HLA typing in Hematopoietic Stem Cell Transplantation

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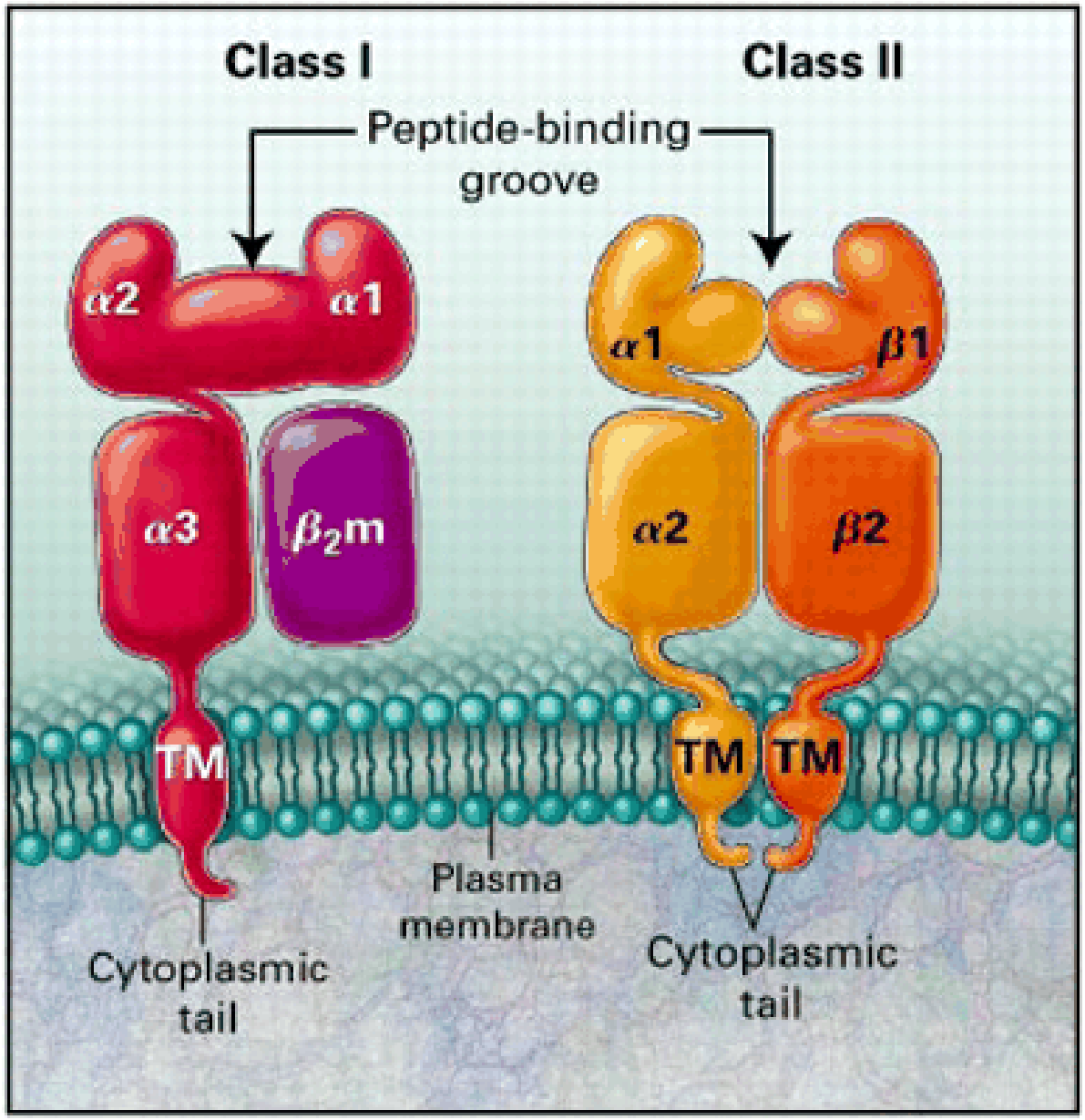
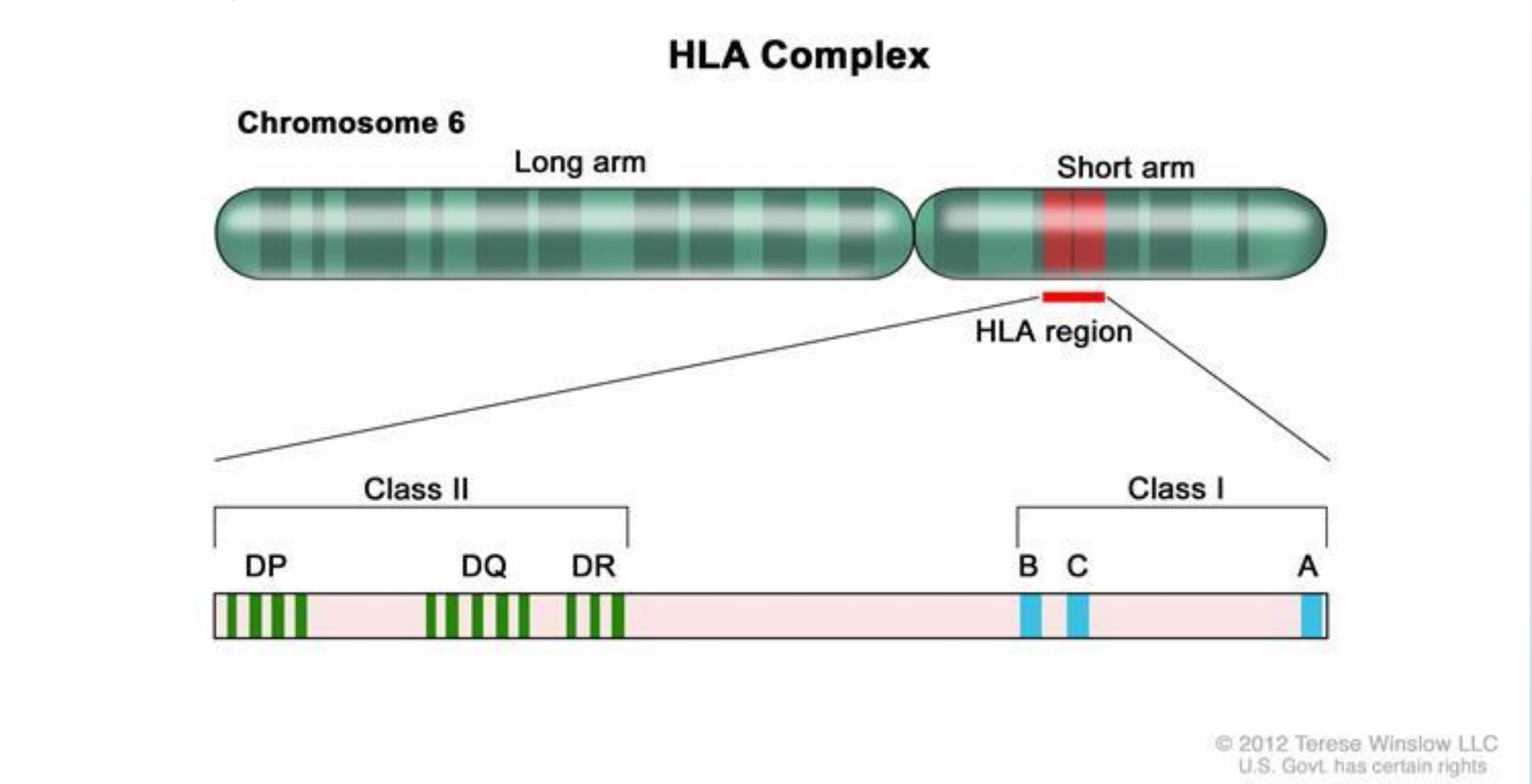
HLA molecules



MHC locus


HLA Complex
Chromosome 6
Long arm
Short arm
HLA region
Class II
Class I
DP
DQ
DR
B
C
A
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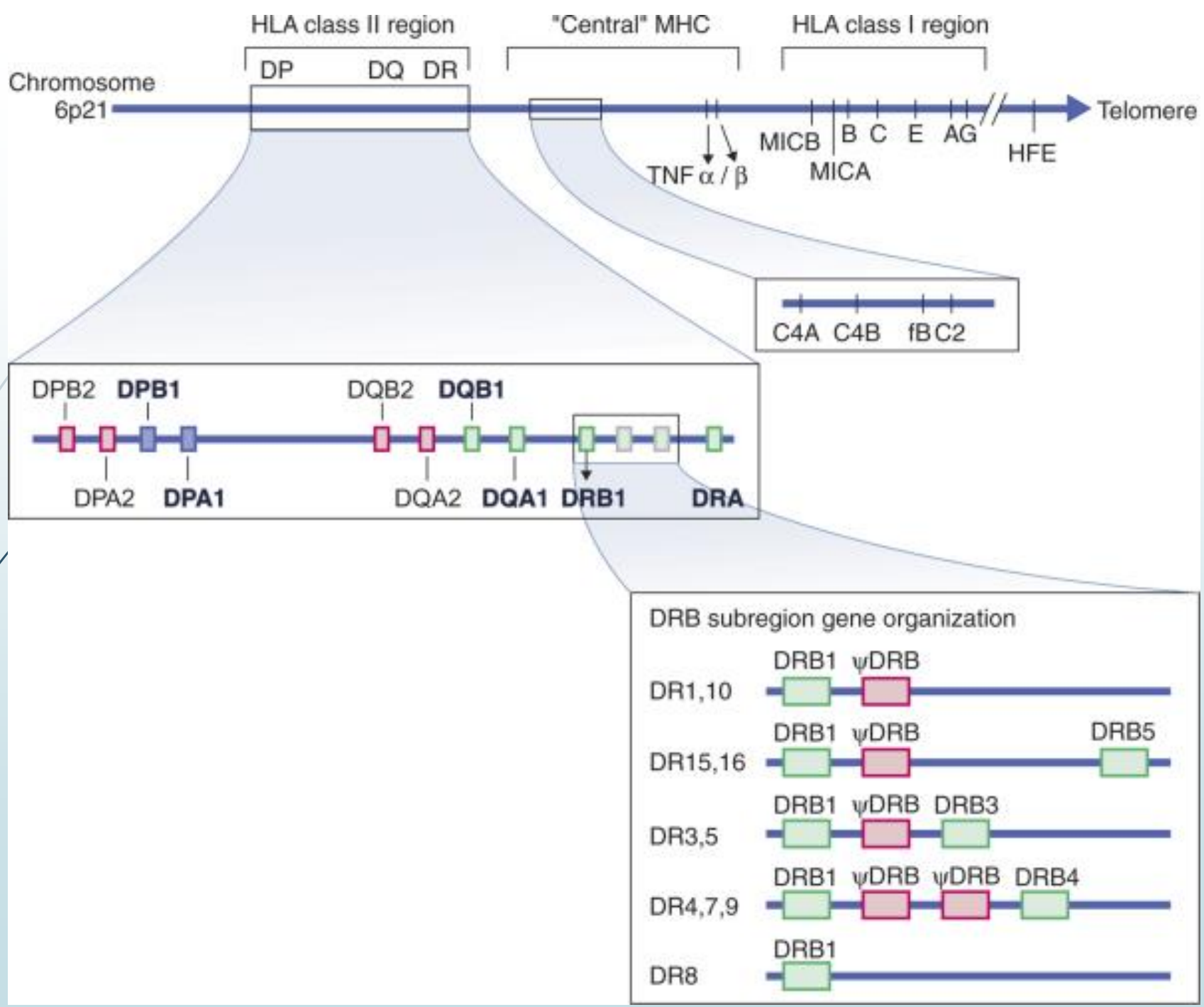

HLA class II region
"Central" MHC
HLA class I region
DP
DQ
DR
Chromosome
6p21
Telomere
TNF α / β
MICB
MICA
B
C
E
AG
HFE
C4A
C4B
fB
C2
DPB2
DPB1
DQB2
DQB1
DPA2
DPA1
DQA2
DQA1
DRB1
DRA
DRB subregion gene organization
DR1,10
DRB1
ψDRB
DR15,16
DRB5
DR3,5
DRB3
DR4,7,9
DRB4
DR8

Classic HLA loci

High expression loci (HEL)

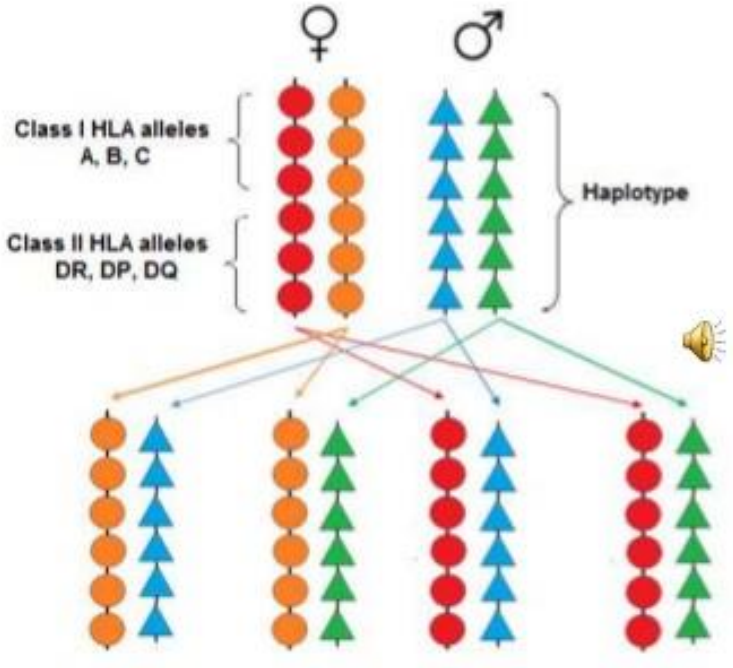
- A
- B
- C
- DRB1

Low expression loci (LEL)

- DRB3
- DRB4
- DRB5
- DQA1
- DQB1
- DDPA1
- DPB1

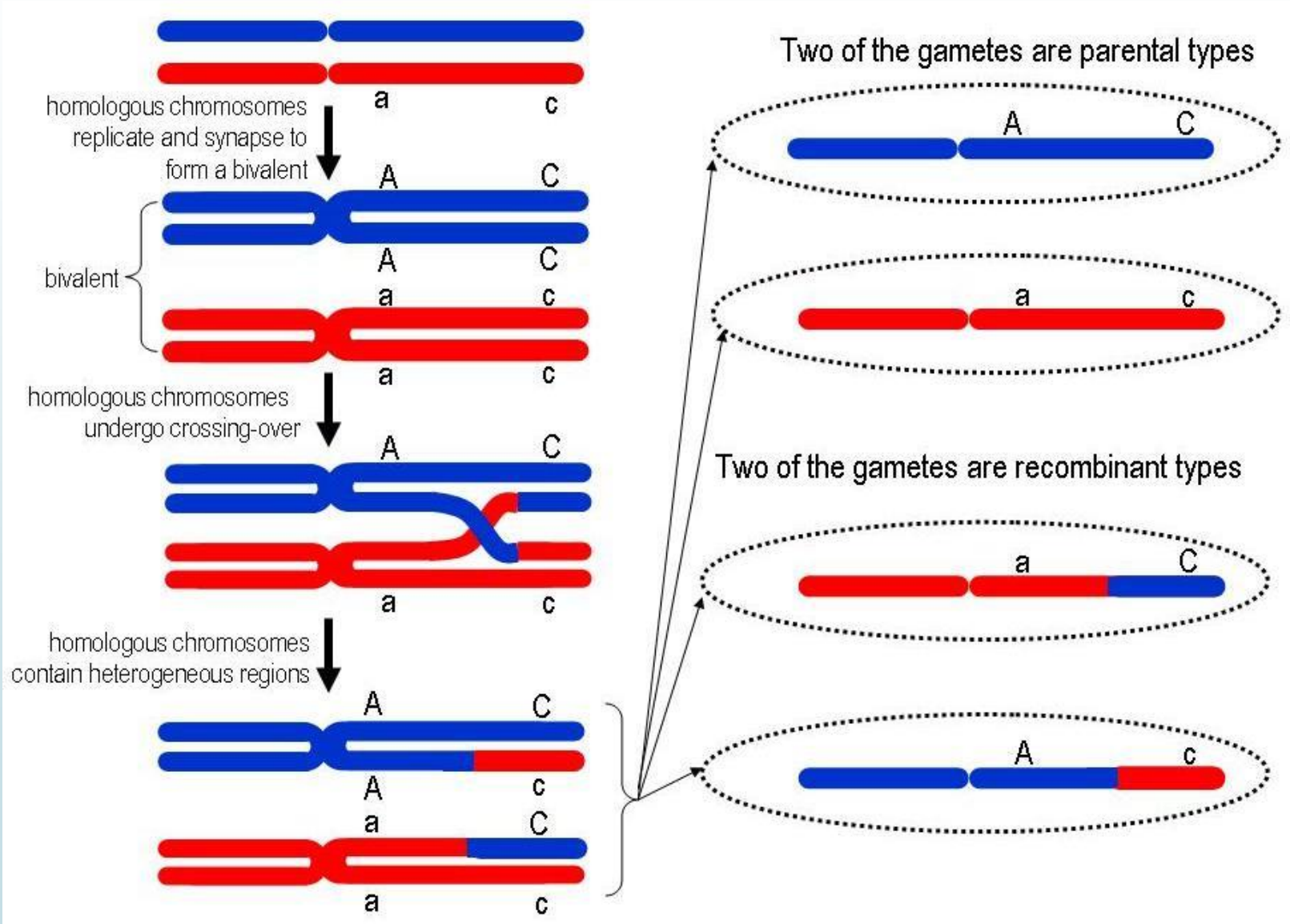
HLA haplotypes

HLA inheritance and familial matching



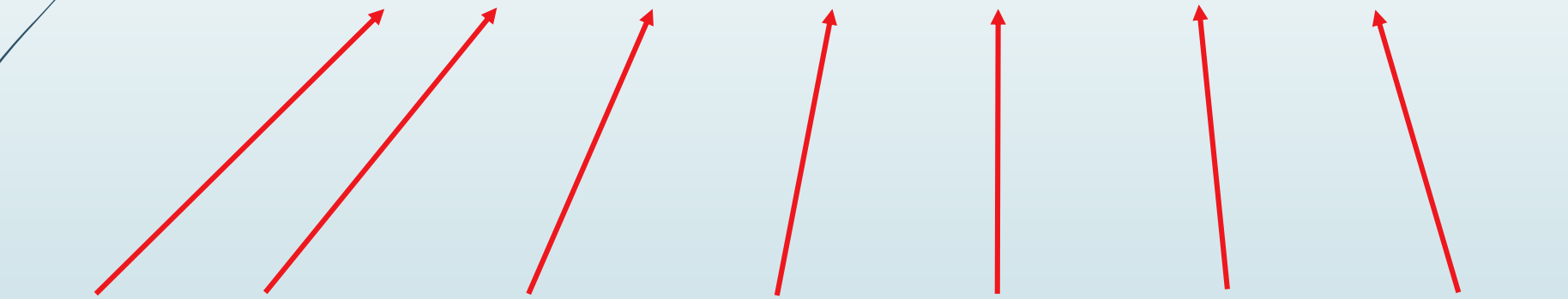
- 'Haplotype': a combination of alleles at adjacent loci on a chromosome that are inherited together.
- Breeding between two heterozygous individuals results in children with 4 possible genotypes
- There is a 1 in 4 chance of a complete match between two siblings

Recombination (crossing over)



HLA Allele Nomenclature

HLA - A * 24:02:01: 01
HLA - A * 24:02:01: 02 L

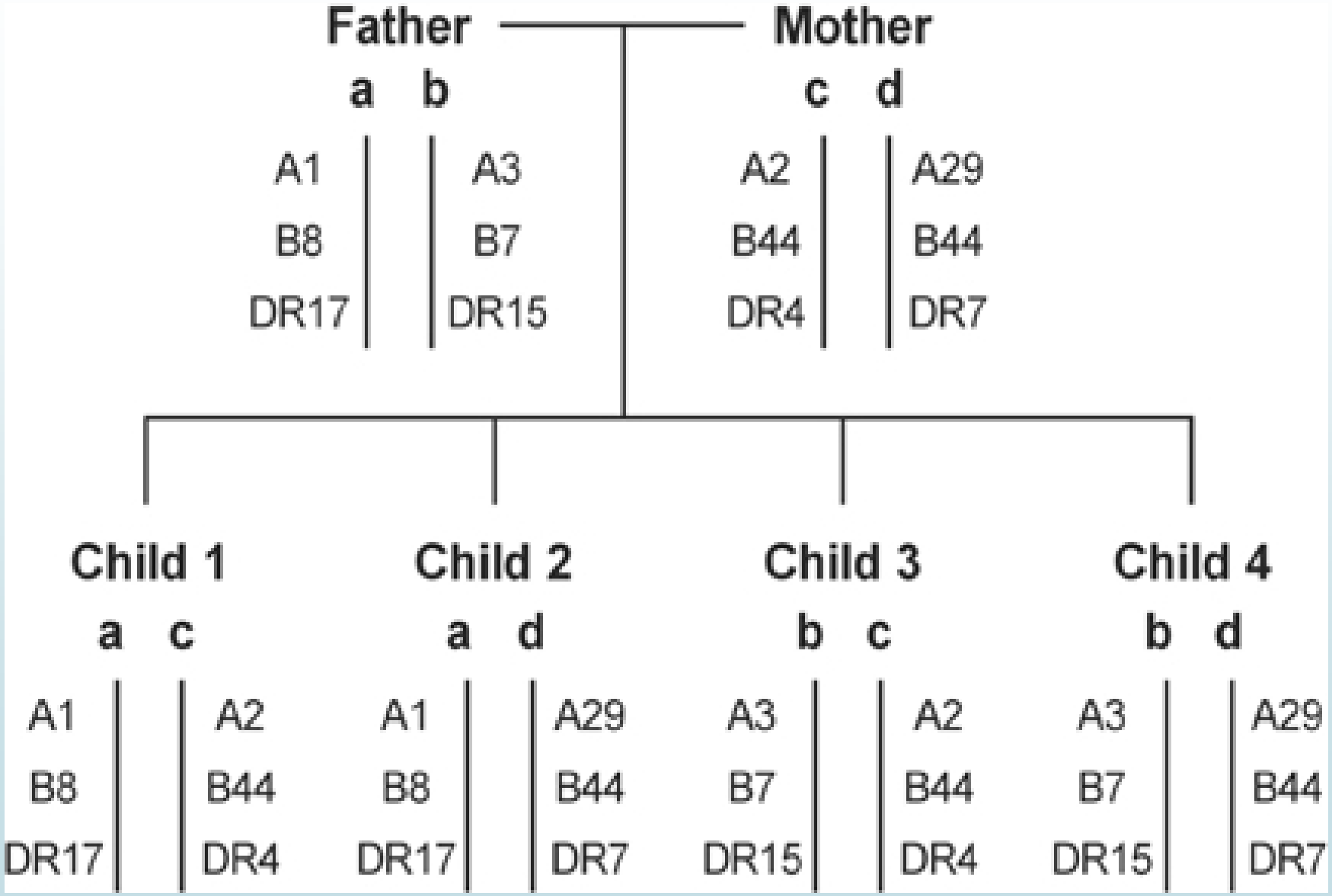


How we can find donors?

Matched sibling donors

- Primary low resolution typing for all available first degree relatives.
- Low or high resolution confirmatory typing of the patient and phenotypically matched donor based on HLA pedigree.
- In most cases high resolution typing is not needed.

Example


Father
a b
A1 A3
B8 B7
DR17 DR15
Mother
c d
A2 A29
B44 B44
DR4 DR7
Child 1
a c
A1 A2
B8 B44
DR17 DR4
Child 2
a d
A1 A29
B8 B44
DR17 DR7
Child 3
b c
A3 A2
B7 B44
DR15 DR4
Child 4
b d
A3 A29
B7 B44
DR15 DR7

An Apparently 6/6 But Really Haploidentical sibling

- Patient and sibling:

  A*01,*02; B*35,*41; DRB1*11,*15

- Father: A*01, - ; B*35, - ; C*01,*04; DRB1*11, -
- Father's haplotypes: A*01 B*35 C*01 DRB1*11

  A*01 B*35 C*04 DRB1*11
- Patient's confirmatory typing:
- A*01,*02; B*35,*41; C*01,*16; DRB1*11,*15
- Sibling's confirmatory typing:
- A*01,*02; B*35,*41; C*04,*16: DRB1*11,*15

An Apparently 10/10 But Really Haploidentical siblings

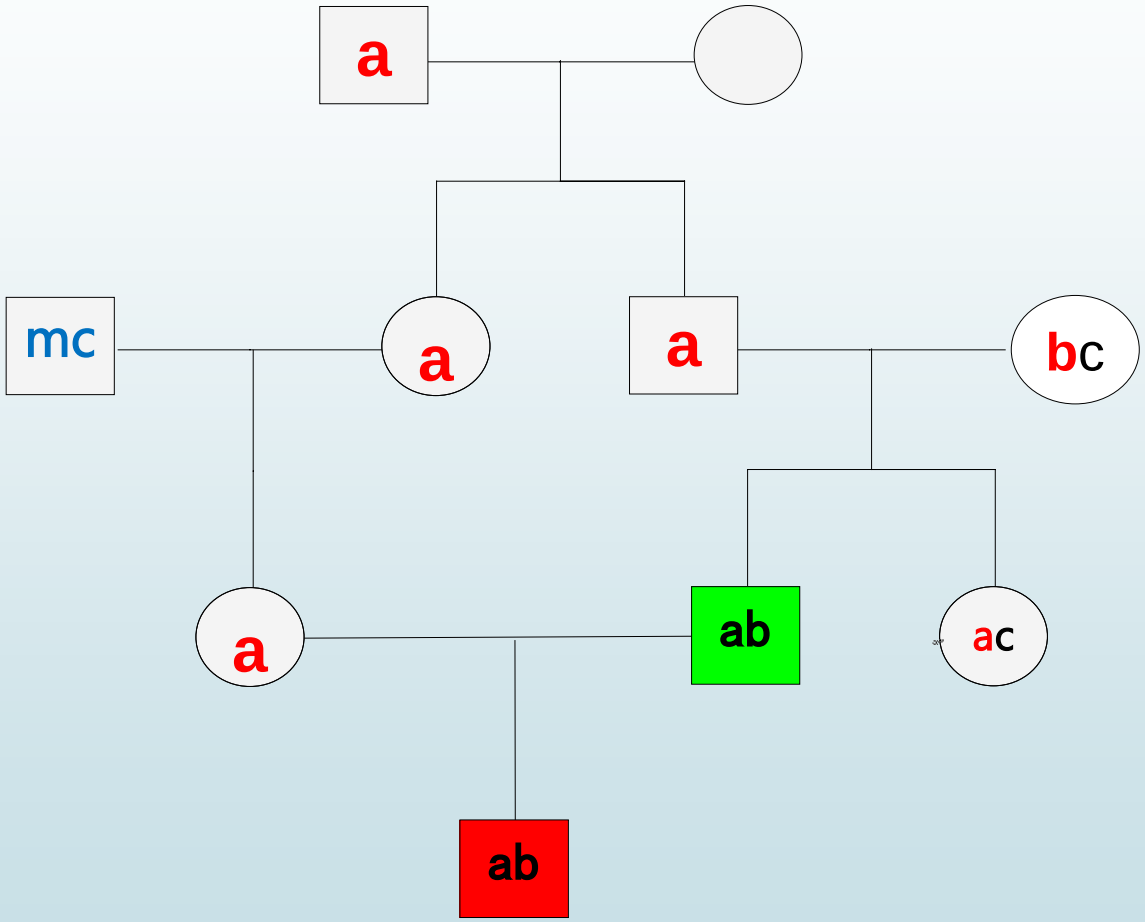
Siblings' typing	Mother's typing	Sibling 1 maternal haplotype	Sibling 2 maternal haplotype
A*02,*03	A*03, -	A*03:01	A*03:02
B*35,*51	B*35, -	B*35:08	B*35:01
C*04,*14			
DRB1*11,*15	DRB1*11, -	DRB1*11:01	DRB1*11:01
DQB1*03,*06			

Related parents

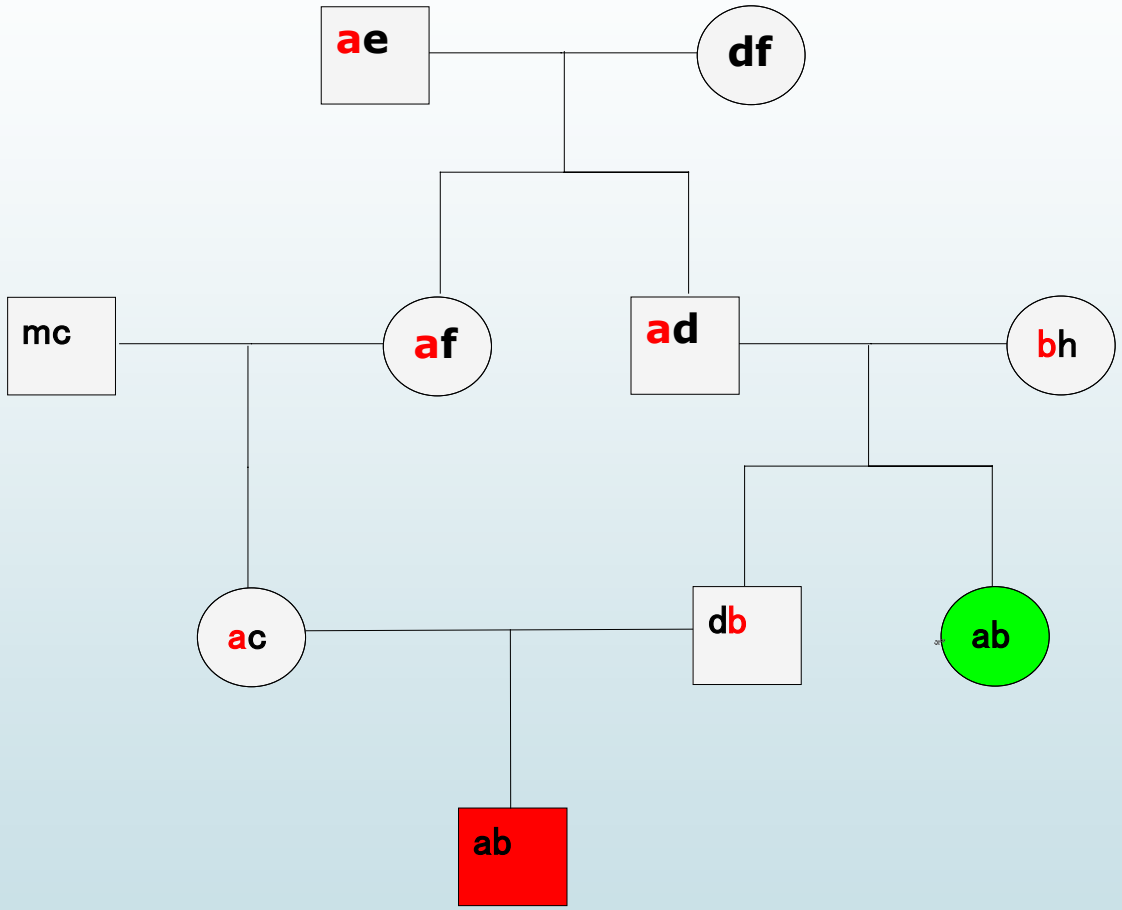
ab X ac

aa ac ab bc

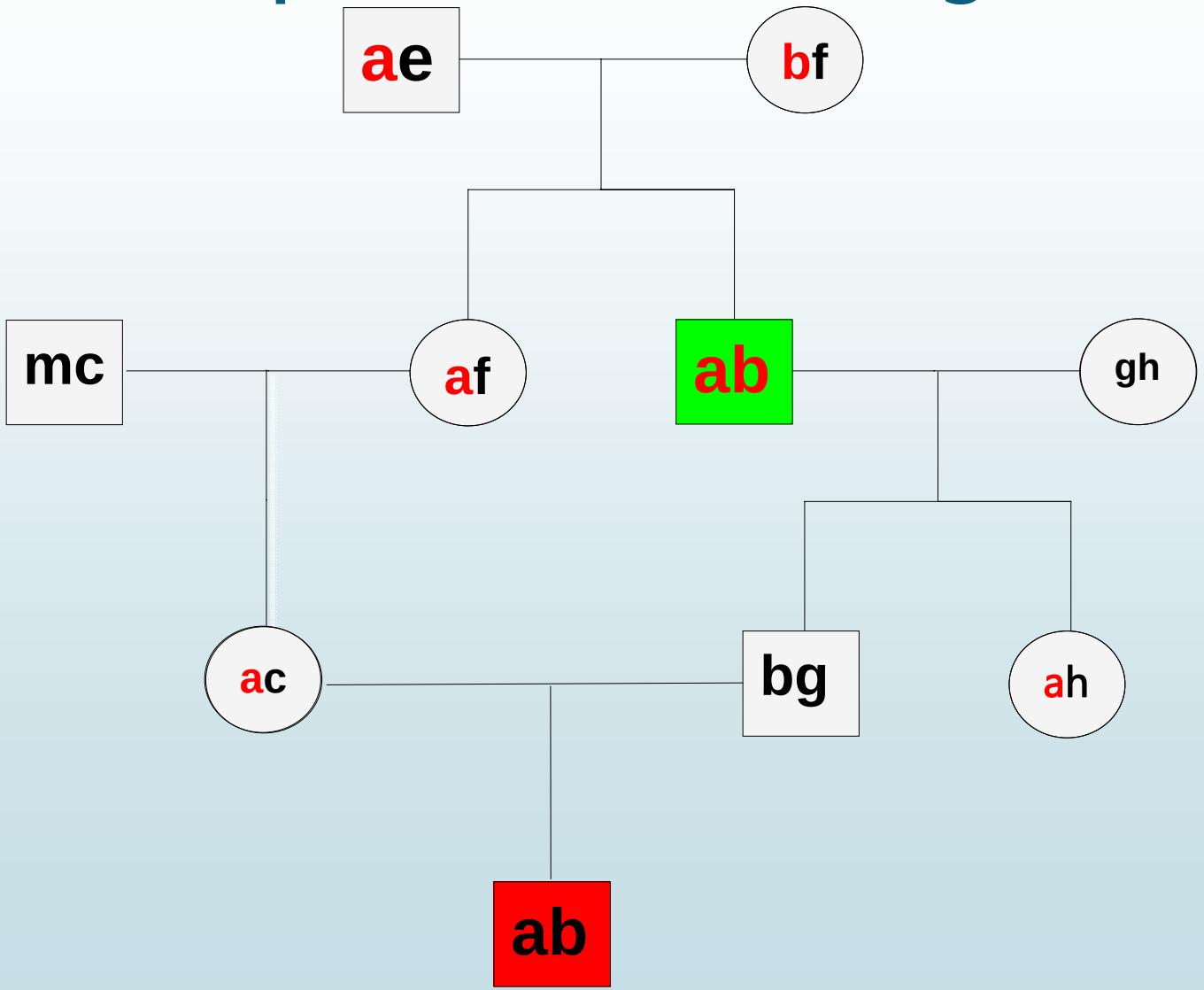
Related parents



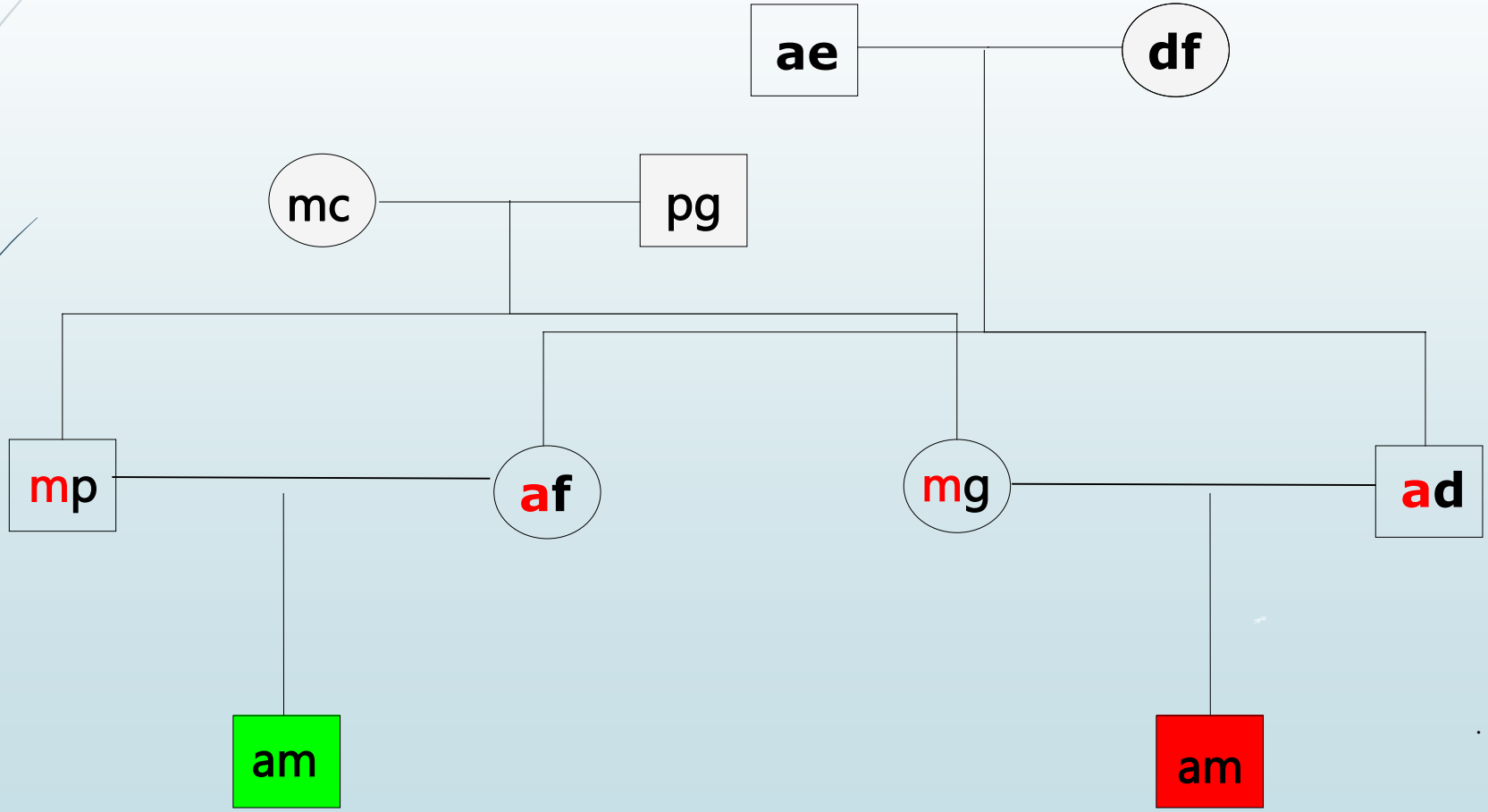
Related parents, matched aunt



Related parents, matched grandfather



Unrelated parents, other marriage between mother's and father's families



Matched other related donors

- ABDR Typing of second degree relatives or beyond based on intra familial marriages.
- Low resolution ABCDRDQ confirmatory typing of the patient and ABDR matched donor.
- In most cases high resolution typing is needed.

An Apparently 8/8 But Really Haploidentical Donor

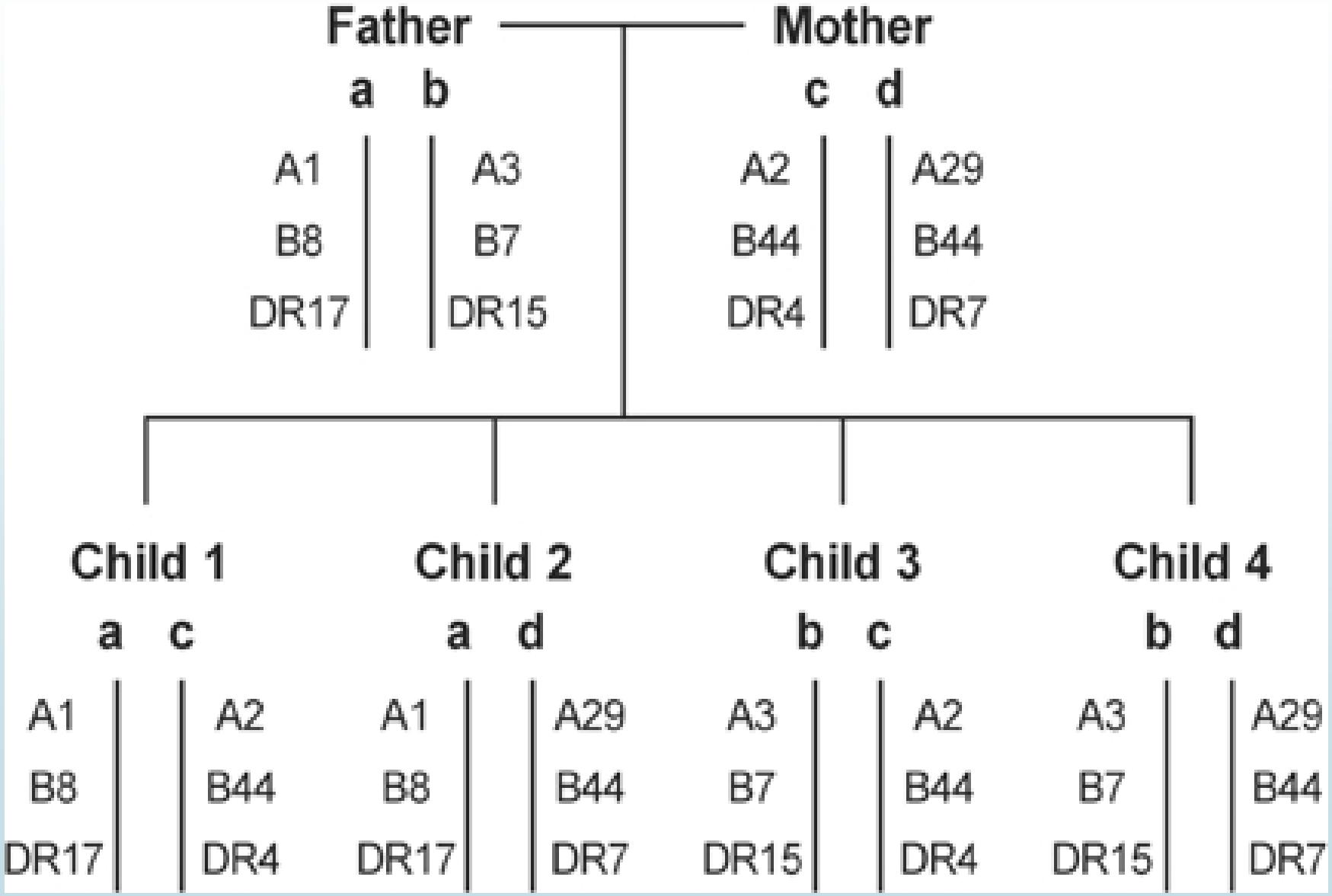
- Patient and his uncle:

A*02,*24; B*35,*51; C*04,*16; DRB1*11,*12

- High resolution HLA typing results:
- Patient: A*24:02:01 B*35:01 DRB1*11:04
- Uncle: A*24:02:01 B*35:02 DRB1*11:01

Haploidentical donors

Example


Father
a b
A1 A3
B8 B7
DR17 DR15
Mother
c d
A2 A29
B44 B44
DR4 DR7
Child 1
a c
A1 A2
B8 B44
DR17 DR4
Child 2
a d
A1 A29
B8 B44
DR17 DR7
Child 3
b c
A3 A2
B7 B44
DR15 DR4
Child 4
b d
A3 A29
B7 B44
DR15 DR7

Mismatched/haploidentical related donors

- Genotypic matching of the shared alleles must be confirmed by HLA pedigree or high resolution typing.
- Two way WBC crossmatch should be done.

An Apparently 5/6 But Really Haploidentical sibling

- Patient: A*02, A*30, B*13, B*51, DRB1*04,07
- Siblings: A*02, A*30, B*13, B*51, DRB1*11,07

- Father: A*02,*30; B*13,*50; DRB1*07, -
- Mother: A*02, -, B*51, -, DRB1*04,*11
- Mother haplotypes: A*02 B*51 DRB1*04
  A*02, B*51, DRB1*11
- Patient: A*02:04 B*51:01 CW*16 DRB1*04
- Sibling: A*02:34 B*51:05 CW*04 DRB1*11

Apparanrly haploidentical siblings

Patient

- A*02,*11
- B*18,*50
- DRB1*11,*13

Sibling

- A*02,*24
- B*50,*55
- DRB1*07,*13

Apparanrly haploidentical siblings

Patient		Sibling	
A*02	A*11	A*02	A*24
B*50	B*18	B*50	B*55
DRB1*13	DRB1*11	DRB1*07	DRB1*13

Mother		Father	
A*02	A*02	A*11	A*24
B*50	B*50	B*18	B*55
DRB1*13	DRB1*07	DRB1*11	DRB1*13

Unrelated donors

- The recipient-donor matching must be confirmed by high resolution typing:
  - Allele level matching
  - G group matching
  - P group matching
- Common Null alleles must be ruled out.
- Donor specific anti-HLA antibody in the case of mismatched transplantations should be ruled out and if possible two way WBC crossmatch should be done.

Thank You