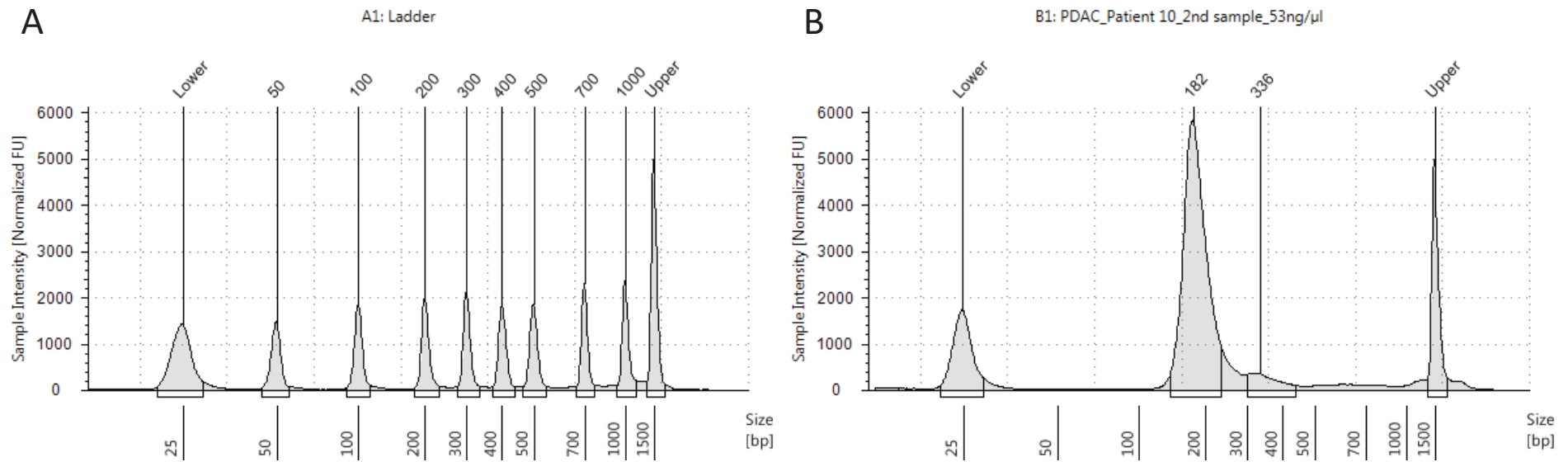


Supplementary Figure S1

Quality control of extracted cfDNA with TapeStation system. The electropherogram profiles are showing the electronic ladder (internal reference) (A) and three representative PDAC samples in the range of 0.49-4.76ng/μl (B-D). These PDAC samples are showing a broad peak at ~180bp, which represents the mononucleosomal fragment and a less abundant dinucleosomal fragment at ~330bp. There is little to no genomic DNA contamination detectable.



Supplementary Figure S2

Quality control of cfDNA with 53ng/μl concentration with TapeStation System. The electropherogram profiles are showing the ladder (internal reference) (A) and the cfDNA sample with 53ng/μl concentration (B). Despite of the high concentration, the electropherogram profile of this cfDNA reveals little to no genomic DNA contamination and shows a broad peak at ~180bp and a less abundant peak at ~330bp.

Supplementary Table S1: Pathogenic variants detected with GP15

Patient #	Sample	Gene Symbol	Amino Acid Change	Variant Frequency (%)	Detection threshold controls (GP15)	Codon Change
1	1st sample	KRAS	p.G12D	4.43	0.053	c.35G>A
	2nd sample	KRAS	p.G12D	2.01	0.053	c.35G>A
2	1st sample	PIK3CA	p.Q546L	4.40	0.000	c.1637A>T
		KRAS	p.G12V	6.96	0.000	c.35G>T
		TP53	p.R273H	1.91	0.050	c.818G>A
	2nd sample	PIK3CA	p.Q546L	0.00	0.000	c.1637A>T
		KRAS	p.G12V	0.00	0.000	c.35G>T
		TP53	p.R273H	0.00	0.050	c.818G>A
3	1st sample	PIK3CA	p.G1007V	0.25	0.104	c.3020G>T
		EGFR	p.Q791H	0.22	0.023	c.2373G>T
		PDGFRA	p.L839P	0.00	0.034	c.2516T>C
	2nd sample	PIK3CA	p.G1007V	1.58	0.104	c.3020G>T
		EGFR	p.Q791H	1.50	0.023	c.2373G>T
		PDGFRA	p.L839P	1.25	0.034	c.2516T>C
4	1st sample	KRAS	p.G12R	1.37	0.015	c.34G>C
		TP53	p.D208V	1.82	0.000	c.623_624delACinsTT
	2nd sample	KRAS	p.G12R	0.19	0.015	c.34G>C
		TP53	p.D208V	0.33	0.000	c.623_624delACinsTT
5	1st sample	MET	p.G1201V	2.06	0.212	c.3602G>T
	2nd sample	MET	p.G1201V	0.00	0.212	c.3602G>T
6	1st sample	/				
	2nd sample	/				
7	1st sample	KRAS	p.G12D	4.54	0.053	c.35G>A
		TP53	p.P152T	1.66	0.000	c.454C>A
		KRAS	p.A146T	0.19	0.049	c.437C>T
	2nd sample	KRAS	p.G12D	0.09	0.053	c.35G>A
		TP53	p.P152T	0.00	0.000	c.454C>A
		KRAS	p.A146T	0.15	0.049	c.437C>T
8	1st sample	KRAS	p.G12V	0.79	0.000	c.35G>T
	2nd sample	KRAS	p.G12V	0.17	0.000	c.35G>T
9	1st sample	/				
	2nd sample	/				
10	1st sample	KRAS	p.G12V	0.87	0.000	c.35G>T
	2nd sample	KRAS	p.G12V	0.43	0.000	c.35G>T
11	1st sample	KRAS	p.G12D	0.41	0.053	c.35G>A
	2nd sample	KRAS	p.G12D	0.12	0.053	c.35G>A

12	1st sample	KRAS	p.A146T	0.24	0.049	c.437C>T
	2nd sample	KRAS	p.A146T	0.00	0.049	c.437C>T
13	1st sample	KRAS	p.Q61R	21.73	0.037	c.182A>G
		TP53	p.F212SfsTer3	16.58	0.000	c.635_636delTT
	2nd sample	KRAS	p.Q61R	8.04	0.037	c.182A>G
		TP53	p.F212SfsTer3	2.90	0.000	c.635_636delTT
14	1st sample	KRAS	p.G12R	15.18	0.015	c.34G>C
		TP53	p.G245V	16.74	0.000	c.734G>T
	2nd sample	KRAS	p.G12R	0.87	0.015	c.34G>C
		TP53	p.G245V	1.67	0.000	c.734G>T
15	1st sample	KRAS	p.A134S	0.00	0.000	c.400G>T
		TP53	p.Y126D	1.41	0.009	c.376T>G
	2nd sample	KRAS	p.A134S	1.47	0.000	c.400G>T
		TP53	p.Y126D	0.36	0.009	c.376T>G
16	1st sample	KRAS	p.G12D	2.79	0.053	c.35G>A
		TP53	p.R282W	1.32	0.090	c.844C>T
	2nd sample	KRAS	p.G12D	1.83	0.053	c.35G>A
		TP53	p.R282W	1.10	0.090	c.844C>T
17	1st sample	KRAS	p.G12R	0.85	0.015	c.34G>C
	2nd sample	KRAS	p.G12R	0.00	0.015	c.34G>C
18	1st sample	/				
	2nd sample	/				
19	1st sample	/				
	2nd sample	/				
20	1st sample	/				
	2nd sample	/				
21	1st sample	KRAS	p.G12D	0.46	0.053	c.35G>A
	2nd sample	KRAS	p.G12D	0.08	0.053	c.35G>A

Supplementary Table S2: Pathogenic variants detected with GP50

Patient #	Sample	Gene Symbol	Amino Acid Change	Variant Frequency (%)	Detection threshold controls (GP50)	Codon Change
1	1st sample	KRAS	p.G12D	3.40	0.045	c.35G>A
		SMAD4	p.Y131D	1.84	0.008	c.392A>G
	2nd sample	KRAS	p.G12D	0.00	0.045	c.35G>A
		SMAD4	p.Y131D	0.00	0.008	c.392A>G
2	1st sample	PIK3CA	p.Q546L	4.17	0.040	c.1637A>T
		KRAS	p.G12V	5.91	0.000	c.35G>T
		TP53	p.R273H	4.71	0.086	c.818G>A
		SMAD4	p.Q256*	0.00	0.061	c.766C>T
	2nd sample	PIK3CA	p.Q546L	0.00	0.040	c.1637A>T
		KRAS	p.G12V	0.00	0.000	c.35G>T
		TP53	p.R273H	0.00	0.086	c.818G>A
		SMAD4	p.Q256*	0.56	0.061	c.766C>T
3	1st sample	/				
	2nd sample	/				
4	1st sample	KRAS	p.G12R	3.34	0.006	c.34G>C
		TP53	p.D208V	1.32	0.000	c.623_624delACinsTT
	2nd sample	KRAS	p.G12R	0.00	0.006	c.34G>C
		TP53	p.D208V	0.45	0.000	c.623_624delACinsTT
5	1st sample	SMAD4	p.R496H	0.00	0.035	c.1487G>A
	2nd sample	SMAD4	p.R496H	0.43	0.035	c.1487G>A
6	1st sample	SMAD4	p.R445*	0.17	0.062	c.1333C>T
		CDKN2A	p.Y129C	0.23	0.029	c.385A>G
	2nd sample	SMAD4	p.R445*	0.24	0.062	c.1333C>T
		CDKN2A	p.Y129C	0.48	0.029	c.385A>G
7	1st sample	KRAS	p.G12D	2.40	0.045	c.35G>A
		TP53	p.P152T	1.51	0.054	c.454C>A
	2nd sample	KRAS	p.G12D	0.00	0.045	c.35G>A
		TP53	p.P152T	0.00	0.054	c.454C>A
8	1st sample	KRAS	p.G12V	1.01	0.000	c.35G>T
	2nd sample	KRAS	p.G12V	0.00	0.000	c.35G>T
9	1st sample	/				
	2nd sample	/				
10	1st sample	KRAS	p.G12V	0.25	0.000	c.35G>T
	2nd sample	KRAS	p.G12V	0.96	0.000	c.35G>T
11	1st sample	KRAS	p.G12D	0.22	0.045	c.35G>A
	2nd sample	KRAS	p.G12D	0.00	0.045	c.35G>A

12	1st sample	/					
	2nd sample	/					
13	1st sample	KRAS	p.Q61R	23.41	0.149	c.182A>G	
		TP53	p.F212SfsTer3	17.22	0.000	c.635_636delTT	
	2nd sample	KRAS	p.Q61R	9.21	0.149	c.182A>G	
		TP53	p.F212SfsTer3	4.65	0.000	c.635_636delTT	
14	1st sample	KRAS	p.G12R	15.94	0.006	c.34G>C	
		TP53	p.G245V	16.13	0.057	c.734G>T	
	2nd sample	KRAS	p.G12R	1.55	0.006	c.34G>C	
		TP53	p.G245V	0.87	0.057	c.734G>T	
15	1st sample	TP53	p.Y126D	0.94	0.014	c.376T>G	
	2nd sample	TP53	p.Y126D	0.33	0.014	c.376T>G	
16	1st sample	KRAS	p.G12D	2.75	0.045	c.35G>A	
		TP53	p.R282W	1.83	0.088	c.844C>T	
	2nd sample	KRAS	p.G12D	1.58	0.045	c.35G>A	
		TP53	p.R282W	1.38	0.088	c.844C>T	
17	1st sample	TP53	p.R282W	0.47	0.088	c.34G>C	
		CDKN2A	p.Y129C	0.40	0.029	c.385A>G	
	2nd sample	TP53	p.R282W	0.00	0.088	c.34G>C	
		CDKN2A	p.Y129C	0.00	0.029	c.385A>G	
18	1st sample	/					
	2nd sample	/					
19	1st sample	TP53	p.R282W	0.43	0.088		
	2nd sample	TP53	p.R282W	0.00	0.088		
20	1st sample	/					
	2nd sample	/					
21	1st sample	SMAD4	p.R135*	0.64	0.073	c.403C>T	
	2nd sample	SMAD4	p.R135*	0.00	0.073	c.403C>T	