



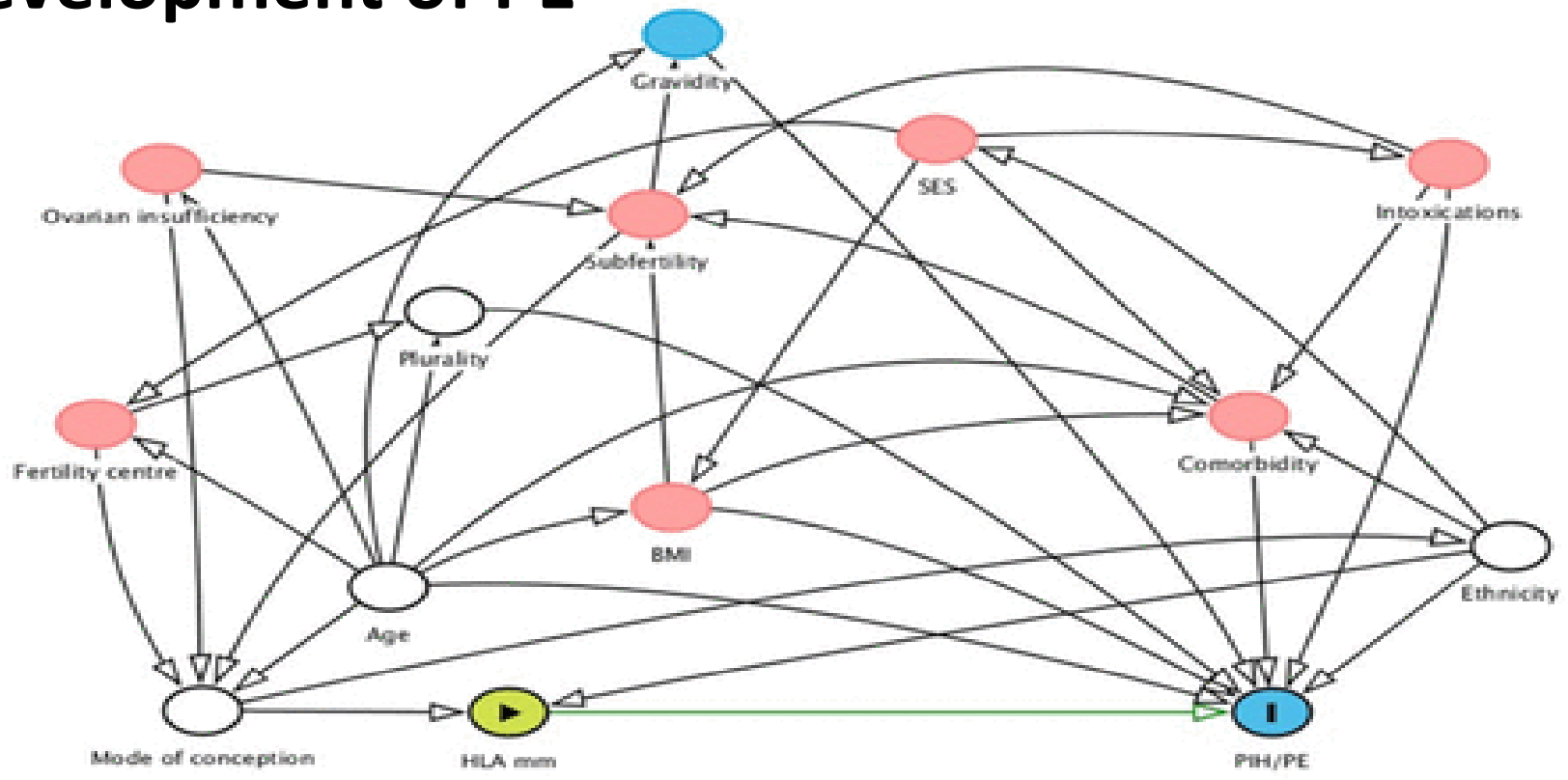
The study of polymorphism of HLA genes as a predictor of the development of hypertensive complications of pregnancy

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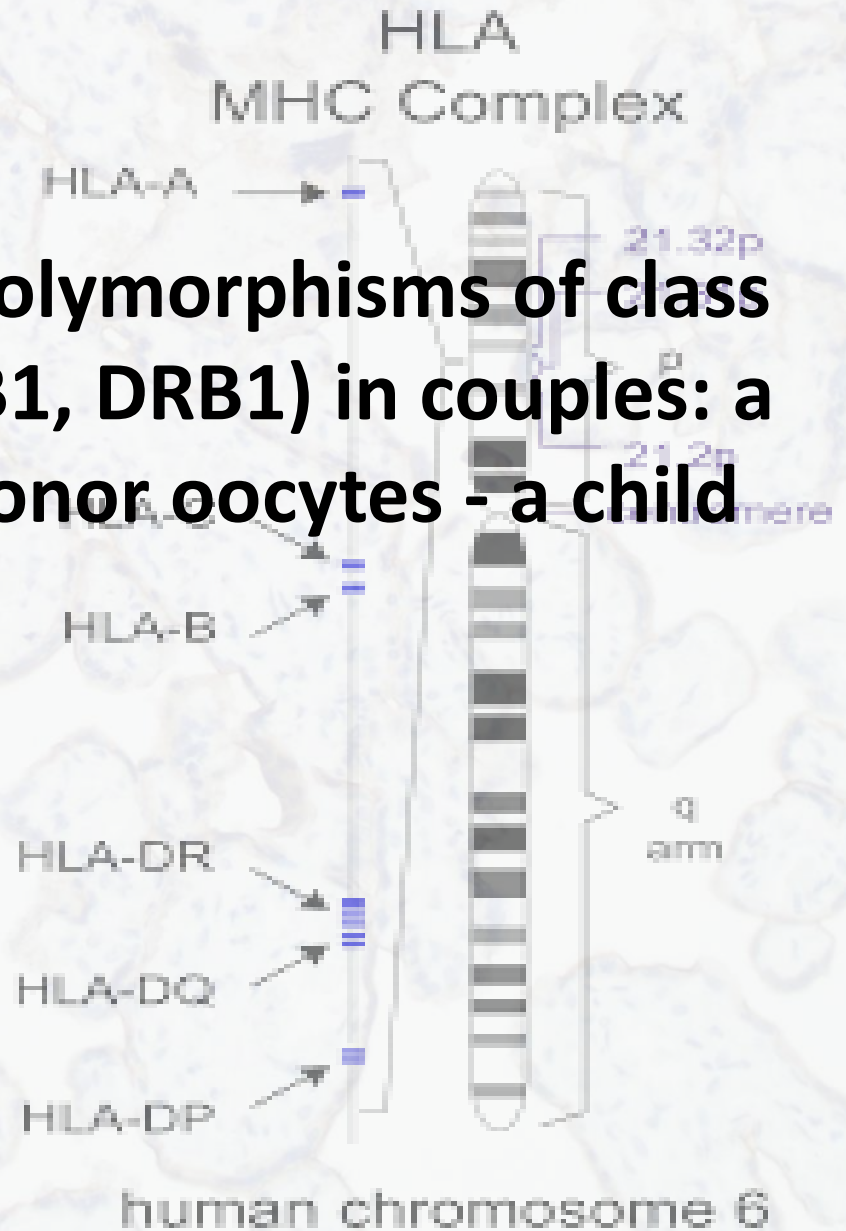
HLA polymorphism in the pathogenesis of the development of PE



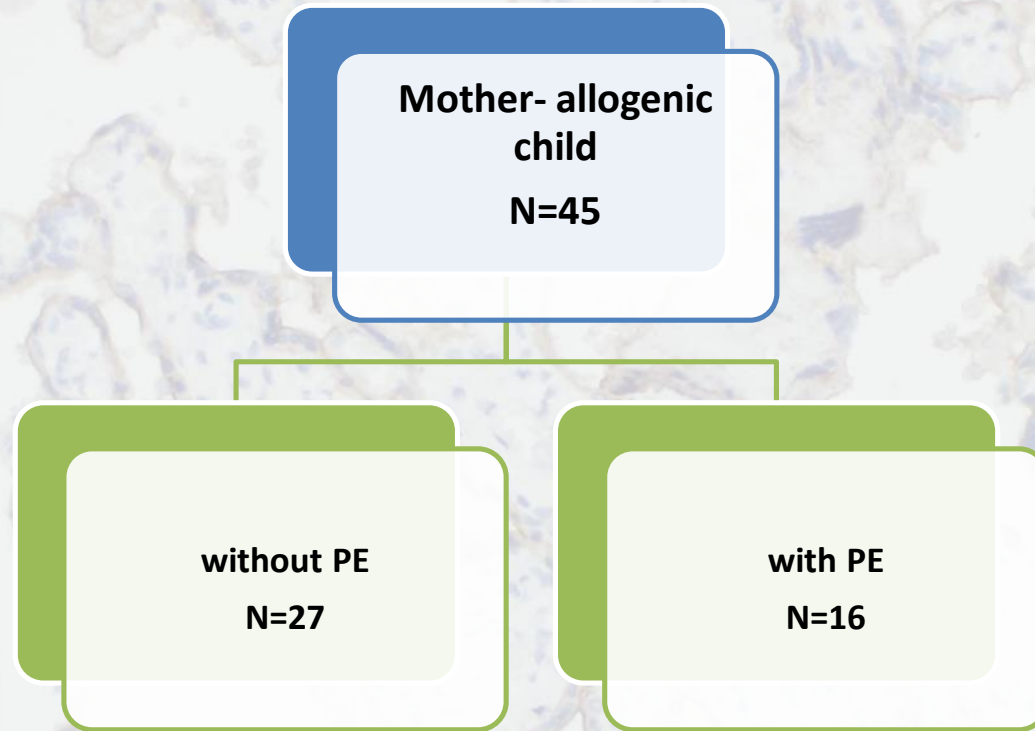
- exposure (HLA mismatches)
- outcome (PIH/PE)
- ancestor of outcome (intoxications, BMI, comorbidity (endothelial dysfunction), subfertility and gravity)
- ancestor of exposure and outcome (SES (social economic status), fertility centre, ovarian insufficiency)
- adjusted variable (mode of conception, plurality, ethnicity, age)
- causal path

Aim of study

To Investigate of allelic polymorphisms of class HLA II genes (DQA1, DQB1, DRB1) in couples: a woman after IVF using donor oocytes - a child



Design



DNA was isolated from EDTA-stabilized venous blood using the QIAamp DNA Blood Mini Kit (QIAGEN, Germany). HLA-DNA-TECH reagent kits were used for typing the genes of the main human histocompatibility complex (HLA) class II (DQA1, DQB1 and DRB1) by polymerase chain reaction (DNA technology, Russia). Typing was performed using a DT96 detection amplifier (DNA technology, Russia) according to the manufacturer's protocol

The study of gene polymorphism class HLA II (DQA1, DQB1, DRB1)

Номер	DQA1			DQB1			DRB1		
	мать	ребёнок		мать	ребёнок		мать	ребёнок	
1	*0102,*0301	*0201,*0501	0	*0302,*0602-8	*02,*0303	0	*04,*13	*03,*07	0
2	*0102,*0103	*0101,*0201	0	*0502/*0504,*0602-8	*02,*0503	0	*13,*16	*07,*14	0
3	*0102,*0501	*0301,*0301	0	*0301,*0502/*0504	*0302,*0401/*0402	0	*11,*16	*04,*04	0
4	*0201,*0501	*0101,*0102	0	*02,*0301	*0501,*0602-8	0	*07,*13	*01,*15	0
5	*0101,*0102	*0301,*0501	0	*0501,*0602-8	*02,*0301	0	*01,*15	*02,*04	0
6	*0401,*0501	*0102,*0501	1	*02,*0301	*0301,*0602-8	1	*03,*02	*11,*13	0
7	*0101,*0102	*0401,*0501	0	*0501,*0502/*0504	*02,*0301	0	*01,*16	*03,*11	0
8	*0101,*0501	*0102,*0102	0	*0301,*0501	*0602-8,*0602-8	0	*01,*11	*15,*15	0
9	*0201,*0301	*0101,*0301	1	*0302,*0303	*0301,*0301	0	*04,*07	*13,*13	0
10	*0102,*0501	*0101,*0301	0	*02,*0502/0504	*0301,*0501	0	*03,*15	*01,*04	0
11	*0401,*0501	*0102,*0103	0	*02,*0301	*0502/*0504,*0602-8	0	*03,*11	*13,*16	0
12	*0103,*0201	*0301,*0501	0	*02,*0602-8	*02,*0302	1	*07,*13	*03,*04	0
13	*0301,*0501	*0101,*0201	0	*0301,*0302	*02,*0503	0	*04,*11	*07,*14	0
14	*0201,*0401	*0401,*0501	1	*02,*0401/*0402	*0301,*0301	0	*07,*08	*11,*12	0
15	*0101,*0501	*0201,*0301	0	*0301,*0501	*02,*0302	0	*01,*11	*04,*07	0
16	*0401,*0501	*0101,*0101	0	*02,*0301	*0501,*0602-8	0	*03,*11	*01,*15	0
17	*0102,*0501	*0101,*0201	0	*0301,*0602-8	*02,*0503	0	*11,*15	*07,*14	0
18	*0101,*0301	*0102,*0501	0	*0303,*0501	*0301,*0502/*0504	0	*01,*09	*11,*16	0
19	*0102,*0103	*0101,*0501	0	*0601,*0602-8	*0302,*0501	0	*13,*15	*01,*11	0
20	*0301,*0501	*0401,*0501	1	*0301,*0302	*0301,*0401/*0402	1	*04,*12	*08,*13	0
21	*0101,*0101	*0201,*0501	0	*0501,*0501	*02,*0303	0	*01,*01	*03,*07	0
22	*0101,*0301	*0102,*0102	0	*0302,*0501	*0502/*0504,*0602-8	0	*01,*04	*13,*16	0

The number of matches in mother-child couples and their relationship with the development of PE

The number of matches	All (n=45)	N (n=27)	PE (n=18)
0	22 (48,9%)	15 (55,5%)	7 (38,9%)
1	9 (20%)	4 (14,8%)	5 (27,7%)
2	5 (11,1%)	3 (11,1%)	2 (11,1%)
>2	9 (20%)	5 (18,5%)	4 (22,2%)

The frequency of occurrence and the strength of the connection with the development of hypertensive complications of protective alleles (8 /33) in the group of mothers

allele	All, N=45		frequency %	Pearson Conjugation Ratio (C)	Normalized Pearson coefficient(C')	Criterion ϕ	Communication strength
	N	PE					
DQA1 *0102	10	5	33,3	0.163	0.231	0.215	medium
DQA1 *0501	18	8	53,3				
DQB1 *0301	14	7	46,6	0.210	0.366	0.215	medium
DQB1 *0302	4	2	13,3				
DQB1*0502/*0504	4	0	8,8				
DQB1*0601	3	0	6,6				
DRB1 *11	12	3	33,3	0.259	0.366	0.268	medium
DRB1*16	3	0	6,60				

The frequency of occurrence and the strength of the connection with the development of hypertensive complications of protective alleles(7\33) in the group of children

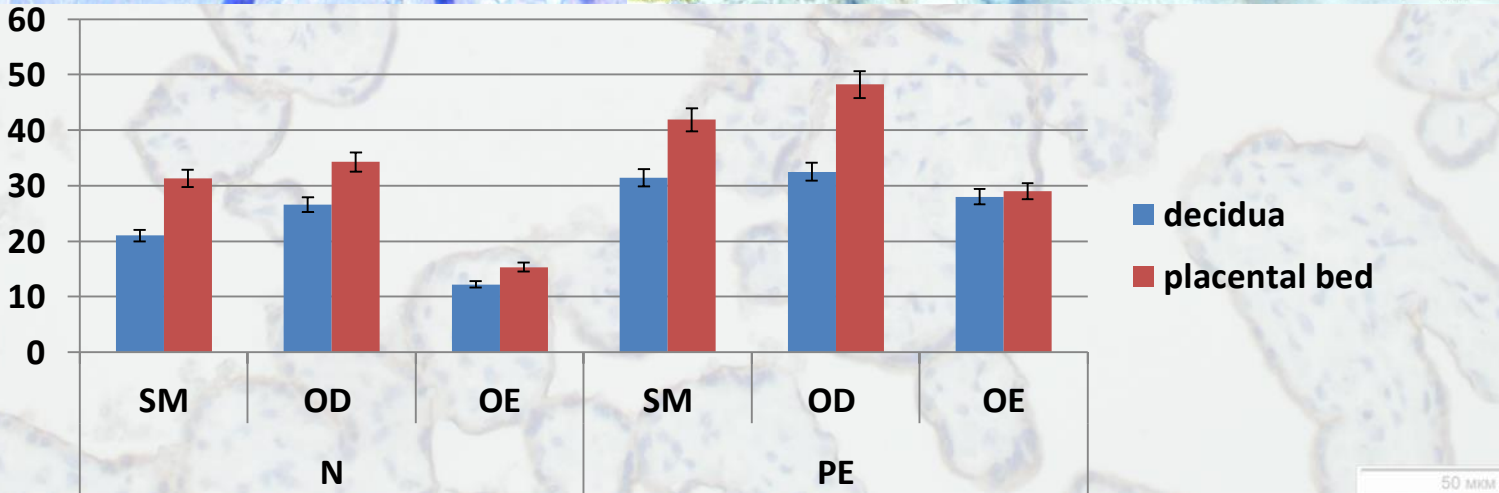
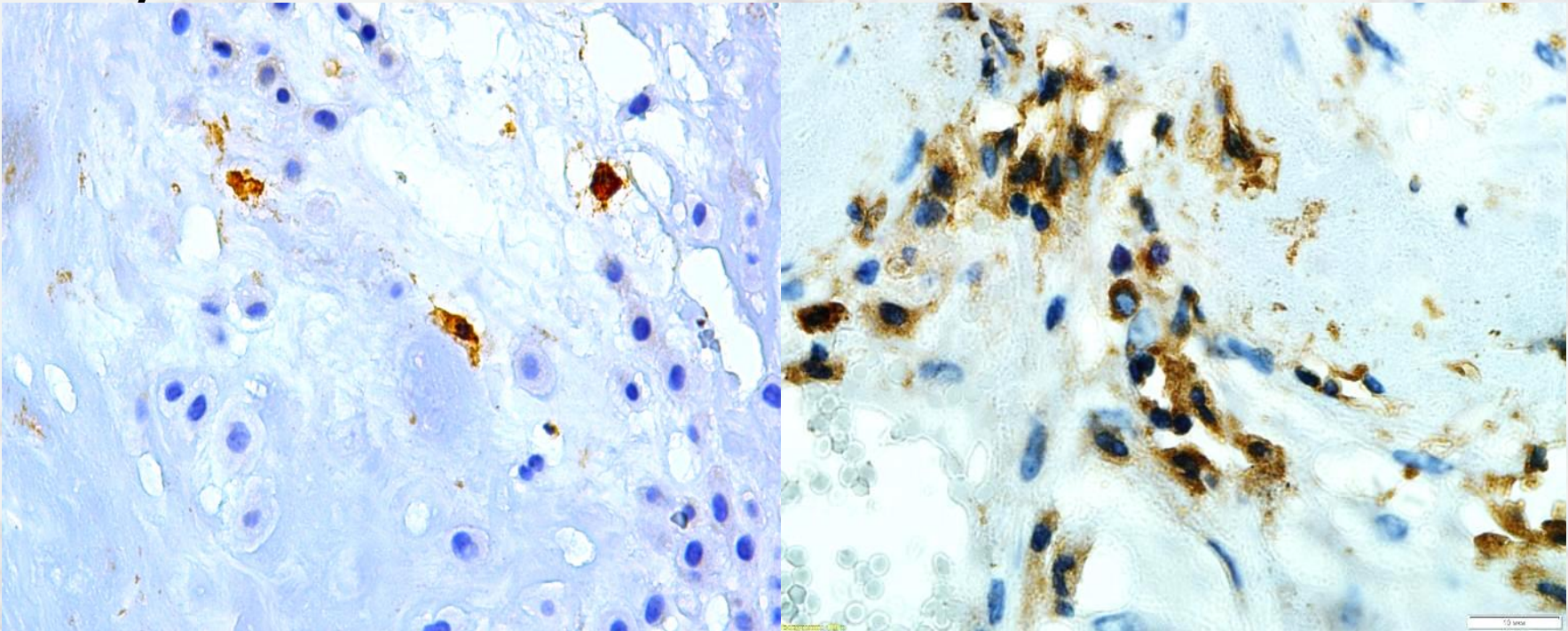
allele	All, N=45		frequency %	Pearson Conjugation Ratio (C)	Normalized Pearson coefficient(C')	Criterion ϕ	Communication strength
	N	PE					
DQB1*0601	9	2	26,6	0.163	0.231	0.215	medium
DQB1 *0401/*0402	5	0	11,1				
DQB1*0502/*0504	4	1	11,1	0.210	0.366	0.215	medium
DQB1*0503	3	0	6,6				
DRB1 *01	5	1	13,3				
DRB1*08	4	0	8,8				
DRB1 *16	4	0	8,8	0.259	0.366	0.268	medium

Protective alleles in mother-child couples and the relationship of their number with the development of PE

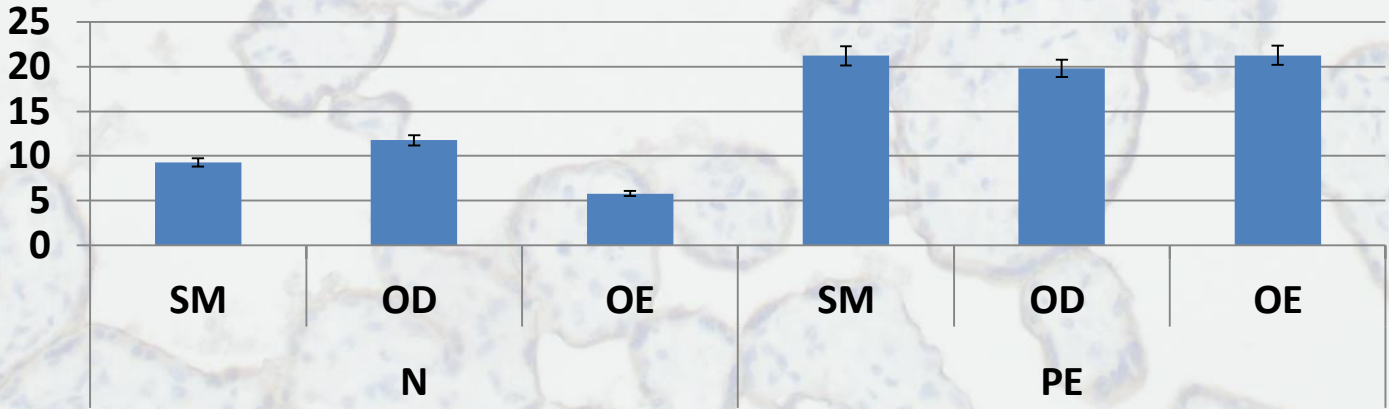
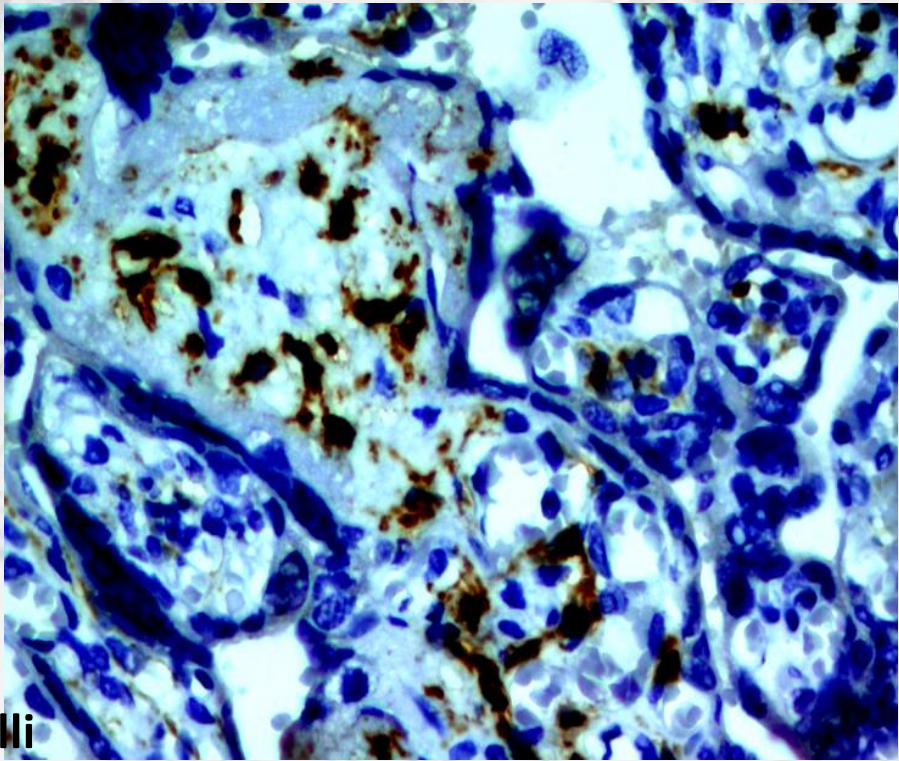
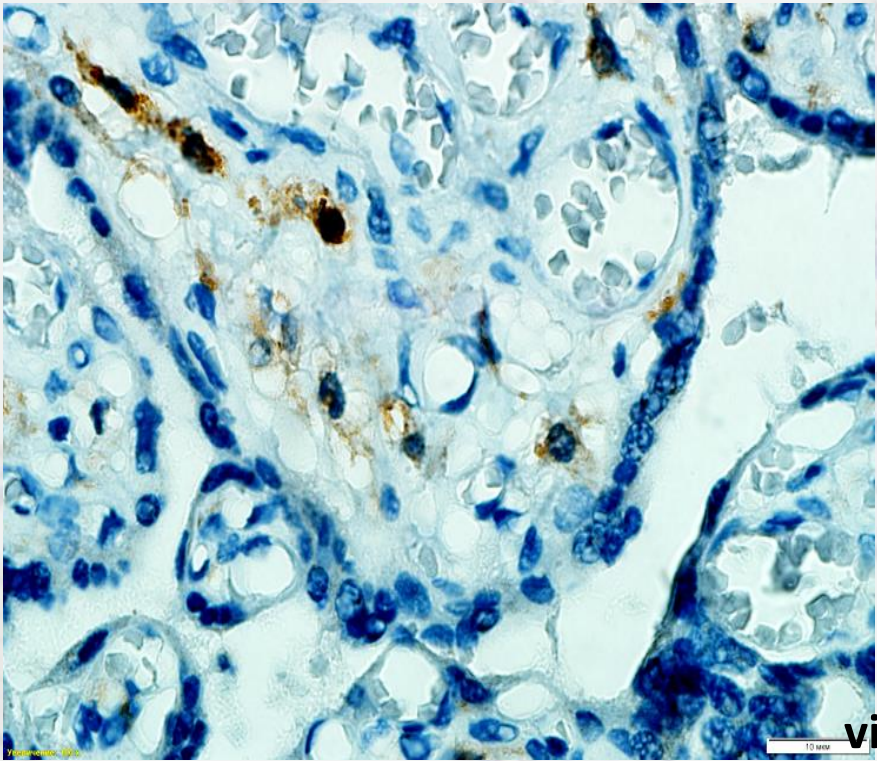
The number of protective alleles in the mother-child couples	N	PE	Chi-square test	Fisher's exact test (two-way)	Pearson Conjugation Ratio (C)	Communication strength*
The number of protective alleles 3-8	21	4	$p < 0,01$	$p < 0,05$	0.502	relatively strong
The number of protective alleles 0 - 2	5	14				

* - interpretation of the obtained values of statistical criteria according to the recommendations of Rea & Parker

HLA-DR in the basal plate and endometrial segment of the placental bed, x400 (cytoplasmic staining with enlightened nucleus)



HLA-DR in the villi, x400 (cytoplasmic staining with enlightened nucleus)



HLA polymorphism in the pathogenesis of the development of PE


decrease in protective alleles HLA II in the mother and fetus



anti-fetal antibodies increased production



violation of tolerance - trophoblast damage



increased risk of PE development

Conclusion

The series of protective alleles have been detected in the blood of the mother and fetus: DQA1 * 0501 (53.3%) in mothers, and DQB1 * 0601 (26.6%) in children. Presence of this alleles significantly lowers the risk of preeclampsia development.

Thank you for your attention!

