



16 mars 2018

Grossesse et Immunité

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L'imposteur



Je ne suis pas jeune

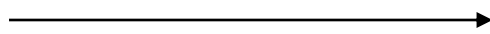
Je ne suis même pas immunologiste
(merci à Julien Zuber !)

Grossesse et Immunité

- Le placenta
- Grossesse et allo-immunité
- Grossesse et auto-immunité



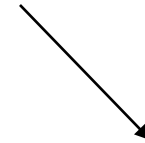
300,000 years



65 millions of years



THERIANS

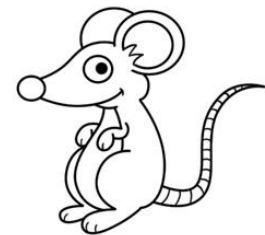


Metatherians

Eutherians

(marsupials)

(placenta)

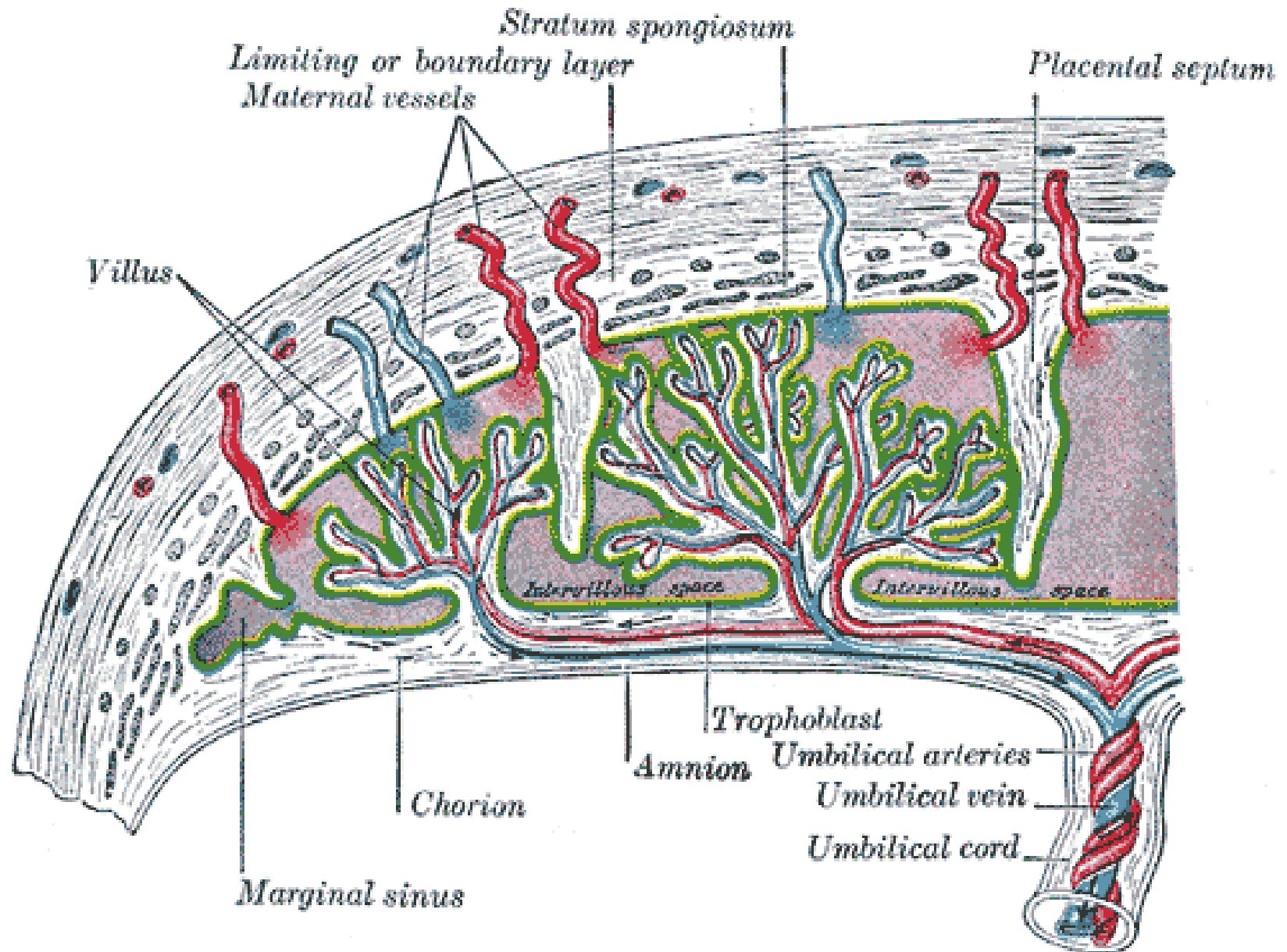


(Eutherian) Mammals

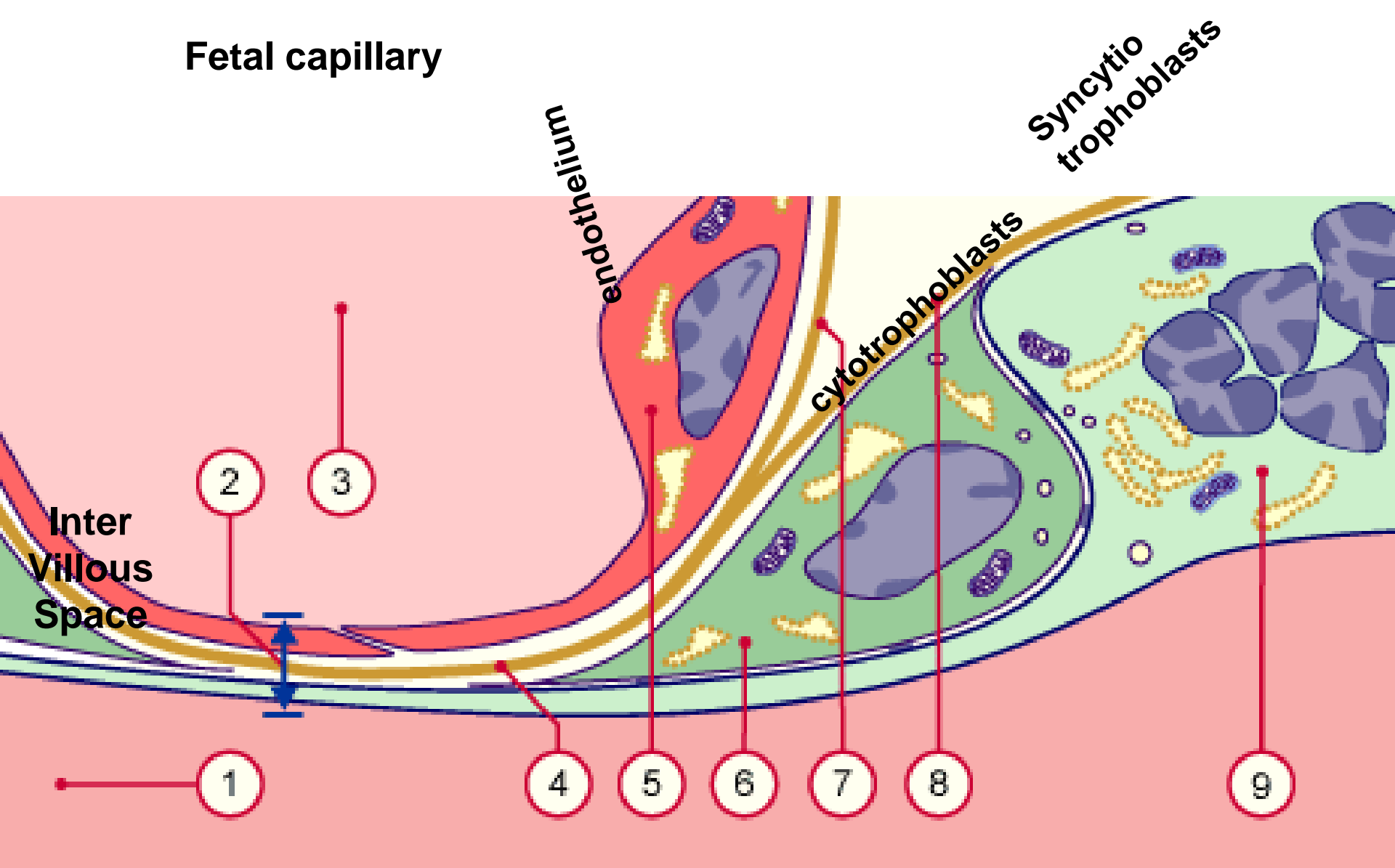




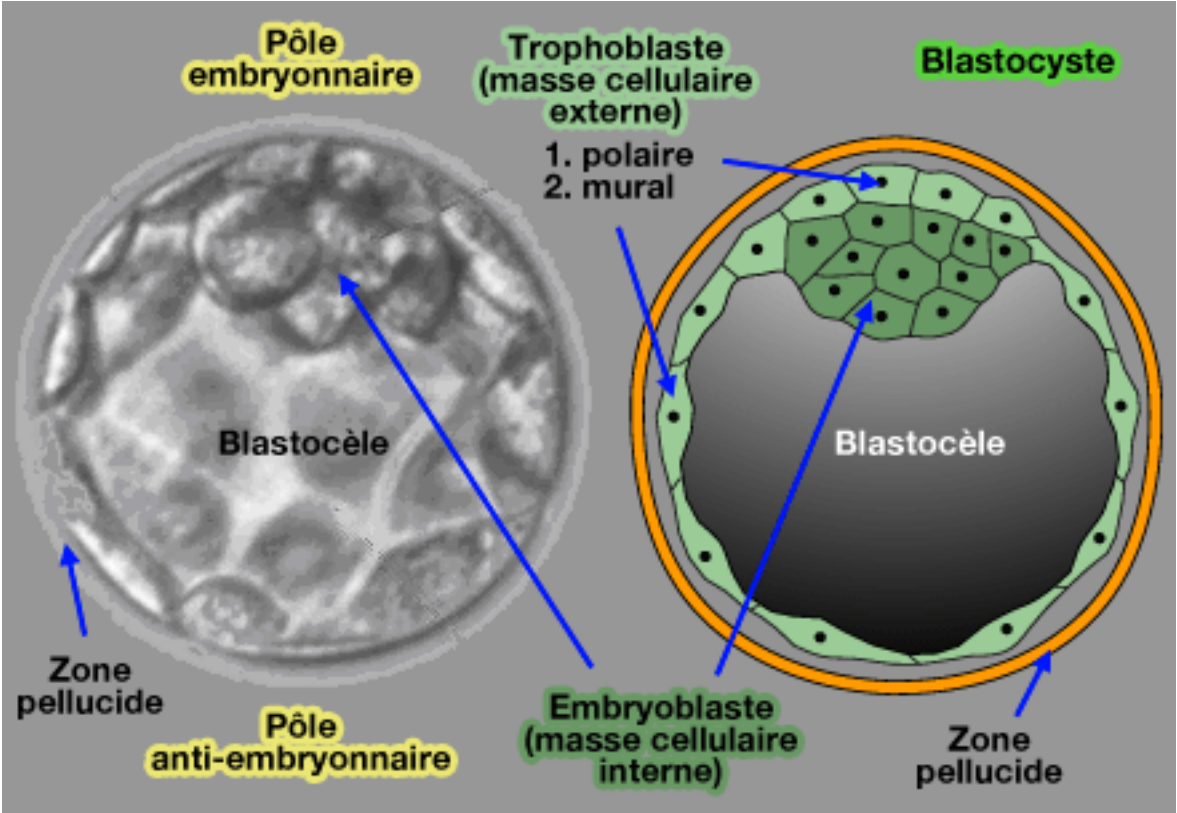
Placentation hémochoriale



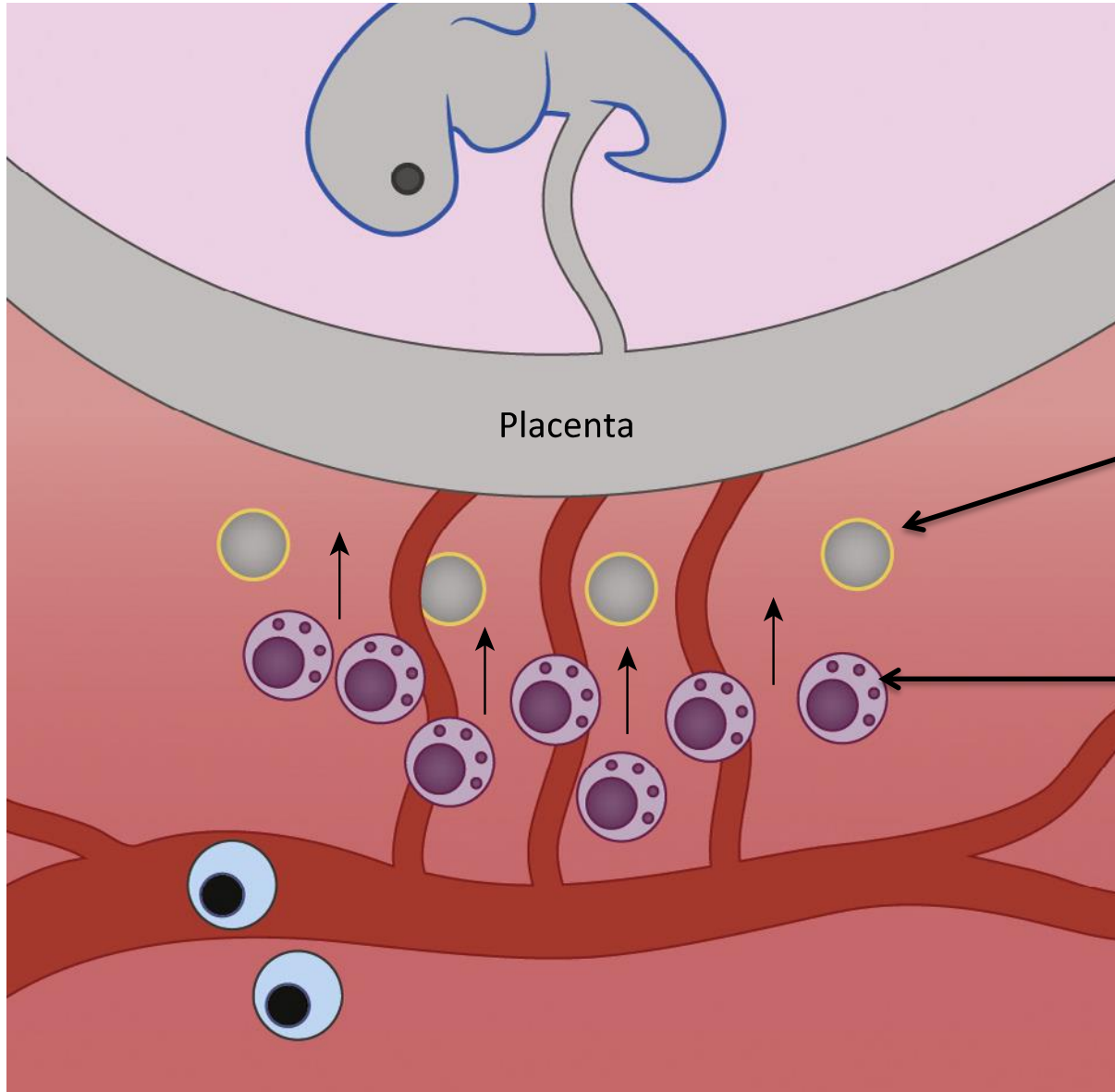
Fetal capillary



Le trophoblaste dérive du blastocyste

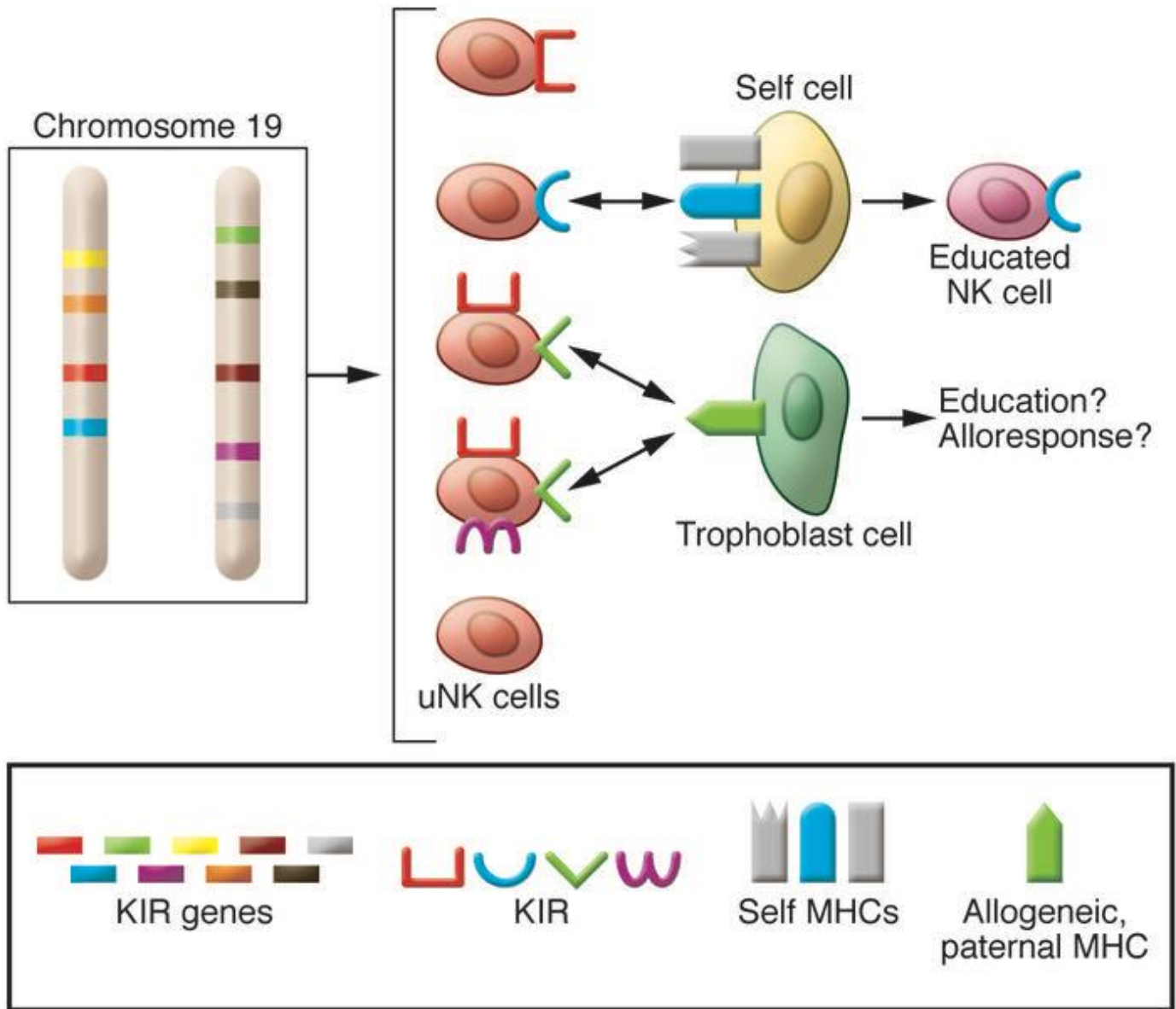


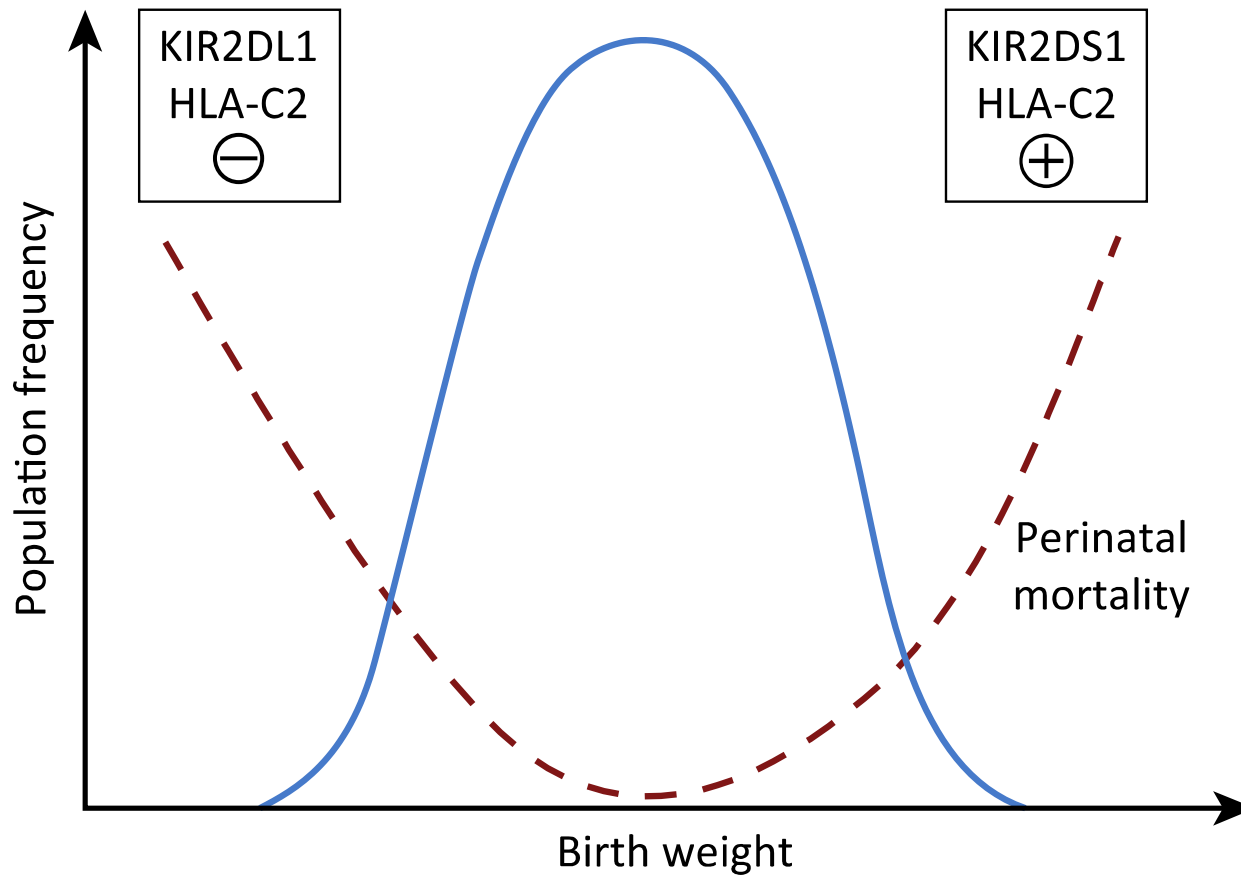
Le remodelage utérin est déterminé par l'interaction uNK / Trophoblastes



**Trophoblasts
(HLA-C, E and G)**

**NK Cells
(KIR)**
70% leucocytes
sur le site d'implantation





Grossesse et Immunité

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- Grossesse et auto-immunité

5	++	+	+	-
6	++	++	-	-
7	+++	+	-	-

No. 4625 **June 21, 1958**

may not be utilized for production
another purpose.

The evidence suggests that, in he
is attacked by monoamine oxidase
that the secondary reaction in w
formed may be concerned with c
aldehyde, probably by the enzy

leucocytes from dor
es from donors 8 and
ucocytes from donor
H. B.'s serum did r

Nature, 1958

Pregnancy allo-immunization

Complement dependent cytotoxic assay:

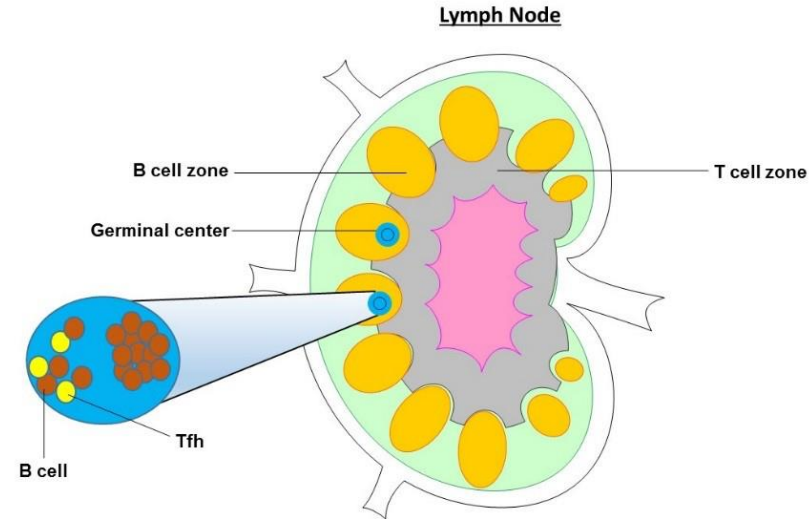
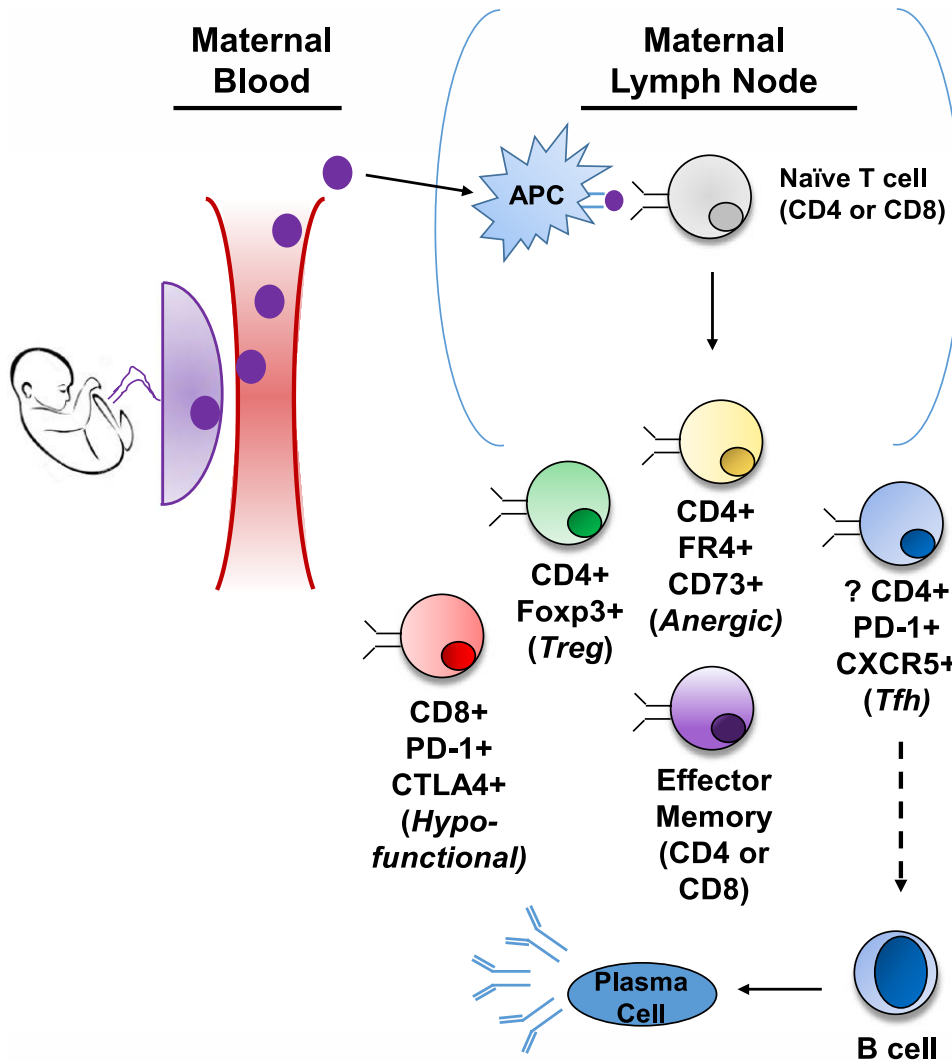
30% des femmes s'immunisent

Single-Antigen Beads (sérum pris à l'accouchement)

50 à 75%

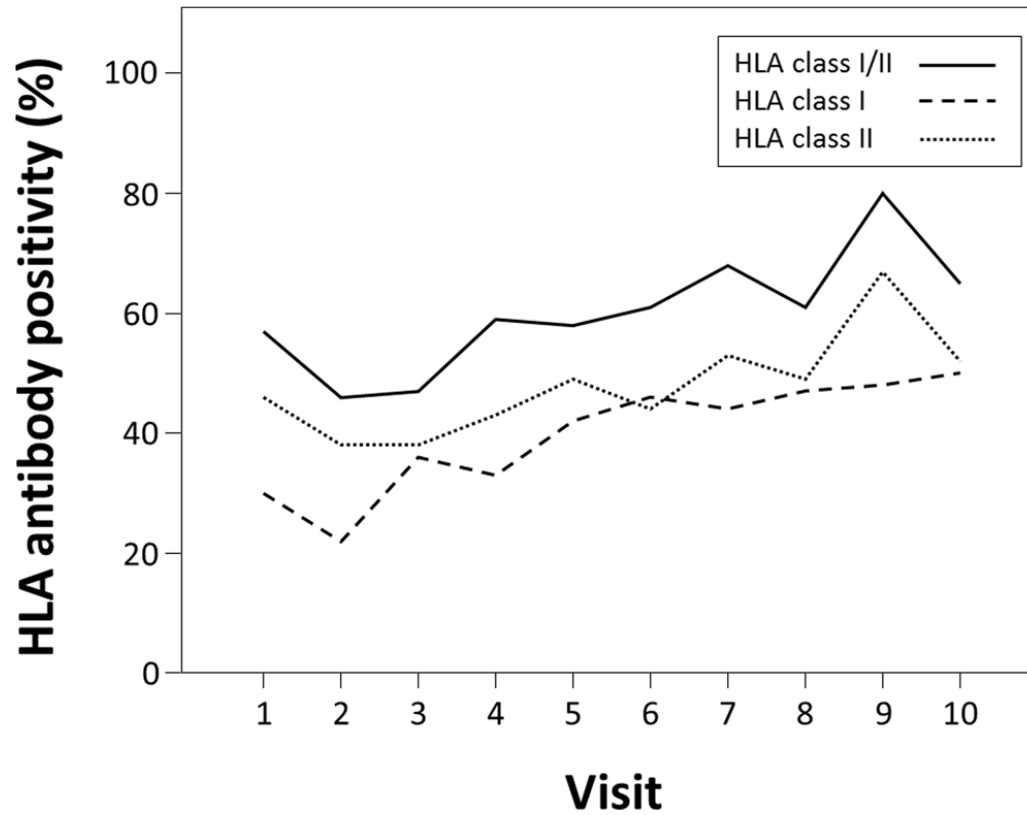
Porrett PM, Am J Transplant 2018

Pregnancy allo-immunization

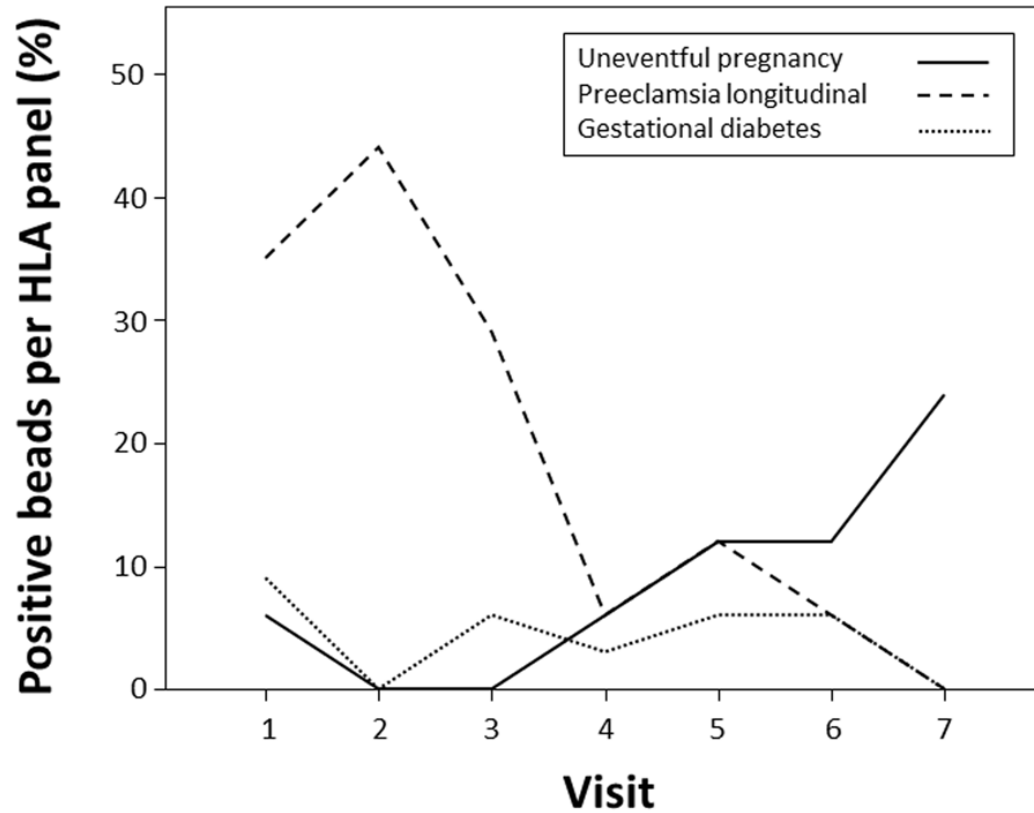


Tfh: T Follicular Helper Cells

1047 serum samples from 101 uneventful pregnancies



1047 serum samples from 101 uneventful pregnancies

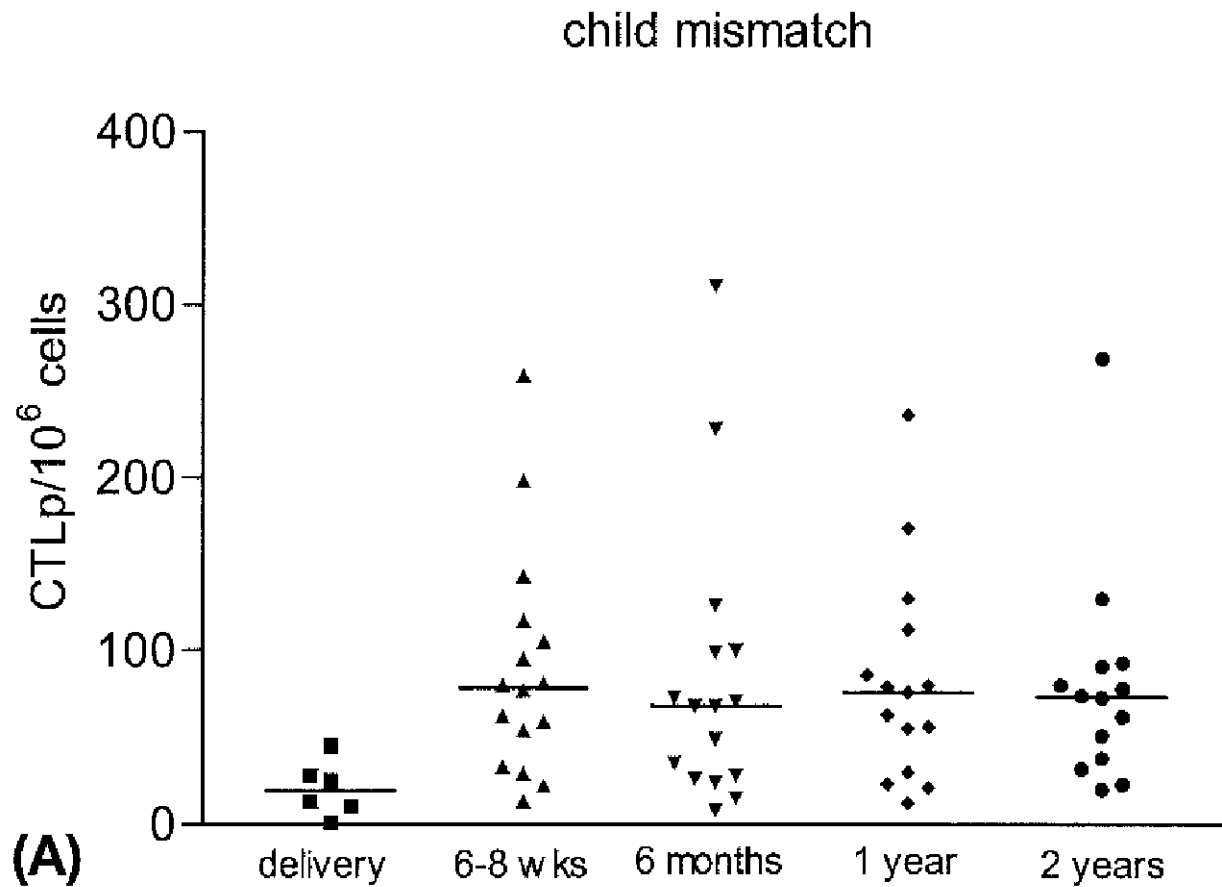


Kussel L, Sci Rep 2017

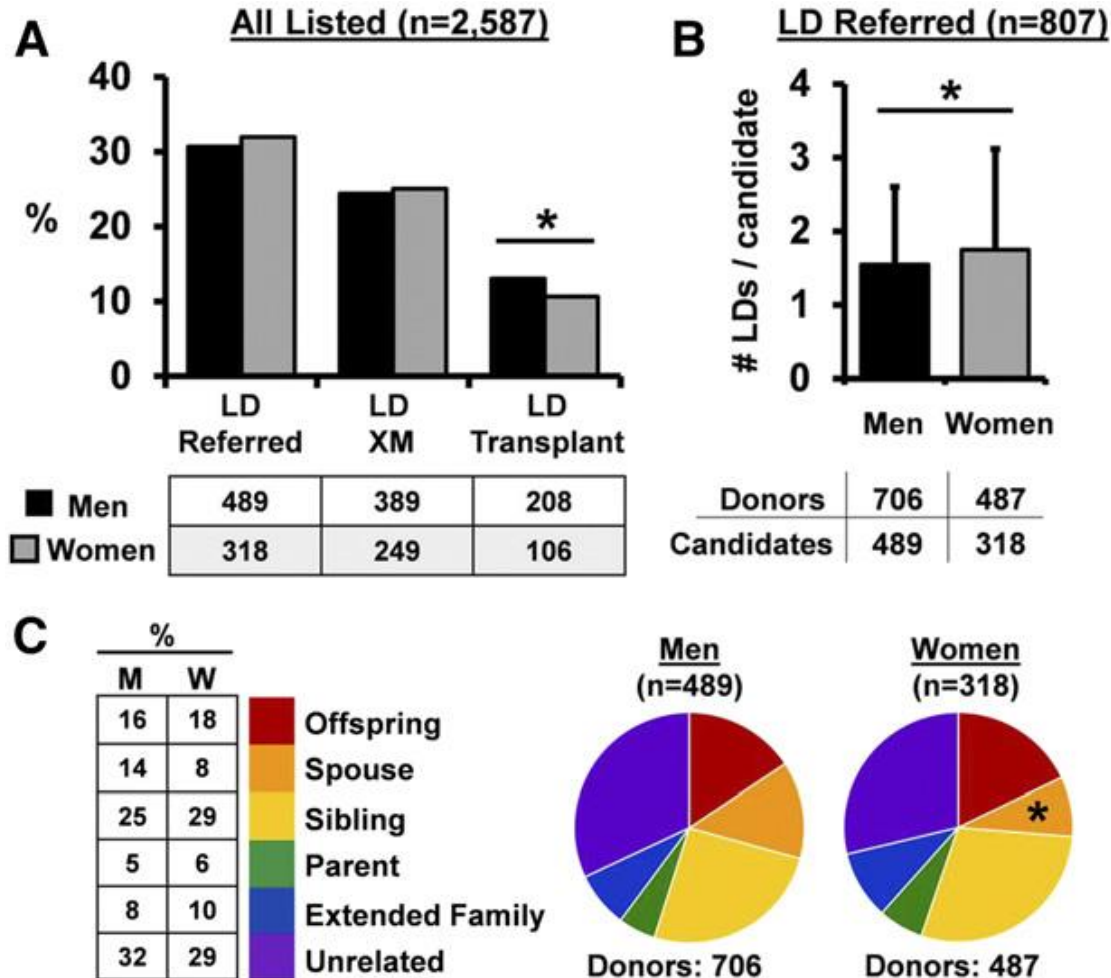
1047 serum samples from 101 uneventful pregnancies

			Primigravidae (n = 28)	Primi-/multipara (n = 73)	P-value
Gestation week 11–13	HLA class I and/or II positive	%	30	67	0.003
	HLA class I positive	%	26	53	0.03
	HLA class II positive	%	17	43	0.03
	Percent positive beads per panel	median (IQR)	0 (0–6)	18 (0–43)	0.003
	MFImax	median (IQR)	257 (182–331)	2869 (2802–2936)	0.011
Whole pregnancy	HLA class I and/or II positive	%	68	88	0.02
	HLA class I positive	%	61	77	0.11
	HLA class II positive	%	43	62	0.09
	Percent positive beads per panel	median (IQR)	0 (0–18)	12 (0–64)	<0.001
	MFImax	median (IQR)	370 (277–1050)	3073 (509–7370)	<0.001

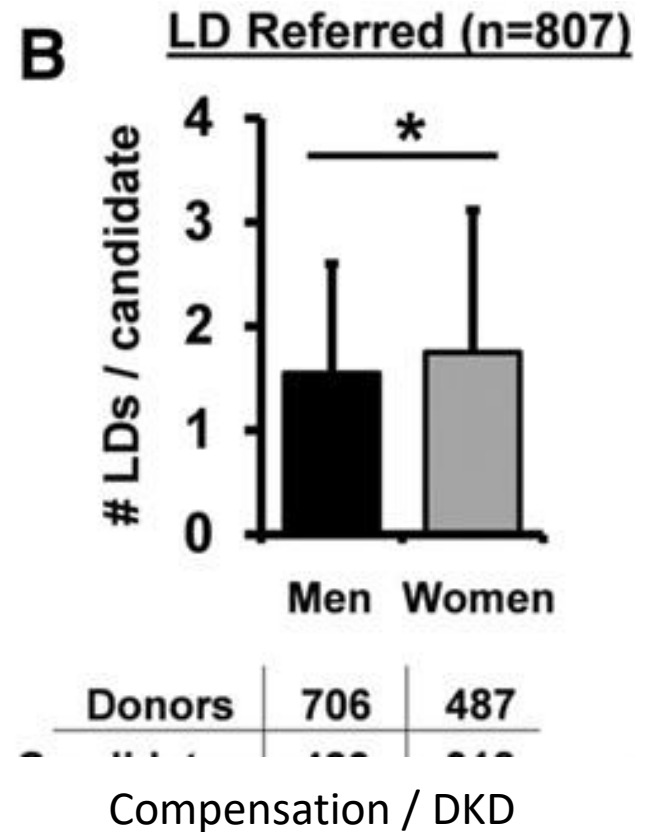
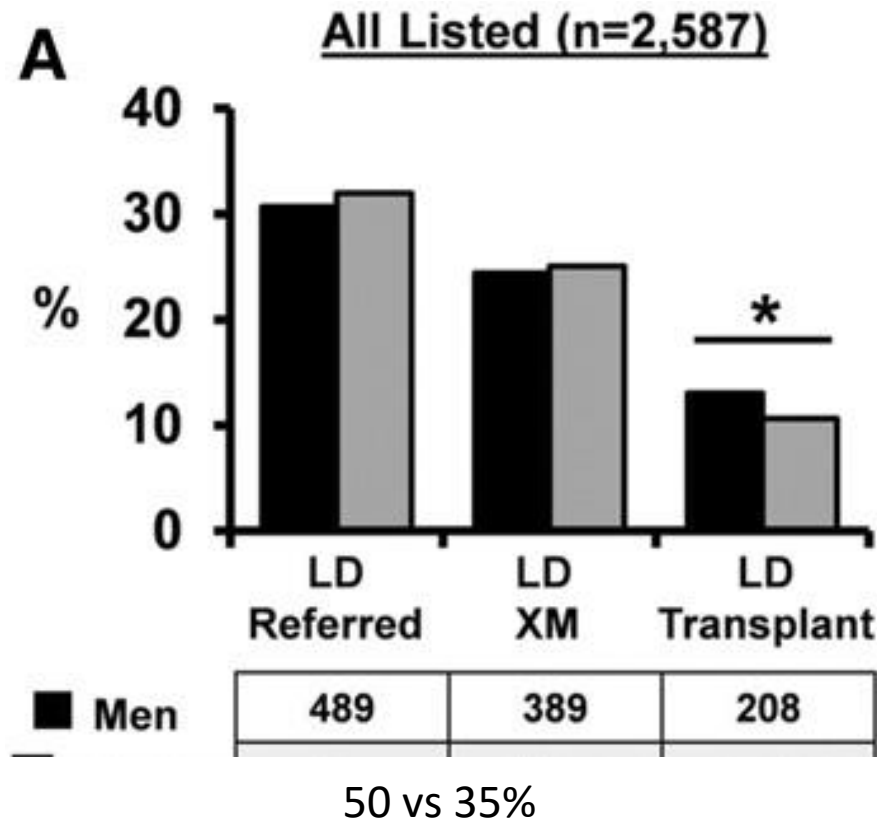
Kinetics of anti-HLA antibodies after delivery



Clinical significance

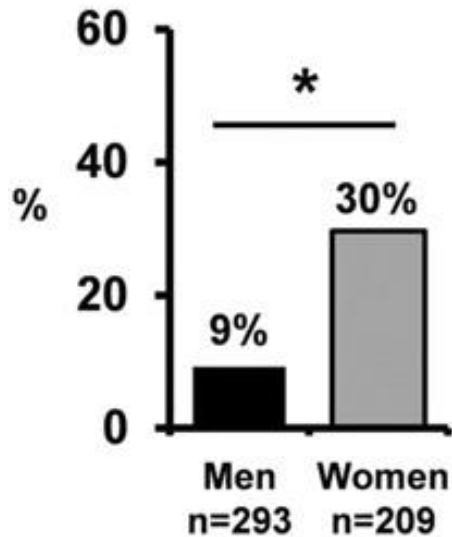


Clinical significance



Clinical significance

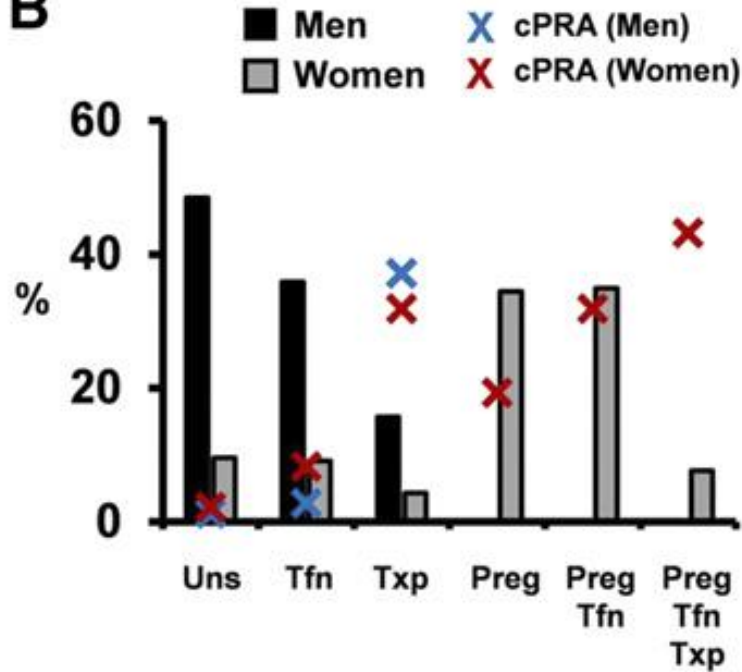
A Incompatible with ≥ 1 Living Donor



51% hommes exposés à un risque cPRA 7%

90% des femmes exposées cPRA 21%

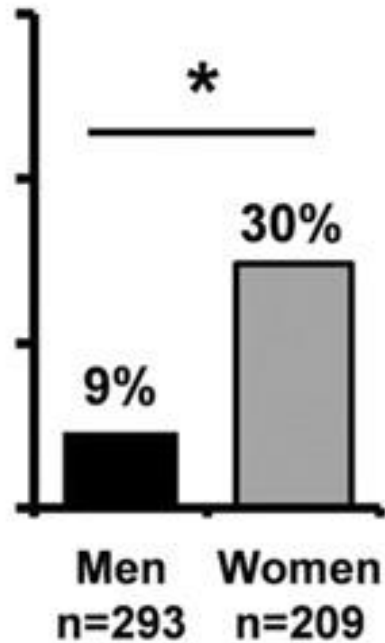
B



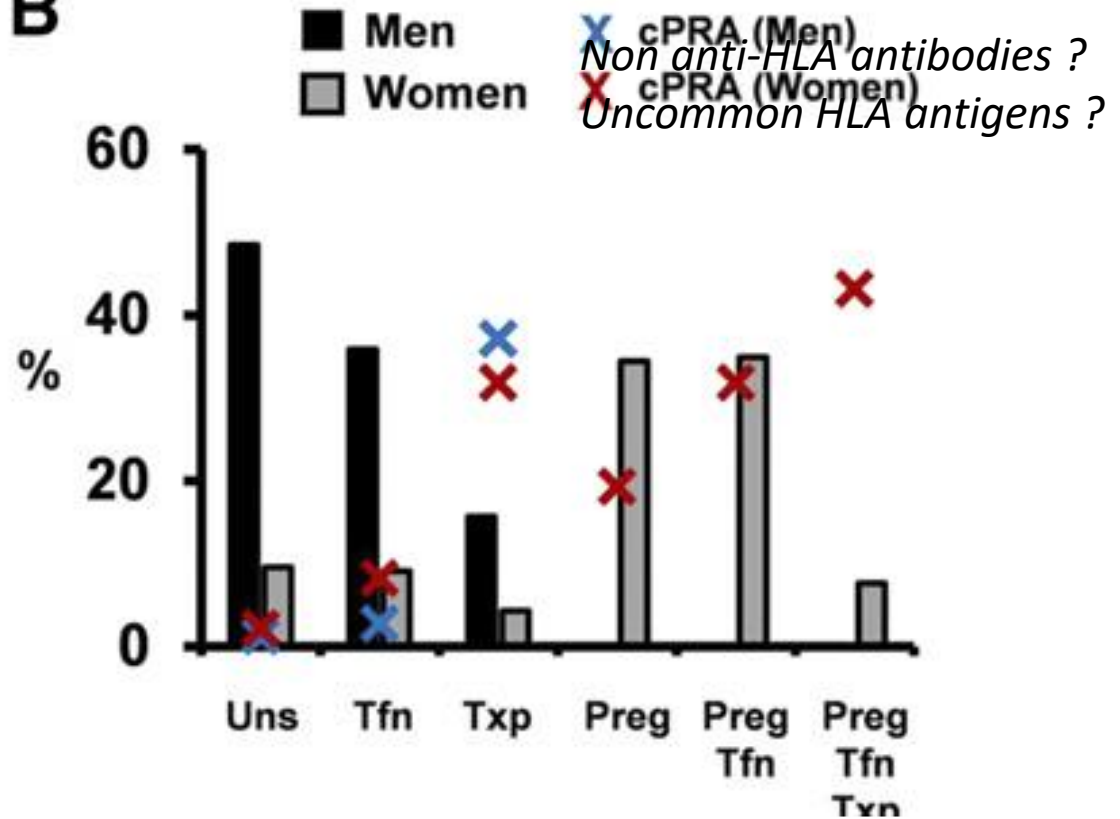
Men	142	105	46	--	--	--
Women	20	19	9	72	73	16

Clinical significance

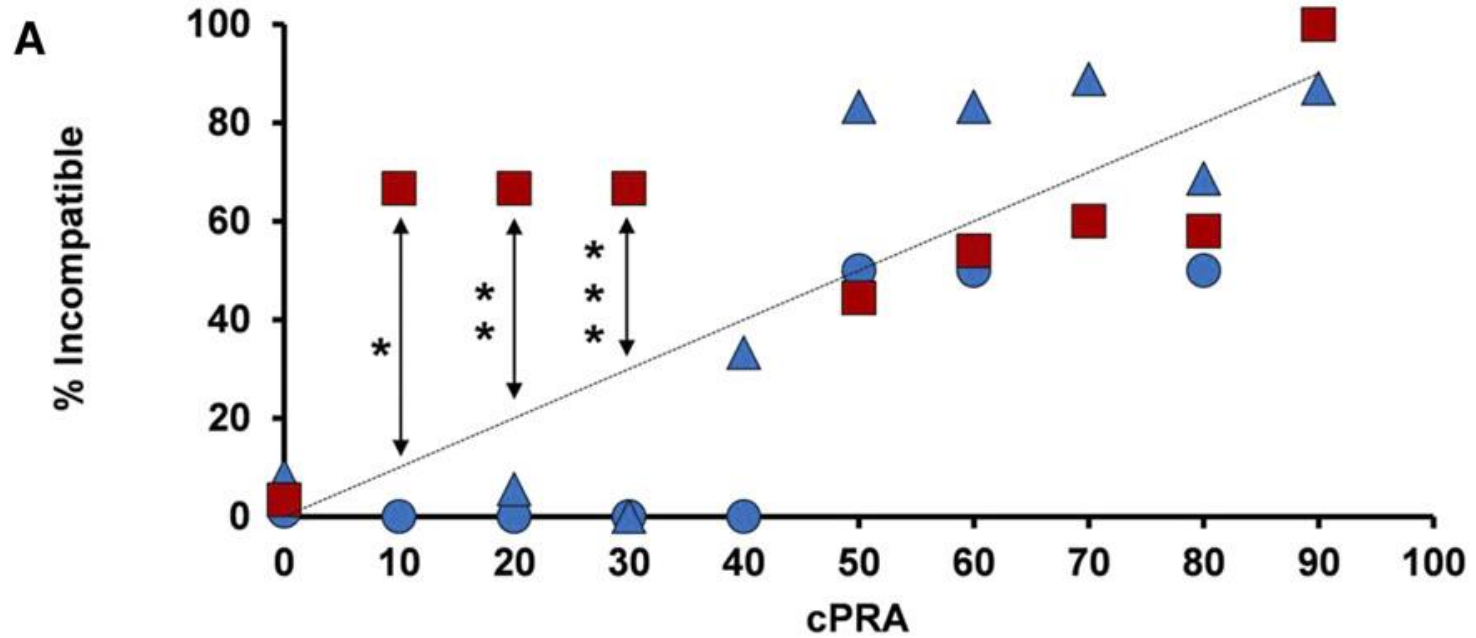
Incompatible with ≥ 1 Living Donor



B

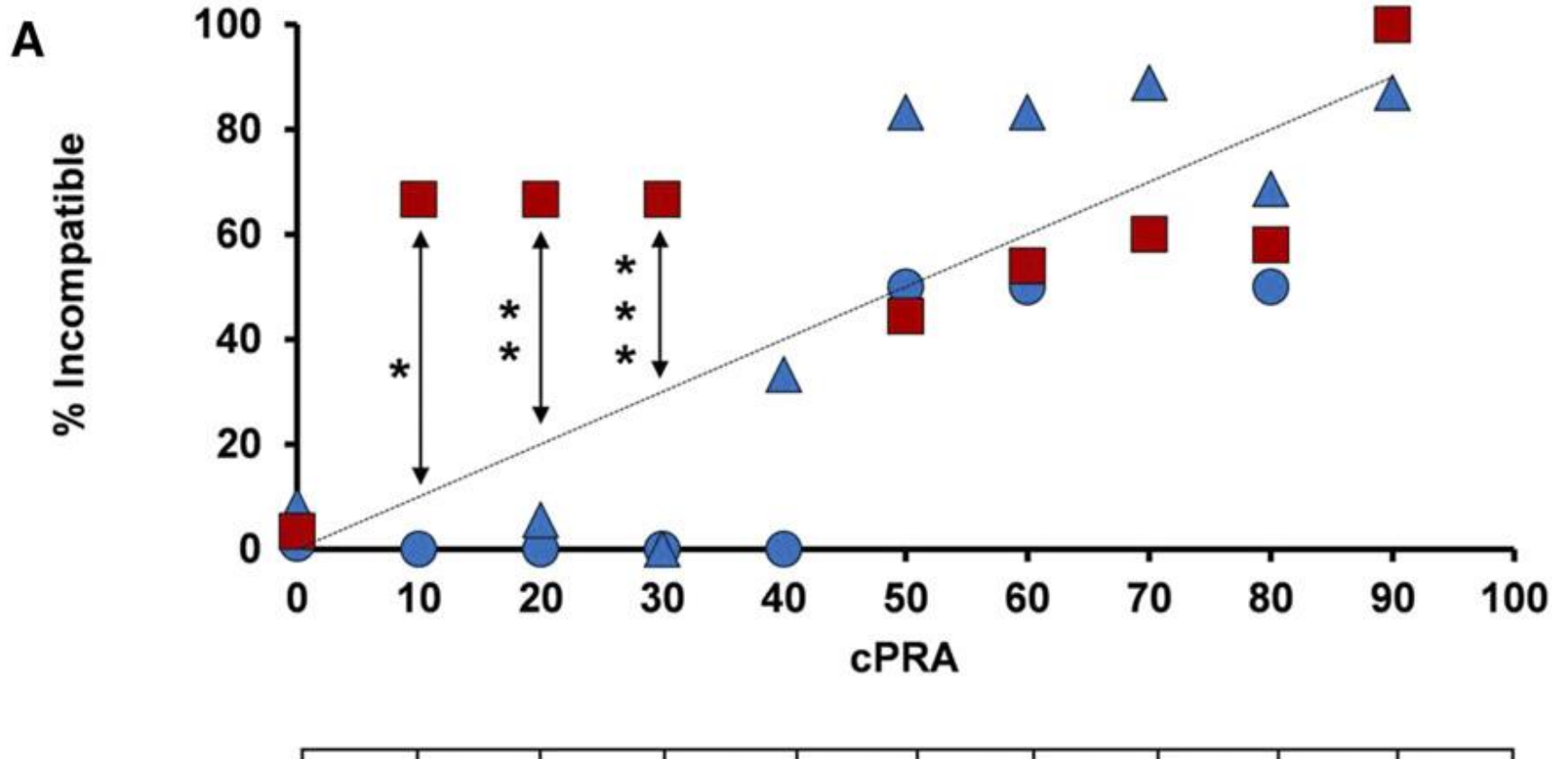


Clinical significance



● Transfusion	167	1	1	7	3	3	2	0	2	1
▲ Transplant	49	0	9	2	4	5	4	7	8	16
■ Pregnancy	66	6	3	10	0	9	11	5	12	7

Clinical significance

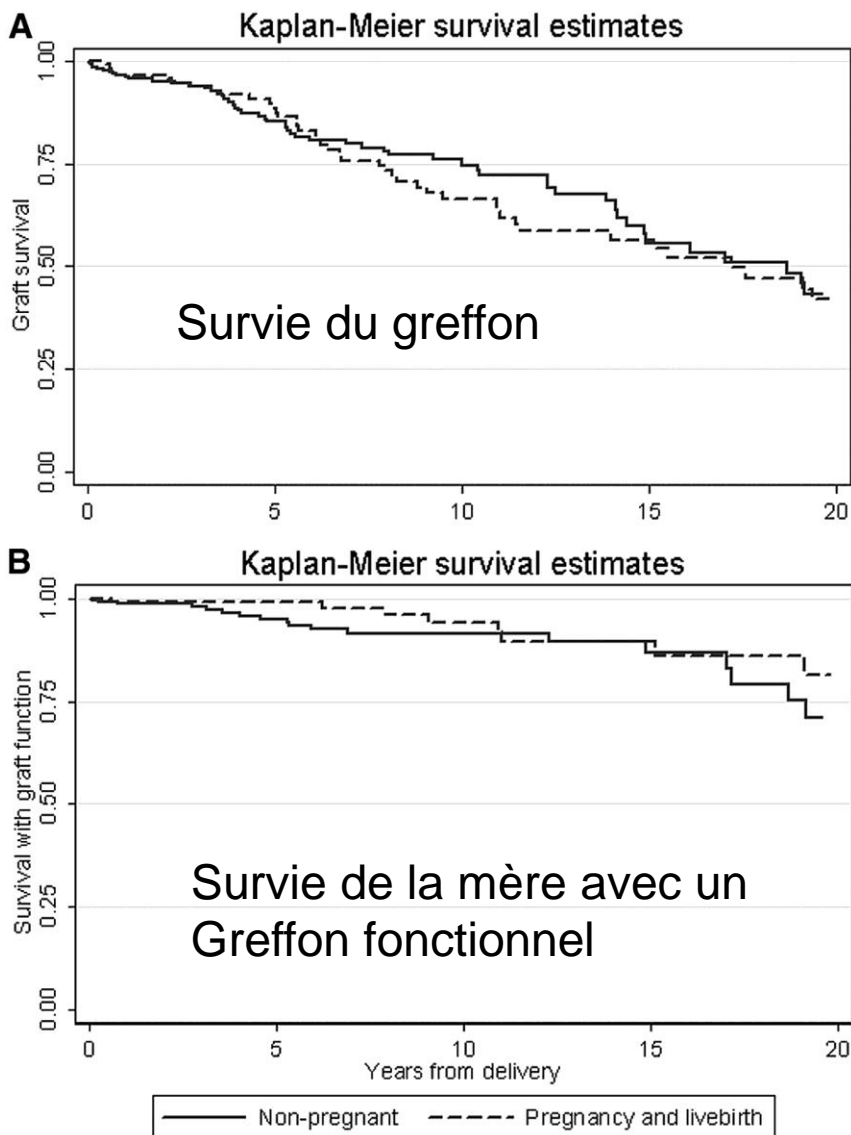


Bromberger B, J Am Soc Nephrol 2017

En cohorte, la grossesse ne compromet pas la survie du greffon

(Australie et Nouvelle Zélande)

Kaplan-Meier graft survival estimates in 120 nulliparous and 120 parous women with a kidney graft



Grossesse et Immunité

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- **Grossesse et auto-immunité**

Lupus erythémateux disséminé

Recommandations pour planifier une grossesse

- **Lupus inactif depuis > 6 mois**
- **Fonction rénale normale**
- **Protéinurie < 50 mg/mmol de créatinine**
- **Ne pas interrompre l'hydroxychloroquine !**

Kidney Outcomes and Risk Factors for Nephritis (Flare/*De Novo*) in a Multiethnic Cohort of Pregnant Patients with Lupus

Lupus quiescent, sans insuffisance rénale ni protéinurie abondante

Patient Characteristics	Total (%)	No Kidney Flare/ <i>De Novo</i> (%)	Kidney Flare/ <i>De Novo</i> (%)	P Value
<i>n</i>	373	356	17	
Demographics				
Ethnicity/race				0.62
<i>Non-Hispanic white</i>	179 (47.99)	171 (48.03)	8 (47.06)	
<i>Hispanic all races</i>	62 (16.62)	59 (16.57)	3 (17.65)	
<i>Black</i>	74 (19.84)	71 (19.94)	3 (17.65)	
<i>Asian</i>	41 (10.99)	40 (11.24)	1 (5.88)	
<i>Other</i>	17 (4.56)	15 (4.21)	2 (11.76)	
Mean age (SD), y	30.9 (4.90)	31.0 (4.87)	29.6 (5.52)	0.26

***Incidence de poussée lupique sous traitement: 17/373=4,5%
(1,6% en l'absence d'antécédent de néphrite lupique)***

La moitié des poussées au 2^e trimestre, l'autre moitié au 3^e

A past history of kidney disease and a low C4 are risk factors

Clinical history

History of kidney disease				<0.001
<i>No kidney disease</i>	255 (68.36)	251 (70.51)	4 (23.53)	
<i>Complete remission</i>	89 (23.86)	82 (23.03)	7 (41.18)	
<i>Partial remission</i>	29 (7.77)	23 (6.46)	6 (35.29)	
aPL status				0.14
<i>aPL+</i>	50 (13.40)	50 (14.04)	0 (0.00)	
<i>aPL-</i>	323 (86.60)	306 (94.74)	17 (100.00)	
C3				0.01
<i>Normal</i>	286 (79.89)	277 (81.23)	9 (52.94)	
<i>Low</i>	72 (20.11)	64 (18.77)	8 (47.06)	
C4				<0.001
<i>Normal</i>	265 (74.23)	259 (76.18)	6 (35.29)	
<i>Low</i>	92 (25.77)	81 (23.82)	11 (64.71)	
Anti-dsDNA				0.63
<i>Negative</i>	218 (58.45)	209 (58.71)	9 (52.94)	
<i>Positive</i>	155 (41.55)	147 (41.29)	8 (47.06)	

Conclusions

- Le placenta est localement peu ou pas immunogène (au maximum HLA-C)
- Le foetus l'est mais pas localement: c'est une réponse systémique (>50% anticorps anti-HLA post accouchement)
- Les anticorps anti-HLA sont pérennes une fois sur 2, et ils limitent l'accès des femmes à la greffe
- La grossesse ne modifie pas le pronostic de la greffe sous traitement
- La grossesse ne représente pas un sur-risque de poussée du lupus quiescent sous traitement