

Allogeenne vereloome tüvirakkude siirdamine

Ain Kaare

Tallinna hematoloogia 30, oktoober 2014



Tartu Ülikooli Kliinikum

Vereloometüvirakkude siirdamine

- Autoloogne
- Allogenne
 - Sugulasdoonor
 - Registridoonor



Vereloometüvirakkude siirdamine

- Luuüdi
- Perifeerse vere
- Platsentaar- ja nabaväädi veri



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Hematopoietic stem cell transplantation in Estonia

1993 first autoBMTt

1996 first autoPBSCt

1995 first alloBMTt

2000 first alloPBSCt

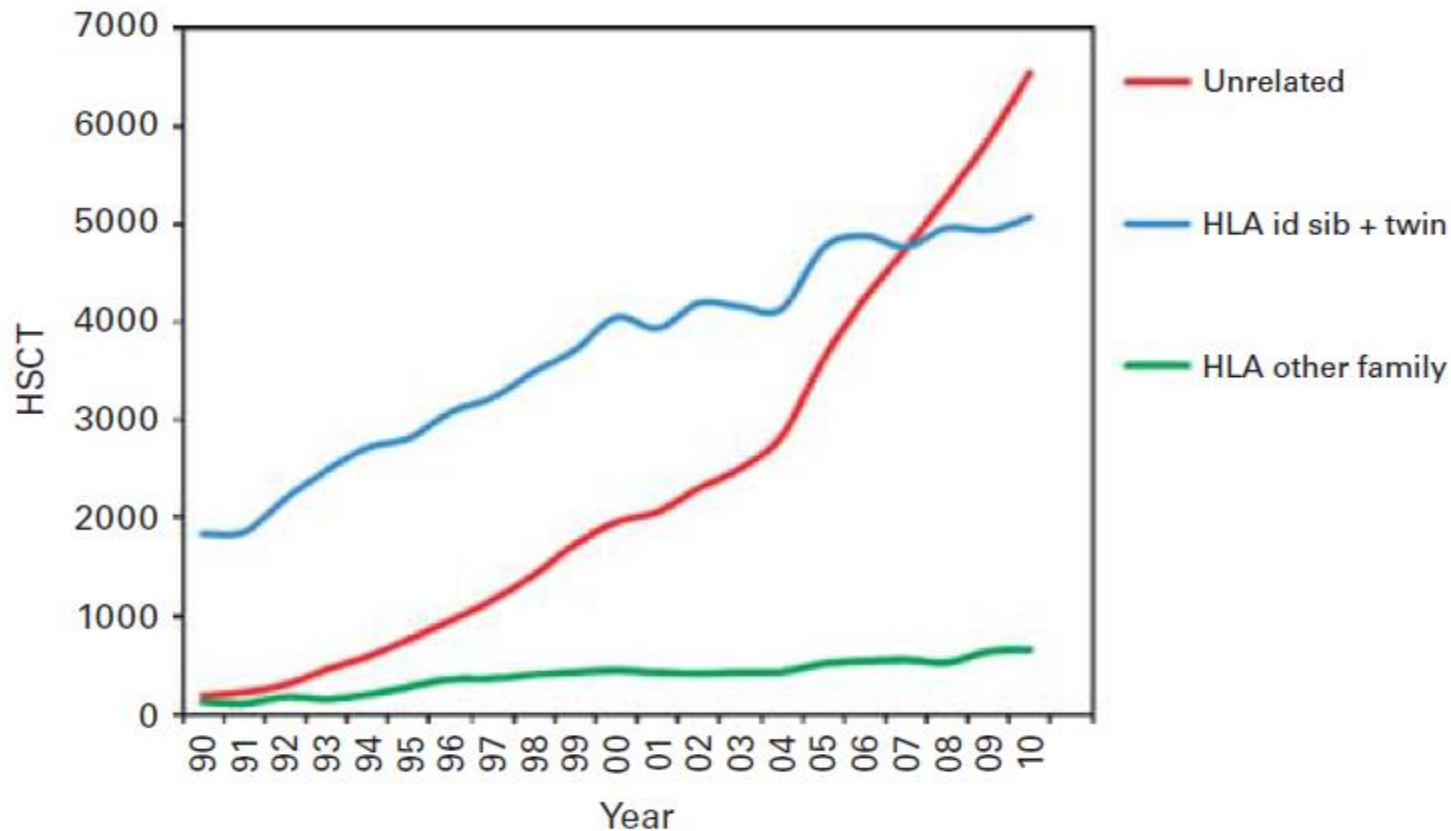
2005 first unrelated allogenic transplantation

2006 first autoPBSCt in Tallinn



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Allogreensete siirdamiste arv



Bone Marrow Transplantation (2012) 47, 906–923



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Vereloome tüvirakkude siirdamiste arv Euroopas 2012



EBMT Activity Survey in 2012: Donor type and stem cell source: all transplants

Donor type	Stem Cell Source			Total
	BM	PBSC	Cord	
Allogeneic total	3476	11117	758	15351
HLA-id	1570	4236	58	5864
HLA-nid	445	766	6	1217
Syngeneic	7	39	0	46
Unrelated	1454	6076	694	8224
Autologous	176	22285	6	22467

Baldomero: Transplant Activity
Survey Dec 2013

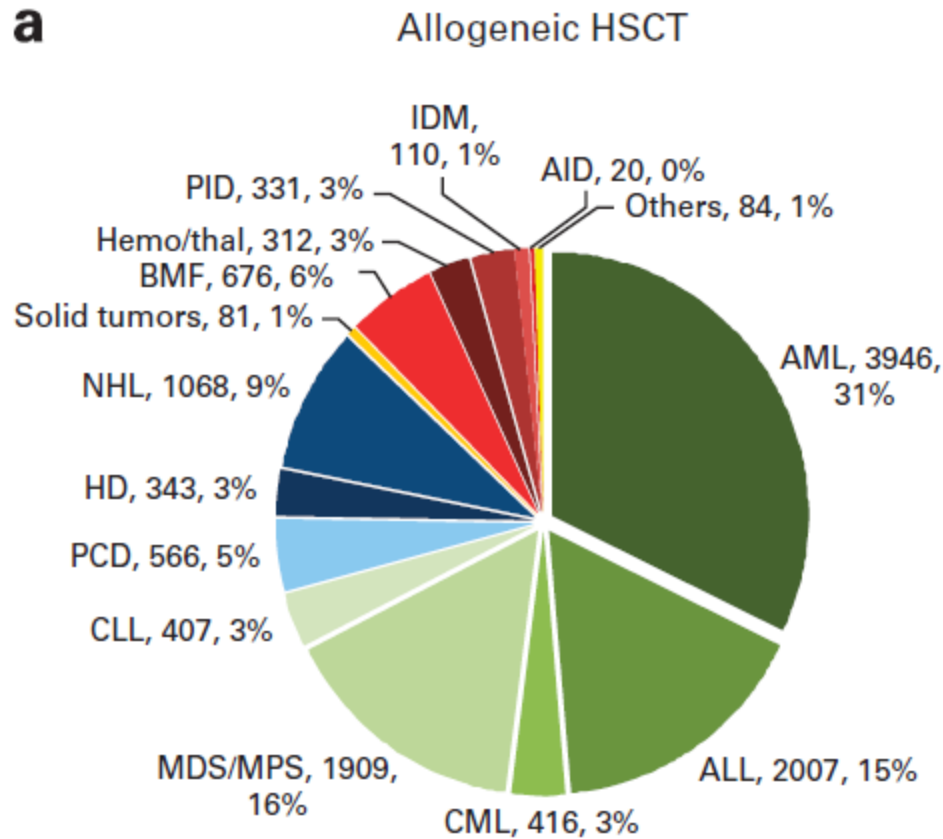
The European Group for Blood and Marrow Transplantation³

www.ebmt.org



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Näidustused

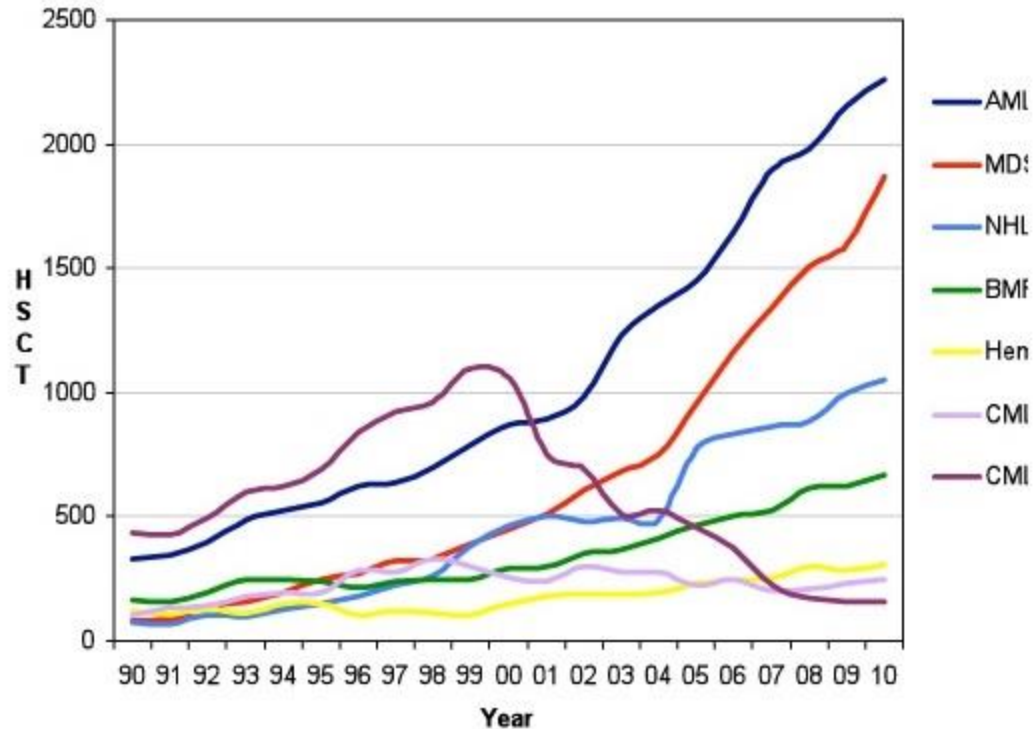


Bone Marrow Transplantation (2012) 47, 906–923



Tartu Ülikooli Kliinikum

Allogeense vereloome tüvirakkude siirdamiste arv Euroopas 1990-2010

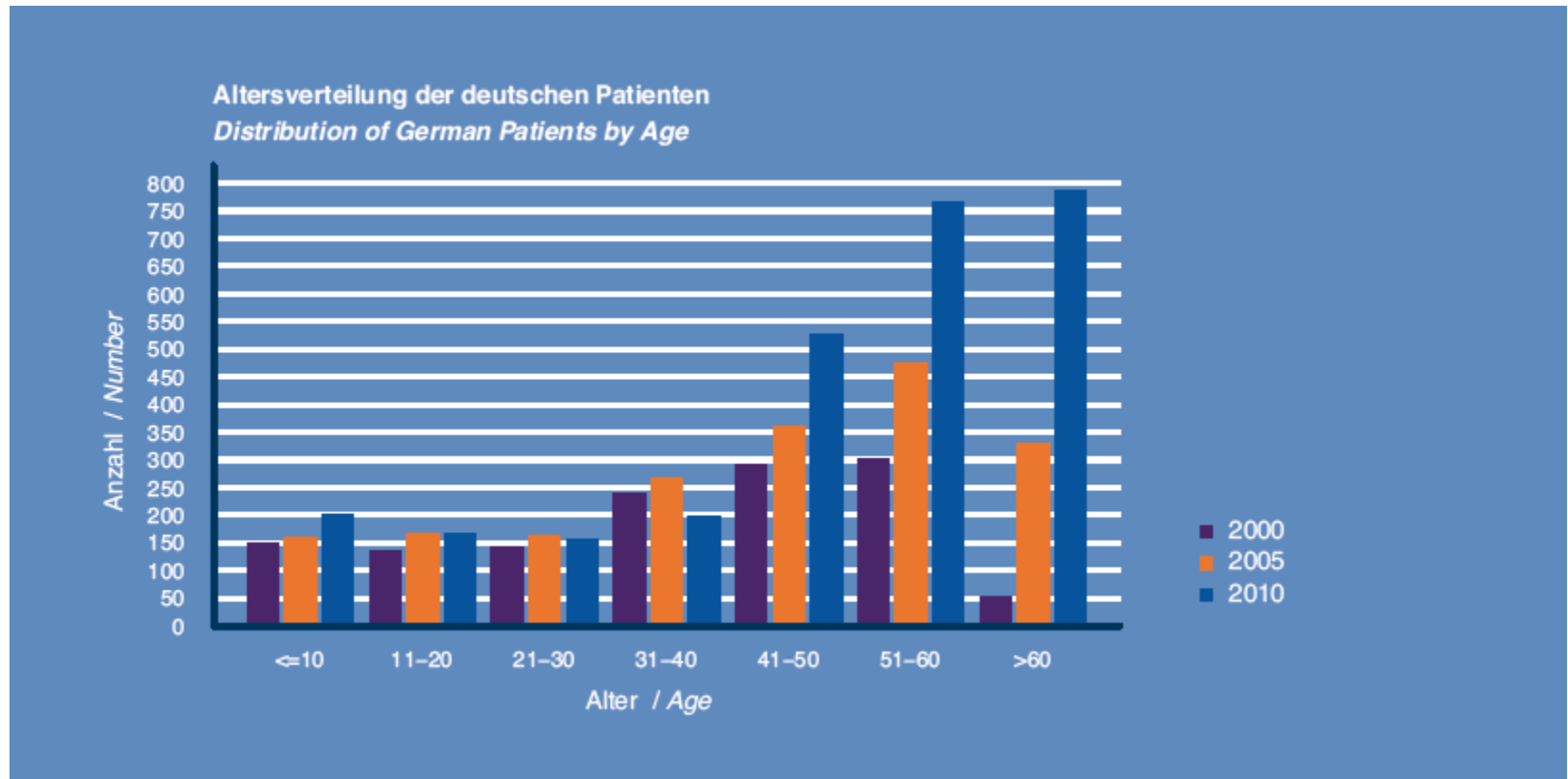


Bone Marrow Transplantation (2012) 47, 906–923



Tartu Ülikooli Kliinikum

Allogeense vereloome tüvirakkude siirdamise retsipientide vanuseline jaotus Saksamaal 2000-2010

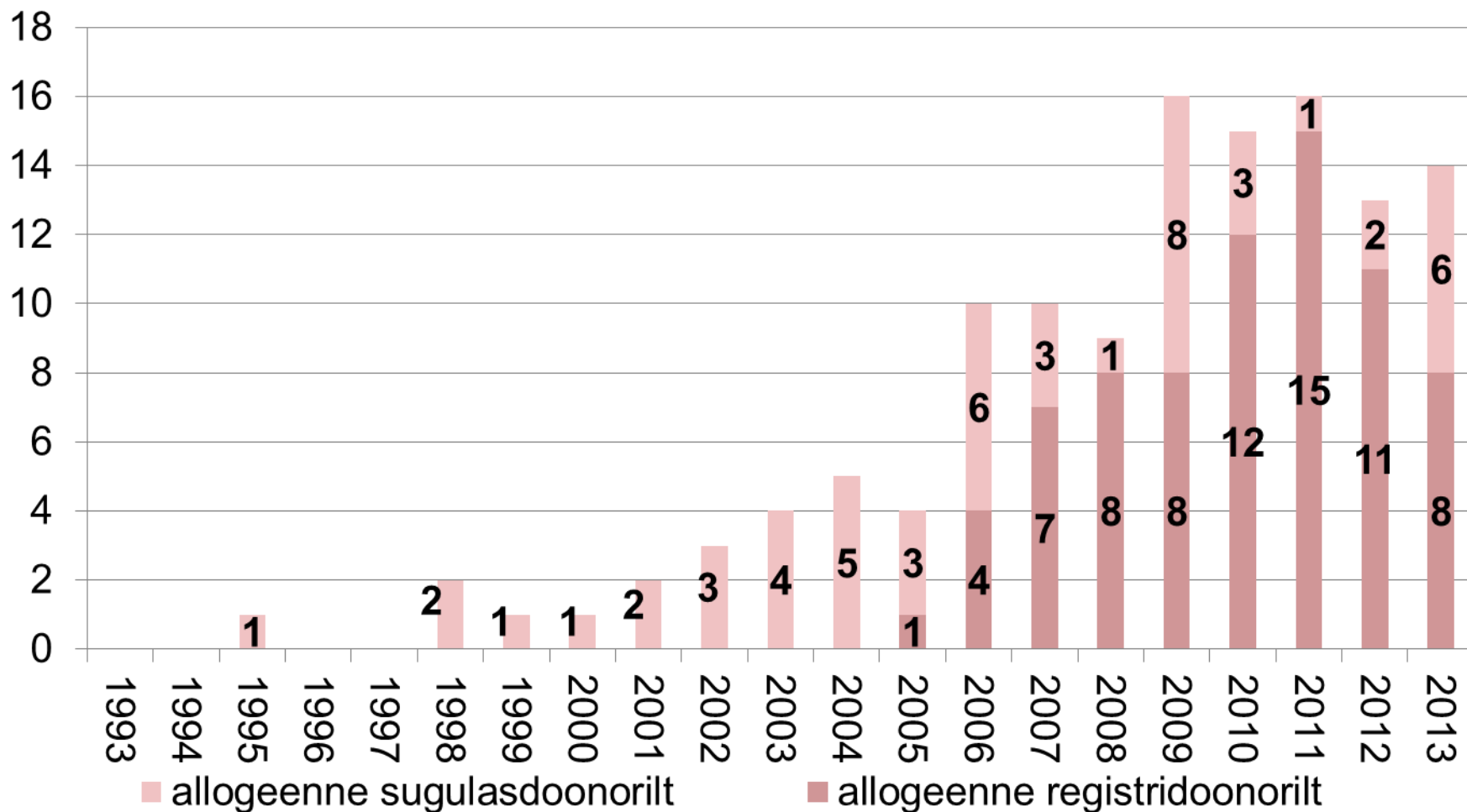


ZKDR (Zentrales Knochenmarkspender Register Deutschland) 2009/2010



Tartu Ülikooli Kliinikum

Vereloome tüvirakkude siirdamine Eestis 1993- 2013

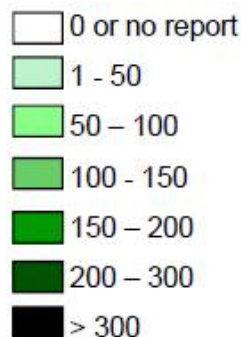


Siirdamiste arv Euroopas

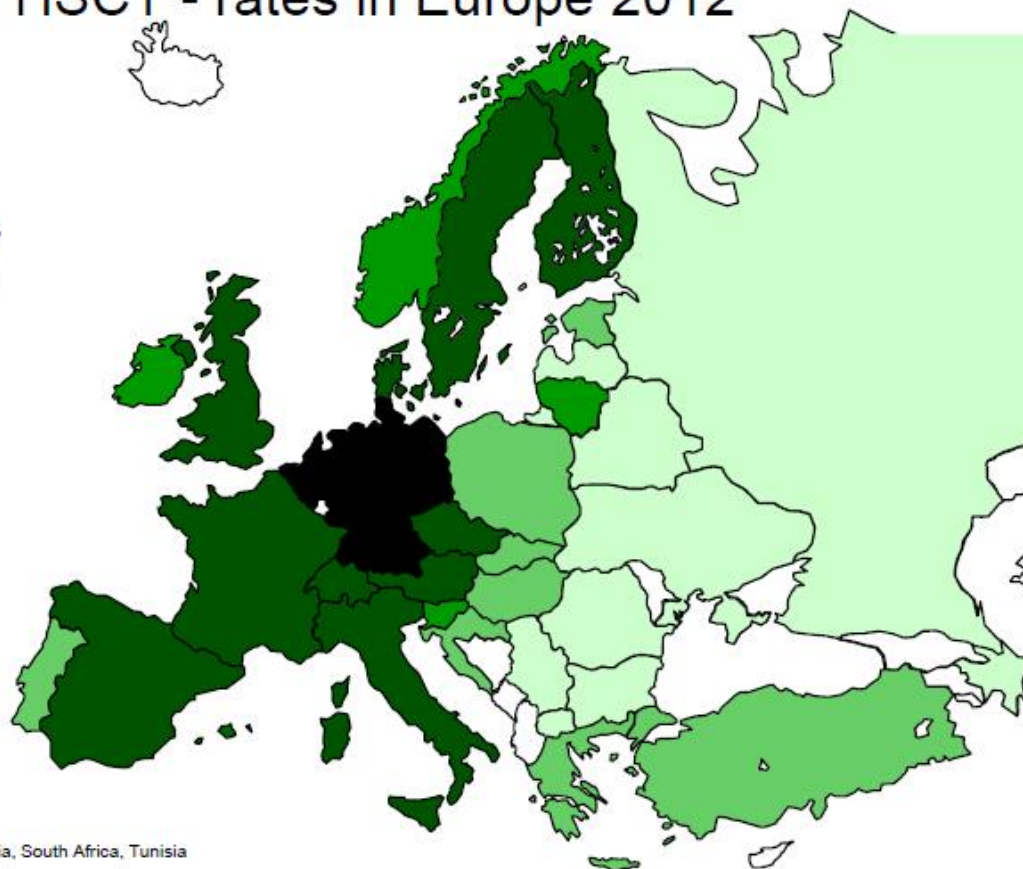


HSCT - rates in Europe 2012

N. allogeneic transplants
per 10 million population



Algeria, Iran, Kazakhstan, Nigeria, South Africa, Tunisia
Jordan, Lebanon, Saudi Arabia
Israel



JR. Passweg, H. Baldomero et al, BMT 2014

www.ebmt.org

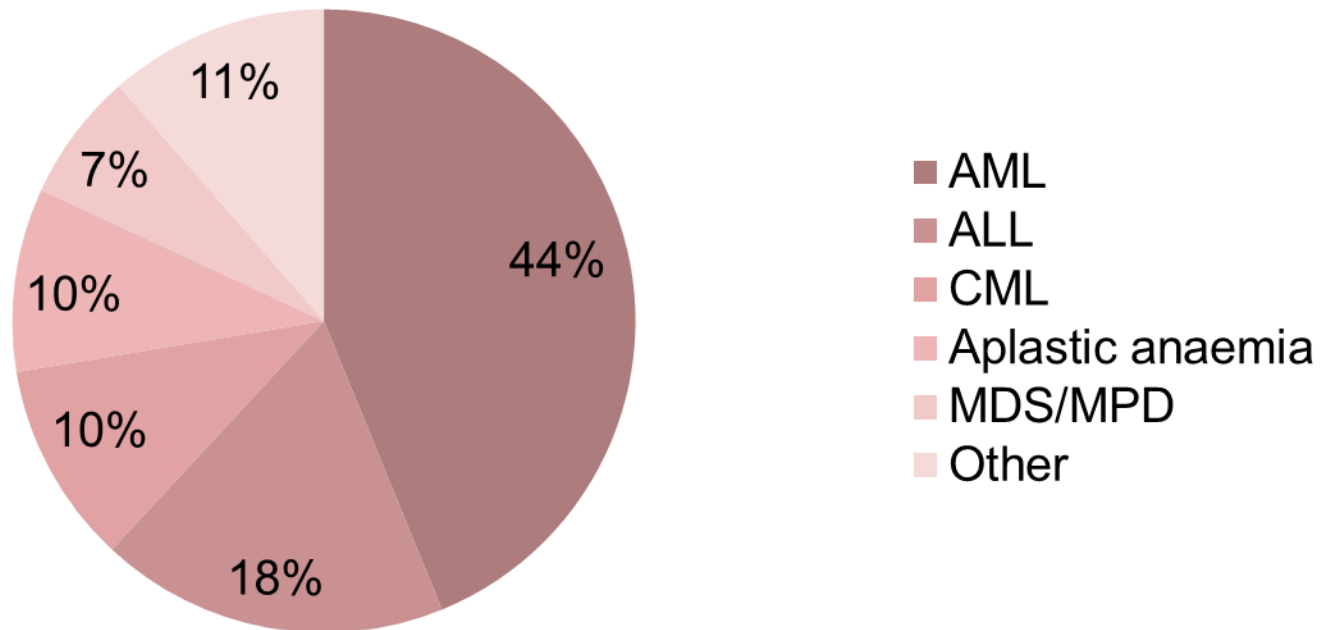
Baldomero: Transplant Activity
Survey Dec 2013

The European Group for Blood and Marrow Transplantation

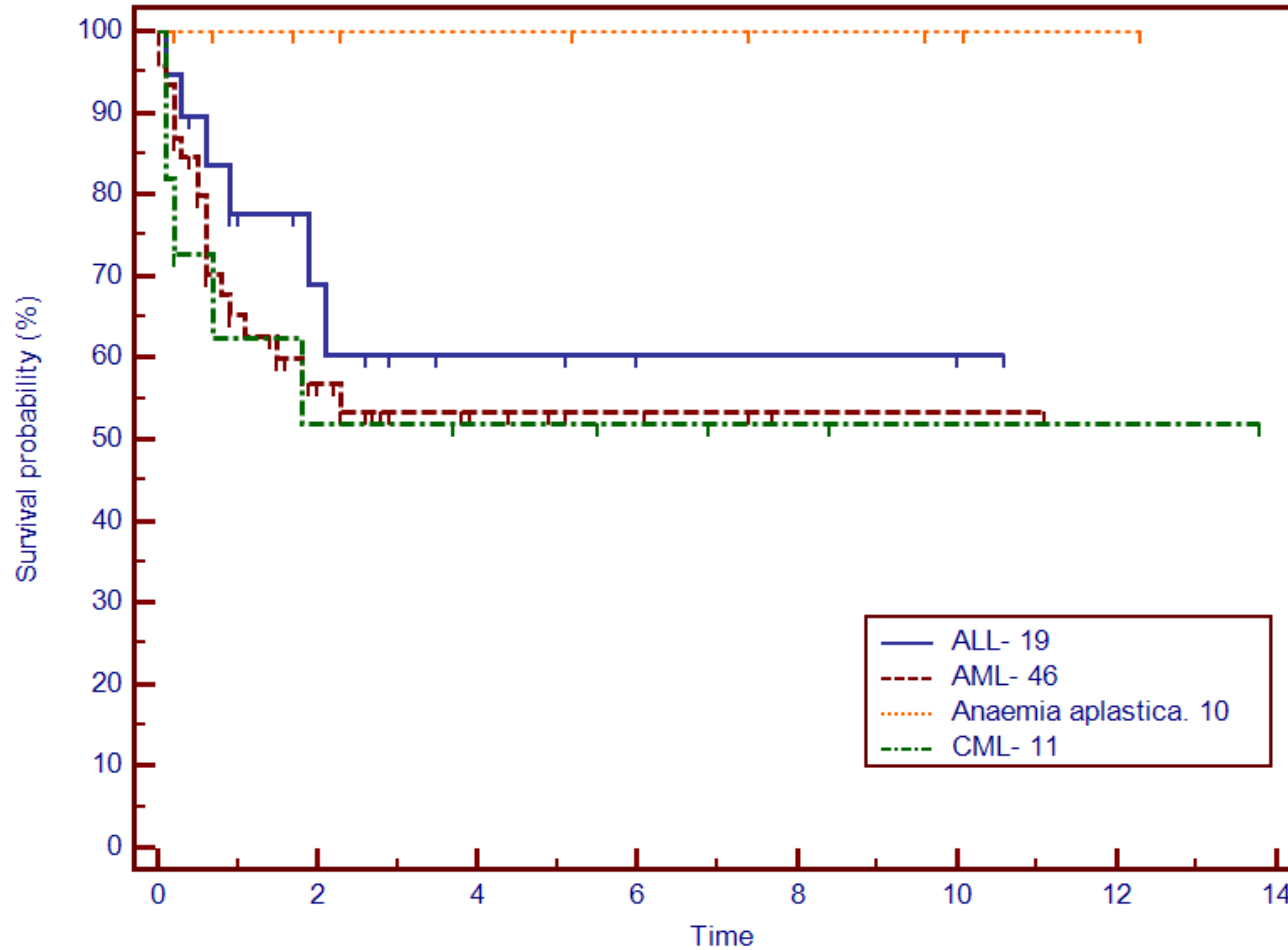


Tartu Ülikooli Kliinikum

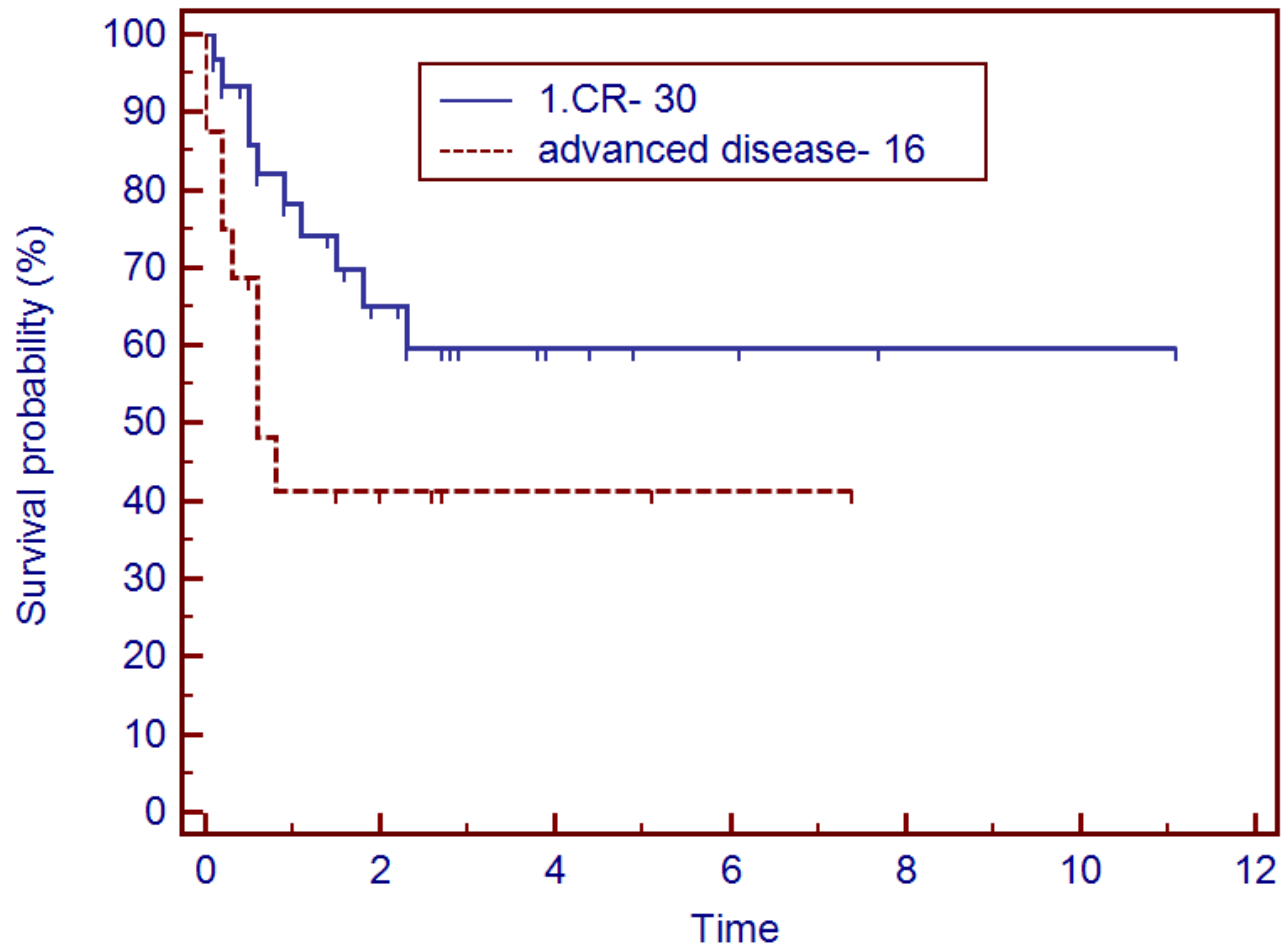
Näidustused Eestis



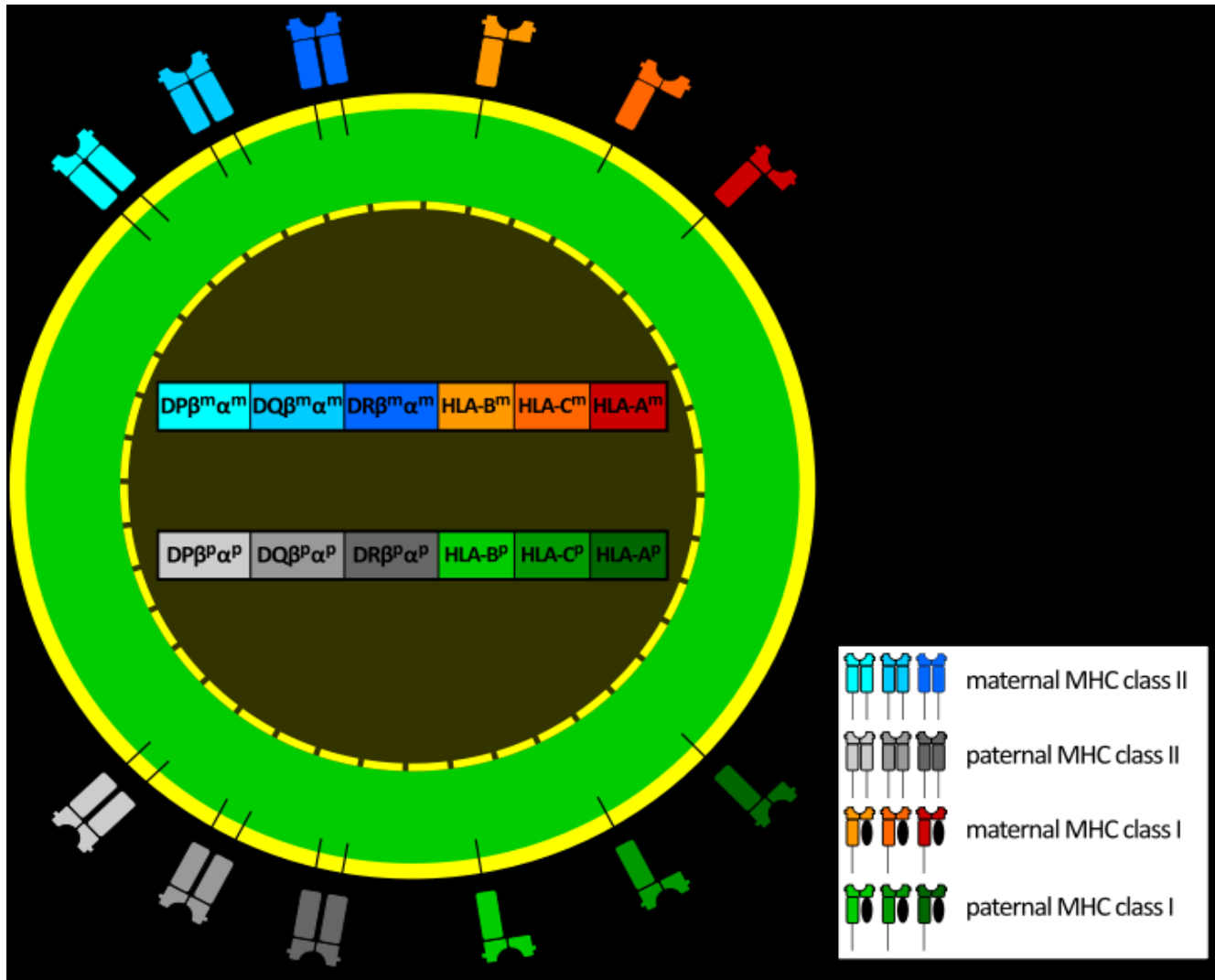
Overall survival by disease group



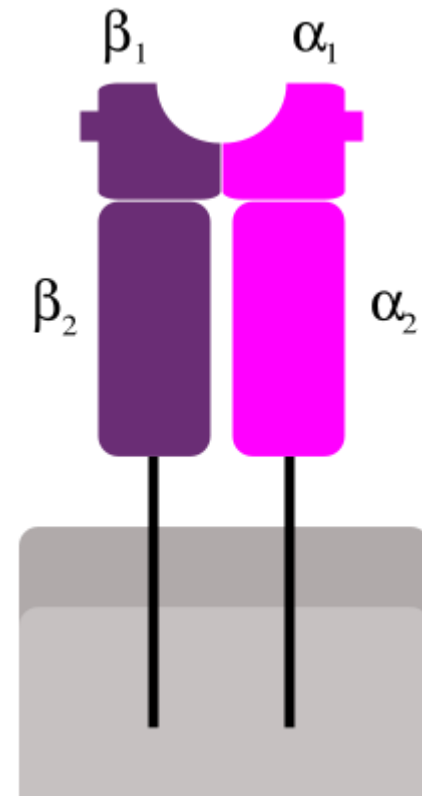
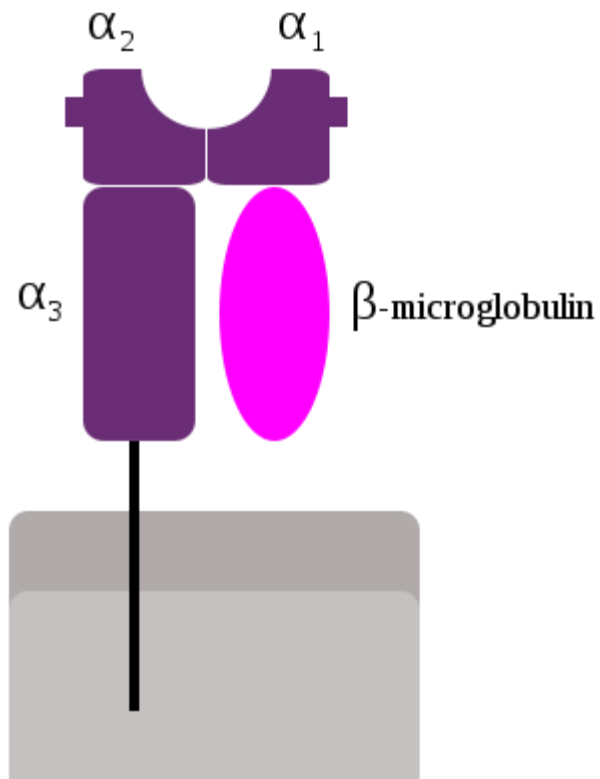
Overall survival of AML patients



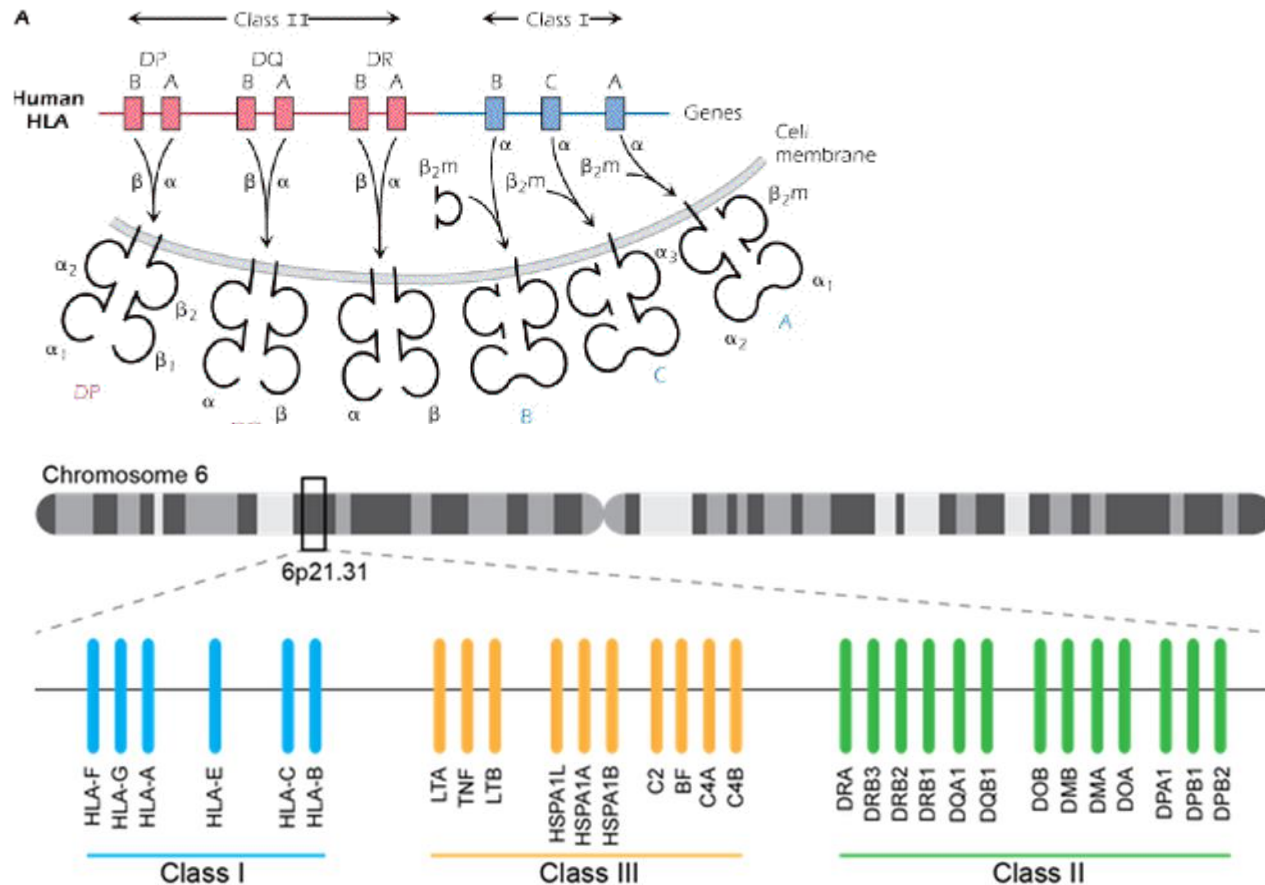
HLA class I and class II antigens



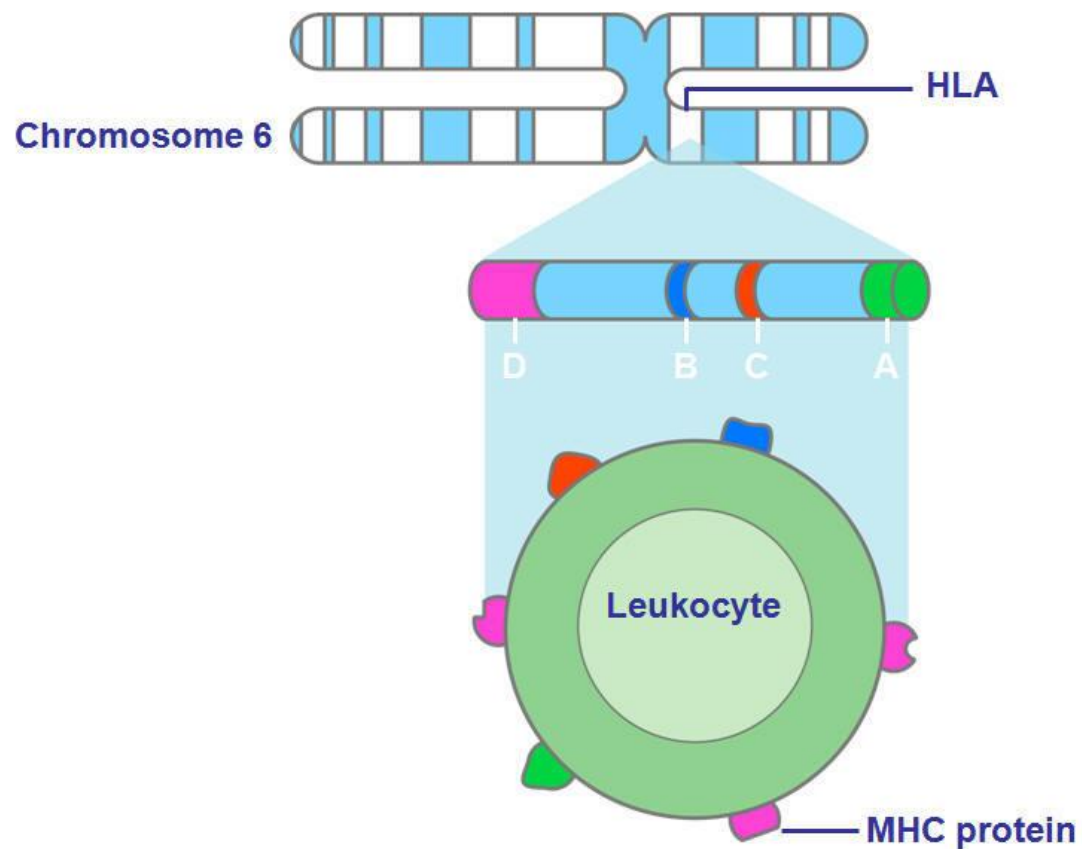
HLA molekulid

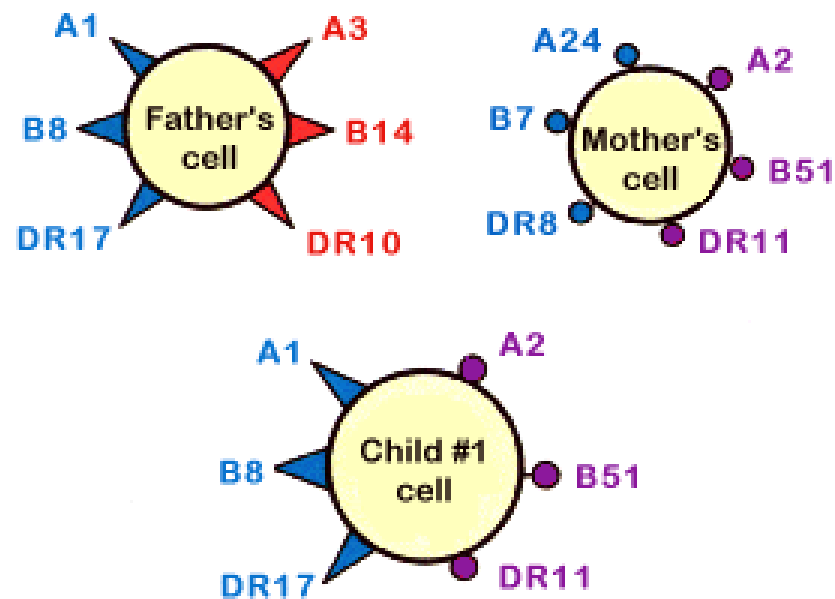


HLA geenid



HLA geenid





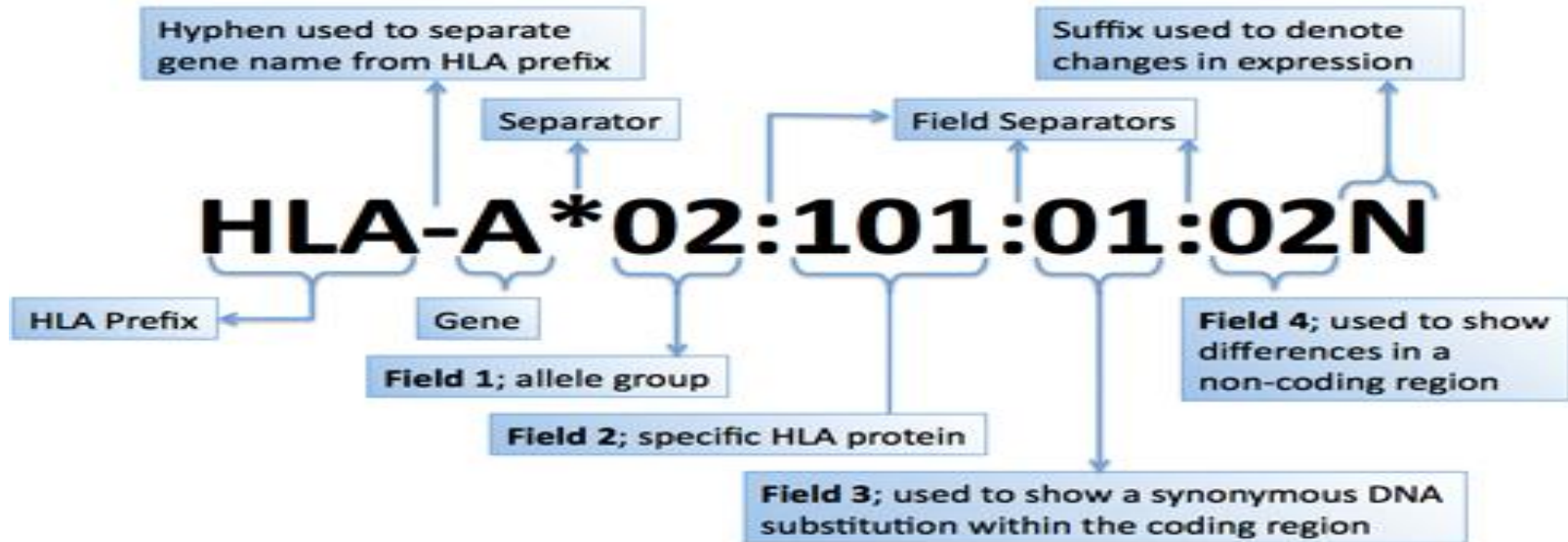
HLA pärandumine

		A*01:01;03:01
		B*08:01;07:02
		C*07:01;07:02
		DRB1*03:01;15:01
		DQB1*02:01;06:02
		DPB1*01:01;02:01

		A*02:01;31:01
		B*07:02;40:01
		C*07:02;03:04
		DRB1*15:01;04:04
		DQB1*06:02;03:02
		DPB1*03:01;04:01

		A*01:01;03:01			A*01:01;31:01			A*03:01;03:01			A*03:01;31:01
		B*08:01;07:02			B*08:01;40:01			B*07:02;07:02			B*07:02;40:01
		C*07:01;07:02			C*07:01;03:04			C*07:02;07:02			C*07:02;03:04
		DRB1*03:01;15:01			DRB1*03:01;04:04			DRB1*15:01;15:01			DRB1*15:01;04:04
		DQB1*02:01;06:02			DQB1*02:01;03:02			DQB1*06:02;06:02			DQB1*06:02;03:02
		DPB1*01:01;03:01			DPB1*01:01;04:01			DPB1*02:01;03:01			DPB1*02:01;04:01

HLA nomenclature



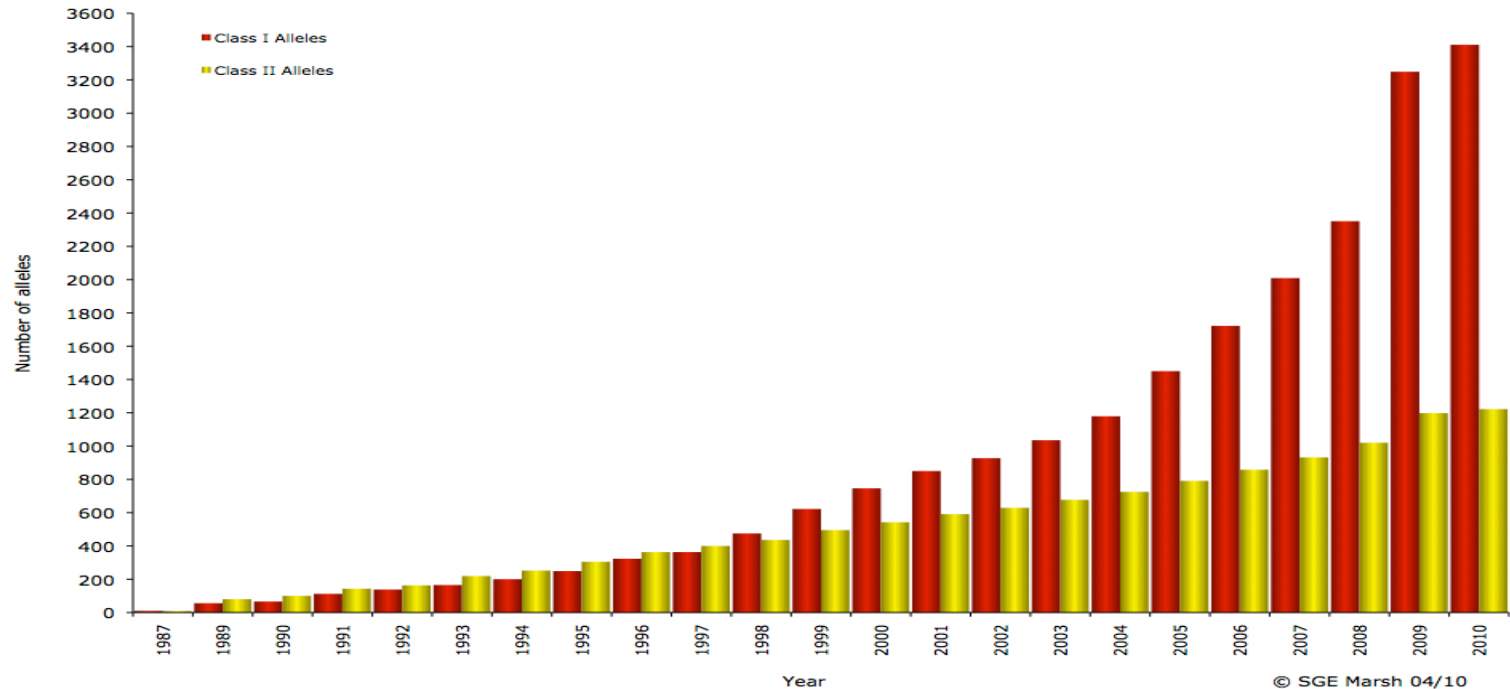
© SGE Marsh 04/10

Nomenclature	Indicates
<i>HLA-A</i>	a particular HLA locus i.e. A
<i>HLA-A*02</i>	a group of alleles which encode the A 02 antigen (one of from 02:01 to 02:199)
<i>HLA-A*02:101</i>	a specific HLA allele



Tartu Ülikooli Kliinikum

Erinevate HLA alleelide arv



HLA geenid on kõige polümorfsem lookus inimese genoomis, tänaseks on identifitseeritud üle 10000 erineva alleeli



Tartu Ülikooli Kliinikum

Alleel	arv
A	2579
B	3285
C	2133
DRB1	1411
DQB1	509
DPB1	248

Potentsiaalsete kombinatsioonide arv $3,2 \times 10^{18}$

Maa elanike arv $7,1 \times 10^9$



Seondumise ebavõrdsus (linkage disequilibrium)

- Erinevate võimalike HLA A;B,C, DRB1;DRQB1;DPB1 kombinatsioonide arv ületab maakera elanike arvu



Seondumise ebavõrdsus (linkage disequilibrium)

Kuid

- Erinevate alleelide esinemissagedus populatsioonis on erinev (HLA DRB1*13:03 on väga harv)
- Mõningad kombinatsioonid esinevad sagedamini kui teised (A1, B8 ja DR3 on väga sage kuid A1, B8, DR9 on väga harv)
- Esineb rassiline erinevus erinevate kombinatsioonide esinemissagedusel

HLA A*01:01 B*08:01 C*07:01 DRB1*03:01 DQB1*02:01
haplotüübi esinemissagedus europiidse rassi seas on 7,8%

HLA A*30:01 B*42:01 C*17:01 DRB1*03:02 DQB1*04:02
haplotüübi esinemissagedus afro-ameeriklaste seas on 1,7%

- Mõningad kombinatsioonid esinevad väga harva ja mõnede esinemissagedus on 0- HLA A*30:01 B*42:01 C*17:01 DRB1*03:02 DQB1*04:02 haplotüüpi europiidse rassi seas ei esine



HLA ABCDRDQ esinemissagedus

	A	B	C	D	E	F	G	H	I	J	K	L	M
1	A	C	B	DRB1	DQB1	EUR_freq	EUR_rank	AFA_freq	AFA_rank	API_freq	API_rank	HIS_freq	HIS_rank
2	0101g	0701g	0801g	0301	0201g	0,07792	1	0,01119	4	0,00108	462	0,03125	2
3	0301g	0702	0702g	1501	0602	0,03544	2	0,00559	9	0,00000	NA	0,01562	3
4	0201g	0501g	4402g	0401	0301g	0,02498	3	0,00000	NA	0,00000	NA	0,00000	NA
5	0201g	0702	0702g	1501	0602	0,02430	4	0,00000	NA	0,00000	NA	0,00000	NA
6	2902	1601	4403	0701	0201g	0,01908	5	0,00336	43	0,00000	NA	0,03277	1
7	0201g	0304	1501g	0401	0302	0,01290	6	0,00000	NA	0,00000	NA	0,00000	NA
8	0101g	0602	5701	0701	0303	0,01277	7	0,00224	57	0,01085	9	0,00625	12
9	0301g	0401g	3501g	0101	0501	0,01272	8	0,00000	NA	0,00027	689	0,00937	6
10	0201g	0701g	0801g	0301	0201g	0,01075	9	0,00000	NA	0,00000	NA	0,00000	NA
11	0201g	0304	4001g	1302	0604	0,00971	10	0,00000	NA	0,00000	NA	0,00000	NA
12	3001	0602	1302	0701	0201g	0,00948	11	0,00000	NA	0,00759	10	0,00156	150
13	2402g	0702	0702g	1501	0602	0,00852	12	0,00224	71	0,00217	61	0,00000	NA
14	0201g	0602	5701	0701	0303	0,00846	13	0,00000	NA	0,00000	NA	0,00000	NA
15	1101g	0401g	3501g	0101	0501	0,00786	14	0,00000	NA	0,00000	NA	0,00156	276
16	3301	0802	1402	0102	0501	0,00728	15	0,00224	117	0,00000	NA	0,00937	5
17	2301g	0401g	4403	0701	0201g	0,00691	16	0,00112	373	0,00000	NA	0,00781	7
18	0201g	0501g	4402g	1501	0602	0,00616	17	0,00000	NA	0,00000	NA	0,00000	NA
19	3101	0304	4001g	0404	0302	0,00608	18	0,00000	NA	0,00027	859	0,00469	26
20	0201g	0602	1302	0701	0201g	0,00602	19	0,00000	NA	0,00000	NA	0,00000	NA

HLA ABCDRDQ esinemissagedus

	A	B	C	D	E	F	G	H	I	J	K	L	M
1	A	C	B	DRB1	DQB1	EUR_freq	EUR_rank	AFA_freq	AFA_rank	API_freq	API_rank	HIS_freq	HIS_rank
4703	3001	1701g	4101	0901	0303	0,00000	NA	0,00000	NA	0,00000	NA	0,00039	727
4704	3001	1701g	4101	1001	0501	0,00000	NA	0,00000	NA	0,00000	NA	0,00039	945
4705	3001	1701g	4102	0301	0201g	0,00000	NA	0,00000	NA	0,00000	NA	0,00039	519
4706	3001	1701g	4102	1501	0602	0,00000	NA	0,00000	NA	0,00000	NA	0,00039	733
4707	3001	1701g	4201	0102	0501	0,00000	NA	0,00224	75	0,00000	NA	0,00000	NA
4708	3001	1701g	4201	0301	0201g	0,00000	NA	0,00112	243	0,00000	NA	0,00000	NA
4709	3001	1701g	4201	0302	0402	0,00000	NA	0,01689	1	0,00000	NA	0,00000	NA
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4711	3001	1701g	4201	0804	0301g	0,00000	NA	0,00559	10	0,00000	NA	0,00000	NA
4712	3001	1701g	4201	1102	0301g	0,00000	NA	0,00131	133	0,00000	NA	0,00000	NA
4713	3001	1701g	4201	1201g	0501	0,00000	NA	0,00382	24	0,00000	NA	0,00000	NA
4714	3001	1701g	4201	1302	0609	0,00000	NA	0,00112	406	0,00000	NA	0,00000	NA
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4716	3001	1701g	4201	1401g	0503	0,00000	NA	0,00112	163	0,00000	NA	0,00000	NA
4717	3001	1701g	4201	1503	0602	0,00000	NA	0,00120	136	0,00000	NA	0,00000	NA
4718	3001	1701g	4202	0804	0301g	0,00000	NA	0,00112	323	0,00000	NA	0,00000	NA
4719	3001	1701g	4202	1503	0602	0,00000	NA	0,00112	339	0,00000	NA	0,00000	NA
4720	3001	1701g	4403	0701	0201g	0,00000	NA	0,00028	877	0,00000	NA	0,00000	NA
4721	3001	1701g	4403	1101	0301g	0,00000	NA	0,00028	590	0,00000	NA	0,00000	NA



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Recipient ID: 002

Extended sorting on DRB1

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0101	0801	07XX	0301	02XX	USA11	3*01XX	
0101	0801	07XX	0301		USA11	3*0101	
0101	0801	0701	0301	0201	USA11	3*0101	
0101	0801		0301	0201	PL4 1		
0101	0801		0301		PL3 2		
0101	0801		0301		PL 1		
0101	0801	07XX	0301	0201	NL 2	3*0101	
0101	0801	07AAS 07AFM	0301	0201	NL 1		
0101	0801	07AAS	0301	0201	NL 1	3*0101	
0101	0801	0701	0301	0201	USA11	3*0101	
0101	0801	0701	0301	0201	AUS 1		
0101	0801	07AG	0301	0201	A 1	3*0101	
0101	0801	0701	0301	0201	A 1	3*0101	
<u>Potentially (Allele) Matched:</u>							
0101	0801		0301	03AD	D 4		
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199

20203



Tartu Ülikooli Kliinikum

HLA ABCDRDQ esinemissagedus

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3	0301g	0702	0702g	1501	0602	0,03544	2	0,00559	9	0,00000	NA	0,01562	3
4	0201g	0501g	4402g	0401	0301g	0,02498	3	0,00000	NA	0,00000	NA	0,00000	NA
5	0201g	0702	0702g	1501	0602	0,02430	4	0,00000	NA	0,00000	NA	0,00000	NA
6	2902	1601	4403	0701	0201g	0,01908	5	0,00336	43	0,00000	NA	0,03277	1
7	0201g	0304	1501g	0401	0302	0,01290	6	0,00000	NA	0,00000	NA	0,00000	NA
8	0101g	0602	5701	0701	0303	0,01277	7	0,00224	57	0,01085	9	0,00625	12
9	0301g	0401g	3501g	0101	0501	0,01272	8	0,00000	NA	0,00027	689	0,00937	6
10	0201g	0701g	0801g	0301	0201g	0,01075	9	0,00000	NA	0,00000	NA	0,00000	NA
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12	3001	0602	1302	0701	0201g	0,00948	11	0,00000	NA	0,00759	10	0,00156	150
13	2402g	0702	0702g	1501	0602	0,00852	12	0,00224	71	0,00217	61	0,00000	NA
14	0201g	0602	5701	0701	0303	0,00846	13	0,00000	NA	0,00000	NA	0,00000	NA
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16	3301	0802	1402	0102	0501	0,00728	15	0,00224	117	0,00000	NA	0,00937	5
17	2301g	0401g	4403	0701	0201g	0,00691	16	0,00112	373	0,00000	NA	0,00781	7
18	0201g	0501g	4402g	1501	0602	0,00616	17	0,00000	NA	0,00000	NA	0,00000	NA
19	3101	0304	4001g	0404	0302	0,00608	18	0,00000	NA	0,00027	859	0,00469	26
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Recipient ID: 1122

Search determinants: **A:** 3, **B:** 27, 56 **DR:** 14, 15

Extended sorting on DRB1

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HLA-DR Allele/Split Antigen Mismatched:							
03 CVAB	56 01 27 EKN	01 02 02 02 02	15 01 01	13:01:01		2	
03:CVAB	56 01 27 EKN		15 01	13:02	D	1	3*01 AYG 5*01 YXC
					USA1	1	

Registry Code Information:

D: Germany

USA1: USA-NMDP

Multiple Allele Code Information:

AYG: 01/02/03/04/05/11

YXC: 01/05/09/11/12

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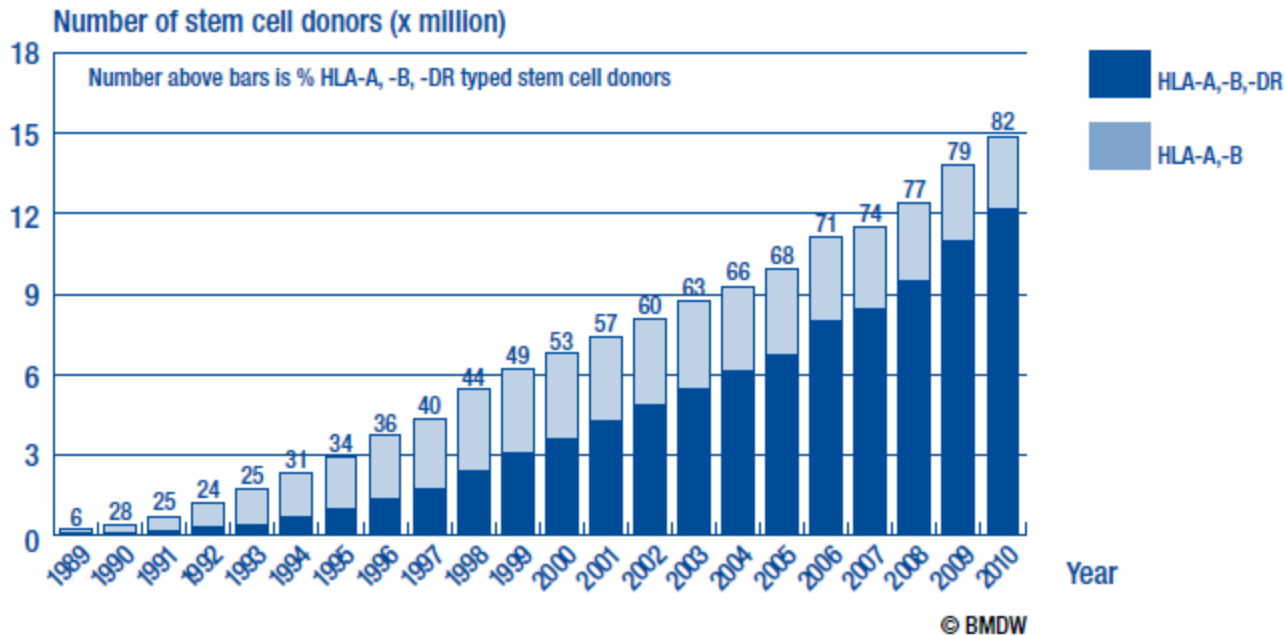
EKN: 05/13



Tartu Ülikooli Kliinikum

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4489	2601g	0102	5502	1407	0502	0,00000	NA	0,00000	NA	0,00027	778	0,00000	NA
4490	2601g	0702	3802	1407	0502	0,00000	NA	0,00000	NA	0,00027	591	0,00000	NA
4491	1102	1202	2704	1418	0503	0,00000	NA	0,00000	NA	0,00108	379	0,00000	NA
4492	0301g	1508	5101g	1419	0301g	0,00000	NA	0,00000	NA	0,00108	138	0,00000	NA
4493	2402g	0303g	1501g	1419	0301g	0,00000	NA	0,00000	NA	0,00108	451	0,00000	NA
4494	0207g	0401g	3915	1422	0301g	0,00000	NA	0,00000	NA	0,00108	357	0,00000	NA
4495	1102	0304	1301	1425	0301g	0,00000	NA	0,00000	NA	0,00027	714	0,00000	NA
4496	1102	0304	4006	1425	0301g	0,00000	NA	0,00000	NA	0,00027	671	0,00000	NA
4497	2601g	0304	1301	1425	0301g	0,00000	NA	0,00000	NA	0,00027	748	0,00000	NA
4498	2601g	0304	4006	1425	0301g	0,00000	NA	0,00000	NA	0,00027	587	0,00000	NA
4499	0101g	0202	0715	1501	0602	0,00008	1945	0,00000	NA	0,00000	NA	0,00000	NA
4500	0101g	0202	2705g	1501	0602	0,00010	1253	0,00000	NA	0,00000	NA	0,00000	NA
4501	0101g	0202	4002g	1501	0602	0,00008	1413	0,00000	NA	0,00000	NA	0,00000	NA
4502	0101g	0202	4405	1501	0502	0,00008	2051	0,00000	NA	0,00000	NA	0,00000	NA
4503	0101g	0303g	5501	1501	0602	0,00006	2801	0,00000	NA	0,00000	NA	0,00000	NA
4504	0101g	0304	4005	1501	0602	0,00000	NA	0,00000	NA	0,00000	NA	0,00039	529
4505	0101g	0401g	1302	1501	0602	0,00008	1721	0,00000	NA	0,00000	NA	0,00000	NA

Registridoonorite arvukus

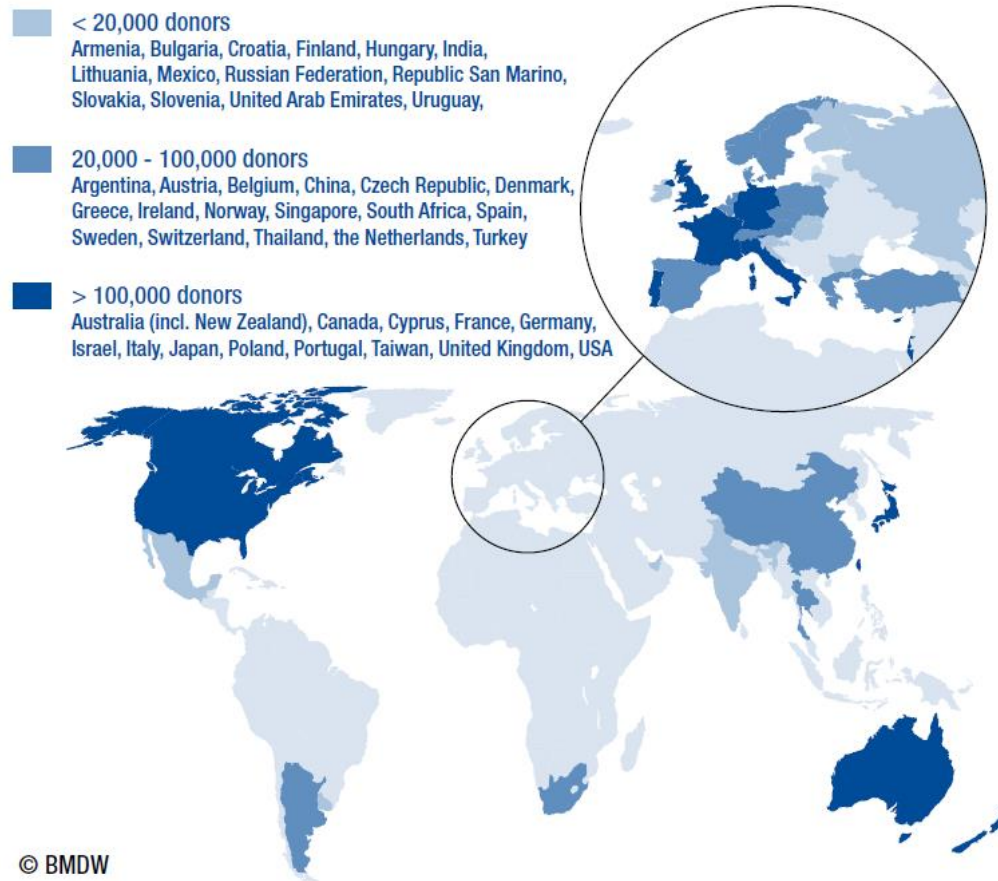


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Suurimad doonorite registrid

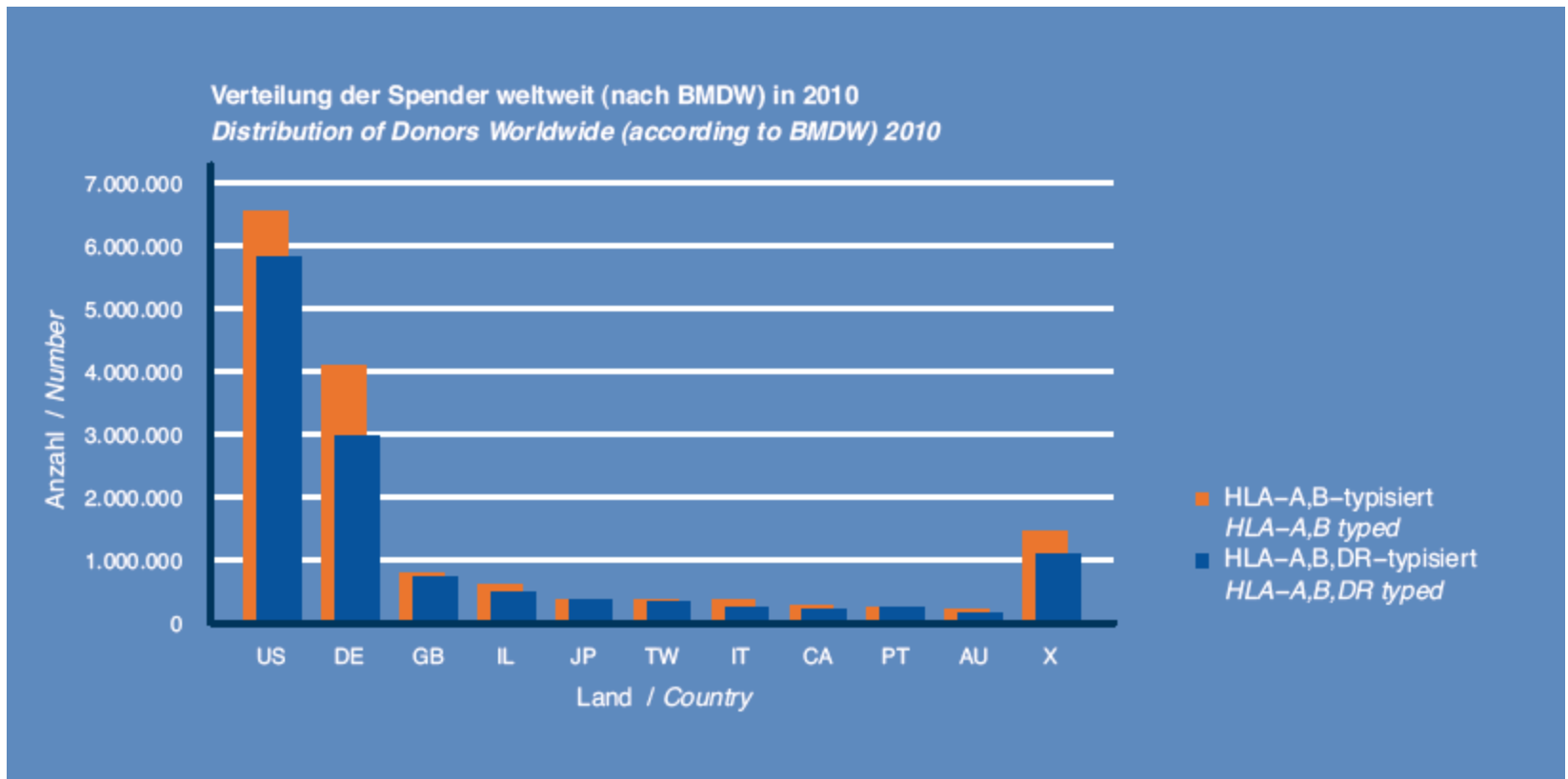


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Suurimad doonorite registrid



ZKDR (Zentrales Knochenmarkspender Register Deutschland) 2009/2010



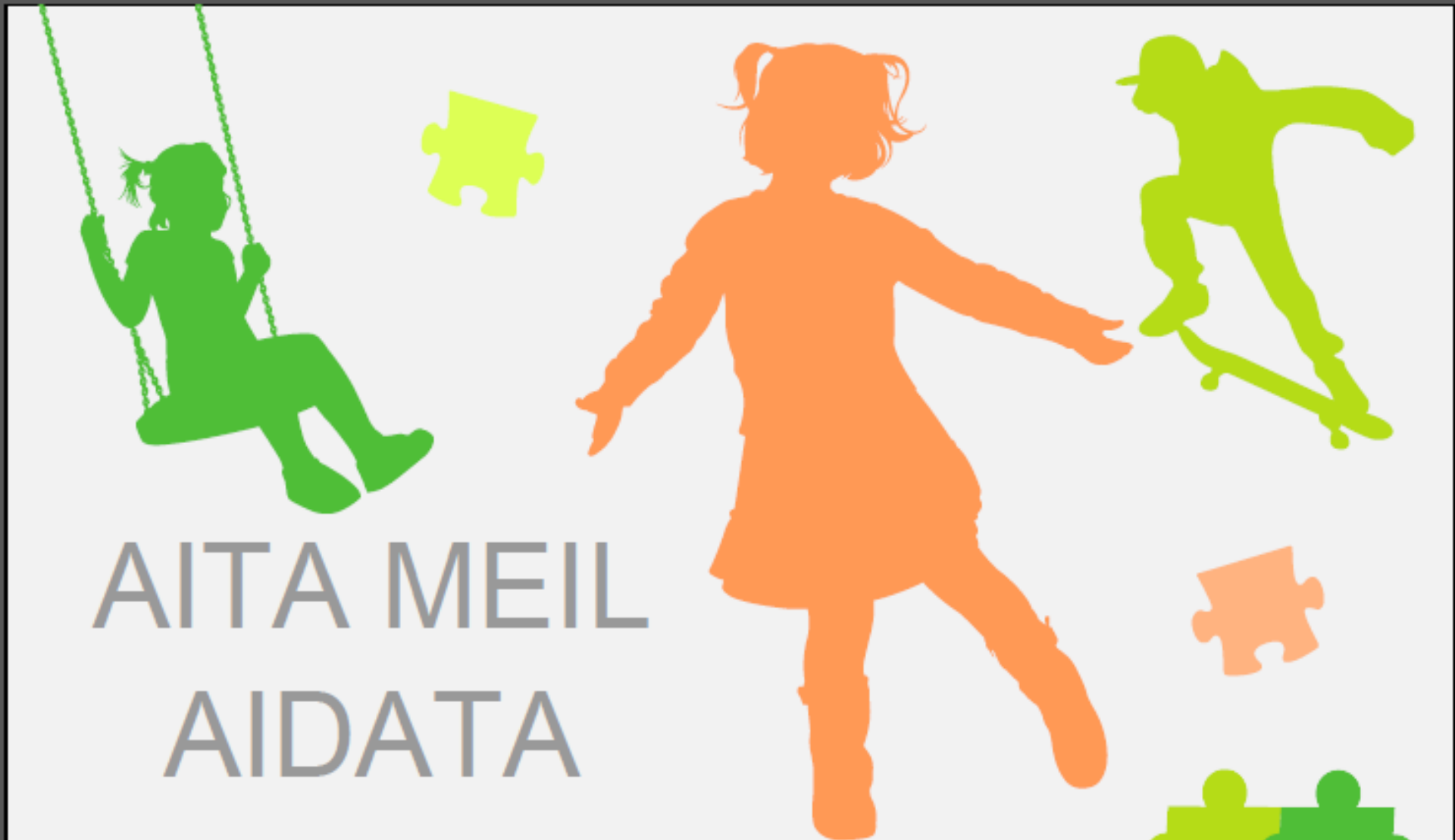
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