

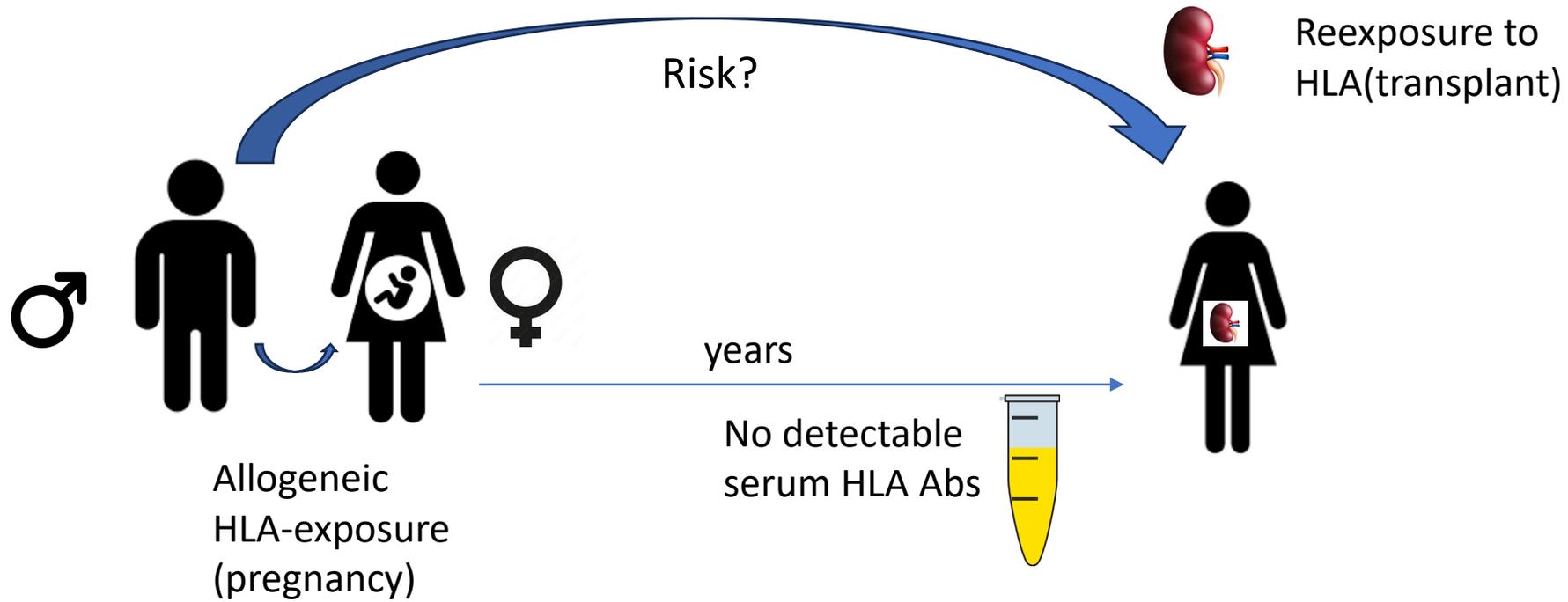
HLA-specific memory B cells in female transplant candidates sensitized by pregnancy

Elisenda Alari-Pahissa^{1*}, Sara Sanz-Ureña^{1,2*}, Laura Llinàs¹, Gonka Karahan³, Judith Federico^{1,2}, Jorge Eguía⁴, José Luís Caro⁵, Sebastian Heidt³, Dolores Redondo-Pachon^{1, 6}, Marta Crespo^{1, 6}.

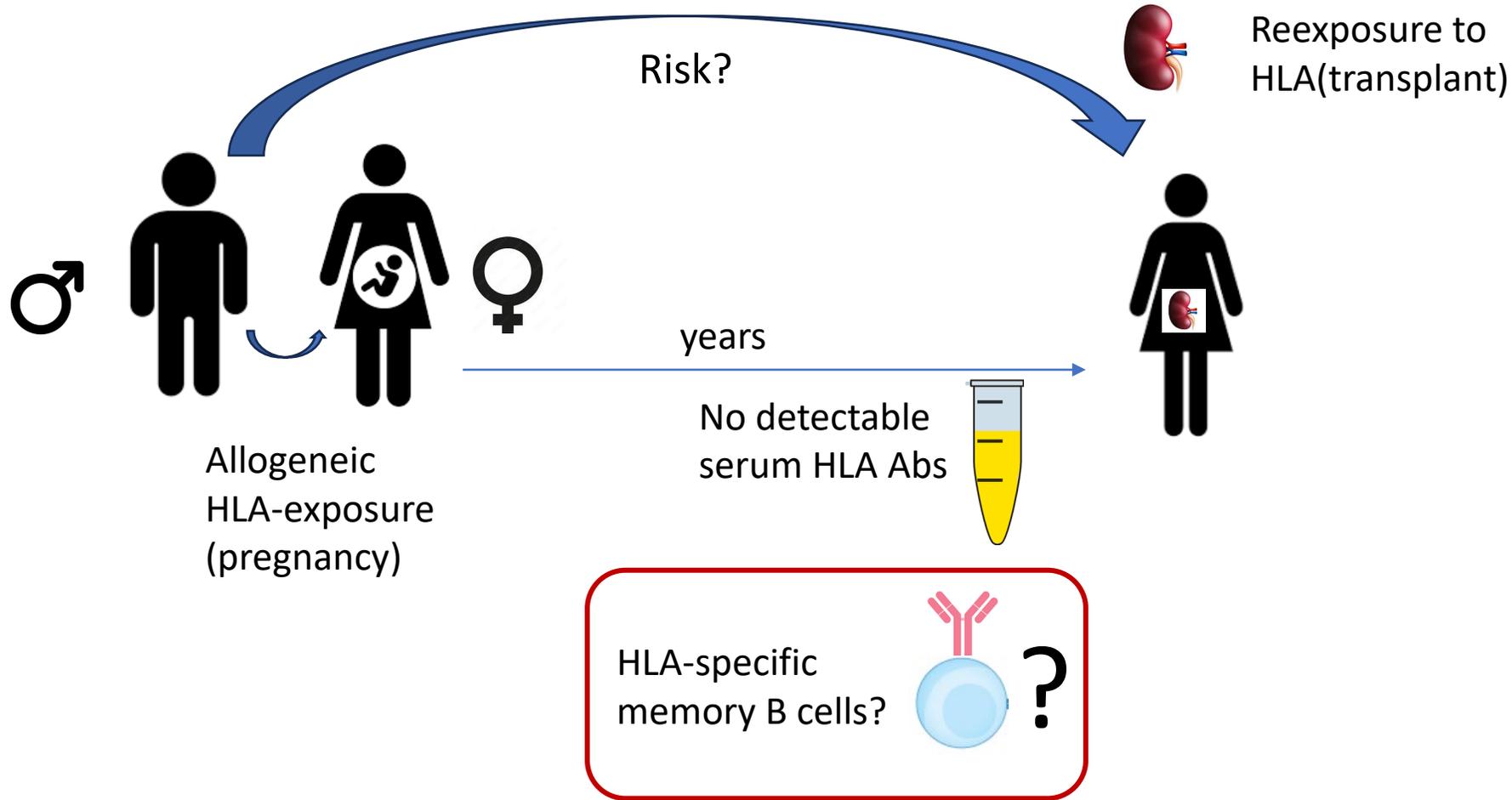
¹Hospital del Mar Research Institute, Barcelona. ²Department of Medicine and Life Sciences, Universitat Pompeu Fabra, Barcelona. ³Department of Immunohematology and Blood Transfusion, Leiden University Medical Center (LUMC), the Netherlands. ⁴Laboratori de Referència de Catalunya, Barcelona. ⁵Histocompatibility Laboratory, Hospital Clinic, Barcelona. ⁶Nephrology Service, Hospital del Mar, Barcelona.



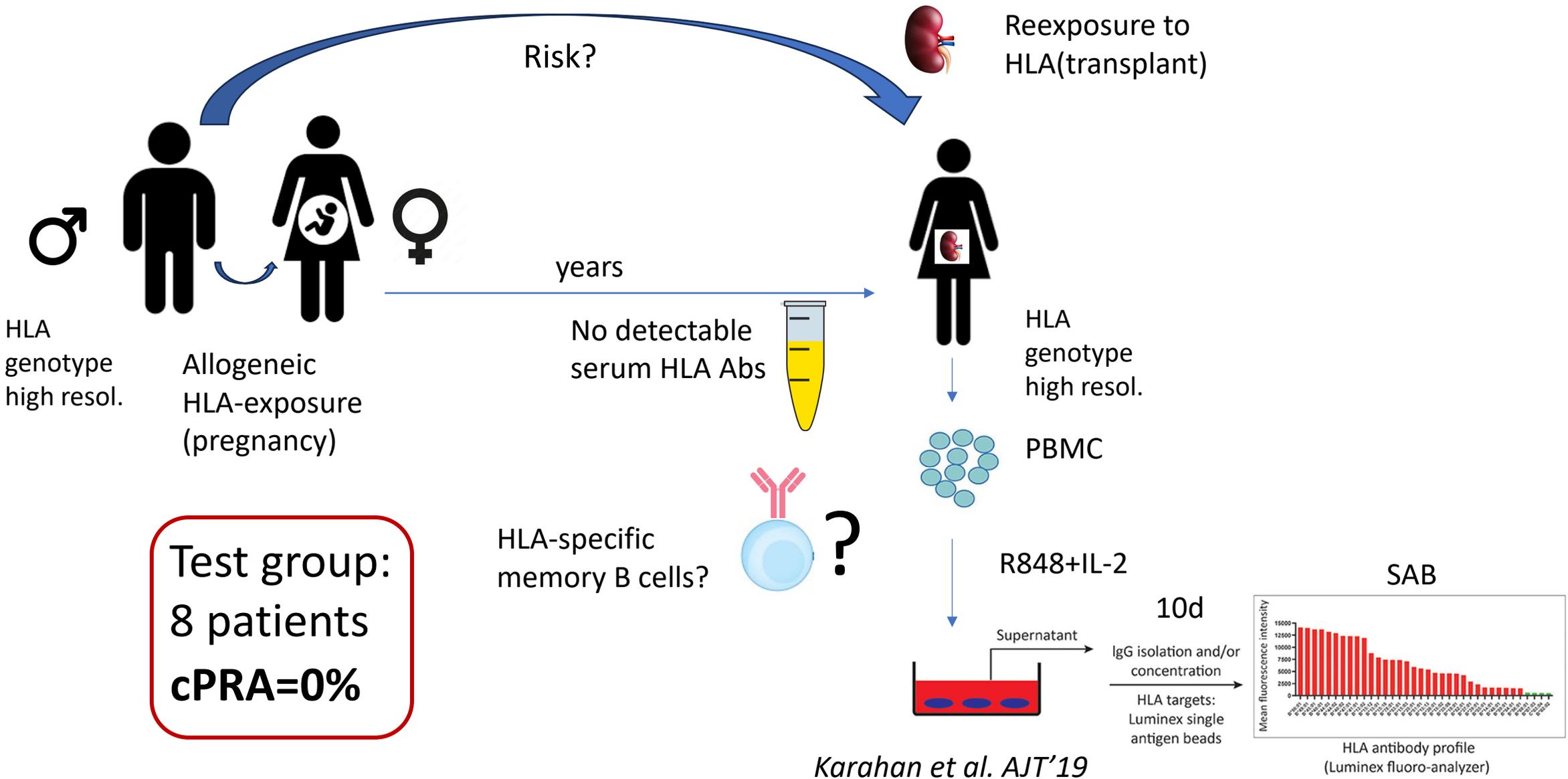
Risk of transplanting HLA-exposed patients without serum HLA Abs with organs bearing the same HLA?



Risk of transplanting HLA-exposed patients without serum HLA Abs with organs bearing the same HLA?



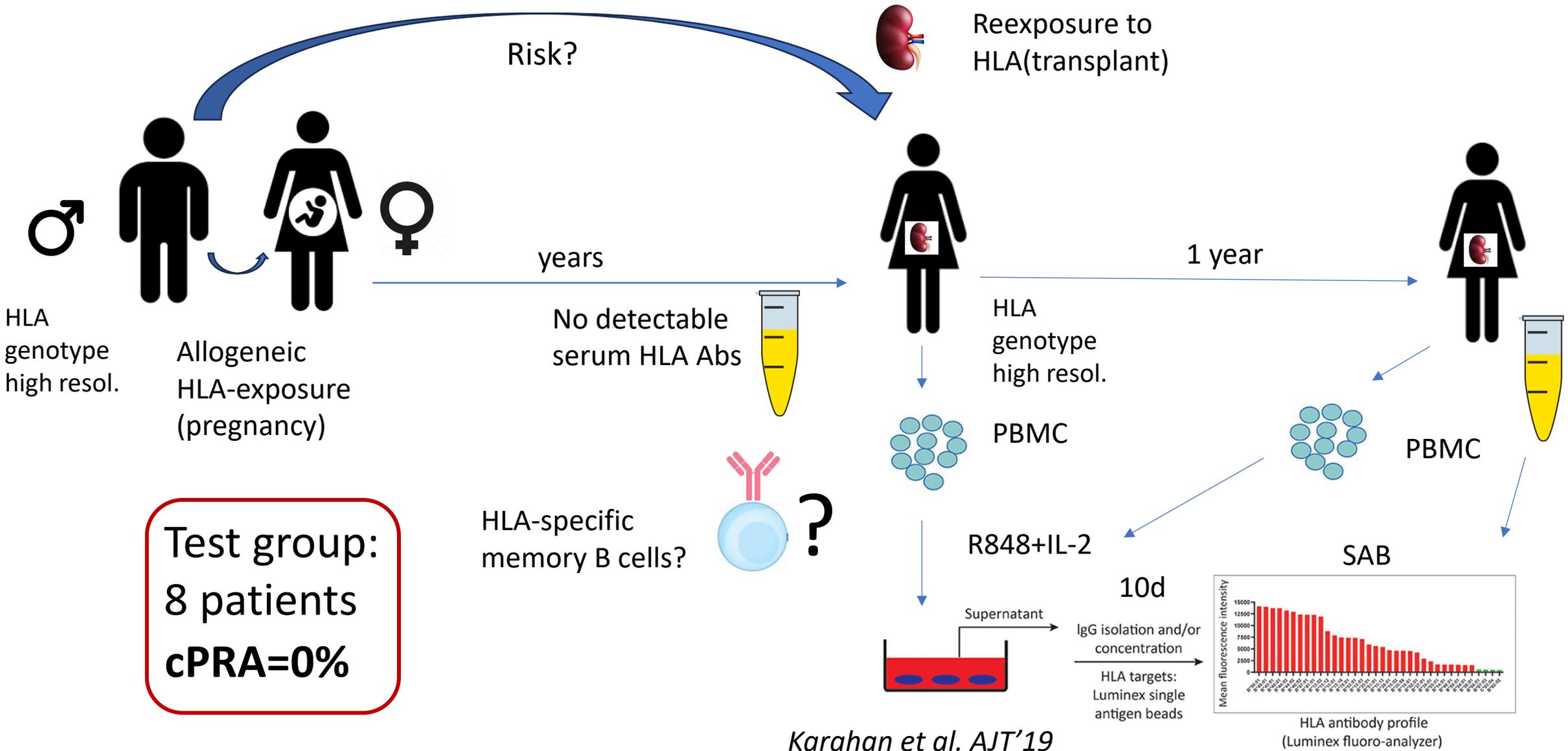
Patient selection and methods for test group:



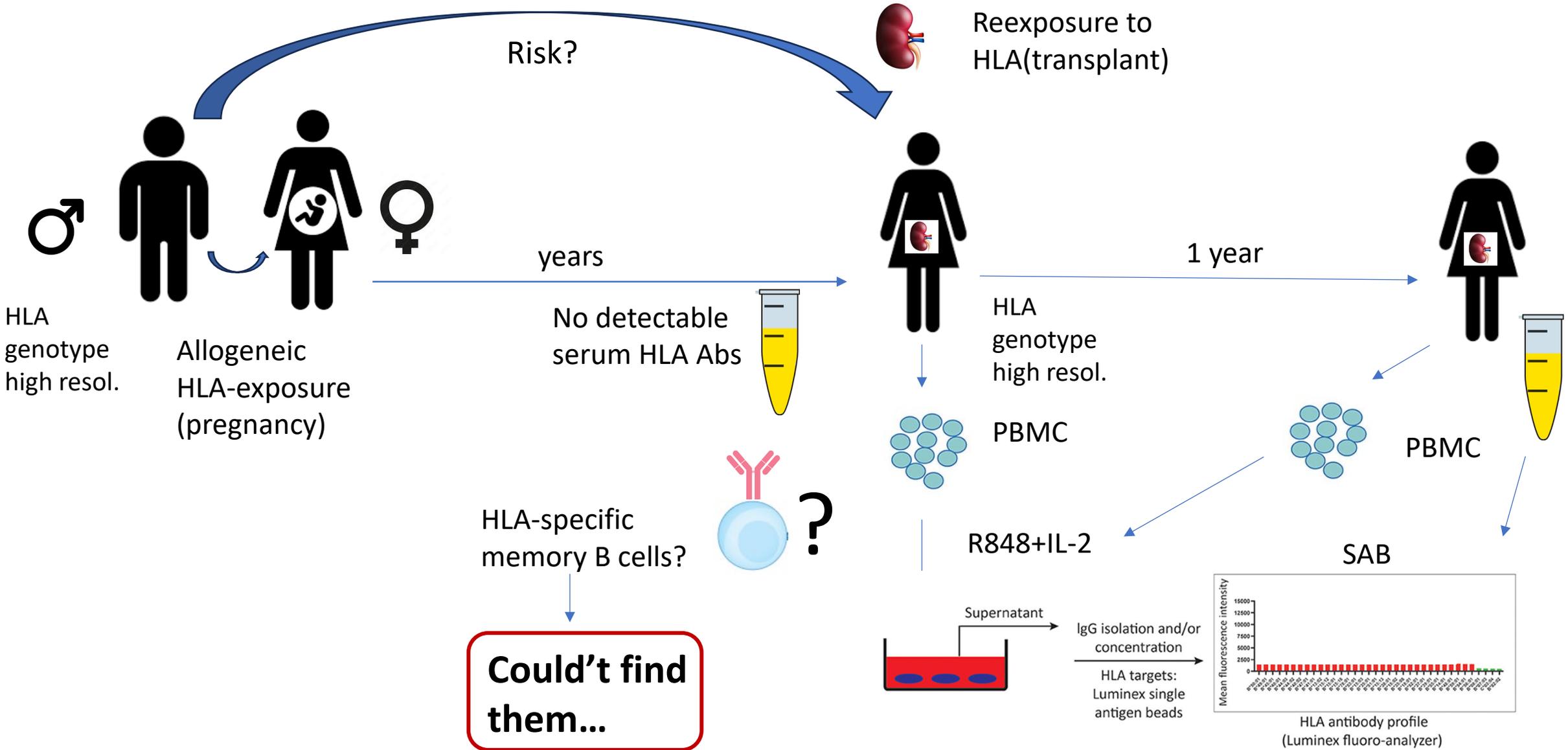
**Test group:
8 patients
cPRA=0%**

Karahan et al. AJT'19

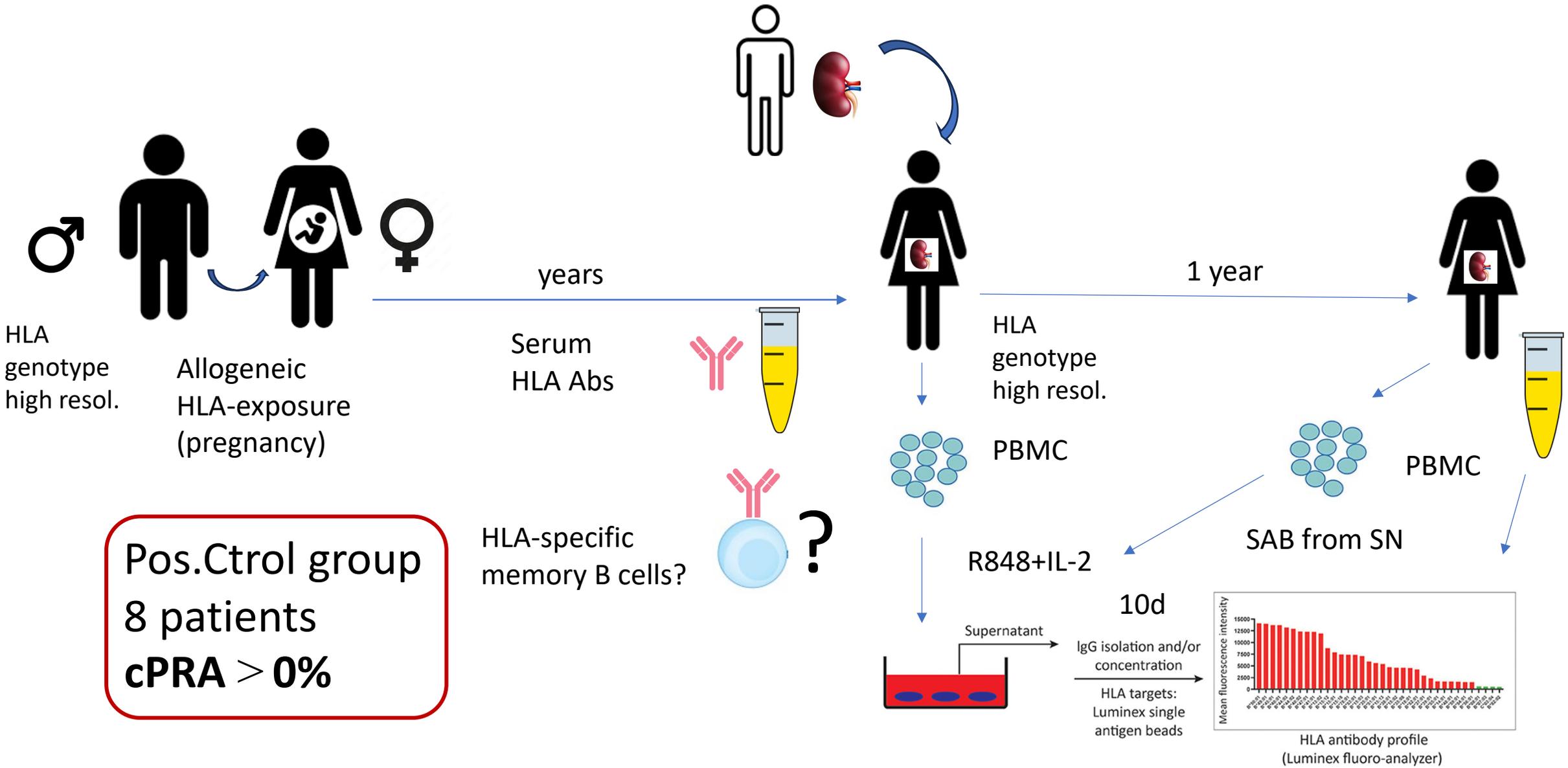
Patient selection and methods for test group:



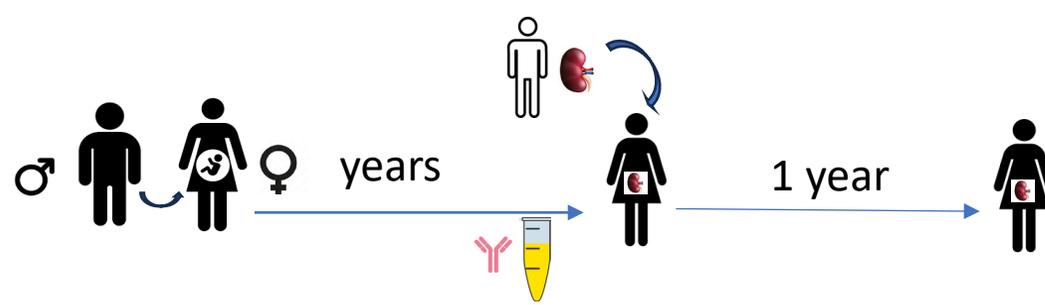
Results of cPRA=0% group:



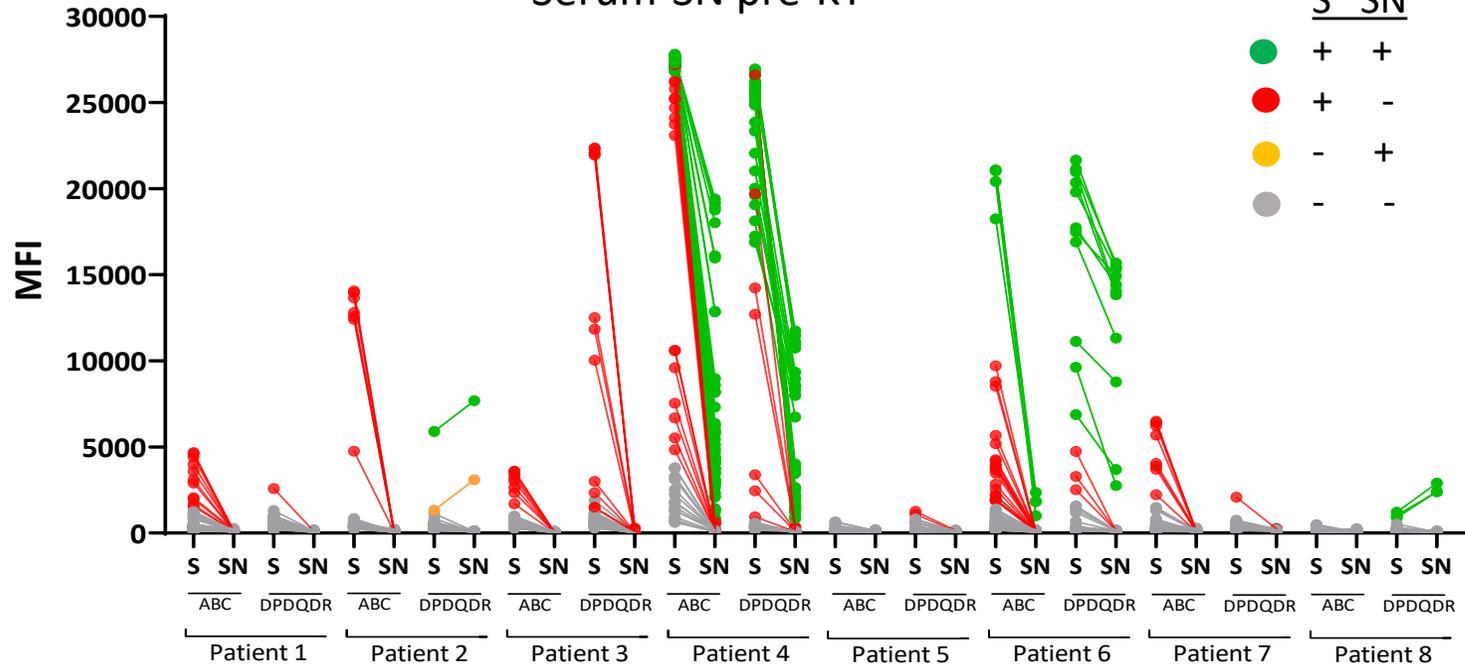
Patient selection and methods for positive control group:



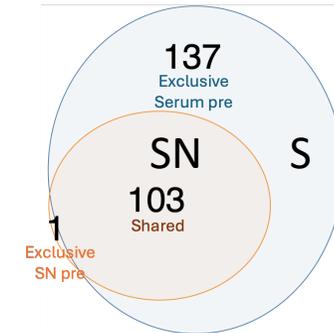
Results of cPRA > 0% group pre-KT:



Serum-SN pre-KT



Serum-SN pre-KT

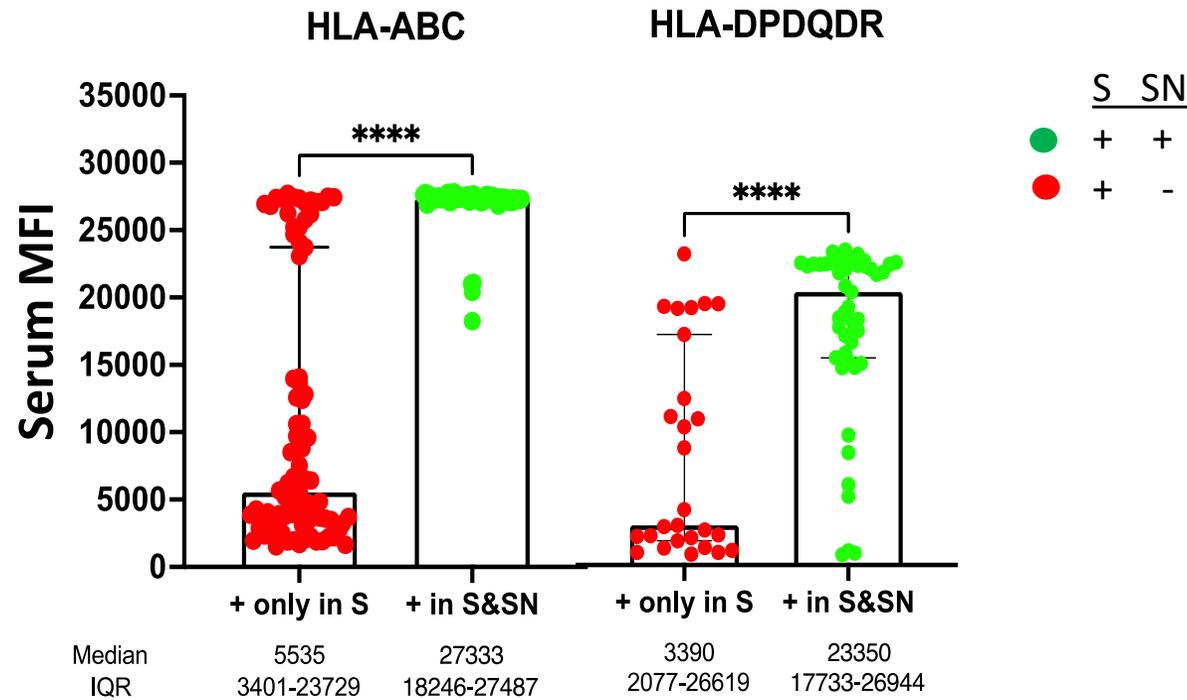


Less positivities in SN than in serum, in less patients, all of them with pre-KT seric anti-HLA-Abs

Agreement test	Patient 1		Patient 2		Patient 3		Patient 4		Patient 5		Patient 6		Patient 7		Patient 8	
	ABC	DPDQDR														
ABC	k = 0.000	k = 0.000	k = 0.000	k = 0.000	k = 0.359	NA	k = 0.270	k = 0.000								
DPDQDR	k = 0.000	k = 0.659	k = 0.000	k = 0.000	k = 0.796	k = 0.000	k = 0.538	k = 0.000	k = 0.422	k = 0.000	k = 0.422					

k=0.58

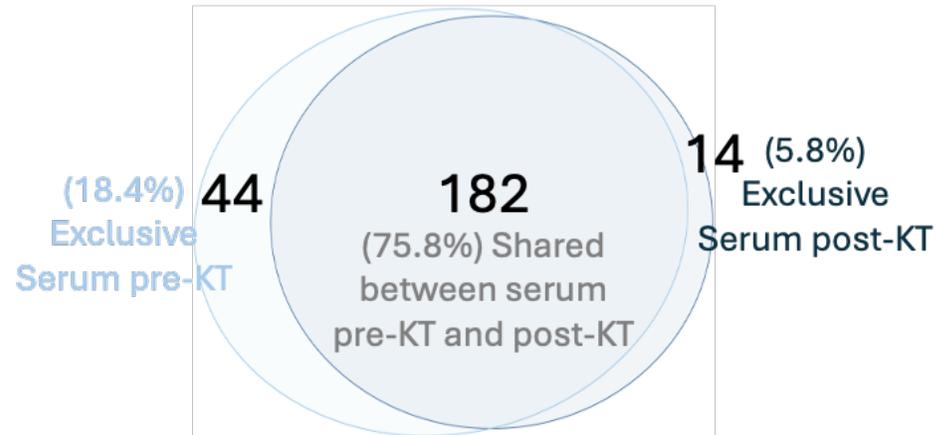
Results of cPRA > 0% group pre-KT:



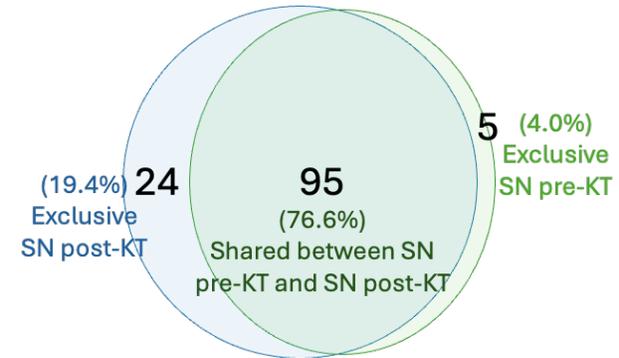
Positivities found
 in both serum and SN
 had higher MFI in serum than
 those detected only in serum

Results of cPRA > 0% group pre-KT vs post-KT:

Serum Pre vs post



SN Pre vs post



New hypothesis:

Does the detection of positive specificities in

<u>S</u>	<u>SN</u>
+	+
+	-
-	-

depend on the immunogenicity of paternal HLA alleles?

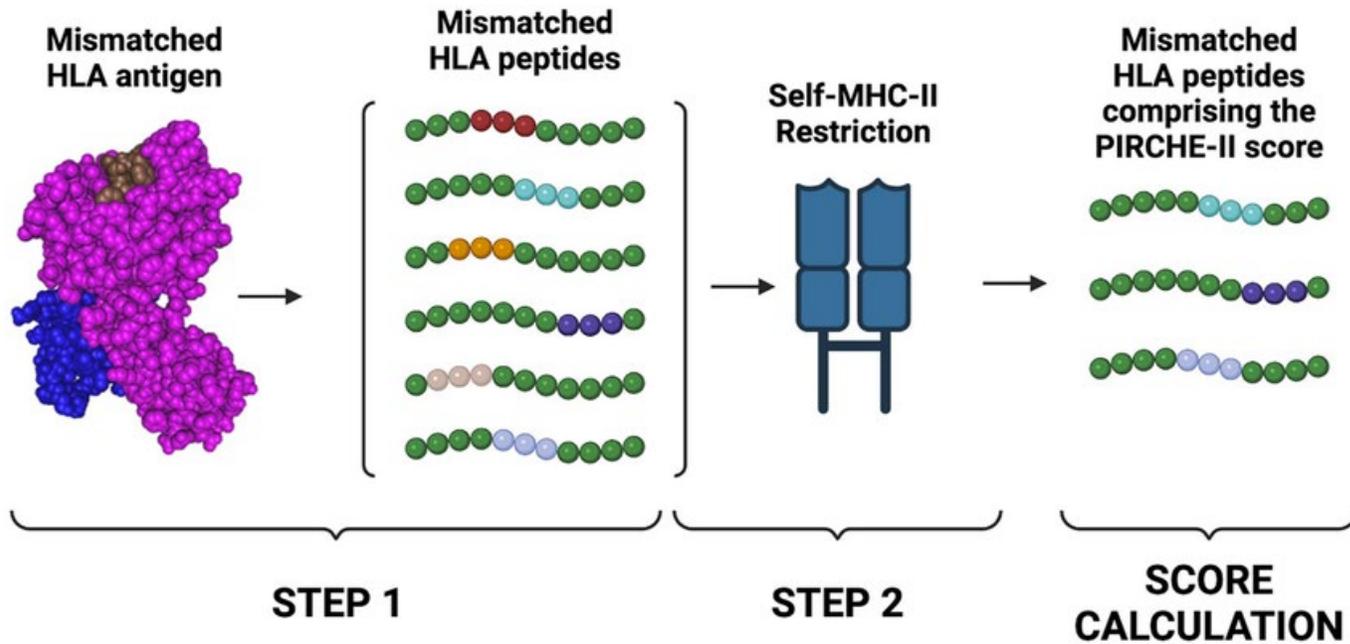


Analyze

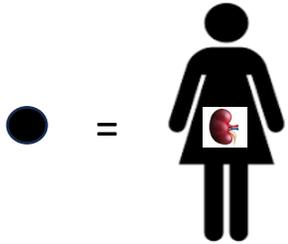
T and B cell epitope loads
of paternal HLA alleles

Method to calculate T cell epitope load:

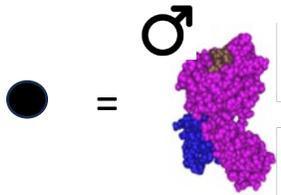
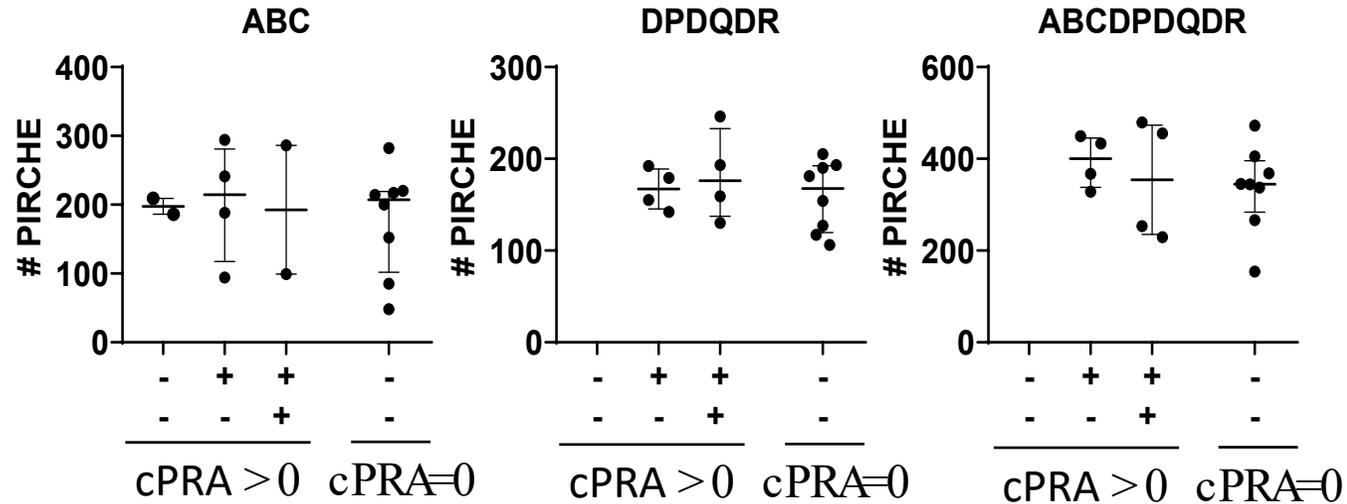
Predicted Indirectly Recognizable HLA Epitopes:



Results of T cell epitope load of paternal HLA alleles:

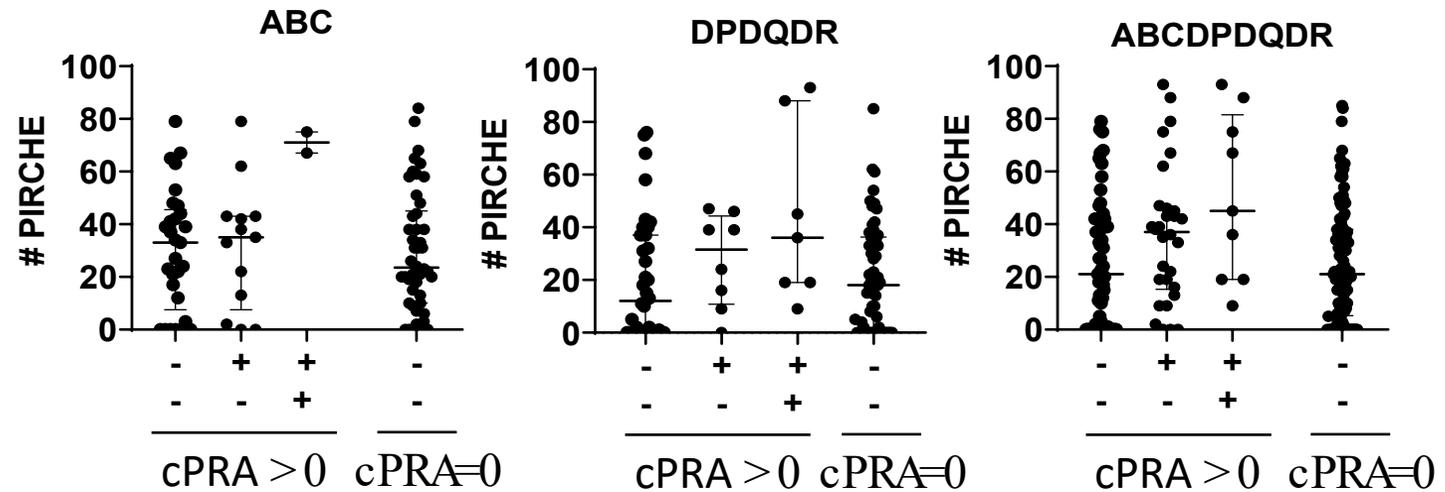


\sum # PIRCHE all paternal HLA alleles of a patient



PIRCHE of each paternal HLA alleles

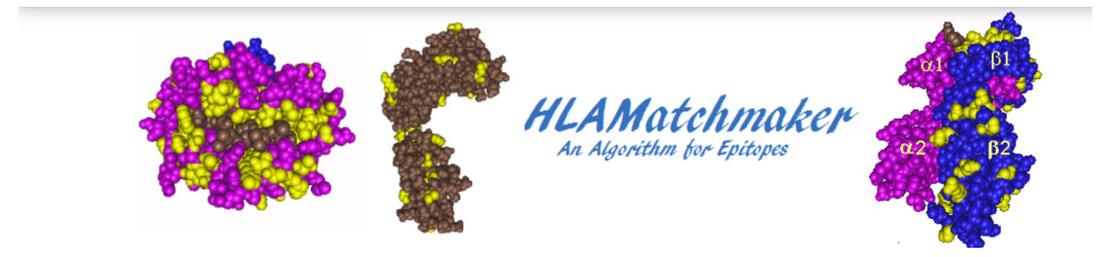
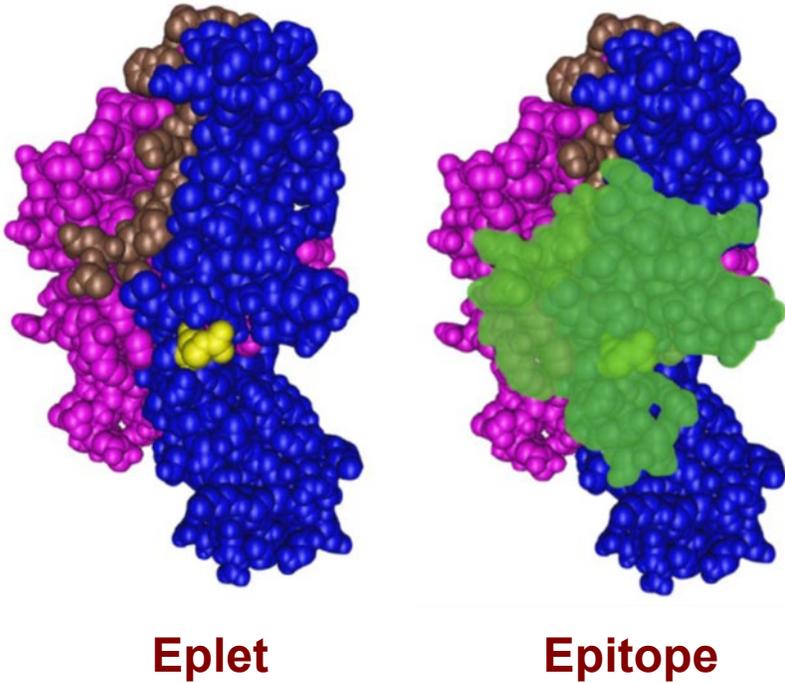
Pool of paternal HLA alleles from patients:



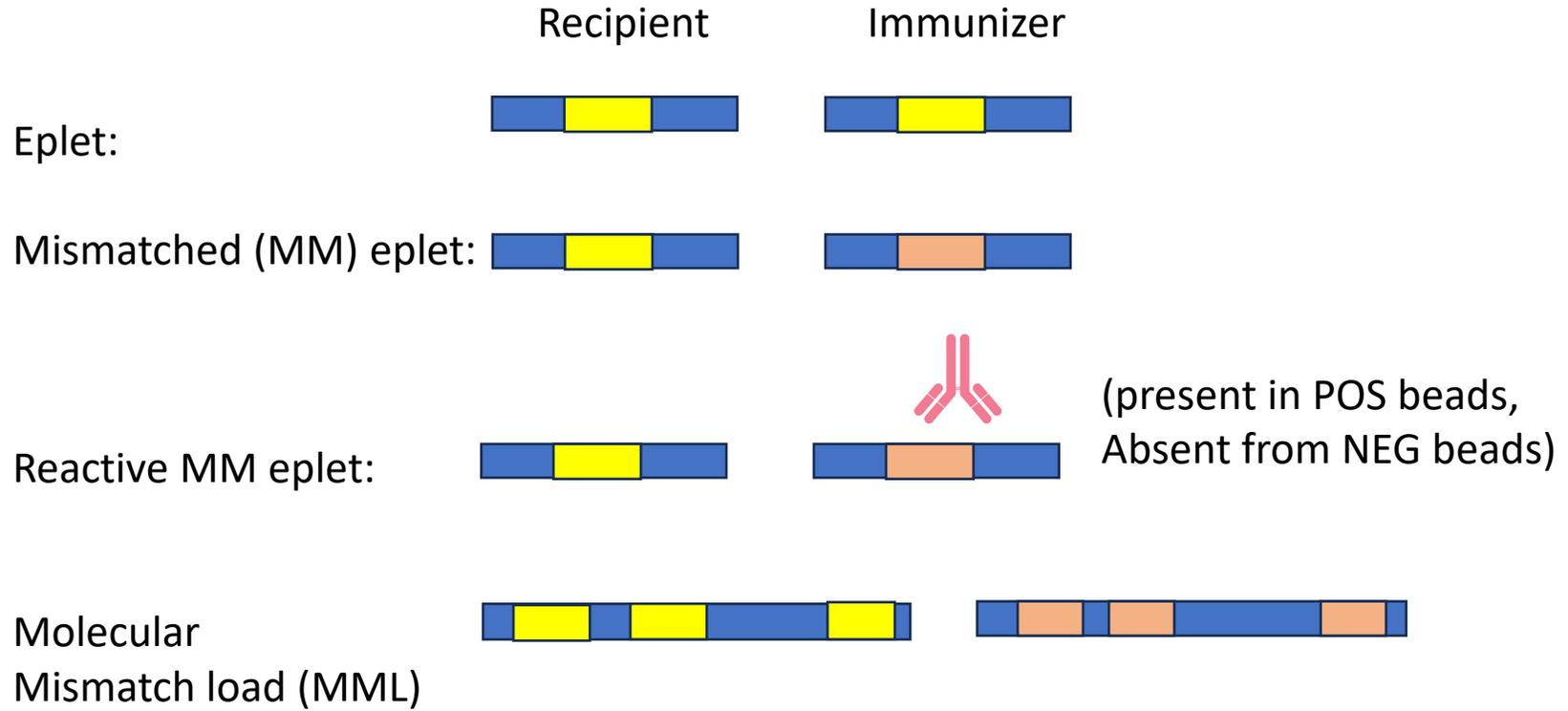
HLA B cells epitopes

EPLET: small patch of **polymorphic** amino acids, contiguous or non-contiguous, that cluster together on the surface of HLA molecules

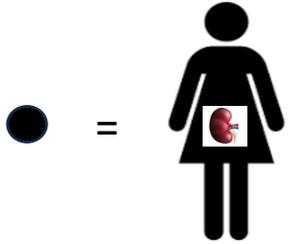
B cell epitope: eplet+ surrounding contact surface



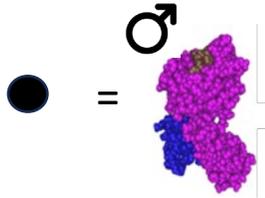
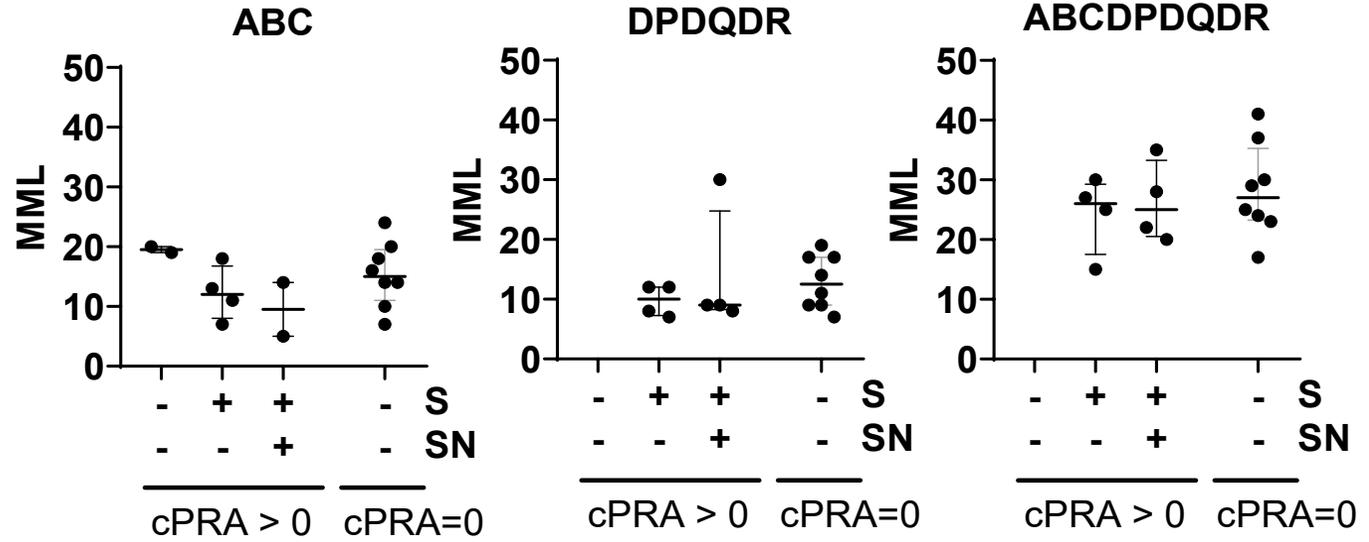
Only considered Ab-verified eplets



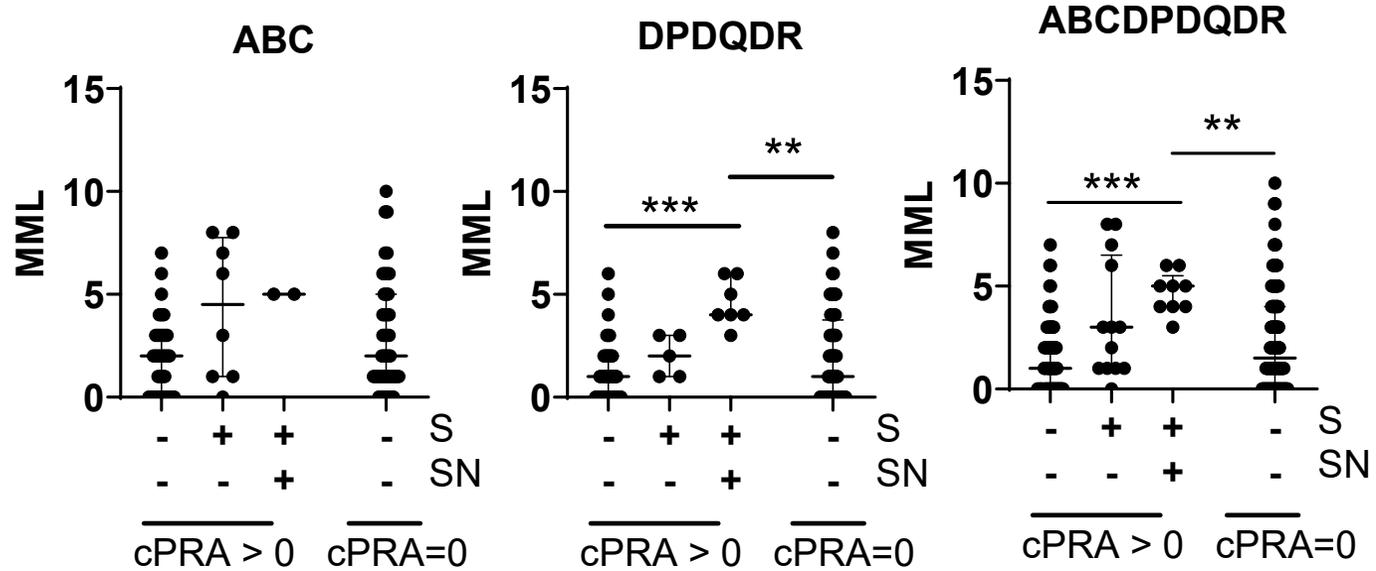
Results of molecular mismatch load (MML) of paternal HLA alleles: :



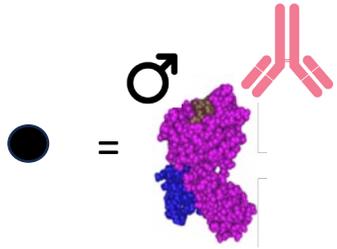
\sum MML all paternal HLA alleles of a patient



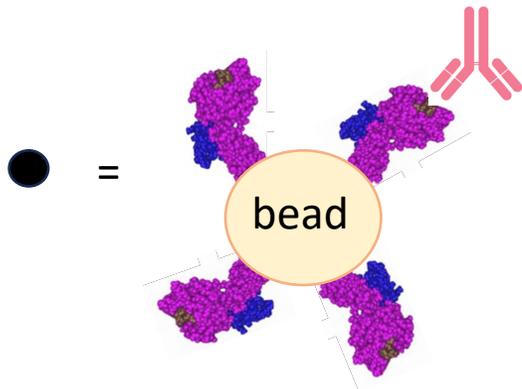
Pool of paternal HLA alleles from patients:



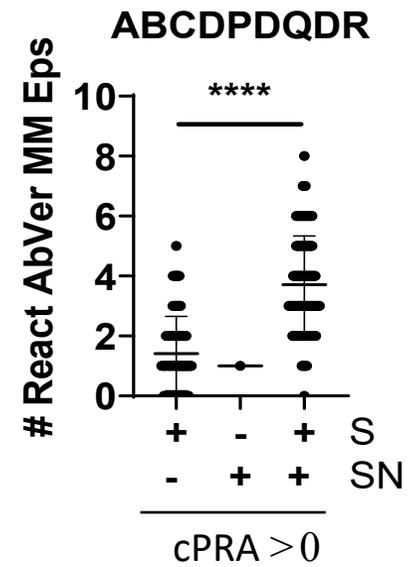
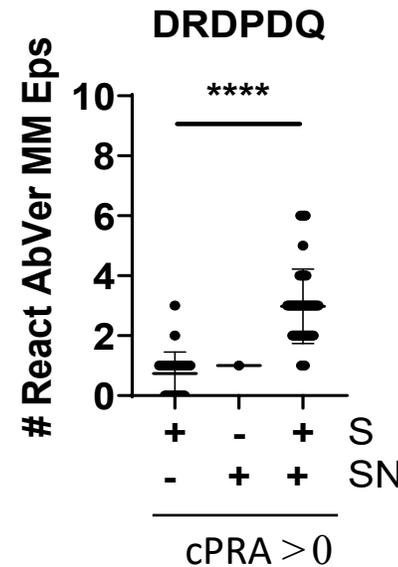
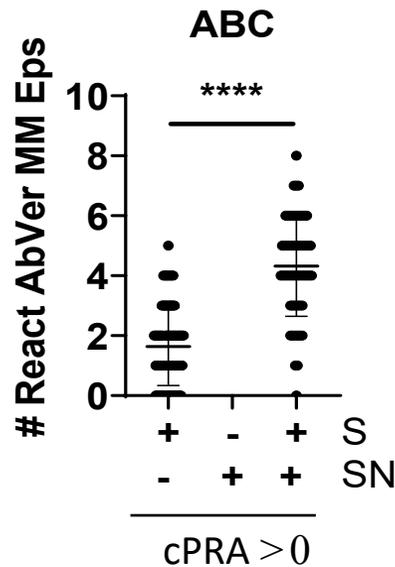
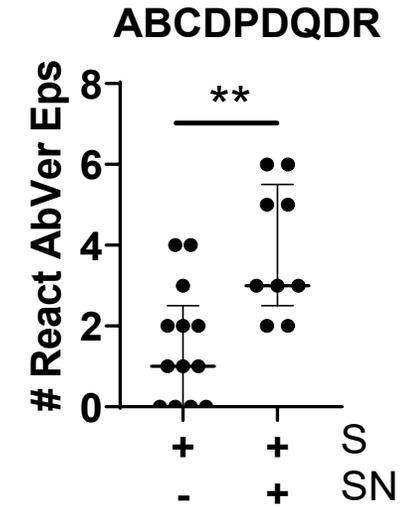
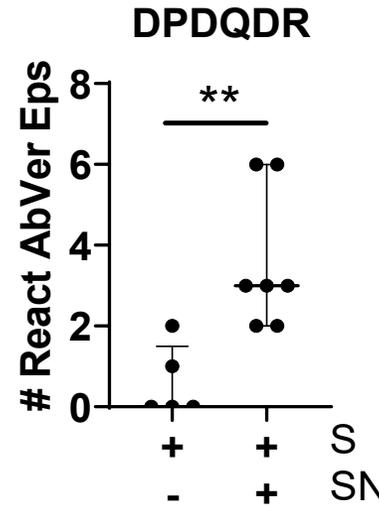
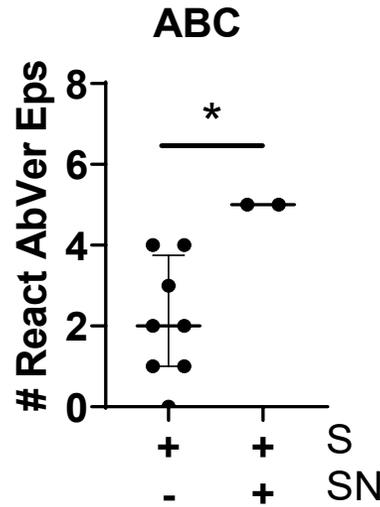
Results of reactive MM eplets of positive specificities:



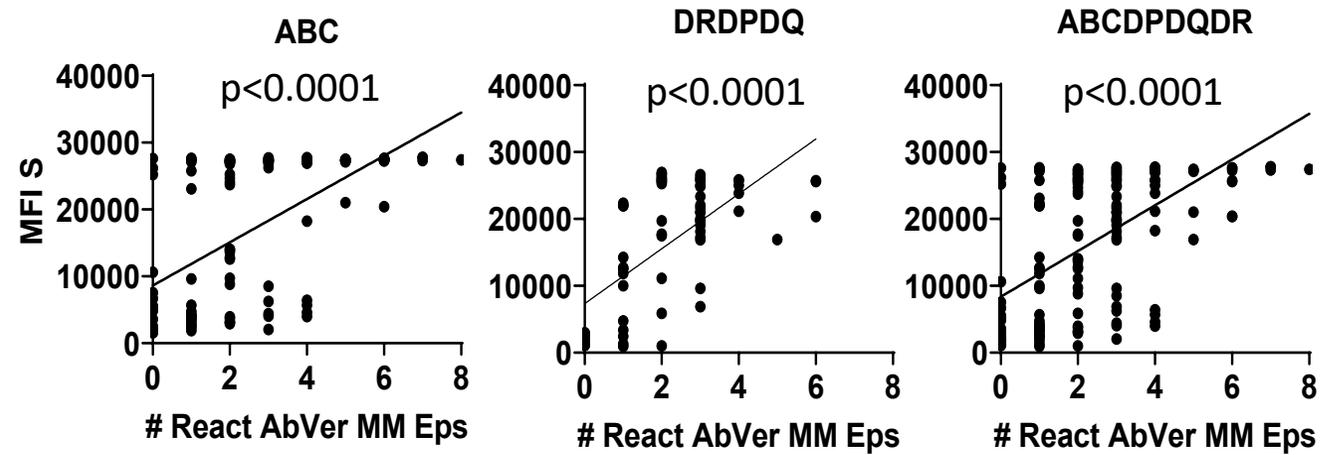
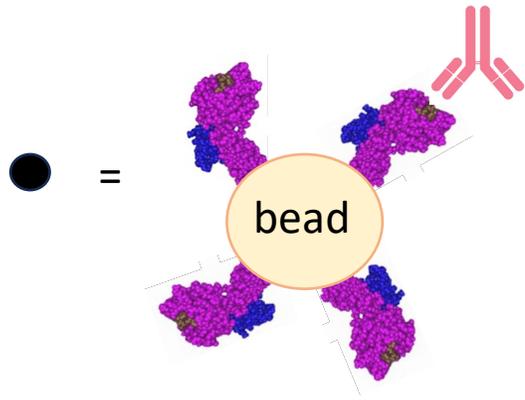
Pool of paternal HLA alleles from cPRA > 0 patients



Pool of positive HLA specificities Of cPRA > 0 patients

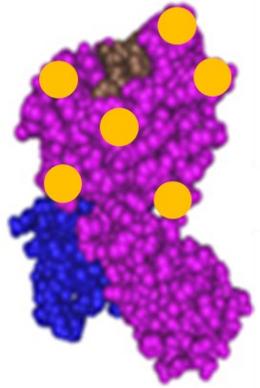


Results of reactive MM eplets of positive specificities:

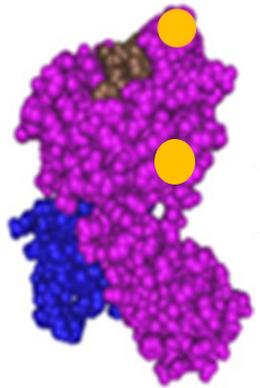


Pool of positive HLA specificities of cPRA > 0 patients

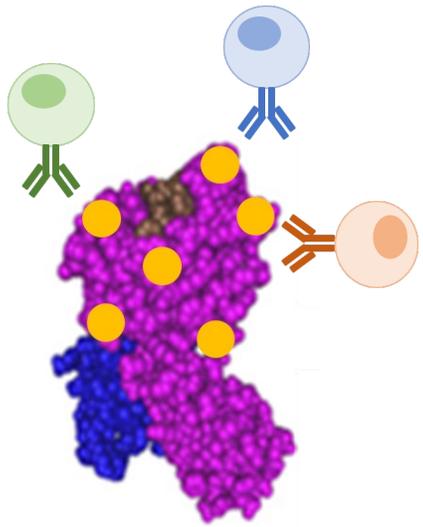
Model:



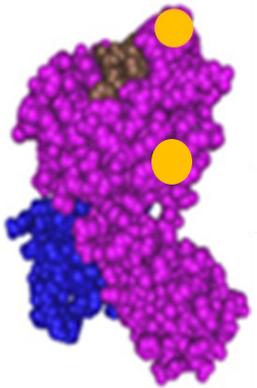
MML of
immunizer HLA



Model:

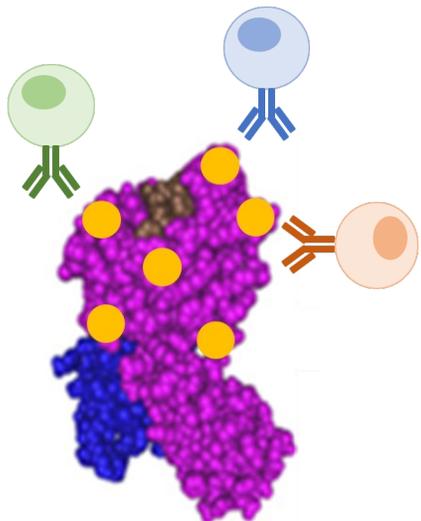


MML of
immunizer HLA

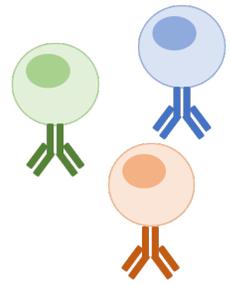


Model:

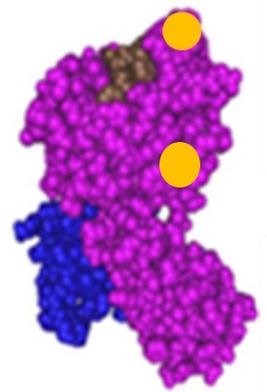
PBMC



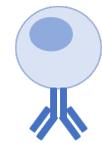
HLA
mBC



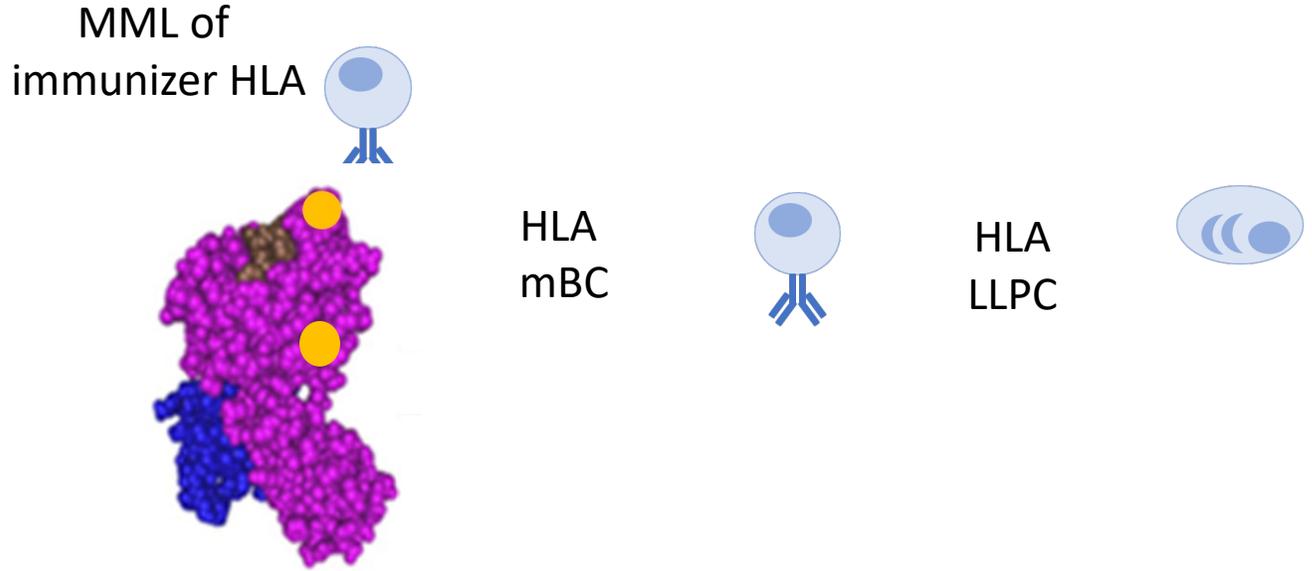
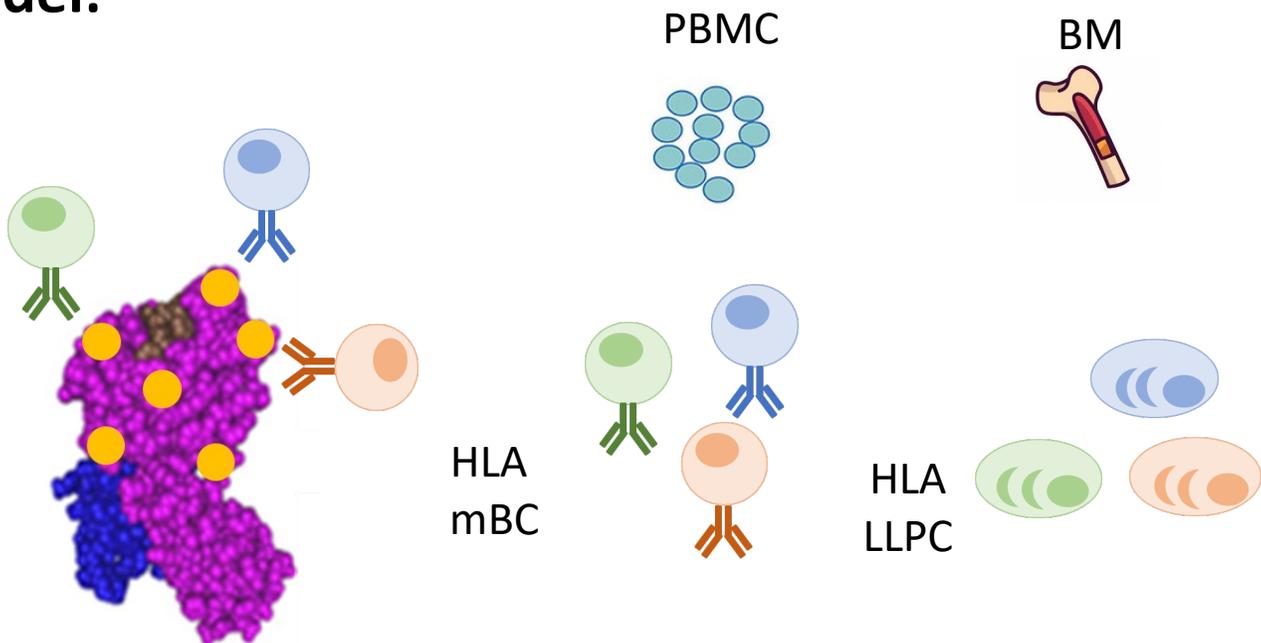
MML of
immunizer HLA



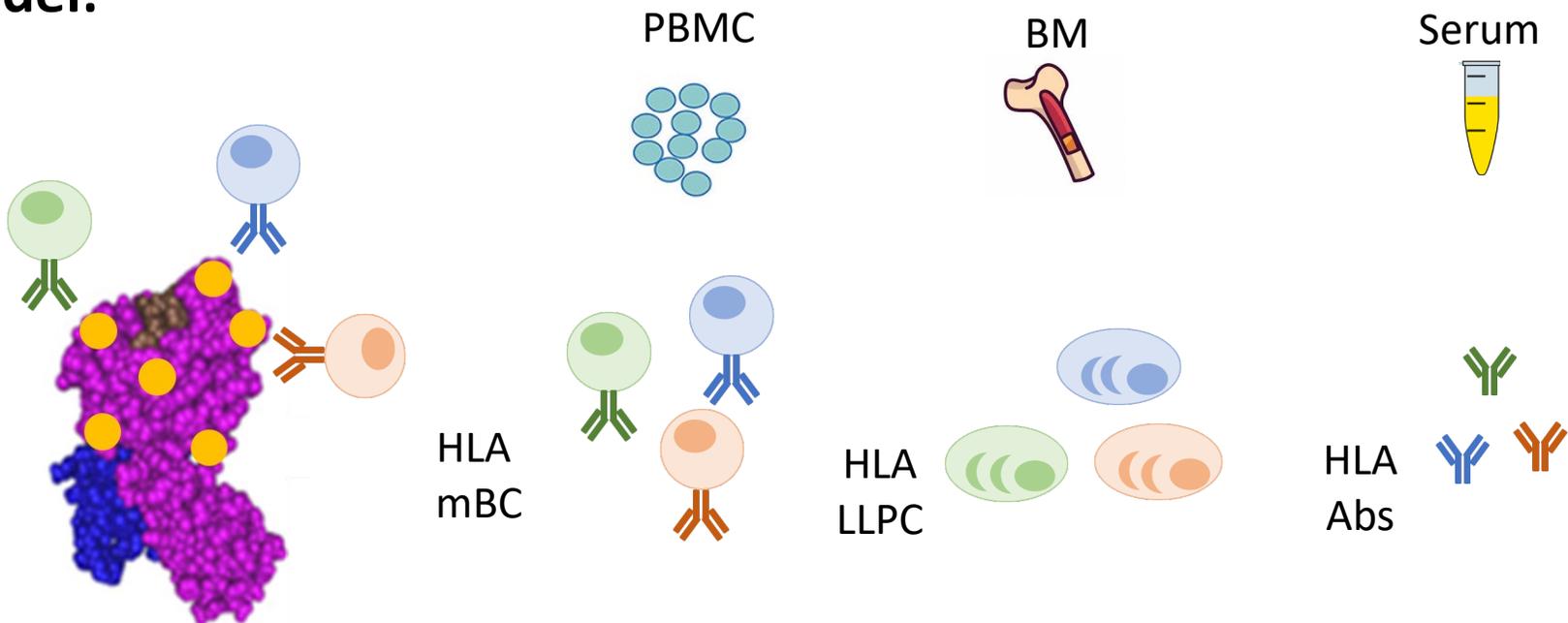
HLA
mBC



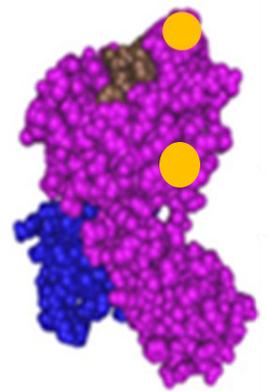
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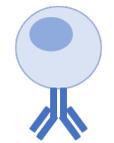
Model:



MML of immunizer HLA



HLA mBC



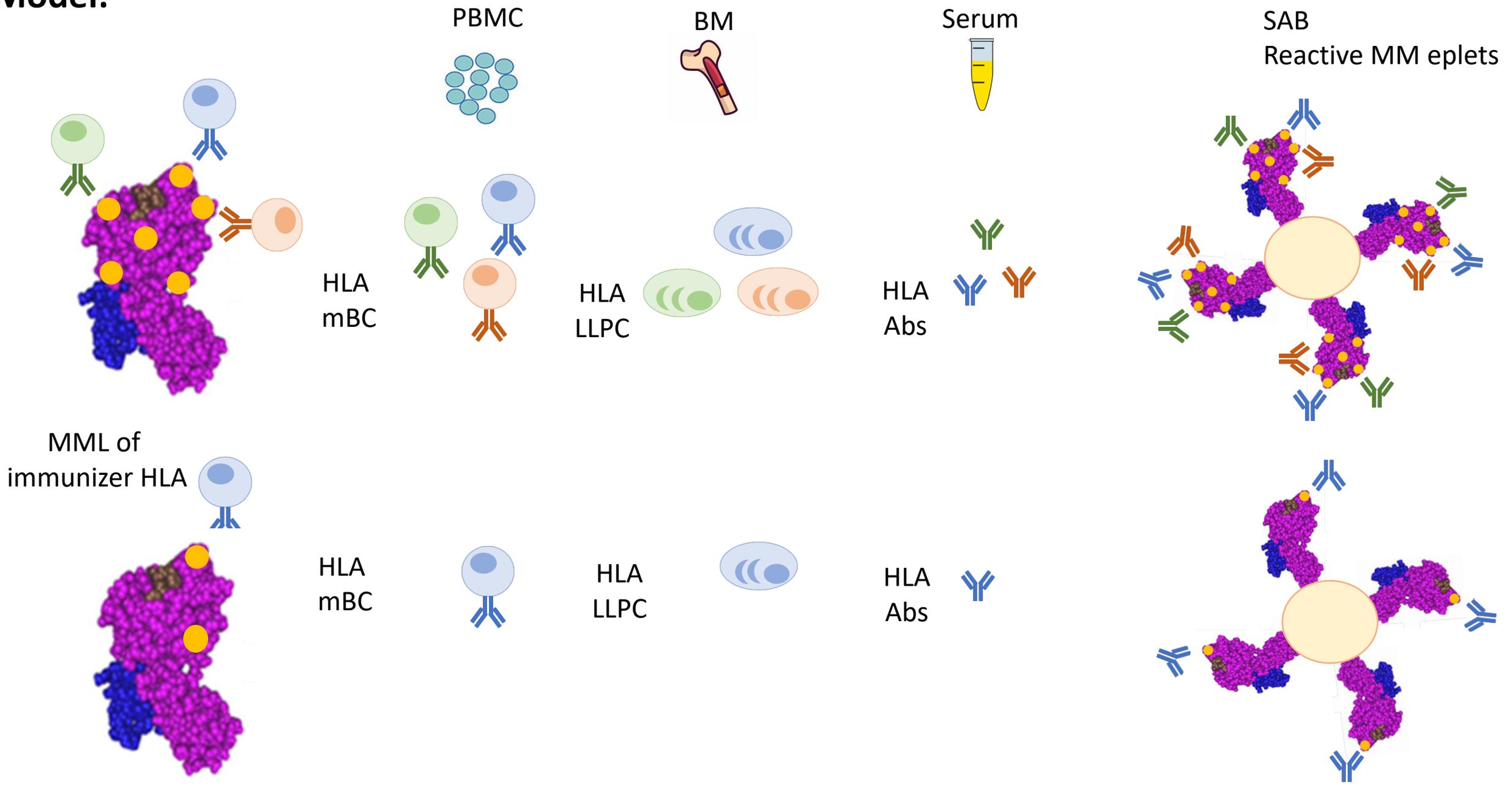
HLA LLPC



HLA Abs



Model:



**Grup de Recerca en Nefropaties
Immunologia del Trasplantament**

Elisenda Alari Pahissa
Sara Sanz Ureña
Judith Federico Vega

Past: Laura Llinàs

**Servei de
Nefrologia**

Marta Crespo
Dolores Redondo Pachón
María José Pérez Sáez
Anna Buxeda
Carla Burballa
Anna Faura

**Servei de
Patologia**

José Yélamos
Dulce Soto

La Marató 



**Department of
Immunoematology
and Blood Transfusion**

Gonka Karahan
Sebastian Heidt



**Laboratori
d'Histocompatibilitat**

José Luís Caro

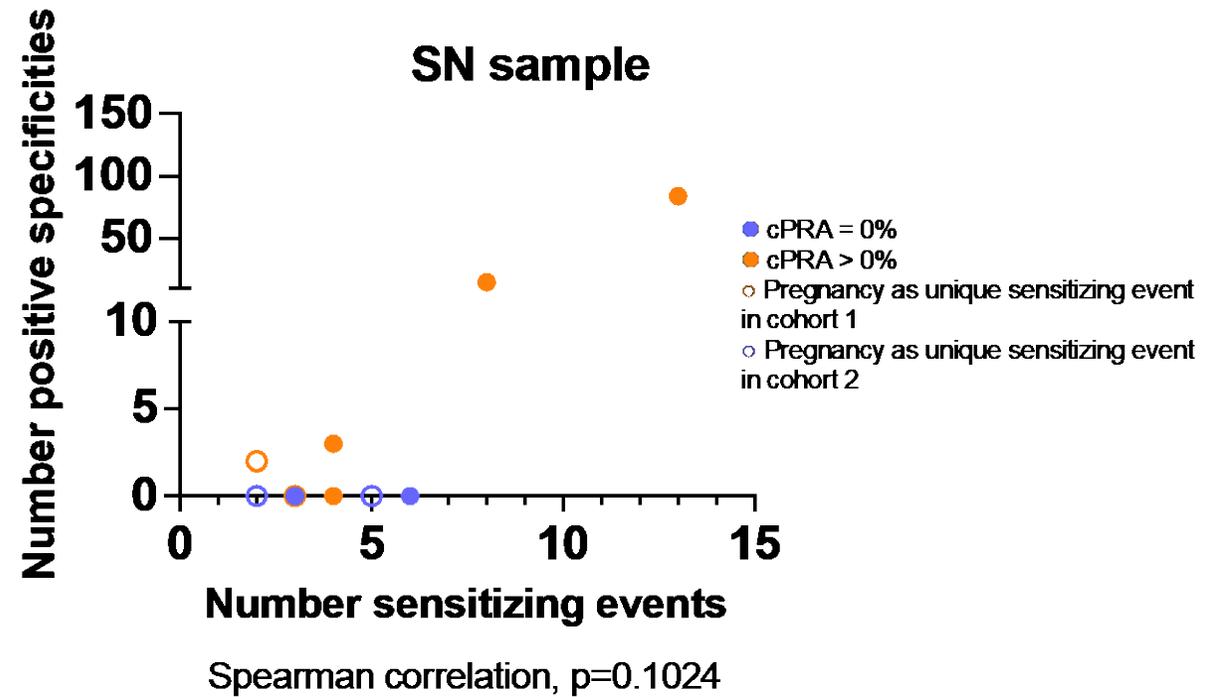
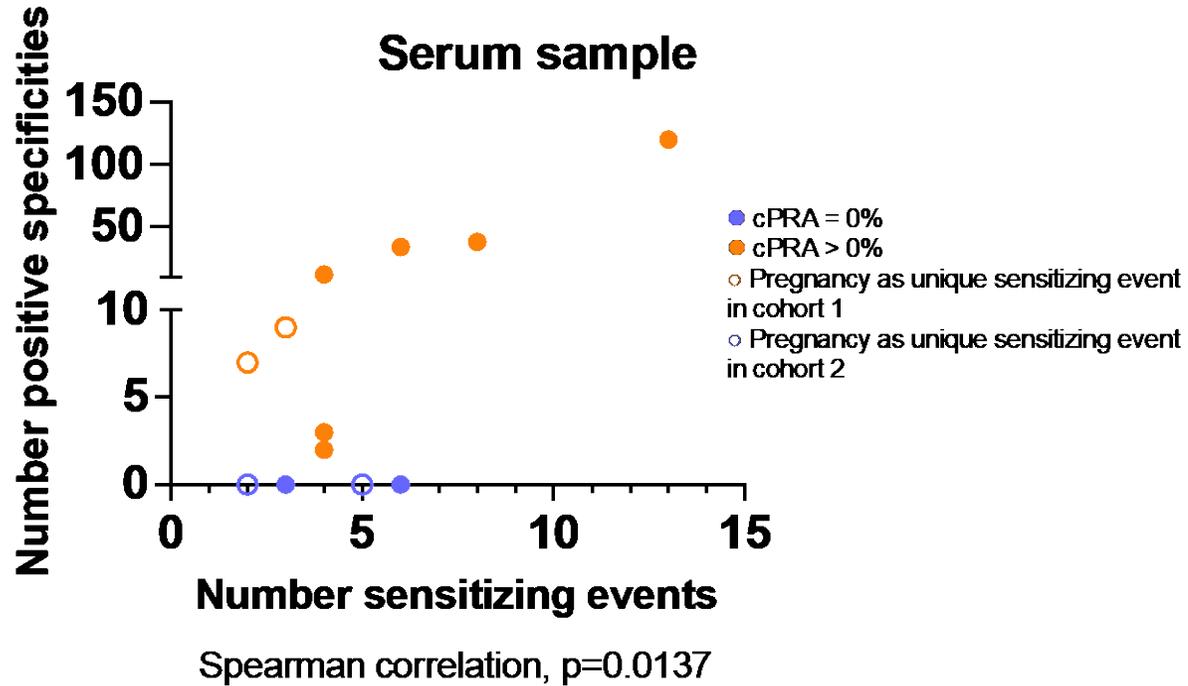


**Laboratori de
Referència de
Catalunya**

Jorge Eguia

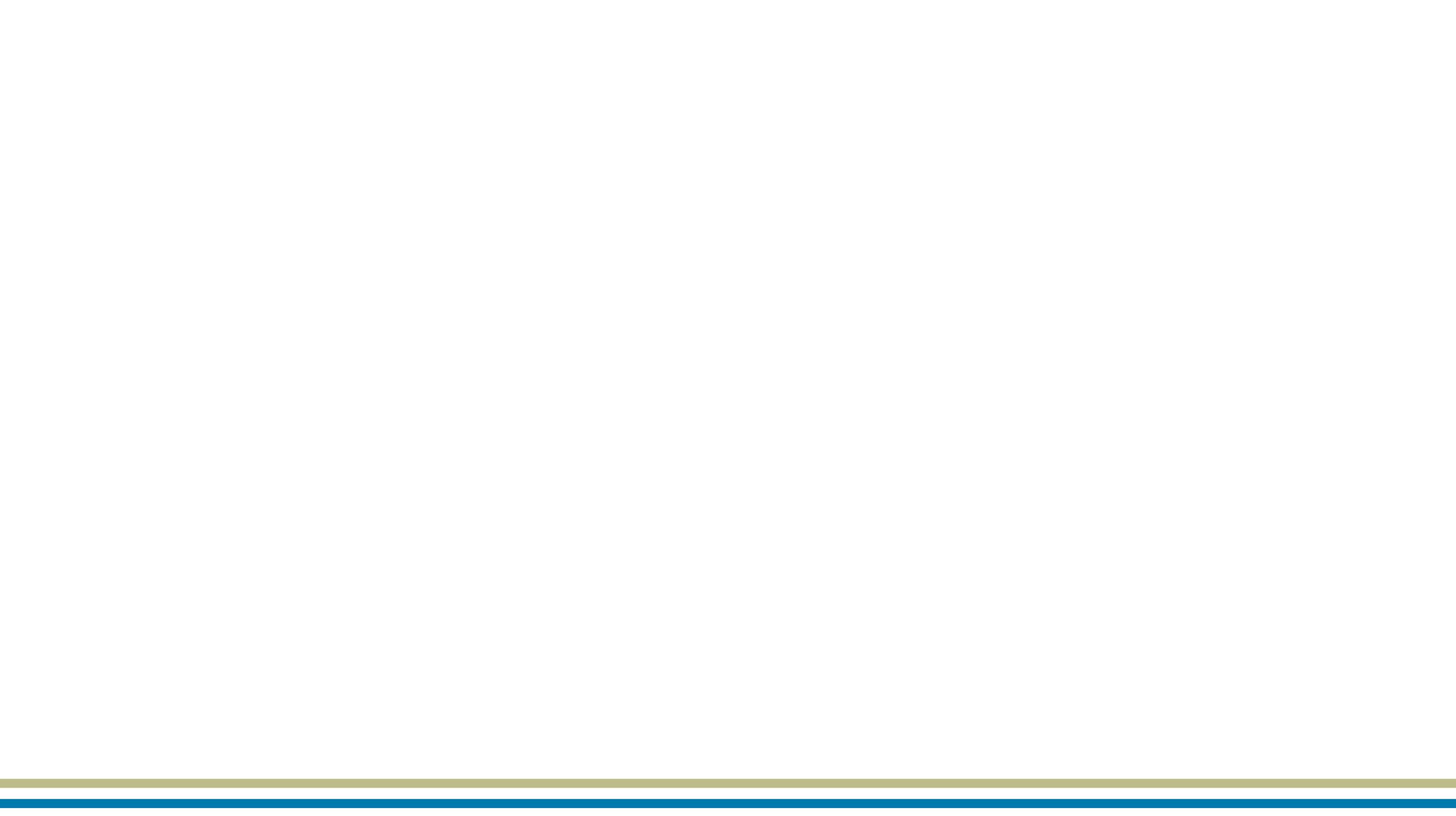
Descriptive table

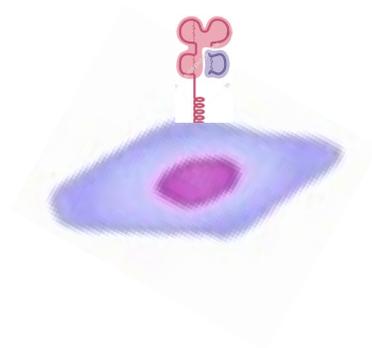
	[ALL]	cPRA > 0	cPRA=0%	P- overall
	<i>N=16</i>	<i>N=8</i>	<i>N=8</i>	
Recipient age at KT time (years) [median (IQR)]	55.5 [51.2;60.0]	57.0 [53.8;60.0]	54.5 [48.0;64.0]	0.560
Recipient ethnicity (caucasian) (n, %)	12 (75.0%)	7 (87.5%)	5 (62.5%)	0.569
cPRA (%) [median (IQR)]	0.00 [0.00;60.5]	62.0 [54.2;75.0]	0.00 [0.00;0.00]	0.001
Pregnancies [median (IQR)]	2.00 [2.00;3.00]	2.00 [2.00;3.00]	2.00 [2.00;2.50]	0.545
Time between last pregnancy and time of study (years) [median (IQR)]	32.0 [25.8;39.0]	34.0 [29.0;39.0]	31.0 [23.0;38.0]	0.599
Blood transfusions before KT (yes) (n, %)	8 (50.0%)	6 (75.0%)	2 (25.0%)	0.132
reTR (yes) (n, %)	1 (6.25%)	1 (12.5%)	0 (0.00%)	1.000
RRT (HD/PD) (n, %)	10 (62.5%)	7 (87.5%)	3 (37.5%)	0.119
Time between dialysis started and KT (months) [median (IQR)]	5.00 [0.00;16.5]	19.5 [9.75;36.0]	1.25 [0.00;3.25]	0.011
Chronic kidney disease (n, %)				0.116
Diabetes	3 (18.8%)	1 (12.5%)	2 (25.0%)	
Glomerular disease	4 (25.0%)	1 (12.5%)	3 (37.5%)	
PKD	1 (6.25%)	0 (0.00%)	1 (12.5%)	
SLE and other autoimmune disease	1 (6.25%)	0 (0.00%)	1 (12.5%)	
Other	7 (43.8%)	6 (75.0%)	1 (12.5%)	
Induction immunosuppression (n, %)				0.007
Basiliximab	10 (62.5%)	2 (25.0%)	8 (100%)	
Thymoglobulin	6 (37.5%)	6 (75.0%)	0 (0.00%)	



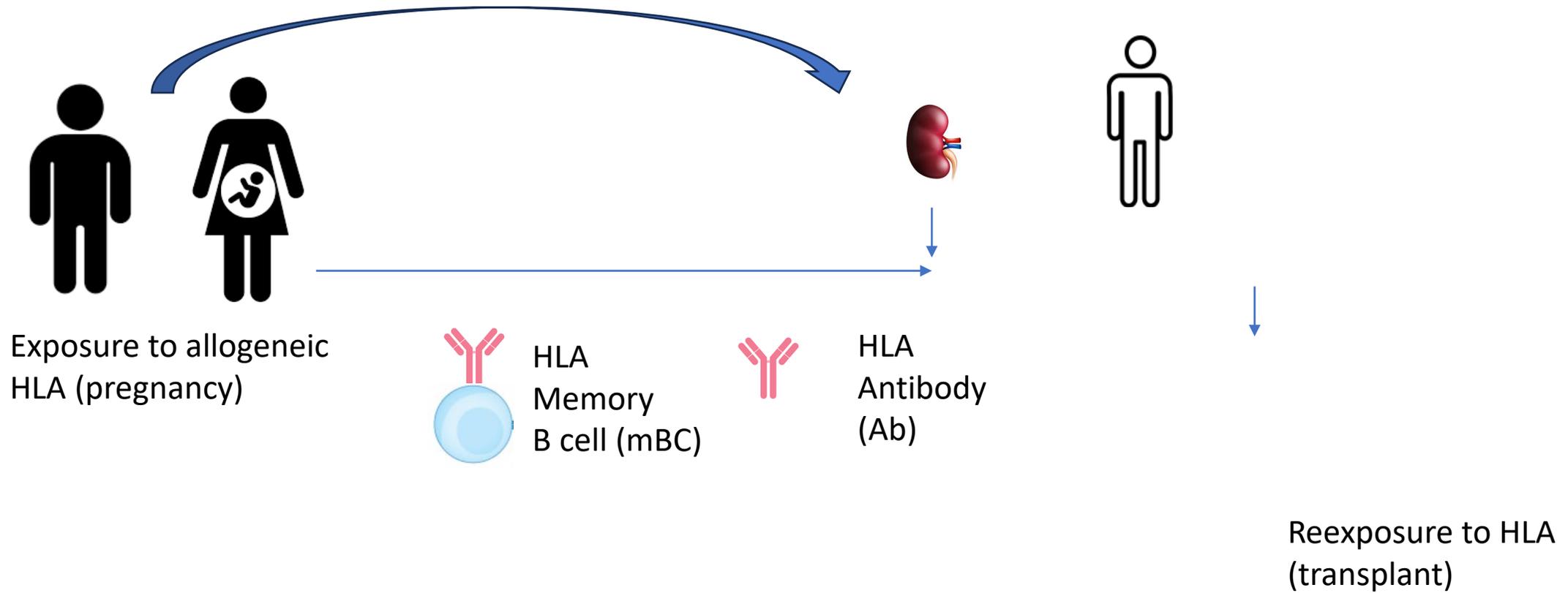




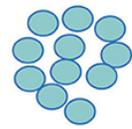




Could HLA-specific memory B cell detection refine immune risk stratification?

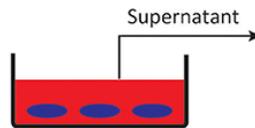


A

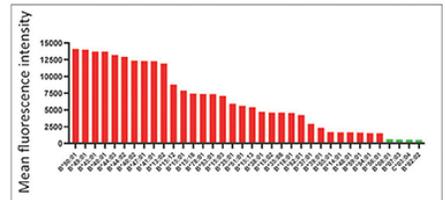


Peripheral
blood B
cells

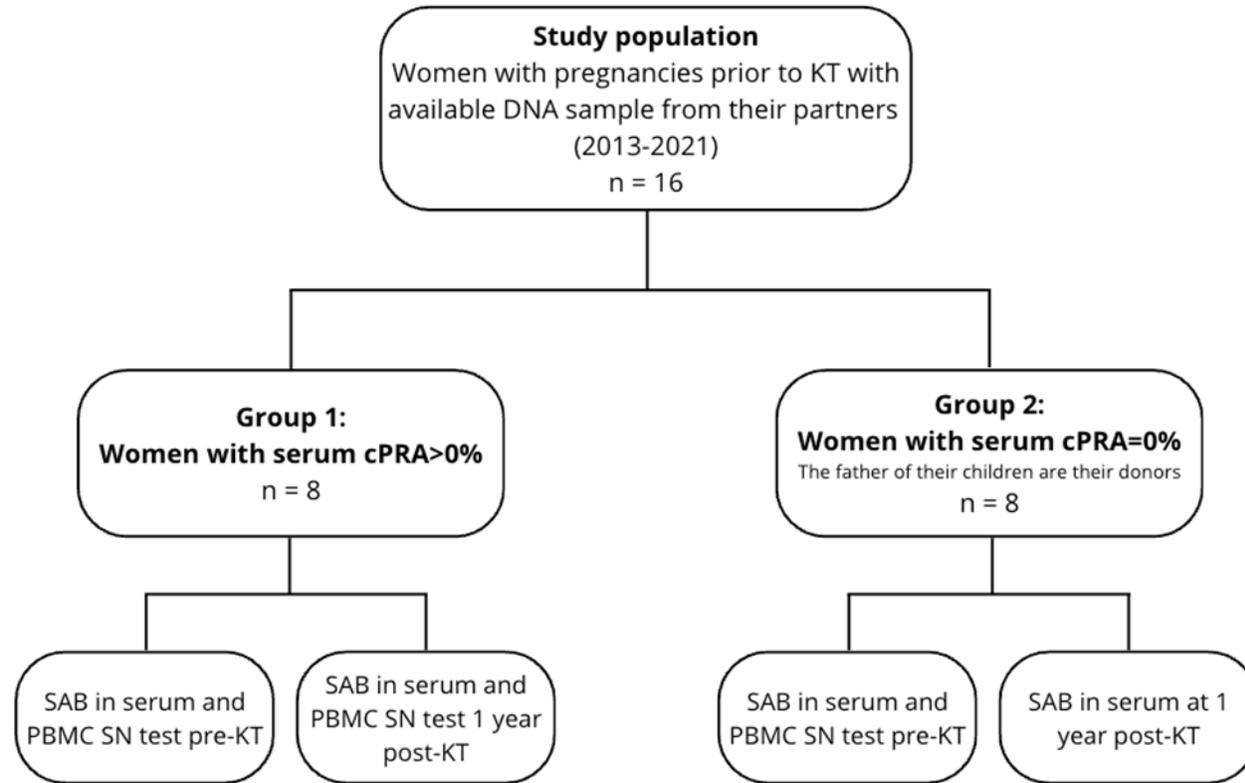
polyclonal
activation



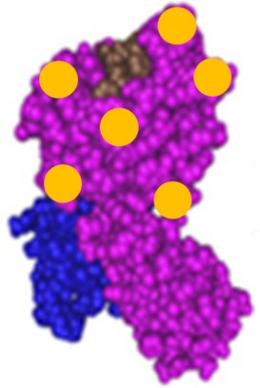
IgG isolation and/or
concentration
HLA targets:
Luminex single
antigen beads



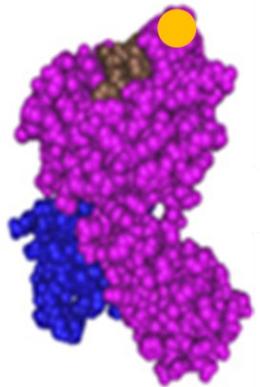
HLA antibody profile
(Luminex fluoro-analyzer)



Model:



MML of
immunizer HLA



Model:

