

Resistance training rejuvenates aging skin by reducing circulating inflammatory factors and enhancing dermal extracellular matrices

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Extended Data 1. Characteristics of participants in the aerobic training and resistance training groups

	All (n = 56)	AT (n = 26)	RT (n = 30)	p-value
Age, y	48.5 ± 5.2	49.5 ± 5.1	47.7 ± 5.1	0.19
Regular menstruation: Yes, n (%)	27 (48)	10 (38)	17 (57)	0.17 ^a
Dietary intake				
Energy, kcal/day	1805.4 ± 319.2	1837.1 ± 241.8	1774 ± 381.5	0.48
Protein, g/day	73.2 ± 13.4	73.6 ± 10.8	72.9 ± 15.8	0.85
Fat, g/day	68.9 ± 16.3	71.1 ± 13.6	66.8 ± 18.6	0.34
Carbohydrate, g/day	214.0 ± 40.9	217.4 ± 33.1	210.8 ± 47.7	0.56
Skin aging parameters				
Skin elasticity, Ur/Uf	0.32 ± 0.05	0.32 ± 0.05	0.32 ± 0.05	0.60
Dermal thickness, mm	1.74 ± 0.16	1.71 ± 0.19	1.77 ± 0.14	0.18
Upper dermal LEP, %	27.0 ± 13.9	27.9 ± 15.4	26.3 ± 12.7	0.69
Body composition				
Height, m	1.61 ± 0.05	1.60 ± 0.06	1.61 ± 0.05	0.77
Body weight, kg	54.4 ± 6.1	54.2 ± 6.5	54.6 ± 5.8	0.84
BMI, kg/m ²	21.1 ± 1.6	21.0 ± 1.7	21.1 ± 1.5	0.94
AppLTM, kg	15.4 ± 1.8	15.4 ± 2.0	15.4 ± 1.7	0.87
TotalLTM, kg	36.5 ± 3.7	36.7 ± 4.1	36.4 ± 3.4	0.8
Body fat, kg	15.6 ± 4.1	15.2 ± 3.9	15.9 ± 4.4	0.57
BMC, kg	2.28 ± 0.30	2.25 ± 0.32	1.31 ± 0.28	0.47
Physical capacity				
VO _{2peak} , mL/kg/min	28.0 ± 4.8	27.1 ± 0.9	28.7 ± 0.9	0.20
1-RM, kg				
Chest press	11.5 ± 3.3	11.2 ± 3.2	11.8 ± 3.3	0.19
Shoulder press	15.7 ± 3.7	14.9 ± 3.8	16.3 ± 3.6	0.49
Arm curl	15.2 ± 3.4	15.0 ± 3.9	15.4 ± 3	0.30
Rowing	22.1 ± 4.0	21.7 ± 4.9	22.5 ± 3.1	0.30
Leg curl	43.4 ± 8.9	42.0 ± 10.1	44.6 ± 7.8	0.44
Leg extension	68.2 ± 17.8	65.5 ± 18.9	70.5 ± 16.7	0.15

Values show the means ± standard deviations (SDs). Statistical analyses were performed with two-sided independent *t* tests and ^achi-squared test to compare the aerobic training and resistance training groups. AppLTM, appendicular lean soft tissue mass; AT, aerobic training; BMC, bone mineral content; BMI, body mass index; LEP, low echogenic pixel; RT, resistance training; TotalLTM, total lean soft tissue mass; VO_{2peak}, peak oxygen uptake; 1-RM, one-repetition maximum

Extended Data 2. Differences in the effect of aerobic training and resistance training on skin aging parameters, body composition, and physical capacity

	ANCOVA 1 ^a			ANCOVA 2 ^b			ANCOVA 3 ^c		
	AT (n = 26)	RT (n = 30)	p value	AT (n = 26)	RT (n = 30)	p value	AT (n = 26)	RT (n = 30)	p value
Skin aging parameters									
ΔSkin elasticity, Ur/Uf	+0.045 ± 0.008	+0.056 ± 0.007	0.29	+0.042 ± 0.007	+0.058 ± 0.007	0.13	+0.043 ± 0.008	+0.057 ± 0.007	0.16
ΔDermal thickness, mm	-0.014 ± 0.023	+0.040 ± 0.021	< 0.10	-0.015 ± 0.023	+0.041 ± 0.022	< 0.10	-0.014 ± 0.023	+0.041 ± 0.022	< 0.10
ΔUpper dermal LEPs, %	-12.1 ± 2.4	-11.0 ± 2.2	0.98	-12.1 ± 2.4	-11.0 ± 2.2	0.98	-12.1 ± 2.4	-11.0 ± 2.2	0.88
Body composition									
ΔBody weight, kg	-0.73 ± 0.26	-0.067 ± 0.25	< 0.10	-0.75 ± 0.27	-0.046 ± 0.25	< 0.10			
ΔBMI, kg/m ²	-0.25 ± 0.10	-0.0091 ± 0.0899	< 0.10	-0.26 ± 0.10	+0.0019 ± 0.091	< 0.10			
ΔAppLTM, kg	+0.0062 ± 0.0733	+0.24 ± 0.07	< 0.05	+0.021 ± 0.073	+0.23 ± 0.07	< 0.05			
ΔTotalTM, kg	-0.054 ± 0.148	+0.43 ± 0.14	< 0.05	-0.041 ± 0.150	+0.42 ± 0.14	< 0.05			
ΔBody fat, kg	-0.36 ± 0.24	-0.21 ± 0.23	0.67	-0.40 ± 0.24	-0.17 ± 0.22	0.49			
ΔBMC, kg	-0.0085 ± 0.0069	-0.0070 ± 0.0064	0.88	-0.0079 ± 0.0070	-0.0076 ± 0.0065	0.97			
Physical capacity									
ΔVO _{2peak} , mL/kg/min	+1.01 ± 0.67	+0.91 ± 0.62	0.91	+1.06 ± 0.68	+0.87 ± 0.63	0.84			
Δ1-RM (kg)									
ΔChest press	+0.46 ± 0.32	+5.9 ± 0.3	< 0.001	+0.49 ± 0.32	+5.8 ± 0.3	< 0.001			
ΔShoulder press	+0.71 ± 0.50	+7.5 ± 0.5	< 0.001	+0.73 ± 0.51	+7.5 ± 0.5	< 0.001			
ΔArm curl	+0.54 ± 0.53	+6.4 ± 0.5	< 0.001	+0.62 ± 0.53	+6.3 ± 0.5	< 0.001			
ΔRowing	-0.94 ± 0.57	+5.4 ± 0.5	< 0.001	-0.84 ± 0.57	+5.3 ± 0.5	< 0.001			
ΔLeg curl	+0.48 ± 1.28	+12.4 ± 1.2	< 0.001	+0.74 ± 1.24	+12.2 ± 1.2	< 0.001			
ΔLeg extension	+2.6 ± 1.6	+16.0 ± 1.5	< 0.001	+2.7 ± 1.7	+15.9 ± 1.6	< 0.001			

Values show the means of delta (Δ) calculated by subtracting the baseline value measured before the training intervention from the value measured after the training intervention, ± standard errors (SEs). Statistical analyses were performed with three types of analysis of co-variance by adjusting for ^athe baseline value measured before training intervention, ^bthe baseline value measured before training intervention and menstruation regularity (regular or irregular), and ^cthe baseline value measured before training intervention, ^bthe baseline value measured before training intervention, ^bthe baseline value measured before training intervention and menstruation regularity (regular/irregular or after menopause), and Δmelanin index as a measure of exposure to ultraviolet rays during the intervention period.

ANCOVA, analysis of co-variance; AppLTM, appendicular lean soft tissue mass; AT, aerobic training; BMC, bone mineral content; BMI, body mass index; LEP, low echogenic pixel; RT, resistance training; TotalLTM, total lean soft tissue mass; VO_{2peak}, peak oxygen uptake; 1-RM, one-repetition maximum

Extended Data 4. Blood factors that increased significantly after both aerobic training and resistance training

Blood factor	Unit	All (n=56)			AT (n=26)			RT (n=30)			Change (Δ)		
		Before	After	p value	Before	After	p value	Before	After	p value	AT	RT	p value ^a
IL-26	FP	4.97 ± 0.69	7.25 ± 0.87	< 0.001	5.65 ± 1.36	8.92 ± 1.34	< 0.01	4.38 ± 0.54	5.80 ± 1.10	< 0.05	+3.27 ± 1.00	+1.42 ± 1.00	0.20
Osteocalcin	ng/mL	3.79 ± 0.27	4.46 ± 0.30	< 0.0001	3.84 ± 0.50	4.29 ± 0.53	< 0.01	3.76 ± 0.27	4.62 ± 0.33	< 0.001	+0.60 ± 0.30	+0.71 ± 0.30	0.78
Osteopontin	ng/mL	15.51 ± 0.75	18.63 ± 0.91	< 0.001	16.21 ± 1.36	19.76 ± 1.46	< 0.01	14.92 ± 0.76	17.66 ± 1.13	< 0.01	+3.55 ± 0.99	+2.74 ± 0.99	0.61
Ghrelin	FP	144.63 ± 43.85	356.91 ± 63.44	< 0.0001	194.22 ± 86.20	340.72 ± 98.53	< 0.05	101.66 ± 33.45	370.93 ± 83.56	< 0.001	+146.50 ± 80.54	+269.28 ± 80.54	0.29
ANGPTL6	ng/mL	4.67 ± 0.26	5.28 ± 0.30	< 0.01	4.38 ± 0.33	4.85 ± 0.42	< 0.05	4.91 ± 0.40	5.66 ± 0.43	< 0.05	+0.46 ± 0.30	+0.76 ± 0.30	0.44
Angiopoietin-2	ng/mL	1.81 ± 0.09	2.10 ± 0.12	< 0.0001	1.79 ± 0.15	2.13 ± 0.21	< 0.01	1.83 ± 0.12	2.08 ± 0.13	< 0.001	+0.34 ± 0.06	+0.24 ± 0.06	0.44
Synuclein- α	pg/mL	490.64 ± 15.82	689.89 ± 23.82	< 0.0001	486.17 ± 16.53	679.71 ± 43.88	< 0.001	494.50 ± 26.09	698.72 ± 23.77	< 0.0001	+193.54 ± 31.45	+204.21 ± 31.45	0.84
TGF- α	FP	20.94 ± 0.38	22.25 ± 0.48	< 0.01	21.02 ± 0.60	22.19 ± 0.75	< 0.05	20.87 ± 0.48	22.30 ± 0.63	< 0.05	+1.17 ± 0.71	+1.43 ± 0.71	0.77
CCL14/HCC-1/HCC-3	ng/mL	42.03 ± 1.07	44.81 ± 0.97	< 0.0001	39.47 ± 1.62	42.88 ± 1.47	< 0.001	44.24 ± 1.31	46.49 ± 1.23	< 0.01	+3.41 ± 0.81	+2.25 ± 0.81	0.34
Glu	μ M	43.10 ± 1.60	51.57 ± 2.31	< 0.001	41.44 ± 1.84	52.57 ± 3.80	< 0.01	44.55 ± 2.52	50.70 ± 2.82	< 0.05	+10.81 ± 2.49	+5.60 ± 2.49	0.25
Homocitrulline	μ M	0.16 ± 0.01	0.19 ± 0.01	< 0.001	0.16 ± 0.01	0.18 ± 0.02	< 0.05	0.16 ± 0.01	0.19 ± 0.02	< 0.01	+0.26 ± 0.07	+0.11 ± 0.07	0.22
SDMA	μ M	0.34 ± 0.01	0.38 ± 0.01	< 0.0001	0.34 ± 0.01	0.38 ± 0.01	< 0.01	0.34 ± 0.01	0.38 ± 0.01	< 0.01	+0.20 ± 0.09	+0.35 ± 0.09	0.26
Urea	μ M	2100.02 ± 54.71	2280.97 ± 55.84	< 0.001	2094.63 ± 84.06	2247.97 ± 84.58	< 0.10	2104.70 ± 72.90	2309.57 ± 75.04	< 0.01	+82.73 ± 68.78	+172.78 ± 68.78	0.35

Values show the means \pm standard errors (SEs). The change value was calculated by subtracting the baseline value measured before the training intervention from the value measured after the training intervention. Statistical analyses were performed with two-sided paired *t* tests for the intragroup difference, ^atwo-sided independent *t* tests for the intergroup difference, and ^bWilcoxon signed-rank sum tests for the intragroup difference in the FI value.

AT, aerobic training; FI, fluorescence intensity; RT, resistance training

Extended Data 6. Blood factors that increased significantly only after aerobic training

Blood factor	Unit	All (n= 56)			AT (n = 26)			RT (n = 30)			Change (Δ)		
		Before	Alter	p value	Before	Alter	p value	Before	Alter	p value	AT	RT	p value ^a
25(OH)VitaminD	ng/mL	37.80 ± 11.89	32.09 ± 3.07	0.64	24.51 ± 2.88	34.09 ± 4.94	< 0.05	49.32 ± 22.02	30.36 ± 3.86	0.40	+9.59 ± 22.37	-18.96 ± 22.37	0.24
Myonectin	ng/mL	2.03 ± 0.13	2.14 ± 0.13	< 0.01	1.86 ± 0.06	2.01 ± 0.05	< 0.01	2.17 ± 0.23	2.26 ± 0.24	0.16	+0.14 ± 0.06	+0.09 ± 0.06	0.47
IL-15	Ff	-7.93 ± 1.06	-6.32 ± 1.25	< 0.05	-8.41 ± 1.78	-6.48 ± 1.67	< 0.05	-7.52 ± 1.25	-6.18 ± 1.86	0.43	+1.93 ± 0.94	+1.34 ± 1.19	0.70
MPIF-1/CCL23	pg/mL	146.02 ± 11.61	158.21 ± 13.35	< 0.05	146.44 ± 17.69	160.84 ± 19.73	< 0.05	145.65 ± 15.60	155.94 ± 18.44	0.16	+14.41 ± 7.12	+10.28 ± 7.12	0.67
CD163	ng/mL	94.57 ± 5.13	98.88 ± 5.37	0.12	92.11 ± 7.80	103.46 ± 7.35	< 0.001	96.70 ± 6.89	94.91 ± 7.78	0.67	+11.34 ± 4.13	-1.79 ± 4.13	< 0.05
Chitinase 3-like 1	ng/mL	15.42 ± 1.05	15.68 ± 1.10	0.67	14.71 ± 1.07	17.75 ± 1.94	< 0.10	16.03 ± 1.73	13.83 ± 1.07	0.22	+3.04 ± 1.63	-2.66 ± 1.63	< 0.05
IL-6Ra	ng/mL	9.03 ± 0.40	9.47 ± 0.43	0.12	8.36 ± 0.61	9.48 ± 0.49	< 0.01	9.62 ± 0.53	9.47 ± 0.69	0.71	+1.12 ± 0.39	-0.14 ± 0.39	< 0.05
IL-12(p70)	Ff	-2.85 ± 0.42	-2.70 ± 0.38	0.33	-2.90 ± 0.85	-2.50 ± 0.66	< 0.10	-2.80 ± 0.29	-2.87 ± 0.44	0.63	+0.40 ± 0.43	-0.07 ± 0.43	0.45
IL-34	Ff	-25.17 ± 1.49	-23.83 ± 1.53	< 0.01	-27.03 ± 2.87	-23.9 ± 2.62	< 0.05	-23.56 ± 1.24	-23.76 ± 1.79	0.24	+3.13 ± 1.59	-0.20 ± 1.59	< 0.10
IL-35	Ff	-7.21 ± 1.84	-5.75 ± 2.14	< 0.10	-8.15 ± 3.53	-3.84 ± 2.93	< 0.05	-6.39 ± 1.63	-7.41 ± 3.10	0.66	+4.31 ± 2.49	-1.02 ± 2.49	0.11
MMP-2	ng/mL	80.10 ± 3.85	92.00 ± 5.09	< 0.01	79.61 ± 5.51	93.72 ± 5.84	< 0.0001	80.52 ± 5.46	90.50 ± 8.14	0.13	+14.11 ± 6.33	+9.98 ± 6.33	0.58
Pentraxin-3	ng/mL	11.71 ± 0.75	12.87 ± 0.79	< 0.10	11.87 ± 1.37	13.02 ± 1.18	< 0.10	11.57 ± 0.76	12.75 ± 1.08	0.22	+1.15 ± 0.94	+1.18 ± 0.94	0.98
TSLP	Ff	10.45 ± 1.10	11.54 ± 1.23	< 0.10	12.02 ± 2.19	13.87 ± 2.16	< 0.10	9.08 ± 0.76	9.52 ± 1.24	0.46	+1.85 ± 1.15	+0.43 ± 1.15	0.34
TWEAK/TNFSF12	pg/mL	354.66 ± 15.48	371.33 ± 13.17	0.13	347.80 ± 28.34	392.14 ± 17.64	< 0.05	360.61 ± 15.68	352.68 ± 18.94	0.63	+44.34 ± 18.13	-19.69 ± 18.13	< 0.05
IL-33	Ff	-4.89 ± 0.27	-4.76 ± 0.27	0.42	-4.81 ± 0.36	-4.37 ± 0.35	< 0.10	-4.97 ± 0.40	-5.10 ± 0.39	0.38	+0.44 ± 0.16	-0.13 ± 0.16	< 0.05
Erythropoietin	Ff	-7.46 ± 0.80	-7.43 ± 0.81	0.63	-8.27 ± 1.14	-7.62 ± 1.19	< 0.05	-6.75 ± 1.12	-7.27 ± 1.11	0.23	+0.65 ± 0.45	-0.52 ± 0.45	< 0.05
FSH	mIU/mL	33.66 ± 5.24	43.88 ± 7.27	< 0.01	38.86 ± 8.03	48.57 ± 10.25	< 0.05	28.85 ± 6.82	39.37 ± 10.41	0.11	+11.2 ± 5.68	+9.47 ± 5.68	0.81
MIA	pg/mL	846.98 ± 44.15	891.83 ± 44.99	< 0.01	816.52 ± 61.96	887.18 ± 66.38	< 0.01	873.38 ± 63.09	895.86 ± 62.23	0.26	+70.66 ± 19.42	+22.48 ± 19.42	0.12
Park7/DJ-1	ng/mL	11.56 ± 0.57	12.25 ± 0.73	0.33	10.60 ± 0.49	12.59 ± 1.34	< 0.10	12.38 ± 0.96	11.95 ± 0.73	0.61	+1.99 ± 0.84	-0.43 ± 0.84	< 0.10
1-Methylnicotinamide	μ M	0.32 ± 0.02	0.40 ± 0.02	< 0.01	0.30 ± 0.03	0.45 ± 0.04	< 0.01	0.33 ± 0.03	0.35 ± 0.03	0.56	+0.22 ± 0.09	+0.09 ± 0.09	0.24
ADWA	μ M	0.35 ± 0.01	0.37 ± 0.01	0.11	0.34 ± 0.01	0.38 ± 0.01	< 0.05	0.36 ± 0.01	0.36 ± 0.01	0.83	+0.30 ± 0.09	+0.01 ± 0.09	< 0.05
Guantinosuccinic acid	μ M	0.34 ± 0.02	0.37 ± 0.02	< 0.05	0.30 ± 0.03	0.35 ± 0.04	< 0.10	0.37 ± 0.03	0.38 ± 0.03	0.35	+0.12 ± 0.08	+0.12 ± 0.08	1.00
His	μ M	131.5 ± 2.26	133.6 ± 2.20	0.23	129.49 ± 3.27	133.50 ± 3.12	< 0.10	133.25 ± 3.15	133.69 ± 3.14	0.87	+2.98 ± 2.56	+0.79 ± 2.56	0.52
Homocysteine	μ M	1.84 ± 0.07	2.04 ± 0.10	< 0.05	1.91 ± 0.13	2.15 ± 0.17	< 0.05	1.78 ± 0.08	1.94 ± 0.12	0.16	+0.29 ± 0.12	+0.18 ± 0.12	0.51
Lys	μ M	342.53 ± 7.10	356.24 ± 8.33	0.14	341.98 ± 10.46	370.27 ± 14.35	< 0.10	343.01 ± 9.83	344.07 ± 8.99	0.92	+23.07 ± 9.99	-4.00 ± 9.99	0.12
Mucic acid	μ M	4.47 ± 0.23	4.90 ± 0.22	< 0.05	4.42 ± 0.32	4.97 ± 0.36	< 0.10	4.51 ± 0.34	4.84 ± 0.27	0.19	+0.60 ± 0.25	+0.32 ± 0.25	0.48
N1-Methyl-4-pyridone-5-carboxamide	μ M	0.31 ± 0.01	0.36 ± 0.02	< 0.05	0.28 ± 0.02	0.36 ± 0.02	< 0.05	0.33 ± 0.02	0.35 ± 0.03	0.41	+0.17 ± 0.08	+0.03 ± 0.08	0.22
Ornithine	μ M	65.49 ± 1.64	68.52 ± 2.30	0.18	67.96 ± 2.03	74.73 ± 4.18	< 0.10	63.34 ± 2.48	63.13 ± 1.89	0.94	+5.04 ± 2.57	+0.14 ± 2.57	0.25

Values show the means ± standard errors (SEs). The change value was calculated as delta (Δ) by subtracting the baseline value measured before training intervention from the value measured after training intervention. Statistical analyses were performed with two-sided paired *t* tests for the intragroup difference, ^atwo-sided independent *t* tests for the intergroup difference, and ^bWilcoxon signed-rank sum tests for the intragroup difference in the FI value. AT, aerobic training; FI, fluorescence intensity; IU, international unit; RT, resistance training

Extended Data 7. Blood factors that decreased significantly only after resistance training

Blood factor	Unit	All (n = 56)			AT (n = 26)			RT (n = 30)			Change (Δ)		
		Before	After	p value	Before	After	p value	Before	After	p value	AT	RT	p value ^a
MCP-3	FP	-3.34 ± 0.55	-3.62 ± 0.56	0.11	-2.48 ± 0.76	-2.63 ± 0.74	0.64	-4.09 ± 0.79	-4.47 ± 0.82	< 0.10	-0.15 ± 0.32	-0.39 ± 0.32	0.60
MIG	pg/mL	185.63 ± 61.71	117.34 ± 9.35	0.25	254.77 ± 132.52	130.6 ± 18.32	0.34	125.71 ± 9.80	105.85 ± 6.98	< 0.05	-124.18 ± 7.54	-19.86 ± 7.54	0.38
ENA-78/CXCL5	ng/mL	1.08 ± 0.39	1.20 ± 0.52	0.51	1.46 ± 0.85	1.76 ± 1.16	0.39	0.77 ± 0.09	0.73 ± 0.09	< 0.10	+0.21 ± 0.03	-0.07 ± 0.03	0.23
Eotaxin-2/CCL24	pg/mL	63.51 ± 3.36	61.49 ± 3.36	0.34	63.92 ± 5.83	65.09 ± 5.91	0.73	63.16 ± 3.82	58.37 ± 3.64	< 0.10	+1.16 ± 2.63	-4.79 ± 2.63	0.16
I-TAC/CXCL11	pg/mL	15.79 ± 2.37	11.44 ± 1.00	< 0.10	17.83 ± 4.73	11.52 ± 1.54	0.21	14.01 ± 1.71	11.37 ± 1.33	< 0.05	-6.31 ± 1.07	-2.64 ± 1.07	0.44
MCP-2/CCL8	pg/mL	66.76 ± 11.99	48.70 ± 2.99	0.11	81.22 ± 24.51	52.41 ± 3.81	0.23	54.24 ± 6.95	45.49 ± 4.47	< 0.10	-28.81 ± 4.87	-8.75 ± 4.87	0.37
MIP-1 α /CCL15	ng/mL	4.45 ± 0.36	4.00 ± 0.28	< 0.10	4.50 ± 0.49	3.94 ± 0.33	0.45	4.39 ± 0.54	4.05 ± 0.45	< 0.05	-0.69 ± 0.43	-0.17 ± 0.43	0.45
MIP-3 β /CCL19	pg/mL	44.80 ± 2.65	40.50 ± 1.54	< 0.10	48.42 ± 5.08	41.69 ± 2.27	0.14	41.65 ± 2.20	39.47 ± 2.12	< 0.10	-6.73 ± 1.27	-2.19 ± 1.27	0.30
IL-17F	FP	3.63 ± 0.71	3.49 ± 0.72	0.13	2.52 ± 1.06	2.48 ± 1.11	0.61	4.59 ± 0.93	4.36 ± 0.91	< 0.10	-0.04 ± 0.13	-0.23 ± 0.13	0.47
IL-23	FP	-1.25 ± 0.14	-1.46 ± 0.14	0.15	-1.33 ± 0.21	-1.17 ± 0.19	0.45	-1.18 ± 0.20	-1.70 ± 0.20	< 0.01	+0.15 ± 0.19	-0.52 ± 0.19	< 0.05
IL-31	FP	4.63 ± 0.76	4.46 ± 0.77	0.15	3.10 ± 1.09	3.19 ± 1.10	0.82	5.97 ± 1.00	5.57 ± 1.05	< 0.05	+0.10 ± 0.20	-0.40 ± 0.20	< 0.10
CD40LG	pg/mL	245.03 ± 11.38	191.94 ± 13.42	< 0.001	224.73 ± 15.42	200.08 ± 22.75	0.19	261.95 ± 16.02	184.87 ± 15.71	< 0.001	-16.00 ± 21.05	-77.07 ± 21.05	< 0.05
FGF21	FP	-269.30 ± 12.32	-280.74 ± 10.92	< 0.001	-253.92 ± 25.00	-260.98 ± 22.46	0.20	-282.63 ± 7.59	-297.87 ± 4.82	< 0.001	-7.06 ± 5.52	-15.23 ± 5.52	0.34
CCL28	pg/mL	145.99 ± 9.40	128.75 ± 9.73	< 0.10	132.45 ± 6.87	132.88 ± 16.68	0.98	157.71 ± 16.36	125.17 ± 11.22	< 0.05	+0.43 ± 12.61	-32.54 ± 12.61	< 0.10
ANGPTL3	ng/mL	45.71 ± 2.61	43.46 ± 2.71	0.14	45.47 ± 4.15	44.08 ± 4.50	0.59	45.91 ± 3.35	42.92 ± 3.31	< 0.10	-1.38 ± 1.74	-3.00 ± 1.74	0.60
GDNF	pg/mL	4.36 ± 0.20	4.11 ± 0.19	< 0.05	4.38 ± 0.34	4.19 ± 0.29	0.23	4.34 ± 0.23	4.04 ± 0.24	< 0.10	-0.19 ± 0.16	-0.30 ± 0.16	0.62
D-Dimer + FDPs	ng/mL	2.83 ± 0.33	2.01 ± 0.17	< 0.05	1.85 ± 0.13	2.01 ± 0.28	0.54	3.65 ± 0.55	2.01 ± 0.22	< 0.01	+0.23 ± 0.56	-1.63 ± 0.56	< 0.01
Reg3A	ng/mL	6.78 ± 0.49	6.39 ± 0.43	< 0.10	6.70 ± 0.68	6.48 ± 0.58	0.49	6.85 ± 0.71	6.32 ± 0.64	< 0.05	-0.23 ± 0.24	-0.53 ± 0.24	0.44
Progranulin/PGRN	ng/mL	37.23 ± 2.11	33.68 ± 1.05	< 0.05	38.5 ± 4.09	33.06 ± 1.91	0.13	36.14 ± 1.79	34.21 ± 1.07	< 0.05	-5.44 ± 0.91	-1.93 ± 0.91	0.30
Complement Factor D/Adpsin	μ g/mL	3.07 ± 0.09	2.83 ± 0.07	< 0.001	2.95 ± 0.10	2.81 ± 0.11	0.12	3.18 ± 0.13	2.85 ± 0.10	< 0.001	-0.14 ± 0.08	-0.32 ± 0.08	0.13
MSP/MST1	μ g/mL	2.69 ± 0.07	2.58 ± 0.06	< 0.05	2.55 ± 0.06	2.50 ± 0.08	0.36	2.81 ± 0.12	2.65 ± 0.09	< 0.05	-0.04 ± 0.06	-0.16 ± 0.06	0.14
LBP	μ g/mL	5.91 ± 0.28	5.31 ± 0.15	< 0.05	6.16 ± 0.54	5.48 ± 0.25	0.19	5.69 ± 0.24	5.16 ± 0.18	< 0.05	-0.69 ± 0.21	-0.53 ± 0.21	0.76
CXCL4/PF4	μ g/mL	11.17 ± 1.22	8.82 ± 0.77	< 0.10	11.18 ± 2.18	8.30 ± 0.97	0.22	11.16 ± 1.32	9.26 ± 1.18	< 0.10	-2.87 ± 1.11	-1.90 ± 1.11	0.69
ADP	μ M	1.23 ± 0.11	1.06 ± 0.09	< 0.10	0.98 ± 0.12	1.01 ± 0.14	0.64	1.45 ± 0.17	1.10 ± 0.12	< 0.10	-0.21 ± 0.20	-0.43 ± 0.20	0.38
Ethanolamine phosphate	μ M	4.15 ± 0.20	3.46 ± 0.18	< 0.01	3.77 ± 0.29	3.29 ± 0.29	0.14	4.47 ± 0.26	3.61 ± 0.23	< 0.05	-0.48 ± 0.33	-0.91 ± 0.33	0.34
NIN-Dimethylglycine	μ M	6.95 ± 0.42	6.53 ± 0.46	< 0.10	7.71 ± 0.80	7.34 ± 0.92	0.40	6.29 ± 0.32	5.83 ± 0.27	< 0.05	-0.39 ± 0.21	-0.45 ± 0.21	0.90
Nicotinamide	μ M	0.35 ± 0.02	0.30 ± 0.01	< 0.05	0.32 ± 0.02	0.29 ± 0.02	0.15	0.37 ± 0.02	0.32 ± 0.02	< 0.05	-0.10 ± 0.08	-0.10 ± 0.08	0.98

Values show the means \pm standard errors (SEs). The change value was calculated as delta (Δ) by subtracting the baseline value measured before the training intervention from the value measured after the training intervention. Statistical analyses were performed with two-sided paired *t* tests for the intragroup difference, ^atwo-sided independent *t* tests for the intergroup difference, and ^bWilcoxon signed-rank sum tests for the intragroup difference in the FI value. AT, aerobic training; FI, fluorescence intensity; RT, resistance training

Supplementary Table 1. Circulating factors measured in this study

Measurement Panel/Method	Catalog No.	Measured circulating factors (>1,487)	Process Ref.
Bio-Plex Cytokine panel	# F-12007283	β-NGF	
		IL-1Ra	IL-1α
		IL-16	IL-13
		IL-17A	IL-15
		IL-18	IL-17
		IL-27	IL-18
		IL-27 (p28)	IL-19
		IL-29/IFN-λ1	IL-20
		Osteocalcin	IL-21
		Osteonectin	IL-22
Bio-Plex Chemokine panel	# F-171-AV98MR2-20	6Kine/CCL21	IL-23
		MCP-2/CCL8	IL-24
		APRIL/TNFSF3	IL-25
		IL-8Ra	IL-26
		IL-27	IL-27
Bio-Plex Inflammation panel	# F-171-AL001M	IL-1Ra	IL-1α
		IL-29/IFN-λ1	IL-13
		Osteocalcin	IL-15
		IL-17F	IL-17
		Apelin	IL-18
		Ghrelin	IL-19
		ACTH	IL-20
		Cortisol	IL-21
		IGF-1	IL-22
		IGF-1	IL-23
Bio-Plex Th17 Cytokine panel	# F-BP-HTH17-plex07	IL-17A	IL-17
		IL-17F	IL-17
		IL-17R	IL-17
		IL-17RC	IL-17
		IL-17E	IL-17
		IL-17F1	IL-17
		IL-17F2	IL-17
		IL-17F3	IL-17
		IL-17F4	IL-17
		IL-17F5	IL-17
Mullepex Myokine panel	# F-MIL-HWOMAG-89K-08	IL-1Ra	IL-1α
		IL-16	IL-13
		IL-17A	IL-15
		IL-18	IL-17
		IL-27	IL-18
		IL-27 (p28)	IL-19
		IL-29/IFN-λ1	IL-20
		Osteocalcin	IL-21
		Osteonectin	IL-22
		Osteopontin	IL-23
Mullepex Metabolic Hormone panel	# F-MIL-HWEMAG-5HK-07	IL-1Ra	IL-1α
		IL-16	IL-13
		IL-17A	IL-15
		IL-18	IL-17
		IL-27	IL-18
		IL-27 (p28)	IL-19
		IL-29/IFN-λ1	IL-20
		Osteocalcin	IL-21
		Osteonectin	IL-22
		Osteopontin	IL-23
Mullepex Pituitary panel	# F-MIL-HPT1MAG-66K-05	IL-1Ra	IL-1α
		IL-16	IL-13
		IL-17A	IL-15
		IL-18	IL-17
		IL-27	IL-18
		IL-27 (p28)	IL-19
		IL-29/IFN-λ1	IL-20
		Osteocalcin	IL-21
		Osteonectin	IL-22
		Osteopontin	IL-23
Mullepex Multi-Species Hormone panel	# MS-HMAG-21K	IL-1Ra	IL-1α
		IL-16	IL-13
		IL-17A	IL-15
		IL-18	IL-17
		IL-27	IL-18
		IL-27 (p28)	IL-19
		IL-29/IFN-λ1	IL-20
		Osteocalcin	IL-21
		Osteonectin	IL-22
		Osteopontin	IL-23
Mullepex IGF panel	# F-MIL-HGFIMAG-52K-02	IL-1Ra	IL-1α
		IL-16	IL-13
		IL-17A	IL-15
		IL-18	IL-17
		IL-27	IL-18
		IL-27 (p28)	IL-19
		IL-29/IFN-λ1	IL-20
		Osteocalcin	IL-21
		Osteonectin	IL-22
		Osteopontin	IL-23
Lumines LISAH	# LXSAMW39	IL-1Ra	IL-1α
		IL-16	IL-13
		IL-17A	IL-15
		IL-18	IL-17
		IL-27	IL-18
		IL-27 (p28)	IL-19
		IL-29/IFN-λ1	IL-20
		Osteocalcin	IL-21
		Osteonectin	IL-22
		Osteopontin	IL-23
CE-TOFMS/LC-TOFMS	# DEIA-X2197	IL-1Ra	IL-1α
		IL-16	IL-13
		IL-17A	IL-15
		IL-18	IL-17
		IL-27	IL-18
		IL-27 (p28)	IL-19
		IL-29/IFN-λ1	IL-20
		Osteocalcin	IL-21
		Osteonectin	IL-22
		Osteopontin	IL-23
Blood biochemistry	The circulating levels of cytokines and hormones in serum were measured with the following multiplex assays: Bio-Plex (Bio-Rad Laboratories - Hercules, CA, USA), Milliplex (Merck Millipore, Burlington, MA, USA) and Lumines (R&D Systems, Minneapolis, MN, USA) and enzyme-linked immunosorbent assay (ELISA). Over 1,200 metabolites in plasma were measured with a capillary electrophoresis and liquid chromatography-mass spectrometry-based system (Duo Scan, Human Metabolome Technologies, Boston, MA, USA); the details of the instruments and measured metabolites are shown on the manufacturer websites (https://en.humanmetabolome.com). ELISA, enzyme-linked immunosorbent assay; HDL, high-density lipoprotein; LDL, low-density lipoprotein; TOFMS, time of flight mass spectrometry	Albumin	
		Cholesterol	
		HDL cholesterol	
		LDL cholesterol	
		Total cholesterol	
		Triglyceride	
		Insulin	
		Urea nitrogen	
		Creatinine	
		Glucose	

Supplementary Table 2. Dermal ECM-related genes analyzed in this study

Gene Symbol	Gene Name	TaqMan® Assay ID
COL1A1	collagen type I alpha 1	Hs00164004_m1
COL1A2	collagen type I alpha 2 chain	Hs01028956_m1
COL3A1	collagen type III alpha 1 chain	Hs00943809_m1
COL5A1	collagen type V alpha 1	Hs00609133_m1
COL6A1	collagen type VI alpha 1	Hs01095585_m1
COL12A1	collagen type XII alpha 1 chain	Hs00189184_m1
COL14A1	collagen type XIV alpha 1 chain	Hs00964045_m1
HAS2	hyaluronan synthase 2	Hs00193435_m1
HAS1	hyaluronan synthase 1	Hs00758053_m1
DCN	decorin	Hs00754870_s1
BGN	biglycan	Hs00156076_m1
VCAN	versican	Hs00171642_m1
CHPF	chondroitin polymerizing factor	Hs00226041_m1
CHSY1	chondroitin sulfate synthase 1	Hs00208704_m1
CHSY3	chondroitin sulfate synthase 3	Hs02380326_s1
ELN	elastin	Hs00355783_m1
GAPDH	glyceraldehyde-3-phosphate dehydrogenase	Hs02786624_g1

The expression level of dermal extracellular matrix-related genes listed above was analyzed by real-time PCR with the primers and probes of TaqMan® gene expression assays.

ECM, extracellular matrix; PCR, polymerase chain reaction