluten-specific CD4 T cells
Native gluten peptide
Neutral charge
P P P Q P
Deamidation
by TG2
P P P E P
Deamidated gluten peptide
(negatively charged)
APC
HLA-DQ2.5
P4 P6 P7
+ + +
−
P P P E P
High avidity
interaction
TCR
low avidity
TCR
High avidity
Gluten-specific
CD4 T cells
Clonal expansion


Haplotype
HLA-DQ molecules
Risk for
CD
T1D
DQB1* DQA1* DRB1*
cis
DR3DQ2
02:01
05:01
03:01
HLA-DQ2.5
X
02:01 - 02
05:01 - 05
+++
trans
DR5DQ7
03:01
05:05
11 - 12
DR7DQ2
02:02
02:01
07
HLA-DQ8
DR4DQ8
03:02
03
04
03:02
03
+
+
X
HLA-DQ8.5(trans)
03:02
05:01
+
+++
DR4DQ8
03:02
03
04
DR3DQ2
02:01
05:01
03:01
+ HLA-DQ2.5, HLA-DQ8 and other…

GENES Y PROTEÍNAS

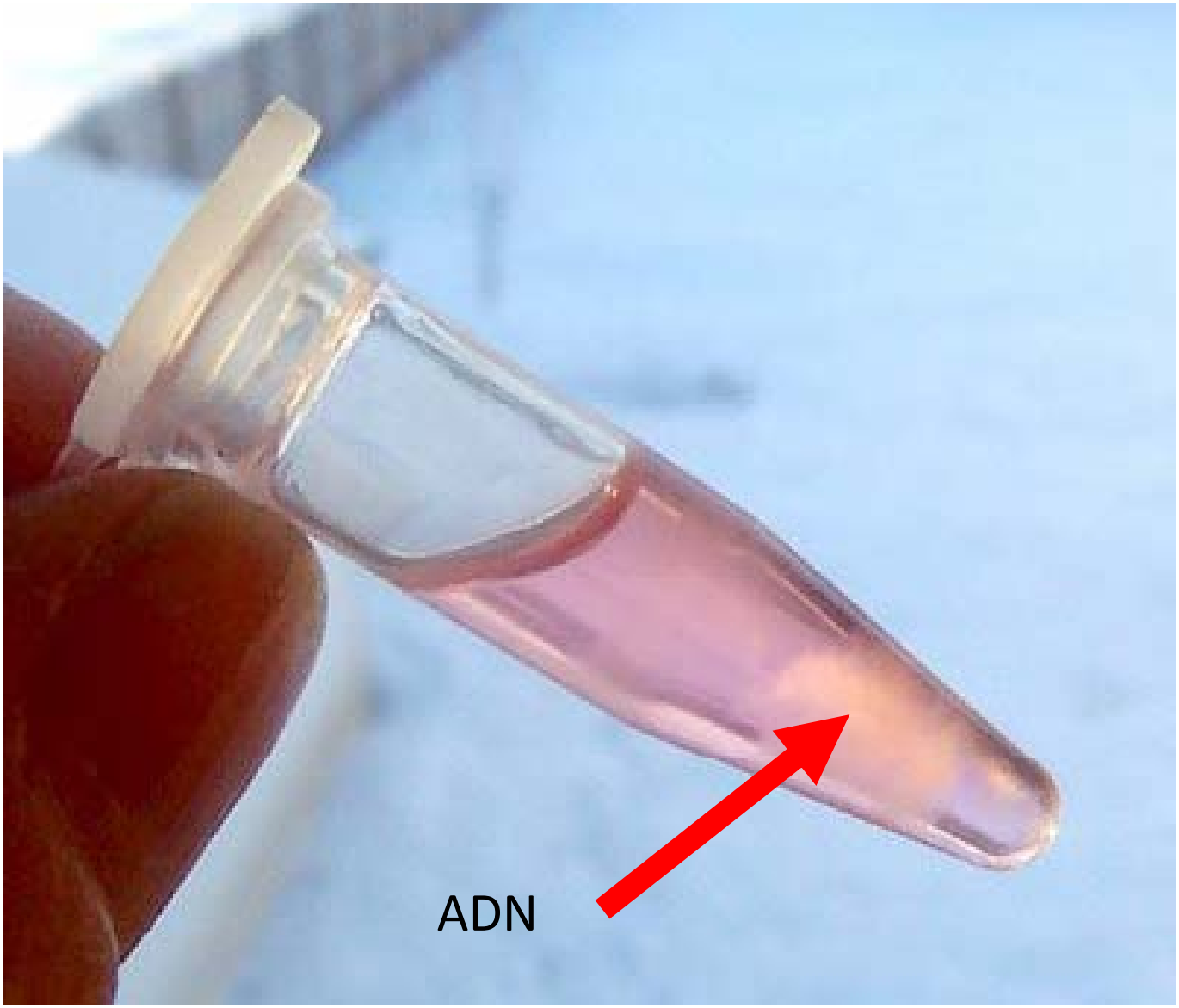
GENES

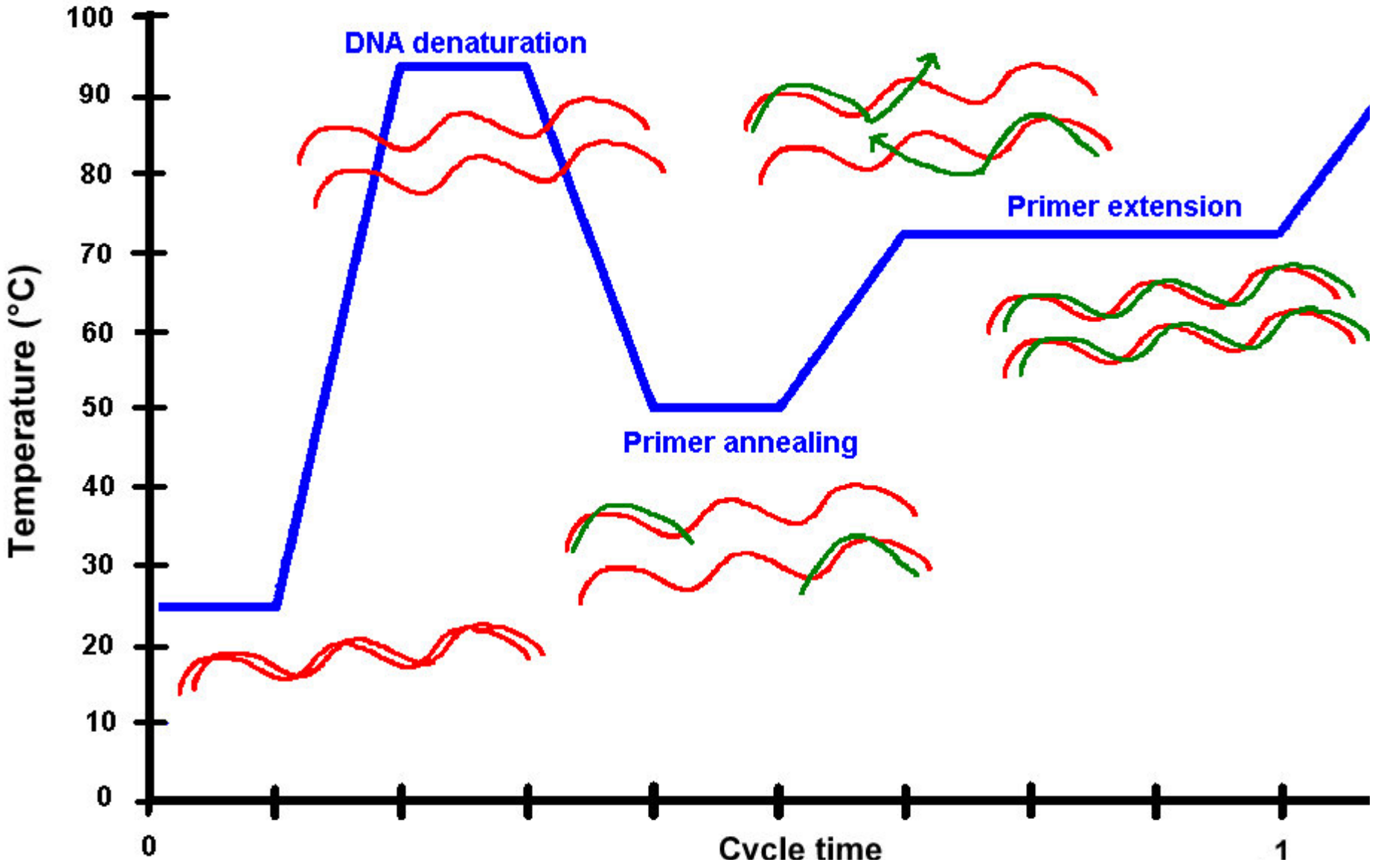
HLA-DQB1*0201

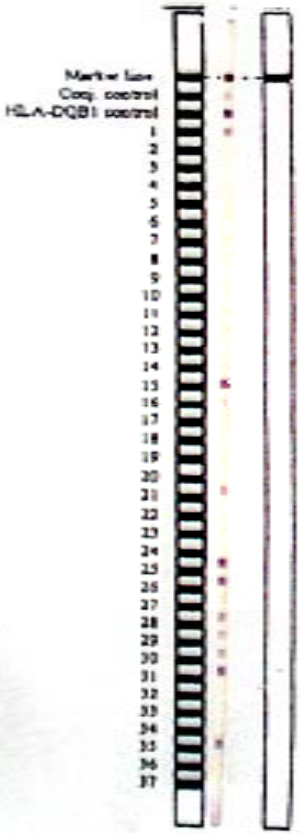
HLA-DQB1*0202

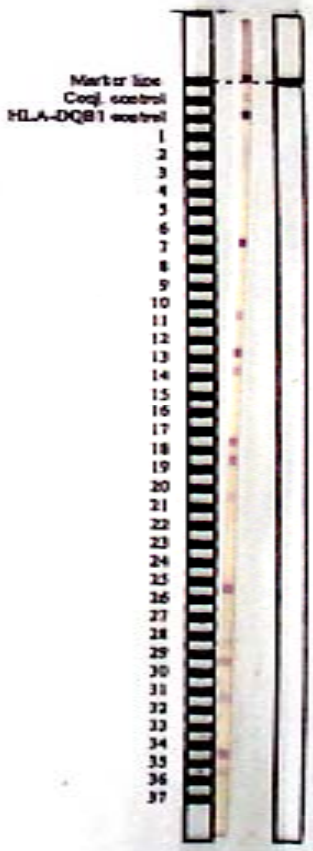
CODIFICAN PARA UN GRUPO DE PROTEÍNAS:

HLA DQ2, CON SIMILARES FUNCIONES


ADN


DNA denaturation
Primer annealing
Primer extension
Temperature (°C)
100
90
80
70
60
50
40
30
20
10
0
0
Cycle time
1

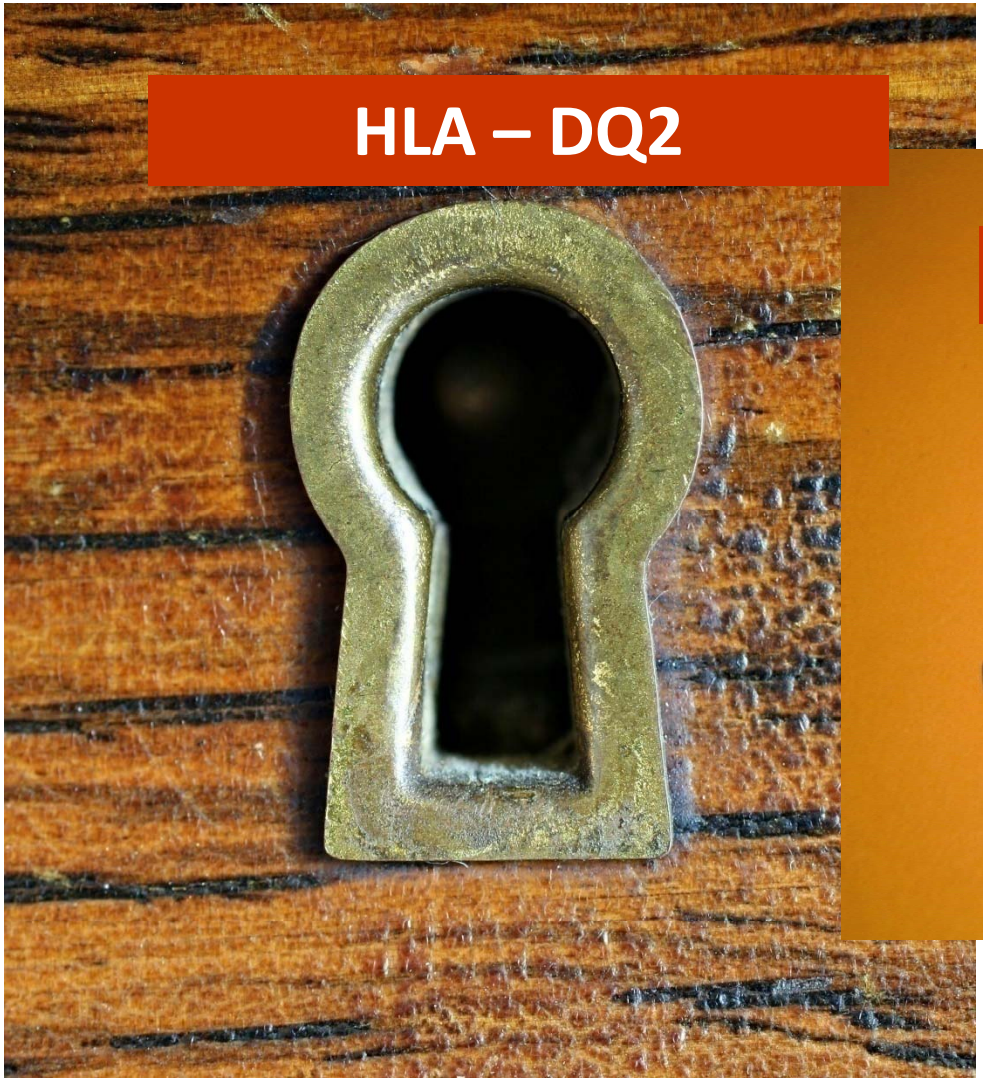




HLA-DQ2

Sondas reactivas	1, 15, (16), 17, 21, 25, 26, 29, 28, 29, 30, 31, 35		Sondas reactivas	7, 11, 13, 14, 17, 19, 21, 29, 30, 32, 35, 37	
Resultado (serologia)	DQ 7	DQ 8	Resultado (serologia)	DQ 2	DQ 6
Tipo DQB1	*03:01:01/03:01:04/03:13/03:19/03:22	*03:02:01/03:02:04	Tipo DQB1	*05:02	*06:03:01
Observaciones					

¿QUÉ ES EL DQ2?



B8, DR3 and DQ2.5 levels in Europeans (given as frequency in %)

	Reference	Population	B8 (&A30B18)	DR17 (DR3)	DRB1 301	Haplo. DR3DQ2	Estimated DQ2.5
	[7]	Sardinian	(20.0)	25.7		21.9	**22.0**
	[7]	Basque (Spain)		-15	19.2	21.9	**22.0**
	[10]	Western Irish [11]				20.8	**21.5**
	[12]	Irish[13][14]	17.7	(17.4)			**17.0**
	[7]	Swedish	16.0			15.9	**15.9**
[15]		Arratia (Spain)	(15.3)		17.3	12.0	**12.0**
	[16]	Wales	16.5		16.6	14.7	**14.7**
[17]		Dutch	12.1	(13.2)		14.4	**13.2**
	[7]	Belgium[18]	5.5	(15.7)		14.2	**14.2**
	[7]	England	13.7	(12.4)			**12.4**
	[7]	Yugoslavia	10.7	(11.5)		12.0	**12.0**
	[7]	Cornish	11.4	(11.4)		11.4	**11.4**
	[7]	Danish	8.9	(11.3)		11.3	**11.3**
[19]		Swiss	10.3	(11.6)			**10.3**
[20]		Poland[21]	10.3	(10.7)		10.7	**10.7**
[22]		Paris	(7.7)	(10.1)		9.7	**9.7**
[23]		Arab Israeli				9.6	**9.6**
[24]		Turk			9.6	9.2	**9.2**
[25]		Finn[26]	8.9	6.0		9.2	**9.0**
[27]		Russian			9.5	9.0	**9.0**
[28]		Svanetian	6.8		8.7		**8.7**
[29]		Croatian	6.4		8.3		**8.3**
[30]		Bulgarian	18.2		8.2		**8.0**
[31]		Greek	3.6		6.5	6.3	**6.3**
[32]		NE. Turk	3.4	5.6			**5.4**
[33]		Macedonian	6.8		6.8	5.0	**5.0**
[34]		non-Ashk Jew.			7.8	4.4	**4.4**

DQ Serotype	DQ cis-isoform	DQ Subtype	DQ A1	B1	Freq %[1]
	α5-β2	2.5	05:01*	02:01	13. 16
DQ2	α2-β2	2.2	02:01	02:02	11. 8
	α3-β2	2.3	03:02*	02:02	0. 8
DQ4	α3-β4	4.3	03:01	04:02	0. 3
			03:02*	04:02	0. 11
	α4-β4	4.4	04:01	04:02	2. 26
DQ5	α1-β5.1	5.1	01:01	05:01	10. 85
			01:02	05:01	0. 3
			01:03	05:01	0. 3
			01:04	05:01	0. 71
	α1-β5.2	5.2	01:02	05:02	1. 20
			01:03	05:02	0. 5
	α1-β5.3	5.3	01:04	05:03	2. 3
	α1-β5.4	5.4	01:02	05:04	0. 8
DQ6	α1-β6.1	6.1	01:03	06:01	0. 66
	α1-β6.2	6.2	01:02	06:02	14. 27
			01:03	06:02	0. 3
			01:04	06:02	0. 3
	α1-β6.3	6.3	01:02	06:03	0. 27
			01:03	06:03	5. 66
	α1-β6.4	6.4	01:02	06:04	3. 40
	α1-β6.9	6.9	01:02	06:09	0. 71
DQ7	α2-β7	7.2	02:01	03:01	0. 5
	α3-β7	7.3	03:01	03:01	0. 16
			03:03*	03:01	6. 45
			03:01	03:04	0. 9
			03:02*	03:04	0. 9
	α4-β7	7.4	04:01	03:01	0. 3
	α5-β7	7.5	05:05*	03:01	11. 6
	α6-β7	7.6	06:01	03:01	0. 11
DQ8	α3-β8	8.1	03:01	03:02	9. 62
			03:02*	03:02	0. 93
DQ9	α2-β9	9.2	02:01	03:03	3. 66
	α3-β9	9.3	03:02	03:03	0. 79

Reference	DQA1	DQB1	Estimated	
	Population	*03	*0302	DQ8.1
[38]	Nenets	40.9	20.9	20.0
	(N. Russia)			
[38]	Murmansk S	38.3	18.5	17.2
	(Russia)			
[39]	Gaza		17.6	17.0
	(Israel/Palestine)			
[40]	Arkhange Po	22.6	17.1	16.4
	(Russia)			
[41]	Swedish	24.2	18.7	16.1
[41]	Caucasian	23.7	16.4	15.9
	(England)			
[41]	Finland		15.7	15.2
[42]	France's CEP	21.3	14.5	13.5
[41]	Dane	20.9	13.2	13.2
[43]	Dutch		11.2	11.0
	Irish			10.6
[44]	NW Slavic	16.0	11.0	10.5
	(Russia)			
[45]	German		10.5	9.9
[46]	Russian		8.9	7.2
[47]	Cantabarian	19.3	8.4	7.0
	(Spain)			
[45]	Spanish		8.9	6.5
[45]	Sardinian		4.9	4.9
[45]	Italian		4.6	4.5
[48]	United Arab Emirates		0.83	0.8
[49]	Jordon	24.1	17.9	17.9
Africa				
[45]	!kung		36.7	36.7
[45]	Khoi		14.9	13.9
[50]	Oromo	17.5	9.0	9.0
[51]	Morocco	17.2	8.9	8.6
[52]	Tunisia	10.31	10.0	8.0
[50]	Amhara	11.2	5.6	5.6
[53]	Aka pygmies		3.2	3.0
[45]	Negroid		3.1	2.7
	(N. Africa)			
[54]	Cameron	11.5	1.5	1.2
[53]	Bantu Congo		0.6	0.5
[55]	Gabonese	7.5		0.5
[56]	Bubi	17.5	0.0	0.0

DQA1*03:DQB1*0302 haplotype frequencies in the Americas

(given as frequency in %)

Reference	Population	DQA1 *03	DQB1 *0302	Estimated DQ8.1
[4]	Lacandon Mayan (Mexico)	79.0	77.9	**77.9**
[5]	Perija-Yucpa (Venezuela)	74.0	75.0	**74.9**
[6]	Mayan (Guatemala)		48.1	**47.6**
[7]	Mazatecans (Mexico)	48.5	48.5	**47.5**
[8]	Lamas (Peru)		45.2	**44.7**
[9]	Dakota Sioux (S. Dakota)	52.1	45.0	**44.5**
[10]	Mixtec (Oaxaca, Mexico)	40.0	35.9	**35.4**
[11]	Lakota Sioux (S. Dakota)		25.7	**25.5**
[12]	Terena (Brazil)		17.5	**17.0**
[13]	Cauc., San Antonio (USA)		11.7	**11.7**
[14]	Caucasian (USA)	18.5	10.5	**10.5**
[15]	African American (SE. USA)		4.9	**4.5**
[16]	Tlinglet (Alaska, USA)	14.0	8.5	**8.5**
[17]	Eskimo (Alaska, USA)		3.8	**3.8**
[18]	Canoncito Navajo (NM, USA)	6.3	3.5	**3.5**
[19]	Eskimo (E. Greenland)	0.0	0.0	**0.0**

NOSOTROS Y LA ENFERMEDAD CELIACA

- DESDE DICIEMBRE 2005
- HASTA
- DICIEMBRE 2014
- 6750 ESTUDIOS GENÉTICOS
- 198 CELÍACOS

ALELOS DQ DE RELEVANCIA EN LA ENFERMEDAD CELÍACA

- **DQ2**
  - –DQA1*0501/DQB1*0201
  - – DQA1*0505/DQB1*0202
- **DQ8**
  - – DQA1*0301-*02-*03/DQB1*0302
- **DQ7 ? RELEVANCIA COMPLEMENTARIA?**
  - – **DQA1*0505/DQB1*0301**

ALELOS DQ SIN RELEVANCIA EN LA ENFERMEDAD CELÍACA

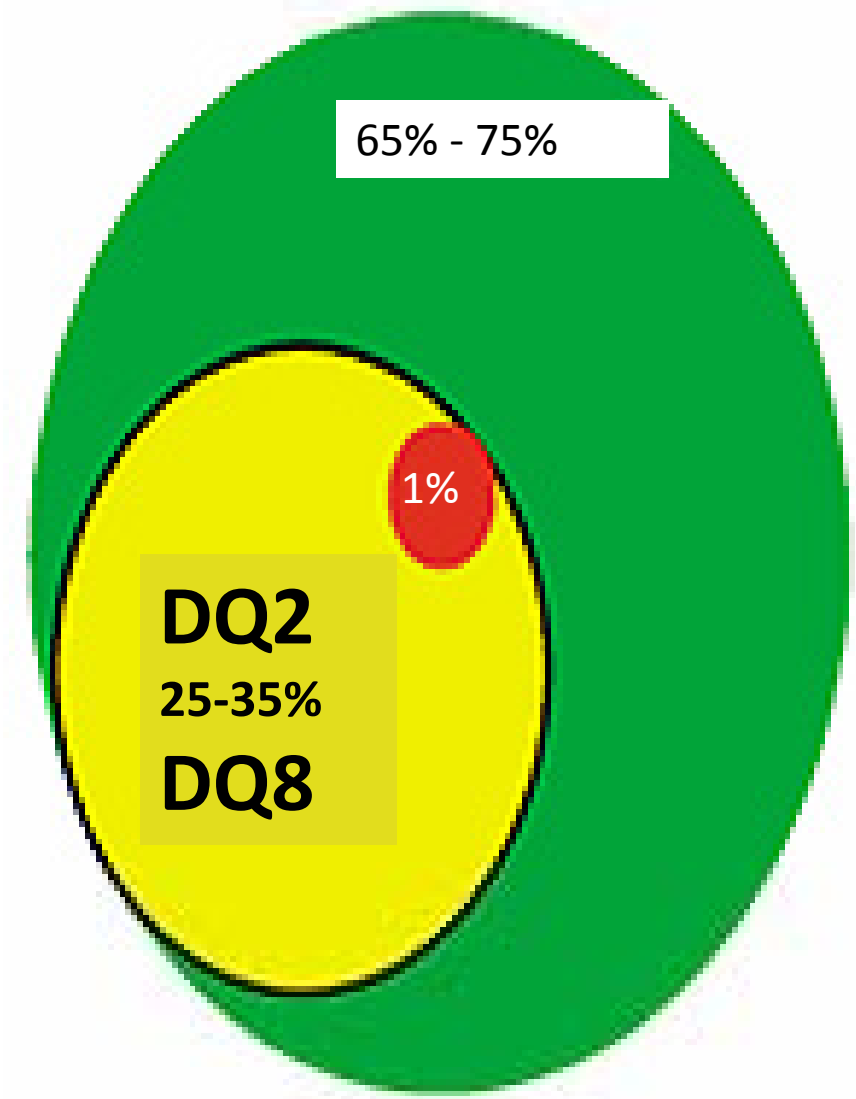
- DQ 4
- DQ 5
- DQ 6
- DQ 9

DISTRIBUCIÓN ALÉLICA EN CELÍACOS

- EL ALELO MÁS FRECUENTE EN NUESTRA POBLACIÓN CELÍACA: DQ2 : 90%
- EL RESTO SON DQ8 : 10 %

- DE TODOS LOS DQ2:
- DQB1*0201 : 89%
- DQB1*0202 : 11%

- MENOS DEL 1% DE LOS CELÍACOS PORTAN EL HAPLOTIPO DQB1*0202 ACOMPAÑADO POR HAPLOTIPOS NO RELEVANTES.
- **EN EL RESTO ESTÁ ACOMPAÑADO POR LOS HAPLOTIPOS**:
  - DQ8: 50%
  - DQ2 (DQB1*0202 HOMOCIGOTA): 40%
  - DQ7: 5%



POBLACION GENERAL

POBLACIÓN DQ2 / DQ8

ENFERMEDAD CELIACA

PARA PODER DESARROLLAR LA ENFERMEDAD CELÍACA

ES NECESARIO POSEER PROTEÍNAS DEL SISTEMA HLA

DQ2/DQ8.

NO TODOS LOS QUE LA POSEEN SERÁN CELÍACOS.

LOS QUE **NO** LA POSEEN

ES MUY POCO PROBABLE

QUE SEAN CELÍACOS ALGÚN DÍA,

¡PERO NO IMPOSIBLE !

MUCHAS GRACIAS