

# Genetic Polymorphisms of ACE1 Rs4646994 Associated with Lung Cancer in Patients with Pulmonary Nodules: A Case–Control Study

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**Table S1.** Correlations of genotype polymorphism in ACE1 rs4646994 and lung cancer risk in patients with pulmonary nodules according to gender.

Gender	Genotype /allele	Case (n=300)	Control (n=100)	p-Value <sup>a</sup>	OR	95%CI
Male		135	44			
	II	52 (38.5%)	13 (29.5%)	Reference		
	ID	63 (46.7%)	28 (63.6%)	0.132	0.559	0.262-1.191
	DD	20 (14.8%)	3 (6.8%)	0.461	1.667	0.429-6.475
	DD vs. ID+II			0.157	2.502	0.702-8.916
	I allele	167 (61.9%)	54 (61.4%)	Reference		
Female	D allele	103 (38.1%)	34 (38.6%)	0.978	0.993	0.604-1.632
		165	56			
	II	69 (41.8%)	28 (50%)	Reference		
	ID	69 (41.8%)	25 (44.6%)	0.715	1.126	0.596-2.127
	DD	27 (16.4%)	3 (5.4%)	0.041	3.783	1.057-13.536
	DD vs. ID+II			0.044	3.570	1.036-12.307
	I allele	207 (62.7%)	81 (72.3%)	Reference		
	D allele	123 (37.3%)	31 (27.7%)	0.059	1.574	0.982-2.523

CI, confidence interval; OR, odds ratio. <sup>a</sup> Logistic regression adjusted for age.

Case group versus control group.

**Table S2.** Correlations of genotype polymorphism in ACE1 rs4646994 with histological types of SCC and adenocarcinoma according to gender.

Gender	Genotype /allele	LUAD (n=282)	SCC (n=14)	p-Value <sup>a</sup>	OR	95%CI
Male		118	14			
	II	43 (36.4%)	7 (50%)	Reference		
	ID	57 (48.3%)	6 (42.9%)	0.363	1.751	0.524-5.857
	DD	18 (15.3%)	1 (7.1%)	0.492	2.169	0.239-19.728
	DD vs. ID+II			0.426	2.340	0.288-19.012
	I allele	143 (60.6%)	20 (71.4%)	reference		
	D allele	93 (39.4%)	8 (28.6%)	0.647	1.649	0.194-14.040

<b>Female</b>		164	0			
	II	69 (42.1%)	0	Reference		
	ID	69 (42.1%)	0	-	-	-
	DD	26 (15.9)	0	-	-	-
	DD vs. ID+II			-	-	-
	I allele	207 (63.1%)	0	Reference		
	D allele	121 (36.9%)	0	-	-	-

CI, confidence interval; OR, odds ratio. <sup>a</sup> Logistic regression adjusted for age.

LUAD group versus SCC group.

**Table S3.** Correlations of ACE1 rs4646994 genotype polymorphism with EGFR mutation in lung adenocarcinoma according to gender.

<b>Gender</b>	<b>Genotype /allele</b>	<b>EGFR+ (n=75)</b>	<b>EGFR (n=62)</b>	<b>p-Value <sup>a</sup></b>	<b>OR</b>	<b>95%CI</b>
<b>Male</b>		29	32			
	II	10 (34.5%)	11 (34.4%)	Reference		
	ID	18 (62.1%)	14 (43.8%)	0.612	1.335	0.436-4.086
	DD	1 (3.4%)	7 (21.9%)	0.129	0.171	0.018-1.670
	DD vs. ID+II			0.083	0.145	0.016-1.284
	I allele	38 (65.5%)	36 (56.2%)	Reference		
	D allele	20 (34.5%)	28 (43.8%)	0.253	0.662	0.325-1.344
<b>Female</b>		46	30			
	II	22 (47.8%)	11 (36.7%)	Reference		
	ID	19 (41.3%)	12 (40%)	0.759	0.848	0.296-2.409
	DD	5 (10.9%)	7 (23.32%)	0.176	0.384	0.096-1.534
	DD vs. ID+II			0.180	0.416	0.115-1.501
	I allele	63 (68.5%)	34 (56.7%)	Reference		
	D allele	29 (31.5%)	26 (43.3%)	0.190	0.630	0.315-1.257

CI, confidence interval; OR, odds ratio. <sup>a</sup> Logistic regression adjusted for age.

EGFR+ group versus EGFR group.

**Table S4.** Correlations of genotype polymorphism in ACE1 rs4646994 and lung cancer risk in patients with pulmonary nodules according to age.

<b>Age</b>	<b>Genotype /allele</b>	<b>Case (n=300)</b>	<b>Control (n=100)</b>	<b>p-Value <sup>a</sup></b>	<b>OR</b>	<b>95%CI</b>
<b>≤45</b>		48	17			
	II	20 (41.7%)	7 (41.2%)	Reference		
	ID	21 (43.8)	9 (52.9%)	0.669	0.767	0.227-2.590
	DD	7 (14.6)	1 (5.9%)	0.498	2.216	0.222-22.154
	DD vs. ID+II			0.399	2.573	0.287-23.077
	I allele	201 (63.8%)	50 (61.0%)	Reference		
	D allele	114 (36.2%)	32 (39.0%)	0.625	0.882	0.534-1.458
<b>&gt;45</b>		252	83			
	II	101 (40.1%)	34 (41.0%)	Reference		

ID	111 (44.0%)	44 (53.0%)	0.512	0.838	0.493-1.423
DD	40 (15.9%)	5 (6%)	0.030	3.111	1.119-8.651
DD vs. ID+II			0.014	3.423	1.284-9.126
I allele	313 (62.1%)	112 (67.5%)	Reference		
D allele	191 (37.9%)	54 (32.5%)	0.146	1.322	0.908-1.926

CI, confidence interval; OR, odds ratio. <sup>a</sup> Logistic regression adjusted for sex and age.

Case group versus control group.

**Table S5.** Correlations of genotype polymorphism in ACE1 rs4646994 with histological types of SCC and adenocarcinoma according to age.

Age	Genotype /allele	LUAD (n=282)	SCC (n=14)	<i>p</i> -Value <sup>a</sup>	OR	95%CI
≤45		48	0			
	II	20 (41.7%)	0		Reference	
	ID	21 (43.8%)	0	-	-	-
	DD	7 (14.6%)	0	-	-	-
	DD vs. ID+II	-	-	-	-	-
	I allele	61 (63.5%)	0		Reference	
	D allele	35 (36.5%)	0	-	-	-
>45		234	14			
	II	92 (39.3%)	7 (50%)		Reference	
	ID	105 (44.9%)	6 (42.9%)	0.458	1.556	0.484-4.996
	DD	37 (15.8%)	1 (7.1%)	0.342	2.872	0.326-25.268
	DD vs. ID+II			0.441	2.286	0.279-18.707
	I allele	289 (61.8%)	20 (71.4%)	Reference		
	D allele	179 (38.2%)	8 (28.6%)	0.277	1.615	0.680-3.835

CI, confidence interval; OR, odds ratio. <sup>a</sup> Logistic regression adjusted for sex.

LUAD group versus SCC group.

**Table S6.** Correlations of ACE1 rs4646994 genotype polymorphism with EGFR mutation in lung adenocarcinoma according to age.

Age	Genotype /allele	EGFR+ (n=75)	EGFR (n=62)	<i>p</i> -Value <sup>a</sup>	OR	95%CI
≤45		9	10			
	II	4 (44.4%)	3 (30%)		Reference	
	ID	5 (55.6%)	4 (40%)	0.942	0.929	0.126-6.842
	DD	0	3 (30%)	0.999	0	0
	DD vs. ID+II			0.999	0	0
	I allele	13 (72.2%)	10 (50%)		Reference	
	D allele	5 (27.8%)	10 (50%)	0.183	0.396	0.102-1.548
>45		66	52			
	II	28 (42.4%)	19 (36.5%)		Reference	
	ID	32 (48.5%)	22 (42.3%)	0.824	1.097	0.485-2.481
	DD	6 (9.1%)	11 (21.2%)	0.084	0.356	0.110-1.148

DD vs. ID+II			0.053	0.340	0.114-1.013
I allele	88 (66.7%)	60 (57.7%)		Reference	
D allele	44 (33.3%)	44 (42.3%)	0.175	1.451	0.848-2.484

CI, confidence interval; OR, odds ratio. <sup>a</sup> Logistic regression adjusted for sex.

EGFR+ group versus EGFR group.