Supplementary table 1. Relative expression of miRNA in plasma and bile among individuals with PDAC, CP, and controls

Candidate miRNA	PDAC	CP	Normal	P value	PDAC vs. CP	PDAC vs. Normal	CP vs. Normal
Training Cohort - Plasma							
	N=40	**N=30**	**N=24**				
miR-10b	13.1 (13.2)	0.9 (1.2)	1.1 (0.6)	<0.001	<0.001	<0.001	1.000
	21.2 (30.8)	1.2 (0.8)	1.0 (0.4)				
miR-21	0.9 (0.7)	1.2 (1.7)	0.8 (0.7)	0.426			
	1.0 (0.8)	1.5 (1.4)	1.0 (0.6)				
miR-30c	8.4 (11.8)	1.3 (3.0)	0.8 (0.8)	<0.001	<0.001	<0.001	0.126
	14.5 (18.8)	2.2 (2.1)	1.0 (0.7)				
miR-106b	8.4 (13.6)	1.4 (1.2)	0.9 (0.9)	<0.001	<0.001	<0.001	0.378
	14.2 (12.3)	1.4 (0.9)	1.0 (0.6)				
miR-132	1.9 (2.8)	1.0 (1.2)	0.7 (0.7)	0.001	0.073	0.001	0.341
	2.4 (1.8)	1.5 (1.4)	1.0 (0.9)				
miR-155	164.1 (826.8)	1.1 (2.1)	1.1 (0.8)	<0.001	<0.001	<0.001	0.558
	1051.1 (2080.2)	2.4 (2.9)	1.0 (0.6)				
miR-181a	2.0 (2.4)	1.0 (1.3)	1.0 (0.7)	0.007	0.016	0.025	1.000
	2.6 (3.5)	1.1 (0.9)	1.0 (0.5)				
miR-181b	1.8 (1.9)	0.5 (0.5)	0.9 (0.6)	<0.001	<0.001	0.001	0.096
	2.2 (1.5)	0.7 (0.7)	1.0 (0.6)				
miR-196a	2.0 (3.1)	0.6 (0.9)	0.8 (1.2)	<0.001	<0.001	<0.001	1.000
	2.8 (2.5)	1.2 (1.7)	1.0 (0.9)				
miR-212	7.3 (6.7)	1.0 (1.5)	0.8 (0.9)	<0.001	<0.001	<0.001	0.578
	7.3 (5.0)	1.7 (1.9)	1.0 (0.9)				
Training cohort - bile							
	N=25	**N=23**	**N=22**				
miR-10b	10.2 (8.6)	0.7 (1.0)	1.0 (0.5)	<0.001	<0.001	<0.001	1.000
	19.5 (27.0)	1.1 (0.7)	1.0 (0.4)				
miR-21	1.4 (1.4)	1.3 (1.3)	1.0 (0.6)	0.151			
	1.5 (1.0)	1.5 (1.1)	1.0 (0.4)				
miR-30c	11.3 (8.5)	1.5 (1.2)	1.0 (0.6)	<0.001	<0.001	<0.001	0.051
	13.7 (9.4)	1.6 (1.1)	1.0 (0.5)				
miR-106b	19.9 (19.7)	1.2 (1.3)	1.1 (0.4)	<0.001	<0.001	<0.001	0.622
	25.0 (19.9)	1.5 (1.1)	1.1 (0.6)				
miR-132	1.2 (1.6)	1.0 (1.1)	1.1 (0.7)	0.535			
	1.5 (1.1)	1.1 (1.0)	1.2 (1.2)				
miR-155	24.7 (20.2)	1.1 (1.2)	0.9 (0.4)	<0.001	<0.001	<0.001	0.761
	31.5 (26.8)	1.2 (0.8)	1.0 (0.4)				
miR-181a	1.5 (1.1)	1.2 (1.1)	1.0 (0.4)	0.016	0.115	0.015	1.000

	1.8 (1.3)	1.2 (0.8)	1.0 (0.4)				
miR-181b	1.1 (1.0)	1.3 (1.1)	1.0 (0.8)	0.297			
	1.5 (1.1)	1.5 (1.0)	1.1 (0.7)				
miR-196a	1.6 (1.0)	1.2 (0.9)	0.9 (0.8)	0.009	0.198	0.006	0.527
	1.9 (1.3)	1.3 (0.9)	1.0 (0.5)				
miR-212	10.7 (8.5)	1.0 (0.9)	0.8 (0.7)	<0.001	<0.001	<0.001	1.000
	12.2 (6.6)	1.2 (0.8)	1.1 (0.5)				
Validation Cohort - Plasma							
	N=29	**N=37**	**N=38**				
miR-10b	31.5 (58.5)	1.0 (1.0)	1.0 (0.7)	<0.001	<0.001	<0.001	1.000
	70.4 (93.4)	1.2 (0.7)	1.0 (0.6)				
miR-30c	11.6 (12.7)	1.3 (1.2)	0.9 (1.1)	<0.001	<0.001	<0.001	0.942
	13.1 (10.0)	1.4 (0.8)	1.3 (1.0)				
miR-106b	19.4 (12.8)	1.1 (1.4)	0.7 (1.0)	<0.001	<0.001	<0.001	0.851
	22.4 (16.7)	1.2 (1.0)	0.9 (0.7)				
miR-155	80.2 (717.6)	1.5 (1.7)	1.0 (0.5)	<0.001	<0.001	<0.001	<0.001
	841.2 (1428.2)	2.0 (1.6)	1.1 (0.8)				
miR-212	13.9 (12.4)	1.2 (1.1)	0.8 (0.7)	<0.001	<0.001	<0.001	0.003
	17.4 (12.7)	1.5 (0.8)	0.9 (0.5)				
Validation cohort - bile							
	N=28	**N=28**	**N=33**				
miR-10b	9.6 (7.1)	1.0 (0.7)	1.0 (0.6)	<0.001	<0.001	<0.001	1.000
	14.0 (14.8)	1.1 (0.7)	1.0 (0.4)				
miR-30c	7.3 (5.9)	1.1 (1.0)	1.0 (0.5)	<0.001	<0.001	<0.001	1.000
	10.4 (10.0)	1.3 (0.9)	1.0 (0.4)				
miR-106b	11.3 (12.4)	1.2 (1.1)	1.1 (0.7)	<0.001	<0.001	<0.001	1.000
	16.0 (16.5)	1.3 (0.8)	1.1 (0.5)				
miR-155	21.0 (25.9)	0.9 (1.0)	0.8 (0.8)	<0.001	<0.001	<0.001	0.468
	31.6 (28.4)	1.2 (0.8)	1.0 (0.7)				
miR-212	8.1 (6.1)	0.9 (0.4)	1.0 (0.4)	<0.001	<0.001	<0.001	1.000
	9.4 (5.4)	0.9 (0.3)	0.9 (0.4)				

All miRNA levels are nonparametric and hence median (interquartile range) is reported. We also include mean (standard deviation) in gray font for descriptive purposes. P-values are obtained based using the Kruskal-Wallis test and pairwise p-values are adjusted using the Bonferroni multiple comparison approach.

Supplementary Table 2. Performance characteristics of miRNA for distinguishing PDAC from CP and control subjects (training cohort, n=95)

| Candidate miRNA	PDAC vs. CP	PDAC vs. Control	CP vs. Control	PDAC vs. Other	Threshold
Plasma					
miR-10b	0.982	1.000	0.494	**0.980**	**3.579**
miR-21	0.589	0.485	0.572	0.556	
miR-30c	0.902	0.984	0.625	**0.938**	**4.873**
miR-106b	0.998	1.000	0.609	**0.999**	**2.92**
miR-132	0.659	0.757	0.634	0.703	
miR-155	0.971	0.979	0.601	**0.975**	**10.68**
miR-181a	0.687	0.698	0.495	0.692	
miR-181b	0.873	0.786	0.680	0.834	
miR-196a	0.763	0.773	0.466	0.767	
miR-212	0.878	0.927	0.596	**0.900**	**2.013**
Bile					
miR-10b	0.974	0.965	0.458	**0.970**	**3.497**
miR-21	0.485	0.645	0.646	0.578	
miR-30c	0.991	1.000	0.678	**0.996**	**3.933**
miR-106b	0.983	0.991	0.597	**0.987**	**5.261**
miR-132	0.590	0.562	0.538	0.576	
miR-155	0.986	0.995	0.586	**0.990**	**5.232**
miR-181a	0.671	0.733	0.569	0.701	
miR-181b	0.550	0.580	0.636	0.513	
miR-196a	0.637	0.772	0.599	0.703	
miR-212	0.981	0.982	0.538	**0.981**	**4.163**

AUC = Area under the curve;

Threshold denotes the miRNA expression level corresponding to the AUC for PDAC vs. All other (CP + controls).

For reference, accuracy is graded from fail to excellent based on the following AUC thresholds:

Accuracy	AUC
Excellent	≥ 0.90
Good	≥ 0.80
Fair	≥ 0.70
Poor	≥ 0.60
Fail	< 0.60

Supplemental Figure 1. Plasma and bile miRNA expression by smoking status
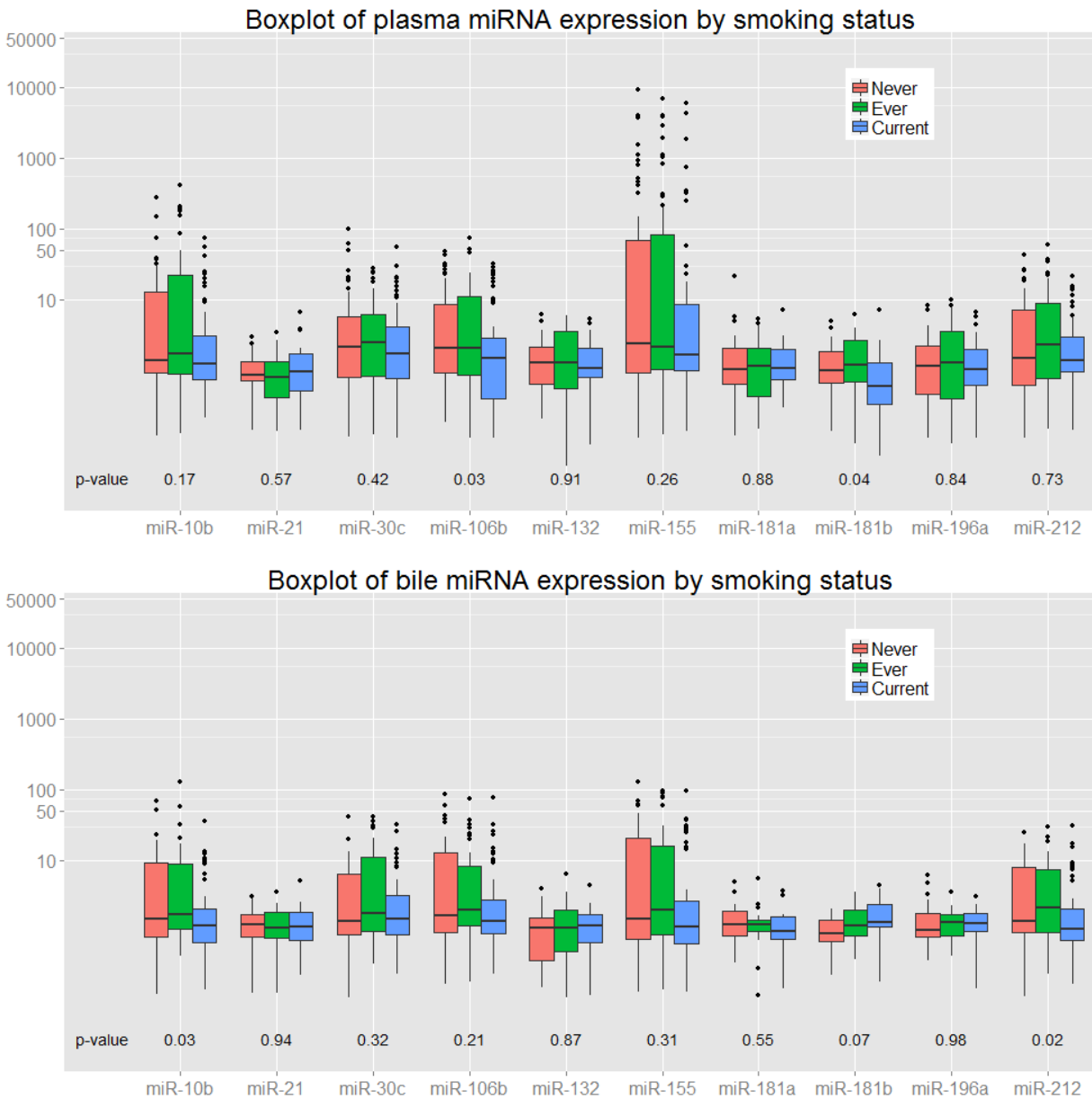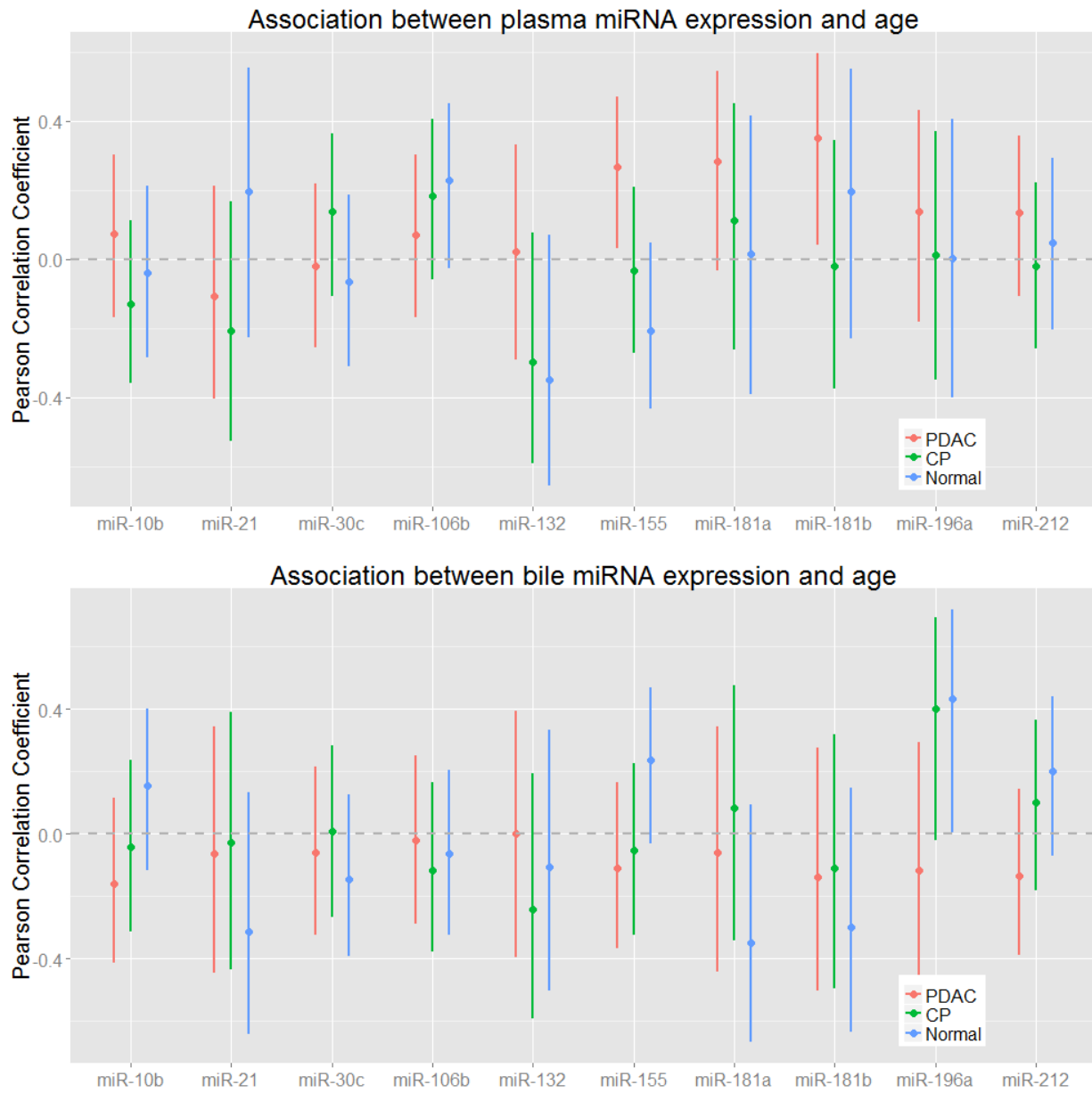

Differential expression of miRNA in plasma (top panel) and bile (bottom panel) is illustrated as a function of smoking status (never, ever, or current). The inclusion of smoking status in our regression models to establish Signature Panels did not impact the results.

Supplemental Figure 2. Plasma and bile miRNA expression by serum bilirubin elevation
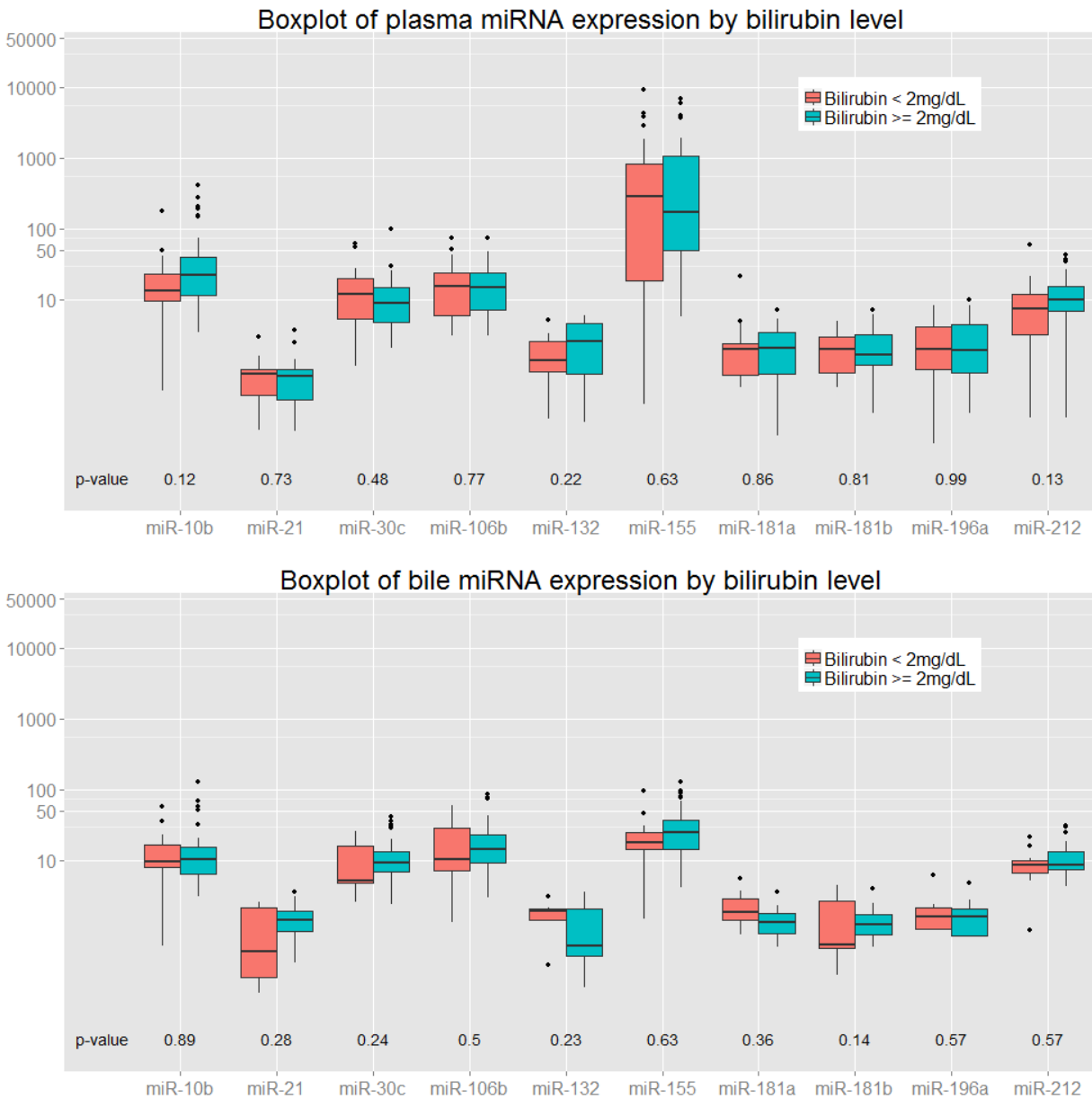
Differential expression of miRNA in plasma (top panel) and bile (bottom panel) is illustrated as a function of serum bilirubin elevation, defined as > 2mg/dL. The inclusion of serum bilirubin in our regression models to establish Signature Panels did not impact the results.

Supplemental Figure 3. Plasma and bile miRNA expression by age

Differential expression of miRNA in plasma (top panel) and bile (bottom panel) is illustrated as a function of age. The inclusion of age in our regression models to establish Signature Panels did not impact the results.