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Original Article

Aberrant methylation of cell-free DNA as a promising biomarker for esophageal cancer

Huanqiang Wang[1,Δ], Congying Yang[6,Δ], Siyuan Wang[2,Δ], Tian Wang[1], Jingling Han[1], Kai Wei[1], Fucun Liu[1], Jida Xu[1], Xianzhen Peng[1,3,✉], Jianming Wang[3,4,5,✉]

[1] *Department of Public Health and Preventive Medicine;* [2] *Department of Clinical Medicine, Kangda College of Nanjing Medical University, Lianyungang, Jiangsu 222000, China;*
[3] *Departments of Epidemiology;* [4] *Department of Social Medicine and Health Education;* [5] *The Innovation Center for Social Risk Governance in Health, School of Public Health, Nanjing Medical University, Nanjing, Jiangsu 211166, China;*
[6] *Department of Pathology, The First People's Hospital of Lianyungang, Lianyungang, Jiangsu 222000, China*

Supplementary Table1 **Clinic information of specimens whose samples were used for Infinium Methylation 450k array.**

Specimen	Age(year)	Gender	TNM	G (histologic grade)	Tumor location	Stage
1	70	female	T1N0M0	G2	Lower	I
2	72	male	T1N0M0	G2	Middle	I
3	66	male	T1N0M0	G2	Middle	I
4	71	male	T2N0M0	G2	Middle	II
5	62	male	T1N0M0	G3	Middle	I

*Tumor stages were evaluated according to the TNM classification of the American Joint Committee on Cancer (AJCC).

Supplementary Table2 **Gene ontology annotation (GOA) analysis**

ID	Term	Function	Genes
GO:0007165	Signal transduction	The cellular process in which a signal is conveyed to trigger a change in the activity or state of a cell.	*ING2, IQGAP2*
GO:0007275	Multicellular organismal development	The biological process whose specific outcome is the progression of a multicellular organism over time from an initial condition (e.g. a zygote or a young adult) to a later condition (e.g. a multicellular animal or an aged adult).	*ADAMTS9, EBF3*
GO:0005737	Cytoplasm	All of the contents of a cell excluding the plasma membrane and nucleus, but including other subcellular structures.	*CDH13, AIM2, TRIT1, CASZ1*
GO:0016020	Membrane	Double layer of lipid molecules that encloses all cells, and, in eukaryotes, many organelles; may be a single or double lipid bilayer; also includes associated proteins	*TMEFF2*
GO:0005515	Protein binding	Interacting selectively and non-covalently with a nucleotide, any compound consisting of a nucleoside that is esterified with orthophosphate or an oligophosphate at any hydroxyl group on the ribose or deoxyribose	*ING2, IQGAP2, EBF3*

[Δ]These authors contributed equally to this work

[✉]Corresponding author: Xianzhen Peng, Department of Public Health and Preventive Medicine, Kangda College of Nanjing Medical University, Lianyungang, Jiangsu 222000, China. Tel:86-518-83083543. E-mail: xianzhenpeng@njmu.edu.cn; Jianming Wang, Department of Epidemiology, School of Public Health, Nanjing Medical University, Nanjing, Jiangsu 211166, China. Tel: 86-25-86868438. E-mail: jmwang@njmu.edu.cn.

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Table 2 **Gene ontology annotation (GOA) analysis (**continued)

ID	Term	Function	Genes
GO:0000166	Nucleotide binding	Interacting selectively and non-covalently with a nucleotide, any compound consisting of a nucleoside that is esterified with orthophosphate or an oligophosphate at any hydroxyl group on the ribose or deoxyribose.	*TRIT1*
GO:0005524	ATP binding	Interacting selectively and non-covalently with ATP, adenosine 5'-triphosphate, a universally important coenzyme and enzyme regulator.	*TRIT1*
GO:0003700	Sequence specific DNA binding transcription factor activity	Interacting selectively and non-covalently with a specific DNA sequence in order to modulate transcription.	*KLF6*
GO:0005509	Calcium ion binding	Interacting selectively and non-covalently with calcium ions (Ca2 +).	*CDH13*

Supplementary Table3 **Diagnostic information of cumulative methylation of specific genes in cell-free plasma DNA**

Gene	Cut-point	Sensitivity (%)	Specificity (%)	Correctly classified (%)
CASZ1	2.74	100.00	0.00	76.92
	2.95	100.00	33.33	84.62
	3.21	100.00	66.67	92.31
	3.82	100.00	100.00	100.00
	3.9	80.00	100.00	84.62
	4.01	70.00	100.00	76.92
	4.09	60.00	100.00	69.23
	4.17	50.00	100.00	61.54
	4.23	40.00	100.00	53.85
	4.33	20.00	100.00	38.46
	4.34	10.00	100.00	30.77
CDH13	1.04	100.00	0.00	76.92
	1.22	100.00	33.33	84.62
	1.56	100.00	66.67	92.31
	2.34	100.00	100.00	100.00
	2.8	70.00	100.00	76.92
	2.85	60.00	100.00	69.23
	2.9	50.00	100.00	61.54
	3.42	40.00	100.00	53.85
	3.54	30.00	100.00	46.15
	3.61	10.00	100.00	30.77
ING2	0.48	100.00	0.00	76.92
	0.81	100.00	33.33	84.62
	0.92	100.00	66.67	92.31
	2.28	100.00	100.00	100.00
	2.65	80.00	100.00	84.62
	2.71	70.00	100.00	76.92
	2.72	60.00	100.00	69.23
	2.75	50.00	100.00	61.54
	2.78	40.00	100.00	53.85
	2.8	20.00	100.00	38.46
	2.81	10.00	100.00	30.77