NHS Blood and Transplant

Human Neutrophil Antigen specific antibodies are associated with early and chronic antibody mediated rejection in kidney transplant recipients

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Retrospective review of kidney transplant outcome in 7 individuals with Human Neutrophil Antigen (HNA) specific antibodies

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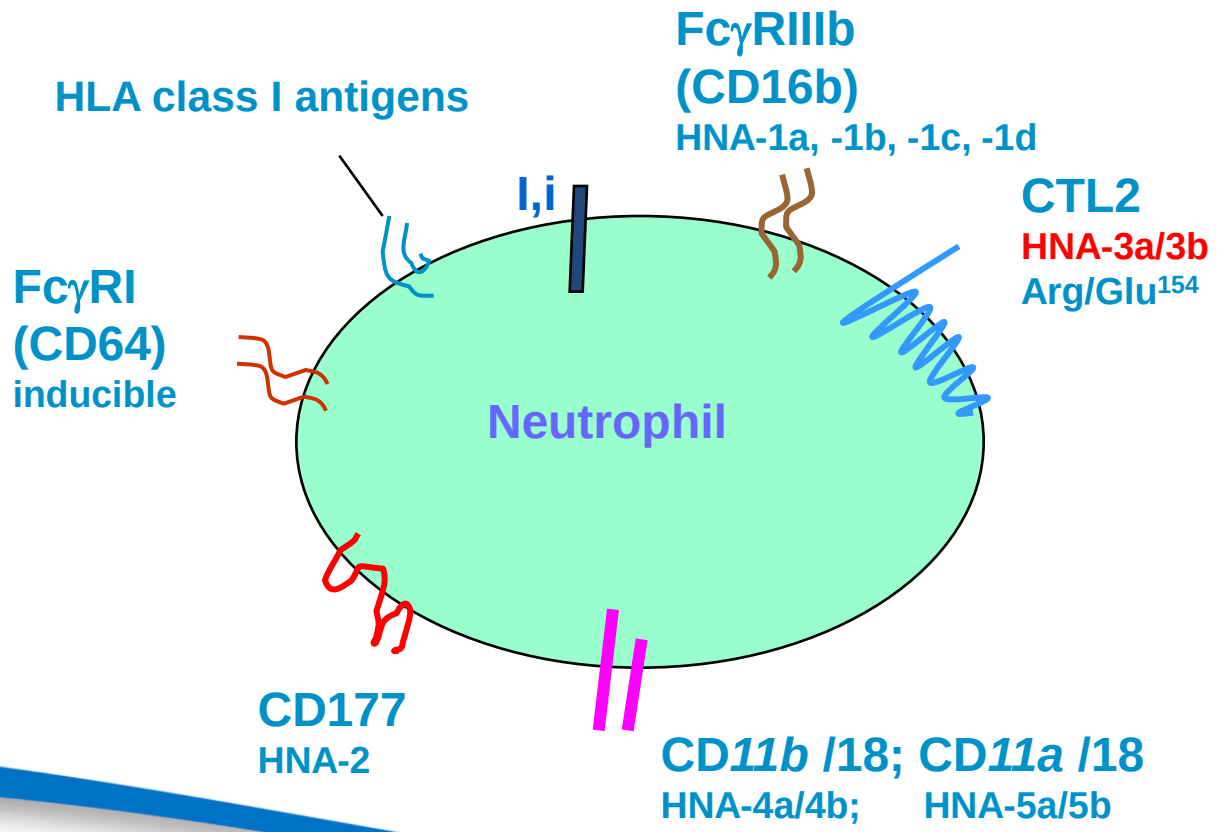
Human Neutrophil Antigen (HNA) system



System	Genotype Frequency	Glycoprotein
HNA-3a/3a	60%	CTL2
HNA-3a/3b	35%	
HNA-3b/3b	5%	

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Approximately 5% individuals are HNA3b/3b

Associated with a single amino acid substitution at position 154 on choline transporter like protein 2 (CTL2)

Can become allo-sensitised through exposure to HNA3a/3a or HNA3a/3b

HNA-3 expressed on platelets, lymphocytes, endothelial, kidney, spleen & placental cells

Anti-HNA-3a has been implicated in the more severe cases of TRALI

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Seven kidney transplant recipients

Transplanted at five different UK centres

‘Unexplained’ positive donor T and B cell Flow cytometry crossmatch

No HLA donor specific antibodies

Previous non proceeding transplants due to positive FCxm

Retrospective testing using GIFT LIFT and Luminex® identified HNA-3a specific antibodies in all recipients

Donors typed as HNA 3a/3a or 3a/3b

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Patient	Gender	Age	Primary renal disease	Transplanted	Donor type	Sensitisation	Previous non proceeding transplant	Induction therapy
1	F	43	Small kidneys Cause Unknown	2006	DBD	Pregnancy	3	ATG
2	F	57	ADPKD	2013	DCD	Pregnancy + Transfusion	1	Basiliximab
3	F	55	ADPKD	2014	LKD	Pregnancy + Transfusion	6	ATG
4	F	37	Cystinosis	2015	LKD	Transplant	2	Basiliximab
5	F	60	ADPKD	2016	DCD	Pregnancy + Transfusion	1	Basiliximab
6	F	61	Renovascular disease	2017	DCD	Pregnancy	0	Basiliximab
7	F	57	ADPKD	2018	DBD	Pregnancy	0	Basiliximab

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Patient	HLA-A B DR mm	Donor HNA-3	FCxm T cell RMF	FCxm B cell RMF	ABMR	Biopsy	Histology	Graft Loss
1	1.1.0	3a/3a	9.0	4.2	Y	Day 5	Banff 2, acute antibody mediated rejection	N
2	1.1.0	3a/3b	6.4	5.6	Y	Day 5,13,25	Banff 4, IIa	Y
3	0.1.0	3a/3a	10.1	3.4	Y	36 months	Banff 2, chronic antibody mediated rejection	N
4	0.0.1	3a/3b	4.0	4.0	Y	Day 18	Banff 2, acute antibody mediated rejection	N
5	1.1.1	3a/3a	4.0	4.0	Y	Day 5	Banff 2, acute antibody mediated rejection	Y
6	1.1.1	3a/3b	4.3	2.0	N	n/a	No post-transplant dysfunction: no biopsy	N
7	0.0.0	3a/3a	2.7	3.2	Y	Day 4	Banff 2, acute antibody mediated rejection	N

Summary

- All female HNA-3b/3b with HNA-3a antibodies
- Most have history of previous pregnancies
- Donor expressed HNA-3a
- May be HLA sensitised but no detectable HLA DSA
- Positive FCxm (T and B cell)
- High incidence of ABMR
- 2 graft failures at 10 and 12 months
- >95% of Donors will express HNA-3a

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