Supplementary Appendix 1

Effects of cannabidiol on *TAFAZZIN*-deficient B-lymphoblastoid cells

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Supplementary Table 1: List of human primers sequences used in qPCR analyses

Gene	Forward Sequence, 5’ → 3’	Reverse Sequence, 5’ → 3’	Product size
GPAT4	TGCCGGAAAGGAATGGAGAC	CCAGTGCTATCCTGAGCGG	193 bp
AGPAT1	AACGTGGCGCCTTCCA	GAAGTCTTGGTAGGAGGACATGACT	77 bp
PGPS	GTCAAGCTCCAGAGGCTGTT	CAGCCATGGTGACCTAAGGA	95 bp
CLS	CTTGGTGGCAGCTTCTTTGG	GGCCCTGTTCCCATTGATGT	210 bp
ALCAT1	TGGAAGGATGACAAGAGCCAT	TCGAGACTTGCTGTTTTCTGTG	120 bp
αTFP	TCGGCATCTGGGTTTTAGTC	GGTCAGCAAAGCAGAAGACC	234 bp
ABHD18	ACAAGGACTCTTCAGACAAGC	TCACAGGATGAAGCTCCCTT	132 bp
PLA2G6	CGTCAGGAAACCCAAGGTGAT	CCGGACAGTTTCTGGAGCAT	100 bp
PNPLA8	AGGAGTGGCTGTCAAGGAAAG	TCGTAGGGTCTGGAGAGCAA	196 bp
HSD17B10	CTTCTGGACCTGCCCAACTC	CCTTCTCAGAGGTCACGTCG	94 bp
GAPDH	AGAAGGCTGGGGCTCATTTG	AGGGGCCATCCACAGTCTTC	258 bp

Supplementary Table 2: Cell Growth Data[1]

Group	Cell Line	Condition	Day 0	Day 1	Day 2	Day 3	Day 4
Healthy	AG15022	VEH	1174833	1515500	2473333	3801000	4643333
	AG15022	CBD	1171800	1494500	2473333	3776500	4613000
BTHS	GM22192	VEH	1211000	1435000	1862000	2919000	3584000
	GM22192	CBD	1260000	1477000	2380000	3927000	4760000
Healthy	AG14750	VEH	1274000	1561000	2324000	3633000	4648000
	AG14750	CBD	1239000	1505000	2240000	3864000	4732000
BTHS	GM22163	VEH	1202250	1307250	1932000	2780750	3669750
	GM22163	CBD	1174250	1421000	2338000	3440500	4575375
Healthy	AG14948	VEH	1183000	1452500	2499000	4137000	5068000
	AG14948	CBD	1172500	1400000	2453500	4179000	5054000
BTHS	GM22193	VEH	1200500	1239000	1981000	3412500	4707500
	GM22193	CBD	1169000	1197000	2576000	4452000	6146000
Healthy	AG14731	VEH	1204000	1281000	2254000	4903500	5628000
	AG14731	CBD	1200500	1242500	2226000	4830000	5698000
BTHS	GM22150	VEH	1302000	1575000	2317000	2856000	3097500
	GM22150	CBD	1323000	1652000	2835000	3696000	4121250
Healthy	AG14947	VEH	1205750	1454250	3097500	5108250	5950000
	AG14947	CBD	1198750	1471750	3048500	5003250	6072500
BTHS	GM22194	VEH	1211000	1400000	2139667	3145917	3624833
	GM22194	CBD	1186500	1509667	2402167	3804500	4627000

[1] Data show cell counts for each cell line on each day.

Supplementary Table 3. Cell Cycle Analysis[1]

Group	Cell Line used	Condition	Sample	Sub G1	G1	S	G2/M
Healthy	AG15022	VEH	1	4.47	68.66	4.3	20.8
	AG15022	TREAT	2	2.03	69.27	11.88	15.91
BTHS	GM22192	VEH	3	1.96	67.37	14.65	16.15
	GM22192	CBD	4	6.45	66.1	12.03	14.39
Healthy	AG14750	VEH	5	3.42	70	12.62	12.45
	AG14750	TREAT	6	4.11	69.97	12.99	12.66
BTHS	GM22163	VEH	7	2.65	70.03	14.63	12.16
	GM22163	CBD	8	3.45	68.41	13.72	13.76
Healthy	AG14948	VEH	9	4.16	74.71	9.59	10.79
	AG14948	TREAT	10	3.88	73.8	10.56	11.44
BTHS	GM22193	VEH	11	11.95	64.37	10.11	13.23
	GM22193	CBD	12	3.48	69.09	11.42	15.67
Healthy	AG14731	VEH	13	20.5	58.77	10.85	9.4
	AG14731	TREAT	14	12.35	59.75	11.53	15.5
BTHS	GM22159	VEH	15	15.06	58.34	7.77	16.1
	GM22150	CBD	16	11.06	65.31	8.73	13.18
Healthy	AG14947	VEH	17	9.94	64.48	17.7	7,49
	AG14947	TREAT	18	8.62	62.47	11.48	16.73
BTHS	GM22194	VEH	19	11.66	61.79	13.22	12.52
	GM22194	CBD	20	15.23	58.7	11.7	13.4

[1] Data show percent of cells in each cell cycle phase.

Supplementary Table 4: Concentration of cardiolipin fatty acids in vehicle- or CBD-treated BTHS and healthy B-lymphoblastoids.[1]

Cardiolipin fatty acid species	Healthy vehicle (μg/mg of protein)	Healthy CBD (μg/mg of protein)	BTHS vehicle (μg/mg of protein)	BTHS CBD (μg/mg of protein)
C 10:0	0.049 ± 0.020	0.049 ± 0.018	0.052 ± 0.028	0.055 ± 0.034
C 12:0	0.022 ± 0.004	0.018 ± 0.004	0.026 ± 0.009	0.028 ± 0.006
C 14:0	0.130 ± 0.024	0.134 ± 0.034	0.079 ± 0.022	0.124 ± 0.026
C 15:0	0.036 ± 0.007	0.035 ± 0.008	0.033 ± 0.007	0.052 ± 0.006
C 16:0	0.998 ± 0.028^{a}	0.896 ± 0.087^{a}	1.063 ± 0.104^{a}	1.674 ± 0.181^{b}
C 17:0	0.075 ± 0.015^{ab}	0.068 ± 0.009^{ab}	0.061 ± 0.006^{a}	0.118 ± 0.025^{b}
C 18:0	0.607 ± 0.067^{bc}	0.514 ± 0.114^{a}	0.569 ± 0.099^{ab}	0.992 ± 0.177^{c}
C 20:0	0.048 ± 0.017	0.032 ± 0.006	0.025 ± 0.005	0.055 ± 0.014
C 22:0	0.028 ± 0.007^{b}	0.030 ± 0.009^{b}	0.017 ± 0.005^{ab}	0.042 ± 0.010^{c}
C 23:0	0.008 ± 0.001^{ab}	0.006 ± 0.001^{a}	0.009 ± 0.002^{ab}	0.019 ± 0.004^{b}
C 24:0	0.042 ± 0.015	0.048 ± 0.021	0.041 ± 0.010	0.070 ± 0.023
SFAs	2.057 ± 0.042^{a}	1.847 ± 0.188^{a}	1.993 ± 0.186^{a}	3.256 ± 0.376^{b}
C 12:1	0.010 ± 0.00^{ab}	0.009 ± 0.004^{ab}	0.006 ± 0.001^{a}	0.023 ± 0.007^{b}
C 14:1	0.017 ± 0.002	0.026 ± 0.009	0.012 ± 0.001	0.025 ± 0.012
C 16:1n-7	0.738 ± 0.121^{b}	0.795 ± 0.196^{b}	0.070 ± 0.010^{a}	0.144 ± 0.028^{a}
C 18:1n-7	1.252 ± 0.164	1.256 ± 0.220	0.721 ± 0.104	1.040 ± 0.111
C 18:1n-9	1.018 ± 0.141^{a}	1.010 ± 0.170^{a}	0.232 ± 0.046^{b}	0.373 ± 0.039^{b}
C 20:1n-7	0.013 ± 0.005^{ab}	0.012 ± 0.005^{ab}	0.007 ± 0.002^{a}	0.016 ± 0.003^{b}
C 20:1n-9	0.016 ± 0.004	0.014 ± 0.004	0.011 ± 0.001	0.025 ± 0.008
C 20:1n-11	0.009 ± 0.001	0.004 ± 0.002	0.007 ± 0.002	0.013 ± 0.006
C 22:1n-7	0.006 ± 0.001^{ab}	0.008 ± 0.002^{ab}	0.007 ± 0.003^{a}	0.018 ± 0.005^{b}
C 22:1n-9	0.017 ± 0.005	0.021 ± 0.009	0.014 ± 0.004	0.040 ± 0.007
C 22:1n-11	0.011 ± 0.003^{ab}	0.008 ± 0.002^{ab}	0.006 ± 0.002^{a}	0.020 ± 0.006^{b}
C 24:1n-9	0.015 ± 0.005	0.009 ± 0.002	0.016 ± 0.007	0.023 ± 0.011
MUFAs	3.121 ± 0.381^{b}	3.172 ± 0.568^{b}	1.107 ± 0.144^{a}	1.760 ± 0.142^{ab}
C 18:2n-6	0.248 ± 0.030^{a}	0.243 ± 0.050^{a}	0.021 ± 0.005^{b}	0.044 ± 0.013^{b}
C 18:3n-6	0.011 ± 0.003	0.009 ± 0.001	0.011 ± 0.003	0.022 ± 0.010
C 20:2n-6	0.005 ± 0.002	0.011 ± 0.004	0.008 ± 0.002	0.007 ± 0.003
C 20:3n-6	0.082 ± 0.017^{a}	0.092 ± 0.020^{a}	0.012 ± 0.004^{b}	0.014 ± 0.002^{b}
C 20:4n-6	0.043 ± 0.010	0.047 ± 0.011	0.024 ± 0.010	0.047 ± 0.016
C 22:2n-6	0.012 ± 0.005	0.011 ± 0.004	0.007 ± 0.002	0.014 ± 0.005
C 22:4n-6	0.009 ± 0.002	0.007 ± 0.002	0.011 ± 0.004	0.019 ± 0.004
C 22:5n-6	0.008 ± 0.002	0.008 ± 0.002	0.010 ± 0.001	0.014 ± 0.005
N-6	0.417 ± 0.050^{a}	0.430 ± 0.083^{a}	0.105 ± 0.019^{b}	0.181 ± 0.043^{b}
C 18:3n-3	0.027 ± 0.001	0.024 ± 0.006	0.028 ± 0.005	0.037 ± 0.009
C 18:4n-3	0.013 ± 0.004	0.008 ± 0.003	0.010 ± 0.002	0.027 ± 0.011
C 20:3n-3	0.016 ± 0.009^{ab}	0.008 ± 0.003^{a}	0.010 ± 0.004^{a}	0.044 ± 0.012^{b}

C 20:4n-3	0.006 ± 0.003^{a}	0.004 ± 0.001^{a}	0.006 ± 0.002^{a}	0.024 ± 0.007^{b}
C 20:5n-3	0.012 ± 0.003^{ab}	0.005 ± 0.001^{a}	0.009 ± 0.001^{ab}	0.013 ± 0.003^{b}
C 22:5n-3	0.008 ± 0.002	0.011 ± 0.003	0.012 ± 0.003	0.017 ± 0.007
C 22:6n-3	0.009 ± 0.005^{ab}	0.006 ± 0.002^{ab}	0.005 ± 0.003^{a}	0.019 ± 0.007^{b}
N-3	0.092 ± 0.022^{ab}	0.065 ± 0.014^{a}	0.080 ± 0.010^{a}	0.181 ± 0.036^{b}
Total	5.716 ± 0.434^{b}	5.539 ± 0.781^{ab}	3.305 ± 0.336^{a}	5.399 ± 0.563^{b}

[1] Data are presented as mean ± S.E.M; n = 5. ^{abc}Groups with different superscript letters are significantly different, $P<0.05$.

Supplementary Table 5A. RT-qPCR Ct values

Sample	**Cell Line ID#**	***GAPDH***	***AGPAT1***	***GPAT4***	***CLS***
H-Veh-1	AG15022	17.21	25.18	22.27	21.77
H-Veh-2	AG14750	17.27	25.70	22.65	22.15
H-Veh-3	AG14948	17.46	25.01	22.07	21.53
H-Veh-4	AG14731	17.74	25.29	23.23	22.75
H-Veh-5	AG14947	17.09	25.00	22.36	21.64
H-CBD-1	AG15022	17.54	25.03	22.24	21.58
H-CBD-2	AG14750	17.12	25.39	22.54	21.99
H-CBD-3	AG14948	17.66	25.29	22.26	21.64
H-CBD-4	AG14731	17.15	25.38	22.58	22.23
H-CBD-5	AG14947	17.04	24.97	22.39	21.47
BTHS-Veh-1	GM22192	17.64	25.45	22.59	22.02
BTHS-Veh-2	GM22163	17.62	25.55	22.86	21.97
BTHS-Veh-3	GM22193	18.13	25.47	22.37	22.04
BTHS-Veh-4	GM22150	18.13	25.49	22.89	22.32
BTHS-Veh-5	GM22194	17.42	24.56	22.52	21.74
BTHS-CBD-1	GM22192	17.34	25.55	22.89	22.10
BTHS-CBD-2	GM22163	17.48	25.22	22.59	22.03
BTHS-CBD-3	GM22193	17.65	25.38	22.63	22.31
BTHS-CBD-4	GM22150	17.98	25.17	22.87	22.20
BTHS-CBD-5	GM22194	17.14	24.58	22.45	21.59

H-Veh = Vehicle-treated healthy B-lymphoblastoid cells
H-CBD = CBD-treated healthy B-lymphoblastoid cells
BTHS-Veh = Vehicle-treated Barth's B-lymphoblastoid cells
BTHS-CBD = CBD-treated Barth's B-lymphoblastoid cells

Supplementary Table 5B. RT-qPCR Ct values

Sample	Cell Line ID#	*GAPDH*	*PGPS*
H-Veh-1	AG15022	17.60	31.00
H-Veh-2	AG14750	17.52	30.60
H-Veh-3	AG14948	17.41	30.25
H-Veh-4	AG14731	18.36	30.92
H-Veh-5	AG14947	17.06	29.49
H-CBD-1	AG15022	17.58	30.49
H-CBD-2	AG14750	17.47	29.94
H-CBD-3	AG14948	17.96	30.21
H-CBD-4	AG14731	17.67	30.41
H-CBD-5	AG14947	17.30	29.74
BTHS-Veh-1	GM22192	17.86	29.51
BTHS-Veh-2	GM22163	17.71	30.29
BTHS-Veh-3	GM22193	17.84	31.00
BTHS-Veh-4	GM22150	18.11	30.16
BTHS-Veh-5	GM22194	17.51	29.63
BTHS-CBD-1	GM22192	17.72	29.43
BTHS-CBD-2	GM22163	17.56	29.99
BTHS-CBD-3	GM22193	17.71	31.06
BTHS-CBD-4	GM22150	18.04	29.42
BTHS-CBD-5	GM22194	17.97	29.89

H-Veh = Vehicle-treated healthy B-lymphoblastoid cells
H-CBD = CBD-treated healthy B-lymphoblastoid cells
BTHS-Veh = Vehicle-treated Barth's B-lymphoblastoid cells
BTHS-CBD = CBD-treated Barth's B-lymphoblastoid cells

Supplementary Table 5C. RT-qPCR Ct values

Sample	**Cell Line ID#**	***GAPDH***	***ALCAT1***	***αTFP***
H-Veh-1	AG15022	17.14	23.57	26.25
H-Veh-2	AG14750	17.03	23.75	25.94
H-Veh-3	AG14948	17.04	23.79	25.19
H-Veh-4	AG14731	17.84	23.79	26.91
H-Veh-5	AG14947	16.53	23.26	25.07
H-CBD-1	AG15022	17.32	23.67	26.20
H-CBD-2	AG14750	16.89	23.53	25.81
H-CBD-3	AG14948	17.33	24.02	25.60
H-CBD-4	AG14731	17.14	23.32	26.27
H-CBD-5	AG14947	16.63	23.21	25.14
BTHS-Veh-1	GM22192	17.20	23.79	26.37
BTHS-Veh-2	GM22163	17.22	23.73	26.37
BTHS-Veh-3	GM22193	17.31	23.79	26.52
BTHS-Veh-4	GM22150	17.65	24.02	26.27
BTHS-Veh-5	GM22194	16.75	23.35	25.87
BTHS-CBD-1	GM22192	17.33	23.90	26.55
BTHS-CBD-2	GM22163	17.14	23.64	26.60
BTHS-CBD-3	GM22193	17.15	23.62	26.41
BTHS-CBD-4	GM22150	17.62	24.04	26.03
BTHS-CBD-5	GM22194	16.77	23.67	26.36

H-Veh = Vehicle-treated healthy B-lymphoblastoid cells
H-CBD = CBD-treated healthy B-lymphoblastoid cells
BTHS-Veh = Vehicle-treated Barth's B-lymphoblastoid cells
BTHS-CBD = CBD-treated Barth's B-lymphoblastoid cells

Supplementary Table 5D. RT-qPCR Ct values

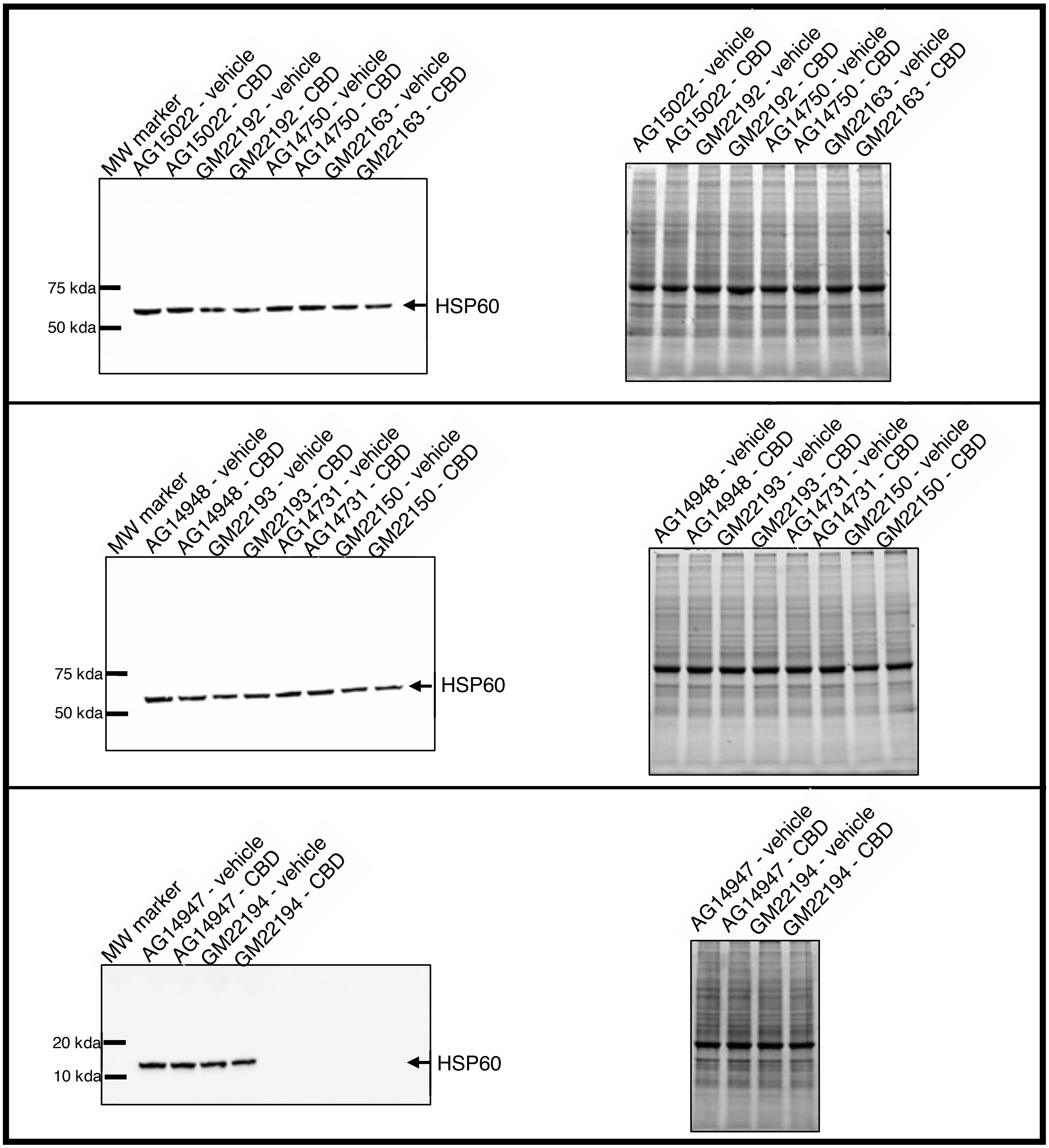
Sample	Cell Line ID#	*GAPDH*	*ABHD18*	*PLA2G6*	*PNPLA8*
H-Veh-1	AG15022	17.37	24.72	25.43	23.72
H-Veh-2	AG14750	17.27	25.28	26.52	24.22
H-Veh-3	AG14948	17.32	25.36	25.98	24.45
H-Veh-4	AG14731	18.07	25.81	26.61	25.12
H-Veh-5	AG14947	17.28	25.01	25.44	24.10
H-CBD-1	AG15022	17.47	25.05	25.48	24.07
H-CBD-2	AG14750	17.25	25.12	26.18	24.19
H-CBD-3	AG14948	17.52	25.64	26.35	24.74
H-CBD-4	AG14731	17.44	25.40	25.72	24.79
H-CBD-5	AG14947	17.02	24.80	25.50	24.24
BTHS-Veh-1	GM22192	17.51	25.47	25.46	24.88
BTHS-Veh-2	GM22163	17.69	25.56	26.31	25.03
BTHS-Veh-3	GM22193	17.47	25.55	26.10	24.99
BTHS-Veh-4	GM22150	18.00	25.27	25.99	24.36
BTHS-Veh-5	GM22194	17.30	25.10	26.04	24.72
BTHS-CBD-1	GM22192	17.45	25.46	25.93	24.83
BTHS-CBD-2	GM22163	17.45	25.51	25.92	24.85
BTHS-CBD-3	GM22193	17.45	25.72	26.11	25.14
BTHS-CBD-4	GM22150	18.09	25.37	25.79	24.63
BTHS-CBD-5	GM22194	17.11	24.95	25.70	24.01

H-Veh = Vehicle-treated healthy B-lymphoblastoid cells
H-CBD = CBD-treated healthy B-lymphoblastoid cells
BTHS-Veh = Vehicle-treated Barth's B-lymphoblastoid cells
BTHS-CBD = CBD-treated Barth's B-lymphoblastoid cells

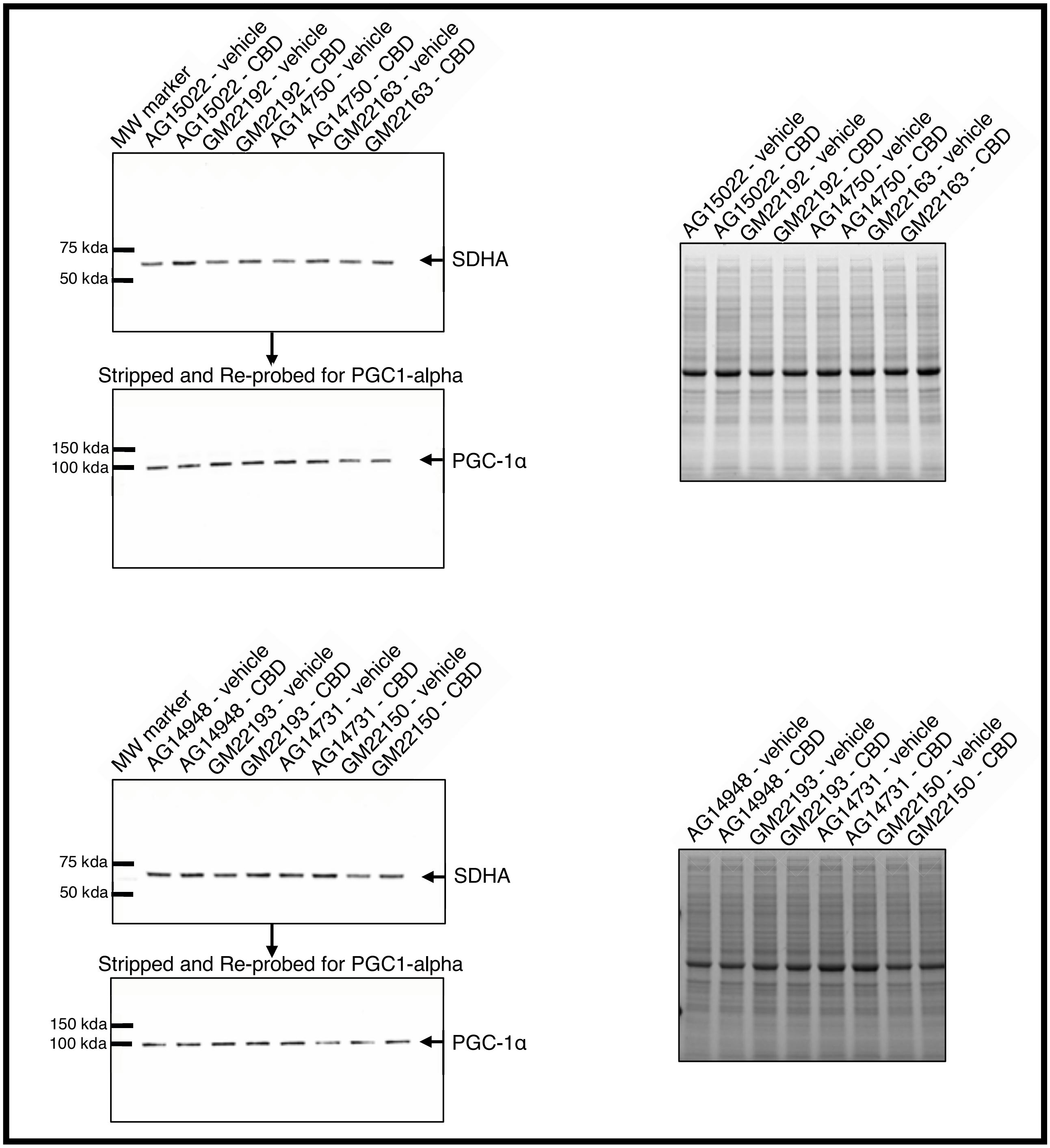
Supplementary Table 5E. RT-qPCR Ct values

Sample	**Cell Line ID#**	***GAPDH***	***HSD17B10***
H-Veh-1	AG15022	18.11	23.92
H-Veh-2	AG14750	18.15	24.27
H-Veh-3	AG14948	18.16	23.75
H-Veh-4	AG14731	19.05	25.20
H-Veh-5	AG14947	18.01	23.94
H-CBD-1	AG15022	18.17	24.02
H-CBD-2	AG14750	18.09	24.26
H-CBD-3	AG14948	18.36	24.24
H-CBD-4	AG14731	18.19	24.50
H-CBD-5	AG14947	17.86	23.79
BTHS-Veh-1	GM22192	18.30	24.10
BTHS-Veh-2	GM22163	18.40	24.05
BTHS-Veh-3	GM22193	18.26	24.22
BTHS-Veh-4	GM22150	18.83	24.36
BTHS-Veh-5	GM22194	18.11	24.02
BTHS-CBD-1	GM22192	18.17	24.32
BTHS-CBD-2	GM22163	18.35	23.72
BTHS-CBD-3	GM22193	18.38	24.46
BTHS-CBD-4	GM22150	18.93	24.06
BTHS-CBD-5	GM22194	17.95	24.17

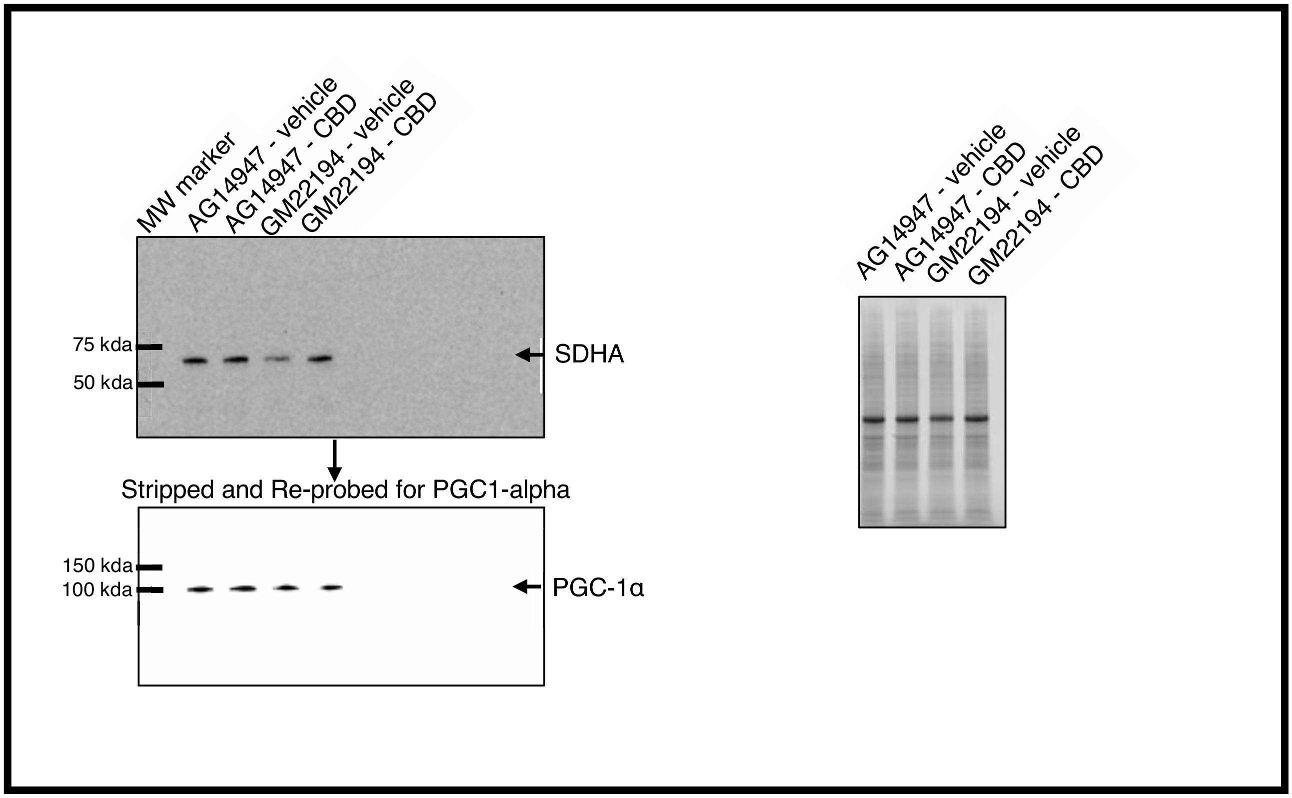
H-Veh = Vehicle-treated healthy B-lymphoblastoid cells
H-CBD = CBD-treated healthy B-lymphoblastoid cells
BTHS-Veh = Vehicle-treated Barth's B-lymphoblastoid cells
BTHS-CBD = CBD-treated Barth's B-lymphoblastoid cells



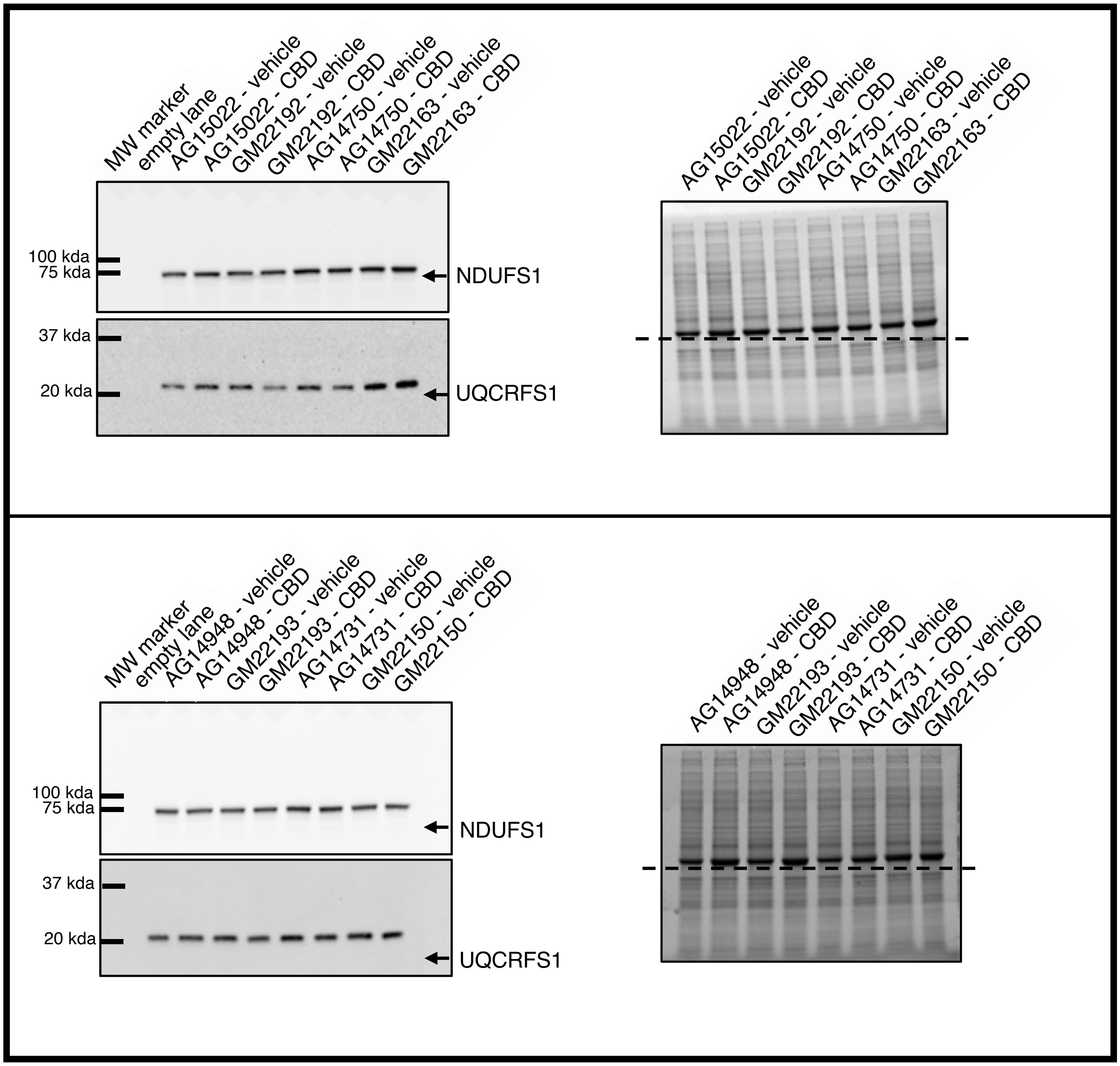
Supplementary Figure 1: Uncropped and unadjusted immunoblots of HSP60. Total protein loading for each gel was visualized by UV-imaging of stain-free gels (Bio-Rad Canada, Mississauga, Ontario, Canada), located to the right of each immunoblot.



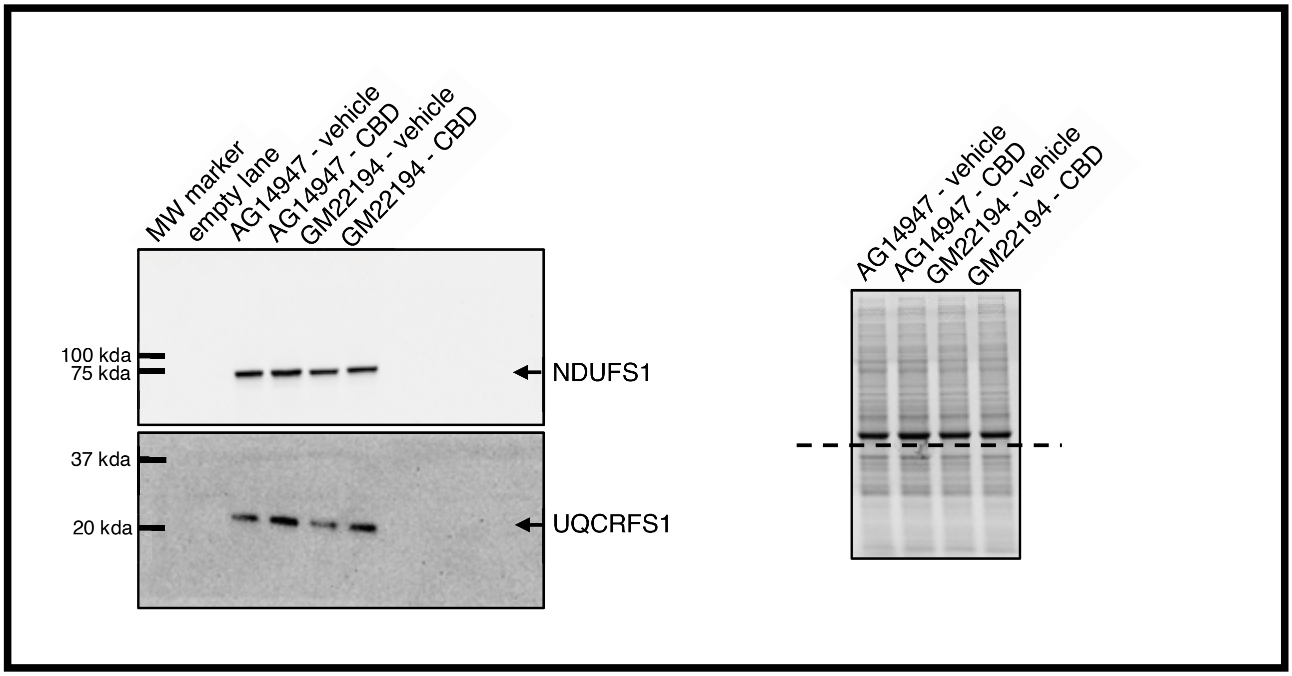
Supplementary Figure 2: Uncropped and unadjusted immunoblots of SDHA and PGC-1α. Total protein loading for each gel was visualized by UV-imaging of stain-free gels (Bio-Rad Canada, Mississauga, Ontario, Canada), located on the right of each blot.



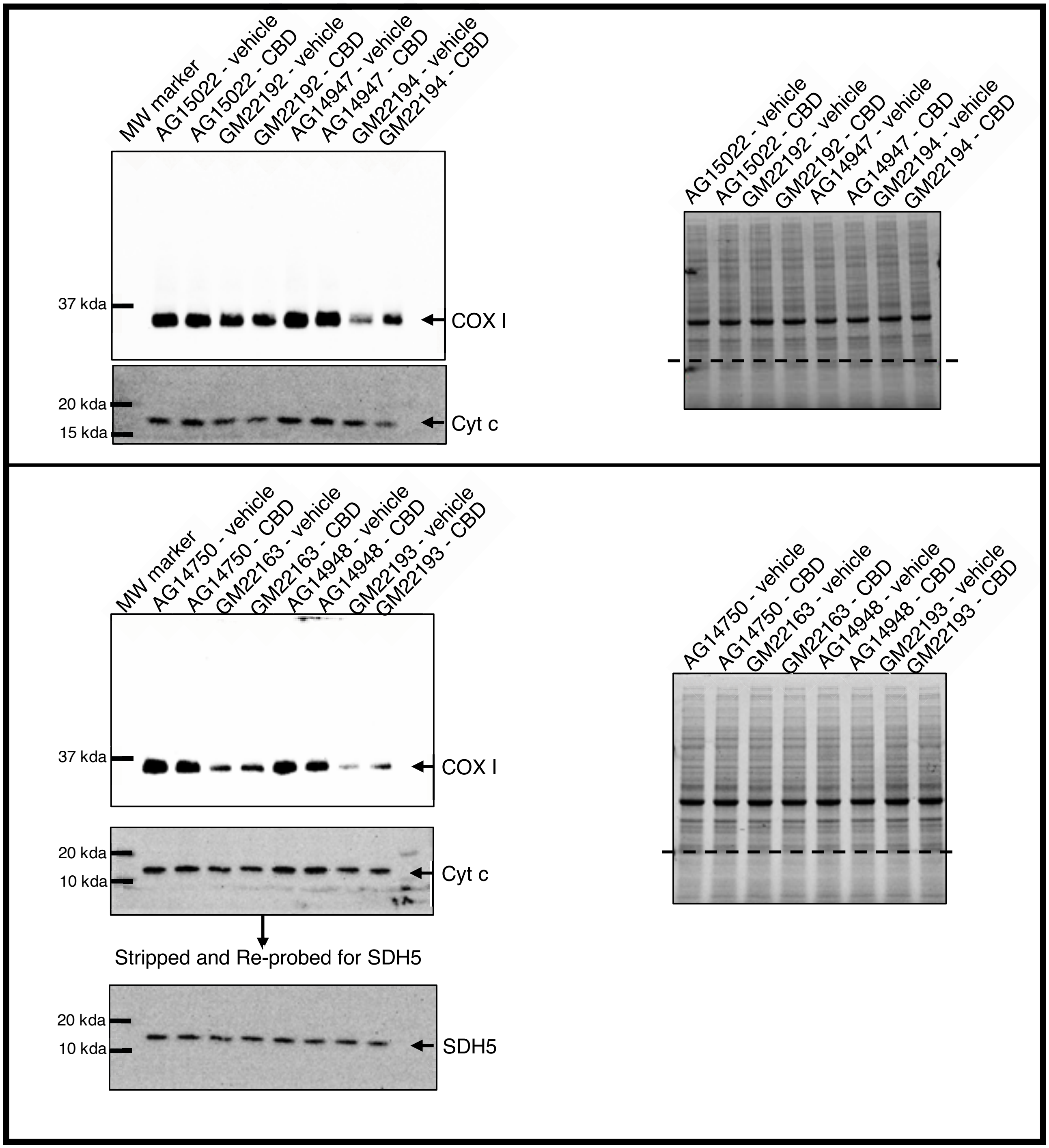
Supplementary Figure 3: Uncropped and unadjusted immunoblots of SDHA and PGC-1α. Total protein loading for each gel was visualized by UV-imaging of Stain-free gels (Bio-Rad Canada, Mississauga, Ontario, Canada), located to the right of each immunoblot.



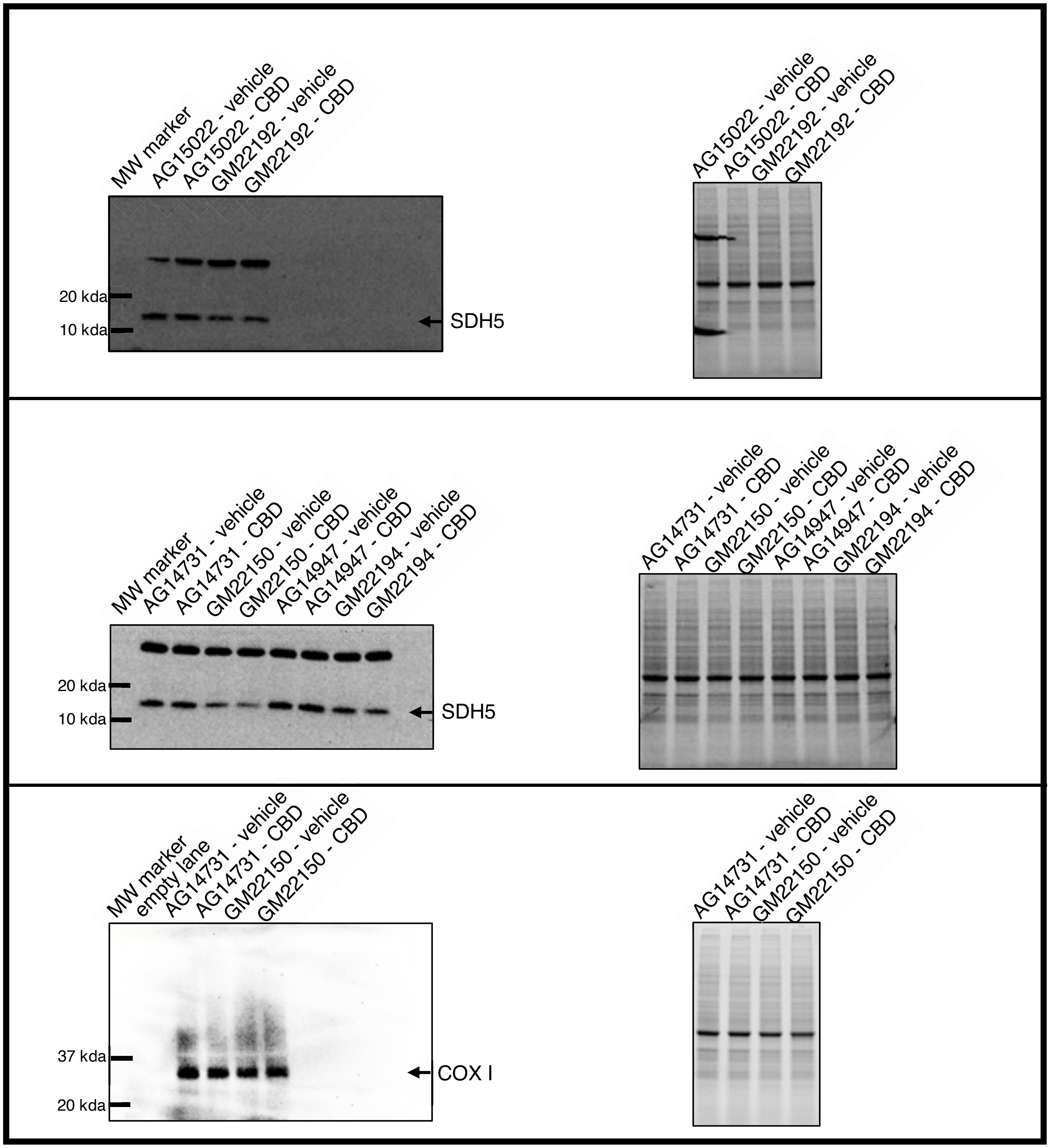
Supplementary Figure 4: Uncropped and unadjusted immunoblots of NDUFS1 and UQCRFS1. Total protein loading for each gel was visualized by UV-imaging of Stain-free gels (Bio-Rad Canada, Mississauga, Ontario, Canada), located to the right of each immunoblot.



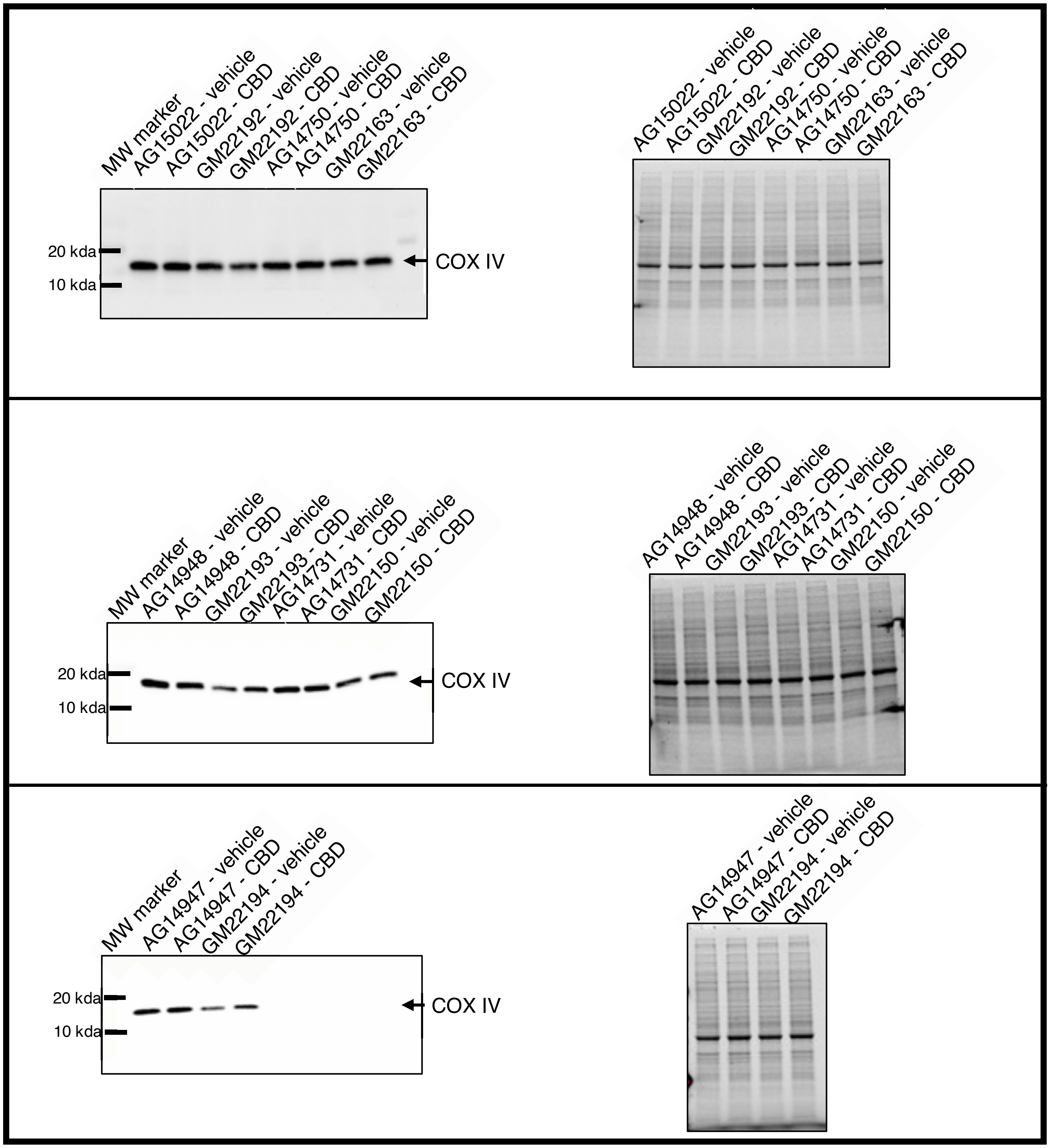
Supplementary Figure 5: Uncropped and unadjusted immunoblots of NDUFS1 and UQCRFS1. Total protein loading for each gel was visualized by UV-imaging of Stain-free gels (Bio-Rad Canada, Mississauga, Ontario, Canada), located to the right of each immunoblot.



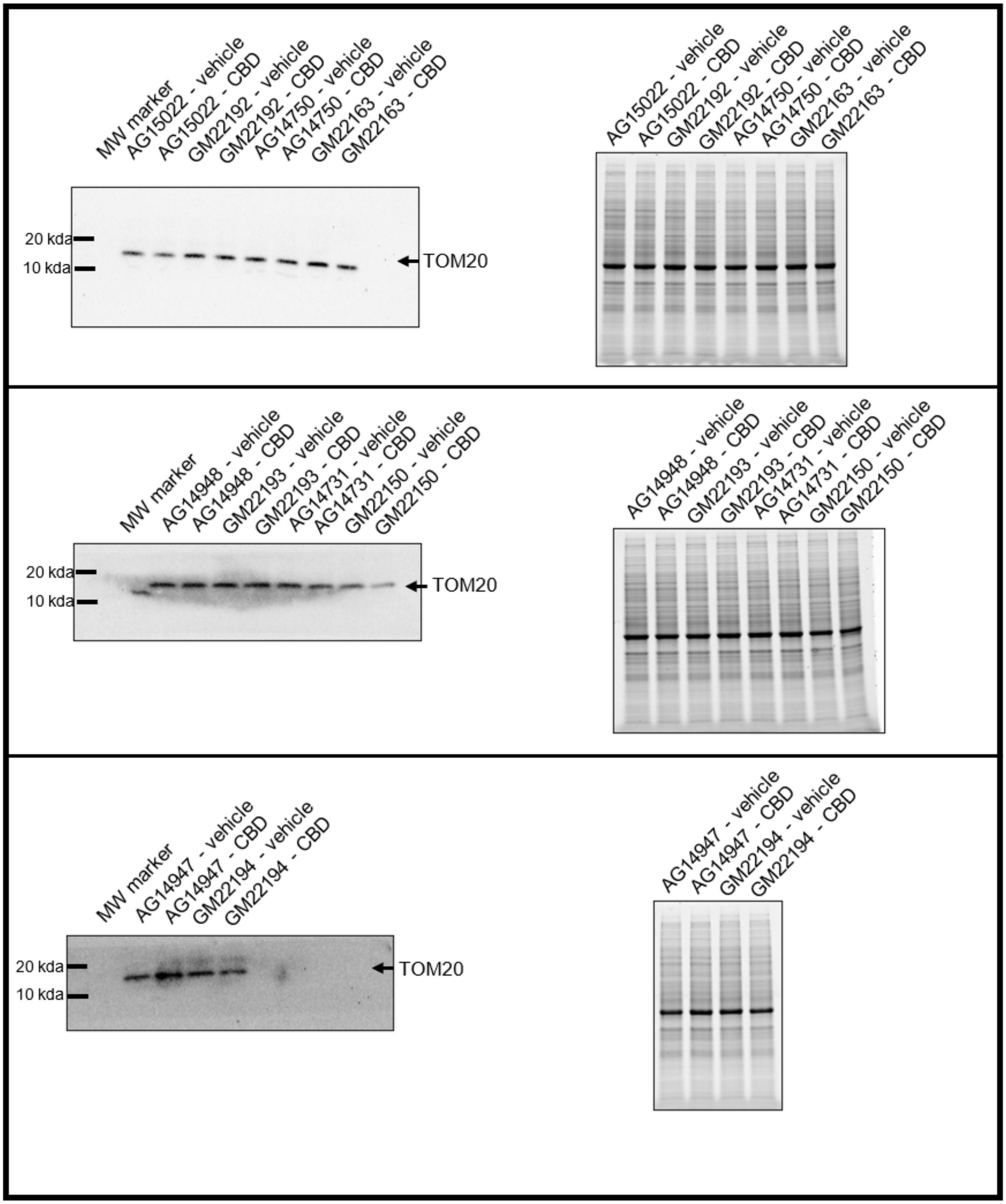
Supplementary Figure 6: Uncropped and unadjusted immunoblots of COX I, Cyt c and SDH5. Total protein loading for each gel was visualized by UV-imaging of Stain-free gels (Bio-Rad Canada, Mississauga, Ontario, Canada), located to the right of each immunoblot.



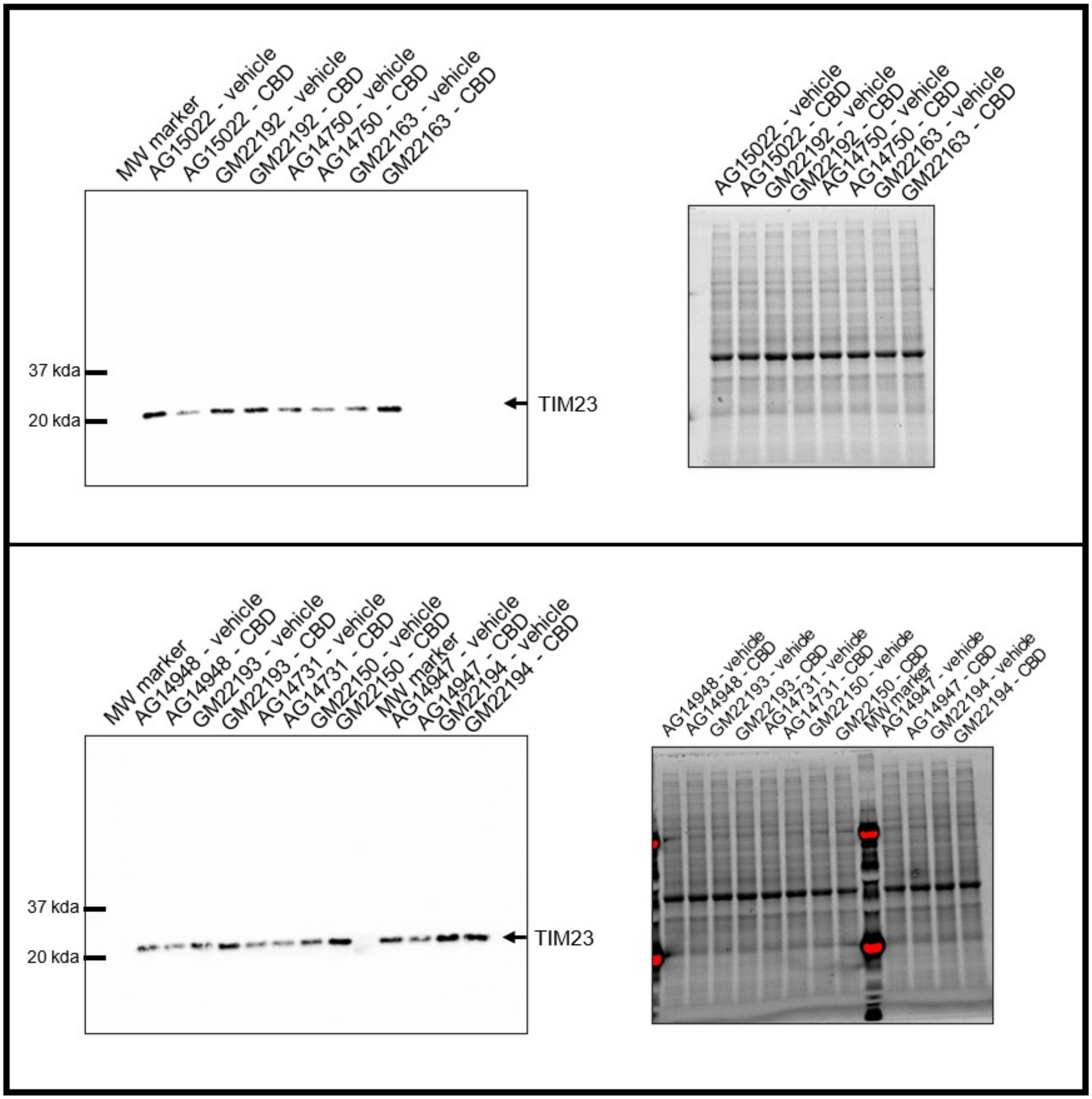
Supplementary Figure 7: Uncropped and unadjusted immunoblots of COX I, and SDH5. Total protein loading for each gel was visualized by UV-imaging of Stain-free gels (Bio-Rad Canada, Mississauga, Ontario, Canada), located to the right of each immunoblot.



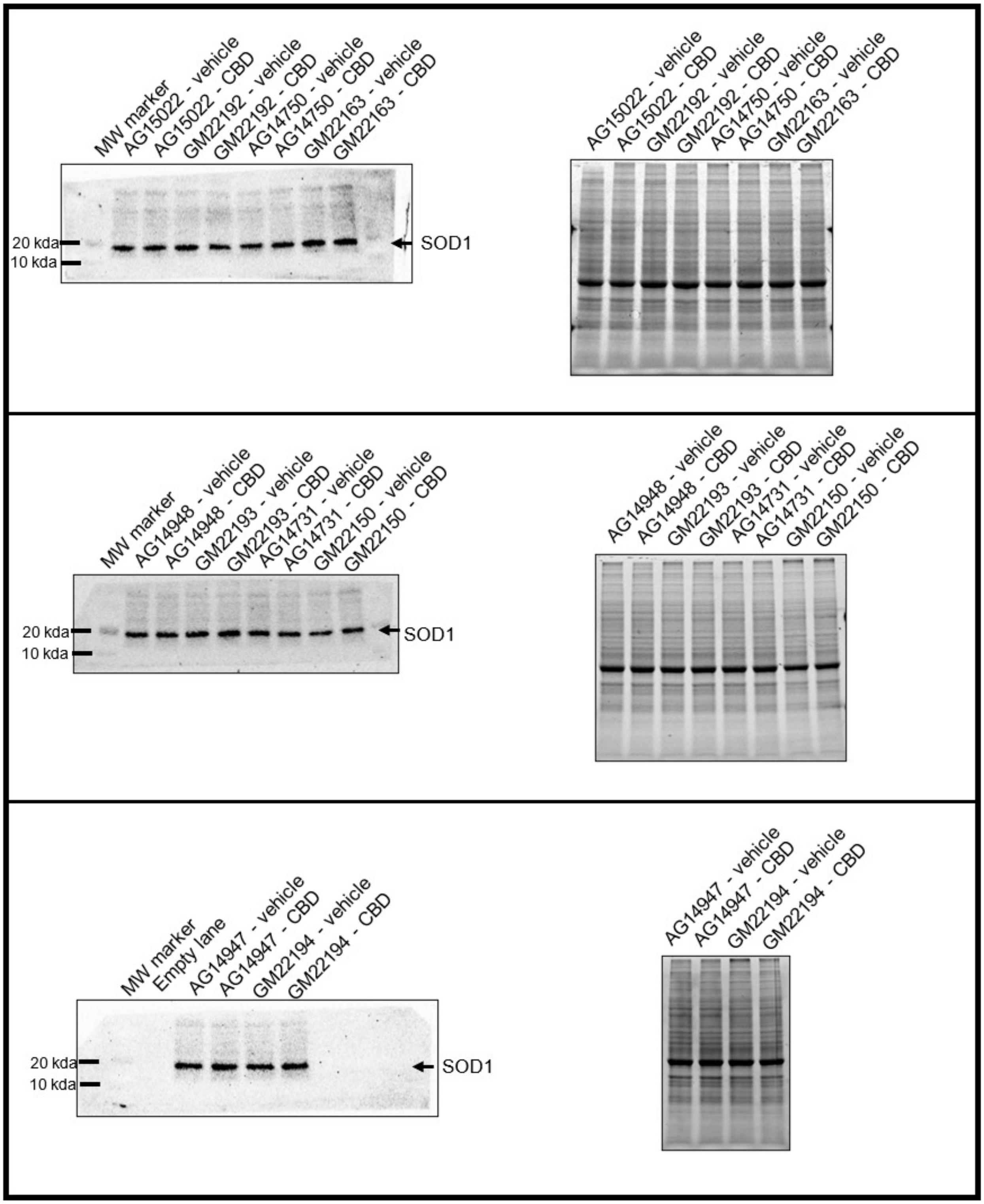
Supplementary Figure 8: Uncropped and unadjusted immunoblots of COX IV. Total protein loading for each gel was visualized by UV-imaging of stain-free gels (Bio-Rad Canada, Mississauga, Ontario, Canada), located to the right of each immunoblot.



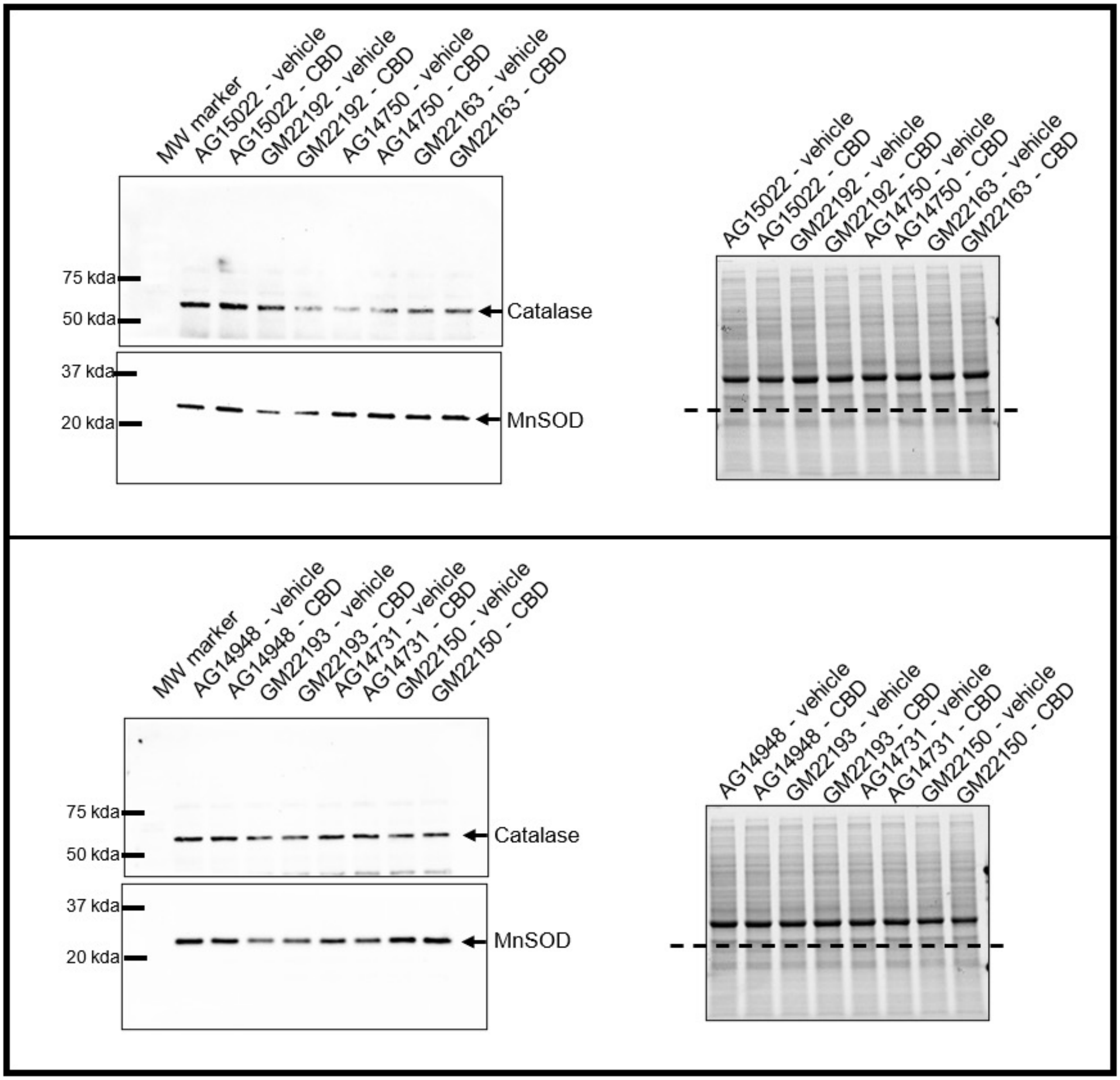
Supplementary Figure 9: Uncropped and unadjusted immunoblots of TOM20. Total protein loading for each gel was visualized by UV-imaging of stain-free gels (Bio-Rad Canada, Mississauga, Ontario, Canada), located on the right of each blot.



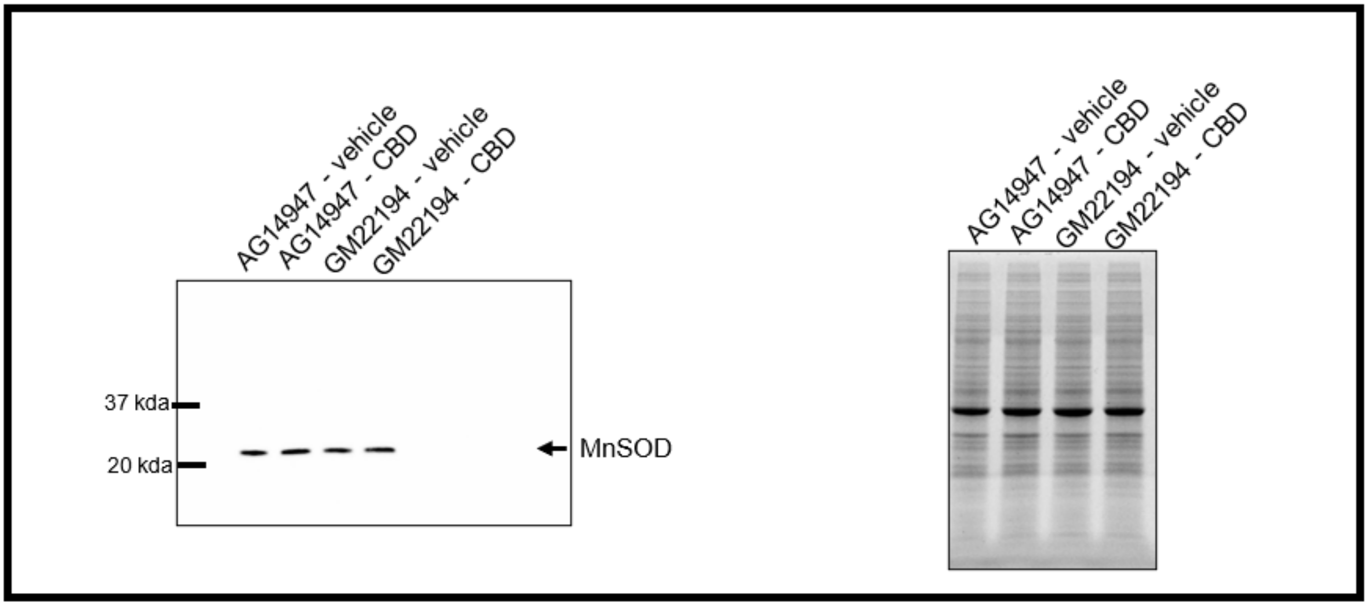
Supplementary Figure 10: Uncropped and unadjusted immunoblots of TIM23. Total protein loading for each gel was visualized by UV-imaging of stain-free gels (Bio-Rad Canada, Mississauga, Ontario, Canada), located on the right of each blot.



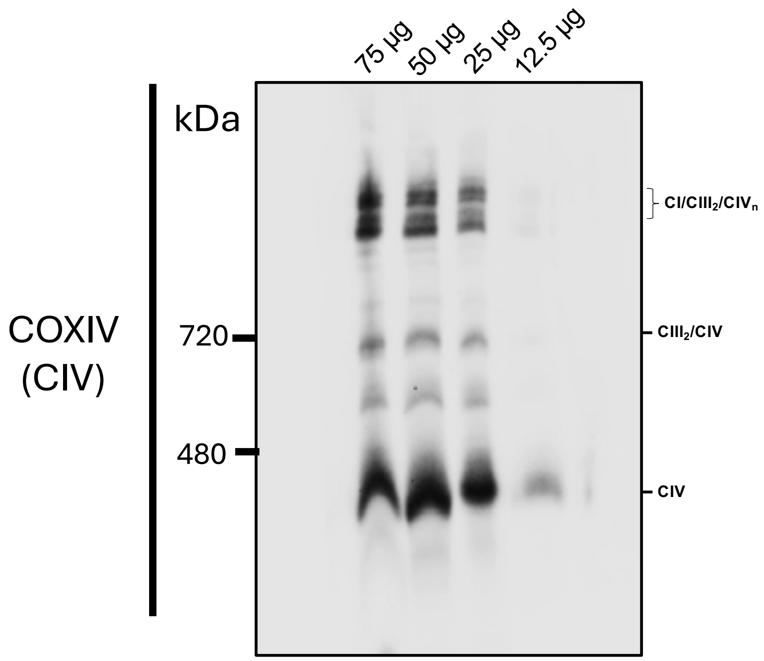
Supplementary Figure 11: Uncropped and unadjusted immunoblots of SOD1. Total protein loading for each gel was visualized by UV-imaging of stain-free gels (Bio-Rad Canada, Mississauga, Ontario, Canada), located on the right of each blot.



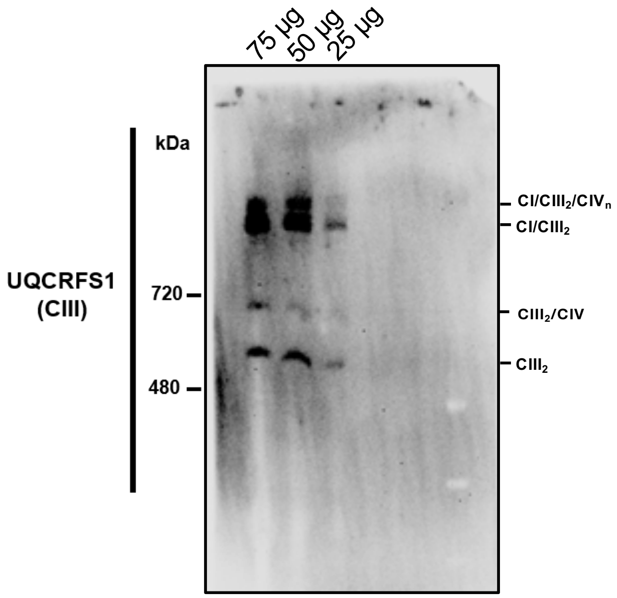
Supplementary Figure 12: Uncropped and unadjusted immunoblots of MnSOD and Catalase. Total protein loading for each gel was visualized by UV-imaging of stain-free gels (Bio-Rad Canada, Mississauga, Ontario, Canada), located on the right of each blot.



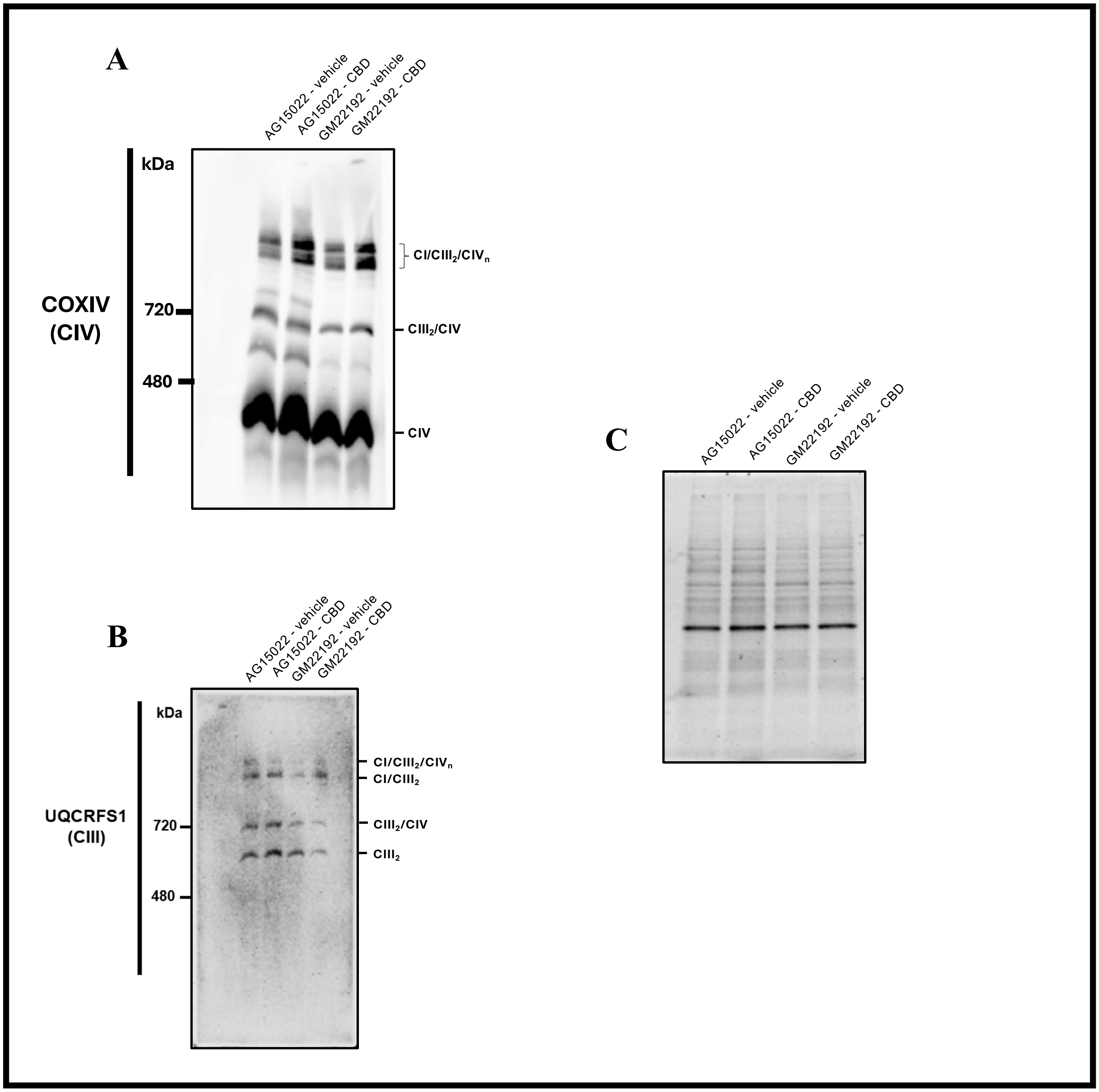
Supplementary Figure 13: Uncropped and unadjusted immunoblots of MnSOD. Total protein loading for each gel was visualized by UV-imaging of stain-free gels (Bio-Rad Canada, Mississauga, Ontario, Canada), located on the right of each blot.



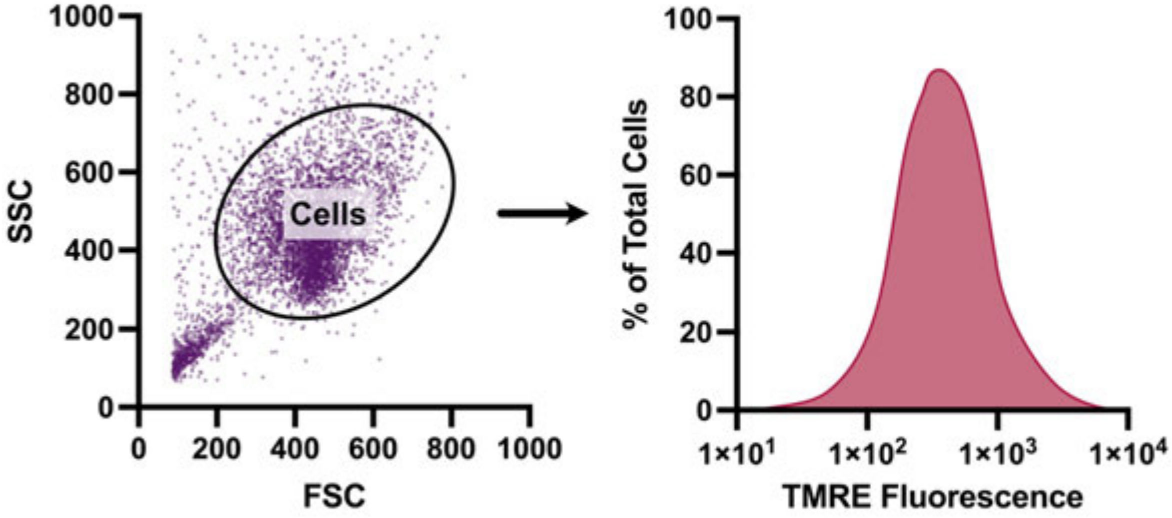
Supplementary Figure 14: Assessment of the optimal range of total protein loading in BN-PAGE for analysis of complexes containing COXIV. Mitochondrial protein isolated from all five healthy B-lymphoblastoid cells lines was pooled and loaded in descending masses (75, 50, 25, and 12.5 *μ*g) onto a BN-PAGE gel. Protein complexes were probed using anti-COXIV antibodies to assess signal saturation.



Supplementary Figure 15: Assessment of the optimal range of total protein loading in BN-PAGE for analysis of supercomplexes containing UQCRFS1. Mitochondrial protein isolated from all five healthy B-lymphoblastoid cells lines was pooled and loaded in descending masses (75, 50, and 25 *µ*g) onto a BN-PAGE. Protein complexes were probed using anti-UQCRFS1 antibodies and then imaged to assess signal saturation.



Supplementary Figure 16: Digitonin solubilized mitochondrial proteins (50 μg) from AG15022 (healthy) and GM22192 (BTHS) B-lymphoblastoids treated with vehicle or 1 μM CBD were separated by BN-PAGE and probed with antibodies against COXIV (CIV) (A) and UQCRFS1 (CIII) (B). The corresponding stain-free SDS-PAGE gel are shown on the right panel (C).



Supplementary Figure 17: Flow cytometry gating strategy for the measurement of TMRE. Lymphoblastoids were gated on FSC vs SSC to exclude debris, and TMRE fluorescence was quantified as the mean intensity of this primary population. Given that lymphoblastoids remain in a uniform suspension under our preparation conditions, additional singlet gating did not improve population resolution and was therefore omitted. Nonetheless, to ensure optimal data quality, cells were gently resuspended prior to data acquisition to ensure consistency across samples.