

**Table S1.** Variations of training measures/cardiorespiratory fitness, body composition and metabolic parameters before and after the 12-week training intervention program

Variable	Intervention Effect		
	<i>BDC</i> <i>Mean ± SD</i>	<i>PTDC</i> <i>Mean ± SD</i>	<i>Paired Samples Test</i> <i>P value</i>
VO2 peak (ml)	2952.5±736.1	3268.6±776.9	.000
VO2 peak/weight (ml/kg)	28.0±6.0	32.9±6.7	.000
HR (bpm)	72.7±10.7	62.0±9.8	.000
SBP (mmHg)	126.9±14.2	126.5±12.4	.818
DBP mmHg)	74.2±10.4	68.6±10.1	.003
DAI (kcal/die)	2058.9±652.1	1657.4±529.8	.000
Weight (kg)	105.3±14.4	99.4±14.4	.000
BMI (kg/mq)	35.6±4.4	33.6±4.5	.000
Waist (cm)	113.3±11.6	109.3±12.4	.000
FM (kg)	38.0±9.5	32.7±9.4	.000
FM (%)	36.5±8.3	33.2±8.8	.000
FFM (kg)	67.3±13.7	66.6±13.8	.240
FFM (%)	63.5±8.3	66.7±8.8	.000
Glucose (mg/dl)	98.7±9.3	96.9±8.8	.145
Insulin (μU/ml)	10.2±5.2	9.6±10.0	.651
HOMA index	2.5±1.4	2.4±2.8	.715
IGF1 (ng/ml)	207.2±76.3	208.9±74.6	.788
Cortisol (ng/ml)	96.5±34.2	85.6±25.9	.072
hsCRP (mg/dl)	.3±.4	.4±.5	.444
Total-C (mg/dl)	220.0±37.2	202.0±37.0	.001
LDL-C (mg/dl)	145.3±30.1	129.7±33.7	.001
HDL-C (mg/dl)	50.0±13.0	48.2±10.9	.163
Triglycerides (mg/dl)	123.6±71.4	120.9±72.6	.811
Irisin (μg/ml)	6.5±1.3	5.6±1.1	.000
FNDC5 gene expression (RQ)	1.3±.4	1.3±.6	.596
VO2, Volume of Oxygen; HR, Heart rate; SBP, Systolic Blood Pressure; DBP, Diastolic Blood Pressure; DCI, Daily Calorie Intake; BMI, Body Mass Index; Waist, Waist circumference; FM, Fat Mass; FFM, Free Fat Mass; HOMA IR index, HOmeostasis Model Assessment Insulin Resistance; IGF1, Insulin-like Growth Factor 1; hsCRP, high-sensitivity C-Reactive Protein; Total-C, Total Cholesterol; LDL-C, LDL Cholesterol calculated using Friedewald's Equation; HDL-C, HDL Cholesterol. BDC, Baseline Data Collection; PTDC, Post Training Data Collection. Data analysed with Paired Samples Test and expressed as means±SD.			

**Table S2.** Bivariate Correlation Analyses between Irisin Plasma Levels or FNDC5 Gene Expression and Clinical Characteristics of Participants before and after the 12-week Training Program

		Irisin (µg/ml)						FNDC5 gene expression (RQ)					
		BDC		PTDC		Change PTDC vs BDC		BDC		PTDC		Change PTDC vs BDC	
		Rho	P value	Rho	P value	Rho	P value	Rho	P value	Rho	P value	Rho	P value
Age (years)		.065	.723	-.086	.644	-.157	.399	-.300	.114	-.534	.003	-.244	.211
Education (years)		.068	.710	.052	.780	.020	.914	-.134	.487	.246	.208	.199	.311
Max. weight in adulthood (kg)		-.257	.216	-.440	.031	-.201	.346	.229	.294	-.002	.992	-.119	.597
Metabolic Syndrome score (n)		-.059	.749	-.181	.331	.060	.749	.019	.924	.097	.625	.074	.709
		median [IQ range]		median [IQ range]		median [IQ range]		median [IQ range]		median [IQ range]		median [IQ range]	
Sex	male	5.6	.005	5.0	.001	-.5	.892	1.4	.988	1.1	.104	-.1	.164
	female	6.8		6.3		-.9		1.3		1.4		.1	
Overweight/obesity in childhood	no	6.19	.677	5.22	.482	-.51	.726	1.21	.392	1.28	.815	.17	.482
	yes	6.43		6.01		-.79		1.41		1.21		-.13	
Overweight/obesity at puberty/menarche	no	5.58	.158	4.79	.251	-.43	.581	1.15	.319	1.24	.704	.16	.649
	yes	6.47		5.85		-.82		1.41		1.22		-.07	
Previous attempts to weight loss	no	5.60	.238	5.44	.877	-.46	.725	2.82	.016	1.88	.455	-.18	.818
	yes	6.29		5.67		-.65		1.31		1.22		.06	
Elevated Glucose criteria	no	6.39	.455	5.88	.247	-.99	.520	1.33	.813	1.19	.910	-.12	.667
	yes	6.19		5.47		-.50		1.30		1.22		.10	
Insulin Resistance according to HOMA IR model	<2.0	6.04	.823	5.22	.653	-1.19	.200	1.29	.101	1.17	.599	.00	.956
	≥2.0	6.21		5.89		-.36		1.54		1.36		.07	
Hypertension criteria	no	6.58	.536	5.66	.830	-.50	.468	1.32	.897	1.15	.274	.06	.618
	yes	5.89		5.51		-.65		1.37		1.32		.11	
Lipid criteria	no	6.15	.716	5.72	.296	-.65	.751	1.32	.799	1.21	.745	.01	.672
	yes	6.37		4.93		-.51		1.44		1.17		.07	
Metabolic Syndrome	<3.0	6.15	.863	5.75	.164	-.50	.952	1.37	.512	1.17	.654	-.12	.598
	≥3.0	6.20		4.91		-.68		1.21		1.28		.10	
Metabolic Syndrome, revised NCEP ATP III criteria for Metabolic Syndrome*; Elevated Glucose criteria, revised NCEP/ATP III criteria for elevated Glucose (Fasting Glucose ≥100 mg/dl and/or on drug treatment for elevated glucose); Hypertension criteria, revised NCEP/ATP III criteria for hypertension (history of hypertension and/or drug treatment for elevated blood pressure and/or blood pressure ≥130/85 mm Hg); Lipid criteria, revised NCEP/ATP III criteria for Lipid (TG ≥150 mg/dL and/or HDL-C <40 mg/dL in male or <50 mg/dL in female or On drug treatment for elevated triglycerides); BDC, Baseline Data Collection; PTDC, Post Training Data Collection. Data are expressed as Spearman's Rho or median [IQ, interquartile range] unless otherwise stated.													

\*Grundy SM, Cleeman JI, Daniels SR, Donato KA, Eckel RH, Franklin BA, Gordon DJ, Krauss RM, Savage PJ, Smith SC Jr. et al. Diagnosis and management of the metabolic syndrome: an American Heart Association/National Heart. Lung. and Blood Institute Scientific Statement. Circulation. 2005;112(17):2735–52.

**Table S3.** Bivariate Correlation Analyses between Irisin Plasma Levels or FNDC5 Gene Expression and Physical capacities/Training measures

		Irisin (µg/ml)						FNDC5 gene expression (RQ)					
		BDC		PTDC		Change PTDC vs BDC		BDC		PTDC		Change PTDC vs BDC	
		Rho	P value	Rho	P value	Rho	P value	Rho	P value	Rho	P value	Rho	P value
Number session (n)				.413	.021	.298	.104			.210	.283	.043	.828
Time for session (min)				-.228	.217	.030	.871			.027	.891	.061	.759
EEE/session (kcal/session)				-.422	.018	.091	.626			-.198	.313	-.150	.447
EEE/minute (kcal/min)				-.138	.459	.035	.850			-.204	.297	-.183	.352
EEE/weight/session (kcal/kg/session)				.141	.450	.098	.600			.082	.678	.077	.698
VO <sub>2</sub> peak (ml)	BDC	-.374	.035	-.422	.018	.088	.637	-.062	.751	-.196	.316	-.193	.326
	PTDC			-.372	.039	.139	.455			-.214	.274	-.150	.447
	Change PTDC vs BDC			-.036	.846	.078	.676			-.115	.558	.038	.849
VO <sub>2</sub> peak/weight (ml/kg)	BDC	-.243	.180	-.286	.119	.082	.660	-.063	.747	-.186	.344	-.203	.300
	PTDC			-.240	.194	.104	.578			-.253	.194	-.187	.342
	Change PTDC vs BDC			-.027	.884	.062	.742			-.247	.205	-.135	.493
HR (bpm)	BDC	-.042	.821	.258	.162	.363	.045	-.024	.903	.301	.120	.301	.120
	PTDC			.305	.095	.267	.147			.030	.881	.062	.754
	Change PTDC vs BDC			.014	.941	-.180	.333			-.395	.037	-.301	.120
SBP (mmHg)	BDC	-.177	.331	-.109	.559	.059	.754	.141	.467	.090	.649	-.073	.710
	PTDC			.207	.265	.159	.392			.208	.289	.133	.499
	Change PTDC vs BDC			.454	.010	.055	.767			.136	.489	.188	.337
DBP (mmHg)	BDC	-.141	.440	-.032	.863	.158	.396	-.077	.690	-.076	.702	-.062	.752
	PTDC			-.074	.691	-.107	.566			.009	.965	.001	.994
	Change PTDC vs BDC			-.019	.921	-.228	.218			-.027	.891	-.052	.795
DCI (kcal/die)	BDC	-.171	.349	-.152	.416	.096	.608	.168	.384	.070	.725	-.157	.426
	PTDC			-.221	.231	.134	.473			.068	.729	.011	.954
	Change PTDC vs BDC			-.136	.465	.080	.669			.037	.853	.342	.075
EEE, Energy Expenditure Exercise; VO <sub>2</sub> , Volume of Oxygen; HR, Heart rate; SBP, Systolic Blood Pressure; DBP, Diastolic Blood Pressure; DCI, Daily Calorie Intake. BDC, Baseline Data Collection; PTDC, Post Training Data Collection. Data are expressed as Spearman's Rho.													

**Table S4.** Bivariate Correlation Analyses between Irisin Plasma Levels or FND5 Gene Expression and Anthropometric and Body Composition Measures

		Irisin (μg/ml)						FNDc5 gene expression (RQ)					
		BDC		PTDC		Change PTDC vs BDC		BDC		PTDC		Change PTDC vs BDC	
		Rho	P value	Rho	P value	Rho	P value	Rho	P value	Rho	P value	Rho	P value
Weight (kg)	BDC	-.356	.045	-.330	.070	.070	.709	.067	.730	-.018	.929	-.014	.944
	PTDC			-.296	.106	.030	.871			.090	.649	.093	.637
	Change PTDC vs BDC			.126	.501	-.038	.840			.249	.202	.210	.284
BMI (kg/mq)	BDC	-.019	.917	.271	.140	.299	.102	.156	.418	.183	.350	.094	.636
	PTDC			.247	.180	.229	.215			.228	.243	.124	.529
	Change PTDC vs BDC			-.018	.925	-.077	.680			.241	.216	.227	.246
Waist (cm)	BDC	-.252	.164	-.092	.623	.123	.511	.091	.638	-.259	.183	-.257	.187
	PTDC			-.025	.895	.224	.225			-.136	.490	-.230	.239
	Change PTDC vs BDC			.179	.336	.177	.342			.211	.282	.093	.640
FM (kg)	BDC	.118	.520	.210	.257	.060	.746	.267	.162	.463	.013	.221	.259
	PTDC			.255	.166	-.008	.966			.434	.021	.218	.265
	Change PTDC vs BDC			.057	.760	-.205	.267			.253	.194	.221	.259
FM (%)	BDC	.379	.032	.432	.015	-.064	.732	.168	.384	.506	.006	.359	.061
	PTDC			.419	.019	-.080	.668			.460	.014	.260	.182
	Change PTDC vs BDC			.092	.621	-.148	.427			.253	.194	.230	.239
FFM (kg)	BDC	-.454	.009	-.518	.003	.072	.700	-.092	.634	-.298	.124	-.204	.299
	PTDC			-.490	.005	.083	.658			-.236	.227	-.163	.407
	Change PTDC vs BDC			-.016	.930	-.015	.936			.264	.175	.175	.372
FFM (%)	BDC	-.376	.034	-.432	.015	.064	.732	-.174	.367	-.506	.006	-.359	.061
	PTDC			-.418	.019	.085	.649			-.428	.023	-.224	.252
	Change PTDC vs BDC			-.063	.737	.157	.399			-.175	.373	-.165	.402
BMI, Body Mass Index; Waist, Waist circumference; FM, Fat Mass; FFM, Free Fat Mass. BDC, Baseline Data Collection; PTDC, Post Training Data Collection. Data are expressed as Spearman's Rho.													

**Table S5.** Bivariate Correlation Analyses between Irisin Plasma Levels or FNDC5 Gene Expression and Metabolic Measures

		Irisin (µg/ml)						FNDC5 gene expression (RQ)					
		BDC		PTDC		Change PTDC vs BDC		BDC		PTDC		Change PTDC vs BDC	
		Rho	P value	Rho	P value	Rho	P value	Rho	P value	Rho	P value	Rho	P value
Glucose (mg/dl)	BDC	-.057	.758	-.005	.980	.257	.163	-.194	.313	.085	.669	.172	.380
	PTDC			.023	.903	.107	.567			.105	.593	.217	.268
	Change PTDC vs BDC			.024	.899	-.200	.280			.028	.888	.003	.989
Insulin (µU/ml)	BDC	-.093	.612	.066	.725	.322	.077	.136	.483	.136	.489	.040	.840
	PTDC			-.095	.611	.174	.348			.094	.635	.021	.914
	Change PTDC vs BDC			-.123	.510	-.007	.968			-.080	.685	-.108	.584
HOMA IR index	BDC	-.127	.488	.029	.877	.357	.049	.106	.583	.210	.284	.132	.503
	PTDC			-.130	.484	.187	.313			.086	.664	.026	.894
	Change PTDC vs BDC			-.142	.445	-.056	.766			-.101	.610	-.131	.505
IGF1 (ng/ml)	BDC	.068	.711	-.177	.340	-.231	.210	-.010	.960	.313	.105	.327	.089
	PTDC			-.197	.288	-.041	.826			.273	.161	.336	.080
	Change PTDC vs BDC			.243	.188	.415	.020			.159	.418	.122	.538
Cortisol (ng/ml)	BDC	-.057	.757	-.321	.078	-.135	.467	.084	.666	-.094	.636	-.139	.480
	PTDC			.125	.503	-.105	.575			-.031	.875	.171	.385
	Change PTDC vs BDC			.440	.013	.075	.687			.152	.440	.414	.029
hsCRP (mg/dl)	BDC	.355	.046	.280	.127	-.116	.534	-.109	.572	.360	.060	.367	.054
	PTDC			.155	.406	-.174	.348			.269	.167	.169	.391
	Change PTDC vs BDC			-.260	.157	-.124	.507			-.069	.727	-.142	.472
Total-C (mg/dl)	BDC	.018	.921	-.053	.778	.163	.382	-.226	.239	-.163	.407	-.084	.670
	PTDC			.042	.821	.024	.897			.005	.980	.170	.388
	Change PTDC vs BDC			.076	.684	-.143	.442			.140	.477	.201	.304
LDL-C (mg/dl)	BDC	.063	.732	-.094	.615	.073	.696	-.245	.201	-.284	.144	-.171	.385
	PTDC			-.040	.829	-.049	.794			-.151	.445	.038	.847
	Change PTDC vs BDC			-.109	.560	-.221	.232			.117	.553	.282	.145
HDL-C (mg/dl)	BDC	.210	.249	.365	.044	.081	.663	.033	.863	.188	.337	.125	.527
	PTDC			.515	.003	.084	.653			.200	.307	.195	.319
	Change PTDC vs BDC			.193	.298	-.132	.478			.054	.784	-.022	.910
Triglycerides (mg/dl)	BDC	.007	.970	-.183	.324	-.051	.786	-.237	.215	.007	.971	.025	.901
	PTDC			-.202	.276	-.094	.614			-.106	.593	-.130	.511
	Change PTDC vs BDC			.109	.560	.013	.943			-.005	.980	.012	.952
HOMA IR index, HOmeostasis Model Assessment Insulin Resistance; IGF1, Insulin-like Growth Factor 1; hsCRP, high-sensitivity C-Reactive Protein; Total-C, Total Cholesterol; LDL-C, LDL Cholesterol calculated using Friedewald's Equation; HDL-C, HDL Cholesterol. BDC, Baseline Data Collection; PTDC, Post Training Data Collection. Data are expressed as Spearman's Rho.													

**Table S6.** Changes in anthropometrics, body composition, training and metabolic measures stratified by median level of irisin change after 12-week of training program among obese healthy participants.

Measures	Group	Intervention		Intervention Effect			Intervention x Group effect		
	<i>above/below median change Irisin</i>	<i>BDC Mean±SD</i>	<i>PTDC Mean±SD</i>	<i>Change within group MD (95% CI)</i>	<i>P value</i>	<i>Partial η2</i>	<i>Change between group MD (95% CI)</i>	<i>P value</i>	<i>Partial η2</i>
VO2 peak (ml)	<i>below median</i>	2852.4±753.0	3133.5±756.8	300.5 (211.5 – 389.4)	.0001	.622	281.1 (173.3 – 388.9)	.659	.007
	<i>above median</i>	3059.2±754.1	3379.0±819.0				319.8 (165.6 – 474.1)		
VO2 peak/weight (ml/kg)	<i>below median</i>	27.7±6.9	32.1±7.4	4.8 (3.6 – 5.9)	.0001	.713	4.4 (3.0 – 5.8)	.570	.011
	<i>above median</i>	28.6±5.2	33.6±6.2				5.1 (3.1 – 7.1)		
HR (bpm)	<i>below median</i>	68.5±9.7	59.0±8.2	-10.8 (-13.9 – -7.6)	.0001	.626	-9.5 (-14.7 – -4.3)	.414	.023
	<i>above median</i>	77.3±10.1	65.2±10.7				-12.1 (-16.0 – -8.2)		
DBP mmHg)	<i>below median</i>	73.4±10.5	70.3±9.8	-5.7 (-9.2 – -2.2)	.002	.282	-3.2 (-8.3 – 2.0)	.142	.073
	<i>above median</i>	75.1±10.6	66.8±10.4				-8.3 (-13.4 – -3.1)		
DAI (kcal/die)	<i>below median</i>	2022.7±657.1	1592.4±578.4	-411.0 (-625.2 – -196.7)	.0001	.347	-430.3 (-712.6 – -148.0)	.855	.001
	<i>above median</i>	2143.3±660.5	1751.6±488.5				-391.6 (-743.3 – -39.9)		
Weight (kg)	<i>below median</i>	103.3±13.3	98.1±13.0	-5.9 (-7.8 – -4.0)	.0001	.583	-5.3 (-8.0 – -2.5)	.494	.016
	<i>above median</i>	106.8±16.1	100.3±16.5				-6.5 (-9.3 – -3.7 )		
BMI (kg/mq)	<i>below median</i>	34.7±4.4	33.0±4.4	-2.0 (-2.7 – -1.4)	.0001	.583	-1.8 (-2.7 – -.8)	.460	.019
	<i>above median</i>	36.5±4.4	34.2±4.6				-4.1 (-17.6 – 25.8)		
Waist (cm)	<i>below median</i>	111.2±9.0	106.4±8.2	-5.1 (-13.7 – 3.5)	.0001	.425	-4.8 (-7.0 – -2.6)	.370	.028
	<i>above median</i>	115.6±13.9	112.3±15.4				-3.2 (-6.3 – -.2)		
FM (kg)	<i>below median</i>	37.8±11.0	33.3±10.3	-5.5 (-7.3 – -3.7)	.0001	.565	-4.5 (-7.0 – -2.0)	.265	.043
	<i>above median</i>	38.6±8.4	32.1±9.1				-6.5 (-9.4 – -3.6)		
FM (%)	<i>below median</i>	36.6±9.4	34.0±9.3	-3.4 (-4.7 – -2.0)	.0001	.475	-2.6 (-4.0 – -1.1)	.235	.048
	<i>above median</i>	36.5±7.3	32.3±8.5				-4.2 (-6.6 – -1.7 )		
FFM (kg)	<i>below median</i>	65.7±13.6	64.7±13.3	-.5 (-1.7– .6)	.360	.029	-1.0 (-1.9 – -.1)	.398	.025
	<i>above median</i>	68.2±14.3	68.2±14.9				.0 (-2.3 – 2.2)		
FFM (%)	<i>below median</i>	63.4±9.5	65.8±9.2	3.3 (1.9 – 4.7)	.0001	.448	2.4 (.9 – 3.9)	.197	.057
	<i>above median</i>	63.5±7.3	67.7±8.5				4.2 (1.7 – 6.7)		
Total-C (mg/dl)	<i>below median</i>	220.0±27.6	204.6±30.6	-18.1 (-28.3 – -7.9)	.001	.313	-15.4 (-31.2 – .4)	.592	.010
	<i>above median</i>	220.0±46.4	199.3±43.7				-20.8 (-34.9 – -6.7)		
LDL-C (mg/dl)	<i>below median</i>	146.9±25.4	132.8±28.4	-15.6 (-24.3 – -6.9)	.001	.316	-14.1 (-27.7 – -.5)	.727	.004
	<i>above median</i>	143.5±35.2	126.4±39.4				-17.1 (-29.1 – -5.1)		

VO2, Volume of Oxygen; HR, Heart rate; DBP, Diastolic Blood Pressure; DCI, Daily Calorie Intake; BMI, Body Mass Index; Waist, Waist circumference; FM, Fat Mass; FFM, Free Fat Mass; Total-C, Total Cholesterol; LDL-C, LDL Cholesterol calculated using Friedewald's Equation. BDC, Baseline Data Collection; PTDC, Post Training Data Collection. Analysis performed with General Linear Model (GLM) Repeated Measures, Within-Subjects and Between-Subjects test. Mean ± standard deviation (SD); median deviation (MD) and 95% confidence intervals (95% CI).