

SUPPLEMENTAL MATERIAL

Data S1.

Supplemental Materials and Methods

principal component analysis (PCA): PCA was used to establish similarity or dissimilarity between the expression profile of UPR-related genes in aortae from *ApoE*^{-/-} and C57BL6 mice aged at 14 and 30 weeks. The transcriptome dataset for PCA analysis was obtained from Gene Expression Omnibus database: GSE163657, which compared aortic gene expression profiles of *ApoE*^{-/-} and C57BL6 mice at different ages; they are all on a normal chow diet. Data analysis was carried out using the PCA tools package in R (v3.1.2). The obtained five-component model explained 94.58% of the total variance. The five principle components account for 44.31%, 17.19%, 16.13%, 12.83%, and 4.12% of total variability, respectively.

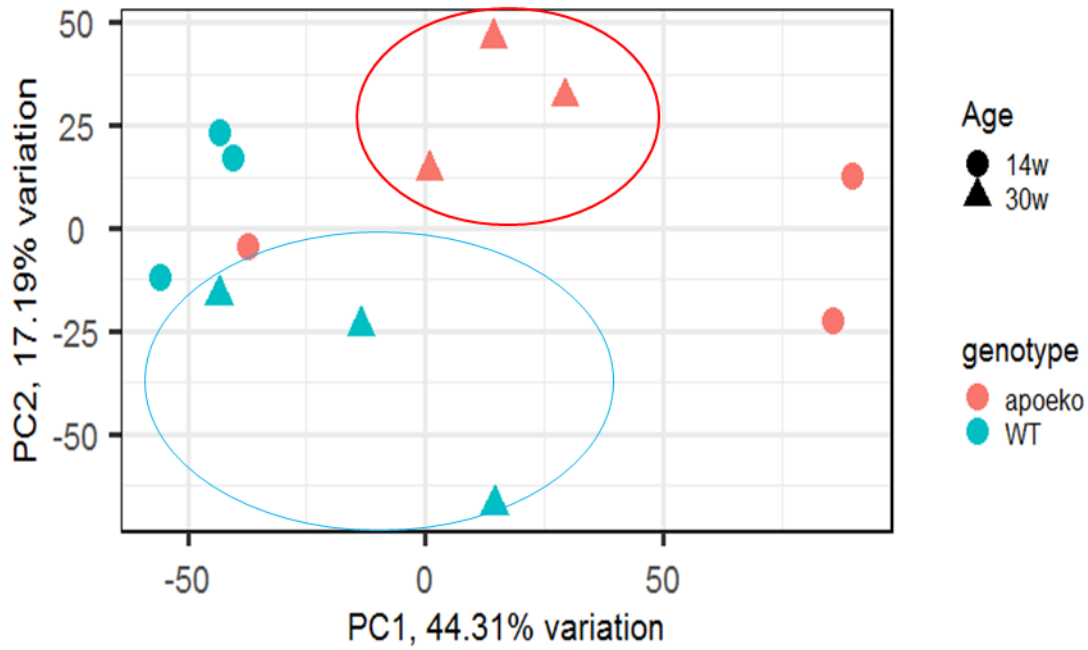
TableS1. Effect size of compared groups.

Variable Name	Groups of comparison	Mean1	Mean2	SD1	SD2	N1	N2	p-value	effect size (cohen's d)
plasma triglyceride	control vs WD	71.38	127.4	13.36	32.68	7	7	0.0175	2.243968927
	control vs aged	71.38	94.68	13.36	47.52	7	7	0.9655	0.667536833
plasma cholesterol	control vs WD	451.6	1307	97.51	116	8	8	0.004	7.98286128
	control vs aged	451.6	537.2	97.51	161.3	8	8	>0.999	0.642267991
Cleaved ATF6a in aorta	control vs WD	1.016	10.39	0.1708	3.94	7	6	0.0012	3.524933529
	control vs aged	1.016	44.31	0.1708	15.39	7	6	0.0012	4.172230956
	WD vs aged	10.39	44.31	3.94	15.39	6	6	0.0022	3.019583706
p-IRE1a protein levels in aorta	control vs WD	1.11714	2.13167	0.17337	0.31884	7	6	<0.0001	4.054775543
IRE1a protein levels in aorta	control vs WD	1.00857	3.37667	0.2166	0.54106	7	6	<0.0001	5.945255658
xBP1s protein levels in aorta	control vs WD	0.99143	2.345	0.13018	0.34807	7	6	<0.0001	5.337452593
xBP1s/total xBP1 mRNA ratio in aorta	WD vs aged	1.204	0.535	0.5093	0.1972	9	12	0.0003	1.843252362
p-PERK protein levels in aorta	control vs WD	0.69429	1.15667	0.09217	0.14052	7	6	0.004	3.963496421
p-eIF2a protein levels in aorta	control vs WD	0.80714	1.74833	0.16408	0.19854	6	7	<0.0001	5.124095839
ATF4 mRNA levels in aorta	control vs WD	0.9193	4.144	0.2781	3.001	8	9	0.0014	1.465879893
	control vs aged	0.9193	2.583	0.2781	1.458	8	12	0.0475	1.443069611
BiP protein levels in aorta	control vs aged	1.15171	0.485	0.30613	0.31984	7	6	0.0087	2.133936023
PDI protein levels in aorta	control vs aged	1.13571	0.52833	0.15608	0.15446	7	6	0.0177	3.909869396
BiP mRNA levels in aorta	control vs WD	0.9813	4.144	0.2693	3.001	8	9	0.00561	1.438030056
	control vs aged	0.9813	6.734	0.2693	3.962	8	8	0.0002	2.048666845
PDI mRNA levels in aorta	control vs WD	1.03	1.303	0.2762	0.328	3	4	>0.999	0.885426214
	control vs aged	1.03	4.722	0.2762	2.33	3	6	0.0129	1.869617105
BIP fluor. intensity in aorta	WD vs aged	1157	769.3	62.51	124.5	4	5	0.0159	3.777825099
CHOP protein levels in aorta	control vs WD	1.01	7.43	0.19459	1.76686	7	6	0.007	5.350641845
	control vs aged	1.01	22.77	0.19459	7.33366	7	6	<0.0001	4.399119777
	WD vs aged	7.43	22.77	1.76686	7.33366	6	6	<0.0001	2.875856956
p-JNK protein levels in aorta	control vs WD	0.90143	7.21833	0.27883	1.97866	7	6	0.0009	4.679834322
	control vs aged	0.90143	11.5733	0.27883	4.44582	7	6	<0.0001	3.552045238
	WD vs aged	7.21833	11.5733	1.97866	4.44582	6	6	0.0335	1.265634319
cleaved caspase 3 levels in aorta	control vs WD	1.03571	2.14167	0.4432	0.53237	7	6	0.0082	2.276718342
	control vs aged	1.03571	3.2	0.4432	0.56391	7	6	0.0012	4.314029088
	WD vs aged	2.14167	3.2	0.53237	0.56391	6	6	0.017	1.929966378

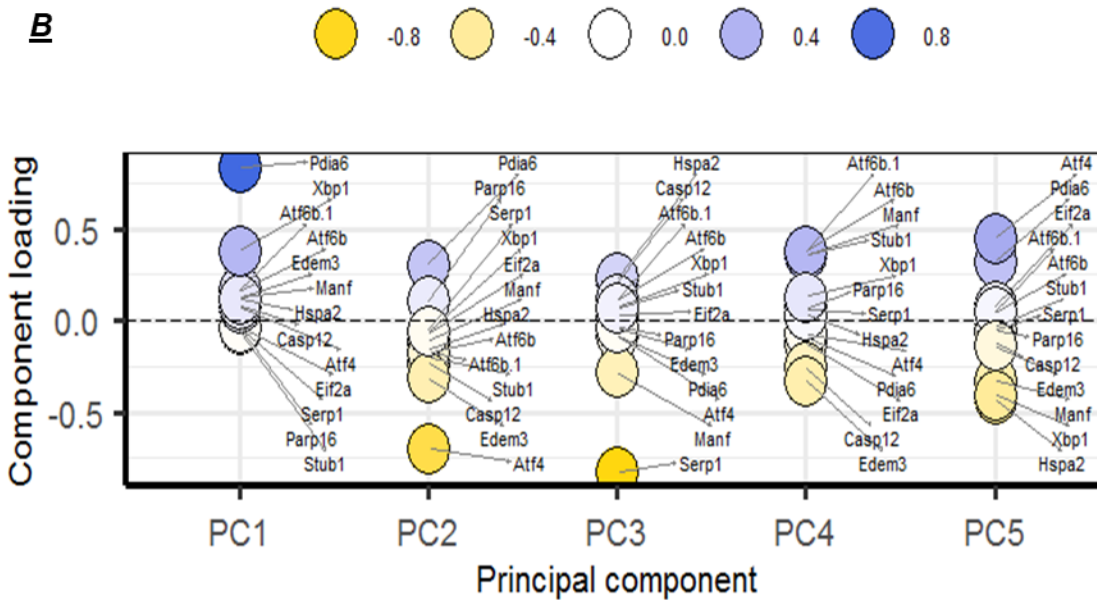
Variable Name	Groups of comparison	Mean1	Mean2	SD1	SD2	N1	N2	p-value	effect size (cohen's d)
CHOP mRNA levels in aorta	control vs WD	0.8867	2.684	0.2951	1.694	8	9	0.0386	1.433893968
	control vs aged	0.8867	5.365	0.2951	4.852	8	12	0.0176	1.179293059
	WD vs aged	2.684	5.365	1.694	4.852	9	12	>0.999	0.696004723
CHOP fluor. intensity in aorta	control vs WD	422.1	686.3	41.14	153.9	5	5	0.1887	2.345425267
	control vs aged	422.1	987.7	41.14	189.3	5	6	0.0016	3.934969612
	WD vs aged	686.3	987.7	153.9	189.3	5	6	0.381	1.727658696
Cleaved caspase 3 fluor. Intensity in aorta	control vs WD	719.9	1055	79.19	141.7	5	5	0.0585	2.91944004
	control vs aged	719.9	1115	79.19	182.4	5	5	0.012	2.809954018
	WD vs aged	1055	1115	141.7	182.4	5	5	>0.999	0.367370713
cleaved ATF6a in lung tissues	control vs WD	1.446	12.67	0.726	2.584	7	6	0.001	6.157632433
	control vs aged	1.446	2.317	0.726	1.191	7	6	0.6457	0.90208946
p-IRE-1a protein levels in lung tissues	control vs WD	1.226	2.48	0.256	0.312	7	6	<0.0001	4.433720747
	control vs aged	1.226	2.427	0.256	0.416	7	6	<0.0001	3.550695504
XBP1s protein levels in lung tissues	control vs WD	1.257	2.318	0.228	0.251	7	6	<0.0001	4.444362496
	control vs aged	1.257	0.675	0.228	0.172	7	6	0.0015	2.84658076
p-eIF2a protein levels in lung tissues	control vs WD	1.33	2.01	0.2812	0.2691	7	6	0.091	2.465860304
	control vs aged	1.33	0.815	0.2812	0.1825	7	6	0.181	2.133457912
	WD vs aged	2.01	0.815	0.2691	0.1825	6	6	0.0003	5.197591562
BiP protein levels in lung tissues	control vs WD	1.1	1.32167	0.26357	0.20527	7	6	0.078	0.928101844
	control vs aged	1.1	0.83	0.26357	0.18144	7	6	0.0262	1.174417714
	WD vs aged	1.32167	0.83	0.20527	0.18144	6	6	0.001	2.537997131
PDI protein levels in lung tissues	control vs WD	0.92429	0.57	0.12205	0.14353	7	6	0.003	2.679043086
	control vs aged	0.92429	0.64	0.12205	0.06164	7	6	0.774	2.864138267
	WD vs aged	0.57	0.64	0.14353	0.06164	6	6	0.0185	0.633750222
CHOP protein levels in lung tissues	control vs WD	0.86	1.14833	0.15481	0.19426	7	6	0.7314	1.658464789
	control vs aged	0.86	1.365	0.15481	0.23628	7	6	0.8482	2.575391192
	WD vs aged	1.14833	1.365	0.19426	0.23628	6	6	0.3888	1.001720406
P-JNK protein levels in lung tissues	control vs WD	1.31	7.54833	0.6758	1.40585	7	6	<0.0001	5.823659265
	control vs aged	1.31	7.08	0.6758	1.27433	7	6	<0.0001	5.807125906
	WD vs aged	7.54833	7.08	1.40585	1.27433	6	6	0.467	0.349058735
cleaved caspase 3 levels in lung tissues	control vs WD	1.00286	1.28667	0.36358	0.24402	7	6	0.7385	0.901229867
	control vs aged	1.00286	1.225	0.36358	0.145	7	6	0.8301	0.777366402
	WD vs aged	1.28667	1.225	0.24402	0.145	6	6	0.9867	0.307237553

Figure S1. PCA analysis of transcriptome datasets for aortae obtained from *ApoE*^{-/-} and C57BL6 mice indicated the aortic expression profile of UPR-related genes was similar between these two groups at 14 weeks of age but showed significant differences at 30 weeks of age.

A



B



A. Score plot of the principle component 1 and 2, which account for more than 60% of total variability.

At 30 weeks of age (closed triangles), UPR-related gene expression profile showed the greatest separation between *ApoE*^{-/-} and C57BL6 mice (blue circle for C57BL6 mice, orange circle for *ApoE*^{-/-} mice), while at 14 weeks of age (closed circle), no clear separation was observed. **B.** component loading plot of UPR-related gene expression in *ApoE*^{-/-} and C57BL6 mice. The UPR-related genes influencing each of the five principle components (PC1- PC5) were illustrated.