



HLA Matchmaker applications

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HLA Matchmaker

- Devised by Rene Duquesnoy
- Based on structure of HLA epitopes
- Determined by polymorphic amino acid residues
- Originally viewed as short linear sequences (triplets)
- Shown to have clinical relevance for solid organ transplantation (sensitisation and graft survival)
- Helped to determine acceptable mismatches

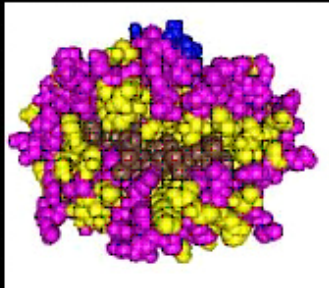


Eplets

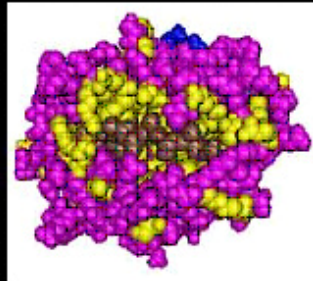
- Triplets provided incomplete description of epitopes
- Modelling studies on crystallised antibody complexes led to determination of “eplets”
- Patches of polymorphic residues within a radius of 3.0-3.5 Ångstroms
- Many eplets identical to triplets
- Correspond to serologically defined HLA determinants
- Free to download



HLA-A2



HLA-B27



HLA-Cw3

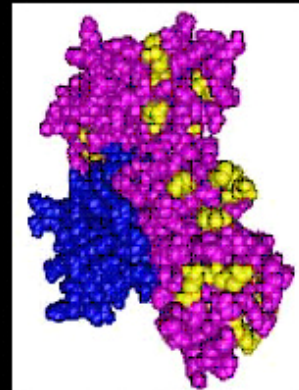
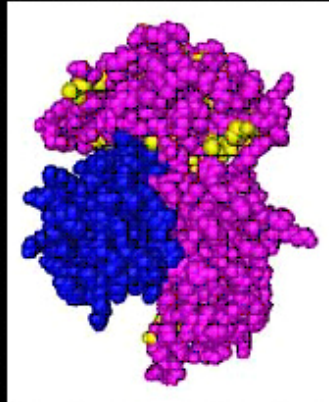
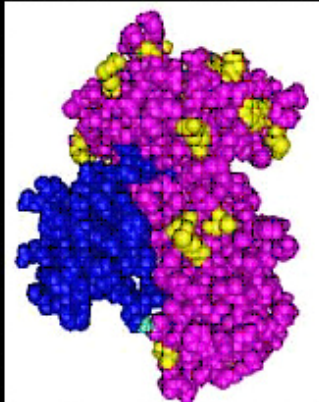
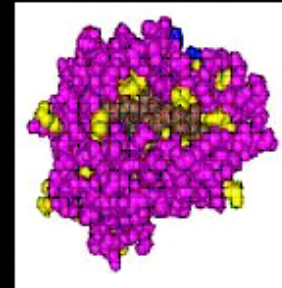


Figure 1 Polymorphic Residues on Class I Antigens



Polymorphic
Residues on B51

"Seen" by
A2, A68;
B27, B44

"Seen" by
A2, A68;
B35, B44

"Seen" by
A2, A24;
B7, B8

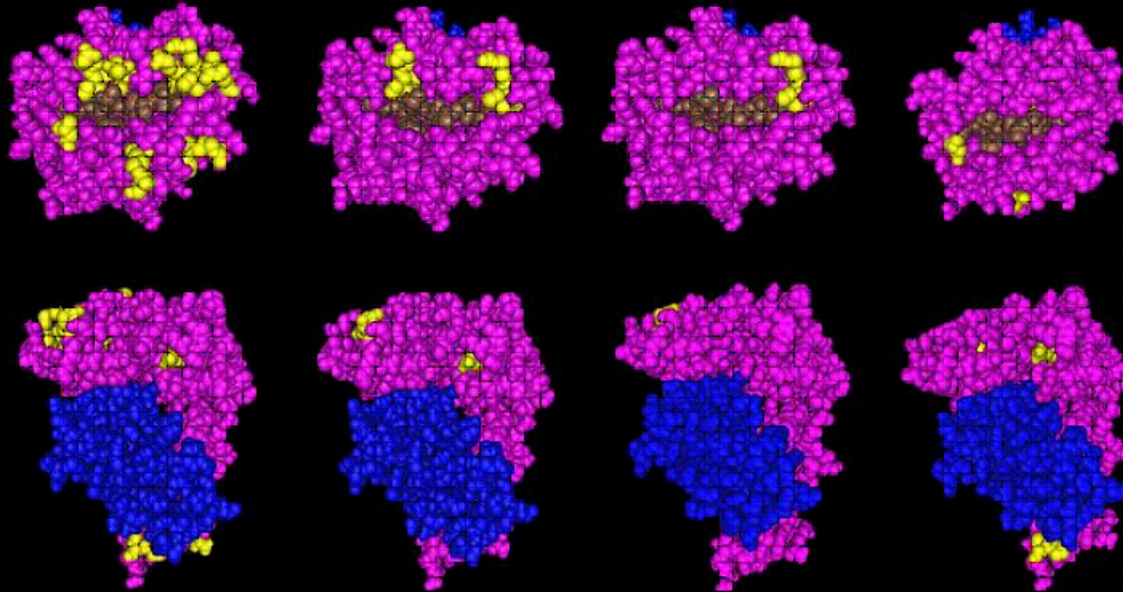


Figure 3 Structural Basis of a HLA-B51 Mismatch

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HLA Matchmaker – main applications in Manchester

- Cw specific antibody analysis
- DQ α antibody analysis
- Allele specific antibodies
- HLA-DP analysis

- Mismatched HSCT donor selection



Male patient.

HLA-CII Ab positive

2 Previous transplants

1- Tpx mm DR103 no DQ mm

2- no mm at DR or DQ

Referred for DSA testing

LABScreen single antigen analysis:-

DR1, 103, 9, 51

?DQA1* 04, 05, 06



Enter patient HLA type and immunising mismatches

	1stDRB1	2ndDRB1	1stDRB345	2ndDRB345	1stDQB	2ndDQB	1stDQA	2ndDQA
Recipient	DRB1*0401	DRB1*1301	DRB4*0101	DRB3*0101	DQB1*0301	DQB1*0603	DQA1*0302	DQA1*0103
Immunizer	DRB1*0103	DRB1*1301	x	DRB3*0101	DQB1*0301	DQB1*0603	DQA1*0501	DQA1*0103

Matchmaker lists mismatched eplets

Immunizing Donor	Total Mismatched DRB Eplets
DRB1*0103	,12LKF2,,14FEH,,25HRL,26RL,,,,,40EFD,47EYR,,,,,,,,,,,,,96EV,,,,,
DRB1*1301	,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,
X	,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,
DRB3*0101	,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,
Donor	Total Mismatched DQ Eplets
DQB1*0301	,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,
DQB1*0603	,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,
DQA1*0501	,,25YT,,41GR3,,,,,56RB,,,,,75SL4,,,,,160AE,,

DQ α associations

DRDQ COMBINATION	DR	DQ	DQA	FREQ OVERALL
DRB1*0101 , DQB1*0501	DRB1*0101	DQB1*0501	DQA1*0101	VERY COMMON
DRB1*0101 , DQB1*0504	DRB1*0101	DQB1*0504	DQA1*0102	VERY RARE
DRB1*0102 , DQB1*0501	DRB1*0102	DQB1*0501	DQA1*0101	VERY COMMON
DRB1*0103 , DQB1*0301	DRB1*0103	DQB1*0301	DQA1*0501	COMMON
DRB1*0103 , DQB1*0501	DRB1*0103	DQB1*0501	DQA1*0101	COMMON
DRB1*0301 , DQB1*0201	DRB1*0301	DQB1*0201	DQA1*0501	VERY COMMON
DRB1*0301 , DQB1*0602	DRB1*0301	DQB1*0602	DQA1*0102	EXTREMELY RARE
DRB1*0302 , DQB1*0402	DRB1*0302	DQB1*0402	DQA1*0401	
DRB1*0401 , DQB1*0301	DRB1*0401	DQB1*0301	DQA1*0302	MOST COMMON
DRB1*0401 , DQB1*0302	DRB1*0401	DQB1*0302	DQA1*0301/2	COMMON
DRB1*0402 , DQB1*0302	DRB1*0402	DQB1*0302	DQA1*0301	VERY COMMON
DRB1*0403 , DQB1*0302	DRB1*0403	DQB1*0302	DQA1*0301	VERY COMMON



Matchmaker determines mismatched eplets

3	DRB1*0101			9	,12LKF2,,14FEH,,25HRL,26RL,,,,,40EFD,47EYR,,,,,,71QRA,,74QRAA,,,,,96EV,,,,,
4	DRB1*0102			10	,12LKF2,,14FEH,,25HRL,26RL,,,,,40EFD,47EYR,,,,,,71QRA,,74QRAA,,81HA,,96EV,,,,,
5	DRB1*0103		IM	7	,12LKF2,,14FEH,,25HRL,26RL,,,,,40EFD,47EYR,,,,,,96EV,,,,,
6	DRB1*0301			1	,,,,,26TYD,,,,,
7	DRB1*0302			3	,,,,,26TFE,,,40EFD,47EYR,,,,,
8	DRB1*0401	Self		0	,,,,,
9	DRB1*0404			2	,,,,,71QRA,,74QRAA,,,,,
10	DRB1*0405			3	,,,,,57SA,,,,,71QRA,,74QRAA,,,,,
11	DRB1*0701			9	,,,,,26QF3,26KFE,,32FYN,,40EFD,47EYR,,,,,67IR,,,,,76GDT,180VM,,98ES,,,,,
12	DRB1*0801			9	,,,14GEY,,25YRF,,,31YFY,32FYN,,,,,57SA,,,67FR,70FDRA,71DRA,73ALDT,,,,,
13	DRB1*0901			7	,,,14FEH,,,26KYH,31QGIY,,,40HFD,,,,,67FR,,,,,180VM,,98ES,,,,,
14	DRB1*1001			7	,12VKF3,,14FEH,,25HRL,26RL,,,,,47EYR,,,,,,180VM,,96QV,,,,,
15	DRB1*1101			7	,,,,,31YFY,32FYN,,,,,57DE,,67FR,70FDRA,71DRA,,74DRAA,,,,,
16	DRB1*1301	Self		0	,,,,,
17	DRB1*1303			5	,,,,,31YFY,32FYN,,,,,57SA,,,67IK,,71DKA,,,,,
18	DRB1*1401			2	,,,,,57AA,,,,,112Y,,,,,
19	DRB1*1501			4	,142M3,,,,,32FYN,,,,,71QAA,,,,,96QV,,,,,
20	DRB1*1502			4	,142M3,,,,,32FYN,,,,,71QAA,,,,,96QV,,,,,
21	DRB1*1601			7	,142M3,,,,,32FYN,,,,,67FR,70FDRA,71DRA,,74DRAA,,,,,96QV,,,,,
22	DRB3*0101	Self		0	,,,,,
23	DRB3*0202			6	,12LKS,,,,,26KFE,,,40EFD,47EYR,,,,,,74QKGQ,,51R,,,,,
24	DRB4*0101	Self		0	,,,,,
25	DRB4*0103			0	,,,,,
26	DRB5*0101			8	,,,,,31QDIY,,,40HFD,,,,,67FR,70FDRA,71DRA,,74DRAA,,,,,96EV,,108T3,,,,,
27	DRB5*0202			7	,6C,,,,,31QGIY,,,40HFD,,,,,71QAA,,,,,81HA,,96EV,,108T3,,,,,



Retrieve bead data from csv. output file

Samples	4 Min Events	0										
Results												
Data Type: Median												
Location	Sample	1	2	3	4	5	6	7	8	9	10	11
1 (A3)	381028	40	4998	925	541	1413	1538	2254.5	2024	1342	2102	1545
2 (B3)	380945	43	32016	149.5	188	173	749	262	866	560	481	177
3 (C3)	369454	30	11103	688.5	1009	316.5	335	402	492	240	1101	178
4 (D3)	381235	32	10692	115.5	182	105.5	309	128	230	214	84.5	15541

Paste into spreadsheet and enter cut-off value

x		x	x	x	x	Avg Self	Avg Self	CutOff	CutOff		Enter	Enter
						1731	#DIV/0!	3000	0		Enter	Enter
DRB	DQB	DQA	sDRB	sDQB	sDQA	Olself	TEPself	OL	TEP	IMM	OLrx	TEPrx
y	y	y						NEG			447.5	x
y	y	y									13648	x
DRB1*0101	y	y									8136.5	x
DRB1*0102	y	y									6300	x
DRB1*0103	y	y								IM	9367.5	x
DRB1*0301	y	y						NEG			720	x
DRB1*0302	y	y						NEG			1053	x
DRB1*0401	y	y	Self			2421					2420.5	x
DRB1*0404	y	y						NEG			1831	x
DRB1*0405	y	y						NEG			822	x
DRB1*0701	y	y						NEG			1053.5	x
DRB1*0801	y	y						NEG			1481	x
DRB1*0901	y	y									4539	x
DRB1*1001	y	y						NEG			2005.5	x
DRB1*1101	y	y						NEG			1337.5	x
DRB1*1301	y	y	Self			801				IM	801	x
DRB1*1303	y	y						NEG			1048	x



Exclude negative beads (eplets) from analysis

			8136.5	x		9	,12LKF2,,14FEH,,25HRL,26RL,,,,,40EFD,47EYR,,,,,71QRA,,74QR/
			6300	x		10	,12LKF2,,14FEH,,25HRL,26RL,,,,,40EFD,47EYR,,,,,71QRA,,74QR/
		IM	9367.5	x		7	,12LKF2,,14FEH,,25HRL,26RL,,,,,40EFD,47EYR,,,,,96EV,,,,,
	NEG		720	x		1	,,,,,26TYD,,,,,,,,,,,,,,,,,,,,,,,,,,,,,
	NEG		1053	x		3	,,,,,26TFE,,,40EFD,47EYR,,,,,,,,,,,,,,,,,,,,,
			2420.5	x		0	,,,
	NEG		1831	x		2	,,,,,71QRA,,74QRAA,,,,,,,,,,,,,
	NEG		822	x		3	,,,,,57SA,,,71QRA,,74QRAA,,,,,,,,,,,,,
	NEG		1053.5	x		9	,,,,,26QF3,26KFE,,32FYN,,40EFD,47EYR,,,,,67IR,,,,,76GDT,180VM
	NEG		1481	x		9	,,,14GEY,,25YRF,,,31YYFY,32FYN,,,,,57SA,,,67FR,70FDRA,71DRA
			4539	x		7	,,,14FEH,,,26KYH,31QGIY,,,40HFD,,,,,67FR,,,,,180VM,,,98ES,,,,,

Enter negative alleles:							
Neg DRB	Neg DRB	Neg DRB	Neg DRB	Neg DQB	Neg DQB	Neg DQA	Neg DQA
DRB1*0701	DRB1*1201	x	x	DQB1*0401	DQB1*0202	DQA1*0201	DQA1*0101
DRB1*1303	DRB1*1503	x	x	DQB1*0201	DQB1*0601	DQA1*0102	x
DRB1*1401	DRB1*0301	x	x	DQB1*0501	x	x	x
DRB1*1101	DRB1*0302	x	x	DQB1*0502	x	x	x
DRB1*0801	DRB3*0301	x	x	DQB1*0604	x	x	x
DRB1*0405	DRB1*1602	x	x	DQB1*0302	x	x	x



Select reactive eplets

OLrx	TEPrx	Commei	#Ep	DRB Ep	DQB Ep	DQA Ep
447.5	x		
13648	x		
8136.5	x		4	,12LKF2,,14FEH,,25HRL,.....96EV,.....
6300	x		4	,12LKF2,,14FEH,,25HRL,.....96EV,.....
9367.5	x		4	,12LKF2,,14FEH,,25HRL,.....96EV,.....
720	x		0
1481	x		0
4539	x		4	,,14FEH,,26KYH,31QGIY,,40HFD,.....
2005.5	x		3	,12VKF3,,14FEH,,25HRL,.....
1337.5	x		0
787	x		0
556	x		0
6270	x		4	,,31QDIY,,40HFD,.....96EV,,108T3,.....
3173	x		5	,6C,,31QGIY,,40HFD,.....96EV,,108T3,.....
430	x		0
403	x		0
20442	x		3	,41GR3,,75SL4,,160AE,
351.5	x		0
887	x		0
841	x		0
16953.5	x		2	,41GR3,,69T,.....
547	x		0
1952	x		0
21172	x		2	,41GR3,,69T,.....

Results list reactive eplets/alleles

Reactive									
Eplets	Reactive DRB Antigens		Reactive DRB Alleles						
14FEH	DR1,9,10	DRB1	*0101 *0102*0103*0106 *0901 *1001						
96EV	DR1,51	DRB1	*0101 *0102*0103*0106 5*0101 5*0102 5*0103 5*0104 5*0105 5*0106 5*0107 5*0109 5*0111						
x		DRB1							
Eplets	Reactive DQB Antigens		Reactive DQB Alleles						
x		DQB1							
x		DQB1							
x		DQB1							
Eplets	Reactive DQA 2-digits		Reactive DQBA Alleles						
41GR3	A4,5,6	DQA1	*0401 *0402 *0404 *0501 *0502 *0503 *0504 *0505 *0601 *0602						
x		DQA1							



Cw analysis

Female patient - pregnancy related sensitisation

No transfusion information. No previous transplant

	1st A	2nd A	1st B	2nd B	1st C	2nd C
Patient	A*0201	A*3201	B*3501	B*4402	Cw*0401	Cw*0501
Immunizer	A*0101	x	B*1501	B*3901	Cw*0702	Cw*0302

LABScreen single antigen analysis:-

B37,38,39,41,42,46,55,61,67,73;

Cw1,7,8,9,10,12,14,16.

Allele specific antibodies

Female patient - pregnancy related sensitisation

No transfusion information. No previous transplant

	1stDRB1	2ndDRB1	1stDRB345	2ndDRB345	1stDQB	2ndDQB	1stDQA	2ndDQA
Recipient	DRB1*0701	DRB1*1301	DRB4*0101	DRB3*0101	DQB1*0202	DQB1*0603	DQA1*0201	DQA1*0103
Immunizer	DRB1*0401	x	DRB4*0101	x	DQB1*0302	x	DQA1*0301	x

LABScreen single antigen analysis:-

DR4,8,11; DQ7,8,9; DRB1*13:03

HLA Matchmaker analysis

Enter eplets on reactive alleles:			
DRB	96YL4	31YYFY	X
DQB	55PPP	X	X
DQA	X	X	X

Results

Eplets	Reactive DRB Antigens																
96YL4	DR4	DRB1	*0401	*0402	*0403	*0404	*0405	*0406	*0407	*0408	*0409	*0410	*0411	*0413	*0415	*0417	*0418
31YYFY	DR8,11,13s	DRB1	*0801	*0802	*0803	*0804	*0805	*0806	*0810	*0811	*0813	*1101	*1102	*1103	*1104	*1105	*1106
			*1107	*1108	*1111	*1114	*1115	*1119	*1303	*1304	*1307	*1311	*1312	*1314	*1321	*1324	
Eplets	Reactive DQB Antigens																
55PPP	DQ3	DQB1	*0301	*0302	*0303	*0304	*0305	*0306	*0307	*0308	*0309	*0310	*0311	*0312	*0313		



Male patient. Multiple transfusions. 1 previous transplant.

	1stDRB1	2ndDRB1	1stDRB345	2ndDRB345	1stDQB	2ndDQB	1stDQA	2ndDQA
Recipient	DRB1*1101	DRB1*1302	DRB3*0202	DRB3*0301	DQB1*0301	DQB1*0609	DQA1*0501	DQA1*0102
Immunizer	DRB1*0101	DRB1*1303	x	DRB3*0101	DQB1*0501	DQB1*0301	DQA1*0101	DQA1*0501

LABScreen single antigen analysis:-

DR1,103,9,10,14; DR51; DQ2,5; DQB1*06:02, *06:03



HLA Matchmaker

- Can explain unusual reaction patterns
- Define allele specific antibodies
- Confirm cross-reactive specificities
- Distinguish DQ α specific antibodies



www.hlamatchmaker.net