Supplementary Table1. Four kinds of primers of present 13 studies

Author	Year	Forward (bp)	Reverse (bp)	Island(bp)
Dong et al (2007, Korea)	2007	chr16:82,660,749-82,660,767	chr16:82,660,652-82,660,673	chr16:82660651-82661813
Feng et al (2008, USA)	2008	chr16:82,660,749-82,660,767	chr16:82,660,652-82,660,673	chr16:82660651-82661813
Hanabata et al (2004, Japan)	2004	chr16:82,660,749-82,660,767	chr16:82,660,652-82,660,673	chr16:82660651-82661813
Hsu et al (2007, Taiwan)	2007	chr16:82,660,749-82,660,767	chr16:82,660,652-82,660,673	chr16:82660651-82661813
Jin et al (2009, Japan)	2009	chr16:82,627,104-82,627,124	chr16:82,627,187-82,627,206	chr16:82660651-82661813
Nikolaidis et al (2012, UK)	2012	chr16:82,660,654-82,660,671	chr16:82,660,705-82,660,726	chr16:82660651-82661813
Toyooka et al (2001, USA)	2001	chr16:82,660,749-82,660,767	chr16:82,660,652-82,660,673	chr16:82660651-82661813
Toyooka et al (2003, USA)	2003	chr16:82,660,749-82,660,767	chr16:82,660,652-82,660,673	chr16:82660651-82661813
Tsou et al (2007, USA)	2007	chr16:82,660,709-82,660,729	chr16:82,660,792-82,660,811	chr16:82660651-82661813
Ulivi et al (2006, Italy)	2006	chr16:82,660,749-82,660,767	chr16:82,660,652-82,660,673	chr16:82660651-82661813
Wang et al (2008, China)	2008	NA	NA	chr16:82660651-82661813
Zhai et al (2014, China)	2014	chr16:82,660,749-82,660,767	chr16:82,660,652-82,660,673	chr16:82660651-82661813
Zhang et al (2011, China)	2011	chr16:82,660,749-82,660,767	chr16:82,660,652-82,660,673	chr16:82660651-82661813

NA: not found in the article.

Supplementary Table 2. Differential CDH13 methylation, odds ratio between adenocarcinoma, squamous cell carcinoma and their counterparts from

Туре	Position	CpG site	МсаМ	МсоМ	Δβ	p-value ^a	p-value ^b
	chr16:82660670	cg08747377	0.32658	0.1609	0.16568	1.11E-51	4.43E-28
	chr16:82660727	cg05374412	0.23438	0.04392	0.19046	9.02E-77	1.29E-22
	chr16:82661421	cg08856946	0.2117	0.07414	0.13756	2.63E-68	1.21E-24
LUAD	chr16:82661521	cg13759328	0.28992	0.17442	0.11549	9.78E-61	1.29E-28
	chr16:82661638	cg09189772	0.28967	0.1819	0.10778	2.63E-49	9.12E-26
	chr16:82661725	cg19369556	0.27121	0.22947	0.04173	6.98E-09	6.44E-09
	chr16:82660670	cg08747377	0.23598	0.1609	0.07507	8.92E-12	1.61E-10
	chr16:82660727	cg05374412	0.12757	0.04392	0.08365	3.65E-33	6.34E-14
	chr16:82661421	cg08856946	0.14118	0.07414	0.06704	3.55E-30	6.01E-17
L030	chr16:82661521	cg13759328	0.24259	0.17442	0.06817	2.59E-26	1.71E-17
	chr16:82661638	cg09189772	0.23064	0.1819	0.04875	9.62E-10	1.51E-10
	chr16:82661725	cg19369556	0.22208	0.22947	0.00739	0.005638311	0.145187084

GSE39279 & GSE52401 dataset

McaM and McoM represent the mean of case methylation (Beta) and mean of control methylation (Beta). Methylation levels are calculated with formula: Beta = (M/M + U).

Position represents the chromosome position of each CpG site according to GRCh37/hg19.

P-value^a was calculated from Wilcoxon rank sum test after false discovery rate(FDR adjustment).

P-value^b was calculated from logistic regression analysis after false discovery rate(FDR adjustment).

Type	CpG site	Position	МсаМ	МсоМ	Λβ	p-value ^a	p-value ^b
	cq08747377	chr16:82660670	0.31	0.07	0.24	3.73E-5	0.009
	cg05374412	chr16:82660727	0.26	0.02	0.24	1.98E-5	0.03
	cg00806490	chr16:82660873	0.25	0.07	0.18	1.20E-5	0.009
LUAD	cg08856946	chr16:82661421	0.18	0.05	0.13	3.80E-5	0.02
	cg13759328	chr16:82661521	0.22	0.10	0.12	3.80E-5	0.01
	cg09189772	chr16:82661638	0.24	0.12	0.12	0.001	0.01
	cg19369556	chr16:82661725	0.20	0.17	0.03	0.85	0.52
	cg08747377	chr16:82660670	0.17	0.07	0.10	0.02	0.08
	cg05374412	chr16:82660727	0.10	0.02	0.08	0.16	0.21
	cg00806490	chr16:82660873	0.15	0.07	0.08	0.003	0.08
LUSC	cg08856946	chr16:82661421	0.11	0.05	0.06	0.14	0.17
	cg13759328	chr16:82661521	0.19	0.10	0.09	0.008	0.08
	cg09189772	chr16:82661638	0.18	0.12	0.06	0.24	0.27
	cg19369556	chr16:82661725	0.15	0.17	0.02	0.15	0.50

Supplementary Table 3. Differential methylation, odds ratio between adenocarcinoma, squamous cell carcinoma and their counterparts from

GSE56044 dataset

McaM and McoM represent the mean of case methylation (Beta) and mean of control methylation (Beta). Methylation levels are calculated with formula: Beta = (M/M + U).

Position represents the chromosome position of each CpG site according to GRCh37/hg19.

P-values^a are calculated from Wilcoxon rank sum test after false discovery rate (FDR adjustment).

P-value^b and OR^b and 95%Cl^b are from logistic regression analysis with P-value^b were also after false discovery rate (FDR adjustment).

	CpGsite	Sensitivity	Specificity	Accuracy	AUC
	cg08747377	0.884	0.774	0.82	0.866
LUAD VS.	cg05374412	0.924	0.886	0.898	0.936
Control	cg08856946	0.894	0.818	0.85	0.896
Control	cg09189772	0.87	0.752	0.8	0.828
	cg08747377	0.756	0.572	0.686	0.658
LU3C VS.	cg05374412	0.806	0.698	0.764	0.744
Control	cg08856946	0.758	0.7	0.734	0.722
Control	cg09189772	0.762	0.524	0.672	0.596
	cg08747377	0.784	0.768	0.776	0.816
LUAD vs. LUSC	cg05374412	0.824	0.832	0.828	0.87
	cg08856946	0.802	0.756	0.78	0.83
	cg09189772	0.776	0.742	0.762	0.78

Supplementary Table 4. Diagnosis sensitivity, specificity, accuracy and AUC based on logistic regression with fivefold cross-validation

Logistic regression was conducted to perform the diagnosis analysis. Sensitivity, specificity, accuracy and AUC were derived from the test result of the model

	QUADAS Question														
Study	1	2	3	4	5	6	7	8	9	10	11	12	13	14	Total Score
Dong et al (2007, Korea)	1	1	1	1	1	1	1	1	1	0	1	1	0	0	11
Feng et al (2008, USA)	1	1	1	1	1	1	1	1	1	0	1	1	1	0	12
Hanabata et al (2004, Japan)	1	1	1	1	1	1	1	1	1	0	1	1	0	0	11
Hsu et al (2007, Taiwan)	1	1	1	1	1	1	1	1	1	0	1	1	1	0	12
Jin et al (2009, Japan)	1	1	1	1	1	1	1	1	1	0	1	1	1	0	12
Nikolaidis et al (2012, UK)	1	1	1	1	1	1	1	1	1	0	1	1	0	0	11
Toyooka et al (2001, USA)	1	1	1	1	1	1	1	1	1	0	1	1	0	0	11
Toyooka et al (2003, USA)	1	1	1	1	1	1	1	1	1	0	1	1	0	0	11
Tsou et al (2007, USA)	1	1	1	1	1	1	1	1	1	0	1	1	1	0	12
Ulivi et al (2006, Italy)	1	1	1	1	0	1	1	1	1	0	1	1	0	0	10
Wang et al (2008, China)	1	1	1	1	1	1	1	1	1	0	1	1	1	0	12
Zhai et al (2014, China)	1	1	1	1	0	1	1	1	1	0	1	1	0	0	10
Zhang et al (2011, China)	1	1	1	1	1	1	1	1	1	0	1	1	0	0	11

Supplementary Table 5. The QUADAS results for the 13 publications in the meta-analysis

Supplementary Figure 1. Funnel plot to diagnosis of the publication bias



Study	TE	seTE	Odds Ratio	OR	95%-CI	W(fixed)	W(random)
Dong at al (2007, Karaa)	1 59	0.4580	1.00	4 85	[1 08- 11 01]	12.6%	11 /0/
Eong et al (2007, Kolea)	2.62	1.0669		4.00	[1.30, 11.31]	2.0%	2.0%
Fenglet al (2006, USA)	2.05	0.7700		0.07	[1.72, 112.44]	2.3%	5.0%
Hanabata et al (2004, Japan)	2.11	0.7720		8.27	[1.82; 37.01]	4.4%	5.3%
Hsu et al (2007, Taiwan)	1.44	0.4280		4.24	[1.83; 9.81]	14.5%	12.4%
Jin et al (2009, Japan)	2.79	0.7600		16.22	[3.66; 71.96]	4.6%	5.4%
Nikolaidis et al (2012, UK)	3.39	1.4609		29.75	[1.70; 521.15]	1.2%	1.7%
Toyooka et al(2001, USA)	2.15	0.8004		8.62	[1.80; 41.41]	4.1%	5.0%
Toyooka et al(2003, USA)	2.14	0.4703		8.51	[3.39; 21.41]	12.0%	11.0%
Tsou et al (2007, USA)	1.22	0.4366		3.39	[1.44; 7.97]	13.9%	12.1%
Ulivi et al (2006, Italy)	2.25	1.4678		9.46	[0.53; 168.06]	1.2%	1.7%
Wang et al (2008, China)	1.24	0.7668	+=	3.46	[0.77; 15.56]	4.5%	5.4%
Zhai et al (2014, China)	4.58	1.4555		- 97.62	[5.63; 1692.22]	1.3%	1.7%
Zhang et al (2011, China)	2.12	0.4366		8.31	[3.53; 19.56]	13.9%	12.1%
Filled: Feng et al (2008, USA)	0.81	1.0668		2.24	[0.28; 18.12]	2.3%	3.0%
Filled: Jin et al (2009, Japan)	0.65	0.7600	- 	1.92	[0.43; 8.51]	4.6%	5.4%
Filled: Nikolaidis et al (2012, UK)	0.04	1.4609		1.05	[0.06; 18.32]	1.2%	1.7%
Filled: Zhai et al (2014, China)	-1.14	1.4555—		0.32	[0.02; 5.53]	1.3%	1.7%
Fixed effect model				5.58	[4.05; 7.67]	100%	
Random effects model			♦	5.64	[3.84; 8.27]		100%
Heterogeneity: I-squared=21.2%, tau-s	quared=0.1	268, p=0.20	71				
				10			

Supplementary Figure 2. Combined estimates for the association between CDH13 methylation and NSCLC after trim-fill treatment.

Supplementary Figure 3. Sensitivity analyses of the overall effect by omitting a single study.

Study	Odds Ratio	OR	95%-CI
Omitting Dong et al (2007, Korea) Omitting Feng et al (2008, USA) Omitting Hanabata et al (2004, Japan) Omitting Hsu et al (2007, Taiwan) Omitting Jin et al (2009, Japan) Omitting Nikolaidis et al (2012, UK) Omitting Toyooka et al (2001, USA) Omitting Toyooka et al (2003, USA) Omitting Tsou et al (2007, USA) Omitting Ulivi et al (2006, Italy) Omitting Wang et al (2008, China) Omitting Zhai et al (2014, China) Omitting Zhang et al (2011, China)		7.84 7.26 7.37 7.04 7.16 7.20 7.20 7.36 7.36 7.36 7.38 7.65 6.80 7.29	[5.51; 11.16] [5.21; 10.13] [5.26; 10.31] [5.61; 11.48] [5.03; 9.87] [5.14; 9.97] [5.26; 10.29] [5.08; 10.20] [5.74; 11.77] [5.30; 10.26] [5.46; 10.71] [4.87; 9.50] [5.11; 10.39]
Fixed effect model	0.5 1 2	7.41	[5.34; 10.29]





The x-axis showed the different CpG sites in CDH13 gene and the y-axis shows the beta value of each CpG site to represent the methylation level of each CpG site.

Supplementary Figure 5. CpG sites on the Illumina Infinium HumanMethylation450 Beadchip array across CDH13 gene region from GSE56044 dataset.



The x-axis showed the different CpG sites in CDH13 gene and the y-axis shows the beta value of each CpG site to represent the methylation level of each CpG site.