

The Use of HLA /HPA Selected Platelets

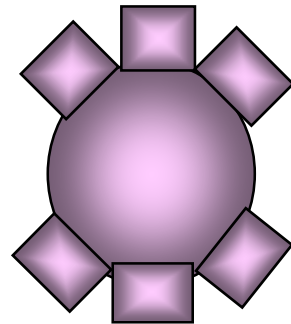
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Histocompatibility and Immunogenetics

HLA and Transfusion

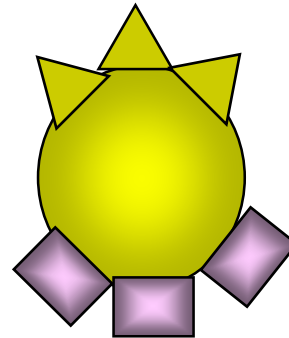
Human Leucocyte Antigens
HLA



LYMPHOCYTES

HLA

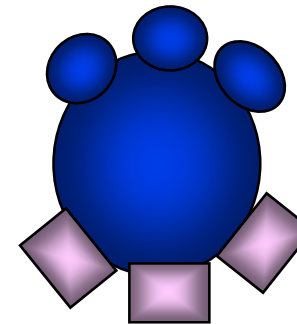
Human Platelet Antigens
HPA



PLATELETS

HPA (+HLA)

Human Neutrophil Antigens
HNA



NEUTROPHILS

HNA (+HLA)

Platelet Refractoriness

Definition:

- Failure to achieve an adequate rise in platelet count after 2 consecutive transfusions of random platelets.

Causes:

- immunological and non-immunological

“Non-immune” refractoriness

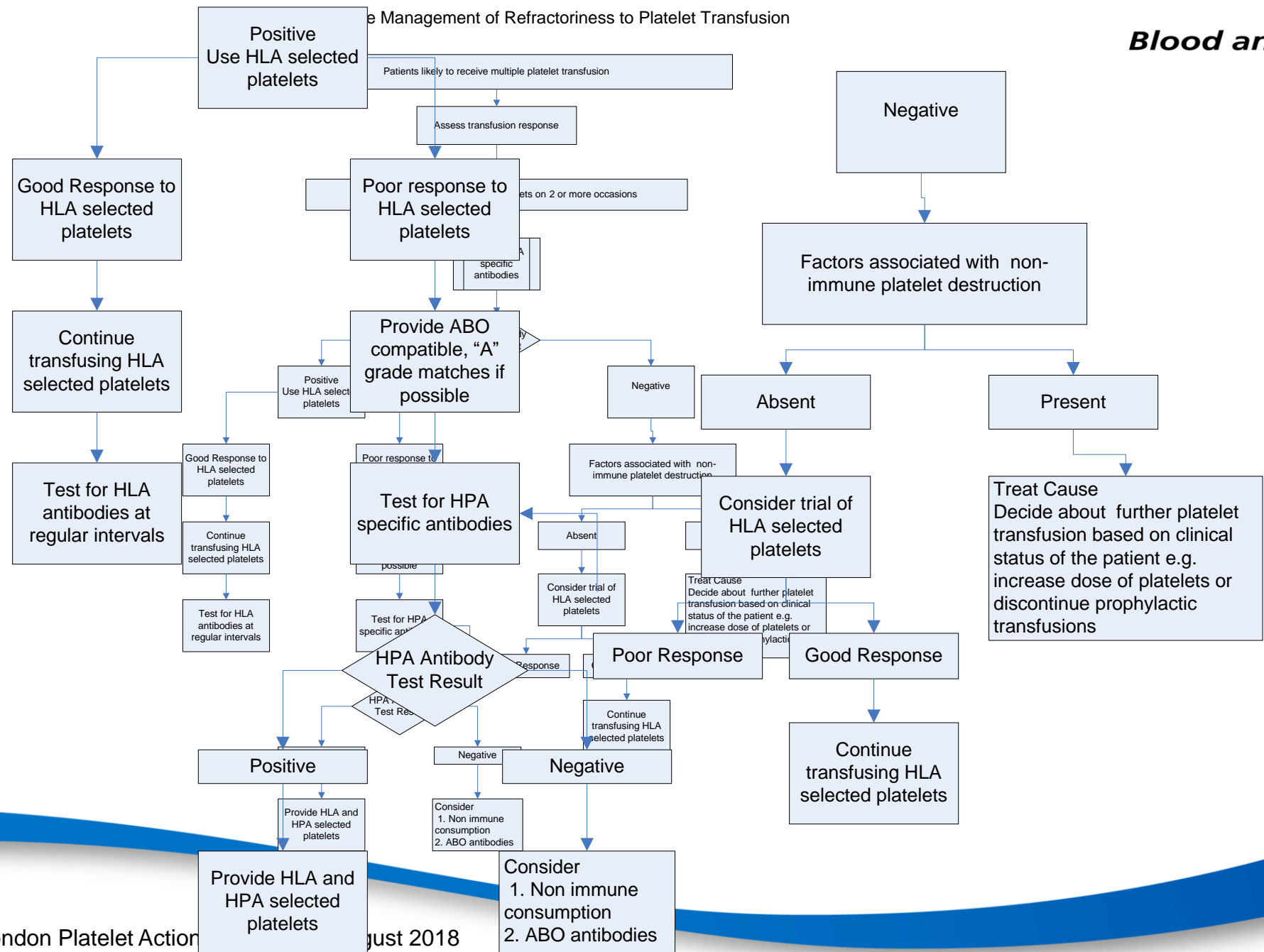
- Old/poorly stored platelets, small dose
- Splenomegaly, hepatomegaly
- DIC (infection, septicaemia, malignancy)
- Infection (CMV)
- Fever
- Antibiotics, esp amphotericin B, ambisome, vancomycin, ciprofloxacin,

Immunological causes of platelet refractoriness

- HLA - class I specific antibodies
- HPA - antibodies
 - incompatibility for HPA is uncommon
- ABO - antibodies
 - Incompatible plts transfused into patients with high titre anti-A or anti-B have a decreased survival

Management of alloimmunised platelet refractory patients

- Provide HLA/HPA compatible donors from an HLA/HPA typed apheresis donor panel
- Define HLA/HPA antibody specificity and select antigen compatible apheresis donors
- Cross-match random apheresis platelets to select compatible donors



The role of the H&I laboratory

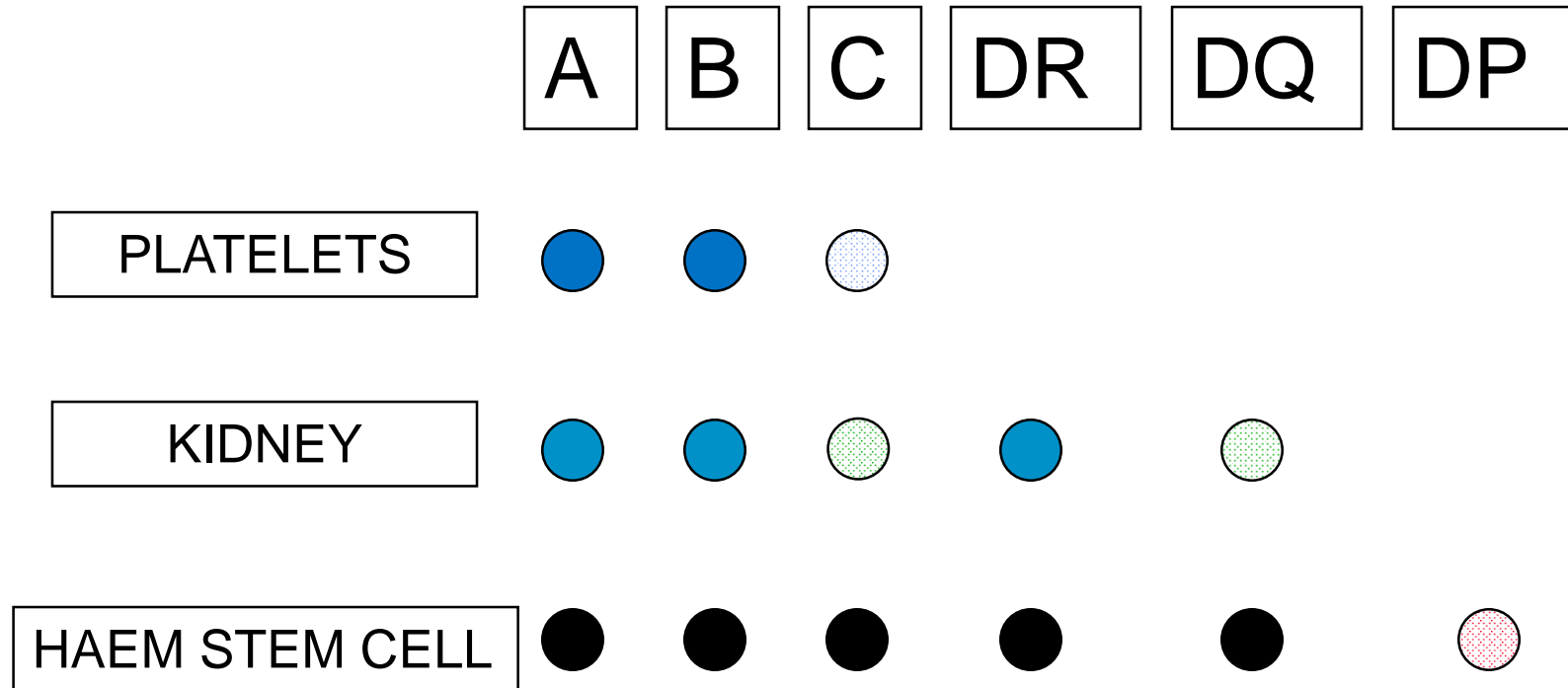
- Detection of HLA specific antibody
- Definition of antibody specificity
- HLA typing of patients and donors
- Selection and issue of HLA compatible platelets
- Documentation of post-transfusion increments
- Advice on patient management

NHSBT Platelet Panel

- 12,000 apheresis donors typed
- HLA class I typed – HLA-A, B, C. by Next Generation Sequencing
- HPA -1, 2, 3, 4, 5, 15. by Real Time PCR (NGS being developed)
- 18 - 20,000 HLA selected platelet units issued per year
- HLA selected platelets issued from:
 - Colindale for hospitals in the South
 - Sheffield for hospitals in the North

HLA Matching

HLA Locus



A match = No mismatch

The donor and patient are not serologically mismatched for the four antigens of the A and B loci.

donor A*01-A*02 / B*08-B*44

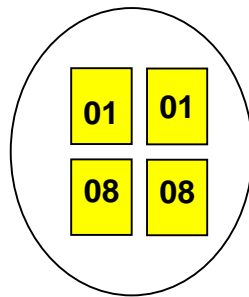
patient A*01-A*02 / B*08-B*44

donor* A*01-A*01 / B*08-B*08

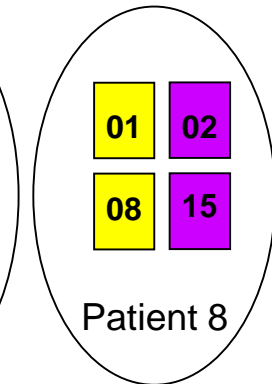
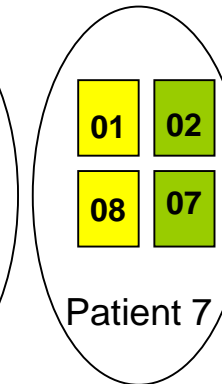
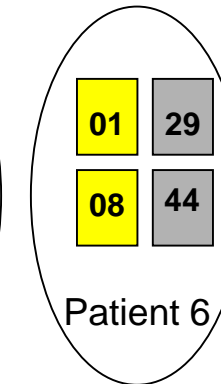
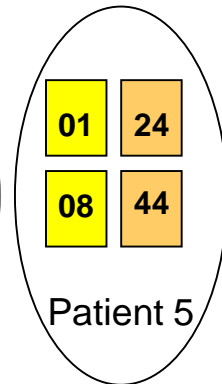
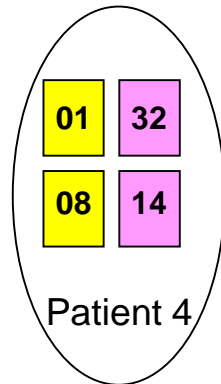
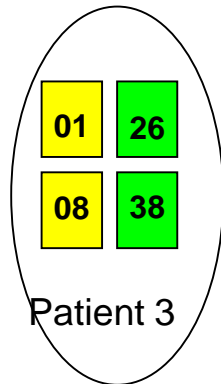
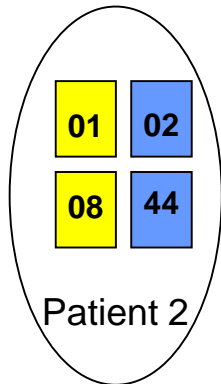
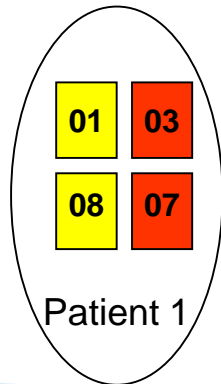
patient A*01-A*02 / B*08-B*44

*homozygous donor

HLA Homozygous Donors



Homozygous donor



B match (B₁-B₄) = Mismatched

The donor and patient are mismatched

B1 donor: A*01-A*02 / B*08-B*27

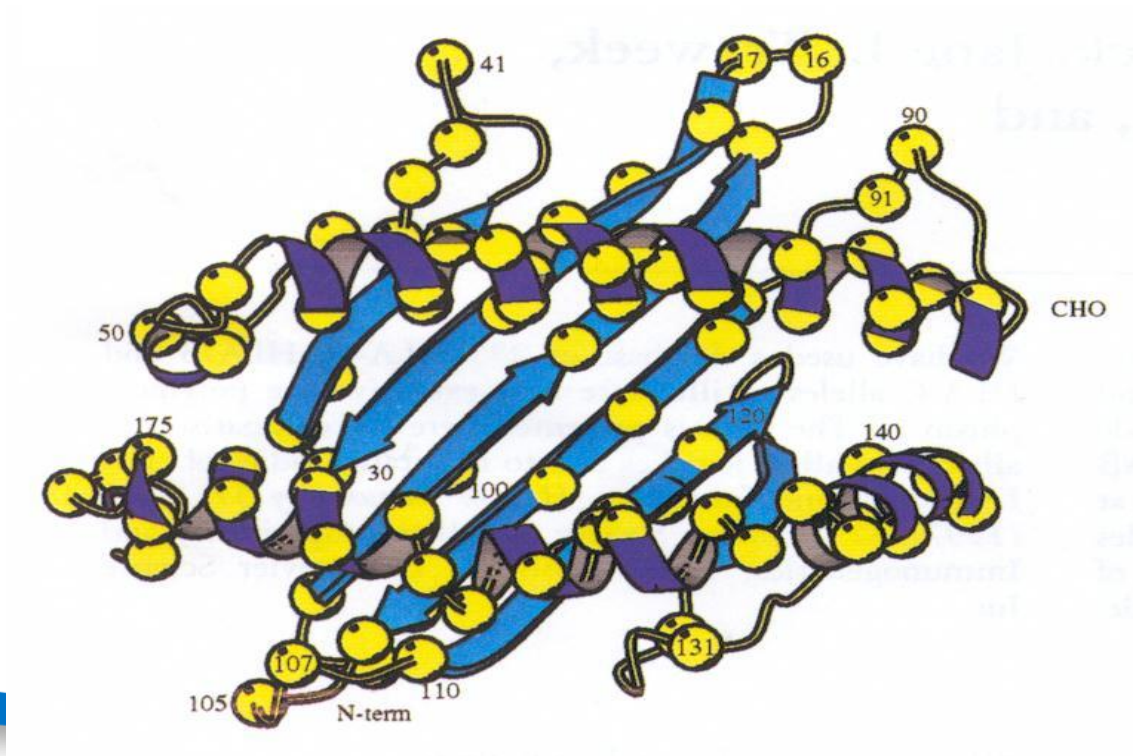
patient: A*01-A*68 / B*08-B*27

B2 donor: A*01-A*02 / B*08-B*07

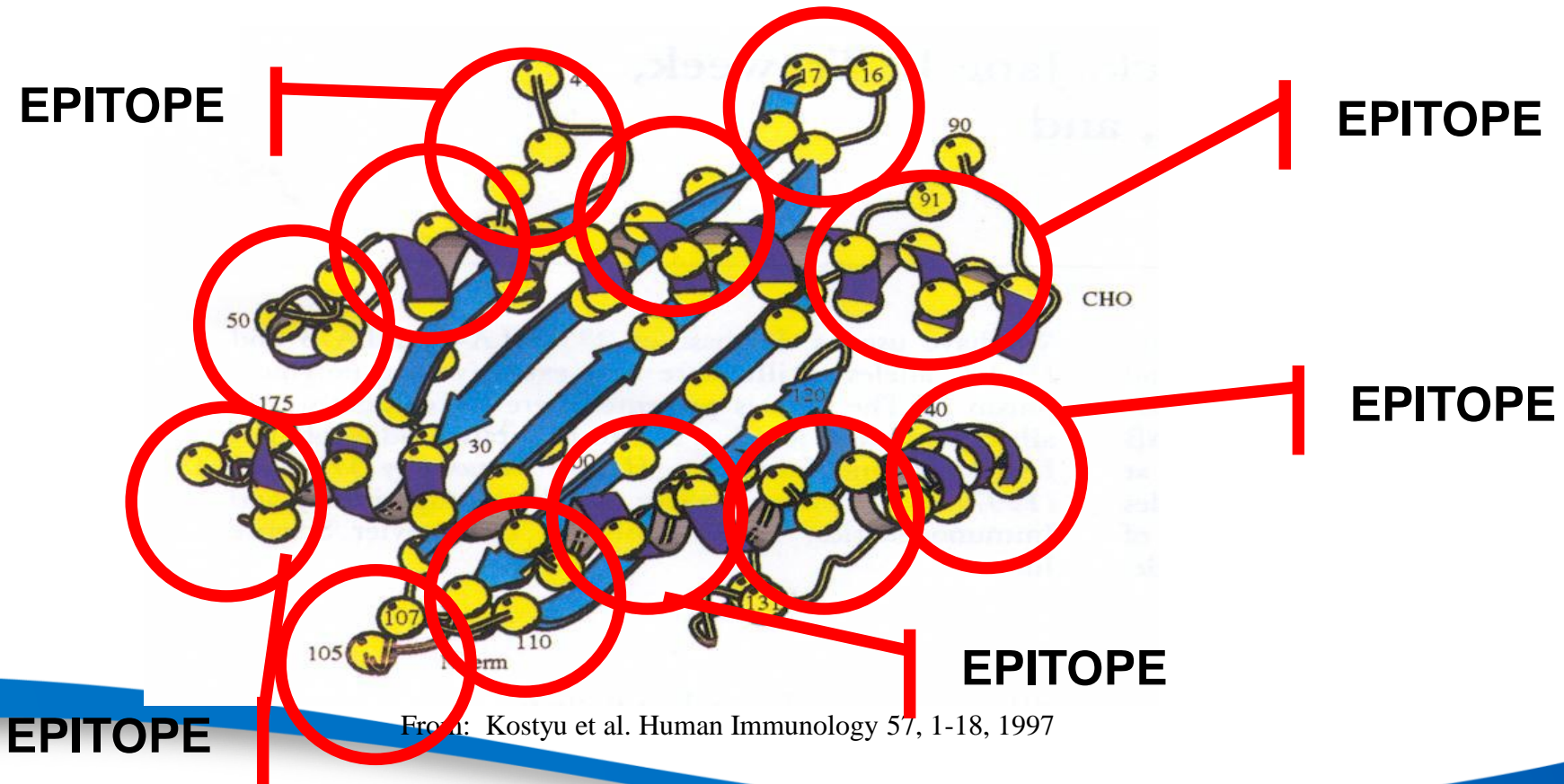
Relevance of HLA High Resolution Technology

- Next Generation Sequencing
 - Allele level HLA typing
 - HLA-B*44 HLA-B*44:02:01:01
- Single Antigen Luminex Beads
 - Allele specific antibodies
 - HLA-B44 HLA-B*44:03 specific antibody

HLA Molecule



HLA Epitopes



From: Kostyu et al. Human Immunology 57, 1-18, 1997

Principles of HLA Epitope Matching

HLAMatchmaker is based on two principles

1. An HLA antigen can be treated as a set of interlocus and intralocus epitopes with each epitope potentially capable of being recognized by antibodies
2. A person cannot make antibodies against one of their own epitopes. A donor who shares those epitopes should therefore be compatible even if the shared epitopes are not at the same HLA antigen

Duquesnoy RJ. HLAMatchmaker: a molecularly based algorithm for histocompatibility determination. I. Description of the algorithm. *Hum Immunol* 2002; 63:339–352.

Antigen vs. Epitope matching

Consider a platelet patient with HLA type A2, A30; B42, B53 and two potential donors D1 and D2 with types as listed

	HLA Type	MM
Patient	A*02, A*30; B*42, B*53	
D1	A*02, A*29; B*07, B*53	B2
D2	A*30, A*69; B*08, B*35	B3

CASE STUDY 1

Patient ID: MO Age: 74 yrs Gender: Female

Diagnosis : Aplastic Anaemia

Blood Group : O RhD pos

HPA Antibodies : NT

HPA Type : NT

HLA Class I Antibodies : A11,A23,A24,A2403,A25,A26,A29,A30,A31,A32,A33,A34,A43,A66,A74,B13,B18,B27,B2708,B35,B37,B38,B39,B41,B44,B45,B46,B47,B48,B49,B50,B51,B52,B53,B54,B55,B56,B57,B58,B59,B60,B61,B62,B63,B64,B65,B67,B71,B72,B75,B76,B77,B78,B82,Cw2,Cw5,Cw6,Cw9,Cw10,Cw15,Cw18,DP9,DP17,DQ7,DQ8,DQ9,DR4,DR7,DR8,DR9,DR11,DR13

HLA Class I Type : HLA-A*01, A*02, B*07, B*08, C*07

CASE STUDY 1

		<u>Match Grade</u>	<u>Pre- Count</u>	<u>Post- Count</u>
Donor 1	O+	Random	26	22
Donor 2	O+	Random	16	17
Donor 3	A+	A	13	48
Donor 4	B-	A	8	35
Donor 5	O+	A	29	55

CASE STUDY 2

Patient ID: PP Age: 72 yrs Gender: Female

Diagnosis : Acute Myeloid Leukaemia

Blood Group : B Positive

HPA Antibodies : HPA-5a ~91% Caucasoids HPA-5a pos

HPA Type : HPA-1a1a, 2a2a, 3a3b, 4a4a, 5b5b, 15a15b

HLA Class I Antibodies : A30, A31

HLA Class I Type : HLA-A*02, A*29, B*15, B*44

CASE STUDY 2

		<u>Match Grade</u>	<u>Pre-Count</u>	<u>Post-Count</u>	
Donor 1	B+	Random	4	7	
Donor 2	B+	Random	3	2	
Donor 3	A+	A	2	6	HLA selected only
Donor 4	O+	A	2	12	
Donor 5	B-	B2	1	49	HLA + HPA selected
Donor 6	O+	B2	9	20	
Donor 7	A-	B2	14	61	

CASE STUDY 3

Patient ID: GR

Age: 17 yrs

Gender: Female

Diagnosis : Hypoplastic MDS

Blood Group : O Positive

HPA Antibodies : NT

HPA Type :

HLA Class I Antibodies : Negative

Awaiting second mismatched
HSCT, HLA selected platelets
to avoid sensitisation to the
donor

HLA Class I Type : HLA-A*02, A*29, B*15, B*44

CASE STUDY 4

Patient ID: KN

Age: 55 yrs

Gender: Female

Diagnosis : Acute Myeloid Leukaemia

Blood Group : A RhD Positive

HPA Antibodies : Negative

HPA Type : nt

HLA Class I Antibodies : A1, A2, A23, A24, A29, A30, A31, A32, A33, A34
A36, A68, A69, A80, B27, B37, B38, B44, B45, B53, B57, B58, B59, B63, B76, B82

HLA Class I Type : HLA-A*03, -, B*07, B*51, C*01, C*07

CASE STUDY 4

- Patient: KN had a BMT in February 2018, Donor was RhD negative, requirement for HLA selected platelets to be RhD negative

		<u>Match</u>	<u>Pre-Count</u>	<u>Post-Count</u>
Donor 1	A-	Random	3	nt
Donor 2	O-	B2	15	24
Donor 3	A-	B2	11	42
Donor 4	A-	B2	11	25
Donor 5	A-	B1	21	34
Donor 6	O-	B1	9	20

HLA + RhD neg selected

HLA Selected Platelets

Post transfusion feedback can assist with patient management and the appropriate use of HLA selected platelets

Please return post transfusion platelet counts