

***ANXA5* AND *VEGFA* GENE VARIANTS IN WOMEN WITH EARLY PREGNANCY LOSSES FROM NORTH MACEDONIA**

Terzikić M^{1, #}, Bozhinovski Gj^{1, #}, Branoski A¹, Dimkovska M¹,
Kubelka-Sabit K^{2,3}, Plaseska-Karanfilska D^{1,*}

***Corresponding Author:** Corresponding author, Prof. Dijana Plaseska-Karanfilska, MD, PhD.
Research Centre for Genetic Engineering and Biotechnology “Georgi D. Efremov”,
Macedonian Academy of Science and Arts, Skopje, North Macedonia, e-mail: dijana@manu.edu.mk

[#] equal contribution

Supplementary Table 1. The results of the haplotypes in the *ANXA5* gene in the group of women with EPLs and Control group based on history of pregnancy loss and previous live births

Haplotype	Women with one EPLs (n=81)	%	p-value	Women with two or more EPLs (n=109)	%	p-value	Controls (n=190)	%
N/N	51	62.96	0.0001	84	77.06	0.06	161	84.73
N/M1	7	8.64	0.12	8	7.34	0.18	8	4.21
M1/M1	0	0.00	/	0	0.00	/	1	0.53
N/M2	21	25.93	<0.00001	15	13.76	0.057	14	7.37
M2/M2	2	2.47	0.21	2	1.83	0.30	1	0.53
M1/M2	0	0.00	/	0	0.00	/	5	2.63
Total	81	100.00		109	100.00		190	100.00
Haplotype	Women with EPLs and no livebirth (n=151)	%	p-value	Women with EPLs and a livebirth (n=39)	%	p-value	Controls (n=190)	%
N/N	106	70.20	0.0010	29	74.36	0.09	161	84.73
N/M1	10	6.62	0.22	5	12.82	0.05	8	4.21
M1/M1	0	0.00	/	0	0.00	/	1	0.52
N/M2	31	20.53	0.0003	5	12.82	0.20	14	7.37
M2/M2	4	2.65	0.12	0	0.00	/	1	0.52
M1/M2	0	0.00	/	0	0.00	/	5	7.90
Total	151	100.00		39	100.00		190	100.00

Supplementary Table 2. The results of the haplotypes in the *ANXA5* gene in the group of women with EPLs and Control group based on maternal age and gestational week of the pregnancy

Haplotypes	Maternal age														
	≤30				31-35				≥36						
	Women with EPLs (n=85)	%	p-value	Controls (n=71)	%	Women with EPLs (n=69)	%	p-value	Controls (n=50)	%	Women with EPLs (n=36)	%	p-value	Controls (n=69)	%
N/N	61	71.76	0.007	63	88.73	51	73.91	0.08	43	86.00	23	63.89	0.1	55	79.70
N/M1	4	4.71	0.7	2	2.82	9	13.04	0.03	1	2.00	2	5.55	0.7	5	7.25
M1/M1	0	0.00	/	0	0.00	0	0.00	/	0	0.00	0	0.00	/	1	1.45
N/M2	19	22.35	0.003	4	5.63	7	10.15	0.5	4	8.00	10	27.78	0.01	6	8.70
M2/M2	1	1.18	/	0	0.00	2	2.90	0.8	1	2.00	1	2.78	/	0	0.00
M1/M2	0	0.00	/	2	2.82	0	0.00	/	1	2.00	0	0.00	/	2	2.90
Total	85	100.00		71	100.00	69	100.00		50	100.00	36	100.00		69	100.00
Haplotypes	Gestational week of the last pregnancy														
	6-9 (n=96)			10-11 (n=17)			Controls (n=190)			ND (n=67)					
	%	p-value	%	p-value	%	p-value	%	p-value	%	p-value	%	p-value			
N/N	68	70.83	0.005	17	62.96	0.01	161	84.73	50	74.63					
N/M1	7	7.29	0.2	2	7.41	0.4	8	4.21	6	8.96					
M1/M1	0	0.00	/	0	0.00	/	1	0.53	0	0.00					
N/M2	17	17.71	0.008	7	25.93	0.007	14	7.37	12	17.91					
M2/M2	3	3.12	0.1	1	3.70	0.2	1	0.53	0	0.00					
M1/M2	0	0.00	/	0	0.00	/	5	2.63	0	0.00					
Total	96	100.00		27	100.00		190	100.00	67	100.00					

Supplementary Table 3. The genotypic frequency of the examined *VEGFA* variants in the group of women with EPLs and Control groups regarding the history of pregnancy losses and previous live births

c.-1154G>A	Women with one EPL (n=81)	%	p-value	Women with two or more EPLs (n=109)	%	p-value	Controls (n=190)	%
GG	39	48.15	0.55	53	48.62	0.56	99	52.11
GA	36	44.44	0.24	40	36.70	1	70	36.84
AA	6	7.41	0.25	16	14.68	0.23	21	11.05
Total	81	100.00		109	100.00		190	100.00
c.*237C>T								
CC	63	77.77	0.32	74	67.89	0.24	141	74.21
CT	17	21.00	0.34	33	30.28	0.25	46	24.21
TT	1	1.23	0.76	2	1.83	0.60	3	1.58
Total	81	100.00		109	100.00		190	100.00
c.-1154G>A	Women with EPLs and no livebirth (n=151)	%	p-value	Women with EPLs and a livebirth (n=39)	%	p-value	Controls (n=190)	%
GG	78	51.66	0.93	14	35.90	0.05	99	52.11
GA	55	36.42	1	21	53.85	0.04	70	36.84
AA	18	11.92	0.80	4	10.25	0.65	21	11.05
Total	151	100.00		39	100.00		190	100.00
c.*237C>T								
CC	108	71.52	0.58	29	74.36	0.45	141	74.21
CT	41	27.15	0.54	9	23.08	0.63	46	24.21
TT	2	1.32	0.73	1	2.56	0.53	3	1.58
Total	151	100.00		39	100.00		190	100.00

Supplementary Table 4. The results of the genotypes in the *VEGFA* gene in the group of women with EPLs and Control group based on maternal age and gestational week of the pregnancy

c.-1154G>A	Maternal age														
	≤30				31-35				≥36						
	Women with EPLs (n=85)	%	p-value	Controls (n=71)	%	Women with EPLs (n=69)	%	p-value	Controls (n=50)	%	Women with EPLs (n=36)	%	p-value	Controls (n=69)	%
GG	40	47.06	0.53	37	52.11	35	50.72	0.43	29	58	17	47.22	1	33	47.83
GA	33	38.82	0.78	26	36.62	26	37.68	0.38	15	30	17	47.22	0.61	29	42.03
AA	12	14.12	0.4	8	11.27	8	11.59	1	6	12	2	5.56	0.4	7	10.14
Total	85	100.0		71	100.0	69	100.0		50	100.0	36	100.0		69	100.0
c.*237C>T															
CC	65	76.47	1	54	76.06	48	69.55	1	35	70	24	66.67	0.3	52	75.36
CT	18	21.18	0.68	17	23.94	20	28.90	1	14	28	12	33.33	0.2	15	21.74
TT	2	2.35	/	0	0.00	1	1.45	0.82	1	2	0	0.00	/	2	2.90
Total	85	100.0		71	100.0	69	100.0		50	100.0	36	100.0		69	100.0
Gestational week of the last pregnancy															
c.-1154G>A	6-9 (n=96)	%	p-value	10-11 (n=17)	%	p-value	Controls (n=190)	%	ND (n=67)	%					
GG	47	48.96	0.6	10	37.04	0.15	99	52.11	35	52.24					
GA	33	34.37	0.7	16	59.26	0.03	70	36.84	27	40.30					
AA	16	16.67	0.2	1	3.70	0.3	21	11.05	5	7.46					
Total	96	100.00		27	100.00		190	100.00	67	100.00					
c.*237C>T															
CC	68	70.83	0.5	25	92.59	0.03	141	74.21	44	65.67					
CT	26	27.08	0.6	2	7.41	0.05	46	24.21	22	32.83					
TT	2	2.08	0.7	0	0.00	/	3	1.58	1	1.50					
Total	96			27			190	100.00	67	100.00					