



Supplementary Materials: Identification of a miRNA Based-Signature Associated with Acute Coronary Syndrome: Evidence from the FLORINF Study

Table S1. Baseline characteristics of the derivation cohort.

	ACS (n=6)	Controls (n=6)	<i>p</i> value
Gender (male %)	100	100	1
Age (years)	59.1 ± 5.5	59.6 ± 5.8	0.89
Diabetes (%)	0	0	1
Obesity (%)	0	16.67	1
Dyslipidaemia (%)	83.3	83.3	1
Hypertension (%)	50	83.3	0.54
Smoking (%)	16.6	16.6	1
Heredity (%)	16.6	33.3	1
Total Cholesterol (mg/mL)	192 ± 48.6	201.2 ± 26.6	0.25
LDL-cholesterol (mg/dL)	117.5 ± 47.2	122.5 ± 31.9	0.78
HDL-cholesterol (mg/dL)	47.8 ± 7.7	56.5 ± 24.4	0.96
Beta-blockers agents (%)	16.6	16.6	1
ACE inhibitors (%)	16.3	33.3	1
Antiplatelet agents(%)	16.6	16.6	1
Statins (%)	50	33.3	1
ARA II inhibitors (%)	16.6	50	0.54

Data are shown as mean ± standard deviation or n (%). LDL; Low-density lipoprotein, HDL; High-density lipoprotein;. ACE; Angiotensin-converting-enzyme, ARA; Angiotensin II receptor.

Table S2. $-\Delta\text{Ct}$ values and fold changes of each detected circulating miRNA (144/758) in ACS and control groups

miRNA	ACS (n=6)		Controls (n=6)		Fold change
	Mean $-\Delta\text{Ct}$	SD	Mean $-\Delta\text{Ct}$	SD	
000268_dme-miR-7	-9.677	5.019	-8.305	5.092	0.386
000377_hsa-let-7a	-5.775	5.429	-8.303	5.966	5.768
000379_hsa-let-7c	-7.965	5.822	-5.625	4.685	0.197
000390_hsa-miR-15b	-7.377	7.006	-0.098	0.678	0.006
000391_hsa-miR-16	3.034	7.437	5.864	2.533	0.141
000395_hsa-miR-19a	-4.582	2.546	-4.371	2.816	0.864
000396_hsa-miR-19b	1.583	1.553	2.301	1.431	0.608
000397_hsa-miR-21	-7.475	5.690	-4.467	7.161	0.124
000402_hsa-miR-24	1.543	0.725	2.745	1.228	0.435
000403_hsa-miR-25	-8.146	5.152	-7.540	5.937	0.657
000405_hsa-miR-26a	-6.560	6.719	-0.717	2.752	0.017
000407_hsa-miR-26b	3.095	1.734	3.206	0.817	0.926
000408_hsa-miR-27a	-12.284	2.065	-9.905	4.235	0.192
000411_hsa-miR-28	-2.720	5.177	-1.280	1.557	0.368
000419_hsa-miR-30c	-13.430	1.056	-7.620	3.960	0.018
000420_hsa-miR-30d	-3.465	7.484	1.324	1.090	0.036
000431_hsa-miR-92a	1.098	2.179	2.722	2.685	0.324
000433_hsa-miR-95	-2.407	1.029	-6.413	5.705	16.064
000436_hsa-miR-99b	-4.204	6.552	0.160	0.900	0.049
000437_hsa-miR-100	-5.986	5.393	-7.480	6.759	2.817
000439_hsa-miR-103	-4.472	9.618	-2.772	8.575	0.308
000442_hsa-miR-106b	-5.131	5.638	-4.377	6.909	0.593
000452_hsa-miR-127	-8.191	5.188	-4.872	4.167	0.100
000454_hsa-miR-130a	-6.932	6.769	-6.778	6.208	0.899
000456_hsa-miR-130b	-9.656	5.145	-6.612	6.198	0.121
000457_hsa-miR-132	-11.388	2.503	-4.813	5.207	0.010
000464_hsa-miR-142-3p	-1.935	5.233	-3.890	4.890	3.875
000468_hsa-miR-146a	3.497	2.003	5.670	0.707	0.222
000473_hsa-miR-150	-2.118	5.757	0.914	7.848	0.122
000475_hsa-miR-152	-10.205	4.367	-6.276	5.483	0.066
000491_hsa-miR-192	0.693	7.135	2.677	1.266	0.253
000494_hsa-miR-195	-6.520	4.821	-6.953	3.389	1.350
000497_hsa-miR-197	-7.095	9.901	2.395	8.366	0.001
000507_hsa-miR-203	-9.532	6.873	-8.434	6.195	0.467
000510_hsa-miR-206	-11.603	4.394	-9.744	6.213	0.276

000512_hsa-miR-210	-2.455	8.182	-2.023	8.404	0.742
000515_hsa-miR-212	-7.675	6.316	-1.392	0.993	0.013
000524_hsa-miR-221	-2.522	4.887	-0.524	4.145	0.250
000542_hsa-miR-326	-12.482	2.467	-6.501	1.532	0.016
000543_hsa-miR-328	-4.082	9.676	5.216	1.152	0.002
000545_hsa-miR-331	-5.339	5.937	-3.366	4.848	0.255
000554_hsa-miR-361	-4.434	7.050	-2.916	5.810	0.349
000563_hsa-miR-374	-5.392	3.625	-7.698	4.460	4.948
000564_hsa-miR-375	-11.667	4.568	-6.347	5.773	0.025
000565_hsa-miR-376a	-11.774	3.277	-6.744	5.395	0.031
000572_hsa-miR-382	-9.879	4.844	-9.410	4.836	0.723
000580_hsa-miR-20a	-1.819	5.784	0.613	0.765	0.185
000587_hsa-miR-29c	-9.105	4.400	-6.259	5.901	0.139
000602_hsa-miR-30b	-9.190	5.878	-1.553	6.570	0.005
001006_RNU48	1.858	3.554	1.166	1.209	1.615
001014_hsa-miR-20b	-2.248	7.901	1.937	1.112	0.055
001027_hsa-miR-432#	-5.763	7.700	-4.864	6.662	0.536
001028_hsa-miR-433	-13.430	1.056	-10.230	3.698	0.109
001090_mmu-miR-93	2.536	7.238	3.801	0.946	0.416
001094_RNU44	-2.281	5.333	-1.519	0.967	0.590
001097_hsa-miR-146b	0.344	6.130	0.829	0.941	0.714
001141_mmu-miR-451	-3.173	7.214	-2.229	5.274	0.520
001159_hsa-miR-518d	-5.593	8.049	3.079	1.023	0.002
001167_hsa-miR-520a	-3.721	10.572	0.328	6.519	0.060
001187_mmu-miR-140	0.815	1.691	-0.137	1.361	1.935
001278_hsa-miR-486	-5.729	7.901	-0.209	6.862	0.022
001285_hsa-miR-487b	-2.564	5.296	-3.713	0.942	2.218
001319_mmu-miR-374-5p	-1.422	5.346	0.981	1.073	0.189
001515_hsa-miR-660	-9.781	4.860	-6.220	6.401	0.085
001516_hsa-miR-425-5p	-6.625	6.978	-5.596	6.620	0.490
001518_hsa-miR-532	-10.274	4.219	-5.746	3.662	0.043
001531_hsa-miR-564	0.244	7.119	1.414	1.449	0.444
001541_hsa-miR-548b	1.937	7.875	2.799	1.181	0.550
001562_hsa-miR-629	-5.748	5.216	-6.506	4.969	1.691
001592_hsa-miR-642	-5.260	8.932	0.257	1.427	0.022
001614_hsa-miR-572	-11.230	5.287	-4.445	7.939	0.009
001630_mmu-miR-491	-0.800	1.749	-1.595	1.169	1.735
001821_hsa-miR-484	-12.197	2.270	-5.110	7.094	0.007
001973_U6 rRNA	4.773	2.910	3.023	1.040	3.364
001986_hsa-miR-766	3.354	1.360	2.480	1.178	1.833

001988_hsa-miR-598	-7.421	4.466	-9.553	3.960	4.384
001992_hsa-miR-668	-7.487	6.318	-5.459	6.386	0.245
001998_hsa-miR-769-5p	6.061	2.771	5.933	1.460	1.093
002087_hsa-miR-505#	-3.331	1.913	-4.865	2.334	2.896
002088_hsa-miR-636	-6.646	4.484	-1.908	1.170	0.037
002098_hsa-miR-223#	-1.419	5.336	-0.177	1.177	0.423
002099_hsa-miR-224	-7.537	6.119	-7.824	6.818	1.220
002122_hsa-miR-376c	-9.986	4.635	-2.903	2.476	0.007
002161_hsa-miR-324-3p	1.150	1.201	0.468	1.082	1.604
002169_hsa-miR-106a	1.131	1.097	1.619	1.533	0.713
002186_hsa-miR-345	-1.266	5.878	0.101	1.310	0.388
002187_hsa-miR-942	0.119	6.107	-0.325	6.212	1.360
002193_hsa-miR-886-5p	-8.841	6.575	-4.164	4.322	0.039
002196_hsa-miR-99b#	-2.337	5.198	-0.128	1.582	0.216
002215_hsa-miR-196b	-5.771	5.760	-7.221	4.554	2.731
002216_hsa-miR-128a	-7.821	5.576	-10.031	5.137	4.629
002227_hsa-miR-323-3p	-10.066	4.557	-12.158	3.794	4.263
002228_hsa-miR-126	1.424	6.706	4.976	1.944	0.085
002234_hsa-miR-140-3p	-9.762	5.168	-1.845	2.913	0.004
002245_hsa-miR-122	-7.704	5.741	-7.380	7.690	0.799
002246_hsa-miR-133a	-9.599	5.692	-4.810	6.544	0.036
002248_hsa-miR-142-5p	-8.191	5.581	-6.838	5.657	0.392
002249_hsa-miR-143	-9.913	5.191	-8.637	5.189	0.413
002258_hsa-miR-340	-4.643	4.890	-4.485	1.782	0.896
002259_hsa-miR-340#	-0.217	1.668	-3.708	5.356	11.246
002260_hsa-miR-342-3p	-2.855	11.252	2.193	1.310	0.030
002271_hsa-miR-185	-5.458	5.597	-3.574	4.913	0.271
002275_hsa-miR-370	-4.109	6.968	-4.591	7.225	1.396
002276_hsa-miR-222	-11.360	5.303	-6.117	6.453	0.026
002277_hsa-miR-320	5.054	1.525	2.556	8.542	5.651
002278_hsa-miR-145	-2.644	4.981	-0.100	1.040	0.172
002282_hsa-let-7g	-0.431	5.768	0.811	0.997	0.423
002283_hsa-let-7d	2.279	1.454	-1.555	5.790	14.256
002285_hsa-miR-186	3.624	1.490	2.871	0.912	1.686
002289_hsa-miR-139-5p	-2.206	1.332	0.931	0.813	0.114
002295_hsa-miR-223	5.308	0.995	5.822	2.561	0.700
002296_hsa-miR-885-5p	-0.967	5.755	1.261	1.911	0.214
002299_hsa-miR-191	2.463	7.175	5.270	2.450	0.143
002302_hsa-miR-425#	0.938	4.348	-1.153	1.524	4.261

002304_hsa-miR-199a-3p	-10.337	4.095	-8.549	3.751	0.290
002308_hsa-miR-17	2.508	7.300	6.148	0.624	0.080
002313_hsa-miR-139-3p	-8.601	6.768	0.327	1.109	0.002
002323_hsa-miR-454	-6.891	6.708	-6.357	7.307	0.691
002324_hsa-miR-744	-1.803	5.088	-0.710	1.545	0.469
002338_hsa-miR-483-5p	-6.233	7.314	1.906	1.120	0.004
002340_hsa-miR-423-5p	-5.053	6.198	-0.363	1.333	0.039
002349_hsa-miR-574-3p	-5.431	5.591	-5.253	3.904	0.884
002365_hsa-miR-494	-6.174	6.314	-9.009	5.145	7.131
002367_hsa-miR-193b	-1.638	8.715	3.191	2.057	0.035
002376_hsa-miR-543	-3.137	5.034	-7.387	6.591	19.025
002392_hsa-miR-301b	-9.955	5.060	-8.940	5.542	0.495
002400_hsa-miR-520c-3p	3.064	9.505	9.594	3.205	0.011
002406_hsa-let-7e	-1.778	8.460	3.032	1.014	0.036
002422_hsa-miR-18a	-5.861	5.266	-4.359	4.222	0.353
002432_hsa-miR-625#	-2.967	10.605	-6.931	1.163	15.597
002434_hsa-miR-628-3p	-3.662	4.426	-5.396	3.753	3.326
002436_hsa-miR-629	-8.731	4.965	-9.574	3.817	1.795
002439_hsa-miR-23a#	4.514	2.853	3.244	1.430	2.411
002442_hsa-miR-25#	-9.447	5.642	-10.258	4.912	1.754
002443_hsa-miR-26a-1#	-9.480	4.338	-10.183	3.549	1.627
002658_hsa-miR-338-5P	-9.581	3.655	-10.592	3.160	2.015
002768_hsa-miR-1233	-9.655	5.724	-1.145	1.197	0.003
002779_hsa-miR-1271	-10.040	3.318	-11.760	3.384	3.293
002838_hsa-miR-1291	-3.668	4.956	-7.870	6.956	18.405
002844_hsa-miR-320b	-5.907	5.544	-5.822	3.688	0.943
002847_hsa-miR-1180	-8.235	5.344	-9.625	4.245	2.622
002883_hsa-miR-1274a	-0.787	6.233	-2.823	8.597	4.103
002884_hsa-miR-1274b	9.493	1.203	9.816	1.328	0.799
002895_hsa-miR-720	5.359	1.094	4.061	1.436	2.459

Circulating miRNAs were detected by using the TaqMan Open Array technology in plasma of ACS patients (n=6) and controls (n=6). Data are shown as relative miRNA expression levels and normalized using the global mean normalization method and expressed as $-\Delta\Delta Ct$. The expression fold change are expressed as $2^{(-\Delta\Delta Ct)}$ in which values represent the fold change miRNA expression of ACS patients relative to miRNA expression of control subjects.

Table S3. Interaction of medical treatment with miRNA expression level.

	Statins	ARA II inhibitors
mir-122	0.35	0.96
mir-150	0.95	0.44
mir-16	0.48	0.63
mir-195	0.67	0.41
mir-92a	0.24	0.56

ARA II ; Angiotensin II receptor. The logistic models were adjusted on statins or ARA II inhibitors and a statistical interaction was sought for each miRNA analyzed.

Table S4. Receiver operating characteristic (ROC) curve analysis comparing predictive of selected circulating miRNAs individually or in combination.

	AUC	95 % CI	<i>p value</i>
MiRNAs			
miR-122	0.655	(0.574-0.736)	-
miR-150	0.665	(0.585-0.745)	-
miR-195	0.680	(0.601-0.759)	-
miR-92a	0.623	(0.541-0.706)	-
miR-16	0.688	(0.610-0.767)	-
miR-122+miR-150	0.722	(0.644-0.799)	0.08
miR-122+miR-195	0.737	(0.661-0.813)	0.02
miR-122+miR-92a	0.690	(0.610-0.771)	0.23
miR-122+miR-16	0.732	(0.655-0.809)	0.03
miR-150+miR-92a	0.678	(0.595-0.760)	0.35
miR-150+miR-195	0.743	(0.667-0.818)	0.01
miR-150+miR-16	0.733	(0.656-0.809)	0.03
miR-195+miR-92a	0.701	(0.621-0.780)	0.47
miR-195+miR-16	0.707	(0.629-0.785)	0.24
miR-16+miR-92a	0.706	(0.627-0.785)	0.11
miR-122+miR-150+miR-92a	0.726	(0.648-0.804)	0.04
miR-122+miR-150+miR-195	0.776	(0.705-0.847)	0.003
miR-122+miR-150+miR-16	0.760	(0.687-0.834)	0.005
miR-150+miR-92a+miR-195	0.754	(0.679-0.829)	0.009
miR-150+miR-92a+miR-16	0.738	(0.661-0.814)	0.04
miR-16+miR-195+miR-92a	0.721	0.643-0.798)	0.15
miR-122+miR-195+miR-92a+miR-16	0.762	(0.689-0.835)	0.005
miR-122+miR-150+miR-195+miR-92a	0.778	(0.706-0.849)	0.002
miR-122+miR-150+miR-195+miR-16	0.785	(0.714-0.855)	0.003
miR-150+miR-195+miR-92a+miR-16	0.757	(0.683-0.831)	0.007
miR-122+miR-150+miR-195+miR-92a+miR-16	0.774	0.702-0.845)	0.003

