

Vietnam Workshop

HLA Compatibility and Ethnicity

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Stem cell source and its

Autologous : availability

Peripheral blood stem cell (PBSC)

Related :

Bone marrow (BM)

PBSC

Unrelated:

Bone marrow

PBSC

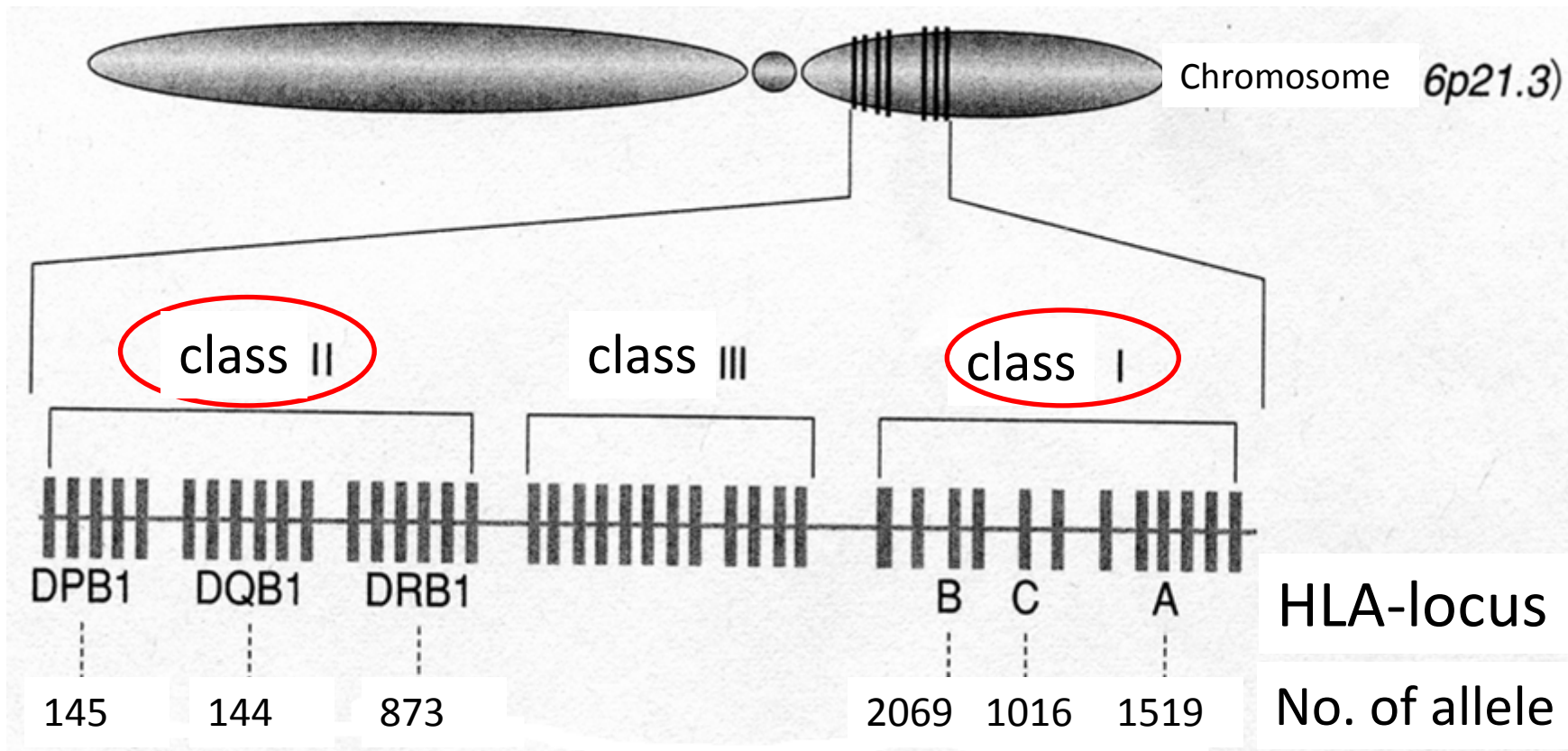
Cord Blood

HLA compatibility
between patient and stem cell (donor)

Characteristics of allo-HSCT

	BMT	PBSCT	CBT
Coordination	yes	yes	no
WBC recovery	2-3 weeks	faster	slower
Immunodeficiency	+	+	+(+)
Acute GVHD	++	++(+)	+
Chronic GVHD	++	+++	+
HLA barrier	<u>A, B, DR compatible</u>		<u>mismatch</u>

HLA region

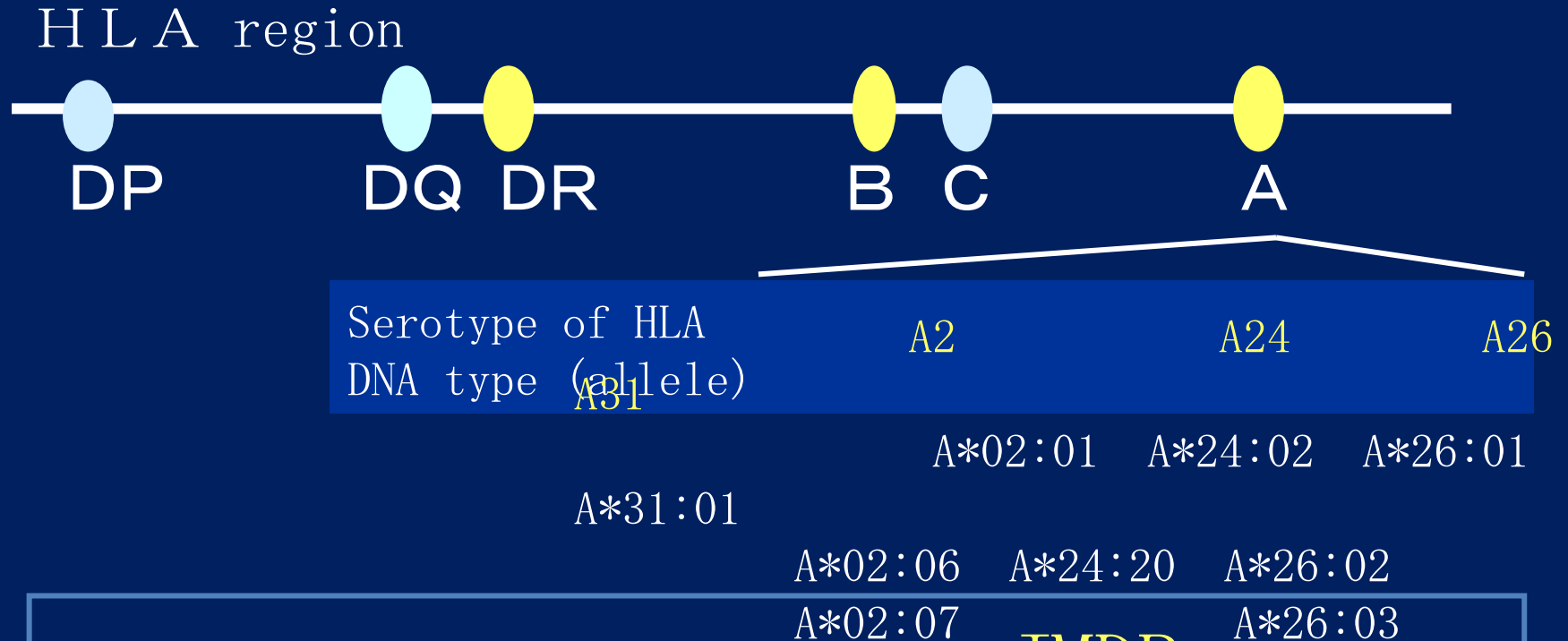


* IMGT/HLA Database <http://hla.alleles.org/nomenclature/stats.html>

HLA compatibility and acute GVHD

Stem cell source		Histocompatibility		acute GVHD
		HLA	non-HLA	
Auto		⊙	⊙	(-)
R	identical twin	⊙	⊙	(-)
	HLA identical sibling	⊙	△	(,+)
	HLA haplo-identical	X	△	(+++)(+)*
UR	HLA identical donor	△	△	(++)
	cord blood	△~X	△	(+)
⊙ complete match in thr region genetically				* T cell depletion
△ allele match or mismatch				
X HLA haplotype mismatch				

HLA compatibility in UR-HSCT



Donor selection in JMDP

HLA-A, B, DR serological match donor

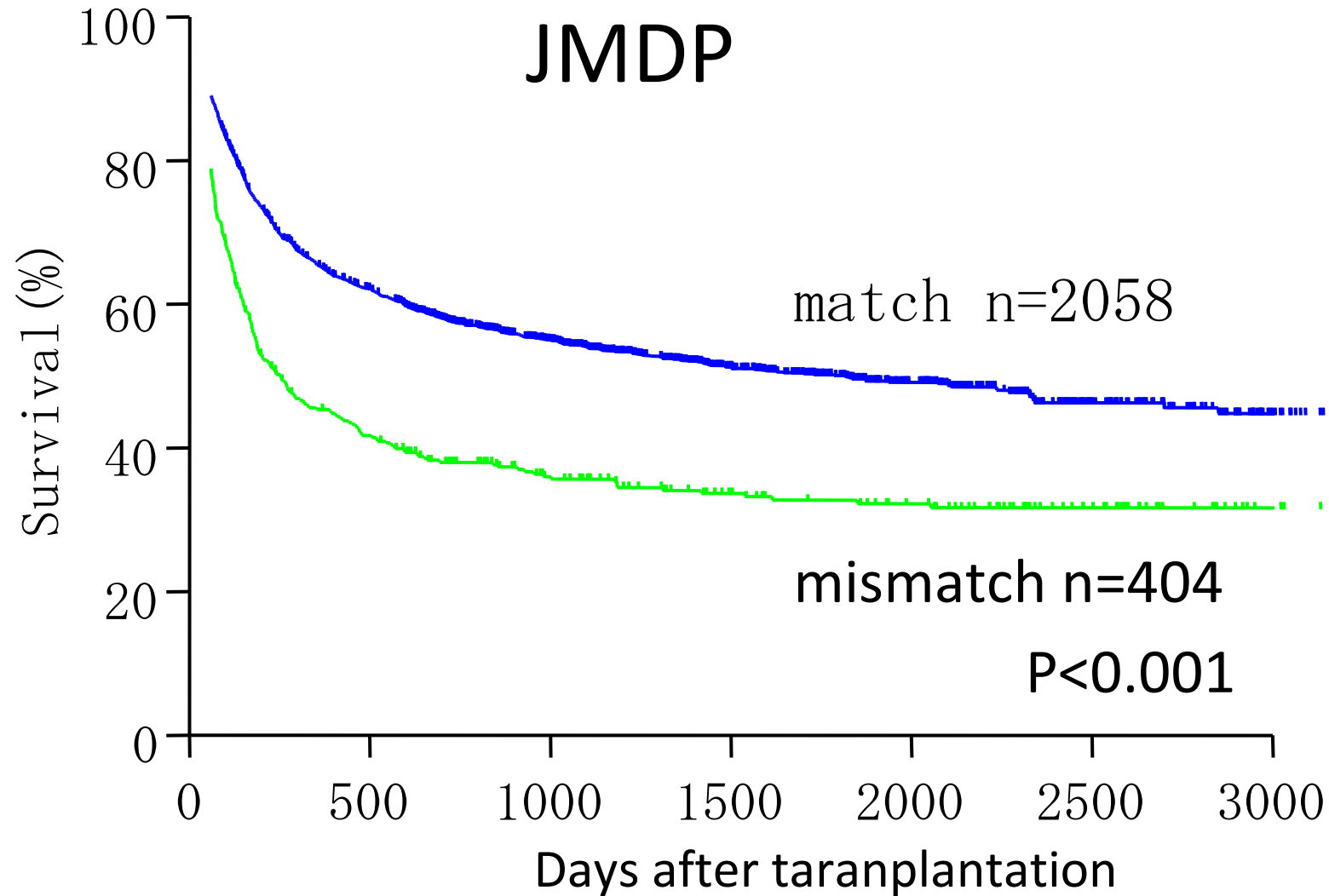


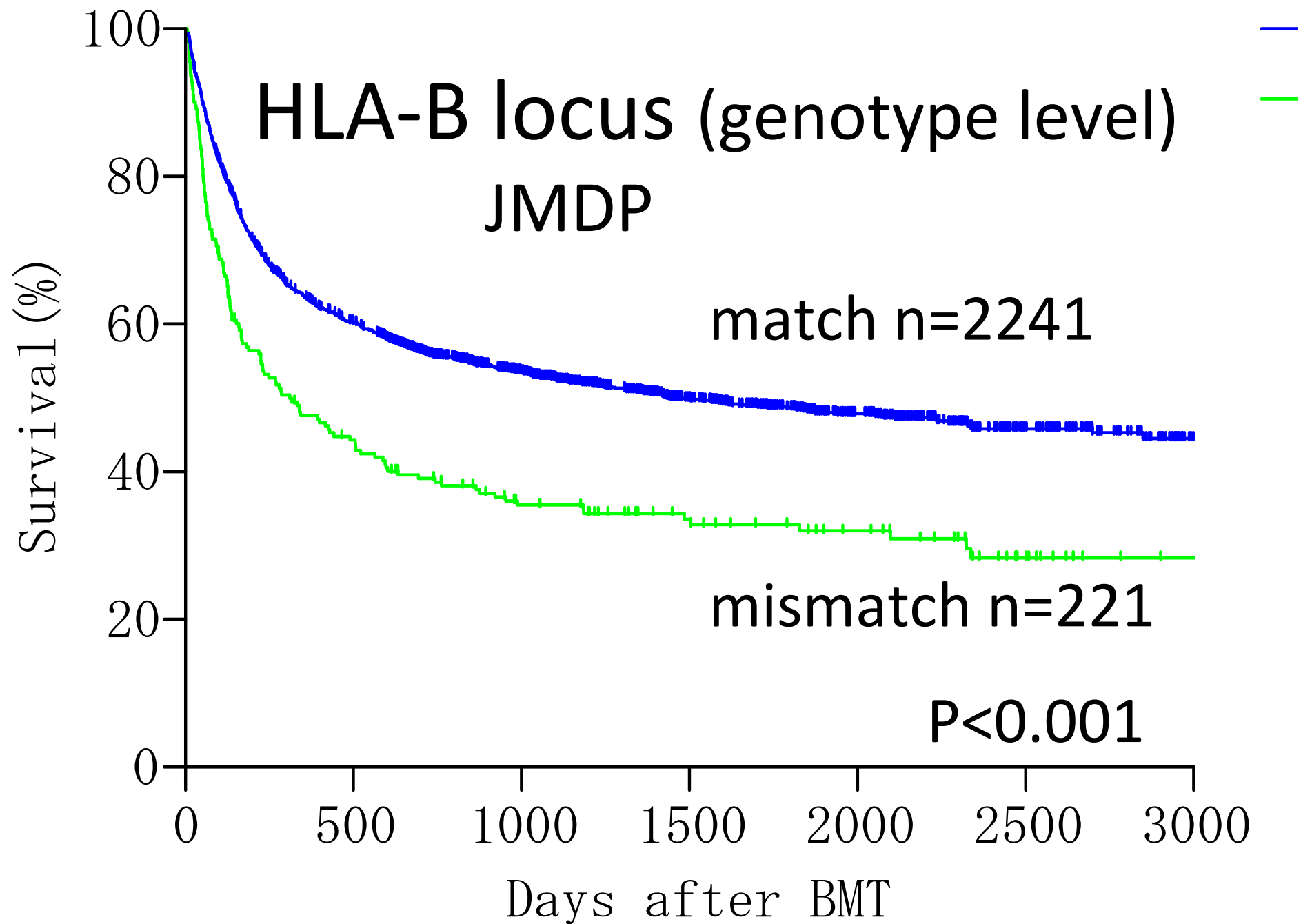
HLA-A, B, DRB1 allele mismatch ?

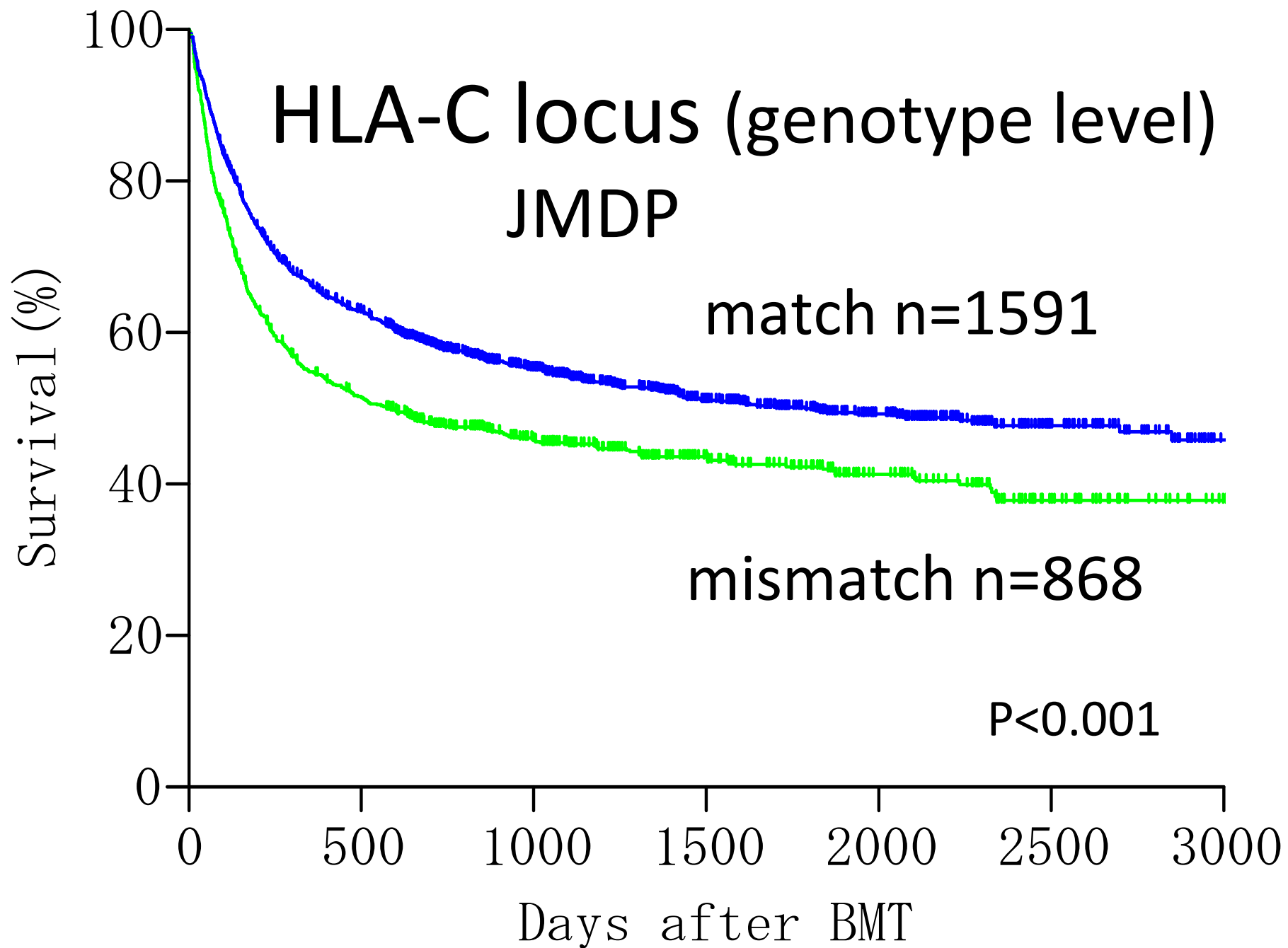
HLA-C, DQB1, DPB1 antigen, allele mismatch?

HLA-A locus (genotype level)

JMDP







Effect of HLA locus matching on clinical outcome in JM DP

5210 patients transplanted with T cell replete marrow from
HLA-A, B, DR serological match unrelated donor

Mismatch		severe a-GVHD		Mortality	
HLA locus	%	Hazard Risk*	p	Hazard Risk*	p
HLA-A	13	1.41	<0.001	1.31	<0.001
HLA-B	6	1.5	<0.001	1.3	0.001
HLA-C	29	1.93	<0.001	1.25	<0.001
HLA-DRB1	20	1.08	0.424	1.03	0.624
HLA-DQB1	23	1.1	0.315	1.08	0.195
HLA-DPB1	66	1.25	0.001	1.11	0.021
		* compared with HLA match			

The difference of HLA-A2 allele mismatch combination by registry (ethnicity)
 (13th International Histocompatibility Workshop Group)
 IHWG

	Non-JMDP	JMDP
A*02:01–A*02:02	7	0
A*02:01–A*02:05	62	0
A*02:01–A*02:06	25	96
A*02:01–A*02:07	0	20
A*02:06–A*02:07	0	50
A*02:01–A*02:10	0	15

Impact of Single Mismatches Relative to Single HLA-DQB1 Mismatch in UR-HSCT

International Histocompatibility Workshop Group
(IHWG study)

Single Mismatch	HR	95% CI	P-Value
HLA-DQB1	1	---	---
HLA-A	1.2	1.05 - 1.37	.007
HLA-B	1.29	1.10 - 1.53	.002
HLA-C	1.18	1.05 - 1.33	.004
HLA-DRB1	1.08	0.89 - 1.32	.45



Model adjusts for disease risk.

Risk of a-GVHD and mortality depend on ethnicity (genetic background)

15th International Histocompatibility Workshop Group
HSCT component study

- UR-HSCT from HLA-A, B, C, DRB1 and DQB1 allele matched donor
- Non-T cell depleted GVHD prophylaxis
- Leukemia case

Acute GVHD and ethnicity

**Asian/Asian: mostly Japanese

Ethnic combination		aGVHD 2-4		aGVHD 3-4	
Donor / Patient	n	HR (95% CI)	p	HR (95% CI)	p
Asian / Asian	*2062	1.00 (Ref.)		1.00 (Ref.)	
Cauc. / Cauc.	2414	1.63 (1.48-1.8)	<0.001	1.54 (1.31-1.79)	<0.001
Black / Black	39	1.27 (0.8-2.01)	0.309	2.16 (1.2-3.88)	0.01
Hisp. / Hisp.	21	1.39 (0.74-2.6)	0.3	1.84 (0.76-4.46)	0.179
Mismatch ethnicity*	268	1.59 (1.33-1.91)	<0.001	1.62 (1.22-2.16)	0.001

* in non-JMDP

Relapse and Survival multivariate analysis

Ethnic combination		relapse		mortality	
Donor / Patient	n	HR (95% CI)	p	HR (95% CI)	p
Asian / Asian	2062	1.00 (Ref.)		1.00 (Ref.)	
Cauc. / Cauc.	2414	1.61 (1.4-1.85)	<0.001	1.51 (1.38-1.66)	<0.001
Black / Black	39	1.94 (1.03-3.65)	0.041	2.59 (1.77-3.8)	<0.001
Hisp. / Hisp.	21	2.18 (0.9-5.29)	0.084	2.25 (1.32-3.82)	0.003
Mismatch ethnicity*	268	1.75 (1.36-2.26)	<0.001	1.69 (1.43-2.01)	<0.001

* in non-JMDP

Other clinical factor
(p<0.01)

HLA-DPB1
Leukemia risk
Disease

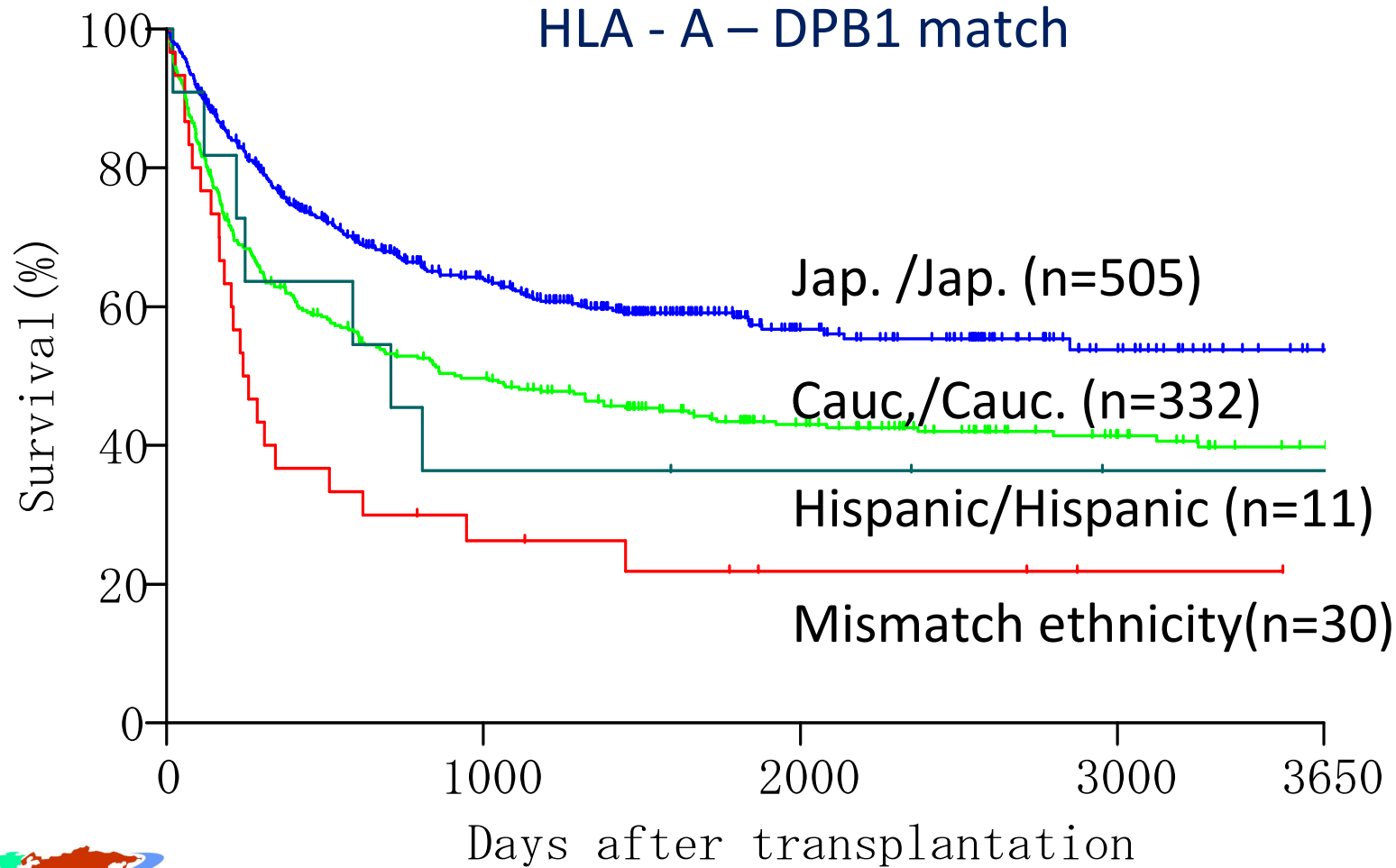
GVHD prophylaxis
Leukemia risk
Patient age
Disease



Survival

Low and intermediate leukemia

HLA - A – DPB1 match



Common HLA Haplotypes and acute GVHD

Comparisin of Caucasian and Japanese

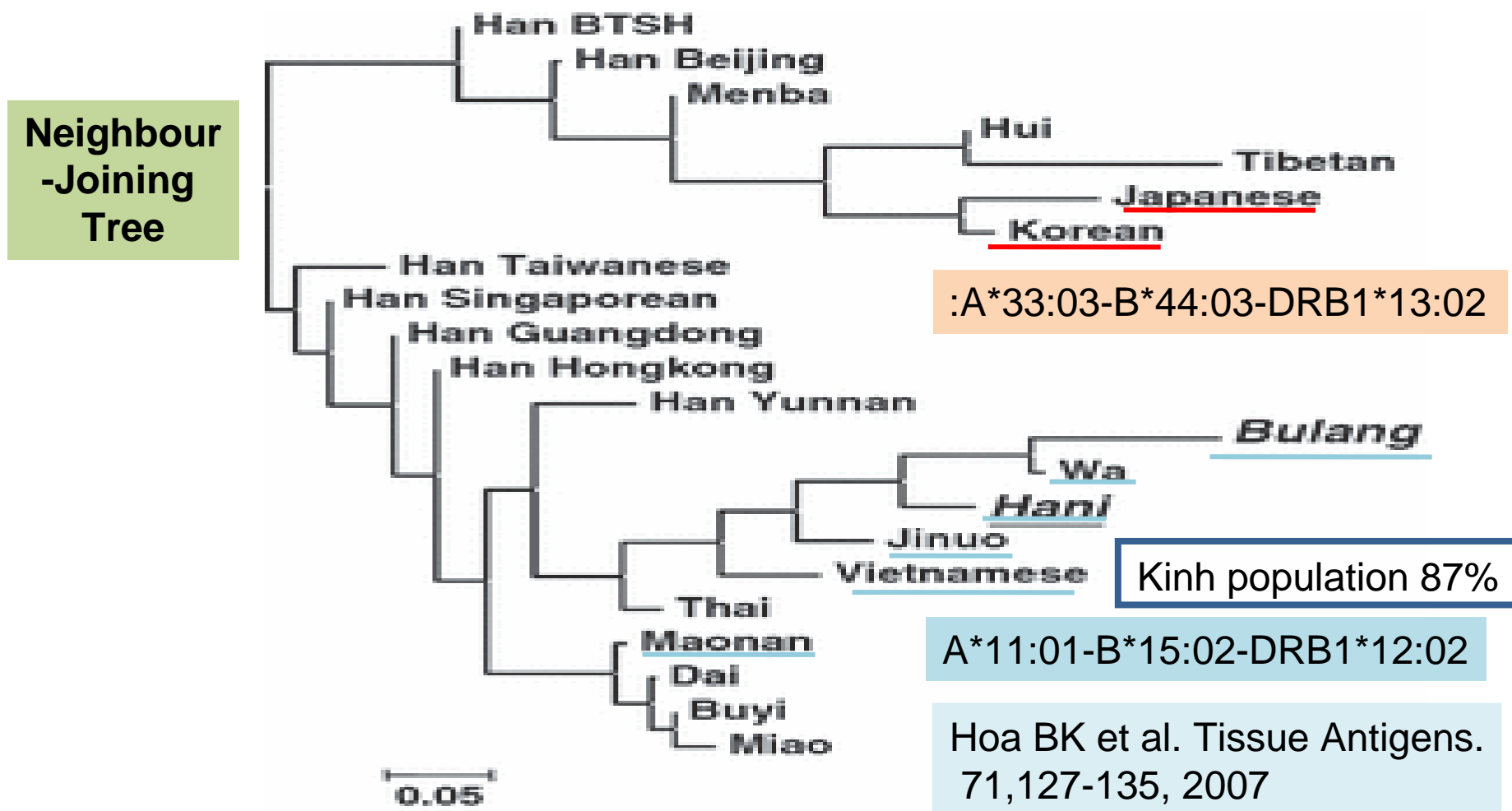
						EUR_freq	
Cauc.	HPC1	A*0101	Cw*0701	B*0801	DRB1*0301	DQB1*0201	7.408
Cauc.	HPC2	A*0301	Cw*0702	B*0702	DRB1*1501	DQB1*0602	3.547
Cauc.	HPC3	A*0201	Cw*0501	B*4402	DRB1*0401	DQB1*0301	2.436
Cauc.	HPC4	A*0201	Cw*0702	B*0702	DRB1*1501	DQB1*0602	2.341
						JAP_freq	
Japanese	HPA1	A*2402	Cw*1202	B*5201	DRB1*1502	DQB1*0601	5.451
	HPA2	A*3303	Cw*1403	B*4403	DRB1*1302	DQB1*0604	2.935

Common HP	n	Incidence of acute GVHD	
		Grade 2-4	Grade 3-4
Cauc. HPC1	707	54.2%	21.8%
Cauc. HPC2	410	50.9%	18.9%
Cauc. HPC3	239	48.7%	22.5%
Cauc. HPC4	263	49.9%	17.8%
Japanese			
HPA1	764	36.3%	13.8%
HPA2	390	33.6%	11.9%



Genetic link among Hani, Bulang and other Southeast Asian populations: evidence from HLA -A, -B, -C, -DRB1 genes and haplotypes distribution

Shi L. et al. Intern J Immunogenetics 37:467-476, 2010




Registry and Donor selection based on HLA

1. ethnic group (genetic background) specific
2. stem cell source (donor) specific

When HLA identical sibling donor is not found, alternative stem cell source ?

Unrelated donor
from donor registry

Cord blood
from cord blood bank



Organization
Size
HLA typing

Haploidentical related donor (non-T cell depleted?)