Supplementary Materials

IL-10 Gene Rs1800871, Rs1800872, and Rs1800896 Polymorphisms and IL-10 Serum Levels Association with Pituitary Adenoma

Table S1. Distributions of *IL – 10* rs1800871, rs1800872, rs1800896 genotypes and alleles in patients with PA and control groups.

Gene	Genotype/allele	PA (n=106), *n* (%)	Control (n=192), *n* (%)	p-value	p-value HWE
IL – 10 (rs1800871)	GG	67 (63.2)	103 (53.6)	0.202	0.449
	AG	32 (30.2)	78 (40,6)		
	AA	7 (6.6)	11 (5,7)		
	Viso:	106 (100)	192 (100)		
	Allele: G A	166 (78.3) 46 (21.7)	284 (74.0) 100 (26.0)	0.238	
IL – 10 (rs1800872)	GG	68 (64.2)	103 (53.6)	0.148	0.449
	TG	31 (29.2)	78 (40.6)		
	TT	7 (6.6)	11 (5.7)		
	Viso:	106 (100)	192 (100)		
	Allele: G T	167 (78.8) 45 (21.2)	284 (74.0) 100 (26.0)	0.190	
IL – 10 (rs1800896)	TT	30 (28.3)	49 (25.5)	0.851	0.554
	TC	52 (49.1)	100 (52.1)		
	CC	24 (22.6)	43 (22.4)		
	Viso:	106 (100)	192 (100)		
	Allele: T C	112 (52.8) 100 (47.2)	198 (51.6) 186 (48.4)	0.767	

Table S2. Binary logistic regression analysis of *IL – 10* rs1800871, rs1800872, rs1800896 in patients with PA and control groups.

IL – 10 (rs1800871)

Model	Genotype/allele	OR (95% CI)	p - value	AIC

Codominant	AG *vs.* GG	0.631 (0.377 – 1.054)	0.079	388.697
	AA *vs.* GG	0.978 (0.361 – 2.649)	0.966	
Dominant	AG+AA *vs.* GG	0.674 (0.414 – 1.095)	0.111	389.849
Recessive	AA *vs.* GG+AG	1.163 (0.437 – 3.096)	0.762	386.699
Overdominant	AG *vs.* AA+GG	0.632 (0.381 – 1.047)	0.075	388.204
Additive	G	0.787 (0.528 – 1.173)	0.239	388.531
IL − 10 (**rs1800872**)				
Codominant	TG *vs.* GG	0.602 (0.359 – 1.009)	0.054	386.059
	TT *vs.* GG	0.964 (0.356 – 2.609)	0.942	
Dominant	TG+TT *vs.* GG	0.647 (0.397 – 1.053)	0.080	389.849
Recessive	TT *vs.* GG+TG	1.163 (0.437 – 3.096)	0.762	386.064
Overdominant	TG *vs.* GG+TT	0.604 (0.363 – 1.004)	0.052	389.829
Additive	G	0.766 (0.513 – 1.144)	0.192	386.059
IL − 10 (**rs1800896**)				
Codominant	TC *vs.* TT	1.177 (0.669 – 2.071)	0.571	391.618
	CC *vs.* TT	1.073 (0.588 – 1.959)	0.818	
Dominant	TC+CC *vs.* TT	1.129 (0.702 – 1.814)	0.617	389.938
Recessive	CC *vs.* TT+TC	1.014 (0.575 – 1.789)	0.961	389.671
Overdominant	TC *vs.* TT+CC	1.152 (0.676 – 1.963)	0.603	389.671
Additive	T	1.051 (0.785 – 1.408)	0.738	389.618

OR: odds ratio; CI: confidence interval; AIC: Akaike information criterion; p-value: significance level (statistically significant when $p < 0.05$).

Table S3. Distributions of *IL − 10* rs1800871, rs1800872,rs1800896 genotypes and alleles in patients with PA and control groups by gender.

Gene	Genotype	Males		p - value	Females		p - value
		PA (n=46) *n*(%)	Control (n=63) *n* (%)		PA (n=60) *n* (%)	Control (n=129) *n* (%)	
IL − 10 (rs1800871)	AA	3 (6.5)	4 (6.3)	0.393	4 (6.7)	7 (5.4)	0.361
	AG	16 (34.8)	30 (47.6)		16 (26.7)	48 (37.2)	
	GG	27 (58.7)	29 (46.0)		40 (66.7)	74 (57.4)	
	Allele: A	22 (23.9)	38 (30.2)	0.308	24 (20.0)	62 (24.0)	0.384
	G	70 (76.1)	88 (69.8)		96 (80.0)	196 (76.0)	
IL − 10 (rs1800872)	GG	28 (60.9)	29 (46.0)	0.276	40 (66.7)	74 (57.4)	0.361
	TG	15 (32.6)	30 (47.6)		16 (26.7)	48 (37.2)	
	TT	3 (6.5)	4 (6.3)		4 (6.7)	7 (5.4)	
	Allele: G	71 (77.2)	88 (69.8)	0.229	96 (80.0)	196 (76.0)	0.384
	T	21 (22.8)	38 (30.2)		24 (20.0)	62 (24.0)	
IL − 10 (rs1800896)	CC	12 (26.1)	9 (14.3)	0.261	12 (20.0)	34 (26.4)	0.306
	TC	24 (52.2)	35 (55.6)		28 (46.7)	65 (50.4)	
	TT	10 (21.7)	19 (30.2)		20 (33.3)	30 (23.3)	
	Allele: C	48 (52.2)	53 (42.1)	0.139	52 (43.3)	133 (51.6)	0.137
	T	44 (47.8)	73 (57.9)		68 (56.7)	125 (48.4)	

Table S4. Binary logistic regression analysis of *IL − 10* rs1800871, rs1800872, rs1800896 in the PA and control groups by gender.

Females				
IL − 10 (rs1800871)				
Model	**Genotype/allele**	**OR (95% CI)**	**p - value**	**AIC**
Codominant	AG *vs.* GG AA *vs.* GG	1.463 (0.891 − 2.402) 1.295 (0.477 − 3.522)	0.132 0.612	393.069
Dominant	AG+AA *vs.* GG	1.439 (0.894 − 2.314)	0.134	391.124
Recessive	AA *vs.* GG+AG	1.111 (0.417 − 2.954)	0.834	393.330
Overdominant	AG *vs.* AA+GG	1.426 (0.878 − 2.316)	0.151	391.322
Additive	G	1.290 (0.879 − 1.893)	0.194	391.690

IL – 10 (rs1800872)

Model	Genotype/allele	OR (95% CI)	p - value	AIC
Codominant	TG *vs.* GG TT *vs.* GG	0.786 (0.289 – 2.135) 1.105 (0.398 – 3.069)	0.636 0.848	393.522
Dominant	TG+TT *vs.* GG	0.721 (0.448 – 1.160)	0.178	391.559
Recessive	TT *vs.* GG+TG	1.111 (0.417 – 2.954)	0.834	393.330
Overdominant	TG *vs.* GG+TT	1.373 (0.845 – 2.233)	0.201	391.742
Additive	G	1.259 (0.858 – 1.847)	0.240	391.997

IL – 10 (rs1800896)

Model	Genotype/allele	OR (95% CI)	p - value	AIC
Codominant	TC *vs.* TT CC *vs.* TT	0.914 (0.521 – 1.604) 0.720 (0.391 – 1.325)	0.754 0.291	394.238
Dominant	TC+CC *vs.* TT	0.821 (0.512 – 1.317)	0.413	392.703
Recessive	CC *vs.* TT+TC	0.742 (0.415 – 1.326)	0.313	392.336
Overdominant	TC *vs.* TT+CC	1.008 (0.591 – 1.719)	0.977	393.373
Additive	T	0.857 (0.638 – 1.151)	0.305	392.309

Males

IL – 10 (rs1800871)

Model	Genotype/allele	OR (95% CI)	p - value	AIC
Codominant	AG *vs.* GG AA *vs.* GG	0.683 (0.416 – 1.122) 0.772 (0.284 – 2.099)	0.683 0.772	393.069
Dominant	AG+AA *vs.* GG	0.695 (0.432 – 1.118)	0.134	391.124
Recessive	AA *vs.* GG+AG	0.900 (0.339 – 2.395)	0.834	393.330
Overdominant	AG *vs.* AA+GG	0.701 (0.432 – 1.139)	0.151	391.322
Additive	G	0.775 (0.528 – 1.138)	0.194	391.690

IL – 10 (rs1800872)

Model	Genotype/allele	OR (95% CI)	p - value	AIC
Codominant	TG *vs.* GG TT *vs.* GG	0.711 (0.433 – 1.168) 0.786 (0.289 – 2.135)	0.178 0.636	393.522
Dominant	TG+TT *vs.* GG	0.721 (0.448 – 1.160)	0.178	391.559
Recessive	TT *vs.* GG+TG	0.900 (0.339 – 2.395)	0.834	393.330
Overdominant	TG *vs.* GG+TT	0.728 (0.448 – 1.184)	0.201	391.742
Additive	G	0.794 (0.541 – 1.166)	0.240	391.997

IL – 10 (rs1800896)

Model	Genotype/allele	OR (95% CI)	p - value	AIC
Codominant	TC *vs.* TT CC *vs.* TT	1.094 (0.624 – 1.919) 1.390 (0.755 – 2.559)	0.754 0.291	394.238

Dominant	TC+CC *vs.* TT	1.218 (0.759 – 1.954)	0.413	392.703
Recessive	CC *vs.* TT+TC	1.348 (0.754 – 2.409)	0.313	392.336
Overdominant	TC *vs.* TT+CC	0.992 (0.582 – 1.692)	0.977	393.373
Additive	T	1.167 (0.869 – 1.569)	0.305	392.309

OR: odds ratio; CI: confidence interval; AIC: Akaike information criteria; p-value: significance level (statistically significant when $p < 0.05$).

Table S5. Distributions of $IL-10$ rs1800871, rs1800872, rs1800896 genotypes and alleles in patients with PA and control groups by PA invasiveness.

Gene	Genotype	Control (n=192) n (%)	Non-invasive PA (n=34) n (%)	p - value	Invasive PA (n=71) n (%)	p - value
IL – 10 (rs1800871)	AA	11 (5.70)	1 (2.9)	0.458	6 (8.5)	0.233
	AG	78 (40.6)	11 (32.4)		21 (29.6)	
	GG	103 (53.6)	22 (64.7)		44 (62.0)	
	Allele: A	100 (26.0)	13 (19.1)	0.224	33 (23.2)	0.512
	G	284 (74.0)	55 (80.9)		109 (76.8)	
IL – 10 (rs1800872)	GG	103 (53.6)	22 (64.7)	0.458	45 (63.4)	0.163
	TG	78 (40.6)	11 (32.4)		20 (28.2)	
	TT	11 (5.7)	1 (2.9)		6 (8.5)	
	Allele: G	284 (74.0)	55 (80.9)	0.224	110 (77.5)	0.410
	T	100 (26.0)	13 (19.1)		32 (22.5)	
IL – 10 (rs1800896)	CC	43 (22.4)	4 (11.8)	0.371	20 (28.2)	0.450
	TC	100 (52.1)	20 (58.8)		31 (43.7)	
	TT	49 (25.5)	10 (29.4)		20 (28.2)	
	Allele: C	186 (48.4)	28 (41.2)	0.269	71 (50.0)	0.750
	T	198 (51.6)	40 (58.8)		71 (50.0)	

Table S6. Binary logistic regression analysis of $IL-10$ rs1800871, rs1800872, rs1800896 in the PA and control groups by PA invasiveness.

$IL-10$ (rs1800871)

Model	Genotype/allele	OR (95% CI)	p - value	AIC
Non-invasive PA				
Codominant	AG *vs.* GG	1.515 (0.693 – 3.308)	0.298	193.779
	AA *vs.* GG	2.350 (0.288 - 19.153)	0.425	

Dominant	AG+AA *vs.* GG	1.584 (0.742 – 3.382)	0.234	191.958
Recessive	AA *vs.* GG+AG	2.006 (0.250 - 16.061)	0.512	192.896
Overdominant	AG *vs.* AA+GG	1.431 (0.660 – 3.102)	0.365	192.566
Additive	G	1.521 (0.784 – 2.951)	0.215	191.780
Invasive PA				
Codominant	AG *vs.* GG AA *vs.* GG	1.587 (0.873 – 2.883) 0.783 (0.273 – 2.250)	0.130 0.650	307.816
Dominant	AG+AA *vs.* GG	1.408 (0.807 – 2.457)	0.228	307.305
Recessive	AA *vs.* GG+AG	0.658 (0.234 – 1.852)	0.428	308.171
Overdominant	AG *vs.* AA+GG	1.629 (0.907 – 2.925)	0.102	304.018
Additive	G	1.163 (0.741 – 1.825)	0.513	305.816
IL – 10 **(rs1800872)**				
Non-invasive PA				
Codominant	TG *vs.* GG TT *vs.* GG	1.515 (0.693 – 3.308) 2.350 (0.288 - 19.153)	0.298 0.425	193.779
Dominant	TG+TT *vs.* GG	1.584 (0.742 – 3.382)	0.234	191.958
Recessive	TT *vs.* GG+TG	2.006 (0.250 - 16.061)	0.512	192.896
Overdominant	TG *vs.* GG+TT	1.431 (0.660 – 3.102)	0.365	192.566
Additive	G	1.521 (0.784 – 2.951)	0.215	191.780
Invasive PA				
Codominant	TG *vs.* GG TT *vs.* GG	1.704 (0.932 – 3.115) 0.801 (0.279 – 2.299)	0.083 0.680	307.073
Dominant	TG+TT *vs.* GG	1.496 (0.854 – 2.618)	0.159	306.757
Recessive	TT *vs.* GG+TG	0.658 (0.234 – 1.852)	0.428	308.171
Overdominant	TG *vs.* GG+TT	1.745 (0.965 – 3.153)	0.065	305.240
Additive	G	1.209 (0.768 – 1.903)	0.413	308.091
IL – 10 **(rs1800896)**				
Non-invasive PA				
Codominant	TC *vs.* TT CC *vs.* TT	0.980 (0.426 – 2.253) 2.150 (0.694 – 6.665)	0.962 0.185	193.194
Dominant	TC+CC *vs.* TT	1.314 (0.627 – 2.753)	0.469	192.881
Recessive	CC *vs.* TT+TC	2.164 (0.723 – 6.483)	0.168	191.197
Overdominant	TC *vs.* TT+CC	0.822 (0.367 – 1.841)	0.634	193.189

Additive	T	1.338 (0.820 – 2.185)	0.244	191.983

Invasive PA

Codominant	TC *vs.* TT CC *vs.* TT	0.760 (0.393 – 1.466) 0.667 (0.342 – 1.297)	0.412 0.233	309.182
Dominant	TC+CC *vs.* TT	0.713 (0.412 – 1.233)	0.226	307.301
Recessive	CC *vs.* TT+TC	0.736 (0.396 – 1.366)	0.331	307.847
Overdominant	TC *vs.* TT+CC	0.874 (0.475 – 1.609)	0.665	308.588
Additive	T	0.812 (0.585 – 1.127)	0.213	307.234

OR: odds ratio; CI: confidence interval; AIC: Akaike information criteria; p-value: significance level (statistically significant when $p < 0.05$).

Table S7. Distributions of *IL – 10* rs1800871, rs1800872, rs1800896 genotypes and alleles in patients with PA and control groups by PA recurrence.

Gene	Genotype	Control (n=192), *n* (%)	Without recurrence (n=81), *n* (%)	p - value	With recurrence (n=21), *n* (%)	p - value
IL – 10 (rs1800871)	AA	11 (5.7)	6 (7.4)	0.226	1 (4.8)	0.771
	AG	78 (40.6)	24 (29.6)		7 (33.3)	
	GG	103 (53.6)	51 (63.0)		13 (61.9)	
	Allele: A G	100 (26.0) 284 (74.0)	36 (22.2) 126 (77.8)	0.346	9 (21.4) 33 (78.6)	0.515
IL – 10 (rs1800872)	GG	103 (53.6)	52 (64.2)	0.159	13 (61.9)	0.771
	TG	78 (40.6)	23 (28.4)		7 (33.3)	
	TT	11 (5.7)	6 (7.4)		1 (4.8)	
	Allele: G T	284 (74.0) 100 (26.0)	127 (78.4) 35 (21.6)	0.272	33 (78.6) 9 (21.4)	0.515
IL – 10 (rs1800896)	CC	43 (22.4)	18 (22.2)	0.878	5 (23.8)	0.924
	TC	100 (52.1)	40 (49.4)		10 (47.6)	
	TT	49 (25.5)	23 (28.4)		6 (28.6)	
	Allele: C T	186 (48.4) 198 (51.6)	76 (46.9) 86 (53.1)	0.745	20 (47.6) 22 (52.4)	0.920

Table S8. Binary logistic regression analysis of *IL – 10* rs1800871, rs1800872, rs1800896 in the PA and control groups by PA recurrence.

Model	Genotype/allele	OR (95% CI)	p - value	AIC
IL – 10 (rs1800871)				
Without recurrence				
Codominant	AG *vs.* GG AA *vs.* GG	1.609 (0.912 – 2.838) 0.908 (0.318 – 2.594)	0.100 0.857	332.957
Dominant	AG+AA *vs.* GG	1.496 (0.862 – 2.503)	0.157	331.963
Recessive	AA *vs.* GG+AG	0.760 (0.271 – 2.129)	0.601	333.726
Overdominant	AG *vs.* AA+GG	1.625 (0.931 – 2.837)	0.088	330.989
Additive	G	1.232 (0.797 – 1.905)	0.347	333.091
With recurrence				
Codominant	AG *vs.* GG AA *vs.* GG	1.406 (0.536 - 3.691) 1.388 (0.166 - 11.646)	0.488 0.762	140.636
Dominant	AG+AA *vs.* GG	1.404 (0.557 - 3.542)	0.472	138.636
Recessive	AA *vs.* GG+AG	1.215 (0.149 - 9.912)	0.855	139.127
Overdominant	AG *vs.* AA+GG	1.368 (0.528 - 3.545)	0.518	138.734
Additive	G	1.307 (0.594 - 2.879)	0.506	138.703
IL – 10 (rs1800872)				
Without recurrence				
Codominant	TG *vs.* GG TT *vs.* GG	1.712 (0.966 – 3.034) 0.926 (0.324 – 2.643)	0.066 0.885	332.228
Dominant	TG+TT vs. GG	1.549 (0.907 – 2.647)	0.109	331.379
Recessive	TT *vs.* GG+TG	0.760 (0.271 – 2.129)	0.601	333.726
Overdominant	TG *vs.* GG+TT	1.725 (0.983 – 3.028)	0.057	331.248
Additive	G	1.276 (0.824 – 1.978)	0.275	332.772
With recurrence				
Codominant	TG *vs.* GG TT *vs.* GG	1.406 (0.536 – 3.691) 1.388 (0.166 - 11.646)	0.488 0.762	140.636
Dominant	TG+TT *vs.* GG	1.404 (0.557 – 3.542)	0.472	138.636
Recessive	TT *vs.* GG+TG	1.215 (0.149 – 9.912)	0.855	139.127
Overdominant	TG *vs.* GG+TT	1.368 (0.528 – 3.545)	0.518	138.734
Additive	G	1.307 (0.594 – 2.879)	0.506	138.703

IL − 10 (rs1800896)				
Without recurrence				
Codominant	TC *vs.* TT CC *vs.* TT	0.852 (0.460 – 1.578) 0.956 (0.493 – 1.851)	0.611 0.893	335.734
Dominant	TC+CC *vs.* TT	0.898 (0.534 – 1.509)	0.683	333.826
Recessive	CC *vs.* TT+TC	1.010 (0.541 – 1.885)	0.975	333.992
Overdominant	TC *vs.* TT+CC	0.864 (0.483 – 1.546)	0.623	333.752
Additive	T	0.962 (0.698 – 1.326)	0.813	333.937
With recurrence				
Codominant	TC *vs.* TT CC *vs.* TT	0.817 (0.281 – 2.377) 0.860 (0.270 – 2.666)	0.710 0.794	141.005
Dominant	TC+CC *vs.* TT	0.836 (0.339 – 2.061)	0.698	139.011
Recessive	CC *vs.* TT+TC	0.923 (0.320 – 2.665)	0.883	139.141
Overdominant	TC *vs.* TT+CC	0.857 (0.315 – 2.330)	0.762	139.072
Additive	T	0.916 (0.530 – 1.583)	0.753	139.064

OR: odds ratio; CI: confidence interval; AIC: Akaike information criteria; p-value: significance level (statistically significant when $p < 0.05$).
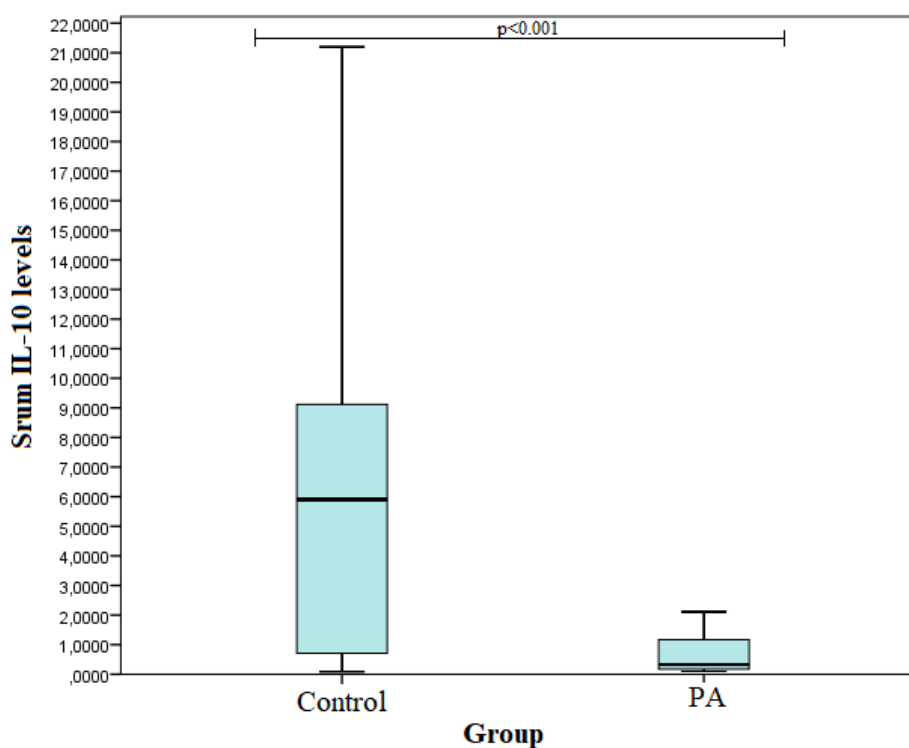
Figure S1. Serum IL-10 levels in PA and control groups.

Table S9. Associations between *IL-10* haplotypes and risk of pituitary adenoma.

Haplotype	rs1800871	rs1800872	rs1800896	Frequency (%)			OR (95% CI)	p-value
				PA	Controls	Total		
1	G	G	C	47.17	48.08	47.75	1.00	---
2	G	G	T	31.13	25.88	27.75	1.24 (0.83 – 1.86)	0.29
3	A	T	T	21.23	25.68	24.10	0.84 (0.54 – 1.29)	0.42
rare	*	*	*	NA	NA	0.40	2.02 (0.12 – 33.38)	0.62

OR – odds ratio; CI – confident interval; p – significance level when p=0.05; AIC – Akaike information criteria; NA – not applicable; rare – pooled haplotypes with frequencies <1%.