Eşler arası Erkekten Kadına ya da Çocuktan Anneye Transplantasyon

Prof.Dr. Tülay Kılıçaslan Ayna

İzmir Katip Çelebi Üniversitesi Tıbbi Biyoloji AD

İKÇÜ Hücre Doku Organ Nakli Araştırma ve Uygulama Merkezi

Diyarbakır 1-2 Kasım 2024

NAKİL SAYISI								
Akrabalık Dereceleri	**2016**	**2017**	**2018**	**2019**	**2020**	**2021**	**2022**	**2023**
1	546	992	1.062	1.084	760	1.094	1.143	1.122
2	296	530	584	621	489	646	722	688
3	53	91	106	104	61	90	118	106
4	34	50	71	96	74	171	143	139
Akraba Değil	992	291	354	308	208	331	332	246
Çapraz	123	104	181	174	169	201	229	154
Eşler Arası	595	593	657	668	489	544	653	696
Genel Toplam	**2.639**	**2.651**	**3.015**	**3.055**	**2.250**	**3.077**	**3.340**	**3.151**

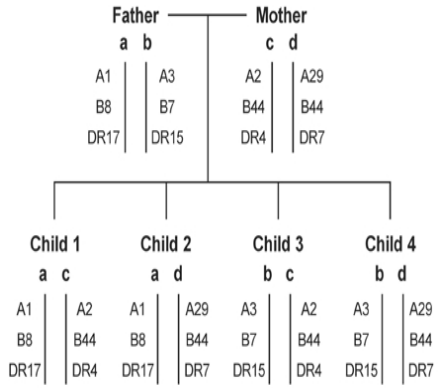
https://nefroloji.org.tr/tr/icerik/genel-5/turk-nefroloji-dernegi-registry-raporlari-508

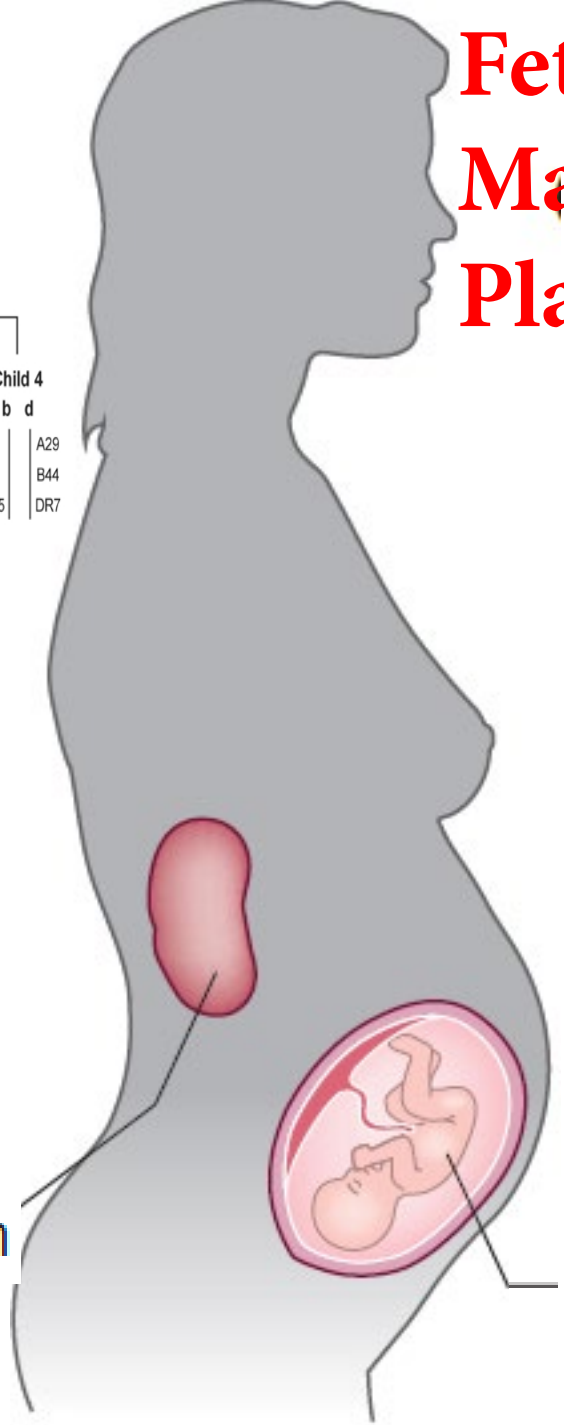
Anti-HLA alloimmunizasyonu

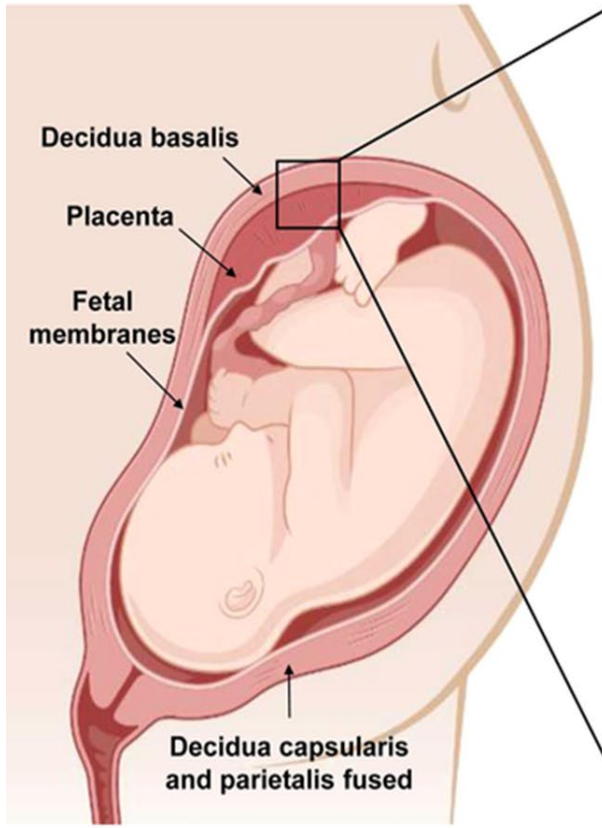
- ✓Kan transfüzyonları
- ✓Transplantasyonlar
- ✓**Gebelik**

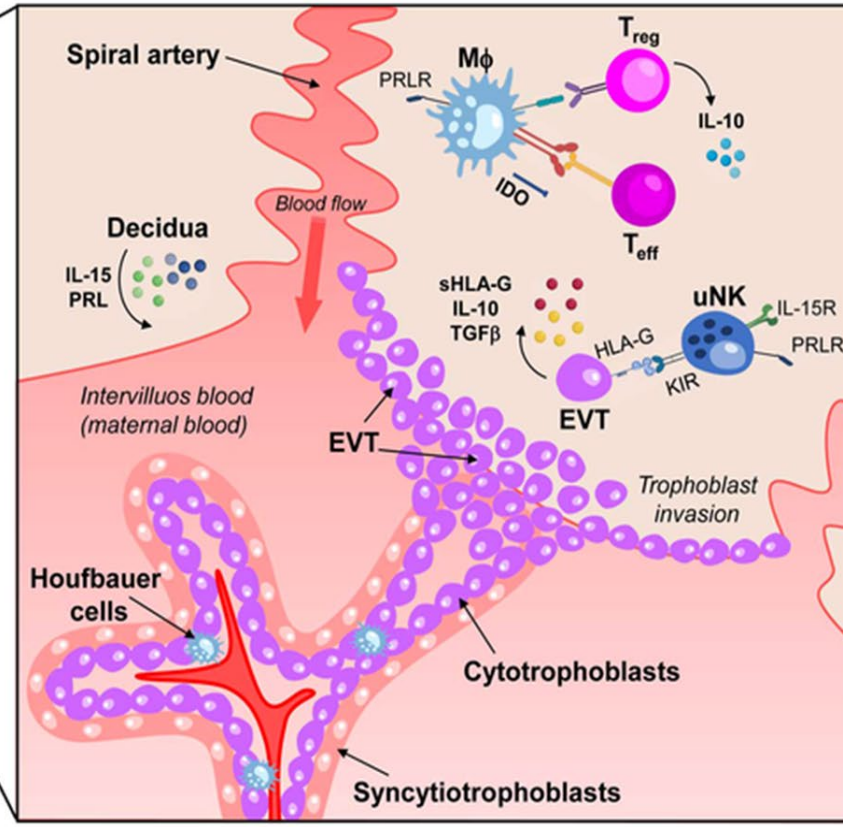
Anti-HLA immunizasyonunun tek doğal kaynağıdır.
-Anti Paternal antikorlar-

Fetal, Maternal, Placental Mekanizmalar

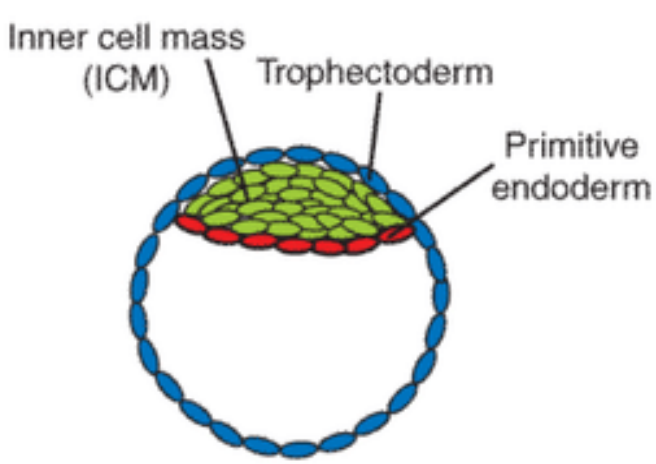


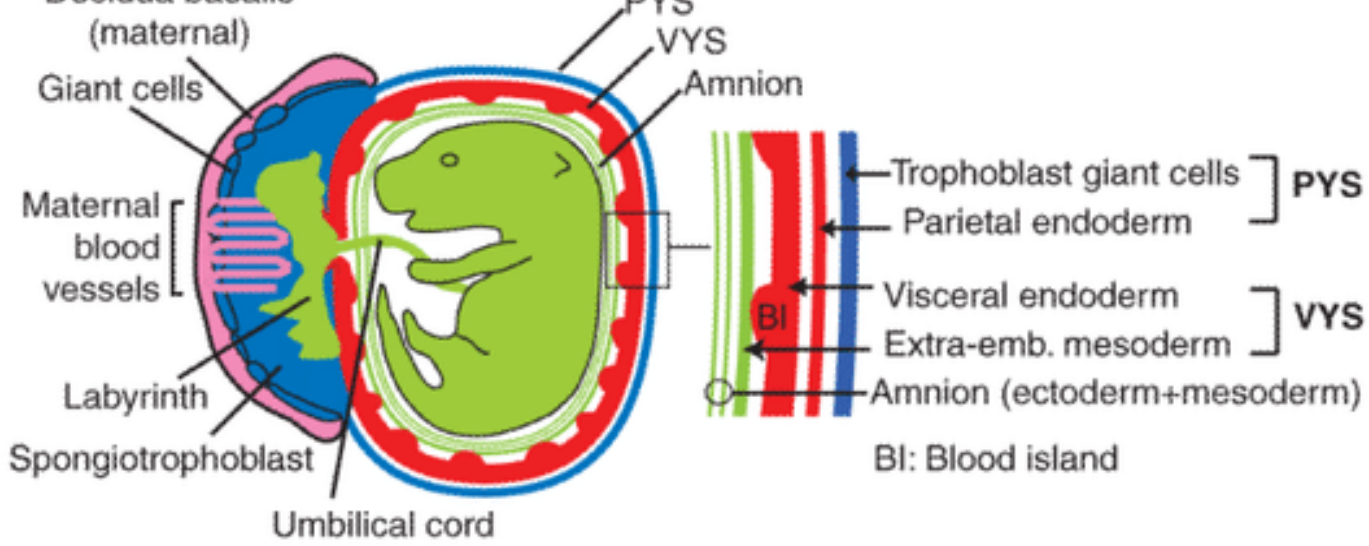


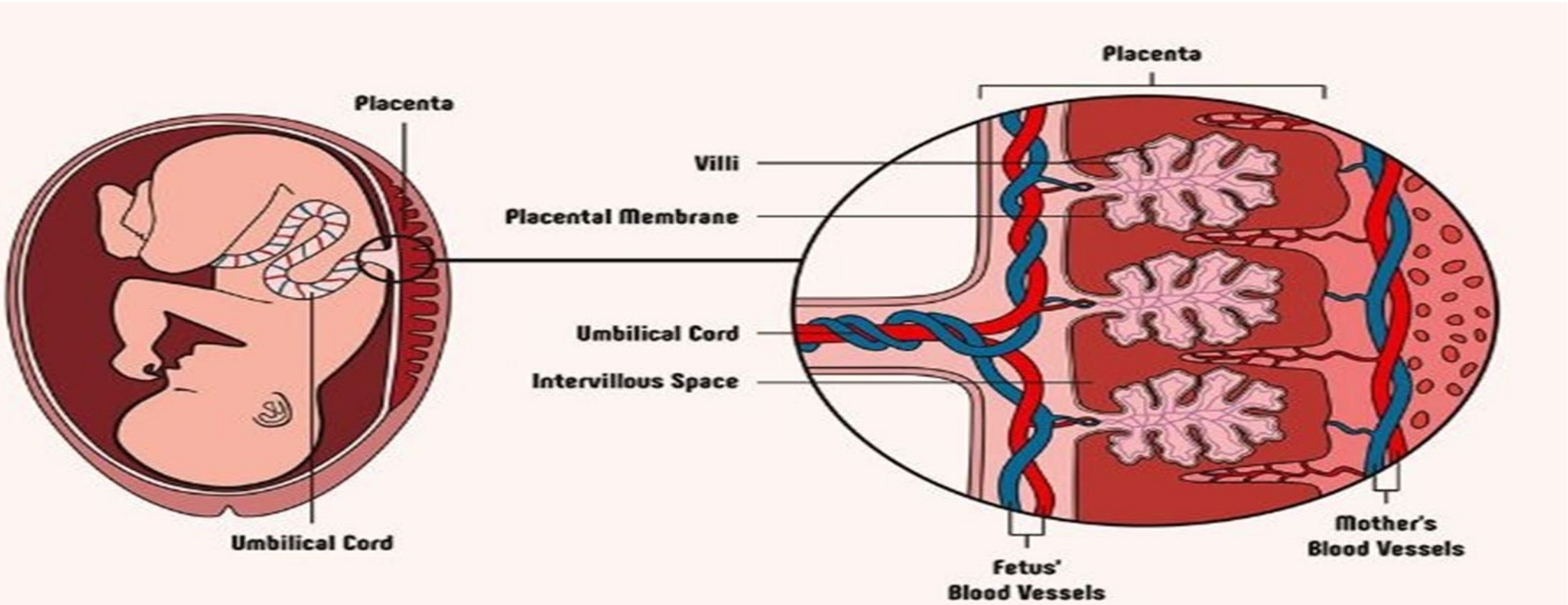




Immune mechanisms at the maternal-fetal interface: perspectives and challenges -2


Inner cell mass
(ICM)
Trophectoderm
Primitive
endoderm

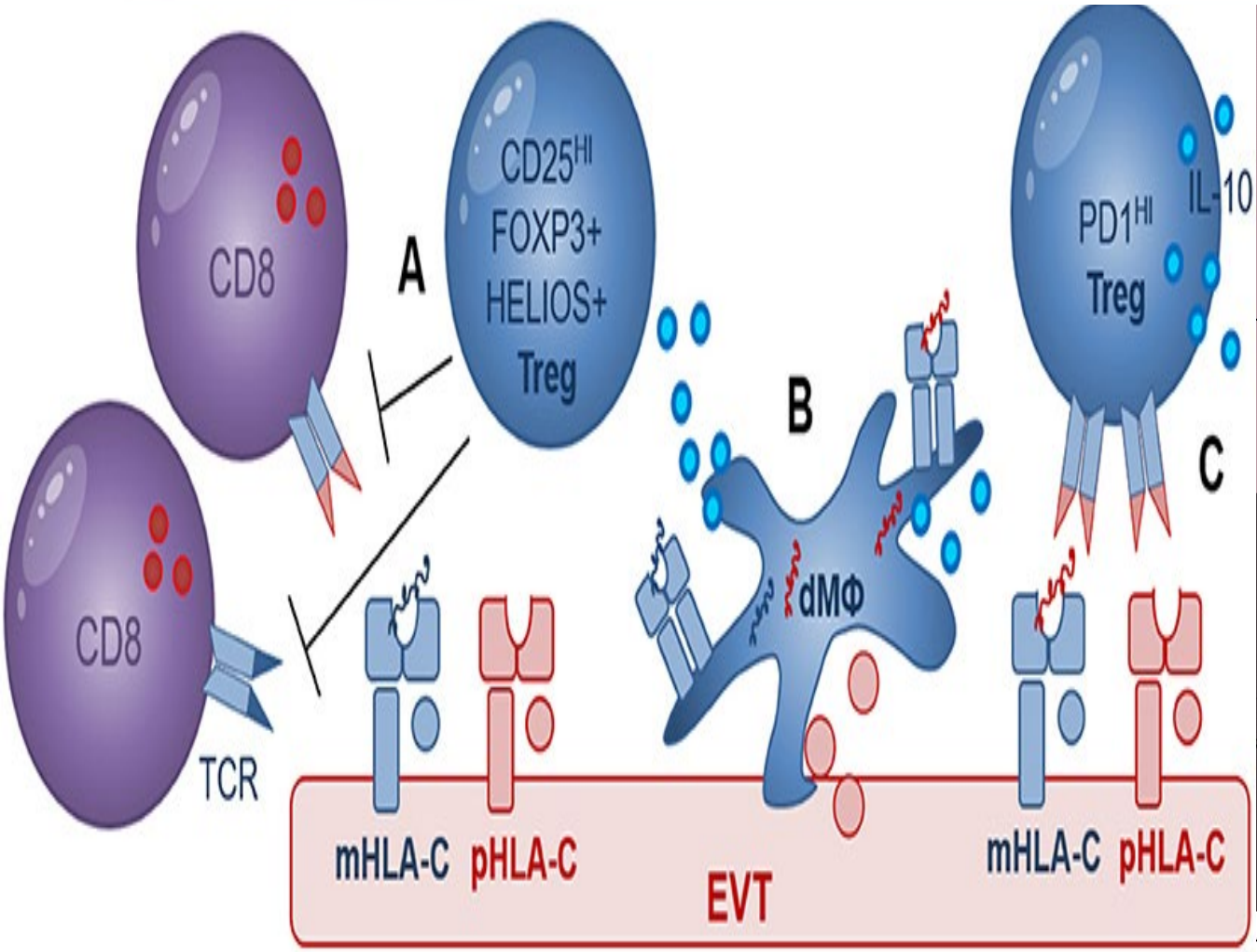

(maternal)
Giant cells
Maternal
blood
vessels
Labyrinth
Spongiotrophoblast
Umbilical cord
PYS
VYS
Amnion
Trophoblast giant cells
Parietal endoderm
PYS
Visceral endoderm
Extra-emb. mesoderm
VYS
Amnion (ectoderm+mesoderm)
BI
BI: Blood island

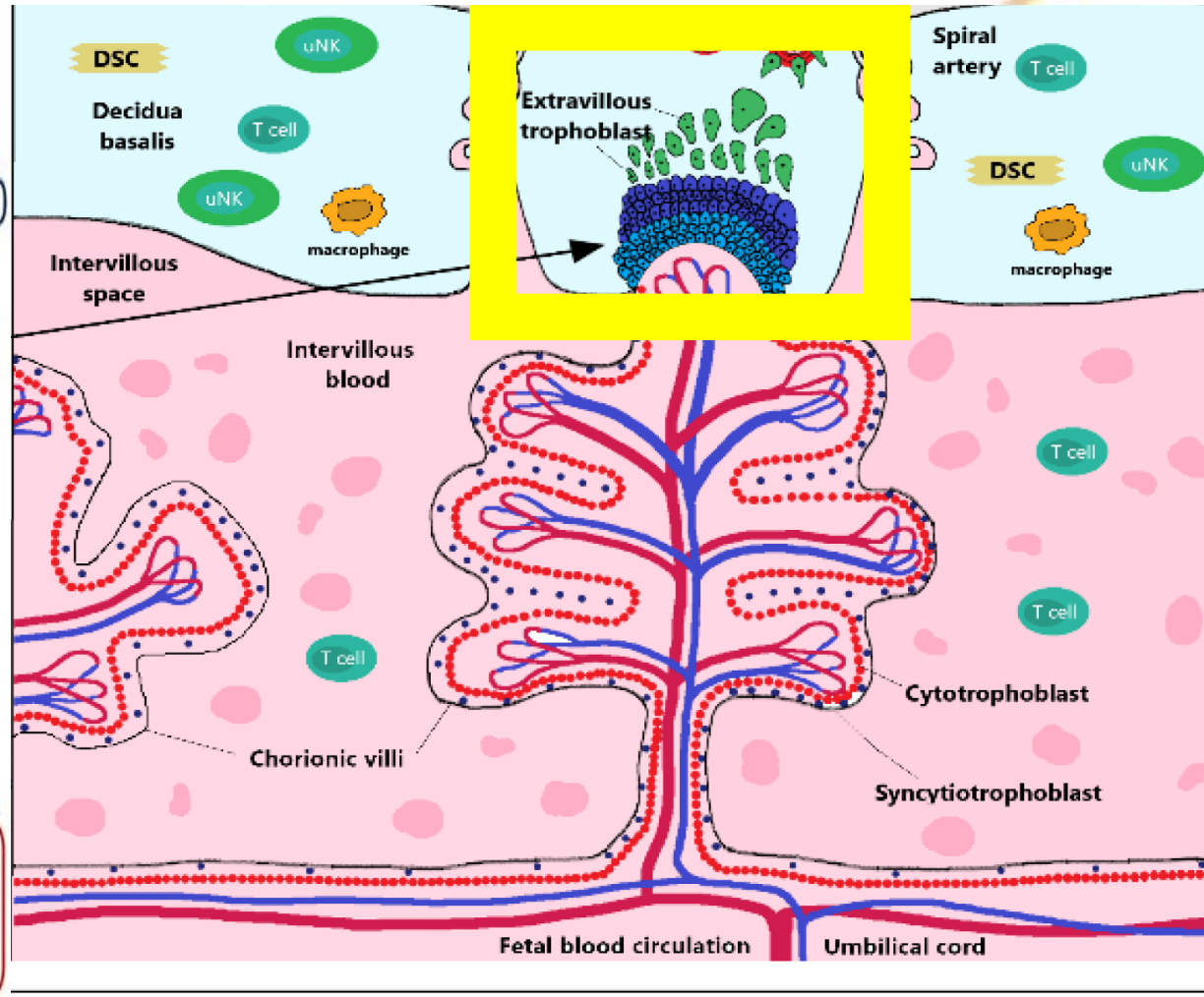

Placenta
Umbilical Cord
Placenta
Villi
Placental Membrane
Umbilical Cord
Intervillous Space
Fetus'
Blood Vessels
Mother's
Blood Vessels

Classic HLA class I | HLA class II | Nonclassic HLA class I

	HLA-A	HLA-B	HLA-C	HLA-DR	HLA-DQ	HLA-G	HLA-E	HLA-F
VT*	(–)	(–)	(–)	(–)	(–)	–	–	–
EVT	(–)	(–)	(+)	(–)	(–)	(+)	(+)	(+)

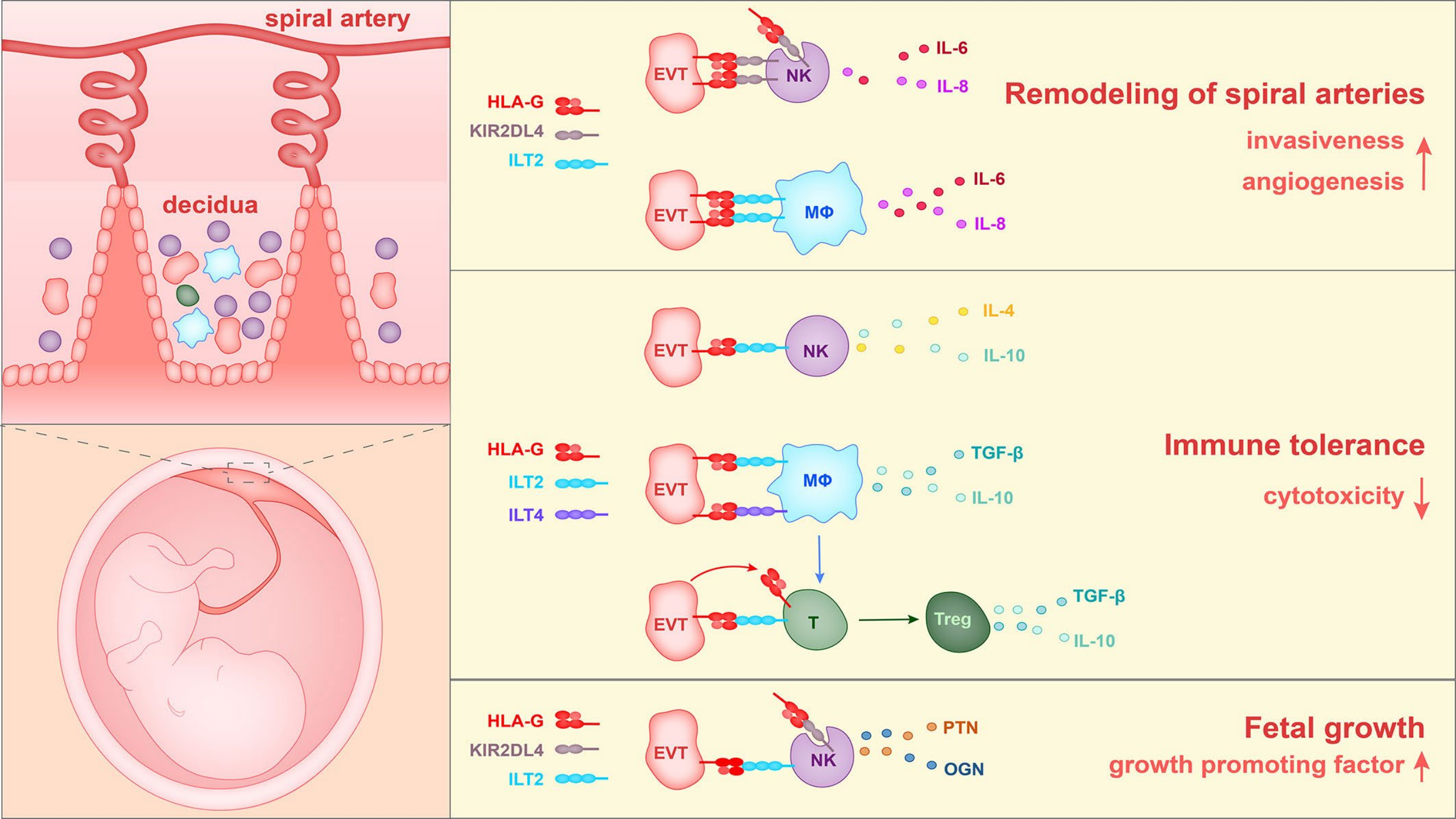
*villous trophoblast

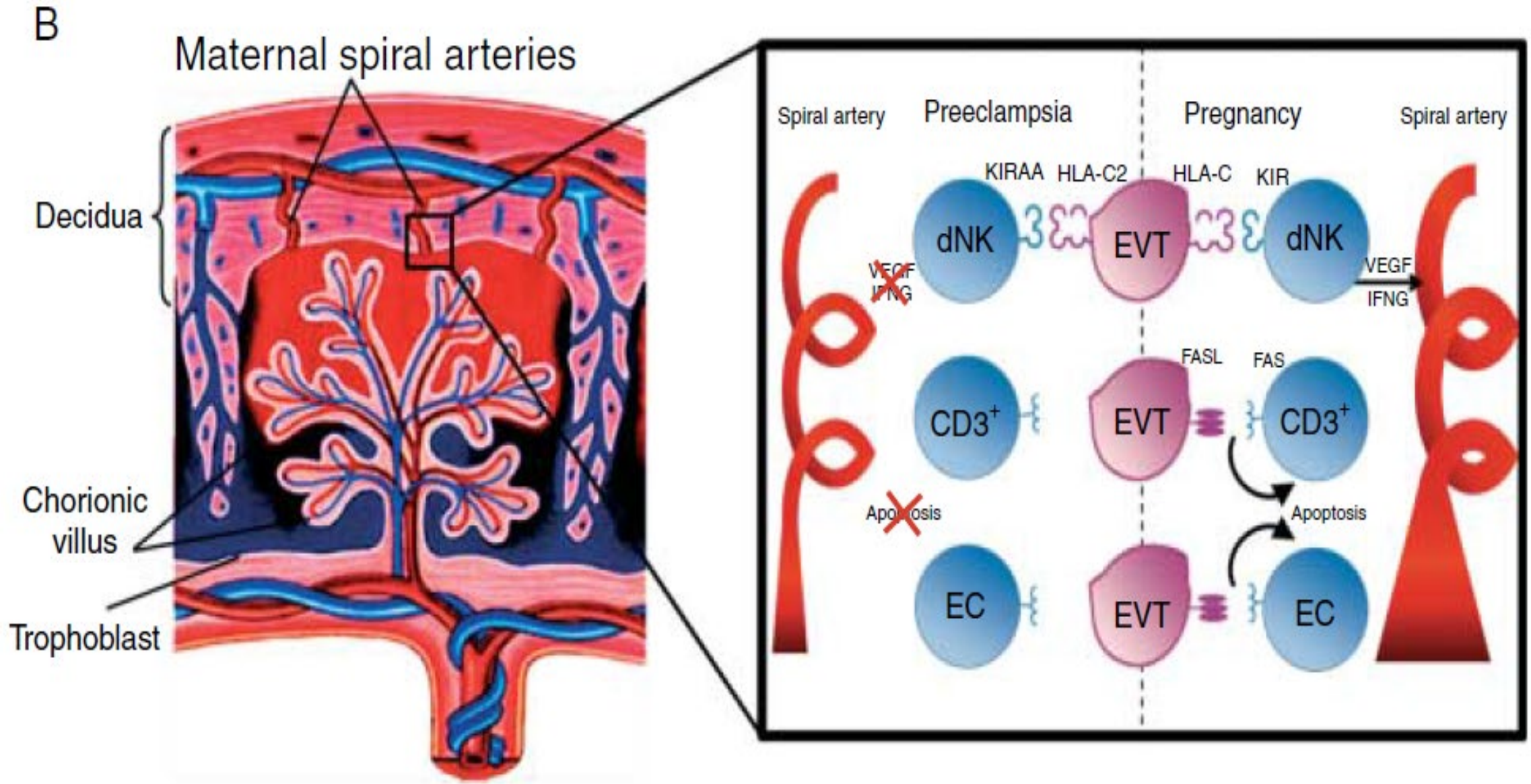


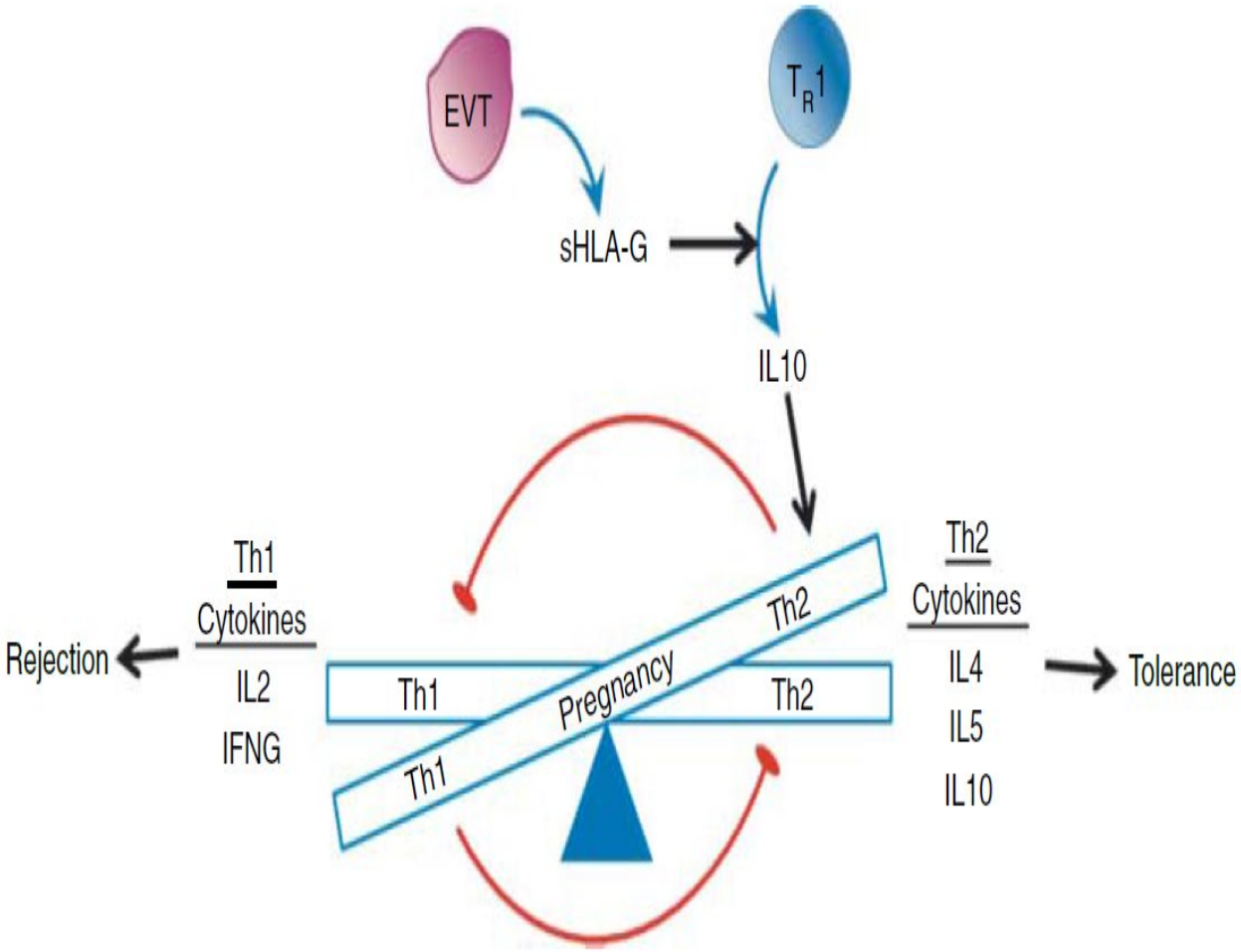


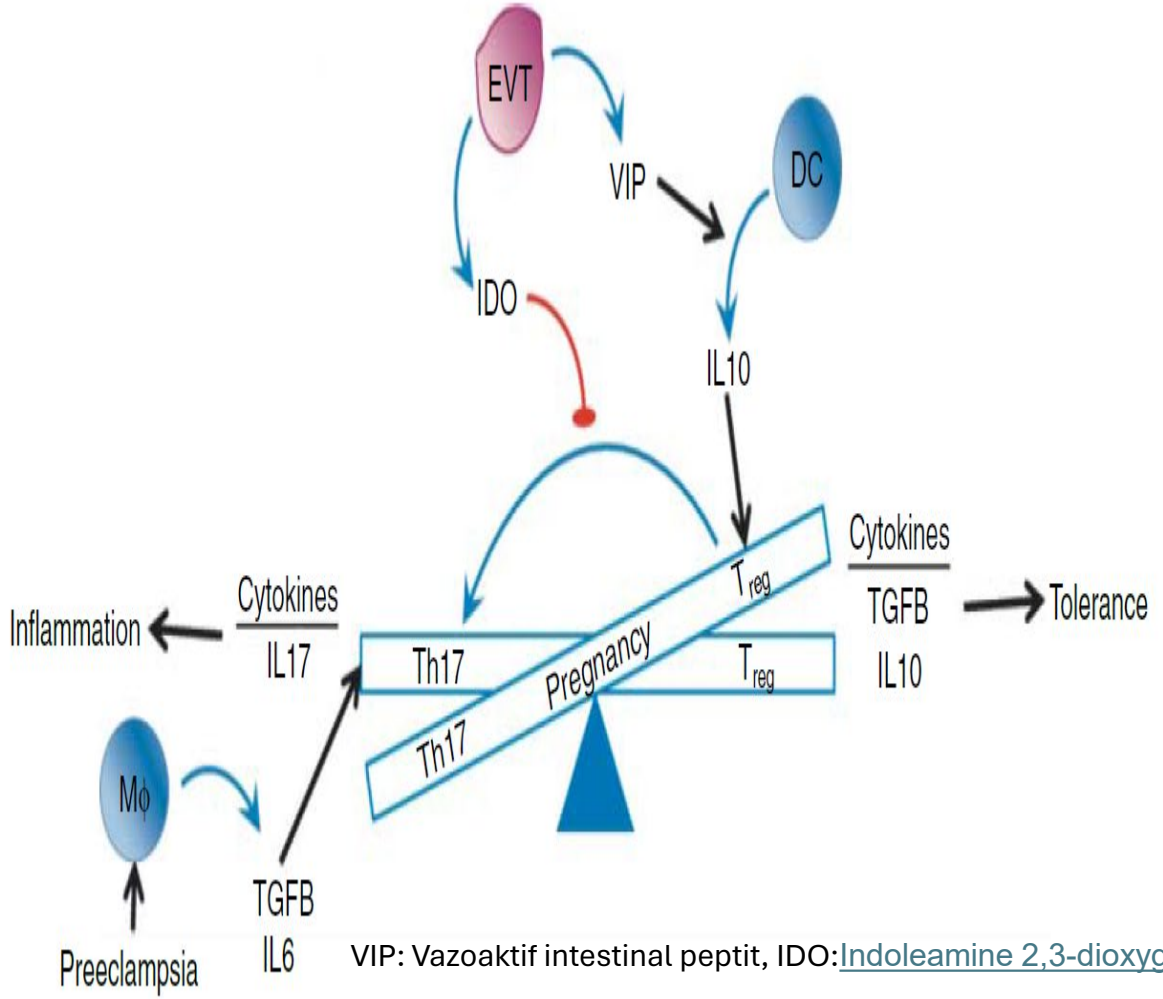
Arayüz 1, invaziv, ekstra-vilöz trofoblast (EVT) ve desidual bağışıklık hücreleri arasındadır ve plasentasyonun başarısının belirlendiği yerdir.

HLA-DR is aberrantly expressed at feto-maternal interface in pre-eclampsia


spiral artery
decidua
HLA-G
KIR2DL4
ILT2
EVT
NK
IL-6
IL-8
Remodeling of spiral arteries
invasiveness
angiogenesis
EVT
MΦ
IL-6
IL-8
EVT
NK
IL-4
IL-10
HLA-G
ILT2
ILT4
EVT
MΦ
TGF-β
IL-10
Immune tolerance
cytotoxicity
EVT
T
Treg
TGF-β
IL-10
HLA-G
KIR2DL4
ILT2
EVT
NK
PTN
OGN
Fetal growth
growth promoting factor

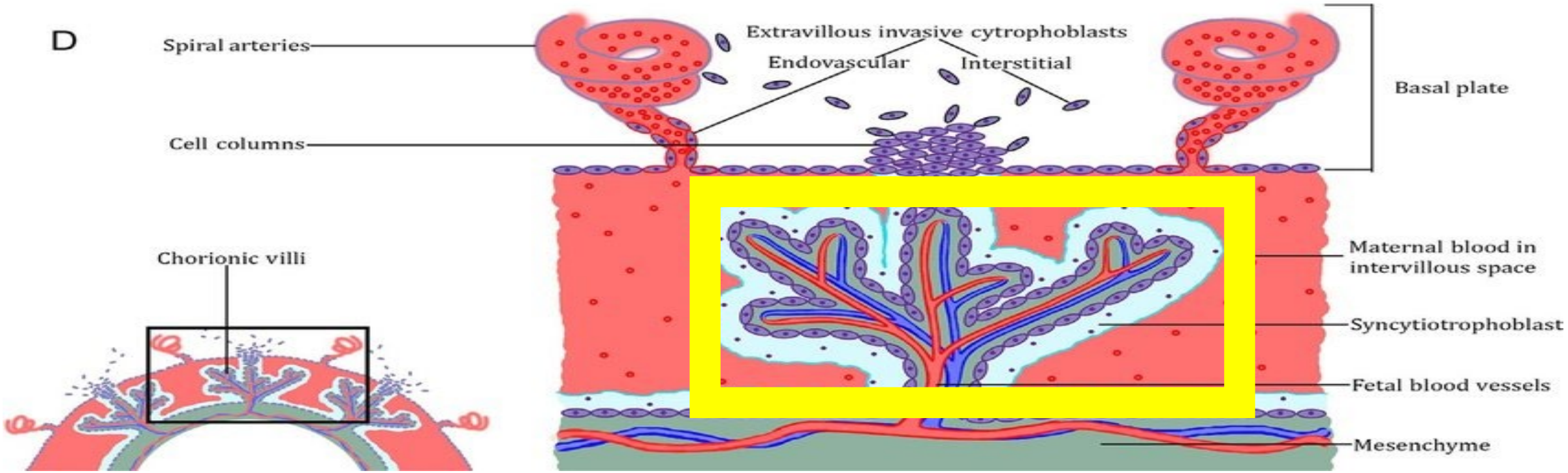

B
Maternal spiral arteries
Decidua
Chorionic villus
Trophoblast
Spiral artery
Preeclampsia
Pregnancy
Spiral artery
KIRAA
HLA-C2
HLA-C
KIR
dNK
EVT
dNK
VEGF
IFNG
VEGF
IFNG
FASL
FAS
CD3+
EVT
CD3+
Apoptosis
Apoptosis
EC
EVT
EC

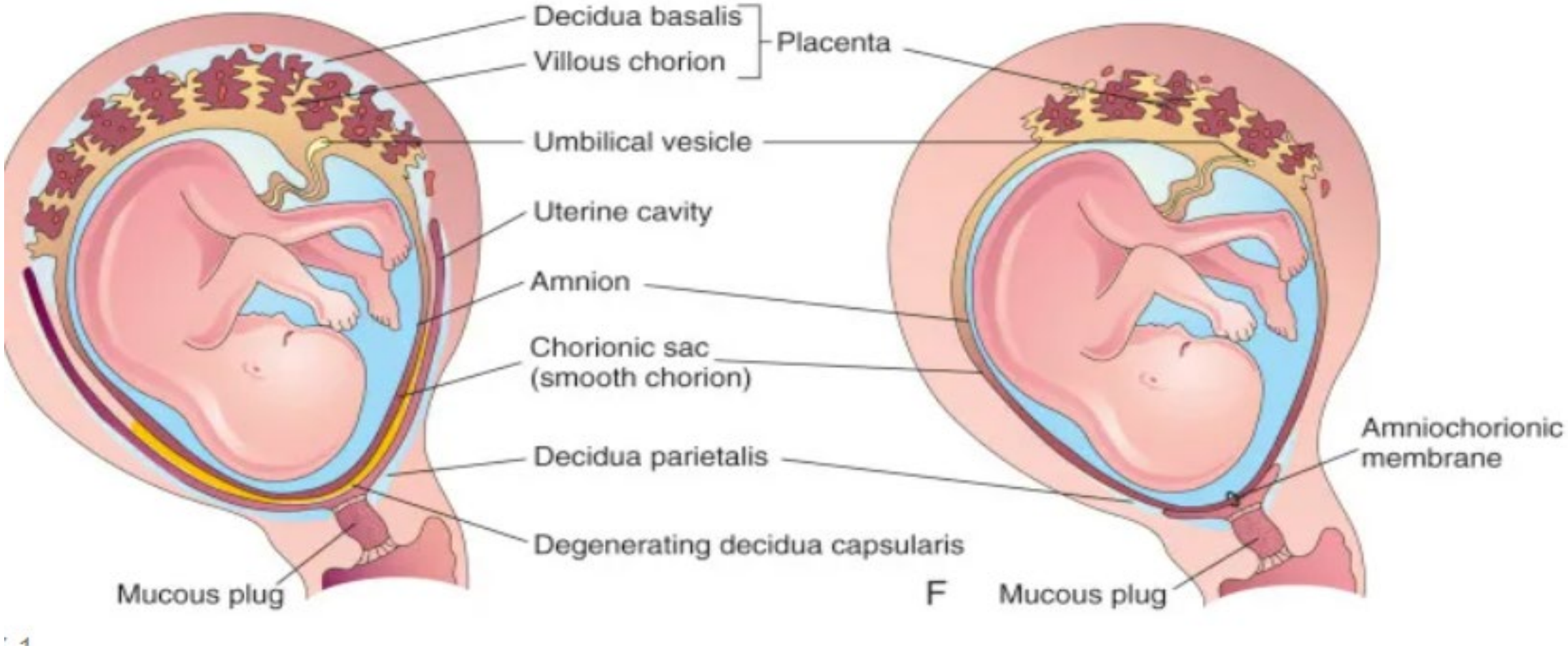




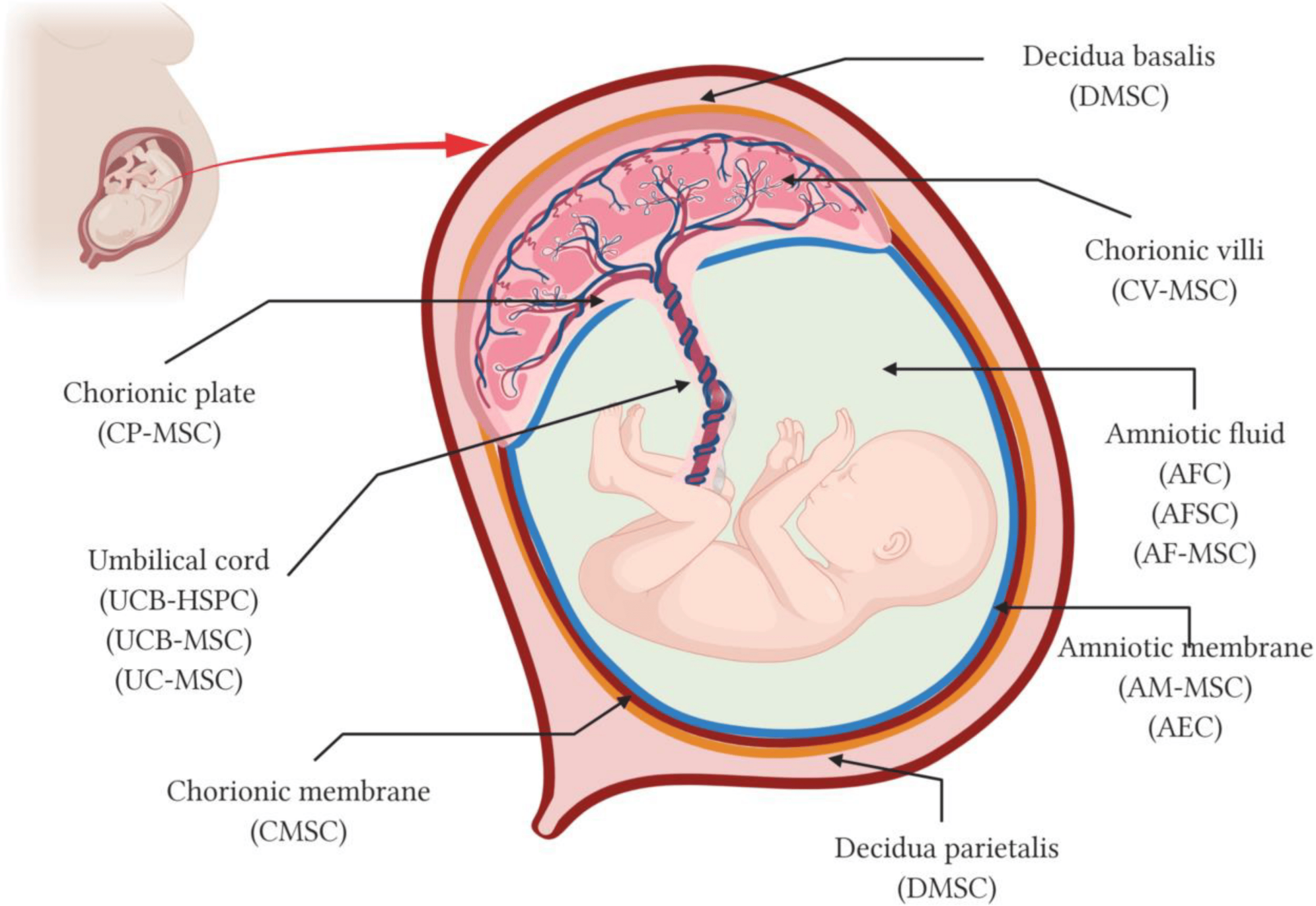
VIP: Vazoaktif intestinal peptit, IDO:Indoleamine 2,3-dioxyger

Arayüz 2, sinsitiyotrofoblast ile maternal kan arasında yer alır. Sinsitiyotrofoblast, koryonik villüsün epitel örtüsünü oluşturur ve gebeliğin ikinci yarısında en aktif olan maternal dolaşımdaki bağışıklık hücrelerinin kanıyla temas halinde geniş bir yüzey alanı sunar. Bu nedenle, maternal dolaşıma dökülen sinsitiyotrofoblast kaynaklı **ekstraselüler veziküller** (STEV'ler) arayüz 2'nin bir uzantısını temsil eder.





Arayüz 3 Decidua parietalis ve the amniokoryon arasındadır.


Decidua basalis
(DMSC)
Chorionic villi
(CV-MSC)
Chorionic plate
(CP-MSC)
Amniotic fluid
(AFC)
(AFSC)
(AF-MSC)
Umbilical cord
(UCB-HSPC)
(UCB-MSC)
(UC-MSC)
Amniotic membrane
(AM-MSC)
(AEC)
Chorionic membrane
(CMSC)
Decidua parietalis
(DMSC)

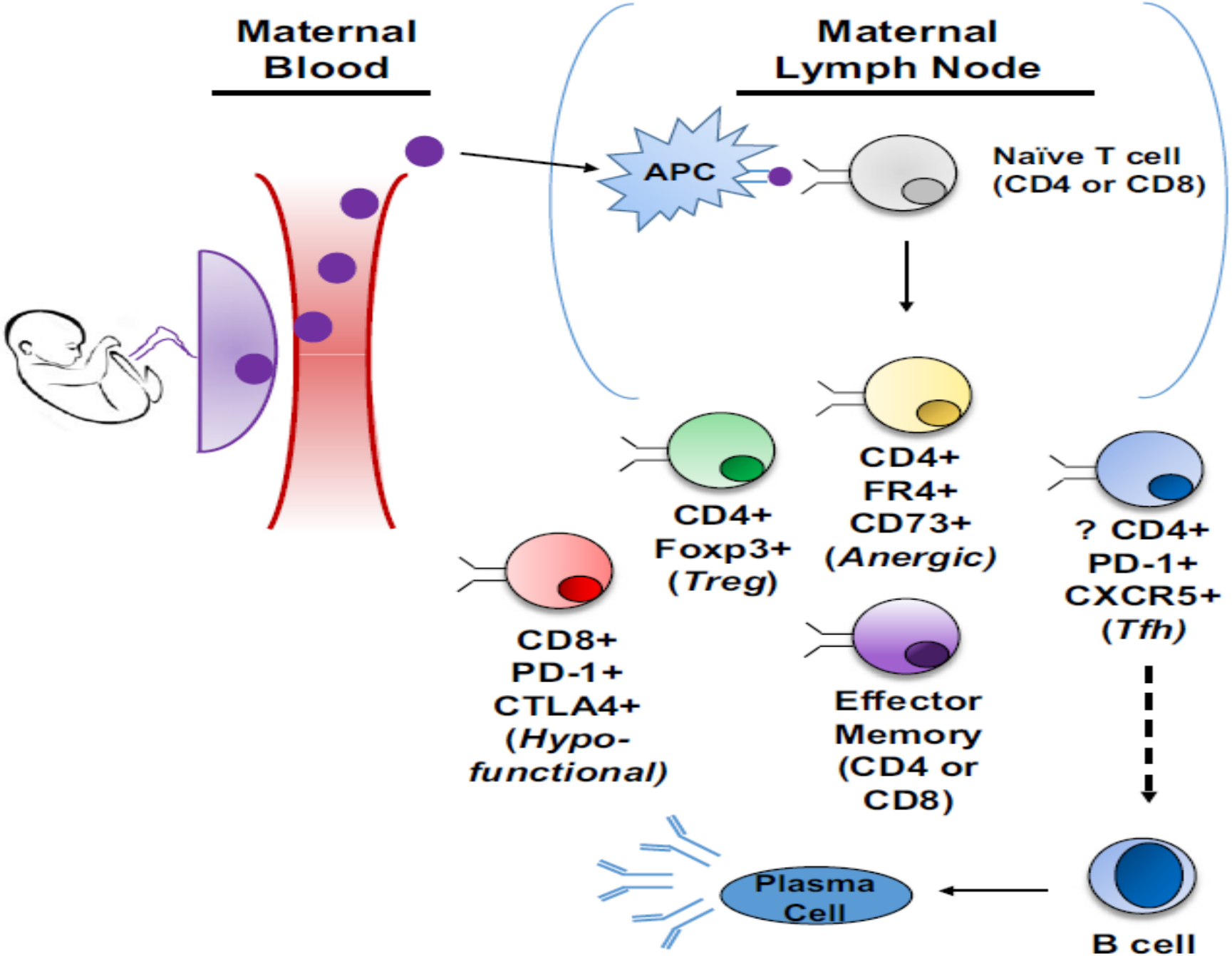


FIGURE 2 Model of maternal T cell priming by fetal antigens. Fetal cells and cellular components (ie, microvesicles) (purple) cross the placenta into the maternal bloodstream, where they circulate to the secondary lymphoid organs. Fetal antigens are presented by the maternal APC and prime maternal CD4 and $CD8^+$ T cells. Potential T cell fates induced by fetal antigen are shown, including $PD\text{-}1^+CTLA4^+$ $CD8^+$ T cells with attenuated effector functions (red), $CD4^+Foxp3^+$ regulatory T cells (green), $CD4^+$ $FR4^+$ $CD73^+$ anergic T cells (yellow), and effector memory cells (purple). While $CD4^+$ $PD\text{-}1^+$ $CXCR5^+$ T follicular helper cells (Tfhs) (blue) have been demonstrated in the placenta, they have yet to be examined in the maternal lymph node. PD-1, programmed cell death protein; CTLA4, cytotoxic T-lymphocyte associated protein 4

Biologic mechanisms and clinical consequences of pregnancy alloimmunization-2018

Gebelikte anti-HLA antikorları ne zaman oluşur?

Comparison of Anti-HLA Antibody Production According to Gestational Periods in Pregnant Women

B. Cerci Gurbuz[a,b,*], M. Soyoz[a,b], D. Ozkale Okyay[c], T. Kilicaslan Ayna[a,b], and I. Pirim[a,b]

[a]Izmir Katip Celebi University Faculty of Medicine, Department of Medical Biology and Genetics, Izmir, Turkey; [b]University of Hea
Science Tepecik Training and Research Hospital, Tissue Typing Laboratory, Izmir, Turkey; and [c]University of Health Science Tep
Training and Research Hospital, Clinic of Gynecology, Izmir, Turkey

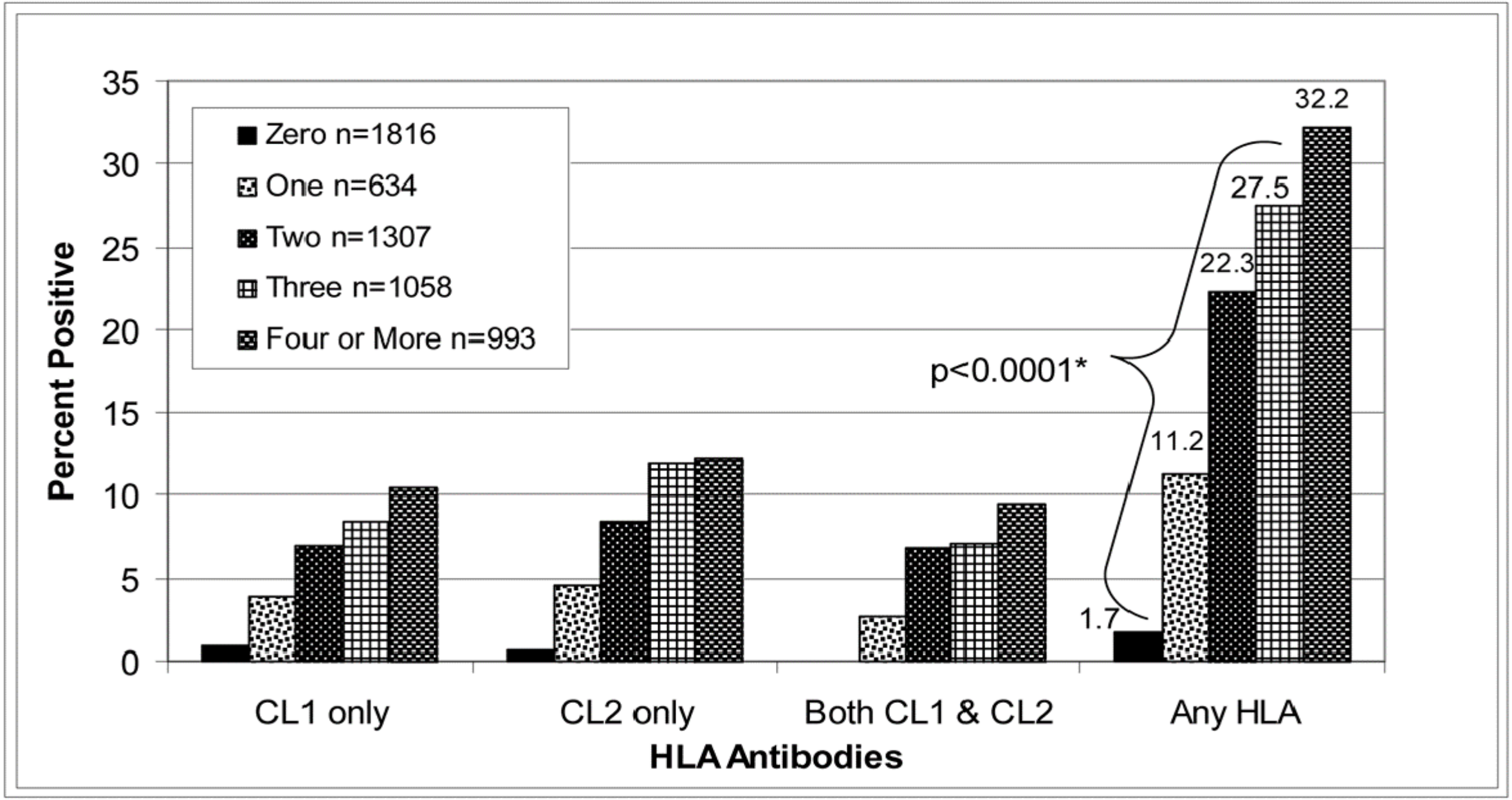
ABSTRACT

Background. To evaluate paternal anti-HLA antibody profiles, sera samples were collected from pregnant women in different trimesters and the panel-reactive antibody (PRA) specificities were identified.

Methods. From 2013 to 2015, serum samples were obtained from 41 pregnant women who had registered at the Izmir Tepecik Education and Research Hospital Gynecology Clinic. Anti-HLA antibodies were screened by using the panel reactive antibody screening and identification tests. Sera samples were obtained at the first, second, and third trimesters. The primary outcome was to determine the anti-HLA antibody production term during pregnancy; the secondary outcome was identification of anti-HLA antibodies.

Results. None of the women had a sensitization history except during pregnancy. We observed that 54% of the women produced paternal antibodies, either class I or II. Class I PRA positivity of the women who had a first or second pregnancy was the same in all 3 trimesters, whereas class II positivity was increased in the third trimester. Class II and both class I and II positivity increased in the third trimester; class I positivity was decreased in the third trimester. PRA positivity could be affected by the history of pregnancy and could be raised, but no impact was observed from the history of abortion and miscarriage (odds ratios, 1.9, 0.4, and 0.5 [95% confidence intervals, 0.5–7.8, 0.1–2.0, and 0.3–0.7], respectively; $P > .05$). The most frequently detected antibodies were A2, B7, DR7, DR4, DR11, DR13, DQ2, and DQ8.

Gebelik sayısının anti-HLA antikor oluşumuna etkisi?



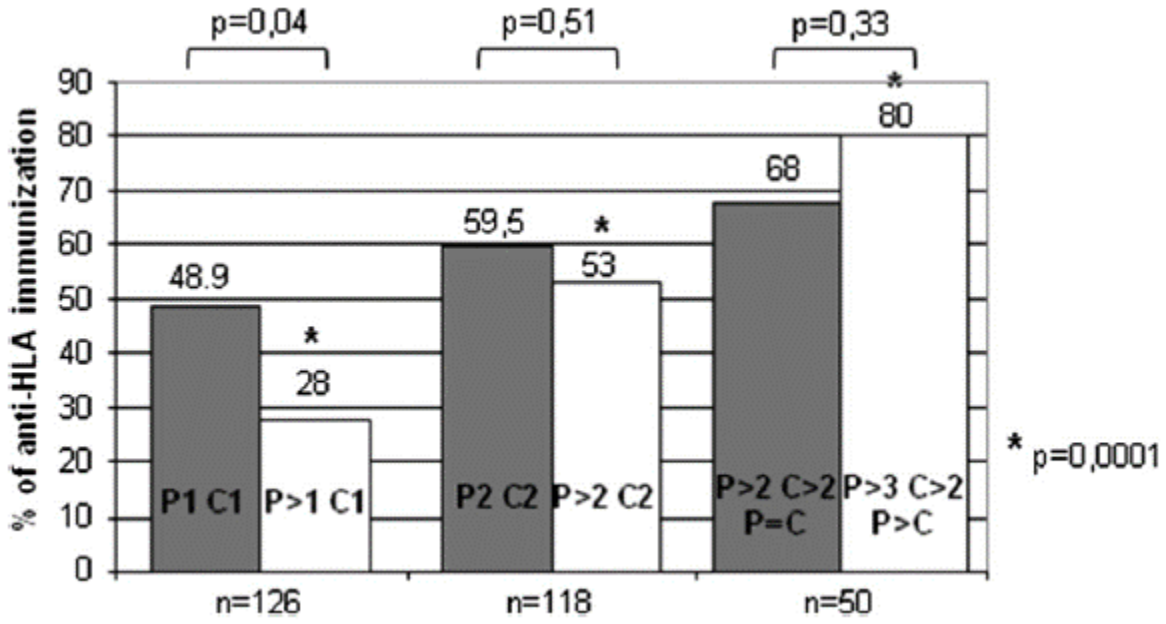
The Effect of Previous Pregnancy and Transfusion on HLA Alloimmunization in Blood Donors-2009

Doğum ve sonrası anti-HLA antikorları

Characteristics of anti-HLA immunization.

	Immunized women sample analysis ($n = 160$)		p value
	At delivery	Second sample	
CDC detection (n,%)	**52 (17.7%)**	**62 (21%)**	0.03
IgM alone	4	3	
IgG + IgM	1	4	
IgG alone	47	55	
Luminex detection (IgG) (n, %)	**131 (44.5%)**	**159 (54.1%)**	<0.001
Anti- class I alone	59	60	
Anti-class II alone	17	22	
Anti-class I + II	55	77	

CDC, complement-dependent cytotoxycity; IgG, Immunoglobulin G; IgM, Immunoglobulin M.



Incidence of immunization for women with only one pregnancy ($n = 94$), depending on their IL-6 gene promoter genotype.

	Immunized	Non immunized	p value
IL-6 gene promoter genotype (n,%)[a]			0.02
WT	25 (62.5%)	15 (37.5%)	
M	21 (38.9%)	33 (61.1%)	

[a] IL-6 gene promoter polymorphism: WT = G/G genotype in position −174; M = G/C or C/C genotype in position −174.

Masson E, Vidal C, Deschamps M, et al. Incidence and risk
factors of anti-HLA immunization after pregnancy. Hum

Gebelikte anti-HLA antikorların ömrü?

Anne yaşı : 47,6±13,1
Gebelik sayısı : 3,4 ± 1,4
Çocuk sayısı : 2,9 ± 1,5
Son doğum sonrası süre: 14,6±12,8

PRA tarama: % 49,3 pozitif
HLA sınıf I : % 52,9
HLA sınıf II : % 61,7

PRA tarama: % 40,5 borderline
HLA sınıf I : % 60,7
HLA sınıf II : % 39,2

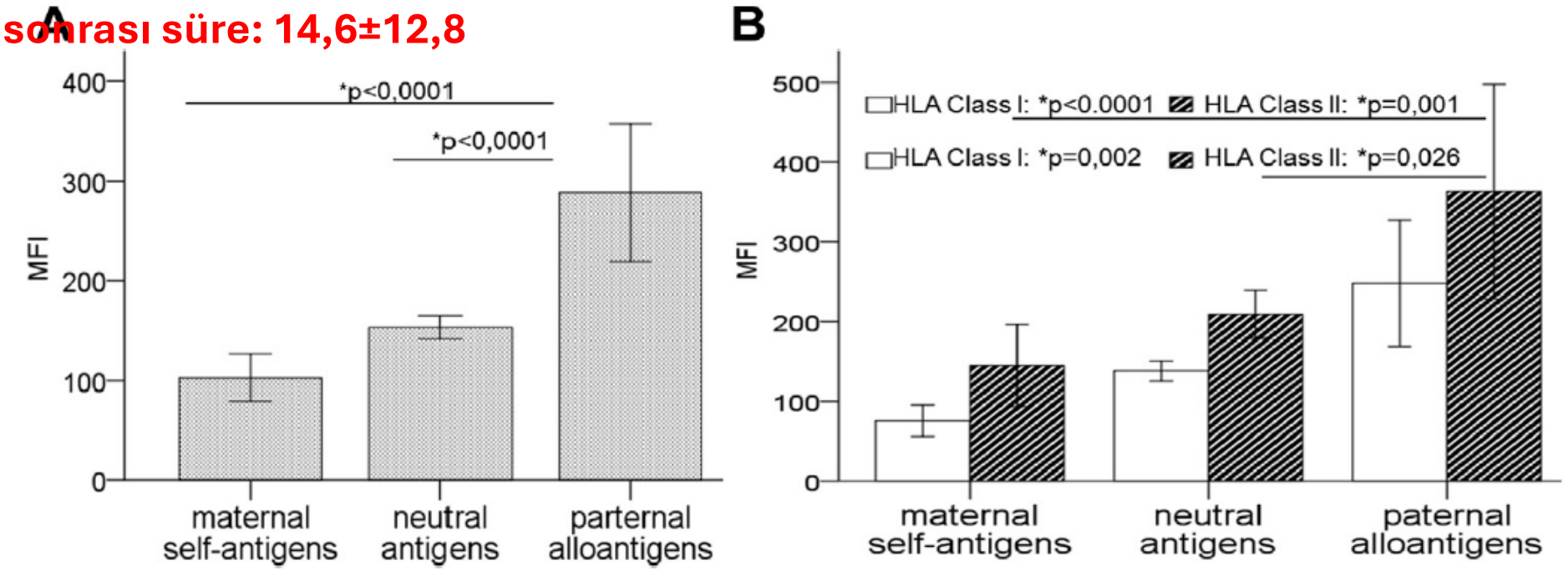


Fig 1. Comparative analysis of the mean of MFI values for the 3 groups established once positive antigens were removed. Maternal self-antigens are HLA antigens present in the mother; paternal alloantigens are HLA antigens mismatched with the mother and present in the children; neutral alloantigens are mismatched antigens not present in any of the children. The results represent the mean of MFIs and confidence intervals at 95%. The significance values (*P*) were obtained with the use of the Mann-Whitney test. (**A**) Comparative analysis of class I and class II antibodies. (**B**) Analysis based on HLA class.

Analysis of Pregnancy-Induced Anti-HLA Antibodies Using Luminex Platform-T proc 2016

Cesarean Section Is a Risk Factor That Prevents Organ Transplantation by Increasing the Development of Anti-HLA Antibodies in Women

Gökhan Akyüz | Hasan Doğan

TABLE 2 | PRA positivity analysis by birth method.

PRA (+)	Cesarean section ($n = 42$)	Normal delivery ($n = 44$)	Control group ($n = 40$)	$p =$	Post-hoc	Total delivery ($n = 86$)	Control group ($n = 40$)	$p =$
Class I (+)	7 (%16.6)	1 (%2.3)	2 (%5)	0.034*	Ces-Norm, Ces-Cont **	8 (%93)	2 (%5)	0.633
Class II (+)	11 (%26)	2 (%4.5)	1 (%2.5)	0.001*	Ces-Norm, Ces-Cont	13 (%15.1)	1 (%2.5)	0.037*
Class I+II (+)	4 (%9.5)	0 (%0)	0 (%0)	0.02*	Ces-Norm, Ces-Cont	4 (%4.6)	0 (%0)	0.306
Total (+)	14 (%32.5)	3 (%8)	3 (%7.5)	0.001*	Ces-Norm, Ces-Cont	17 (%19.8)	3 (%7.5)	0.079

Clinical Transplantation, 2024; 38:e70005.

TABLE 4 | The distribution of MFI values, the % PRA of single antibodies, and the Class I and Class II antibodies.

Pregnant no	Birth method Norm./Ces.	MFI (PRA screening)	% PRA (SAB)	CI antibodies (SAB)	CII antibodies (SAB)
1	Norm.	**CI**: 1830 **CII**: –	**CI**: 4 **CII**: –	A*31, 33, B*35	
2	Norm.	**CI**: – **CII**: 1130	**CI**: – **CII**: 1		DRB1*07
3	Norm.	**CI**: – **CII**: 12 300	**CI**: – **CII**: 27		DRB1*01, 02, 03, 08, 09, 11, 12, 13, DQB1*02
4	Ces.	**CI**: 1590 **CII**: –	**CI**: 1 **CII**: –	B*15	
5	Ces.	**CI**: 1320 **CII**: –	**CI**: 3 **CII**: –	A*03, B*35	
6	Ces.	**CI**: 2540 **CII**: –	**CI**: 13 **CII**: –	A*02, 68, 69, B*15, 45, 50, 57	
7	Ces.	**CI**: 7600 **CII**: 4100	**CI**: 6 **CII**: 26	A*23, 24, 25, 32 B*49, 57, 58	DRB1*08, 11, 13, DQA1*03, DQB1*03
8	Ces.	**CI**: 8040 **CII**: 10200	**CI**: 3 **CII**: 17	A*03, B*27, 35	DRB1*01, 04, DQA1*03, DQB1*03
9	Ces.	**CI**: 1450 **CII**: 5650	**CI**: 3 **CII**: 7	A*02, 11, 33	DRB1*07, 09, DQB1*02
10	Ces.	**CI**: 1330 **CII**: 1100	**CI**: 3 **CII**: 1	A*02, 29, 69	DQB1*06
11	Ces.	**CI**: – **CII**: 1280	**CI**: – **CII**: 6		DRB1*07, 09, DQB1*02
12	Ces.	**CI**: – **CII**: 1150	**CI**: – **CII**: 11		DRB1*04, 07, 09, DQA1*02, DQB1*02, 04
13	Ces.	**CI**: – **CII**: 2630	**CI**: – **CII**: 5		DRB1*04, DQA1*03, DQB1*03
14	Ces.	**CI**: – **CII**: 1680	**CI**: – **CII**: 29		DRB1*03, 04, 09, 10, 11, 13, 14, DQB1*05
15	Ces.	**CI**: – **CII**: 6700	**CI**: – **CII**: 46		DR*01, 02, 08, 11,12, 13, 14, DQA1*01, DQB1*05, 06
16	Ces.	**CI**: – **CII**: 4650	**CI**: – **CII**: 14		DRB1*01, 03, 07, 11, 13, 14
17	Ces.	**CI**: – **CII**: 2760	**CI**: – **CII**: 4		DRB1*07, DQA1*03, DQB1*02

1985-2006

Graft sağkalımı			
	1 yıllık (%)	3 yıllık (%)	5 yıllık (%)
Donör: Erkek (n:10)	83	78	76
Donör: Kadın (n:71)	93	90	83

Results of Kidney Transplantation Between Spouses: A Single-Center Experience

F. Karakayali, G. Moray, T. Colak, F. Boyvat, and M. Haberal

Table 1 Clinical characteristics of transplants from spousal donors and living-related donors

	SD group (n:53) median	LR group (n:116) median	P value
Recipient age (years)	49.73	31.45	<.001
Donor age (years)	44.36	56.14	<.001
Follow-up period (month)	59.18	71.12	ns
Recipients' BMI (kg/m^2)	27.12	28.96	<.001
HLA mismatches	5.06	3.08	<.001
Pre-tx dialysis period (month)	24.17	10.91	<.001
Acute rejection	0	1(0.9%)	ns
DGF	3(5.6%)	5(4.3%)	ns
Patient death (cumulative)	2(3.7%)	3(2.5%)	ns
Graft loss (cumulative)	2(3.7%)	11(9.4%)	<.001
Patient death (first 3 years)	0	0	ns
Graft loss (first 3 years)	1(1.8%)	2(1.8%)	ns

SD spousal donor, *LR* living related

Table 2 (continued)

	Donor	Kinship status	Relationship degree
50.	SA	Father	1
51.	EK	Mother	1
52.	HP	Father	1
53.	SÇ	Mother	1
54.	HG	Mother	1
55.	ÜA	Sister	2
56.	ET	Mother	1
57.	FY	Mother	1
58.	HG	Mother	1
59.	PK	Mother	1
60.	ÖI	Sister	2
61.	HC	Mother	1
62.	İG	Father	1
63.	YT	Father	1
64.	OÇ	Son	1
65.	İŞ	Father	1
66.	MH	Mother	1
67.	SÖ	Mother	1
68.	MV	Father	1
69.	ÖC	Brother	2
70.	EC	Son	1
71.	HÇ	Mother	1
72.	MA	Cousin	4

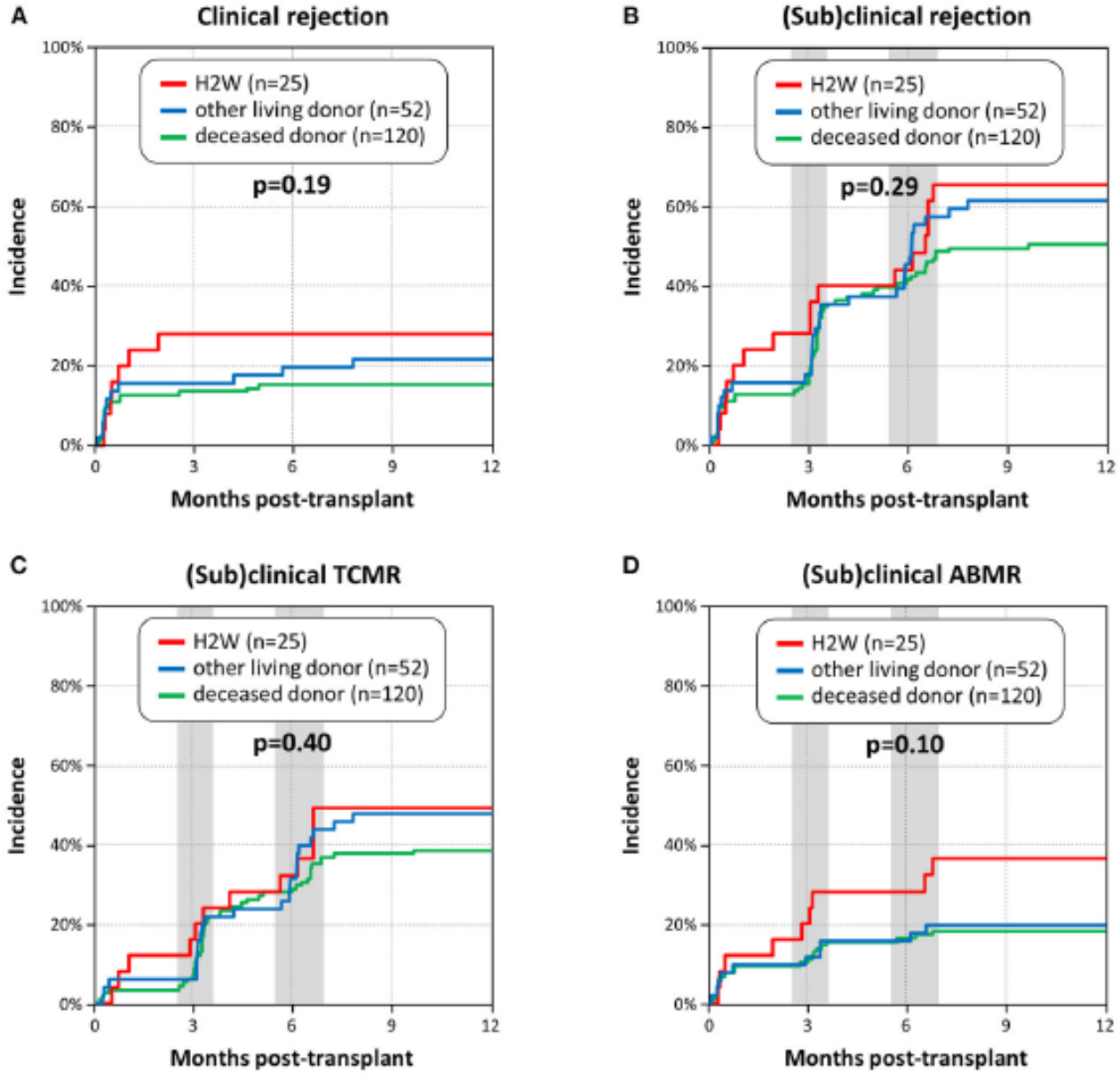


FIGURE 2 | Incidence of rejection within the first year post-transplant. **(A)** Incidence of clinical rejection. **(B)** Incidence of (sub)clinical rejection. **(C)** Incidence of (sub)clinical T cell-mediated rejection (TCMR). **(D)** Incidence of (sub)clinical antibody-mediated rejection (ABMR), including mixed rejection. The gray background areas represent the two time frames, in which surveillance biopsies at 3 and 6 months were performed.

Outcome of Husband-to-Wife Kidney Transplantation With Mutual Children: Single Center Experience Using T Cell-Depleting Induction and Review of the Literature

Table 1. **Retrospective clinical studies assessing the correlation between pregnancy and allograft outcome**

Author	No. of transplants	Outcome
Terasaki et al. (1995)	Husband-to-mother: *n* = 368 Child-to-mother: *n* = 1,411	Comparable allograft survival between spousal donor and unrelated living donor. Pregnancy is a risk factor for loss of allograft
Mahanty et al. (2001)	Offspring-to-mother: *n* = 874 Unrelated living donor to mother: *n* = 310	Fetal tolerance did not translate to a superior allograft survival from offspring donors. Multiple pregnancy trended towards poor allograft survival
Cohen et al. (2003)	Offspring-to-parent: *n* = 3,370 Unrelated living donor: *n* = 8,351 Deceased donor: *n* = 44,792	Comparable death censored 5-yr allograft survival in offspring-to-parent compared to unrelated living donor
Miles et al. (2008)	Offspring to mother: *n* = 3,124 Parent to offspring: *n* = 6,076	Comparable and poor allograft survival in offspring-to-parent and parent-to-offspring transplants
Ghafari (2008)	Offspring-to-mother: *n* = 12 Husband-to-mother: *n* = 9 Unrelated living donor: *n* = 150	Unrelated living donor allografts survival was significantly higher compared to offspring and husband donor allografts
Choi et al. (2012)	Offspring-to-mother: *n* = 49 Parent-to-offspring: *n* = 146	Comparable 5- and 10-yr kidney graft survival between offspring-to-mother and offspring-to-father transplant. Mother-to-child had worse outcome
Redfield et al. (2016)	Highly sensitized: *n* = 7,145 Non-sensitized: *n* = 100,147	Increased graft loss by 23% among women with a history of pregnancy and transfusion compared to non-sensitized
Cohen et al. (2018)	Offspring-to-mother: *n* = 1,332 Unrelated living donor: *n* = 1,435	Comparable allograft survival between offspring and unrelated living donor transplant to mother
Dagan et al. (2020)	Offspring-to-mother: *n* = 148	Offspring donor allograft survival lower compared to unrelated living donor
	Unrelated living donor: *n* = 93	Male offspring donor resulted in poorer survival compared to female offspring donor
Senn et al. (2021)	Husband-to-mother: *n* = 25 Unrelated living donor: *n* = 52 Deceased donor: *n* = 120	Poor allograft survival among mothers who received allograft from spouse compared to unrelated living donor or deceased donor


Teşekkürlerimle