



Supplementary Materials: Moderate Red Wine Consumption Increases the Expression of Longevity-associated Genes in Controlled Human Populations and Extends Lifespan in *Drosophila melanogaster*

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Table S1. Longevity-associated genes whose expression is not affected by moderate wine consumption. Data are expressed as concentration means \pm SD (Molar*10⁻⁵) of 9 different people.

	Before	After	$\Delta\%$	<i>p</i>
AKT1	24 \pm 10	27 \pm 13	115 \pm 24	0.288
CDKN2A	0.19 \pm 0.13	0.23 \pm 0.09	170 \pm 99	0.202
FOXO3	6.4 \pm 4.0	4.9 \pm 3.2	86 \pm 51	0.184
FRAP1	4.0 \pm 2.1	3.0 \pm 0.9	89 \pm 41	0.088
IRS1	0.043 \pm 0.046	0.085 \pm 0.80	273 \pm 257	0.105
SESN2	3.4 \pm 2.3	3.9 \pm 2.5	135 \pm 61	0.346
TERF1	0.05 \pm 0.03	0.05 \pm 0.04	164 \pm 139	0.426
TERF2	8.0 \pm 4.6	7.9 \pm 4.21	112 \pm 68	0.487
TERT	3.9 \pm 7.5	1.9 \pm 1.2	232 \pm 296	0.237

Table S2. Lack of effect of moderate red wine consumption on vitamin E, lipid peroxidation or biomarkers of inflammation. Data are expressed as means \pm SD n=4 before and after wine consumption. Urinary markers are expressed per g creatinine which was not different between the two treatment periods.

	Before	After	<i>p</i>
Plasma			
Gamma-Tocopherol (μM)	0.93 \pm 0.14	0.84 \pm 0.18	0.228
Alpha-Tocopherol (μM)	17.9 \pm 2.7	17.1 \pm 4.0	0.476
Urine			
Gamma-CEHC (μmol/g Creat)	0.73 \pm 0.10	0.54 \pm 0.20	0.21
Alfa-CEHC (μmol/g Creat)	2.37 \pm 0.67	2.30 \pm 0.40	0.86
PGF2a related (μg/g creat.)	2.20 \pm 0.44	2.58 \pm 0.852	0.995
2.3-dinor-F1 metabolites (μg/g creat.)	6.2 \pm 2.2	17.8 \pm 11.4	0.156
2.3-dinor-F2 metabolites (μg/g creat.)	55.4 \pm 17.3	63.3 \pm 25.7	0.853

Table S3. Relative contribution of selected metabolic spectral clusters to overall metabolic content. The value corresponds to the ratio between selected spectral region (labeled as most probable metabolite assignment) and total spectral aliphatic area. The ratio has been multiplied by 1000 for easier readability.

Spectral region metabolite assignment	Before intervention		After intervention		P-value
	Mean	Std	Mean	Std	
2-hydroxyvalerate	8.11	0.49	9.76	2.57	0.301
2-hydroxyvalerate + FFAA β CH ₂	19.42	0.50	20.47	1.20	0.192
acetoacetate	9.14	0.12	9.95	0.49	0.025
alanine	4.05	0.22	4.81	1.10	0.272
alloisoleucine + 2-hydroxyvalerate	9.99	0.31	9.88	0.33	0.674
cholesterol	46.57	2.91	44.20	3.02	0.329
cholesterol + FFAA (-CH ₃)	19.60	0.44	20.42	0.70	0.113
choline + TMA	4.62	0.07	4.92	0.21	0.049
citrate	2.49	0.11	8.86	5.43	0.078
creatine + glucose	5.51	0.36	6.90	2.01	0.270
creatinine	3.59	0.18	4.38	1.27	0.311
cysteine	8.93	0.53	10.22	2.10	0.326
cysteine + lysine	3.63	0.11	3.63	0.17	0.982
cysteine + creatinine	4.92	0.23	5.15	0.47	0.451
FFAA (=CH-CH ₂ -CH=)	17.68	0.48	19.88	3.85	0.351
FFAA (=CH-CH ₂ -CH=) + malate	0.32	0.01	0.70	0.38	0.127
FFAA (=CH-CH ₂ -CH ₂ -)	2.70	0.06	2.77	0.15	0.452
FFAA (=CH-CH ₂ -CH ₂ -) + isoleucine	6.27	0.12	6.72	0.53	0.183
FFAA (-CH ₂) _n	28.01	0.17	26.67	1.01	0.054
FFAA (-CH ₂) _n + isoleucine	82.28	3.50	84.98	4.89	0.438
FFAA (-CH ₃)	51.11	1.64	49.17	2.39	0.261
FFAA (-CH ₃) + valerate	56.82	1.06	58.37	1.42	0.154
FFAA β CH ₂	9.26	0.15	9.56	0.29	0.150
FFAA α CH ₂ + valerate	6.36	0.08	6.57	0.26	0.200
glucose + glycine	3.52	0.10	3.87	0.27	0.067
glucose + lysine	3.88	0.20	4.52	0.90	0.258
glucose + TMAO	3.16	0.29	3.65	0.67	0.262
glutamine	11.43	0.42	11.81	0.90	0.515
isobutyrate + glutamine	5.33	0.18	5.71	0.45	0.200
isobutyrate + malate	3.40	0.11	3.57	0.29	0.368
isoleucine + leucine	37.96	0.71	36.55	0.64	0.028
lactato	2.90	0.11	3.30	0.79	0.398
leucine	4.81	0.16	4.84	0.22	0.868
leucine + 2-hydroxyvalerate	22.55	0.76	22.67	1.08	0.867
leucine + alloisoleucine	11.72	0.28	11.30	0.34	0.118
leucine + glucose	1.91	0.05	2.13	0.32	0.261
leucine + lysine	20.80	0.81	20.81	0.98	0.987
lysine	26.47	0.78	26.20	0.92	0.694
malate	8.46	0.80	10.24	2.67	0.294
malate + proline	1.99	0.07	2.10	0.19	0.370
prolina + lactato	11.53	0.38	12.89	2.84	0.431
proline + alloisoleucine	13.54	0.65	13.92	0.97	0.575
proline + glucose	9.44	0.23	10.07	0.42	0.051
taurine1	9.44	0.26	10.07	0.47	0.043
taurine2	2.04	0.05	2.14	0.11	0.183
threonine	11.62	0.94	13.71	3.51	0.342
unknown1	3.53	0.08	3.93	0.60	0.286
valerate	5.45	0.11	5.52	0.28	0.674
valine	20.15	0.60	22.04	3.16	0.332
valine + FFAA α CH ₂	17.81	0.39	25.14	8.07	0.153

Keys: FFAA, fatty acids; TMA, trimethylamines; TMAO, trimethylamine-oxide.

Table S4. General biochemical and clinical parameters. Data are expressed as means \pm SD of 9 different people. The statistical significance is expressed as *P < 0.05 or **P < 0.01 vs. control.

	Before	After	P
Leucocytes	4.88 \pm 0.68	4.83 \pm 0.74	0.460
Red cells	4.39 \pm 0.17	4.25 \pm 0.20	0.166
Hemoglobin	13.2 \pm 0.5	13.1 \pm 0.6	0.400
Hematocrite	41.1 \pm 1.4	40.4 \pm 2.1	0.285
Average cor. vol.	93.6 \pm 1.7	95.0 \pm 1.4	0.126
Average cor. HB	30.1 \pm 0.6	30.9 \pm 0.4*	0.039
Average cor. [HB]	32.2 \pm 0.2	32.5 \pm 0.5	0.101
Wide distribution hematie	13.7 \pm 0.4	14.2 \pm 0.5	0.071
Platelets	208 \pm 56	263 \pm 27	0.065
MPV	11.2 \pm 1.5	11.3 \pm 1.5	0.464
Immature neutrophils	0.039 \pm 0.023	0.048 \pm 0.005	0.251
Segmented neutrophils	2.60 \pm 0.44	2.65 \pm 0.54	0.451
Basophils	0.015 \pm 0.006	0.023 \pm 0.001	0.114
Eosinophils	0.16 \pm 0.06	0.15 \pm 0.07	0.400
Lymphocytes	1.63 \pm 0.30	1.55 \pm 0.29	0.350
Monocytes	0.43 \pm 0.05	0.32 \pm 0.20	0.160
Reticulocytes	40.3 \pm 19.7	50.7 \pm 21.0	0.249
Glucose	77.8 \pm 6.7	77.2 \pm 10.5	0.463
Total cholesterol	228 \pm 15	242 \pm 33	0.241
HDL	74.7 \pm 4.2	88.4 \pm 4.8**	0.0026
LDL	135 \pm 10	136 \pm 27	0.468
Triglicerides	91.2 \pm 57	84.5 \pm 37	0.424
Total proteins	7.23 \pm 0.34	7.23 \pm 0.28	0.500
Alfa 1 glicoprot ac.	56.8 \pm 6.3	95.8 \pm 9.1**	0.00020
PCR	0.125 \pm 0.066	0.143 \pm 0.060	0.355
Insuline	4.94 \pm 2.29	5.87 \pm 2.90	0.317
Albumin	4.35 \pm 0.01	4.20 \pm 0.18	0.067
Afla 1 globulin	0.222 \pm 0.038	0.230 \pm 0.029	0.382
Afla 2 globulin	0.653 \pm 0.099	0.753 \pm 0.0112	0.115
Beta globuline	0.803 \pm 0.118	0.788 \pm 0.123	0.433
Gamma globuline	0.955 \pm 0.570	1.27 \pm 0.15	0.167
Albumine/globuline	1.53 \pm 0.17	1.40 \pm 0.17	0.163