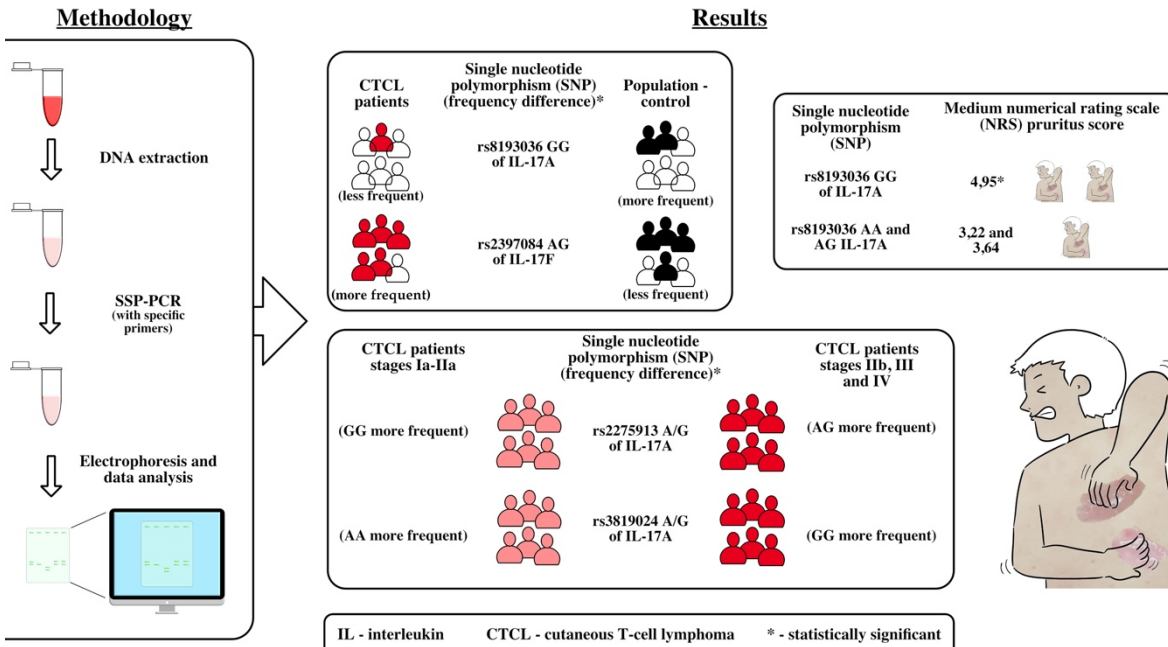


APPENDIX S1

Graphic abstract presenting methods and most important results

Interleukin-17 genes polymorphisms are significantly associated with cutaneous T-cell lymphoma susceptibility



Legend:

Asterix (*) – Statistically significant

IL – Interleukin

CTCL – Cutaneous T-cell lymphoma

SSP-PCR – polymerase chain reaction with specific primers

SNP – single nucleotide polymorphism

Red text – indicates statistical significance

Group	IL-17a/rs2275913	IL-17a/rs2275913	IL-17a/rs2275913	Overall
	GA	GG	AA	
Lymphoma	46	97	7	150
	30,67%	64,67%	4,67%	
Control	62	119	15	196
	31,63%	60,71%	7,65%	
Overall	108	216	22	346

P=0,49

GG p=0,45; GA p=0,85; AA p=0,26

ALLELE	G	A	p
Lymphoma	240	60	0,27
Control	300	92	

Group	IL17a/rs3819024 AA	IL17a/rs3819024 AG	IL17a/rs3819024 GG	Overall
Lymphoma	75	52	23	150
	50,00%	34,67%	15,33%	
control	88	85	23	196
	44,90%	43,37%	11,73%	
Overall	163	137	46	346

P=0,23

GG p=0,33; AG p=0,10; AA p=0,35

ALLELE	G	A	p
Lymphoma	98	202	0,84
Control	131	261	

Group	IL17a/rs8193036 AA	IL17a/rs8193036 GA	IL17a/rs8193036 GG	Overall
Lymphoma	45	84	21	150
	30,00%	56,00%	14,00%	
Control	45	98	53	196
	22,96%	50,00%	27,04%	
Overall	90	182	74	346

P=0,011

GG p=0,003; GA p=0,27; AA p=0,14

Odds ratio GG	0.4392
95 % CI:	0.2512 to 0.7679
Significance level	P = 0.0039

ALLELE	G	A	p
Lymphoma	126	174	0,81
Control	204	272	

Group	IL17F/rs763780 AG	IL17F/rs763780 GG	IL17F/rs763780 AA	Overall
Lymphoma	112	7	31	150
	74,67%	4,67%	20,67%	
Control	136	16	44	196
	69,39%	8,16%	22,45%	
Overall	248	23	75	346

P=0,36

GG p=0,20; AG p=0,28; AA p=0,69

ALLELE	G	A	p
Lymphoma	126	174	0,82
Control	168	224	

Group	IL17F/rs2397084 AG	IL17F/rs2397084 GG	Overall
Lymphoma	133	17	150
	88,67%	11,33%	
Control	146	50	196
	74,49%	25,51%	
Overall	279	67	346

P=0.0009

Odds ratio	2.6793
95 % CI:	1.4729 to 4.8739
Significance level	P = 0.0012

ALLELE	G	A	p
Lymphoma	167	133	0,60
Control	246	146	

Stadium VS Genotype

Early (1a-2a) vs Advanced (2a and higher)

Group	IL-17a/rs2275913 GA	IL-17a/rs2275913 GG	IL-17a/rs2275913 AA	Overall
Advanced (2a and higher)	24	31	6	61
	39,34%	50,82%	9,84%	
Early (1a-2a)	20	64	1	85
	23,53%	75,29%	1,18%	
Overall	44	95	7	146

P=0,003

GG p=0,002; GA p=0,04; AA p=0,043

Odds ratio GG	0.3391
95 % CI:	0.1678 to 0.6852
Significance level	P = 0.0026

Odds ratio GA	2.1081
95 % CI:	1.0285 to 4.3210
Significance level	P = 0.0417

Odds ratio AA	9.1636
95 % CI:	1.0737 to 78.2109
Significance level	P = 0.0429

ALLELE	G	A	p
Advanced (2a and higher)	86	36	0,0005
Early (1a-2a)	148	22	

Odds ratio	0.3551
95 % CI:	0.1962 to 0.6427
Significance level	P = 0.0006

Group	IL17a/rs3819024 AA	IL17a/rs3819024 AG	IL17a/rs3819024 GG	Overall
Advanced (2a and higher)	23	22	16	61
	37,70%	36,07%	26,23%	
Early (1a-2a)	49	30	6	85
	57,65%	35,29%	7,06%	
Overall	72	52	22	146

P=0,003

GG p=0,001; AG p ns; AA p=0,017

Odds ratio GG	4.6815
95 % CI:	1.7099 to 12.8170
Significance level	P = 0.0027

Odds ratio AA	0.4447
95 % CI:	0.2268 to 0.8718
Significance level	P = 0.0183

ALLELE	G	A	P
Advanced (2a and higher)	54	68	0,0005
Early (1a-2a)	42	128	

Odds ratio	2.4202
95 % CI:	1.4692 to 3.9866
Significance level	P = 0.0005

Group	IL17a/rs8193036 AA	IL17a/rs8193036 GA	IL17a/rs8193036 GG	Overall
Advanced (2a and higher)	23	30	8	61
	37,70%	49,18%	13,11%	
Early (1a-2a)	21	52	12	85
	24,71%	61,18%	14,12%	
Overall	44	82	20	146

P=0,23

GG p ns; GA p ns; AA p ns

ALLELE	G	A	p
Advanced (2a and higher)	46	76	0,23
Early (1a-2a)	76	94	

Group	IL17F/rs763780 AG	IL17F/rs763780 GG	IL17F/rs763780 AA	Overall
Advanced (2a and higher)	43	5	13	61
	70,49%	8,20%	21,31%	
Early (1a-2a)	66	2	17	85
	77,65%	2,35%	20,00%	
Overall	109	7	30	146

P=0,25

GG p ns; AG p ns; AA p ns

ALLELE	G	A	p
Advanced (2a and higher)	53	69	0,70
Early (1a-2a)	70	100	

Group	IL17F/rs2397084 AG	IL17F/rs2397084 GG	Overall
0	55	6	61
	90,16%	9,84%	
1	74	11	85
	87,06%	12,94%	
Overall	129	17	146

P=0,56

ALLELE	G	A	p
Advanced (2a and higher)	67	55	0,79
Early (1a-2a)	96	74	

SS vs other stages

ss vs other stages	IL-17a/rs2275913 GA	IL-17a/rs2275913 GG	IL-17a/rs2275913 AA	Overall
other stages	39	91	5	135
	28,89%	67,41%	3,70%	
ss	5	4	2	11
	45,45%	36,36%	18,18%	
Overall	44	95	7	146

P=0,032

GG p=0,04; GA p ns; AA p=0,05

Odds ratio GG	0.2763
95 % CI:	0.0768 to 0.9939
Significance level	P = 0.0489

Odds ratio AA	5.7778
95 % CI:	0.9806 to 34.0415
Significance level	P = 0.0526

ALLELE	G	A	p
other stages	221	49	0,01
ss	13	9	

Odds ratio	3.1224
95 % CI:	1.2638 to 7.7147
Significance level	P = 0.0136

ss vs other stages	IL17a/rs3819024 AA	IL17a/rs3819024 AG	IL17a/rs3819024 GG	Overall
other stages	68	49	18	135
	50,37%	36,30%	13,33%	
ss	4	3	4	11
	36,36%	27,27%	36,36%	

Overall	72	52	22	146
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P=0,12

GG p=0,05; AG p ns; AA p ns

Odds ratio	3.7143
95 % CI:	0.9873 to 13.9729
Significance level	P = 0.0522

ALLELE	G	A	p
other stages	85	185	0,08
ss	11	11	

ss vs other stages	IL17a/rs8193036	IL17a/rs8193036	IL17a/rs8193036	Overall
	AA	GA	GG	
other stages	40	76	19	135
	29,63%	56,30%	14,07%	
ss	4	6	1	11
	36,36%	54,55%	9,09%	
Overall	44	82	20	146

P=0,84

GG p ns; GAp ns; AA p ns

ALLELE	G	A	p
other stages	114	156	0,59
ss	8	14	

ss vs other stages	IL17F/rs763780	IL17F/rs763780	IL17F/rs763780	Overall
	AG	GG	AA	
other stages	102	6	27	135
	75,56%	4,44%	20,00%	
ss	7	1	3	11
	63,64%	9,09%	27,27%	
Overall	109	7	30	146

P=0,63

GG p ns; AG p ns; AA p ns

ALLELE	G	A	p
other stages	114	156	0,90
ss	9	13	

ss vs other stages	IL17F/rs2397084 AG	IL17F/rs2397084 GG	Overall
other stages	119	16	135
	88,15%	11,85%	
ss	10	1	11
	90,91%	9,09%	
Overall	129	17	146

P=0,78

GG p ns; AG p ns; AA p ns

ALLELE	G	A	p
other stages	151	119	0,90
ss	12	10	

Early (1a, 1b) vs advanced

Early (1a, 1b) vs advanced	IL-17a/rs2275913 GA	IL-17a/rs2275913 GG	IL-17a/rs2275913 AA	Overall
Advanced	25	33	6	64
	39,06%	51,56%	9,38%	
Early (1a, 1b)	19	62	1	82
	23,17%	75,61%	1,22%	
Overall	44	95	7	146

P=0,004

GG p=0,002; GA p=0,04; AA p=0,05

Odds ratio GG	0.3434
95 % CI:	0.1700 to 0.6937
Significance level	P = 0.0029

Odds ratio GA	2.1255
95 % CI:	1.0368 to 4.3574
Significance level	P = 0.0395

Odds ratio AA	8.3793
95 % CI:	0.9822 to 71.4847
Significance level	P = 0.0519

ALLELE	G	A	P
Advanced	91	37	0,0006
Early (1a, 1b)	143	21	

Odds ratio	0.3612
95 % CI:	0.1989 to 0.6558
Significance level	P = 0.0008

Early (1a, 1b) vs advanced	IL17a/rs3819024			Overall
	AA	AG	GG	
Advanced	23	25	16	64
	35,94%	39,06%	25,00%	
Early (1a, 1b)	49	27	6	82
	59,76%	32,93%	7,32%	
Overall	72	52	22	146

P=0,0025

GG p=0,003; AG p ns; AA p=0,004

Odds ratio GG	4.2222
95 % CI:	1.5448 to 11.5400
Significance level	P = 0.0050

Odds ratio AA	0.3778
95 % CI:	0.1924 to 0.7420
Significance level	P = 0.0047

ALLELE	G	A	p
Advanced	57	71	0,0002
Early (1a, 1b)	39	125	

Odds ratio	2.5731
95 % CI:	1.5595 to 4.2455
Significance level	P = 0.0002

Early (1a, 1b) vs advanced	IL17a/rs8193036 AA	IL17a/rs8193036 GA	IL17a/rs8193036 GG	Overall
Advanced	23	33	8	64
	35,94%	51,56%	12,50%	
Early (1a, 1b)	21	49	12	82
	25,61%	59,76%	14,63%	
Overall	44	82	20	146

P=0,40

GG p ns; GA p ns; AA p ns

ALLELE	G	A	p
Advanced	49	79	0,28
Early (1a, 1b)	73	91	

Early (1a, 1b) vs advanced	IL17F/rs763780 AG	IL17F/rs763780 GG	IL17F/rs763780 AA	Overall
Advanced	46	5	13	64
	71,88%	7,81%	20,31%	
Early (1a, 1b)	63	2	17	82
	76,83%	2,44%	20,73%	
Overall	109	7	30	146

P=0,32

GG p ns; AG p ns; AA p ns

ALLELE	G	A	p
Advanced	56	72	0,62

Early (1a, 1b)	67	97	
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Early (1a, 1b) vs advanced	IL17F/rs2397084		Overall
	AG	GG	
Advanced	58	6	64
	90,63%	9,38%	
Early (1a, 1b)	71	11	82
	86,59%	13,41%	
Overall	129	17	146

P=0,45

GG p ns; AG p ns

ALLELE	G	A	P
Advanced	70	58	0,73
Early (1a, 1b)	93	71	

Medium VAS scale score of patients according to different genotypes

IL-17a/rs2275913	VAS Medium	VAS Valid	VAS Stand.Dev	VAS Minimum	VAS Maximum	VAS Q25	VAS Median	VAS Q75
GA	3,832051	39	3,264089	0,000000	10,00000	1,400000	2,800000	6,600000
GG	3,273494	83	3,170100	0,000000	10,00000	0,000000	2,500000	5,500000
AA	4,240000	5	2,540276	1,000000	7,50000	3,300000	3,400000	6,000000
Overall	3,483071	127	3,169793	0,000000	10,00000	0,000000	3,000000	6,000000

P=0,31

IL17a/rs3819024	VAS Medium	VAS Valid	VAS Stand.Dev	VAS Minimum	VAS Maximum	VAS Q25	VAS Median	VAS Q75
AA	3,545238	63	3,093707	0,00	10,00000	0,400000	3,000000	5,500000
AG	2,936364	44	2,901090	0,00	10,00000	0,100000	2,000000	5,150000
GG	4,490000	20	3,818363	0,00	10,00000	0,000000	4,700000	7,750000
Overall	3,483071	127	3,169793	0,00	10,00000	0,000000	3,000000	6,000000

P=0,53

IL17a/rs8193036	VAS Medium	VAS Valid	VAS Stand.Dev	VAS Minimum	VAS Maximum	VAS Q25	VAS Median	VAS Q75
AA	3,266667	42	3,257387	0,000000	10,00000	0,000000	2,200000	6,000000
GA	3,346324	68	3,202323	0,000000	10,00000	0,000000	2,650000	5,450000
GG	4,564706	17	2,747258	1,000000	9,50000	2,300000	3,900000	6,100000
Overall	3,483071	127	3,169793	0,000000	10,00000	0,000000	3,000000	6,000000

P=0.74

IL17F/rs763780	VAS Medium	VAS Valid	VAS Stand.Dev	VAS Minimum	VAS Maximum	VAS Q25	VAS Median	VAS Q75
AG	3,380319	94	3,198380	0,00	10,00000	0,000000	2,600000	5,700000
GG	2,300000	6	2,093800	0,00	6,10000	1,400000	1,650000	3,000000
AA	4,103704	27	3,239953	0,00	10,00000	1,000000	4,200000	6,000000
Overall	3,483071	127	3,169793	0,00	10,00000	0,000000	3,000000	6,000000

P=0,22

IL17F/rs2397084	VAS Medium	VAS Valid	VAS Stand.Dev	VAS Minimum	VAS Maximum	VAS Q25	VAS Median	VAS Q75
AG	3,309292	113	3,102106	0,000000	10,00000	0,000000	2,400000	5,700000
GG	4,885714	14	3,478032	1,000000	10,00000	1,500000	3,850000	9,500000
Overall	3,483071	127	3,169793	0,000000	10,00000	0,000000	3,000000	6,000000

P=0,43

VAS pruritus level differences not statistically significant for other genotypes except IL17F/rs2397084

(p=0,01)

	VAS mild pruritus (1-3)	VAS moderate pruritus (4-6)	VAS very severe pruritus (10)	VAS severe pruritus (7-9)	Overall
AG	61	33	6	13	113
	53,98%	29,20%	5,31%	11,50%	
GG	6	4	4	0	14
	42,86%	28,57%	28,57%	0,00%	
Overall	67	37	10	13	127

Medium NRS scale score of patients according to genotypes

IL-17a/rs2275913	NRS Medium	NRS Valid	NRS Stand.Dev	NRS Minimum	NRS Maximum	NRS Q25	NRS Median	NRS Q75
GA	4,040476	42	3,265568	0,00	10,00000	2,000000	3,000000	7,000000
GG	3,497802	91	3,177245	0,00	10,00000	0,000000	3,000000	5,000000
AA	4,000000	7	2,886751	0,00	8,00000	1,000000	4,000000	6,000000
Overall	3,685714	140	3,179240	0,00	10,00000	1,000000	3,000000	6,000000

P=0,81

IL17a/rs3819024	NRS Medium	NRS Valid	NRS Stand.Dev	NRS Minimum	NRS Maximum	NRS Q25	NRS Median	NRS Q75
AA	3,750725	69	3,150519	0,00	10,00000	1,000000	3,300000	6,000000
AG	3,354000	50	3,085265	0,00	10,00000	1,000000	2,500000	5,000000
GG	4,261905	21	3,541253	0,00	10,00000	0,000000	4,000000	7,500000
Overall	3,685714	140	3,179240	0,00	10,00000	1,000000	3,000000	6,000000

P=0,45

IL17a/rs8193036	NRS Medium	NRS Valid	NRS Stand.Dev	NRS Minimum	NRS Maximum	NRS Q25	NRS Median	NRS Q75
AA	3,222727	44	3,203041	0,000000	10,00000	0,000000	2,500000	5,000000
GA	3,638961	77	3,251524	0,000000	10,00000	0,000000	3,000000	6,000000
GG	4,947368	19	2,586797	1,000000	9,00000	3,000000	5,000000	8,000000
Overall	3,685714	140	3,179240	0,000000	10,00000	1,000000	3,000000	6,000000

P=0,26

GG=0,03

IL17F/rs763780	NRS Medium	NRS Valid	NRS Stand.Dev	NRS Minimum	NRS Maximum	NRS Q25	NRS Median	NRS Q75
AG	3,639423	104	3,233634	0,00	10,00000	0,000000	3,000000	6,250000
GG	2,857143	7	2,794553	0,00	8,00000	1,000000	2,000000	5,000000
AA	4,051724	29	3,117763	0,00	10,00000	2,000000	4,000000	5,000000
Overall	3,685714	140	3,179240	0,00	10,00000	1,000000	3,000000	6,000000

P=0,44

IL17F/rs2397084	NRS Medium	NRS Valid	NRS Stand.Dev	NRS Minimum	NRS Maximum	NRS Q25	NRS Median	NRS Q75
AG	3,560484	124	3,172002	0,000000	10,00000	0,000000	3,000000	6,000000
GG	4,656250	16	3,166064	1,000000	10,00000	2,500000	4,000000	6,250000
Overall	3,685714	140	3,179240	0,000000	10,00000	1,000000	3,000000	6,000000

P=0,51

NRS pruritus level differences not statistically significant for other genotypes except IL17a/rs8193036

(p=0,005)

GG	NRS mild pruritus (1-3)	NRS moderate pruritus (4-6)	NRS very severe pruritus (10)	NRS severe pruritus (7-9)	Overall
no	65	38	10	8	121
	53,72%	31,40%	8,26%	6,61%	
yes	7	6	0	6	19
	36,84%	31,58%	0,00%	31,58%	
Overall	72	44	10	14	140