Association of *IL-17A* rs2275913, *IL-17RC* rs708567 and *TGFB1* rs1800469 SNPs with systemic lupus erythematosus in Bulgarian patients

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INTRODUCTION

Background. Systemic lupus erythematosus (SLE) is a multifactorial autoimmune disease resulting from gene-environment interactions. Polymorphisms in the cytokine genes and their receptors are thought to influence the development of SLE.

Objective. The aim of this case-control study was to investigate the association between the *IL-17A* rs2275913, *IL-17RC* rs708567 and *TGFB1* rs1800469 polymorphisms and the susceptibility to SLE in Bulgarian patients as well as their influence on the IL-17A serum levels.

METHODOLOGY

Altogether 152 subjects (57 SLE patients and 95 unrelated healthy controls) were genotyped by TaqMan assay for:

- *TGFB1* rs1800469 A/G
- *IL-17A* rs2275913 G/A
- *IL-17RC* rs708567 C/T

Serum levels were determined using Human IL-17A Platinum ELISA kit Affymetrix eBiosceince™

Demographic	Parameters	SLE
Gender	Male//Female	10/47
Age	Mean ±SD years	40±12.4

RESULTS

SNP	Genotype/ Allele		Subjects (%) SLE (57)	Subjects (%) Controls (95)	OR	95% CI	p-value
rs1800469 *TGF-β*	Genotype	AA	14 (24.6)	14 (14.7)	1.9	0.8 – 4.3	0.09
		AG	28 (49.1)	45 (47.4)	1.1	0.6 – 2.1	0.5
		GG	15 (26.3)	36 (37.9)	0.6	0.3-1.2	0.09
	Allele	**A**	56 (49.1)	73 (38.4)	1.5	1– 2.5	**0.04**
		G	58 (50.9)	117 (61.6)	0.6	0.4 – 1	
rs2275913 *IL-17A*	Genotype	GG	25 (43.9)	43 (45.3)	0.9	0.5 – 1.8	0.5
		GA	28 (49.1)	45 (47.3)	1.1	0.6 – 2.1	0.5
		AA	4 (7.0)	7 (7.4)	0.9	0.3-3.4	0.6
	Allele	G	78 (68.4)	131 (68.9)	1	0.6 – 1.6	0.5
		A	36 (31.6)	59 (31.1)	1	0.6 – 1.7	
rs708567 *IL-17RC*	Genotype	CC	17 (29.8)	21 (22.1)	1.5	0.7 – 3.2	0.2
		CT	22 (38.6)	43 (45.3)	0.8	0.4 – 1.5	0.3
		TT	18 (31.6)	31 (32.6)	1	0.5-1.9	0.5
	Allele	C	57 (50.0)	85 (44.7)	1.2	0.8 – 2	0.2
		T	57 (50.0)	105 (55.3)	0.8	0.5 – 1.3	

Clinical parameters	IL17 GG (n=25)	IL17 GA (n=28)	IL17 AA (n=4)	p	IL17R CC (n=17)	IL17R CT (n=22)	IL17R TT (n=18)	p	*TGF-β* AA (n=14)	*TGF-β* AG (n=28)	*TGF-β* GG (n=15)	p
Malar rash	16 (64.0%)	14 (50.0%)	3 (75.0%)	0.3	11 (64.7%)	12 (57.1%)	11 (61.1%)	0.4	8 (57.1%)	15 (53.6%)	9 (60.0%)	0.6
Discoid rash	4 (16.0%)	7 (25.0%)	0 (0.0%)	0.4	3 (17.7%)	5 (23.8%)	3 (16.7%)	0.6	4 (28.6%)	14 (50.0%)	2 (13.3%)	0.4
Arthritis	16 (64.0%)	18 (64.3%)	3 (75.0%)	0.6	**15 (88.2%)**	11 (50.0%)	11 (61.1%)	**0.03**	8 (57.1%)	17 (60.7%)	10 (66.7%)	0.5
Oral ulcer	3 (12.0%)	1 (3.6%)	0 (0.0%)	0.2	2 (11.7%)	2 (9.1%)	0 (0.0%)	0.3	2 (14.3%)	0 (0.0%)	2 (13.3%)	0.3
Photosensitivity	17 (68.0%)	16 (57.1%)	3 (75.0%)	0.3	8 (32.0%)	15 (34.9%)	13 (54.2%)	0.09	11 (78.6%)	15 (53.6%)	10 (66.7%)	0.1
Serositis	4 (16.0%)	6 (21.4%)	1 (25.0%)	0.4	5 (29.4%)	2 (9.1%)	4 (22.2%)	0.2	3 (21.4%)	5 (17.9%)	3 (20.0%)	0.5
Renal disease	25 (100.0%)	28 (100.0%)	4 (100.0%)	1	17 (100.0%)	22 (100.0%)	18 (100.0%)	1	14 (100.0%)	28 (100.0%)	15 (100.0%)	1
Neurological disease	**9 (36.0%)**	3 (10.4%)	0 (0.0%)	**0.02**	4 (23.5%)	4 (18.2%)	4 (22.2%)	0.4	**6 (42.9%)**	4 (14.3%)	2 (13.3%)	**0.02**
Haematological disease	6 (24.0%)	11 (39.3%)	3 (75.0%)	0.1	8 (47.1%)	6 (27.3%)	6 (33.3%)	0.2	4 (28.6%)	10 (35.7%)	6 (40.0%)	0.6
Immunological disease	15 (60.0%)	16 (57.1%)	2 (50.0%)	0.5	10 (58.8%)	15 (68.2%)	8 (44.4%)	0.6	7 (50.0%)	15 (53.6%)	11 (73.3%)	0.4
ANA	17 (68.0%)	19 (67.9%)	3 (75.0%)	0.6	12 (70.6%)	15 (68.2%)	12 (66.7%)	0.5	10 (71.4%)	17 (60.7%)	12 (8.0%)	0.5

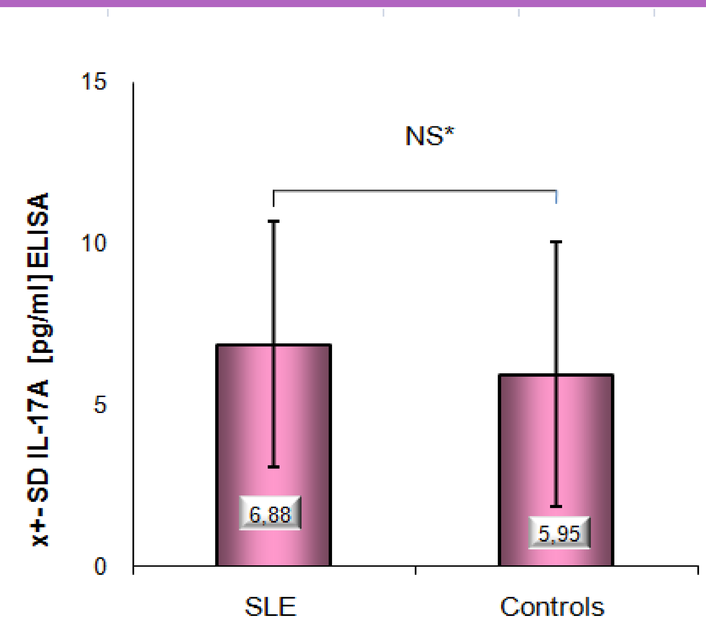

Fig. 1 IL-17A serum levels in SLE and controls determined by Human IL-17A Platinum ELISA kit Affymetrix eBiosceince™ *NS – nonsignificant

Conclusion. Our results indicate that *IL-17A* rs2275913, *IL-17RC* rs708567 and *TGFB1* rs1800469 polymorphisms might play a role in the susceptibility and the development of SLE and IL-17A serum levels should be monitored in the course of the disease.

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