
C1	Normal 1	21915	NA	NA	NA	NA	NA	NA	NA	Jing Zhu
C2	Normal 2	25099	NA	NA	NA	NA	NA	NA	NA	[ref.17]
C3	Normal 3	392	NA	NA	NA	NA	NA	NA	NA	
C4	Normal 4	832	NA	NA	NA	NA	NA	NA	NA	
C5	Normal 5	7849	NA	NA	NA	NA	NA	NA	NA	
C6	Normal 6	10537	NA	NA	NA	NA	NA	NA	NA	

Supplementary Table 2. DNA Quantification by Qubit 3.0 Fluorometer

Sample Name	Conc. (ng/μl)	Volume (μl)	Quantity (μg)	QC Results
Patient 1	624.33	20	12.49	Pass
Patient 2	580.41	20	11.61	Pass
Patient 3	573.33	20	11.47	Pass
Patient 4	639.27	20	12.79	Pass
Patient 5	635.42	20	12.71	Pass
Patient 6	551.42	20	11.03	Pass

Supplementary Table 3. Quality Assessment of Sequencing Library

Sample Name	Size (bp)	Conc. (ng/ μ l)	Conc. (nmol/L)	Volume (μ l)	Total Amount (ng)
Patient 1	334	3.64	16.7	10	36.4
Patient 2	300	3.25	16.4	10	32.5
Patient 3	326	2.71	12.7	10	27.1
Patient 4	318	1.85	8.96	10	18.5
Patient 5	294	3.78	19.8	10	37.8
Patient 6	317	3.42	16.5	10	34.2

Notes: Sequencing library was determined by Agilent 2100 Bioanalyzer using the Agilent DNA 1000 chip kit (Agilent, part # 50671504).

Supplementary Table 4. Information of sequencing reads statistics

Sample Name	Q30	Raw Reads	Clean Reads	Clean Ratio	Mapped Reads	Mapping Ratio
Patient 1	92.42%	128,697,410	128,693,134	100.00%	119,218,714	92.64%
Patient 2	89.10%	135,715,212	135,710,618	100.00%	119,910,588	88.36%
Patient 3	92.71%	138,401,496	138,394,866	100.00%	127,378,834	92.04%
Patient 4	90.76%	117,604,018	117,599,772	100.00%	107,716,908	91.59%
Patient 5	89.72%	121,078,112	121,070,992	99.99%	113,477,028	93.72%
Patient 6	92.06%	127,668,464	127,653,804	99.99%	117,218,652	91.82%

Supplementary Table 5. eccDNA appeared repeatedly in at least 3 LUAD samples

eccDNA position	A1	A2	A3	A4	A5	A6	B1	B2	B3	B4	C1	C2	C3	C4	C5	C6
Chr10:127362840-127363066	5	0	0	0	6	10	0	0	0	0	0	0	0	0	0	0
Chr5-123032458-123032838	0	2	11	1	0	0	0	0	0	0	0	0	0	0	0	0
Chr18:22741002-22741204	0	0	0	2	11	1	0	0	0	0	0	0	0	0	0	0
Chr17:80024304-80024652	0	0	2	0	9	42	0	0	0	0	0	0	0	0	0	0
Chr3:194943264-194943686	0	1	0	9	6	0	0	12	0	0	0	0	0	0	0	0
Chr9:34169256-34169377	11	2	6	0	0	0	10	14	6	0	0	0	0	0	0	0
Chr13:113672394-113672557	0	0	32	34	38	78	60	0	58	135	0	0	0	0	0	0
Chr20:60314368-60314818	0	0	32	0	26	0	30	54	18	57	0	0	0	0	0	0
Chr20:58695019-58695338	1	60	0	24	168	4	28	42	28	39	0	0	0	0	0	0

Notes: Each column represents a sample, and each row represents an eccDNA. The number represents the sample's original split reads of a certain eccDNA in the sample.

Supplementary Table 6. The annotation results of eccDNA appeared repeatedly in LUAD samples

eccDNA position	Width	Annotation	Gene id	Transcript id	Distance to TSS	Gene name
Chr10-127362840-127363066	227	Intron	1793	Enst00000464466.1	114772	DOCK1
Chr5-123032458-123032838	381	Intron	5480	Enst00000306442.5	3887	PPIC
Chr18-22741002-22741204	203	Intron	101927571	Enst00000581177.1	-9437	RP11-370A5.1
Chr17-80024304-80024652	349	Intron	125058	Enst00000310924.7	11220	TBC1D16
Chr3-194943264-194943686	423	Distal intergenic	152002	Enst00000460582.1	143686	XXYLT1
Chr9-34169256-34169377	122	Distal intergenic	51271	Enst00000625521.2	-9628	UBAP1
Chr13-113672394-113672557	164	Intron	6011	Enst00000335678.7	5175	NA*
Chr20-60314368-60314818	451	Intron	693231	Enst00000385067.1	5894	MIR646
Chr20-58695019-58695338	320	Promoter (<=1kb)	100534593	Enst00000533788.1	598	NA*

Notes: Each row represents an eccDNA. TSS, the transcription start site. * NA represents eccDNA mapped to the unnamed regions.