Supplementary Materials

Table S1. Genotypes distribution of *TNF-α* SNPs in the control group using the Hardy-Weinberg equilibrium.

SNP	Group	Allele frequency		Distribution of Genotypes	HWE *p*-Value
TNF-863A/C (rs1800630)	Control	A (0.151)	C (0.849)	10/87/258	645
TNF-308A/G (rs1800629)	Control	A (0.115)	G (0.885)	4/74/277	146
TNF-238A/G (rs361525)	Control	A (0.056)	G (0.944)	1/38/316	16

SNP: single nucleotide polymorphism; HWE: Hardy-Weinberg equilibrium; *p*-value: significance level.

Table S2. Distributions of rs1800630, rs1800629, rs361525 genotypes and alleles in patients with early AMD and control groups.

SNP	Genotypes/ Alleles	Group		*p*-Value
		Control n (%) (n = 355)	Early AMD n (%) (n = 330)	
TNF-863A/C (rs1800630)	CC	258 (72.7)	235 (71.2)	0.594
	AC	87 (24.5)	81 (24.5)	
	AA	10 (2.8)	14 (4.2)	
	C	603 (84.9)	551 (83.5)	0.463
	A	107 (15.1)	109 (16.5)	
TNF-308A/G (rs1800629)	GG	277 (78.0)	267 (80.9)	0.275
	AG	74 (20.8)	56 (17.0)	
	AA	4 (1.1)	7 (2.1)	
	G	628 (88.5)	590 (89.4)	0.579
	A	82 (11.5)	70 (10.6)	
TNF-238A/G (rs361525)	GG	316 (89.0)	303 (91.8)	0.329
	AG	38 (10.7)	27 (8.2)	
	AA	1 (0.3)	0 (0.0)	
	G	670 (94.4)	633 (95.9)	0.186
	A	40 (5.6)	27 (4.1)	

SNP: single nucleotide polymorphism; AMD: age-related macular degeneration; *p*-value: significance level (statistically significant when $p < 0.05$).

Table S3. Distributions of rs1800630, rs1800629, rs361525 genotypes and alleles in patients with early and exudative AMD.

SNP	Genotypes/ Alleles	Group		*p*-Value
		Early AMD n (%) (n = 330)	Exudative AMD n (%) (n = 393)	
TNF-863A/C (rs1800630)	CC	235 (71.2)	263 (66.9)	0.420
	AC	81 (24.5)	108 (27.5)	
	AA	14 (4.2)	22 (5.6)	
	C	551 (83.5)	634 (80.7)	0.164
	A	109 (16.5)	152 (19.3)	
TNF-308A/G (rs1800629)	GG	267 (80.9)	297 (75.6)	0.090
	AG	56 (17.0)	91 (23.2)	
	AA	7 (2.1)	5 (1.3)	
	G	590 (89.4)	685 (87.2)	0.188
	A	70 (10.6)	101 (12.8)	
TNF-238A/G (rs361525)	GG	303 (91.8)	361 (91.9)	0.417
	AG	27 (8.2)	30 (7.6)	
	AA	0 (0.0)	2 (0.5)	
	G	633 (95.9)	752 (95.7)	0.825
	A	27 (4.1)	34 (4.3)	

SNP: single nucleotide polymorphism; AMD: age-related macular degeneration; *p*-value: significance level (statistically significant when $p < 0.05$).

Table S4. Binary logistic regression analysis of rs1800630, rs1800629, rs361525 in patients with early AMD and control groups.

Model	Genotype/Allele	OR (95% CI)	*p*-Value	AIC
TNF-863A/C (rs1800630)				
Additive	**A**	1.106 (0.836–1.464)	0.480	950.200
Codominant	**A/C**	1.022 (0.720–1.451)	0.902	951.654
	A/A	1.537 (0.670–3.527)	0.310	
Dominant	**A/C+A/A**	1.075 (0.770–1.501)	0.670	950.517
Recessive	**A/A**	1.528 (0.669–3.490)	0.314	949.669
Overdominant	**A/C**	1.002 (0.707–1.420)	0.991	950.699
TNF-308A/G (rs1800629)				
Additive	**A**	0.912 (0.654–1.271)	0.586	950.401

Model	Genotype/Allele	OR (95% CI)	p-Value	AIC
Codominant	A/G A/A	0.785 (0.534–1.155) 1.816 (0.525–6.273)	0.219 0.346	950.099
Dominant	A/G+A/A	0.838 (0.578–1.216)	0.352	949.829
Recessive	A/A	1.902 (0.552–6.557)	0.309	949.619
Overdominant	A/G	0.776 (0.528–1.141)	0.197	949.023
TNF-238A/G (rs361525)				
Additive	A	0.709 (0.428–1.176)	0.183	948.898
Codominant	A/G A/A	0.741 (0.441–1.244) –	0.257 –	950.082
Dominant	A/G+A/A	0.722 (0.431–1.209)	0.215	949.145
Recessive	A/A	–	–	949.383
Overdominant	A/G	0.743 (0.443–1.248)	0.262	949.425

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

Table S5. Binary logistic regression analysis of rs1800630, rs1800629, rs361525 in patients with exudative AMD and control groups.

Model	Genotype/Allele	OR (95% CI)	p-Value	AIC
TNF-863A/C (rs1800630)				
Additive	A	1.268 (0.968–1.660)	0.085	984.183
Codominant	A/C A/A	1.169 (0.831–1.645) 1.995 (0.907–4.389)	0.370 0.086	985.604
Dominant	A/C+A/A	1.255 (0.908–1.737)	0.169	985.293
Recessive	A/A	1.912 (0.873–4.184)	0.105	984.410
Overdominant	A/C	1.125 (0.802–1.579)	0.494	986.720
TNF-308A/G (rs1800629)				
Additive	A	1.217 (0.878–1.687)	0.239	985.791
Codominant	A/G A/A	1.235 (0.861–1.772) 1.317 (0.338–5.130)	0.251 0.692	987.754
Dominant	A/G+A/A	1.240 (0.871–1.765)	0.233	985.762
Recessive	A/A	1.254 (0.323–4.872)	0.743	989.081
Overdominant	A/G	1.230 (0.858–1.763)	0.260	985.912
TNF-238A/G (rs361525)				

Additive	**A**	0.734 (0.454–1.184)	0.205	985.570
Codominant	**A/G** **A/A**	0.649 (0.386–1.091) 2.043 (0.171–24.360)	0.103 0.572	986.134
Dominant	**A/G+A/A**	0.681 (0.410–1.133)	0.139	984.985
Recessive	**A/A**	2.121 (0.178–25.257)	0.552	986.813
Overdominant	**A/G**	0.647 (0.385–1.088)	0.101	984.471

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

Table S6. Haplotype association with the predisposition to early AMD occurrence.

TNF -863A/C (rs1800630)	TNF -308A/G (rs1800629)	TNF -238A/G (rs361525)	Frequency		OR (95 % CI)	*p*-Value
			Control	Early AMD		
C	G	G	0.691	0.706	1.00	–
A	A	G	0.134	0.137	0.96 (0.66–1.40)	0.83
C	A	G	0.104	0.09	0.84 (0.58–1.21)	0.35
C	G	A	0.056	0.036	0.70 (0.42–1.18)	0.18
A	G	G	0.016	0.025	1.58 (0.66–3.78)	0.31
A	A	A	0	0.005	–	–

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

Table S7. Distributions of rs1800630, rs1800629, rs361525 genotypes and alleles in patients with early AMD and control groups by gender.

SNP	Geno-types/ Alleles	Female		*p*-Value	Male		*p*-Value
		Control n (%) (n = 222)	Early AMD n (%) (n = 227)		Control n (%) (n = 133)	Early AMD n (%) (n = 103)	
TNF-863A/C (rs1800630)	CC AC AA	163 (73.4) 50 (22.5) 9 (4.1)	169 (74.4) 49 (21.6) 9 (4.0)	0.969	95 (71.4) 37 (27.8) 1 (0.8)	66 (64.1) 32 (31.1) 5 (4.9)	0.105
	C A	376 (84.7) 68 (15.3)	387 (85.2) 67 (14.8)	0.815	227 (85.3) 39 (14.7)	164 (79.6) 42 (20.4)	0.102

TNF-308A/G (rs1800629)	GG AG AA	174 (78.4) 46 (20.7) 2 (0.9)	185 (81.5) 37 (16.3) 5 (2.2)	0.280	103 (77.4) 28 (21.1) 2 (1.5)	82 (79.6) 19 (18.4) 2 (1.9)	0.861
	G A	394 (88.7) 50 (11.3)	407 (89.6) 47 (10.4)	0.661	234 (88.0) 32 (12.0)	183 (88.8) 23 (11.2)	0.771
TNF-238A/G (rs361525)	GG AG AA	199 (89.6) 22 (9.9) 1 (0.5)	207 (91.2) 20 (8.8) 0 (0.0)	0.550	117 (88.0) 16 (12.0) 0 (0.0)	96 (93.2) 7 (6.8) 0 (0.0)	0.179
	G A	420 (94.6) 24 (5.4)	434 (95.6) 20 (4.4)	0.488	250 (94.0) 16 (6.0)	199 (96.6) 7 (3.4)	0.190

SNP: single nucleotide polymorphism; AMD: age-related macular degeneration; p-value: significance level (statistically significant when $p < 0.05$).

Table S8. Binary logistic regression analysis of rs1800630, rs1800629, rs361525 in the early AMD and control groups by gender.

Model	Genotype/Allele	OR (95 proc. CI)	p-Value	AIC
Female				
TNF-863A/C (rs1800630)				
Additive	**A**	0.962 (0.683–1.356)	0.826	624.342
Codominant	**A/C** **A/A**	0.945 (0.603–1.481) 0.964 (0.374–2.491)	0.806 0.940	626.328
Dominant	**A/C+A/A**	0.948 (0.622–1.445)	0.804	624.329
Recessive	**A/A**	0.977 (0.381–2.509)	0.962	624.388
Overdominant	**A/C**	0.947 (0.606–1.480)	0.811	624.333
TNF-308A/G (rs1800629)				
Additive	**A**	0.913 (0.604–1.381)	0.667	624.206
Codominant	**A/G** **A/A**	0.757 (0.468–1.222) 2.351 (0.450–12.278)	0.254 0.311	623.803
Dominant	**A/G+A/A**	0.823 (0.518–1.308)	0.409	623.709
Recessive	**A/A**	2.477 (0.476–12.905)	0.281	623.109
Overdominant	**A/G**	0.745 (0.462–1.203)	0.229	622.933
TNF-238A/G (rs361525)				
Additive	**A**	0.806 (0.438–1.483)	0.488	623.906

Codominant	A/G A/A	0.874 (0.463–1.651) –	0.678 –	624.807
Dominant	A/G+A/A	0.836 (0.445–1.570)	0.577	624.079
Recessive	A/A	–	–	–
Overdominant	A/G	0.878 (0.465–1.659)	0.689	624.230
Male				
TNF-863A/C (rs1800630)				
Additive	A	1.512 (0.925–2.470)	0.099	322.597
Codominant	A/C A/A	1.245 (0.705–2.197) 7.197 (0.822–63.026)	0.450 0.075	322.640
Dominant	A/C+A/A	1.402 (0.808–2.432)	0.230	323.900
Recessive	A/A	6.735 (0.774–58.566)	0.084	321.210
Overdominant	A/C	1.169 (0.665–2.055)	0.587	325.046
TNF-308A/G (rs1800629)				
Additive	A	0.921 (0.526–1.614)	0.775	325.260
Codominant	A/G A/A	0.852 (0.445–1.634) 1.256 (0.173–9.110)	0.630 0.822	327.042
Dominant	A/G+A/A	0.879 (0.469–1.649)	0.688	325.180
Recessive	A/A	1.297 (0.180–9.367)	0.797	325.275
Overdominant	A/G	0.848 (0.443–1.624)	0.619	325.093
TNF-238A/G (rs361525)				
Additive	A	0.533 (0.211–1.349)	0.184	323.474
Codominant	A/G A/A	0.533 (0.211–1.349) –	0.184 –	325.474
Dominant	A/G+A/A	0.533 (0.211–1.349)	0.184	323.474
Recessive	A/A	–	–	–
Overdominant	A/G	0.533 (0.211–1.349)	0.184	323.474

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

Table S9. Binary logistic regression analysis of rs1800630, rs1800629, rs361525 in exudative AMD and control groups by gender.

Model	Genotype/Allele	OR (95 proc. CI)	p-Value	AIC

Female				
TNF-863A/C (rs1800630)				
Additive	**A**	1.288 (0.919–1.803)	0.141	607.226
Codominant	**A/C** **A/A**	1.411 (0.908–2.191) 1.364 (0.558–3.334)	0.126 0.496	608.827
Dominant	**A/C+A/A**	1.403 (0.927–2.123)	0.109	604.832
Recessive	**A/A**	1.240 (0.511–3.008)	0.634	609.190
Overdominant	**A/C**	1.381 (0.893–2.138)	0.147	607.299
TNF-308A/G (rs1800629)				
Additive	**A**	1.304 (0.847–2.007)	0.228	607.948
Codominant	**A/G** **A/A**	1.390 (0.875–2.207) 0.818 (0.102–6.531)	0.163 0.850	609.387
Dominant	**A/G+A/A**	1.363 (0.864–2.148)	0.183	607.629
Recessive	**A/A**	0.762 (0.096–6.044)	0.797	609.353
Overdominant	**A/G**	1.393 (0.878–2.210)	0.160	607.423
TNF-238A/G (rs361525)				
Additive	**A**	0.761 (0.401–1.442)	0.402	608.712
Codominant	**A/G** **A/A**	0.797 (0.411–1.542) –	0.500 –	610.218
Dominant	**A/G+A/A**	0.775 (0.403–1.492)	0.446	608.837
Recessive	**A/A**	–	–	608.673
Overdominant	**A/G**	0.799 (0.413–1.547)	0.506	608.976
Male				
TNF-863A/C (rs1800630)				
Additive	**A**	1.173 (0.741–1.857)	0.495	375.241
Codominant	**A/C** **A/A**	0.835 (0.480–1.452) 7.129 (0.854–59.491)	0.523 0.070	372.042
Dominant	**A/C+A/A**	0.995 (0.585–1.692)	0.985	375.709
Recessive	**A/A**	7.481 (0.901–62.117)	0.062	370.452
Overdominant	**A/C**	0.786 (0.453–1.362)	0.390	374.970
TNF-308A/G (rs1800629)				
Additive	**A**	1.108 (0.668–1.837)	0.691	375.551

Codominant	**A/G** **A/A**	1.042 (0.580–1.870) 1.679 (0.272–10.382)	0.891 0.577	377.382
Dominant	**A/G+A/A**	1.081 (0.613–1.906)	0.787	375.636
Recessive	**A/A**	1.664 (0.270–10.243)	0.583	375.401
Overdominant	**A/G**	1.029 (0.574–1.844)	0.923	375.700
TNF-238A/G (rs361525)				
Additive	**A**	0.739 (0.356–1.532)	0.416	375.042
Codominant	**A/G** **A/A**	0.482 (0.203–1.144) –	0.098 –	372.360
Dominant	**A/G+A/A**	0.588 (0.260–1.330)	0.202	374.053
Recessive	**A/A**	–	–	–
Overdominant	**A/G**	0.474 (0.200–1.125)	0.090	372.719

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

Table S10. Serum TNF-α levels in relation to the genotypes of *TNF-α* polymorphisms.

Model		All Subjects (pg/mL), Median (IQR)	*p*-Value	Exudative AMD (pg/mL), median (IQR)	*p*-Value	Control Group (pg/mL), Median (IQR)	*p*-Value
TNF-863A/C (rs1800630)							
Dominant	AC+AA vs. CC	23.51 (12.25) vs. 23.91 (8.49)	0.908	15.43 (7.45) vs. 16.56 (5.63)	0.724	33.21 (9.52) vs. 29.8 (5.03)	0.309
TNF-308A/G (rs1800629)							
Dominant	AG+AA vs. GG	21.69 (8.35) vs. 24.19 (9.83)	0.563	16.69 (3.88) vs. 16.04 (6.71)	0.858	31.7 (1.64) vs. 30.54 (6.66)	0.812
TNF-238A/G (rs361525)							
Dominant	AG+AA vs. GG	18.6 (5.6) vs. 24.24 (9.74)	0.333	17.12 (7.04) vs. 16.07 (6.22)	0.825	– (–) vs. 31.13 (6.11)	–

p-value: significance level (statistically significant when $p < 0.05$).