immungenetika

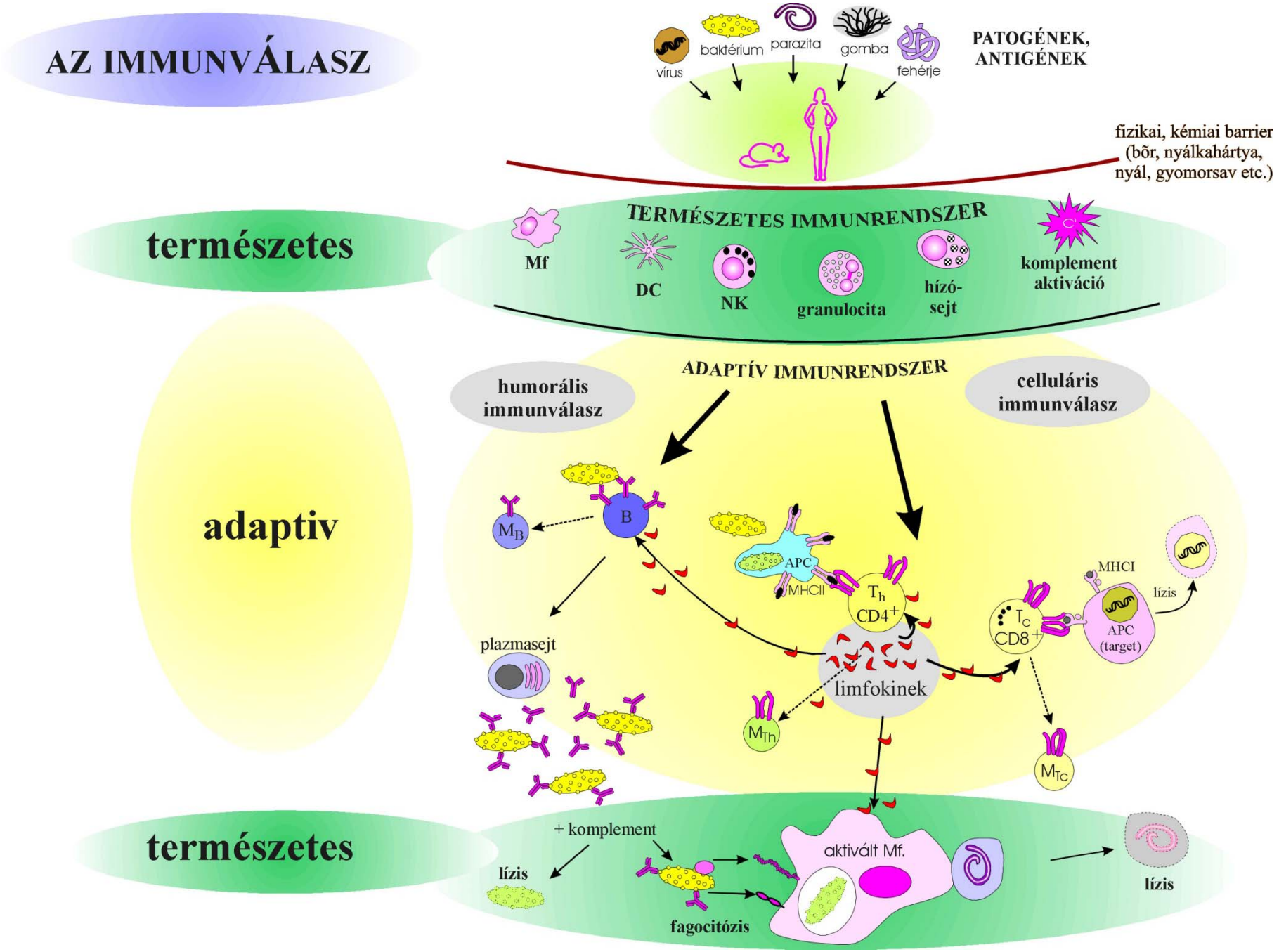
Az immunrendszer génjei – szerepük egészségben és betegségben

2014 május 12

Prechl József

- Immungének – immun és más betegségekben
- Polimorfizmus az immunrendszer génjeiben
  - MHC / HLA
  - KIR
  - BCR, TCR
- adatbázisok

Mi is az az immunológia...


AZ IMMUNVÁLASZ
vírus
baktérium
parazita
gomba
fehérje
PATOGÉNEK, ANTIGÉNEK
fizikai, kémiai barrier (bõr, nyálkahártya, nyál, gyomorsav etc.)
természetes
TERMÉSZETES IMMUNRENDSZER
Mf
DC
NK
granulocita
hízó-sejt
komplement aktiváció
adaptiv
ADAPTÍV IMMUNRENDSZER
humorális immunválasz
celluláris immunválasz
B
MB
APC
MHCII
Th CD4+
MHCI
Tc CD8+
APC (target)
lízis
plazmasejt
limfokinek
MTh
MTc
természetes
+ komplement
lízis
fagocitózis
aktivált Mf.
lízis

Honnan örököltük

ech/article-2030140/Neanderthal-sex-boosted-health-human-race-improving-immune-systems-disease.html

HerMelin iSL Német feladatok

BREAKING NEWS: British police are | BREAKING NEWS: Comedian Freddie | 'I'm White Dee-sus, turning lemonade | Widow is gang-raped as | Skirts are 'too short' and blouses 'too

Neanderthal sex 'boosted health of human race' by improving our immune systems against disease

- **Scientists believe genes that help us fight viruses were inherited from Neanderthals**

By STEPHANIE DARRALL
UPDATED: 07:09 GMT, 26 August 2011

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Virus-fighting genes inherited from different ancient human sub-species have had a positive effect on our fitness, according to U.S. researchers .

Cross- breeding between ancestors of modern humans and their extinct close relatives passed down specific genes which can still be found in our DNA.

Improvements in the Homo sapiens' immune system may also have been inherited from the Denisovans - a now-vanished human sub-

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Biological Process	Genes
Immunity and defense	417
T-cell-mediated immunity	82
Chemosensory perception	45
Biological process unclassified	3,069
Olfaction	28
Gametogenesis	51
Natural killer-cell-mediated immunity	30
Spermatogenesis and motility	20
Inhibition of apoptosis	40
Interferon-mediated immunity	23
Sensory perception	133
B-cell- and antibody-mediated immunity	57

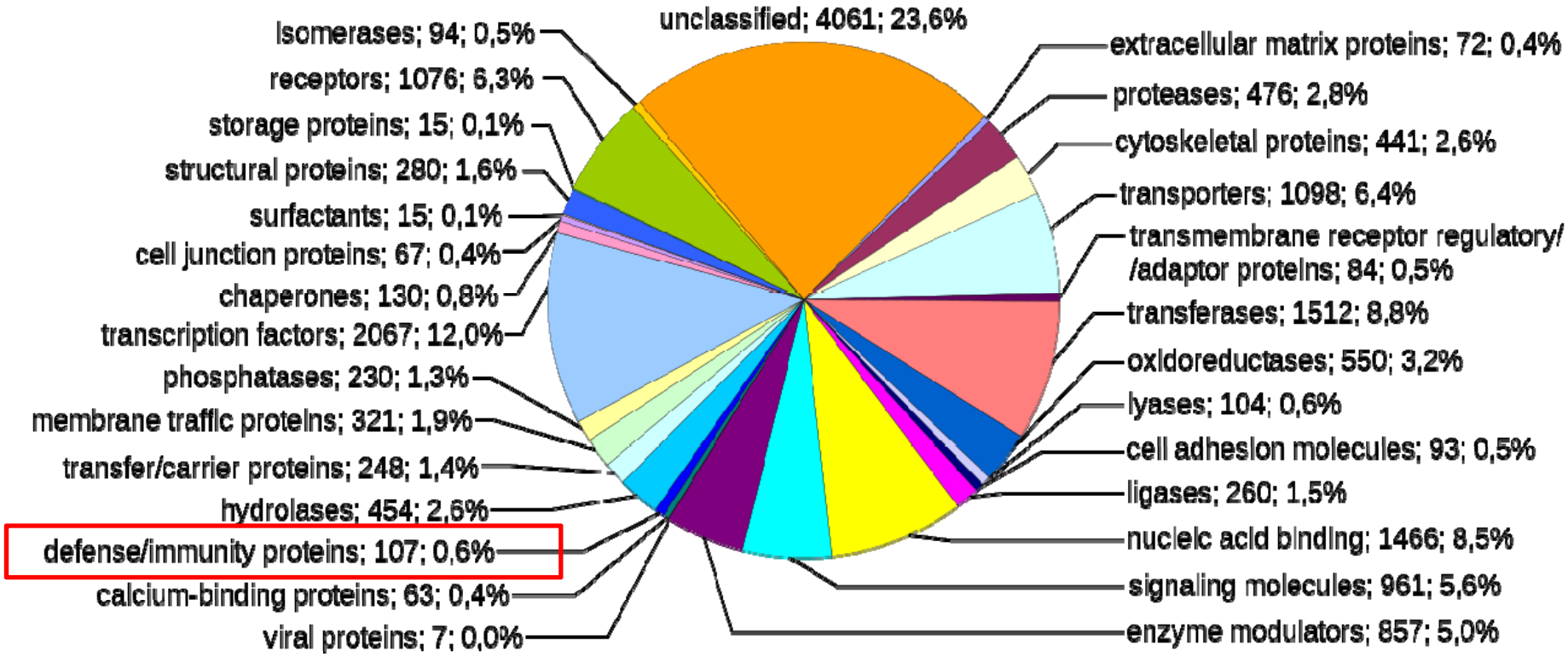
A Scan for Positively Selected Genes in the Genomes of Humans and Chimpanzees

Rasmus Nielsen , Carlos Bustamante, Andrew G Clark, Stephen Glanowski, Timothy B Sackton, Melissa J Hubisz, Adi Fledel-Alon, David M Tanenbaum, Daniel Civello, Thomas J White, John J. Sninsky, Mark D Adams, Michele Cargill

Published: PLoS Biology May 03, 2005

DOI: 10.1371/journal.pbio.0030170

Az emberi gének csoportosítása funkció szerint



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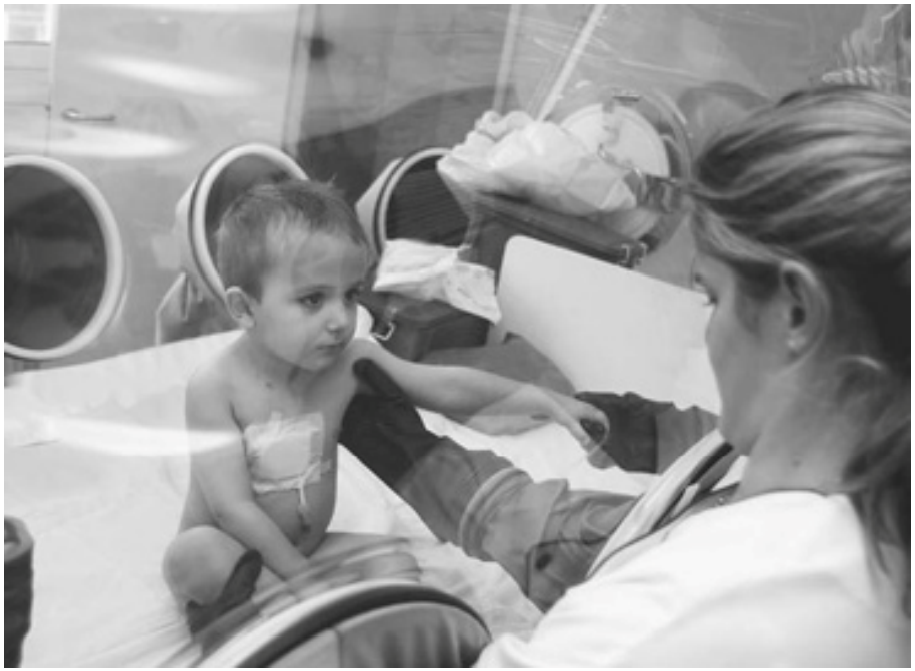
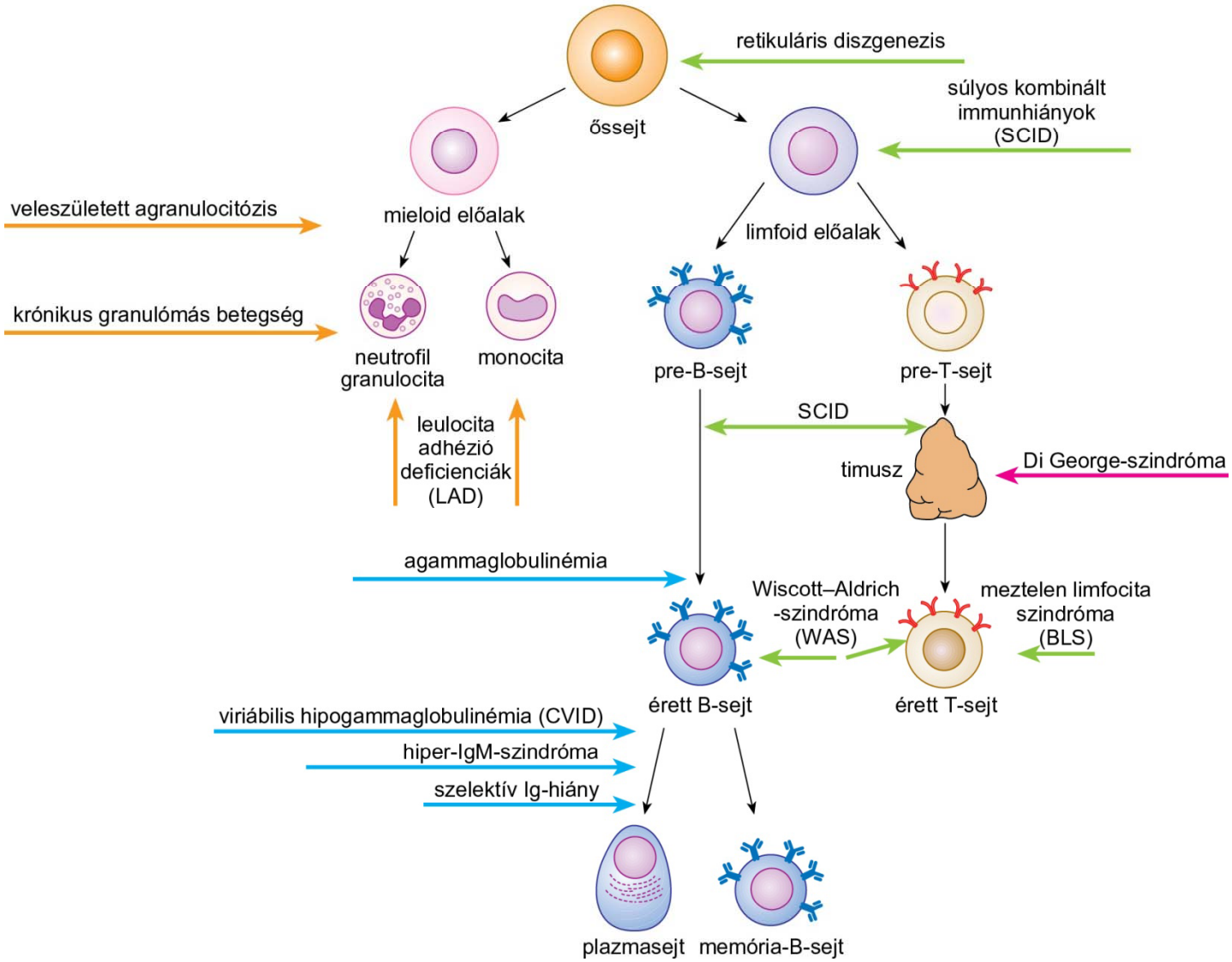
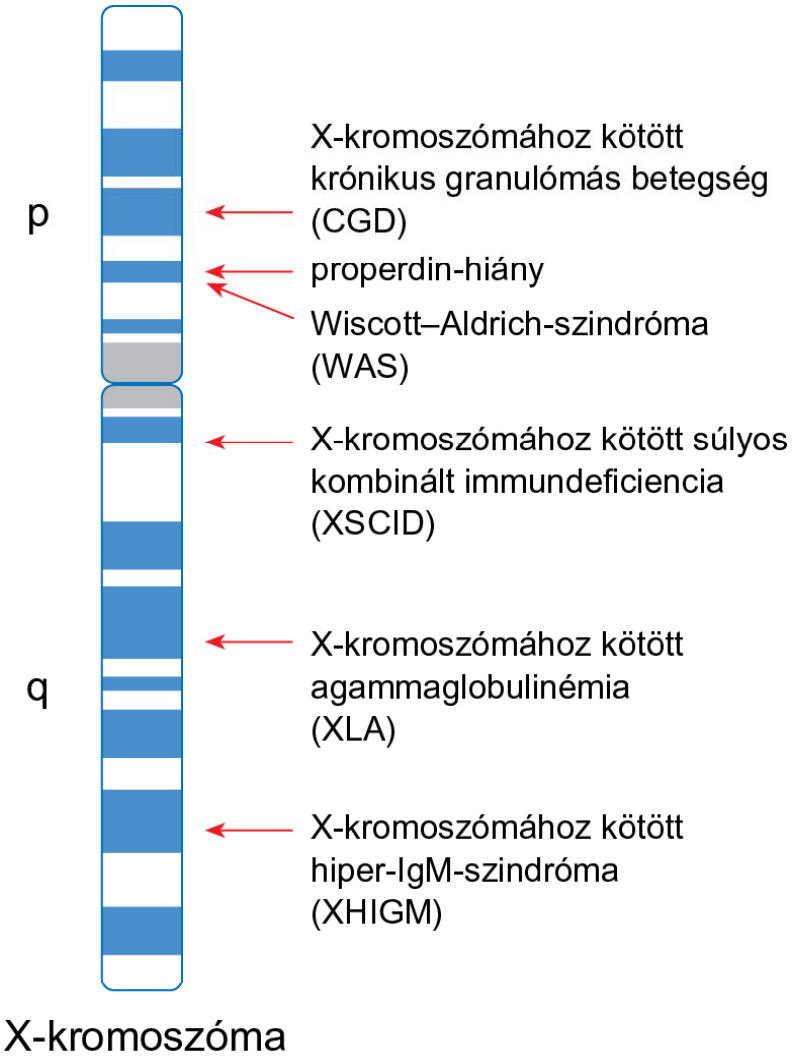
Bubble baby



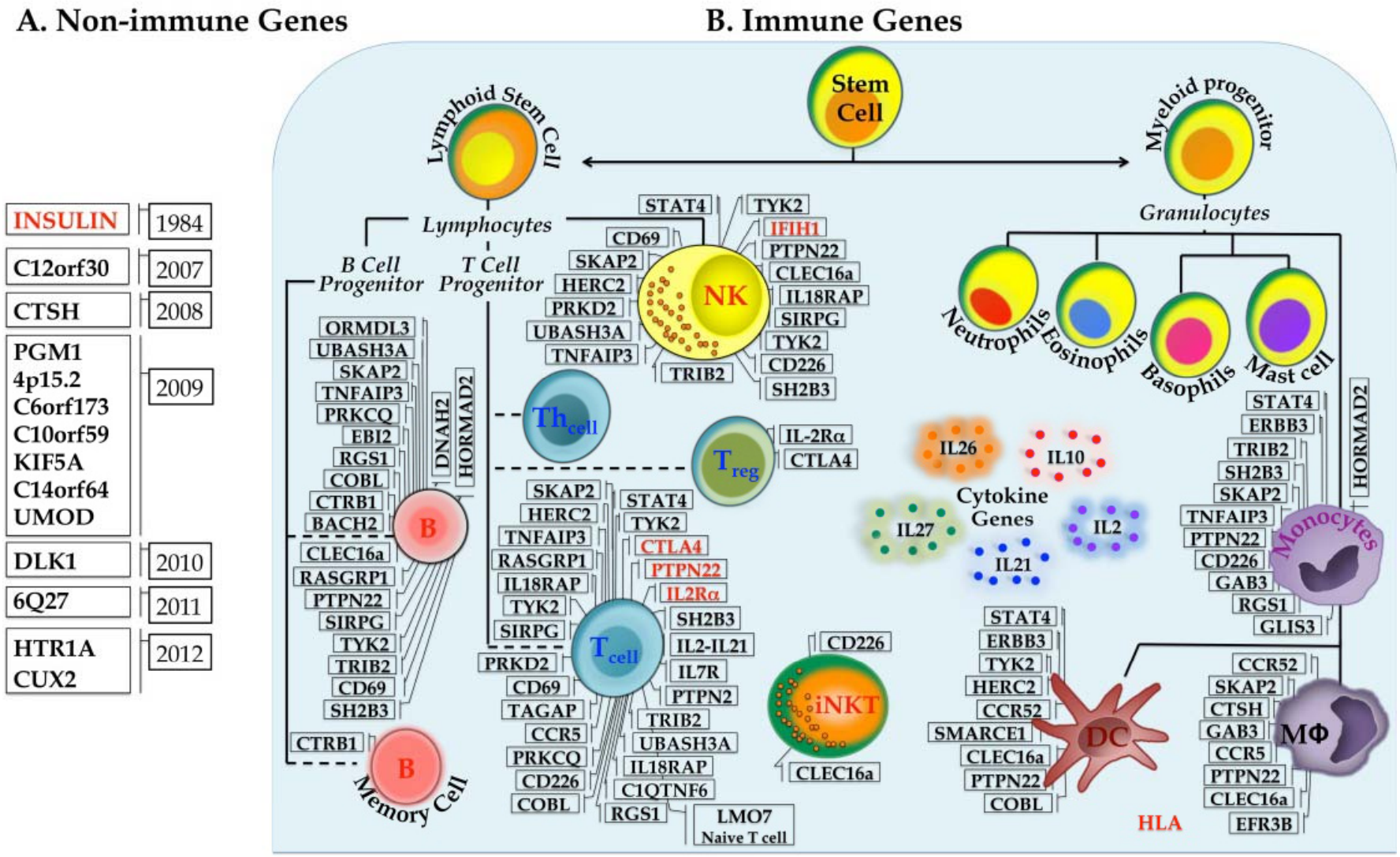
21.1. ábra Öröklött immunhiányos állapotok



21.2. ábra Az X-kromoszómához kötött immunhiányos állapotok



Type 1 diabetes – hajlamosító gének



Genes Involved in Type 1 Diabetes

KIR - skizofrénia

Table Evidence that supports the association between immune system genes and schizophrenia

Study	Gene/gene product	Comments
Stefansson[18]	MHC, *TCF4*	Association with markers spanning the MHC region on 6p21.3-22.1 and a marker in intron 4 of *TCF4*
Li[19]	MHC, *TCF4*	Common variants associated in the Han Chinese population
Lencz[23]	*CSF2RA, IL3RA*	Evidence from genome-wide association, followed by gene sequencing in an independent population
Sun[24,25]	*IL3RA*	Association studies in the Han Chinese population
Paul-Samojedny[26]	*IFNG*	SNP associated with increased risk of schizophrenia in males
Shirts[27]	IL-18 pathway	Genes in the IL-18 pathway and HSV seropositivity are associated with schizophrenia
Ozbey[28]	*IL12* p40	Association of gene promoter variants in a Turkish population
Ozbey[29]	*IL10*	SNP in the *IL10* promoter is associated with schizophrenia
Saviouk[30]	*TNF*	Association of a haplotype in the promoter region of *TNF*
Xu[31]	*IL1* genes: *IL1A, IL1B, IL1RA*	Convergent evidence of association of *IL1* gene complex
Hänninen[32]	*NRG1, IL1B*	Synergistic interaction between *NRG1* and *IL1B* increases risk of schizophrenia
Marballi[34]	*NRG1*	A *NRG1* transmembrane mutation is associated with increased levels of proinflammatory cytokines

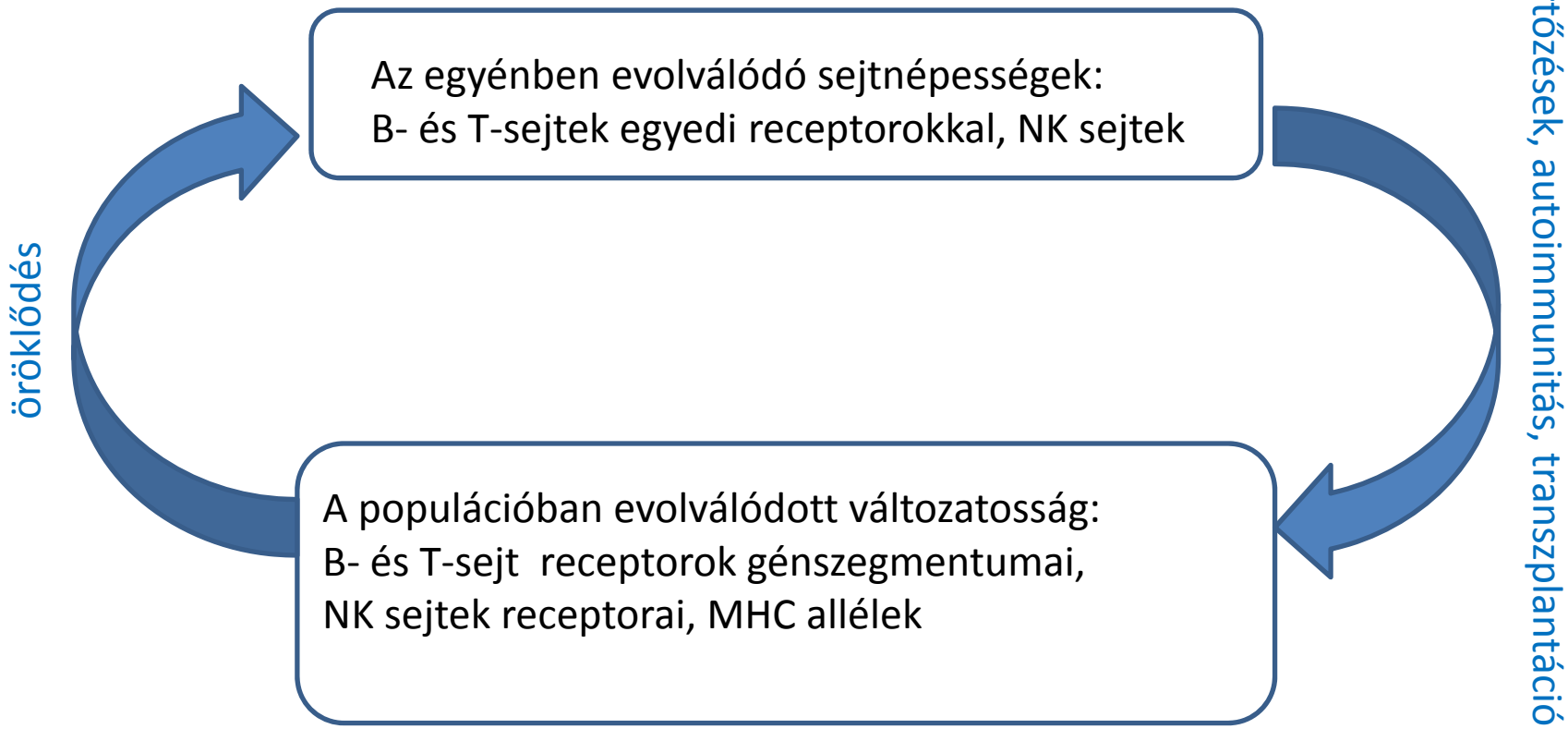
MHC, major histocompatibility complex; *TCF4*, transcription factor 4; *CSF2RA*, colony-stimulating factor 2 receptor α; *IL3RA*, interleukin-3 receptor α; *IFNG*, interferon γ; SNP, single-nucleotide polymorphism; IL-18, interleukin-18; HSV, herpes simplex virus; *IL12* p40, interleukin-12 p40; *IL10*, interleukin-10; *TNF*, tumor necrosis factor; *IL1*, interleukin-1; *IL1A*, interleukin-1α; *IL1B*, interleukin-1β; *IL1RA*, interleukin-1 receptor α; *NRG1*, neuregulin 1.

Hosszú élet

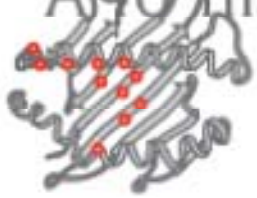
Gene names or genetic defects (symbol)	Protein function	Phenotype	Populations/ study locations	References
Apolipoprotein E (*APOE*)	Ligand for the LDL receptor	Consistently associated with survival and longevity	Multiple	55
Apolipoprotein C3 (*APOC3*)	Major component of VLDL and chylomicron remnants	Associated with cardiovascular risk factors and longevity in one study	Ashkenazi Jews	57
Microsomal triglyceride transfer protein (*MTTP*)	Transport of triglycerides, cholesteryl esters and phospholipids	Inconsistent linkage and association results for longevity	United States France Germany Denmark	44,104 45 58 59
Cholesteryl ester transfer protein (*CETP*)	Transfer of cholesteryl esters	Inconsistent association results for longevity	Ashkenazi Jews Italy	105 106
Angiotensin I-converting enzyme (*ACE*)	Hydrolyses angiotensin I to angiotensin II	Inconsistent association results for longevity	Germany Denmark	61 62,63
Insulin-like growth factor 1 receptor (*IGF1R*)	Energy-status signalling	One study shows association with longevity	Italy	65
Growth hormone 1 (*GH1*)	Growth hormone (insulin signalling component)	One study shows association with survival at age 85+	Holland	66
Catalase (*CAT*)	Catalyses the decomposition of hydrogen peroxide	No association with survival	Denmark	107
Superoxide dismutases 1 and 2 (*SOD1* and *SOD2*)	Catalyses the breakdown of superoxide radicals	One study shows association with longevity	Italy	99
Heat shock proteins (*HSPA1A* and *HSPA1L*)	Protein folding and transport; immune system functions	Various associations but not replicated	Italy Ireland	108 109
Paraoxonase 1 (*PON1*)	Preserves HDL function and protects LDL from oxidative modification	Inconsistent association results for longevity	Denmark Italy and Ireland	110 111
Interleukin 6 (*IL6*)	An immunoregulatory cytokine	Inconsistent, but longitudinal studies show association with longevity	Denmark Finland	79 80
Hereditary haemochromatosis (*HFE*)	Regulation of iron absorption in the intestine	Inconsistent association results for longevity	Denmark France Italy	67 69 112
Methylenetetrahydrofolate reductase (*MTHFR*)	Re-methylation of homocysteine to methionine	Inconsistent association results for longevity	Denmark Switzerland Multiple Ashkenazi Jews	63 113 114 115
Sirtuin 3 (*SIRT3*)	Unknown	Various associations but not replicated	Italy	116,117
Tumour protein p53 (*TP53*)	Tumour suppressor gene	Inconsistent association results for longevity	Holland Italy	66 118
Transforming grow factor β1 (*TGFB1*)	Regulation of proliferation and differentiation; various other functions	One study shows association with longevity	Italy	119
Klotho (KL)	A type-1 membrane protein that is related to β-glucosidases; function is still unclear	Heterozygous survival advantage in two populations	Czech Republic Ashkenazi Jews	120 121
Werner syndrome (*WRN*)	Maintenance and repair of DNA; DNA replication	One study shows association with age but not replicated	Mexico and Finland Holland	122 90
mutL homologue 1 (*MLH1*)	DNA mismatch repair enzyme	One study shows association with age	Korea	123
Mitochondrial mutations (Mt5178A, Mt8414T, Mt3010A and J haplotype)	Mitochondrial energy production	Single studies or inconsistent association results for longevity	Japan Italy	81 82–84

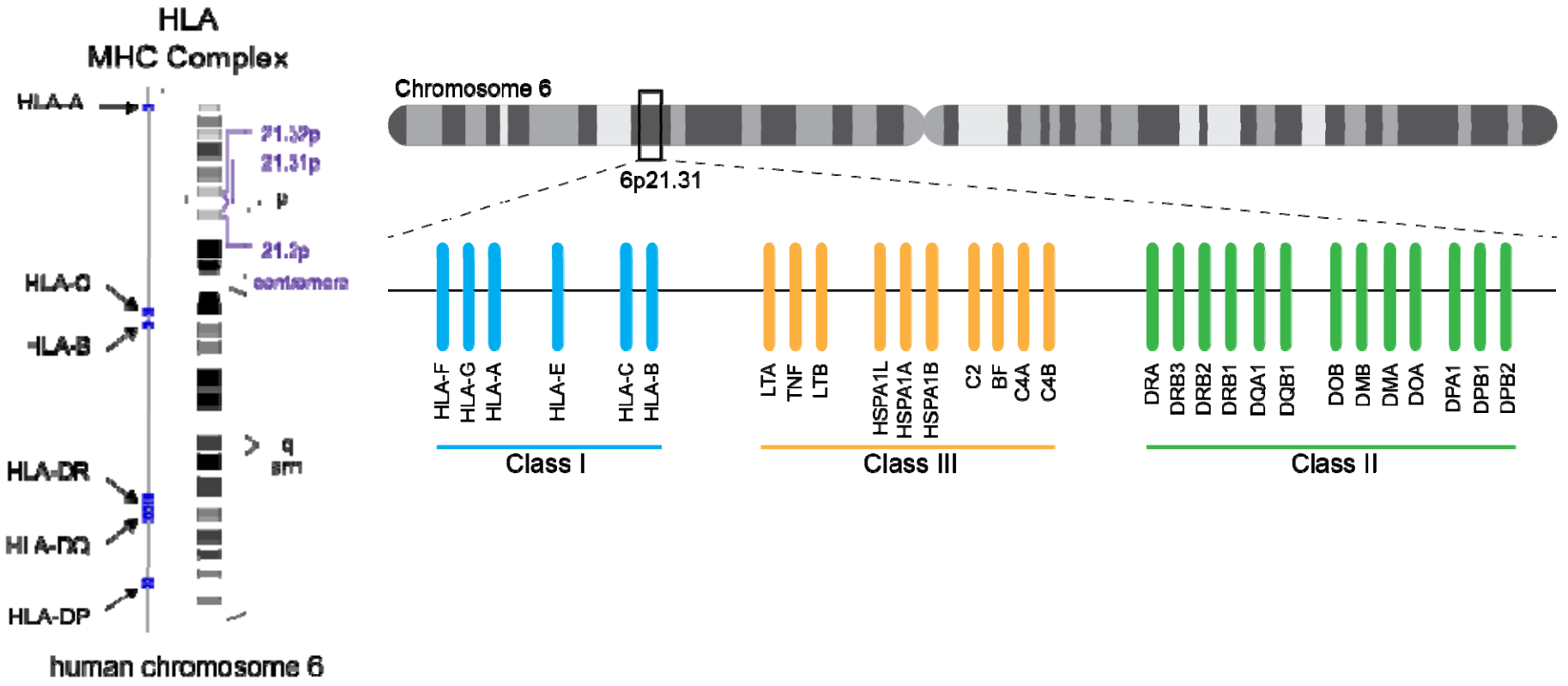
HDL, high-density lipoprotein; LDL, low-density lipoprotein; VLDL, very-low-density lipoprotein.

Az immunrendszer genetikai változatossága egyedi és populációs szinten

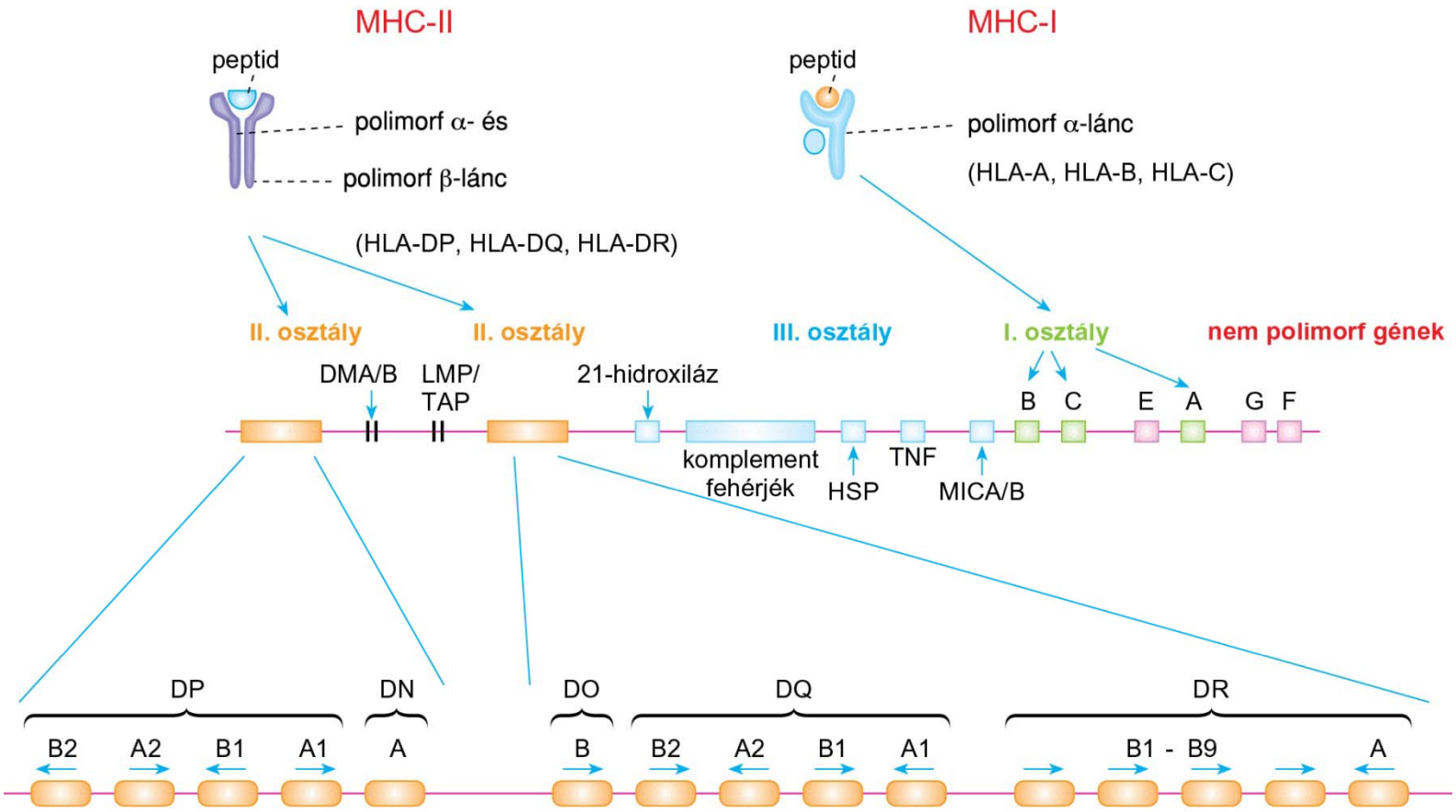


A fő hisztokompatibilitási génkomplex (MHC)

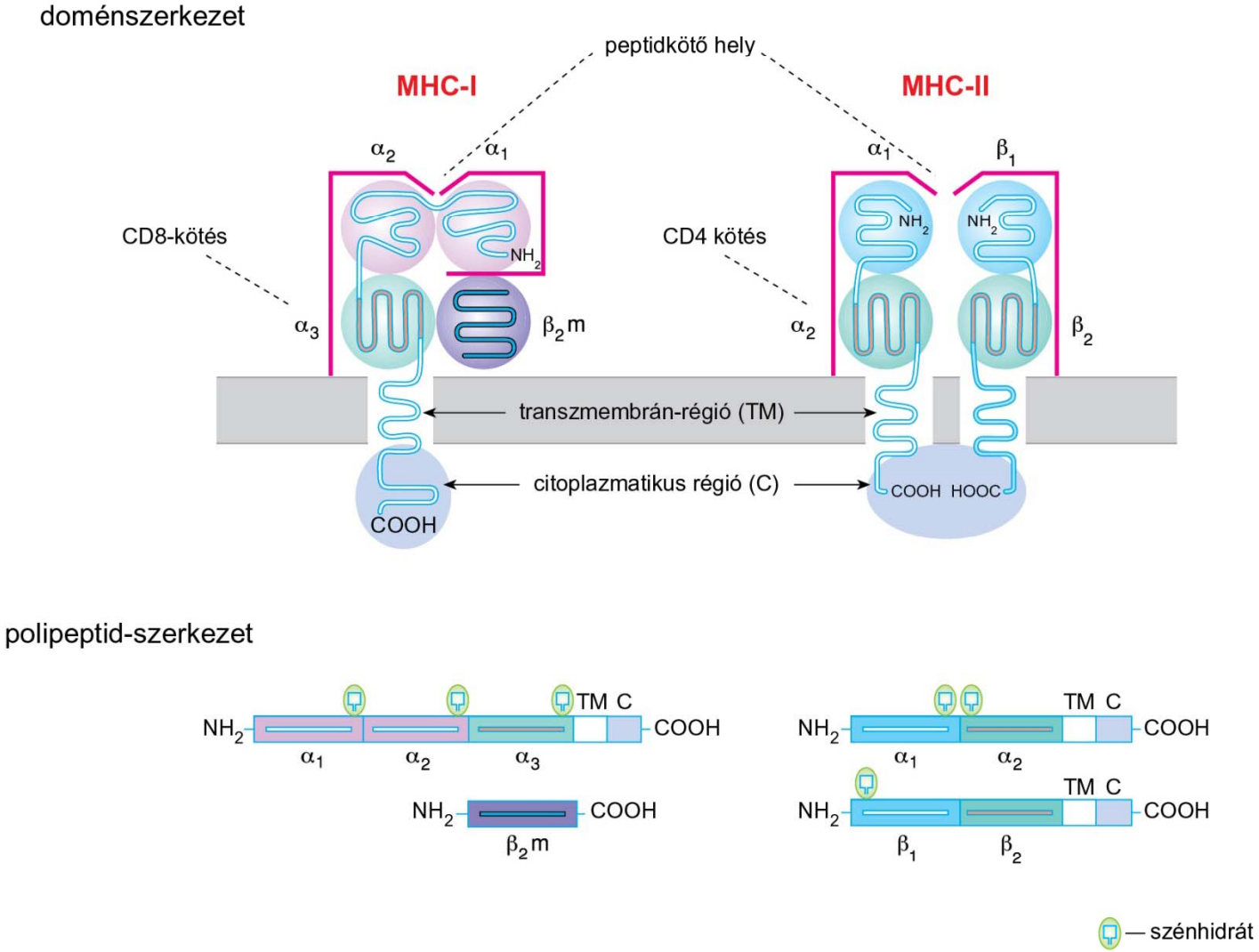




9.1. ábra Az emberi fő hisztokompatibilitási génkomplex (HLA) vázlatos térképe



9.4. ábra Az MHC-I és az MHC-II membránfehérjék doménszerkezete

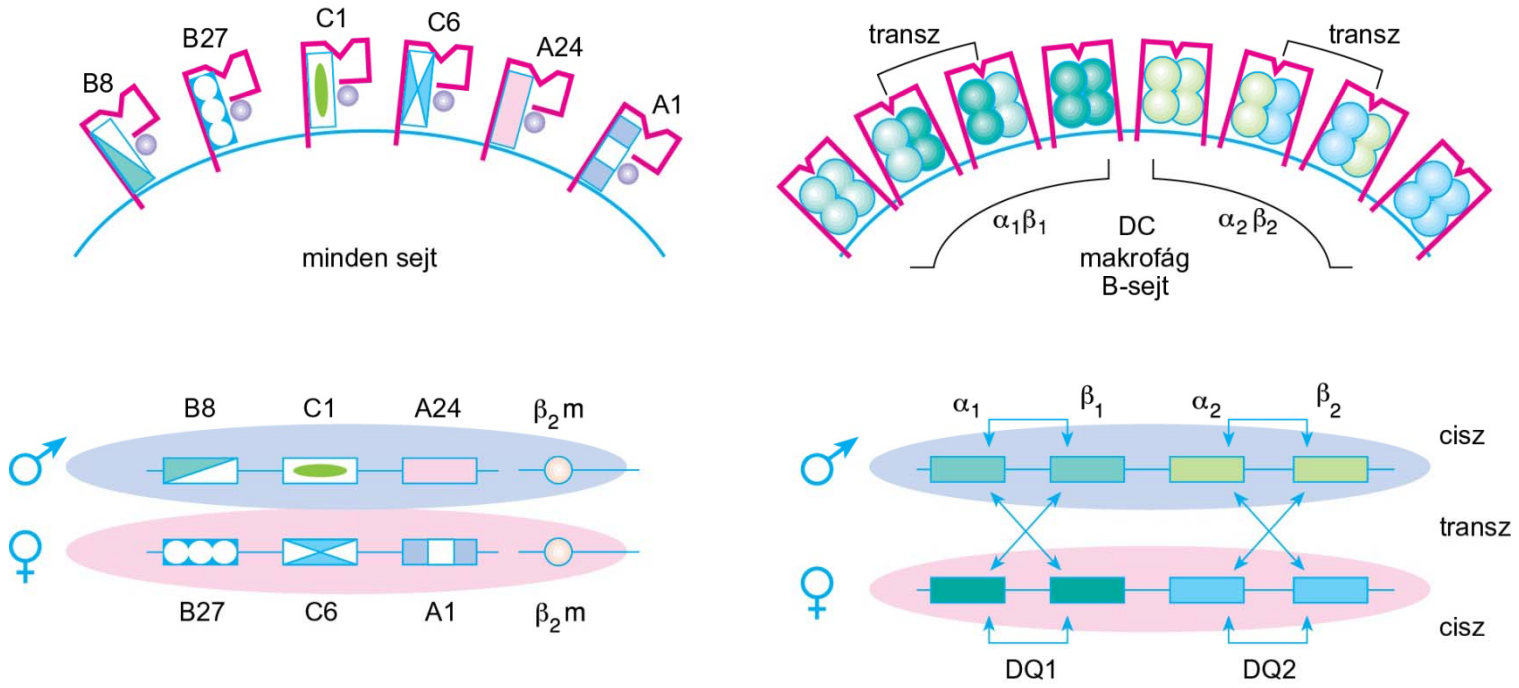


9.2. *táblázat.* **Az MHC-I- és az MHC-II-glikoproteinek szöveti megoszlása**

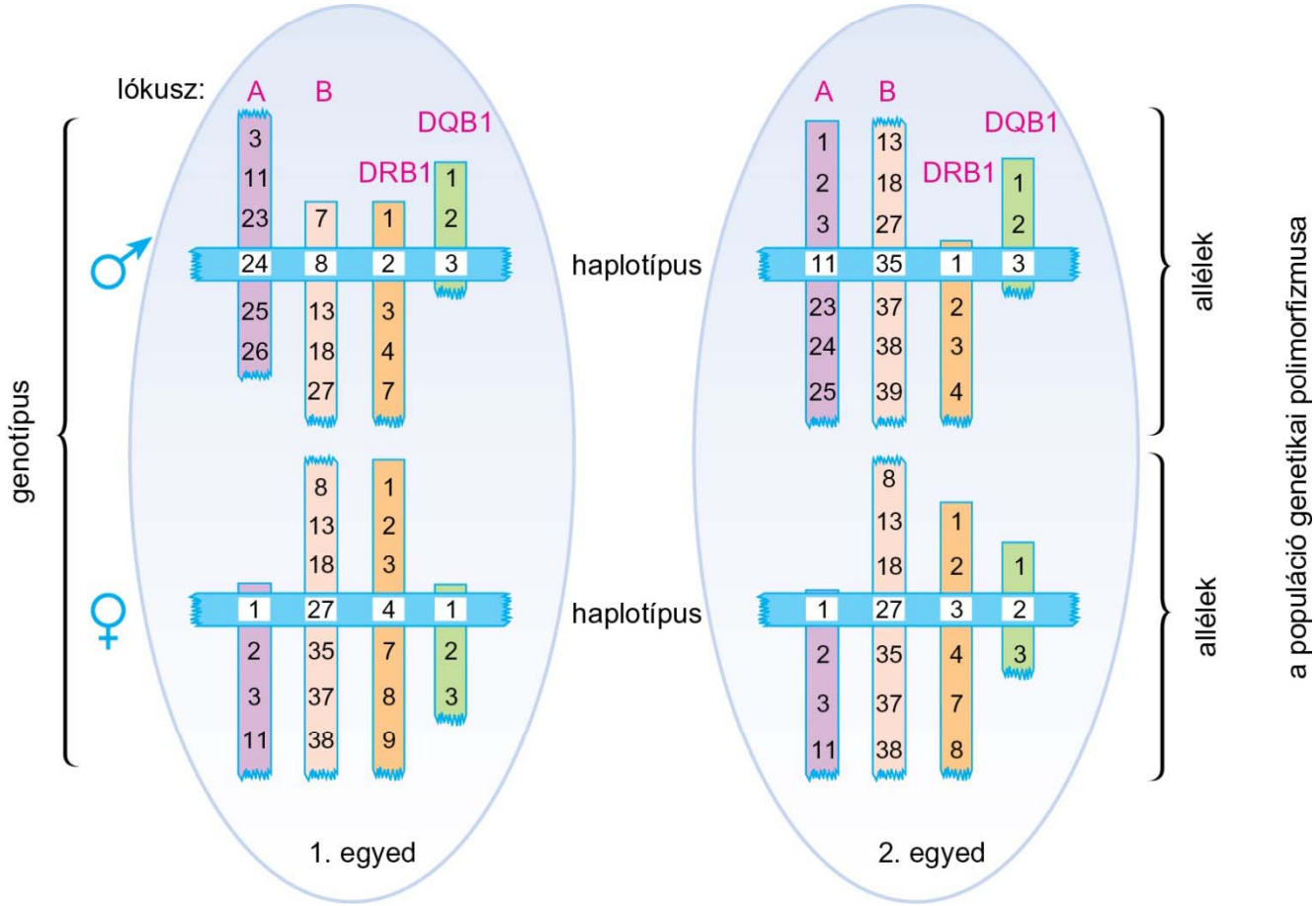
Sejtek, szövetek, szervek	MHC-I	MHC-II
Limfoid sejtek		
T-limfocita	+++	-*
B-limfocita	+++	+++
Mieloid sejtek		
Makrofág	+++	++
Dendritikus sejtek	+++	++++
Egyéb sejtek		
Timuszhámsejtek	+	+++
Neutrofil granulociták	+++	-
Vörösvérsejtek	-	-
*Különböző szervek, szövetek***		
Májsejtek	+	-
Vese	+	-
Agy	+	-***
Ízületek	+	-
Szem	+	-
Méhlepény	+	-
Szívizom	-	-
Gyomor	-	-
Vékonybél	++	++

* az emberi aktivált T-limfocitákon megjelennek az MHC-II-molekulák
** a többféle sejttípusból álló szerveken/szöveteken megjelenő MHC-II-molekuláknak a szervátültetések szempontjából van jelentősége
*** a makrofágokkal rokon mikrogliasejtek MHC-II-molekulákat hordoznak

9.8. ábra Az emberi MHC-I (HLA-B,-C és A) és az MHC-II (HLA-DQ A1B1, A2B2) lókuszok alléljei által kódolt fehérje-termékek sejtfelszíni megjelenése heterozigóta egyedben



9.9. ábra Az MHC-allotípusok kombinálódásának elve az egyedben és a populációban



MHC class I proteins form a functional receptor on most nucleated cells of the body. There are 3 major and 3 minor MHC class I genes in HLA:

HLA-A
HLA-B
HLA-C

minor genes are HLA-E, HLA-F and HLA-G

β_2-microglobulin binds with major and minor gene subunits to produce a heterodimer

Major MHC class II

HLA-DP

- **α**-chain encoded by HLA-**DPA1** locus
- **β**-chain encoded by HLA-**DPB1** locus

HLA-DQ

- **α**-chain encoded by HLA-**DQA1** locus
- **β**-chain encoded by HLA-**DQB1** locus

HLA-DR

- **α**-chain encoded by HLA-**DRA** locus
- **4 β-chains** (only 3 possible per person), encoded by HLA-**DRB1**, **DRB3**,**DRB4**, **DRB5** loci

The other MHC class II proteins, DM and DO, are used in the internal processing of antigens, loading the antigenic peptides generated from pathogens onto the HLA molecules of antigen-presenting cell.

MHC asszociációt mutató betegségek 1.

PHENOTYPE	HLA-A	HLA-C	HLA-B	C4	DRB1	DQA1	DQB1	DPB1	RR	Comments*
Infections										
AIDS progression			*35Px							mostly HLA-B, protective: e.g. B*27/*57/*51
Leprosy/Tuberculosis						*02	*0503			Cambodian, 48 cases, 39 controls
Lyme disease					*0401					
Malaria			*5301							DRB1*1302 protective
SARS			*4601							
Kaposi's sarcoma - HIV associated			*5401		alleles with F13					DRB1 phe13 susceptible/gly13 protective

MHC asszociációt mutató betegségek 2.

PHENOTYPE	HLA-A	HLA-C	HLA-B	C4	DRB1	DQA1	DQB1	DPB1	RR	Comments*
Hypersensitivity										
abacavir			*5701							mapped to class III HSP70?
allopurinol			*5801							
asthma										various class II - not seen in all cases - dependent on allergen. HLA-G associated in recent study
Berylliosis								*0201		DPB1 Glu69 susceptible/Lys69 protective
carbamazepine			*1502							
pigeon breeder's lung										class II
pollen-induced allergic rhinitis						*0302				chinese; 41 cases, 41 controls

MHC asszociációt mutató betegségek 3.

PHENOTYPE	HLA-A	HLA-C	HLA-B	C4	DRB1	DQA1	DQB1	DPB1	RR	Comments*
Autoimunity										
Acute anterior uveitis			*27							
Ankylosing spondylitis			*2702						~90	
			*2704							
			*2705							
Goodpastures syndrome					*1501/2				~16	
Graves disease			*0801		*0301				~4	
Hashimoto's thyroiditis					*0301	*0501				
Multiple sclerosis					*1501	*0102	*0602		~4	
Myasthenia gravis			*0801		*0301	*0501	*0201		~2.5	
Narcolepsy					*1501	*0102	*0602		~90	
Pemphigus vulgaris					*0402				~14	
Rheumatoid arthritis					*0101				~1-2	European descent
					*0401				~7	European descent
					*0404				~8	European descent
					*0405				~8	Oriental
					*1402				~2	Native American
SLE	*0101		*0801	C4AQ*0	*0301	*0501	*0201		~6	
Sjogren's syndrome			*0801		*0301				~3-20	DR2, DR5, DR11 some populations
Type 1 diabetes					*04	*0301	*0302		%	heterozygote
					*03	*0501	*0201			
					*09	*0301	*0303		%	heterozygote
					*03	*0501	*0201			
					*08	*0301	*0402		%	heterozygote
					*04	*0301	*0302			
					*0401	*0301	*0302		%	
					*0402	"	"		%	
					*0403	"	"		%	
					*0404	"	"		%	
Polymyositis/Dermatomyositis										MICA5.1/TNF2/TNFa2/DRB1*03 haplotype (8.1 ancestral haplotype)
										7.1 ancestral haplotype protective

HLA and autoimmune diseases		
HLA allele	Diseases with increased risk	Relative risk
HLA-B27	Ankylosing spondylitis	12[3]
	Postgonococcal arthritis	14[3]
	Acute anterior uveitis	15[3]
HLA-B47	21-hydroxylase deficiency	15[3]
HLA-DR2	Systemic lupus erythematosus	2 to 3[4]
HLA-DR3	Autoimmune hepatitis	14[3]
	Primary Sjögren syndrome	10[3]
	Diabetes mellitus type 1	5[3]
	Systemic lupus erythematosus	2 to 3[4]
HLA-DR4	Rheumatoid arthritis	4[3]
	Diabetes mellitus type 1	6[3]
HLA-DR3 and -DR4 combined	Diabetes mellitus type 1	15[3]
HLA-DQ2 and HLA-DQ8	Coeliac disease	7 [5]

Wikipedia.org - HLA

MHC asszociációt mutató betegségek 4.

PHENOTYPE	HLA-A	HLA-C	HLA-B	C4	DRB1	DQA1	DQB1	DPB1	RR	Comments*
Other diseases										
Haemochromatosis	*03									due to linked HFE-class I gene
21-OH deficiency										CYP21 in class III region
cervical cancer										class II
nasopharyngeal carcinoma	*0207									chinese
smoking behavior				C4AQ*0						
hypertrophic cardiomyopathy			*51							A2-B51-DR2 haplotype, Asian Indian population (14 cases, 81 controls)
non-response to HBV vaccine					*07				relative odds [RO]=5.18	N=164
HCV - Sustained response to therapy			*44							
Gastric cancer					*04051					Japanese; 70 cases, 121 controls

Ismert allélek száma (2012)

MHC class I	
locus	#[9][10]
Major Antigens	
HLA A	1,884
HLA B	2,490
HLA C	1,384
Minor Antigens	
HLA E	11
HLA F	22
HLA G	49

MHC class II				
HLA	**-A1**	**-B1**	**-B3 to -B5**[1]	Theor. possible
locus	**#**[10]	**#**[10]	**#**[10]	combinations
DM-	7	13		91
DO-	12	13		156
DP-	34	155		5,270
DQ-	47	165		7,755
DR-	7	1,094	92	8,302
[1]DRB3, DRB4, DRB5 have variable presence in humans				

40% of these alleles appear to be unique, having only been identified in single individuals
Roughly a third of alleles have been reported more than three times in unrelated individuals.

MHC allélek csoportosítása előfordulási gyakoriságuk alapján

HLA Locus	# Common Alleles[17]	% Common Alleles[17]	# Well-Documented Alleles[17]	% Well-Documented Alleles[17]	# Rare Alleles[15]	% Rare Alleles[15]	# Very Rare Alleles[15]	% Very Rare Alleles[15]	% Alleles Categorized
A	68	3.4%	178	8.8%	145	21.5%	280	41.6%	~75%
B	125	4.8%	242	9.3%	190	17.6%	468	43.5%	~75%
C	44	2.8%	102	6.6%	77	21.4%	154	42.8%	~74%
DRB1	79	6.8%	147	12.7%	133	22.7%	206	35.2%	~77%
DRB3	5	8.6%	7	12.1%					~21%
DRB4	6	40.0%	2	13.3%					~53%
DRB5	5	25.0%	3	15.0%					~40%
DQA1	15	31.9%	4	8.5%	9	26.5%	7	20.6%	~88%
DQB1	22	12.5%	8	4.5%	26	28.9%	42	45.2%	~91%
DPA1	6	17.6%	0	0.0%	4	14.8%	15	55.6%	~88%
DPB1	40	28.8%	14	9.0%	29	22.7%	29	32.8%	~90%
All Loci	415	5.3%	707	9.0%	613	20.6%	1214	40.8%	~76%

MHC allélek meghatározása

-Szerotipizálás
történeti jelentőség, nem ad pontos képet

-Sejtes tipizálás
érzékeny de körülményes, nem konzisztens

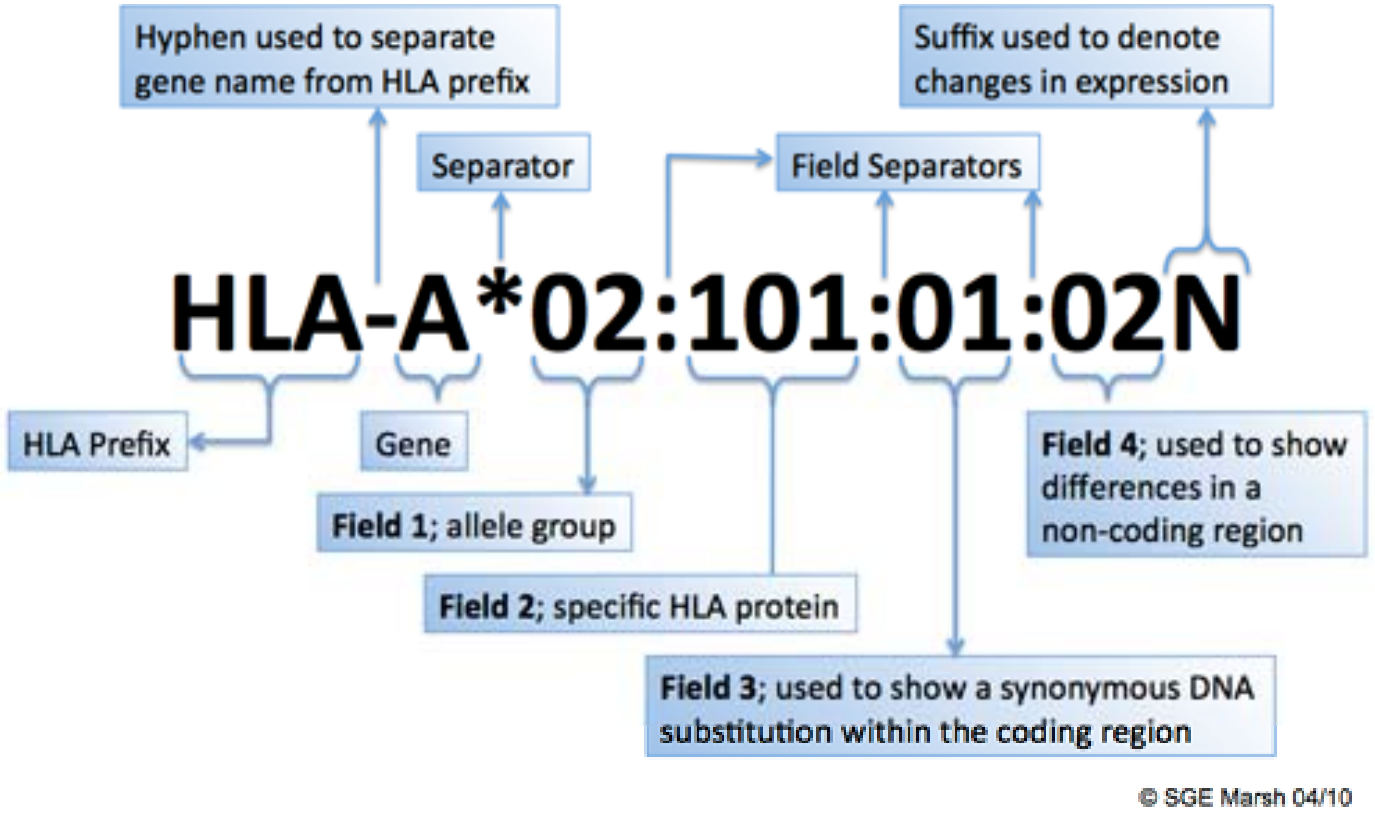
transzplantáció

-Gén tipizálás
új változatokat nem ismer fel

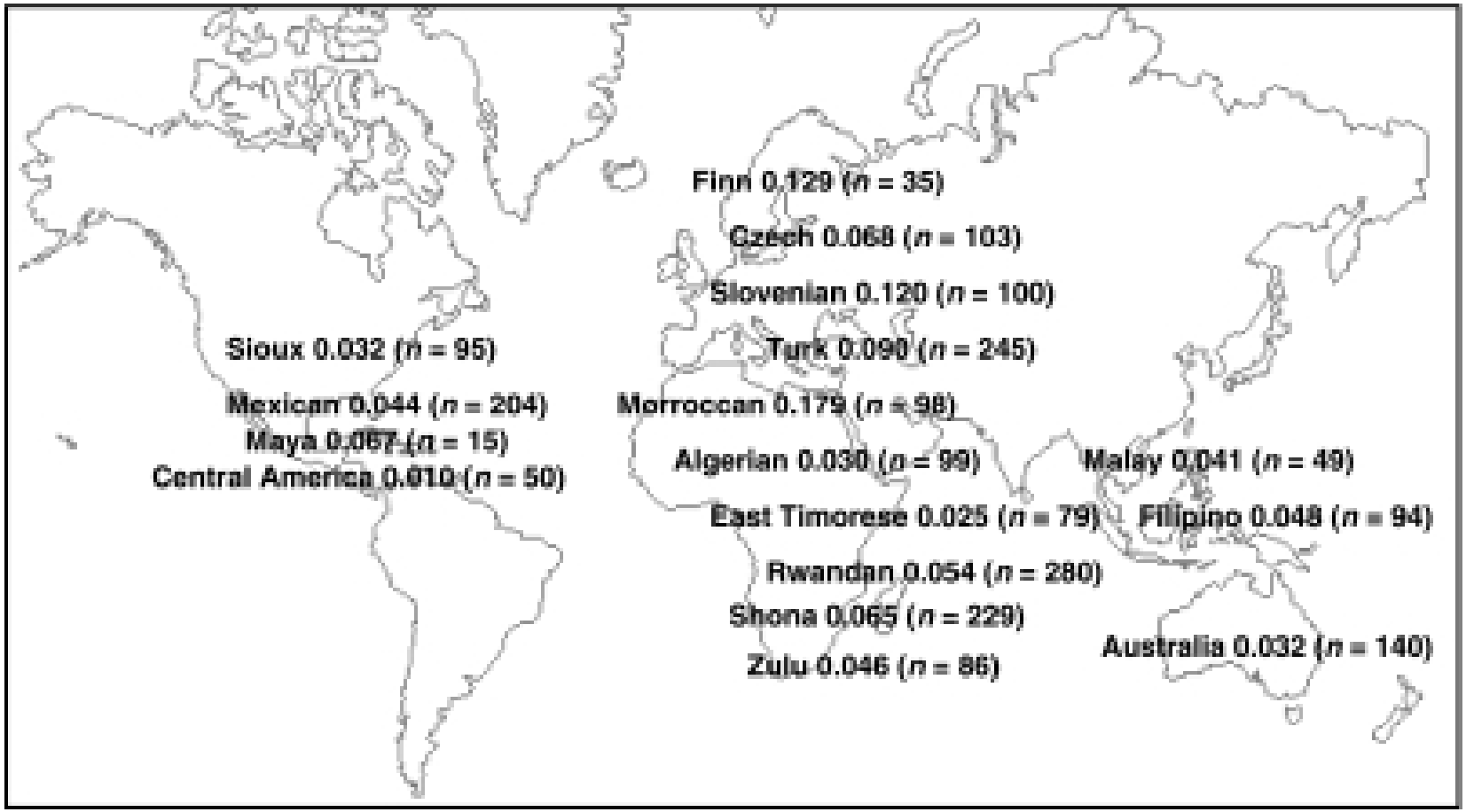
-Gén szekvenálás
definitív de drágább

-Haplotípus meghatározása

HLA allélek nomenklatúrája

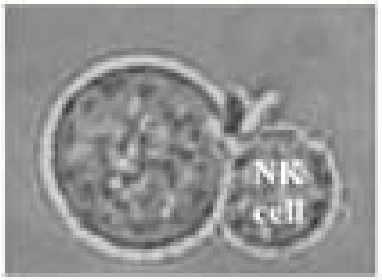


Nomenclature	Indicates
HLA	the HLA region and prefix for an HLA gene
HLA-DRB1	a particular HLA locus i.e. DRB1
*HLA-DRB1*13*	a group of alleles which encode the DR13 antigen or sequence homology to other DRB1*13 alleles
*HLA-DRB1*13:01*	a specific HLA allele
*HLA-DRB1*13:01:02*	an allele that differs by a synonymous mutation from *DRB1*13:01:01*
*HLA-DRB1*13:01:01:02*	an allele which contains a mutation outside the coding region from *DRB1*13:01:01:01*
*HLA-A*24:09N*	a 'Null' allele, an allele which is not expressed
*HLA-A*30:14L*	an allele encoding a protein with significantly reduced or 'Low' cell surface expression
*HLA-A*24:02:01:02L*	an allele encoding a protein with significantly reduced or 'Low' cell surface expression, where the mutation is found outside the coding region
*HLA-B*44:02:01:02S*	an allele encoding a protein which is expressed as a 'Secreted' molecule only
*HLA-A*32:11Q*	an allele which has a mutation that has previously been shown to have a significant effect on cell surface expression, but where this has not been confirmed and its expression remains 'Questionable'

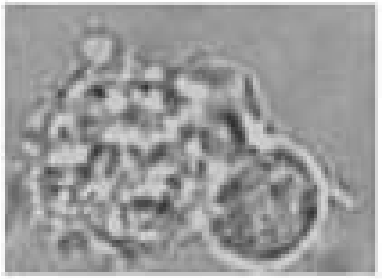

Finn 0.129 (n = 35)
Czech 0.068 (n = 103)
Slovenian 0.120 (n = 100)
Sioux 0.032 (n = 95)
Turk 0.090 (n = 245)
Mexican 0.044 (n = 204)
Moroccan 0.179 (n = 98)
Maya 0.067 (n = 15)
Algerian 0.030 (n = 99)
Malay 0.041 (n = 49)
Central America 0.010 (n = 50)
East Timorese 0.025 (n = 79)
Filipino 0.048 (n = 94)
Rwandan 0.054 (n = 280)
Shona 0.065 (n = 229)
Australia 0.032 (n = 140)
Zulu 0.046 (n = 86)

Natural Killer (NK) cells lyse cells that are deficient in expression of class I MHC proteins

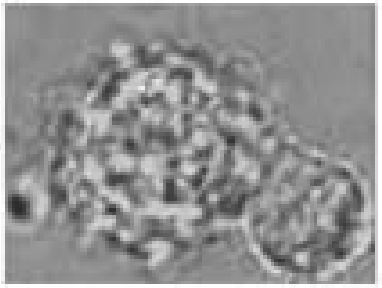
0

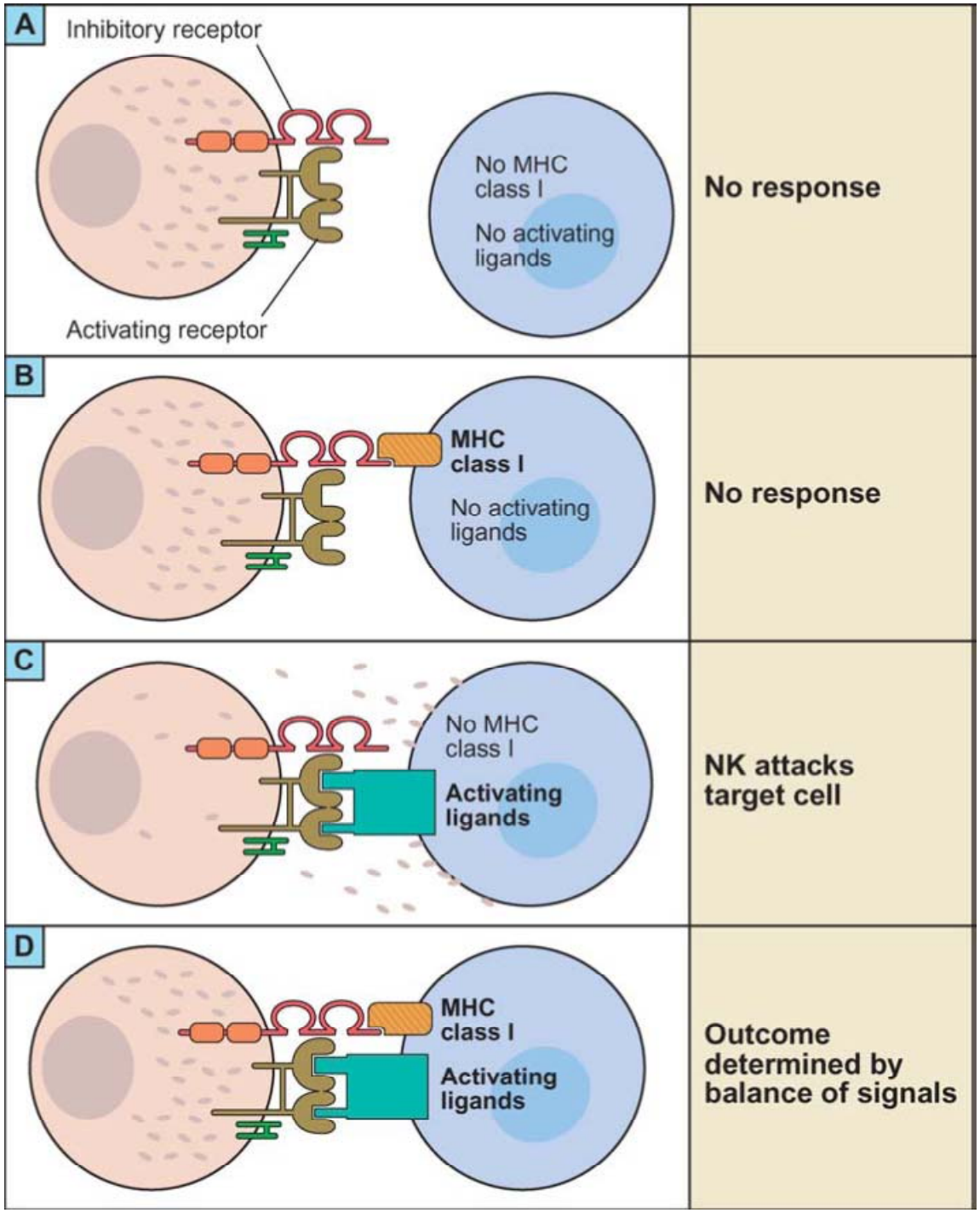


10 min.



15 min.





Annu. Rev. Immunol. 2005. 23:225–74

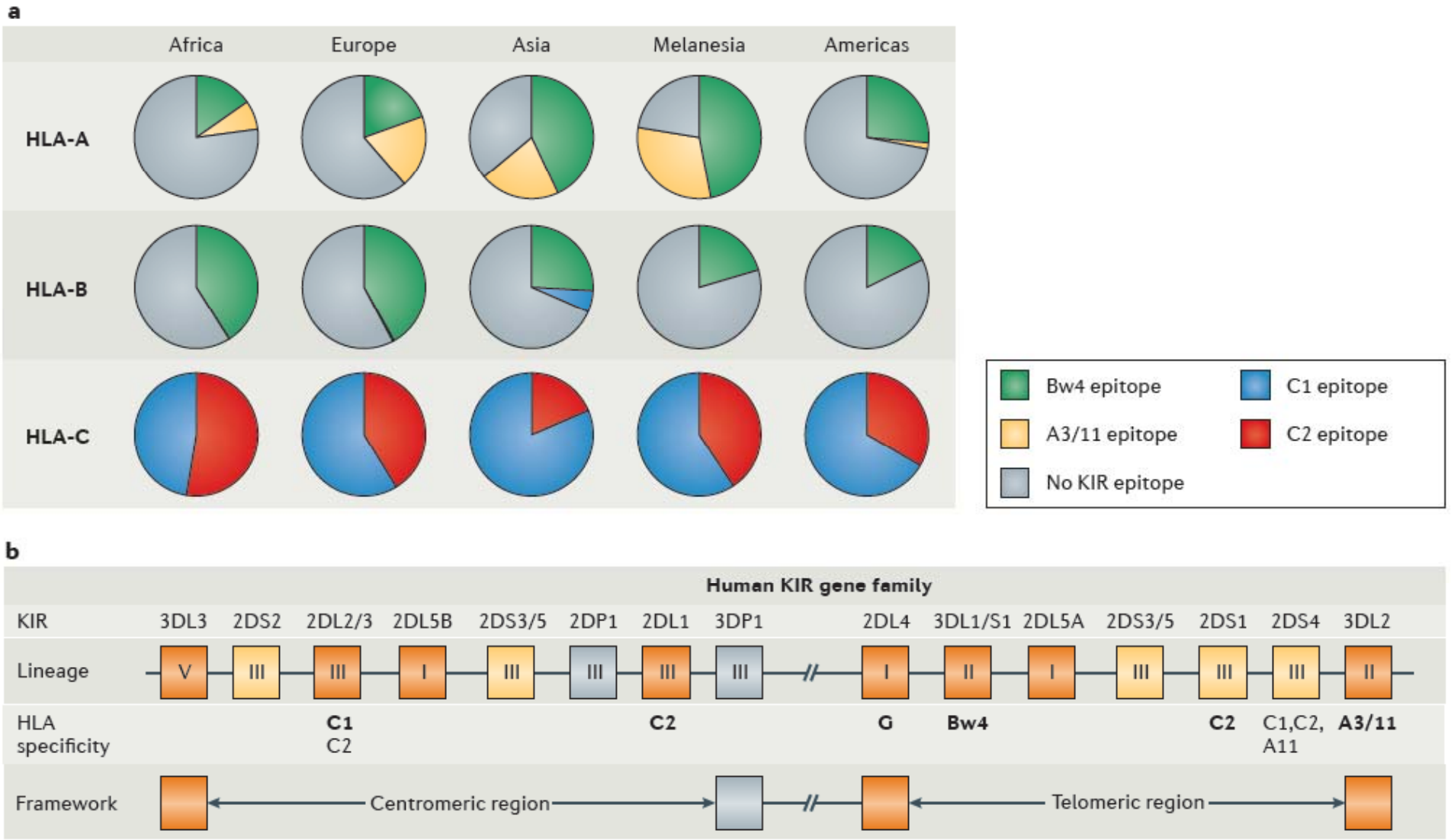
VARIABILITÁS A *KIR* GÉN- KOMPLEX SZERVEZŐDÉSÉBEN

KIR-haplotípus diverzitás

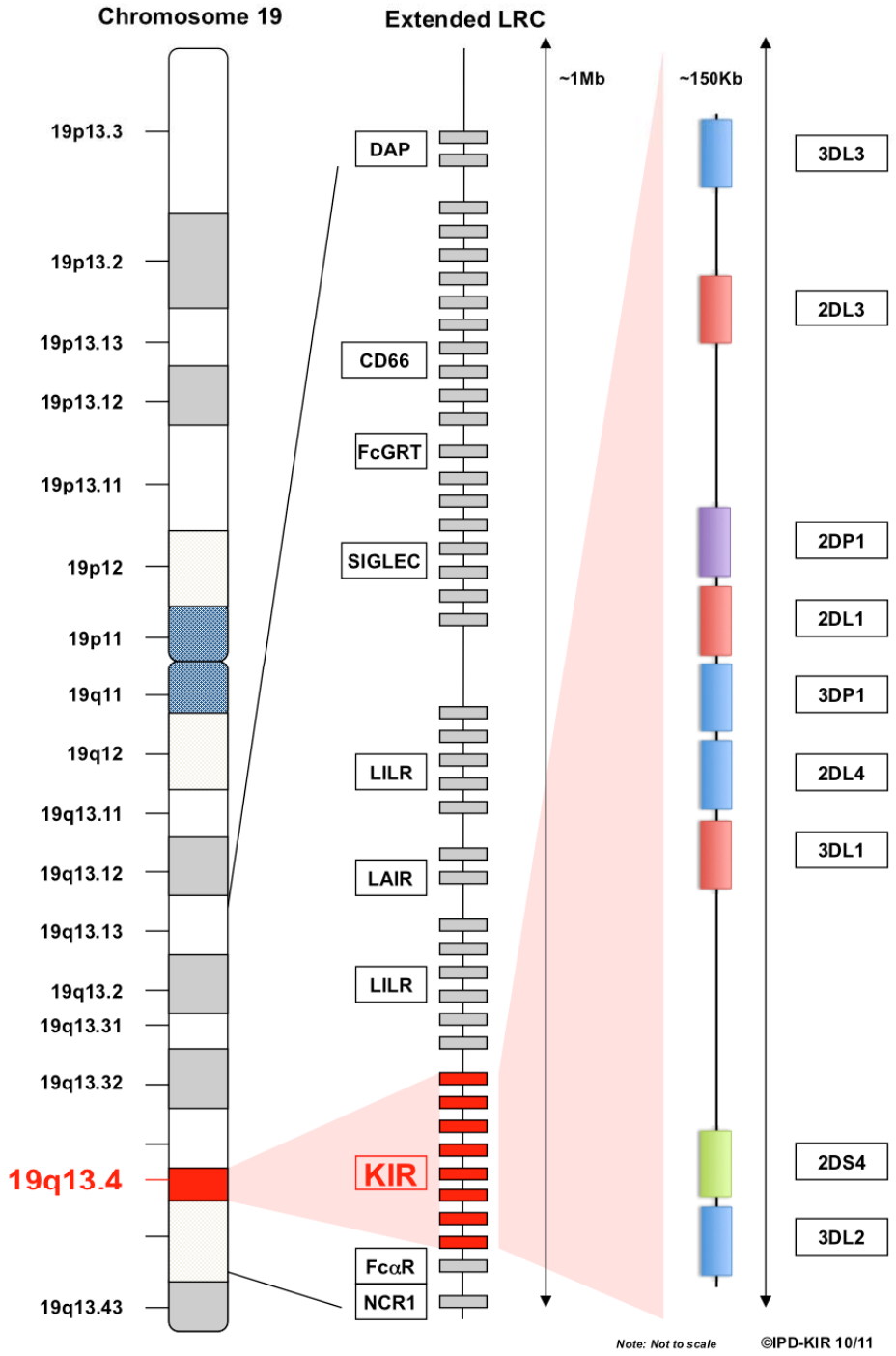
Az emberi KIR haplotípusok változó számú és minőségű gént tartalmaznak

Allélikus polimorfizmus

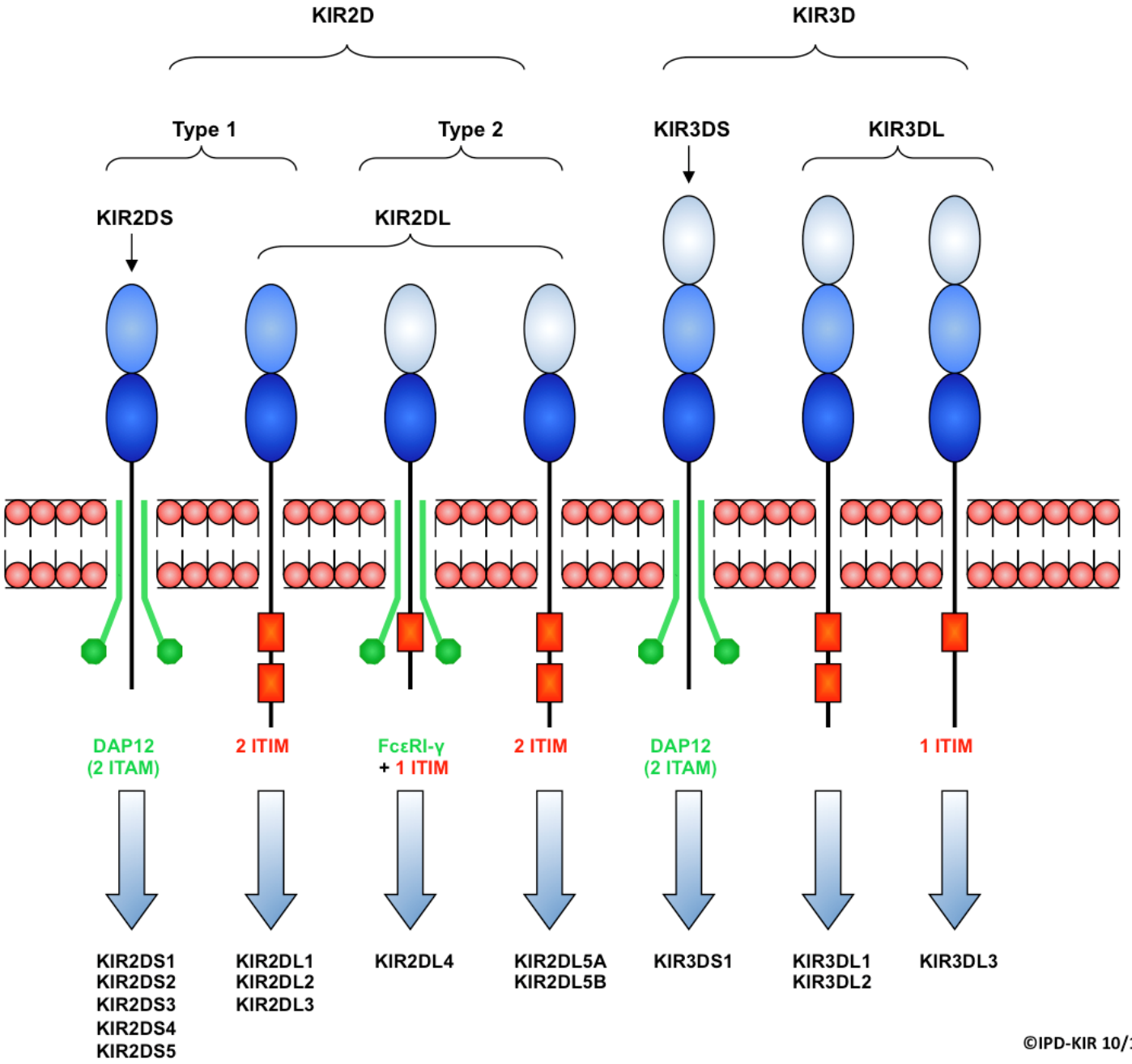
A legtöbb emberi KIR gén polimorfizmust mutat, legtöbbünk heterozigóta egy vagy több KIR szempontjából

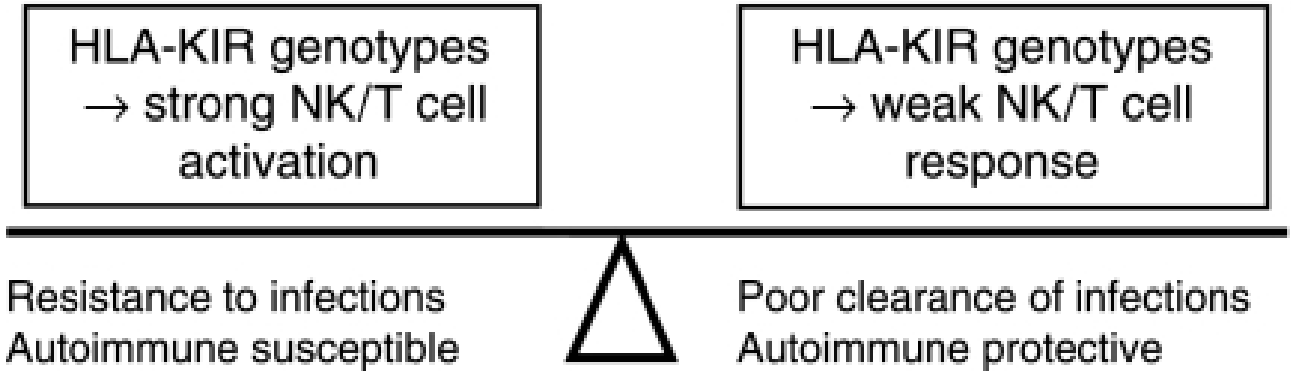

a
Africa
Europe
Asia
Melanesia
Americas
HLA-A
HLA-B
HLA-C
Bw4 epitope
C1 epitope
A3/11 epitope
C2 epitope
No KIR epitope
b
Human KIR gene family
KIR
3DL3
2DS2
2DL2/3
2DL5B
2DS3/5
2DP1
2DL1
3DP1
2DL4
3DL1/S1
2DL5A
2DS3/5
2DS1
2DS4
3DL2
Lineage
V
III
III
I
III
III
III
III
I
II
I
III
III
III
II
HLA specificity
C1
C2
C2
G
Bw4
C2
C1,C2, A11
A3/11
Framework
Centromeric region
Telomeric region

LCR
Leukocyte Receptor Complex)



KIR gene family
currently consists of 15 gene loci
KIR2DL1, KIR2DL2/L3, KIR2DL4, KIR2DL5A, KIR2DL5B, KIR2DS1, KIR2DS2, KIR2DS3, KIR2DS4, KIR2DS5, KIR3DL1/S1, KIR3DL2, KIR3DL3 and two pseudogenes, KIR2DP1 and KIR3DP1

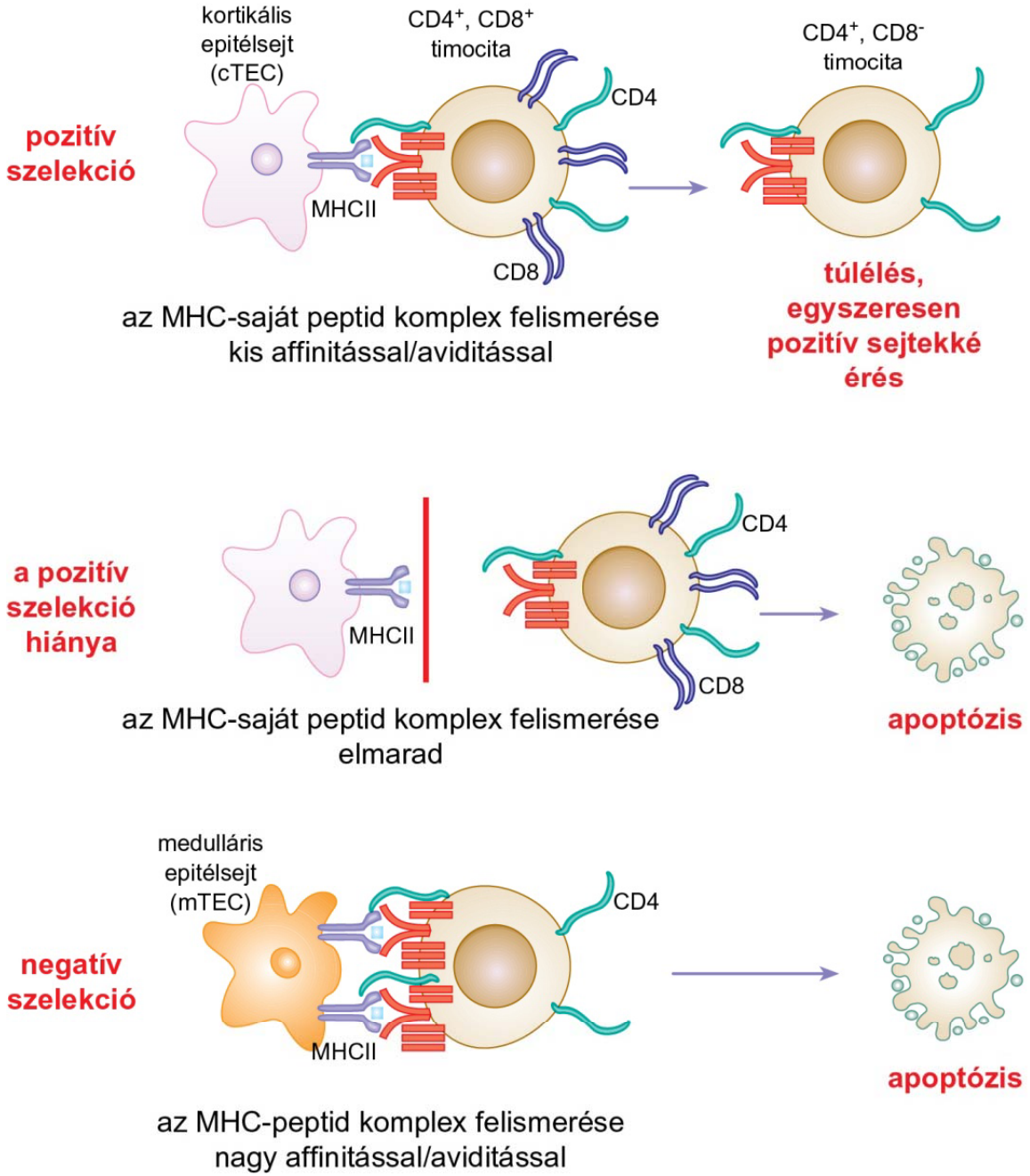

KIR2D
KIR3D
Type 1
Type 2
KIR3DS
KIR3DL
KIR2DS
KIR2DL
DAP12
(2 ITAM)
2 ITIM
FcεRI-γ
+ 1 ITIM
2 ITIM
DAP12
(2 ITAM)
1 ITIM
KIR2DS1
KIR2DS2
KIR2DS3
KIR2DS4
KIR2DS5
KIR2DL1
KIR2DL2
KIR2DL3
KIR2DL4
KIR2DL5A
KIR2DL5B
KIR3DS1
KIR3DL1
KIR3DL2
KIR3DL3


HLA-KIR genotypes → strong NK/T cell activation
HLA-KIR genotypes → weak NK/T cell response
Resistance to infections
Autoimmune susceptible
Poor clearance of infections
Autoimmune protective

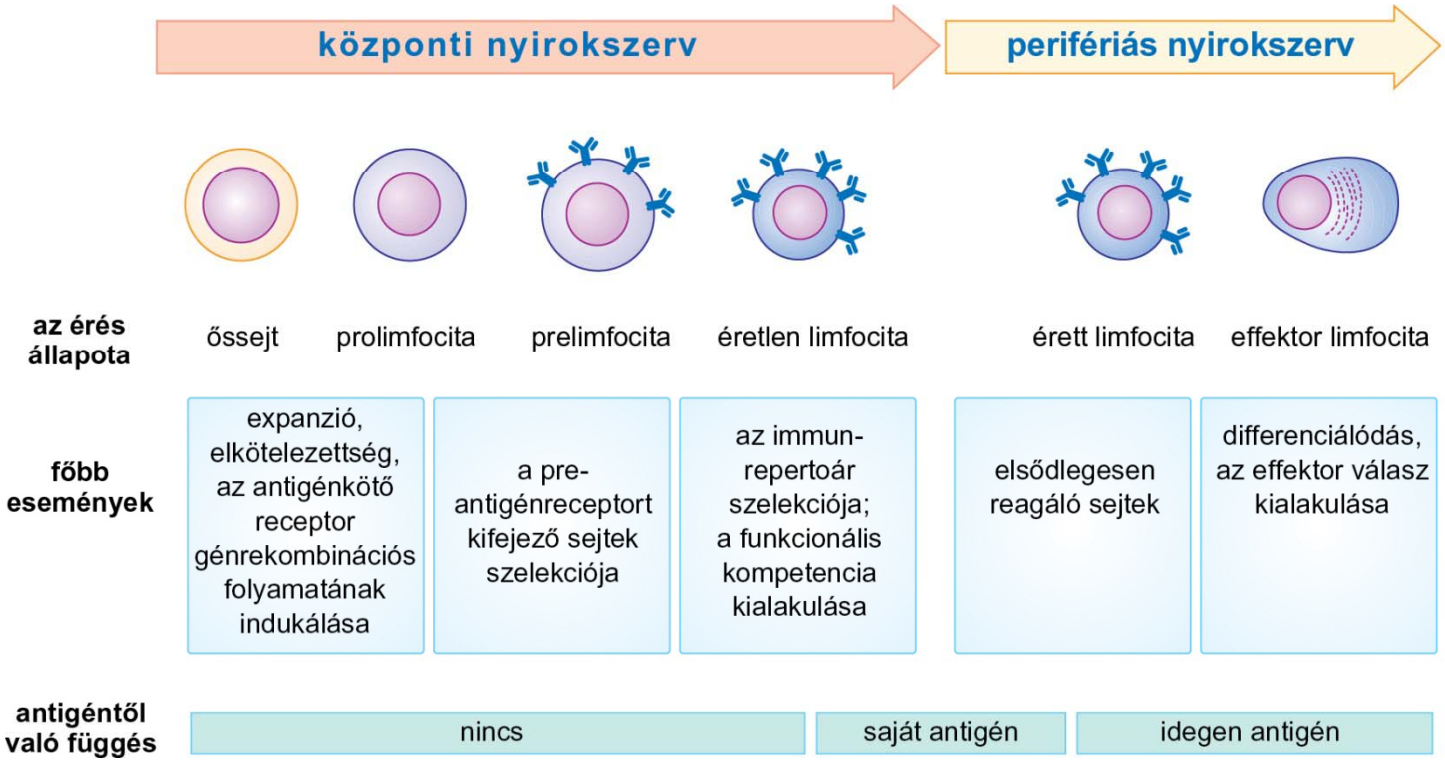
11. fejezet

A limfociták antigén-felismerő receptorkészletének kialakulása, a limfociták túlélése és érése a limfoid szövetekben

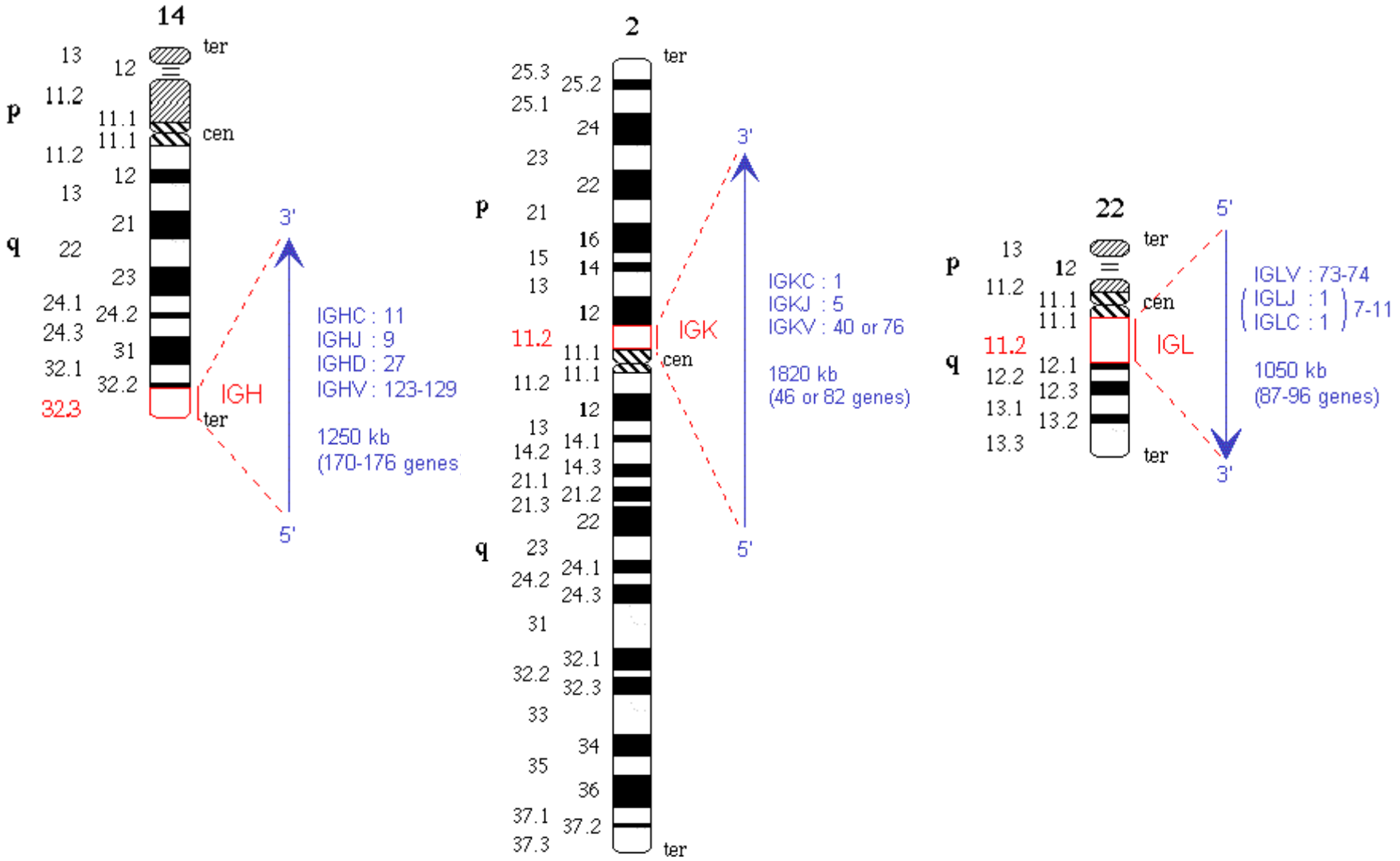
11.22. ábra A tímuszban zajló szelekciós folyamatok



11.1. ábra A limfociták érése

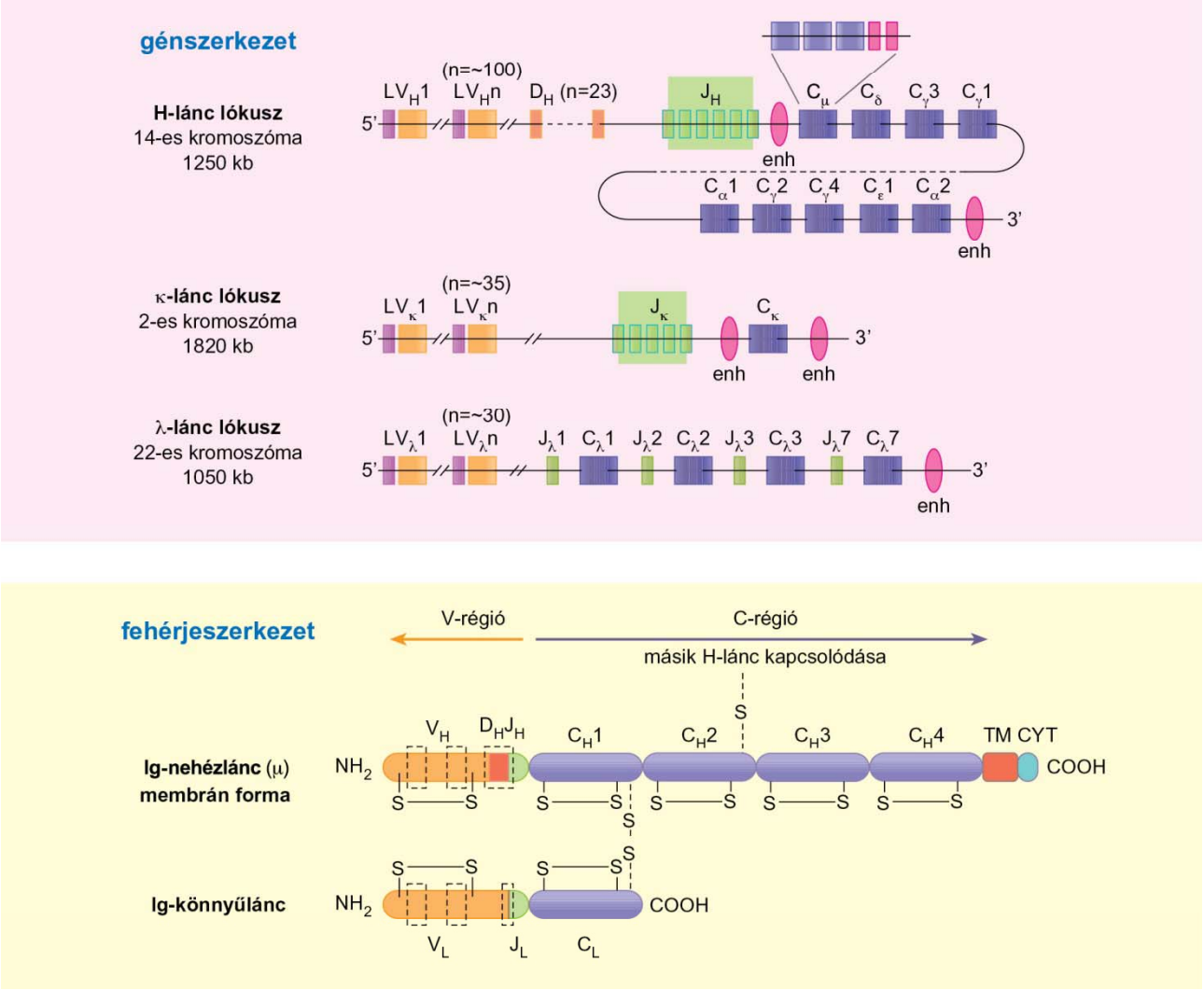


Immunglobulin láncok kromoszomális elhelyezkedése

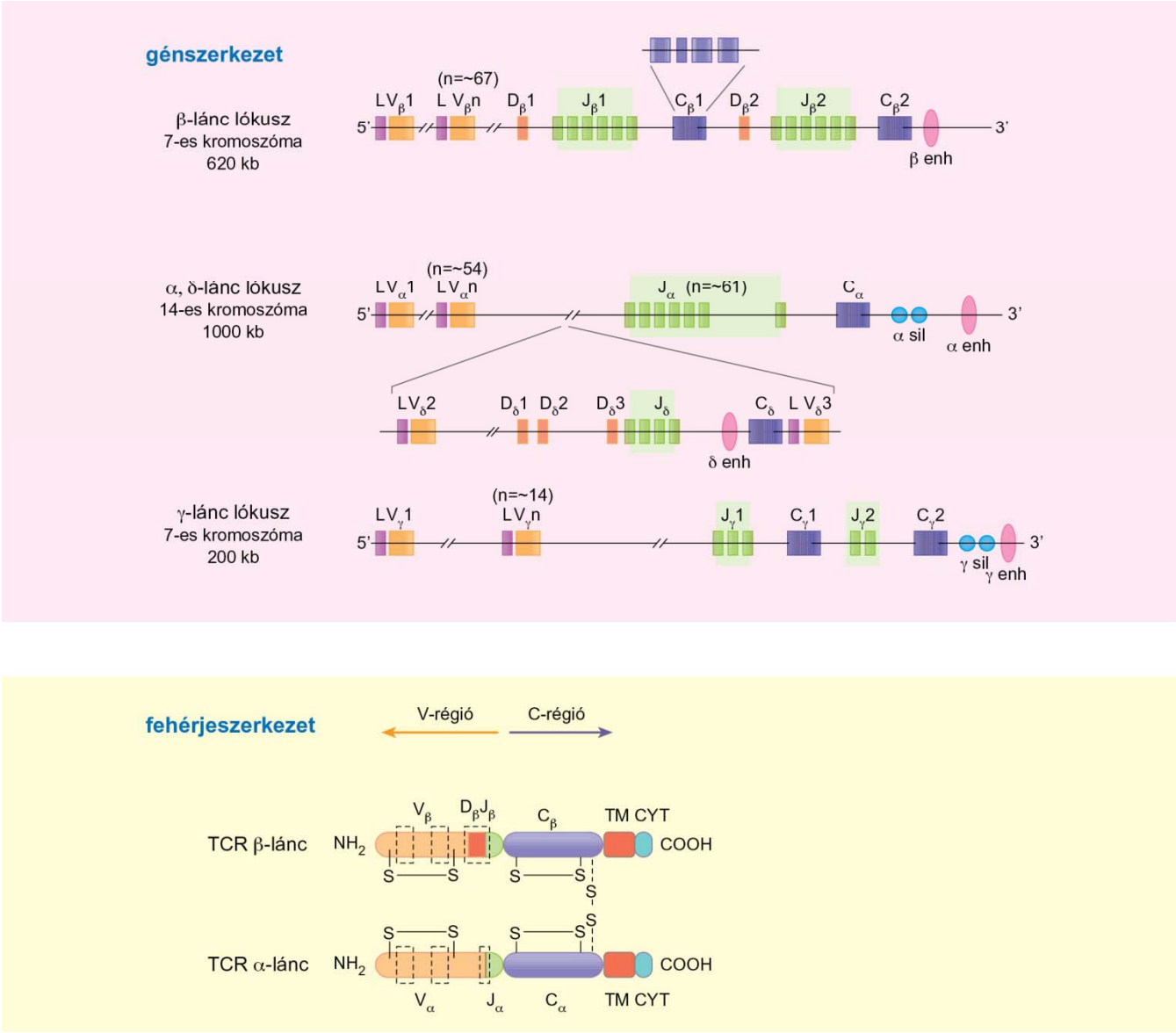


www.imgt.org

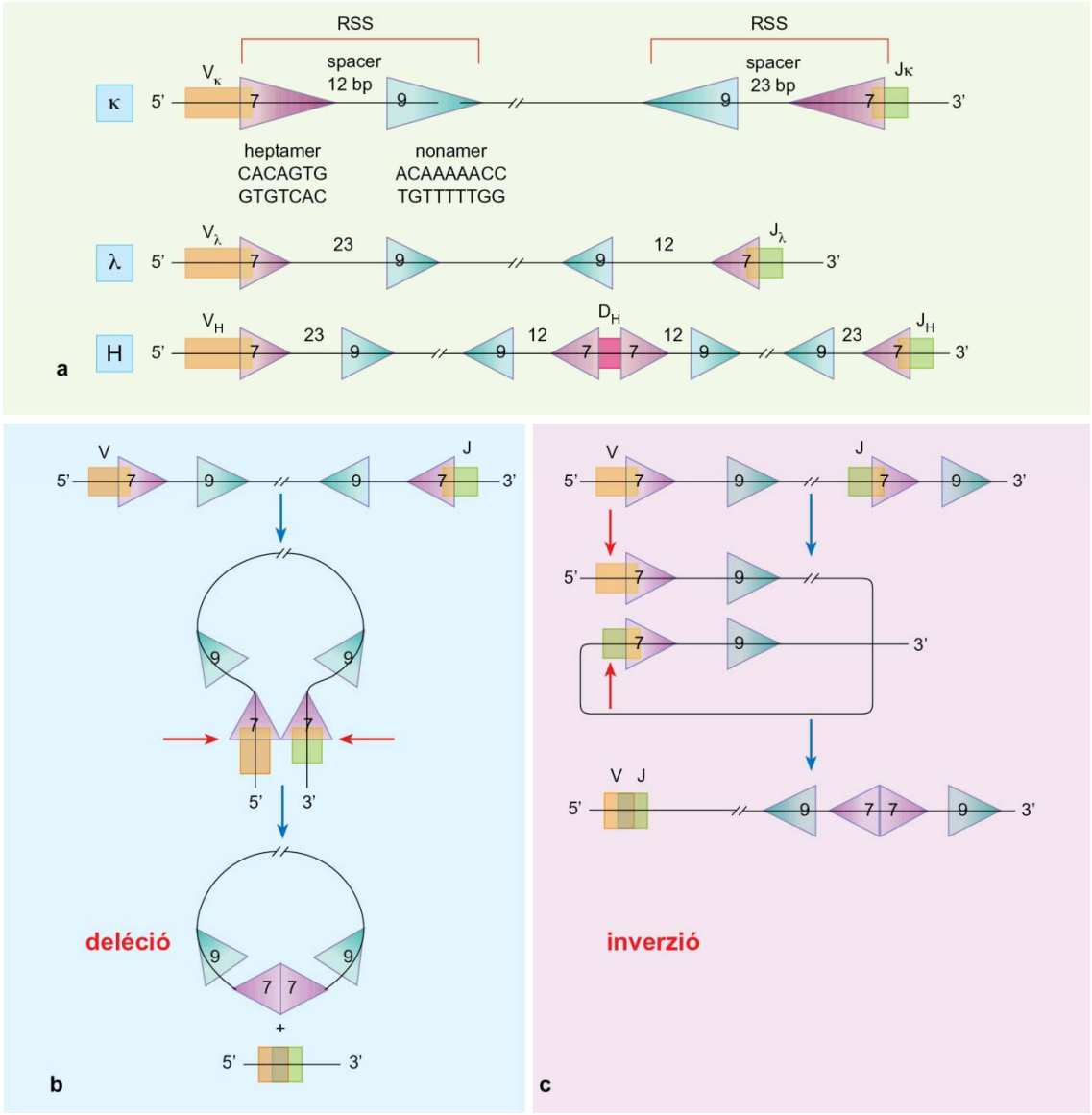
11.6. ábra Az immunglobulin gének szerveződése és a kifejeződő fehérje szerkezete



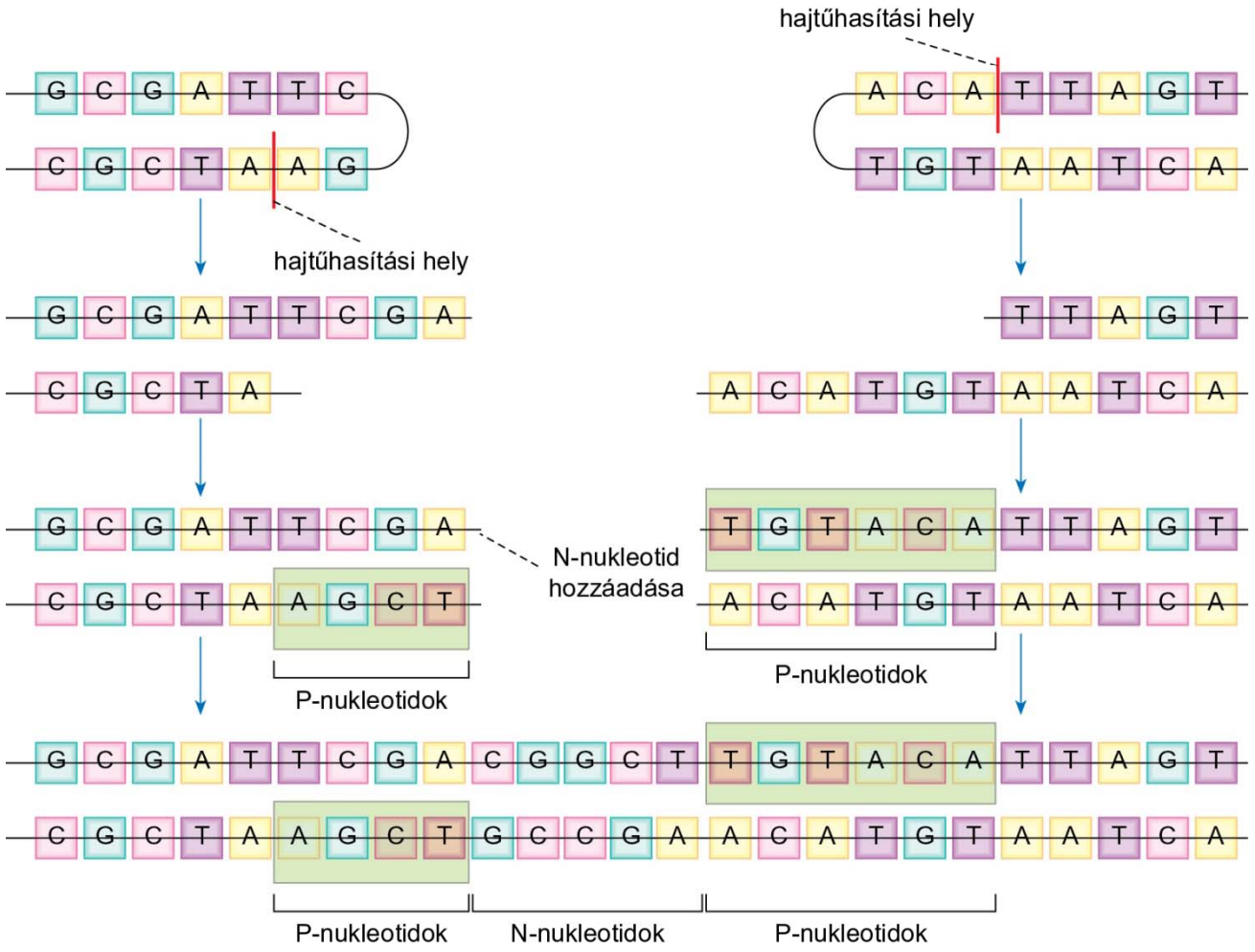
11.7. ábra A humán TCR antigén-felismerő láncait kódoló gének szerveződése és a kifejeződő fehérje szerkezete



11.9. ábra A V(D)J-rekombináció mechanizmusa



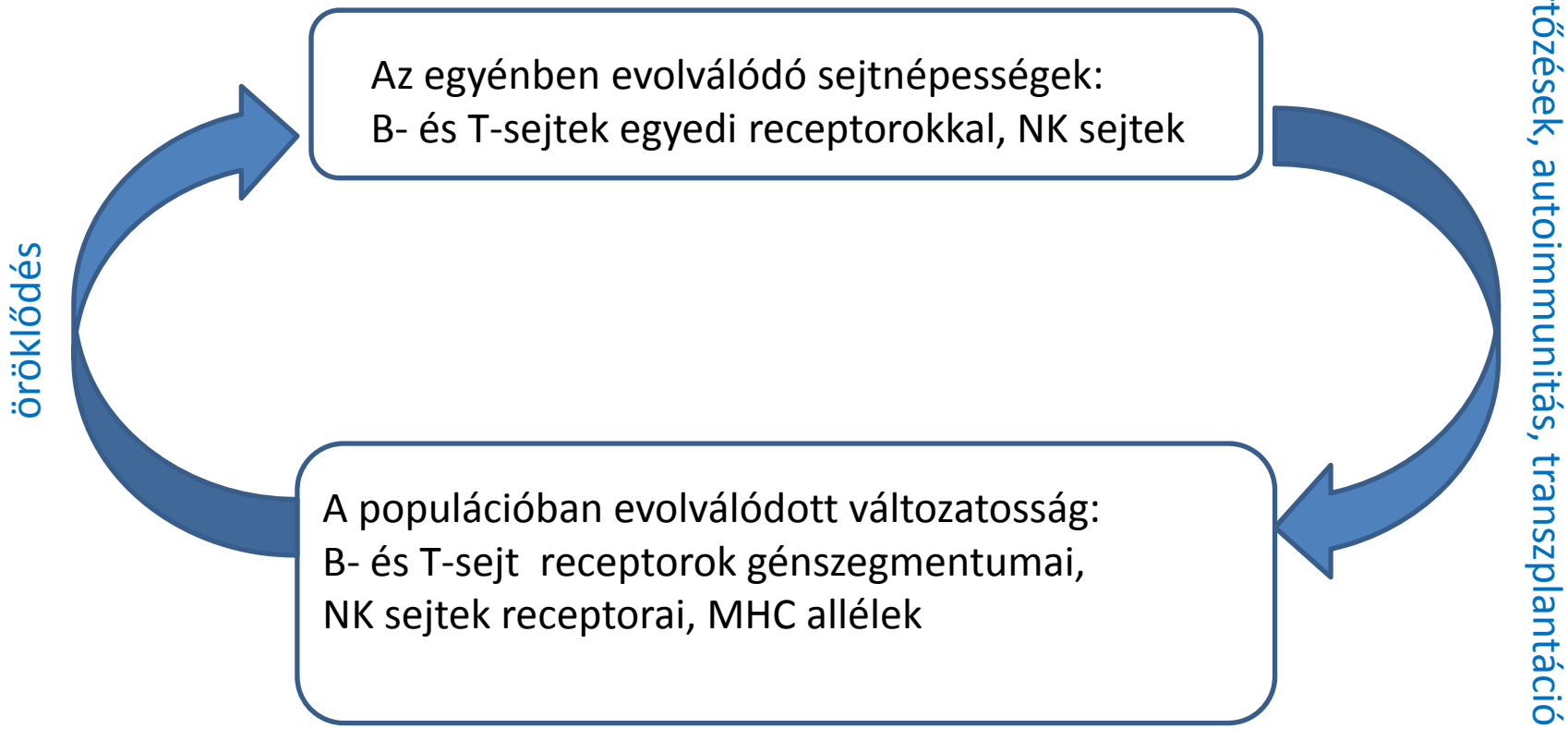
11.12. ábra Az összekapcsolódásból eredő diverzitás kialakulásának mechanizmusa



11.1. táblázat. **A különböző mechanizmusok hatása az Ig- és TCR-repertoár kialakításában**

Mechanizmus	Immunglobulin		TCR-αβ		TCR-γδ	
	Nehézlánc	κ	α	β	γ	δ
Variábilis (V) szegmens	85	35	54	67	14	20-30
Diverzitás (D) szegmens	27	0	0	2	0	3
N-régió diverzitás	V-D, D-J	Nincs	V-J	V-D, D-J	V-J	V-D1, D1-D2, D1-J
Kapcsolódási (J) szegmens	6	5	61	4	5	4
Teljes potenciális repertoár	$\sim 10^{11}$		$\sim 10^{16}$		$\sim 10^{18}$	

Az immunrendszer genetikai változatossága egyedi és populációs szinten



Az immungenetikának dedikált adatbázisok

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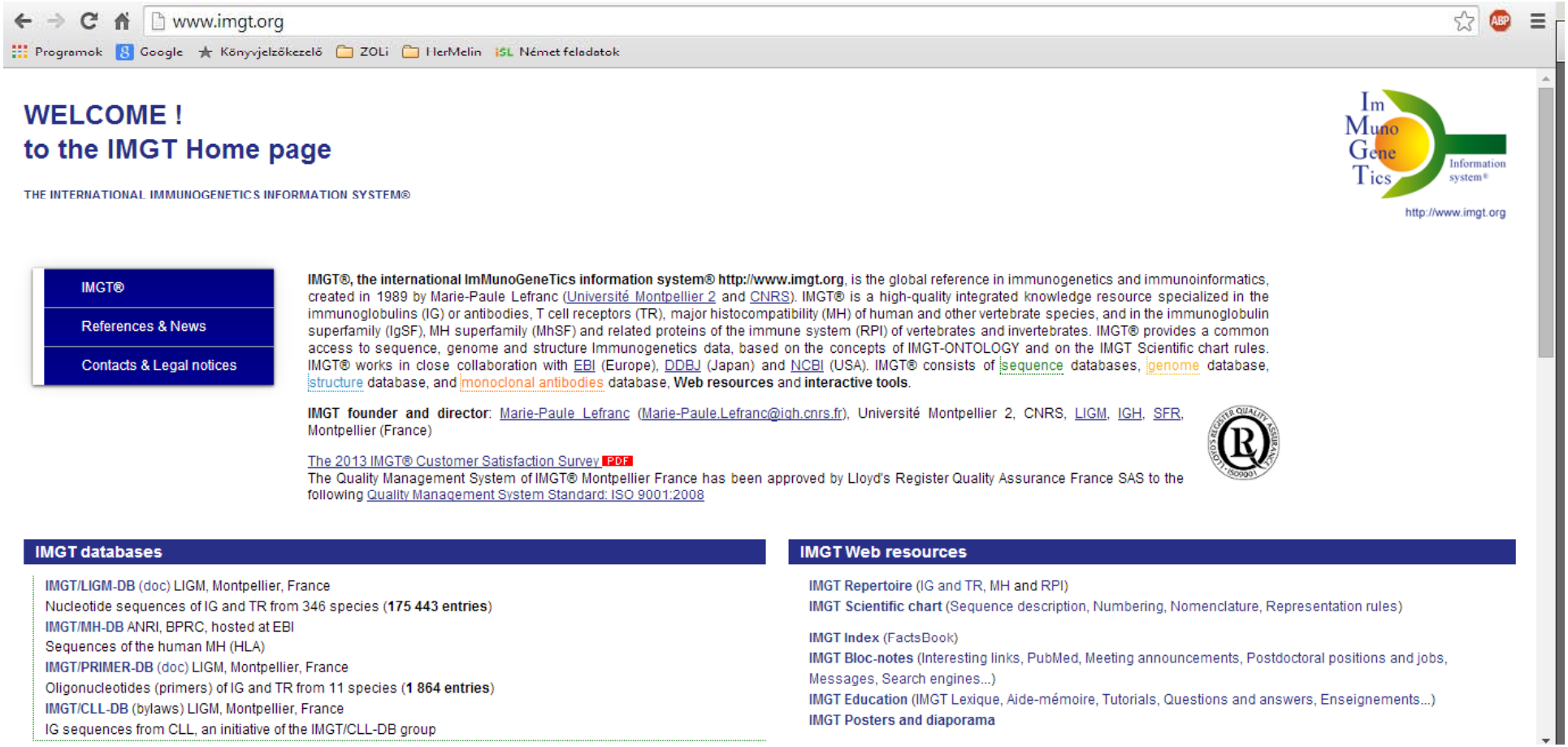
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IMGT founder and director: Marie-Paule Lefranc (Marie-Paule.Lefranc@igh.cnrs.fr), Université Montpellier 2, CNRS, LIGM, IGH, SFR, Montpellier (France)
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Nucleotide sequences of IG and TR from 346 species (175 443 entries)
IMGT/MH-DB ANRI, BPRC, hosted at EBI
Sequences of the human MH (HLA)
IMGT/PRIMER-DB (doc) LIGM, Montpellier, France
Oligonucleotides (primers) of IG and TR from 11 species (1 864 entries)
IMGT/CLL-DB (bylaws) LIGM, Montpellier, France
IG sequences from CLL, an initiative of the IMGT/CLL-DB group
IMGT Web resources
IMGT Repertoire (IG and TR, MH and RPI)
IMGT Scientific chart (Sequence description, Numbering, Nomenclature, Representation rules)
IMGT Index (FactsBook)
IMGT Bloc-notes (Interesting links, PubMed, Meeting announcements, Postdoctoral positions and jobs, Messages, Search engines...)
IMGT Education (IMGT Lexique, Aide-mémoire, Tutorials, Questions and answers, Enseignements...)
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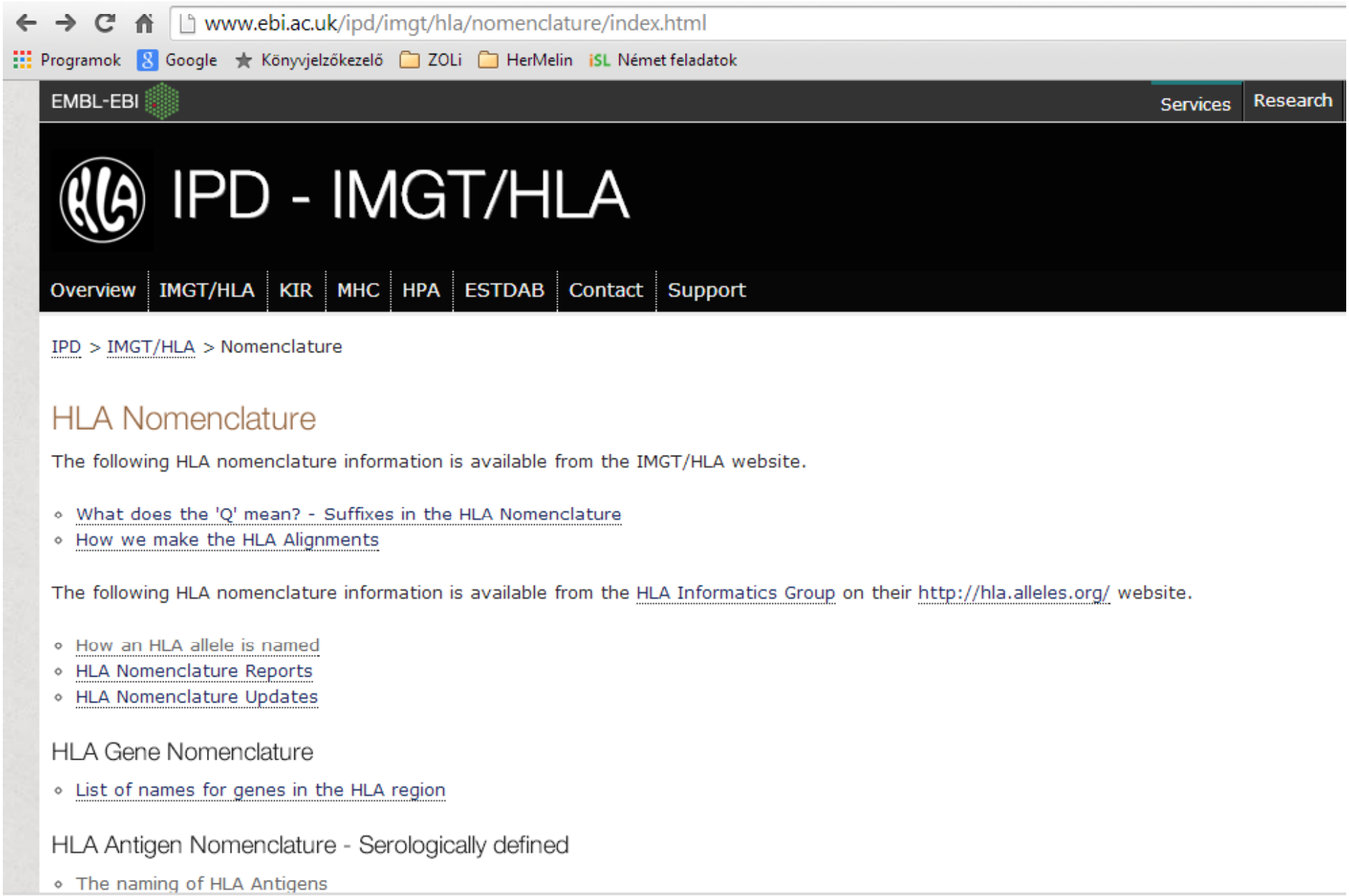
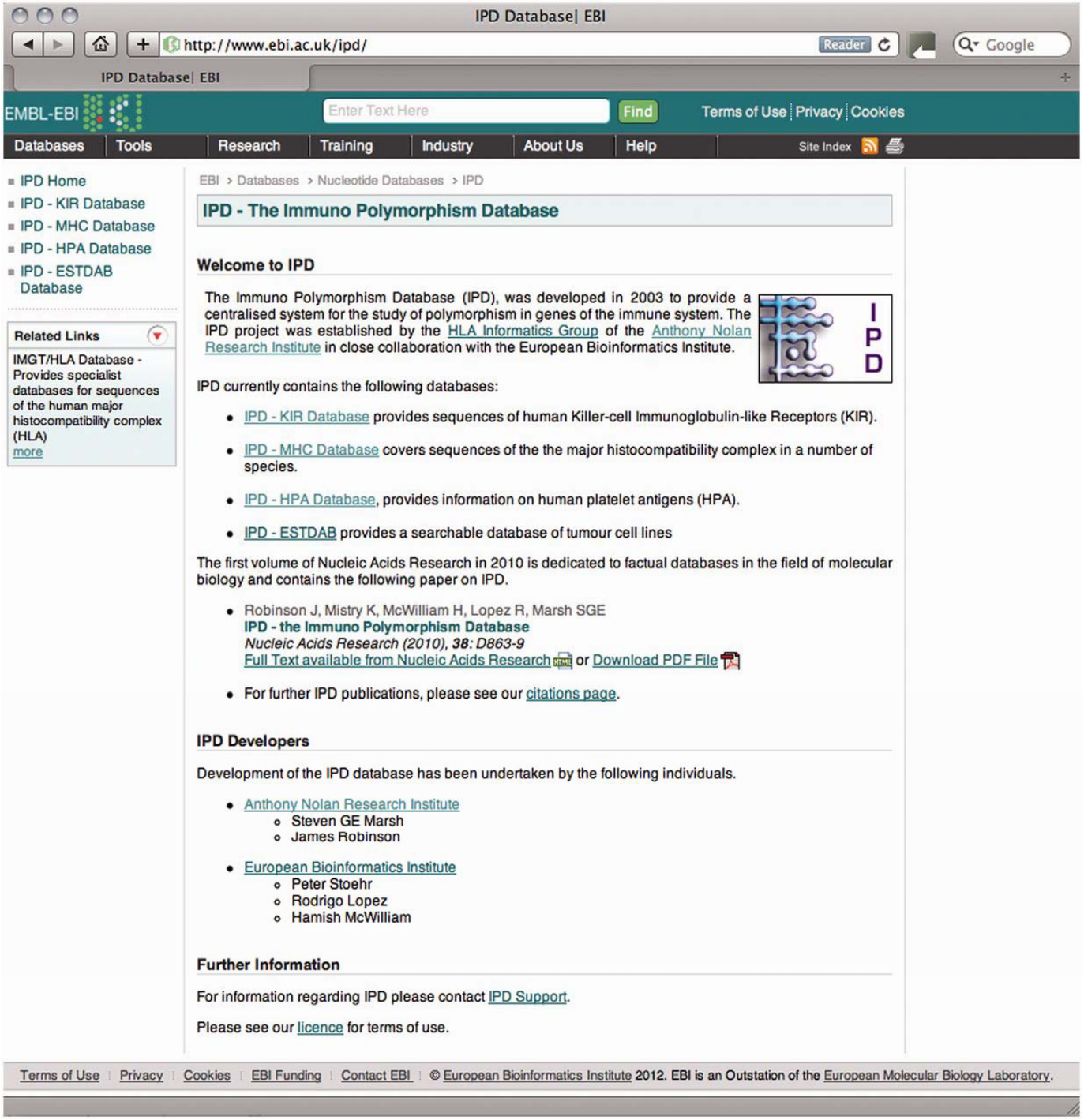
Immune Polymorphism Database

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IPD - KIR Database
IPD - MHC Database
IPD - HPA Database
IPD - ESTDAB Database
Related Links
IMGT/HLA Database - Provides specialist databases for sequences of the human major histocompatibility complex (HLA)
more
EBI > Databases > Nucleotide Databases > IPD
IPD - The Immuno Polymorphism Database
Welcome to IPD
The Immuno Polymorphism Database (IPD), was developed in 2003 to provide a centralised system for the study of polymorphism in genes of the immune system. The IPD project was established by the HLA Informatics Group of the Anthony Nolan Research Institute in close collaboration with the European Bioinformatics Institute.
IPD currently contains the following databases:
IPD - KIR Database provides sequences of human Killer-cell Immunoglobulin-like Receptors (KIR).
IPD - MHC Database covers sequences of the the major histocompatibility complex in a number of species.
IPD - HPA Database, provides information on human platelet antigens (HPA).
IPD - ESTDAB provides a searchable database of tumour cell lines
The first volume of Nucleic Acids Research in 2010 is dedicated to factual databases in the field of molecular biology and contains the following paper on IPD.
Robinson J, Mistry K, McWilliam H, Lopez R, Marsh SGE
IPD - the Immuno Polymorphism Database
Nucleic Acids Research (2010), 38: D863-9
Full Text available from Nucleic Acids Research or Download PDF File
For further IPD publications, please see our citations page.
IPD Developers
Development of the IPD database has been undertaken by the following individuals.
Anthony Nolan Research Institute
Steven GE Marsh
James Robinson
European Bioinformatics Institute
Peter Stoehr
Rodrigo Lopez
Hamish McWilliam
Further Information
For information regarding IPD please contact IPD Support.
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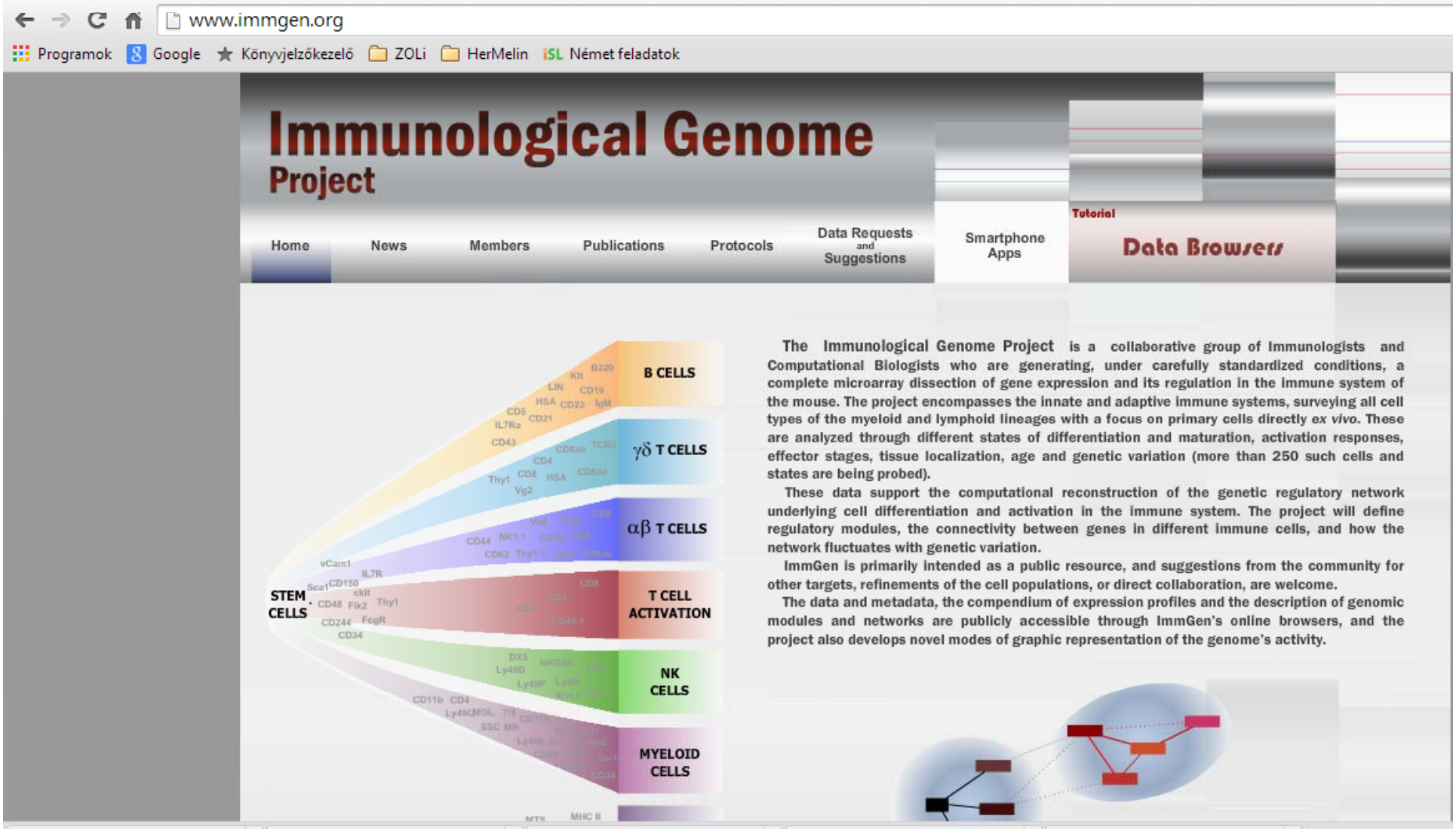
Immgen.org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Tutorial
Data Browsers
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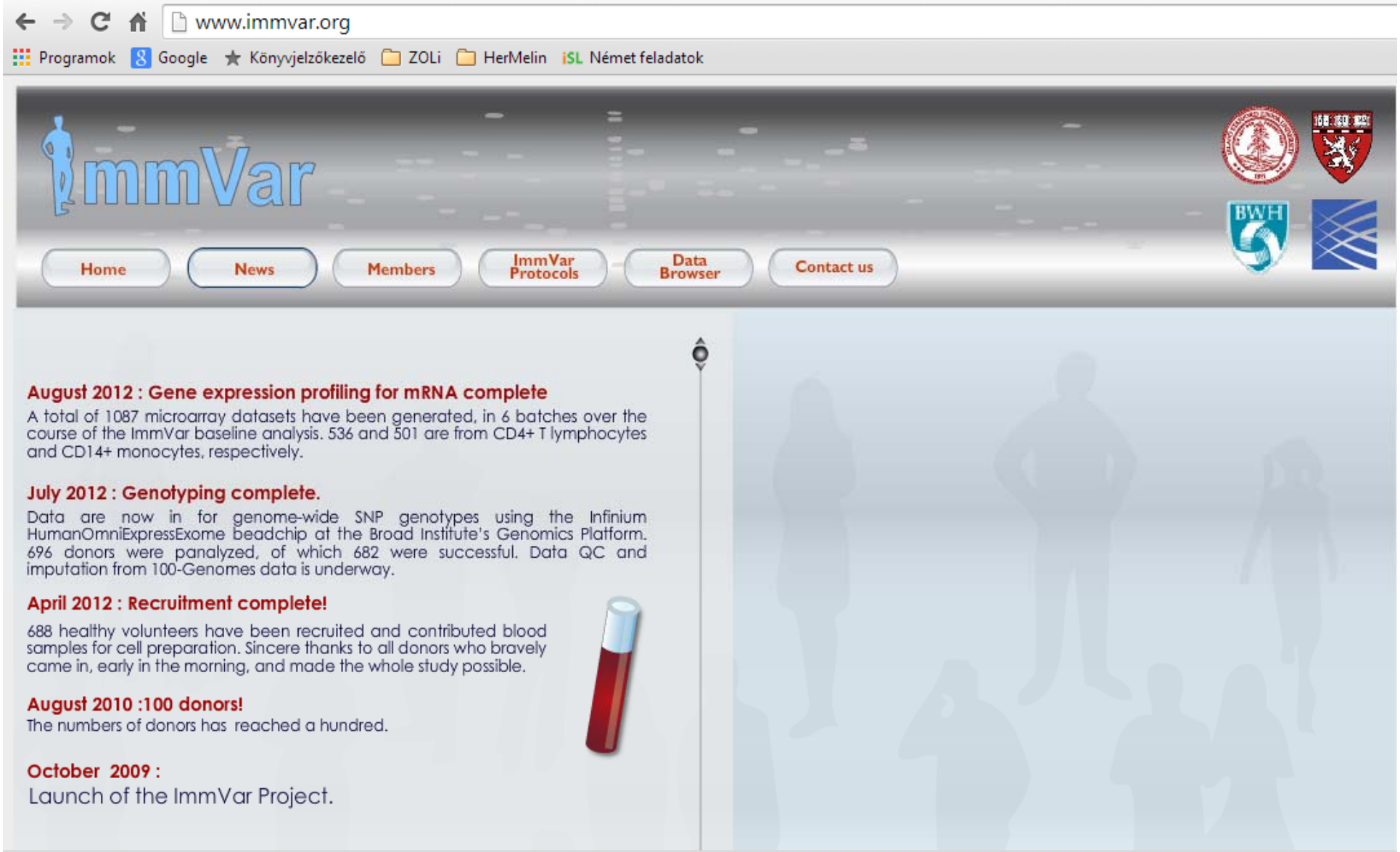
B CELLS
γδ T CELLS
αβ T CELLS
T CELL ACTIVATION
NK CELLS
MYELOID CELLS
The Immunological Genome Project is a collaborative group of Immunologists and Computational Biologists who are generating, under carefully standardized conditions, a complete microarray dissection of gene expression and its regulation in the immune system of the mouse. The project encompasses the innate and adaptive immune systems, surveying all cell types of the myeloid and lymphoid lineages with a focus on primary cells directly ex vivo. These are analyzed through different states of differentiation and maturation, activation responses, effector stages, tissue localization, age and genetic variation (more than 250 such cells and states are being probed).
These data support the computational reconstruction of the genetic regulatory network underlying cell differentiation and activation in the immune system. The project will define regulatory modules, the connectivity between genes in different immune cells, and how the network fluctuates with genetic variation.
ImmGen is primarily intended as a public resource, and suggestions from the community for other targets, refinements of the cell populations, or direct collaboration, are welcome.
The data and metadata, the compendium of expression profiles and the description of genomic modules and networks are publicly accessible through ImmGen's online browsers, and the project also develops novel modes of graphic representation of the genome's activity.

Immvar.org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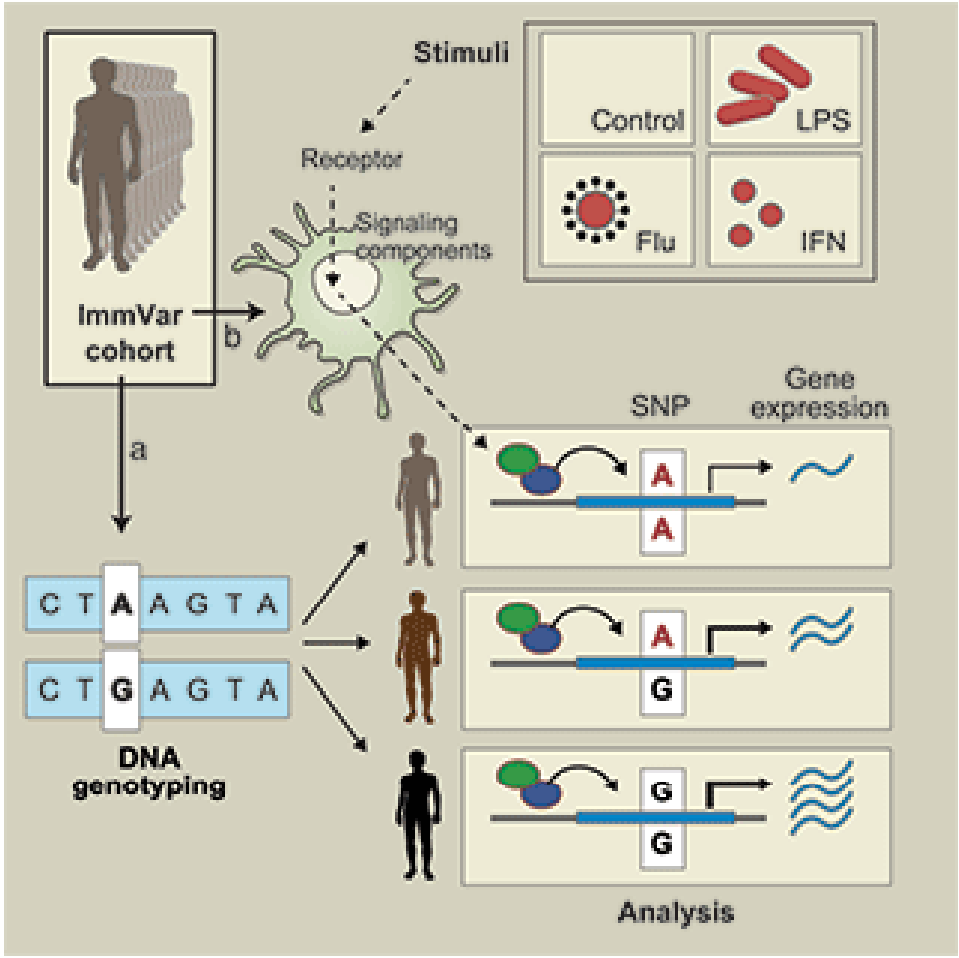
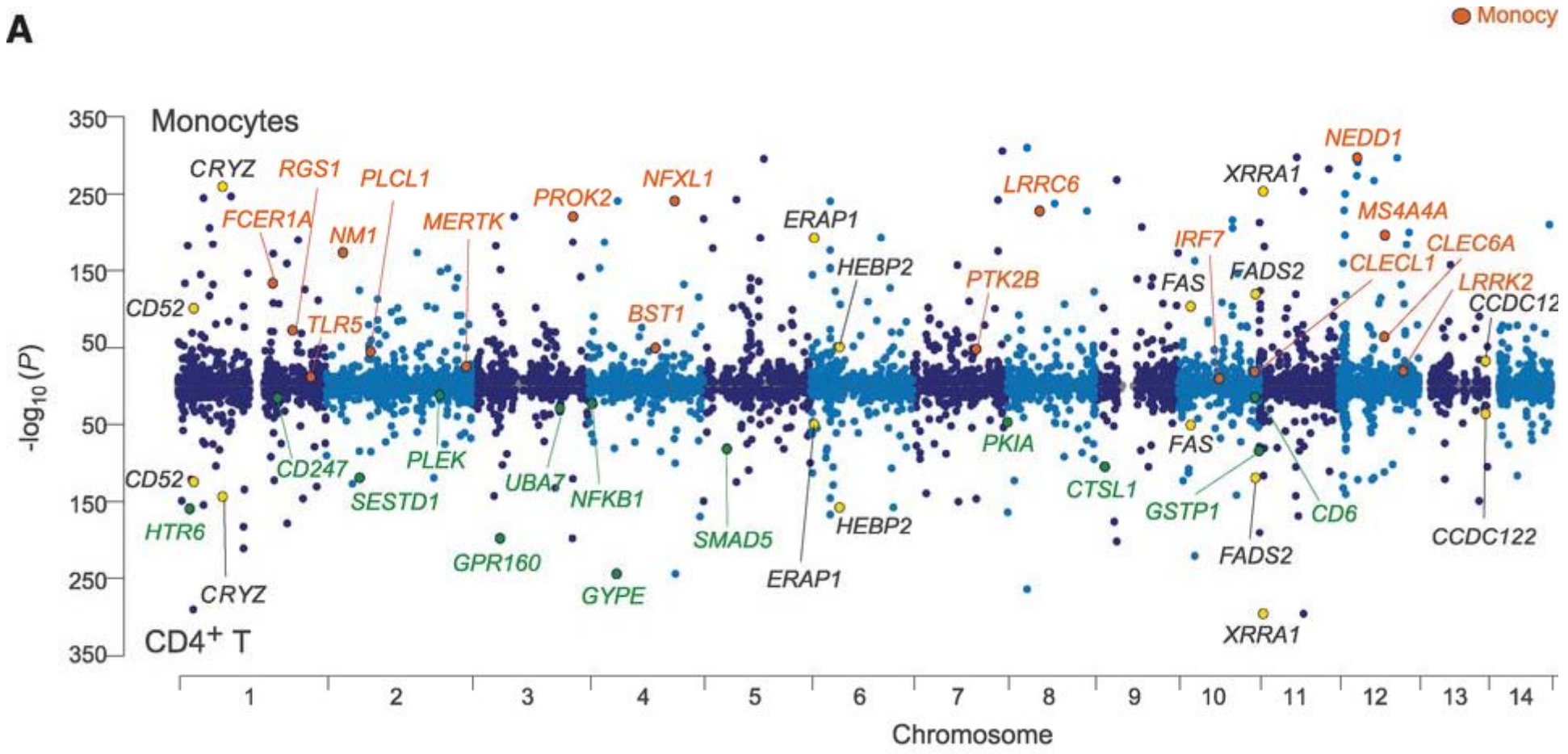
August 2012 : Gene expression profiling for mRNA complete
A total of 1087 microarray datasets have been generated, in 6 batches over the course of the ImmVar baseline analysis. 536 and 501 are from CD4+ T lymphocytes and CD14+ monocytes, respectively.
July 2012 : Genotyping complete.
Data are now in for genome-wide SNP genotypes using the Infinium HumanOmniExpressExome beadchip at the Broad Institute's Genomics Platform. 696 donors were panalyzed, of which 682 were successful. Data QC and imputation from 100-Genomes data is underway.
April 2012 : Recruitment complete!
688 healthy volunteers have been recruited and contributed blood samples for cell preparation. Sincere thanks to all donors who bravely came in, early in the morning, and made the whole study possible.
August 2010 :100 donors!
The numbers of donors has reached a hundred.
October 2009 :
Launch of the ImmVar Project.

- **Identifying the genetic basis of variability in the host response to pathogens.** A cohort of 534 individuals donated blood for (a) genotyping of common DNA variants and (b) isolation of immune DCs. DCs were stimulated with viral and bacterial components, and the variability in individuals' gene expression responses was mapped to specific DNA variants, which were then shown to affect binding of particular transcription factors.
- Science 7 March 2014: Vol. 343 no. 6175




A
Monocy
Monocytes
CD4+ T
-log10 (P)
350
250
150
50
50
150
250
350
CRYZ
RGS1
PLCL1
FCER1A
NM1
MERTK
PROK2
NFXL1
ERAP1
LRRC6
XRRA1
NEDD1
MS4A4A
IRF7
CLEC6A
CLECL1
LRRK2
CCDC12
HEBP2
PTK2B
FAS
FADS2
CD52
TLR5
BST1
CD247
PLEK
UBA7
NFKB1
PKIA
CTSL1
GSTP1
CD6
HTR6
SESTD1
SMAD5
HEBP2
GPR160
GYPE
ERAP1
FADS2
CCDC122
CRYZ
XRRA1
1
2
3
4
5
6
7
8
9
10
11
12
13
14
Chromosome

- Köszönöm a figyelmet!