

# **Supplemental Material**

**Table S1. Adipose tissue samples real-time PCR primer sequences.**

Gene	Forward primer	Reverse Primer
Adiponectin	ATCGGTGAAACCGGAGTACC	GCATGTTGGGGATAGTAACGTAA
CD68	GCTGGCTGTGCTTTTCTCG	GTCACCGTGAAGGATGGCA
CD68(2)	CTTCTCTCATTCCTATGGACA	GAAGGACACATTGTACTCCACC
IL-18	GGCCTCTATTTGAAGATATGACTGATT	CCTCTAGGCTGGCTATCTTTATACATACT
IL-18bp	ATGAGACACAACCTGGACACCA	GCCAGGTCACCTCCAATGC
IL-18R $\beta$	CCACAGTTACTTGGAGAGGCTTAAA	GGCATGTGGTAGCGCATT
IL-1 $\alpha$	ATCATGTAAGCTATGGCCCACT	CTTCCCGTTGGTTGCTACTAC
IL-1Ra	GCCTCCGCAGTCACCTAAT	TCCCAGATTCTGAAGGCTTG
IL-37	CAGCCTCTGCGGAGAAAGGAAGT	GTTTCTCCTTCTTCAGCTGAAGGGATGGAT
Leptin	GGTTGCAAGGCCCAAGAA	ACATAGAAAAGATAGGGCCAAAGC
MCP-1	CCAGTCACCTGCTGTTATAAC	TGGAATCCTGAACCCACTTCT
RPL37A	TAATACGACTCACTATAGGCTTTCTGGGCTC	TCTTCATGCAGGAACCACAG
TNF	CTCTTCTGCCTGCTGCACTTTG	ATGGGCTACAGGCTTGTCCTC

**Table S2 (see separate Excel file). List of 24 genes sequenced and known clonal hematopoiesis hotspots.**

**Table S3 (see separate Excel file). single-molecule Molecular Inversion Probes (smMIP).**

**Table S4 (see separate Excel file). Variant characteristics of candidate clonal hematopoiesis driver mutations in this study.**

**Table S5. ELISA kits.**

Description	Manufacturer	Manufacturer ID	Antibody registry
Human IL-1 $\beta$ ELISA kit	R&D systems	DY201	<a href="#">AB_2848158</a>
Human IL-6 ELISA kit	Sanquin	M9316	<a href="#">AB_10851499</a>
Human TNF- $\alpha$ ELISA kit	R&D systems	DY210	<a href="#">AB_2848160</a>
Human IL-22 ELISA kit	R&D systems	DY782	<a href="#">AB_2928043</a>
Human IL-17 ELISA kit	R&D systems	DY317	<a href="#">AB_2928042</a>
Human IFN $\gamma$ ELISA kit	Sanquin	M9333	<a href="#">AB_2934300</a>
Human IL-1Ra ELISA kit	R&D systems	DRA00B	<a href="#">AB_2916104</a>
Human Resistin ELISA kit	R&D systems	DY1359	<a href="#">AB_2893494</a>
Human Leptin ELISA kit	R&D systems	DY398	<a href="#">AB_2861156</a>
Human Adiponectin ELISA kit	R&D systems	DY1065	<a href="#">AB_2861158</a>
Human AAT ELISA kit	R&D systems	DY1268	<a href="#">AB_2934301</a>
Human IL-1Ra ELISA kit	R&D systems	DY280	<a href="#">AB_2934302</a>
Human IL-18BP ELISA kit	R&D systems	DBP180	<a href="#">AB_2934303</a>
Human hsCRP ELISA kit (Plasma)	R&D systems	DY1707	<a href="#">AB_2928088</a>
Human IL-18 ELISA kit	Simple plex (Biotechne / R&D)	SPCKB-PS-000501	Multi-analyte cartridges no antibody registry ID
Human IL-6 ELISA kit (Plasma)	Simple plex (Biotechne / R&D)	SPCKB-PS-000190	
Human VEGF ELISA kit (Plasma)	Simple plex (Biotechne / R&D)	SPCKB-PS-000330	
Human IL-1 $\beta$ (plasma)	Simple plex (Biotechne / R&D)	SPCKB-PS-000216	

**Table S6. Baseline characteristics of men separated according to CHDM status.**

	<b>No CHDM (n=124)</b>	<b>All CHDM (n=39)</b>	<b>High VAF (n=15)</b>	<b>Low VAF (n=24)</b>	<b>Cor. VAF</b>
Age (years)	66 (62-70)	67 (63-71)	72 (67-77)*	65 (63-69)	0.33
BMI (kg/m <sup>2</sup> )	30 (28.2-32)	30.3 (28.3-32.2)	30 (28.9-30.6)	30.8 (28.2-32.8)	-0.18
Creatinine (μmol/L)	87 (80-95)	88 (81-93)	88 (84-93)	86 (79-93)	-0.067
Glucose (mmol/L)	5.5 (5.1-6)	5.4 (5-5.9)	5.4 (5.2-5.6)	5.5 (5-6.2)	-0.16
Total cholesterol (mmol/L)	5.9 (5.3-6.8)	6 (4.8-6.7)	5.3 (4.7-6.4)	6.1 (4.9-6.8)	-0.1
Triglycerides (mmol/L)	1.7 (1.2-2.2)	1.5 (1.3-1.9)	1.4 (1.4-1.8)	1.5 (1.3-2)	0.0081
Heart rate	61 (54-67)	64 (57-72)	61 (52-64)	67 (61-75)*	-0.39
Antihypertensives (%)	49	39	47	33	
Lipid lowering drugs (%)	33	23	13	29	
Antidiabetic drugs (%)	12	5		8	

BMI: body mass index. All data are given as median (interquartile ranges 1-3). \*indicates p<0.05 compared to No CHDM group. Correlation is indicated with Spearman correlation coefficient.

**Table S7. Baseline characteristics of women separated according to CHDM status.**

	<b>No CHDM (n=88)</b>	<b>All CHDM (n=46)</b>	<b>High VAF (n=18)</b>	<b>Low VAF (n=28)</b>	<b>Cor. VAF</b>
Age (years)	67 (64-71)	68 (63-74)	64 (63-71)	68 (65-74)	-0.22
BMI (kg/m <sup>2</sup> )	30 (28.6-31.9)	29.6 (28.2-31.9)	30.4 (28-32.5)	29.4 (28.4-31.2)	0.1
Creatinine (μmol/L)	67 (63-76)	70 (63-76)	70 (65-72)	72 (61-80)	-0.21
Glucose (mmol/L)	5.4 (5-5.9)	5.4 (4.9-6)	5.4 (5-6.3)	5.2 (5-6)	0.2
Total cholesterol (mmol/L)	6.6 (6-7.3)	6.4 (5.7-7)	6.7 (5.8-6.9)	6.4 (5.8-7.2)	-0.1
Triglycerides (mmol/L)	1.6 (1.3-2.1)	1.5 (1.3-2.2)	1.5 (1.3-2.1)	1.5 (1.3-2.3)	-0.087
Heart rate	62 (57-68)	63.5 (59-69)	65 (59-72)	63 (53-67)	0.025
Antihypertensives (%)	44	41	56	32	
Lipid lowering drugs (%)	21	26	22	29	
Antidiabetic drugs (%)	6	9	11	7	

BMI: body mass index. All data are given as median (interquartile ranges 1-3). \*indicates p<0.05 compared to No CHDM group. Correlation is indicated with Spearman correlation coefficient.

**Table S8. The association between adipose tissue inflammation and CHDM status of the entire study cohort.**

	No CHDM (n=212)	All CHDM (n=85)	High VAF (n=33)	Low VAF (n=52)	Cor. VAF
no. CLS/fields	0.06 (0-0.12)	0.06 (0-0.12)	0.07 (0-0.1)	0.06 (0-0.12)	0.06
no. Adipocytes/fields	20.2 (18.1-22.8)	19.7 (17.7-23.9)	19.8 (18.1-23)	19.7 (17.3-25.6)	0.11
no. CD68/fields	2.3 (1.6-3.2)	2.2 (1.7-3.3)	2.1 (1.8-3.2)	2.2 (1.6-3.3)	0.096
% CD68	11.2 (8.2-15.8)	11.5 (8.9-15.8)	11 (9.3-14.7)	11.5 (8-16.3)	0.071
Area (Median)	2250.21 (1844.29- 2718)	2234 (1853.3- 2696.5)	2224.5 (1929.7- 2601.1)	2238.5 (1829.7- 2776)	0.035
Feretmin (Median)	47.2 (42.1-52.5)	47.1 (43.2-51.4)	47.4 (43.5-51.2)	47.1 (42.3-51.6)	0.042
Area (Mean)	3199.1 (2729- 3779.4)	3282.1 (2761.9- 3698.2)	3257.1 (2853.4- 3576.5)	3285.5 (2738.8- 3858.3)	-0.0013
SQ leptin	0.06 (0.04-0.1)	0.07 (0.05-0.1)	0.07 (0.05-0.1)	0.07 (0.05-0.2)	0.057
SQ IL-18R $\beta$	0.06 (0.02-0.2)	0.07 (0.03-0.2)	0.04 (0.03-0.2)	0.1 (0.03-0.3)	-0.014
SQ IL-1 $\alpha$	0.05 (0.01-0.14)	0.07 (0.02-0.2)	0.04 (0.02-0.1)	0.1 (0.03-0.3)	-0.01
SQ MCP1	0.06 (0.04-0.09)	0.06 (0.04-0.1)	0.05 (0.04-0.07)	0.07 (0.04-0.1)	-0.14
SQ IL-37	0.04 (0.009-0.1)	0.05 (0.02-0.2)	0.03 (0.02-0.09)	0.09 (0.01-0.24)	-0.014
SQ CD68	0.07 (0.03-0.14)	0.08 (0.03-0.18)	0.05 (0.03-0.1)	0.11 (0.05-0.23)*	-0.11
SQ CD68(2)	0.05 (0.02-0.17)	0.07 (0.02-0.23)	0.04 (0.02-0.1)	0.11 (0.03-0.27)	-0.051
SQ Adiponectin	0.08 (0.04-0.14)	0.09 (0.04-0.18)	0.06 (0.04-0.12)	0.1 (0.06-0.22)*	-0.16
SQ TNF	0.04 (0.01-0.15)	0.05 (0.02-0.18)	0.03 (0.02-0.11)	0.1 (0.02-0.25)*	-0.026
SQ IL-18	0.19 (0.099-0.37)	0.16 (0.096-0.27)	0.16 (0.1-0.24)	0.18 (0.09-0.29)	0.07
SQ IL-18Bp	0.03 (0.005-0.36)	0.04 (0.01-0.54)	0.09 (0.01-0.89)	0.04 (0.01-0.33)	0.04
SQ IL-1RA	0.04 (0.02-0.11)	0.04 (0.01-0.09)	0.03 (0.02-0.07)	0.04 (0.01-0.18)	-0.038

CLS: Crown-like structure, SQ: starting quantity, CD68 gene expression measured with 2 primers

All data are given as median (interquartile ranges 1-3). \*indicates  $p < 0.05$  compared to No CHDM group. Correlation is indicated with Spearman correlation coefficient.

**Table S9. Leukocyte numbers and differentiation, and thrombocyte numbers according to CHDM status of men.**

	<b>No CHDM (n=124)</b>	<b>All CHDM (n=39)</b>	<b>High VAF (n=15)</b>	<b>Low VAF (n=24)</b>	<b>Cor. VAF</b>
Leukocytes 10 <sup>9</sup> /l	6 (5-6.7)	6.3 (5.7-7.4)*	6.4 (5.9-7.5)	6.2 (5.6-7.4)	0.18
Neutrophils 10 <sup>9</sup> /l	3.2 (2.7-3.8)	3.6 (2.9-4.8)*	4 (3.4-4.7)*	3.4 (2.7-4.7)	0.2
Lymphocytes 10 <sup>9</sup> /l	1.8 (1.5-2.2)	1.8 (1.6-2.1)	1.7 (1.4-2)	1.9 (1.6-2.3)	0.013
Monocytes 10 <sup>9</sup> /l	0.5 (0.4-0.6)	0.6 (0.5-0.7)	0.6 (0.5-0.7)	0.5 (0.5-0.7)	0.028
Eosinophils 10 <sup>9</sup> /l	0.2 (0.1-0.2)	0.2 (0.1-0.3)	0.1 (0.1-0.3)	0.2 (0.1-0.3)	-0.02
Basophils 10 <sup>9</sup> /l	0.03 (0.02-0.04)	0.03 (0.03-0.05)*	0.03 (0.03-0.05)*	0.03 (0.02-0.04)	0.07
Thrombocytes 10 <sup>9</sup> /l	217 (188-244)	208 (193-254)	215 (199-272)	206 (190-246)	0.31
NLR	1.8 (1.4-2.3)	2 (1.6-2.5)	2.3 (1.9-2.7)*	1.8 (1.2-2.4)	0.18

NLR: Neutrophil to lymphocyte ratio

All data are given as median (interquartile ranges 1-3). \*indicates p<0.05 compared to No CHDM group. Correlation is indicated with Spearman correlation coefficient.



**Table S10. Leukocyte numbers and differentiation, and thrombocyte numbers according to CHDM status of women.**

	<b>No CHDM (n=88)</b>	<b>All CHDM (n=46)</b>	<b>High VAF (n=18)</b>	<b>Low VAF (n=28)</b>	<b>Cor. VAF</b>
Leukocytes 10 <sup>9</sup> /l	5.5 (5-6.3)	5.9 (5-7.2)	6.2 (5-7.3)	5.8 (5.1-6.9)	0.18
Neutrophils 10 <sup>9</sup> /l	3.1 (2.6-3.6)	3.2 (2.6-3.9)	3.2 (2.5-3.9)	3.1 (2.7-3.9)	0.14
Lymphocytes 10 <sup>9</sup> /l	1.9 (1.5-2.3)	2 (1.6-2.3)	2.1 (1.7-2.3)	1.9 (1.5-2.3)	0.2
Monocytes 10 <sup>9</sup> /l	0.4 (0.4-0.5)	0.5 (0.4-0.6)	0.5 (0.4-0.6)	0.4 (0.4-0.5)	0.27
Eosinophils 10 <sup>9</sup> /l	0.1 (0.1-0.2)	0.2 (0.1-0.3)	0.2 (0.1-0.3)	0.2 (0.1-0.2)	0.035
Basophils 10 <sup>9</sup> /l	0.03 (0.02-0.04)	0.03 (0.02-0.04)	0.03 (0.02-0.04)	0.03 (0.02-0.04)	-0.046
Thrombocytes 10 <sup>9</sup> /l	247 (216-283)	247 (215-275)	247 (205-280)	248 (226-272)	-0.024
NLR	1.5 (1.3-2)	1.7 (1.3-2)	1.5 (1.3-1.8)	1.8 (1.4-2)	-0.13

NLR: Neutrophil to lymphocyte ratio

All data are given as median (interquartile ranges 1-3). \*indicates p<0.05 compared to No CHDM group. Correlation is indicated with Spearman correlation coefficient.

**Table S11. *Ex vivo* cytokine production capacity of PBMCs separated according to CHDM status of men.**

	<b>No CHDM (n=124)</b>	<b>All CHDM (n=39)</b>	<b>High VAF (n=15)</b>	<b>Low VAF (n=24)</b>	<b>Cor. VAF</b>
LPS(10 ng/ml)	1029.7	1116.9	1258.9	1099.07 (597.29-	
IL-1 $\beta$	(543.3-1732)	(589-1657.3)	(602.1-1637.)	1630.78)	-0.0086
LPS(100 ng/ml)	2351.1	2809.6	2894.8	2491.5	
IL-1 $\beta$	(1475.1-3770)	(1554.1-4038.1)	(2320.3-4038.1)	(1466.8-4080.9)	-0.024
	280.3	291	287	315	
Pam3Cys IL-1 $\beta$	(112.6-630.6)	(113.9-597.3)	(79-647)	(135.1-475.9)	0.023
LPS(10 ng/ml)	5367.8	5441.3	5342.8	6014.2	
IL-6	(2940-8598.88)	(4307.7-7309.4)	(4307.65-6801.7)	(4204.9-7363)	-0.18
LPS(100 ng/ml)	8103.6	8383.8	7827.2	8455.7	
IL-6	(4800.8-12236.7)	(5730.1-12896.95)	(5580.3-13232.5)	(6762-12011.8)	-0.14
	3750.2	3654.1	3381.5	3744.9	
Pam3Cys IL-6	(1590.5-6675.8)	(1602.85-5778.6)	(1100.6-6721.7)	(1998.4-5465.7)	-0.13

LPS: Lipopolysaccharide, IL: interleukin, IL-1 $\beta$  and IL-6 concentration units are given in pg/ml

All data are given as median (interquartile ranges 1-3). \*indicates  $p < 0.05$  compared to No CHDM group. Correlation is indicated with Spearman correlation coefficient.

**Table S12. *Ex vivo* cytokine production capacity of PBMCs separated according to CHDM status of women.**

	No CHDM (n=88)	All CHDM (n=46)	High VAF (n=18)	Low VAF (n=28)	Cor. VAF
LPS(10 ng/ml)	1194.1	832.2	957.3	790.1	
IL-1 $\beta$	(677.5-2056.9)	(515.1-1682.4)	(450.4-2448.2)	(533.9-1306.8)	0.12
LPS(100 ng/ml)	2548.5	1823.3	2054.4	1724.3	
IL-1 $\beta$	(1575.3-3638.6)	(1103.3-2950.5) *	(992.7-3010.1)	(1231.2-2833.3)	0.11
	291.4	127.04	135.4	104.3	
Pam3Cys IL-1 $\beta$	(110.6-671.6)	(64.9-309.92) *	(55.9-397.1)	(67.9-277.2)*	0.093
LPS(10 ng/ml)	6107.8	4407.8	4407.8	4627	
IL-6	(3837.8-9388.1)	(2468-5910.9)*	(2616.3-6051.7)*	(2444.8-5766.8)*	0.098
LPS(100 ng/ml)	8344.9	6349.7	5121.7	6921.65	
IL-6	(5445.7-13132.3)	(3609.9-8306.8)	(3502-7412)*	(4114.38-10786.5)	0.041
	4185.7	1569.8	1670.3	1569.7	
Pam3Cys IL-6	(2125.9-6202.9)	(811.1-2579.2)*	(684.9-3184.6)*	(828-2256.4)*	0.25

LPS: Lipopolysaccharide, IL: interleukin, IL-1 $\beta$  and IL-6 concentration units are given in pg/ml

All data are given as median (interquartile ranges 1-3). \*indicates p<0.05 compared to No CHDM group. Correlation is indicated with Spearman correlation coefficient

**Table S13. Circulating cytokines and adipokines in plasma separated according to CHDM status of men.**

	<b>No CHDM (n=124)</b>	<b>All CHDM (n=39)</b>	<b>High VAF (n=24)</b>	<b>Low VAF (n=15)</b>	<b>Cor. VAF</b>
IL-6 (pg/ml)	2.3 (1.6-3.3)	2.8 (1.8-4.6)	2.9 (2.1-4.6)	2.7 (1.7-4)	0.052
IL-1 $\beta$ (pg/ml)	0.06 (0.06-0.1)	0.06 (0.06-0.11)	0.06 (0.06-0.01)	0.08 (0.06-0.11)	-0.1
IL-18 (pg/ml)	313 (222.7-515)	300.9 (224.5-510.2)	277.7 (224.5-349.2)	341 (232.5-628.4)	-0.17
IL-18bpa (ng/ml)	17.1 (14.4-20)	16.4 (13.6-20.2)	16.5 (13-17.7)	16.2 (14.1-21.2)	-0.2
hsCRP ( $\mu$ g/ml)	1.4 (0.9-3)	1.9 (1.1-3.1)	1.9 (1-3.7)	1.9 (1.3-2.8)	0.033
AAT (mg/ml)	1 (0.6-1.7)	0.9 (0.6-1.4)	0.9 (0.7-1.1)	0.87 (0.61-1.44)	0.12
Resistin (ng/ml)	10.3 (8-12.8)	11.5 (9.3-15.2)	11.8 (10-14.9)	11.3 (9.2-15.9)	-0.0066
Leptin (ng/ml)	10.2 (7-15)	12.3 (7.5-17)	8.5 (6.9-16.1)	13.3 (8.4-21.3)	-0.22
Adiponectin ( $\mu$ g/ml)	3.1 (2.2-4.5)	3.3 (2.7-4.3)	3.7 (3-4.2)	3.1 (2.3-4.4)	0.092

IL: interleukin, IL-18bp: IL-18 binding protein, CRP: C-reactive protein, AAT: Alpha-1 antitrypsin

All data are given as median (interquartile ranges 1-3). \*indicates  $p < 0.05$  compared to No CHDM group.

Correlation is indicated with Spearman correlation coefficient.

**Table S14. Circulating cytokines and adipokines in plasma separated according to CHDM status of women.**

	No CHDM (n=88)	All CHDM (n=46)	High VAF (n=18)	Low VAF (n=28)	Cor. VAF
IL-6 (pg/ml)	2.7 (1.9-3.4)	2.6 (1.7-4.1)	3.3 (2-4.4)	2.2 (1.5-3)	0.36
IL-1 $\beta$ (pg/ml)	0.06 (0.06-0.11)	0.06 (0.06-0.13)	0.06 (0.06-0.14)	0.07 (0.06-0.11)	0.013
IL-18 (pg/ml)	300.1 (234.1-478.8)	283.7 (204.2-469.9)	411.3 (222.3-489.9)	252.5 (200-379)	0.27
IL-18bpa (ng/ml)	17.5 (14-21.4)	15.8 (13.5-19)	14.9 (12.8-18.7)	16.2 (14.2-19.2)	-0.098
hsCRP ( $\mu$ g/ml)	2.7 (1.1-4.6)	2.1 (1.3-3.7)	2 (0.9-3.7)	2.2 (1.5-3.8)	0.13
AAT (mg/ml)	0.9 (0.6-1.9)	0.9 (0.6-1.3)	0.8 (0.6-1.6)	0.9 (0.6-1.1)	-0.037
Resistin (ng/ml)	10.8 (8.6-15.3)	11.5 (9-14.4)	11.4 (8.3-13)	12.8 (10-16.2)	-0.18
Leptin (ng/ml)	31.5 (21.7-48.1)	27.5 (17.8-51)	25.4 (18.8-47.1)	28.8 (17.5-52.7)	-0.056
Adiponectin ( $\mu$ g/ml)	6 (4.6-7.3)	5.1 (4.2-8)	4.9 (4.2-6.8)	6 (4.2-8)	-0.046

IL: interleukin, IL-18bp: IL-18 binding protein, CRP: C-reactive protein, AAT: Alpha-1 antitrypsin

All data are given as median (interquartile ranges 1-3). \*indicates  $p < 0.05$  compared to No CHDM group. Correlation is indicated with Spearman correlation coefficient.

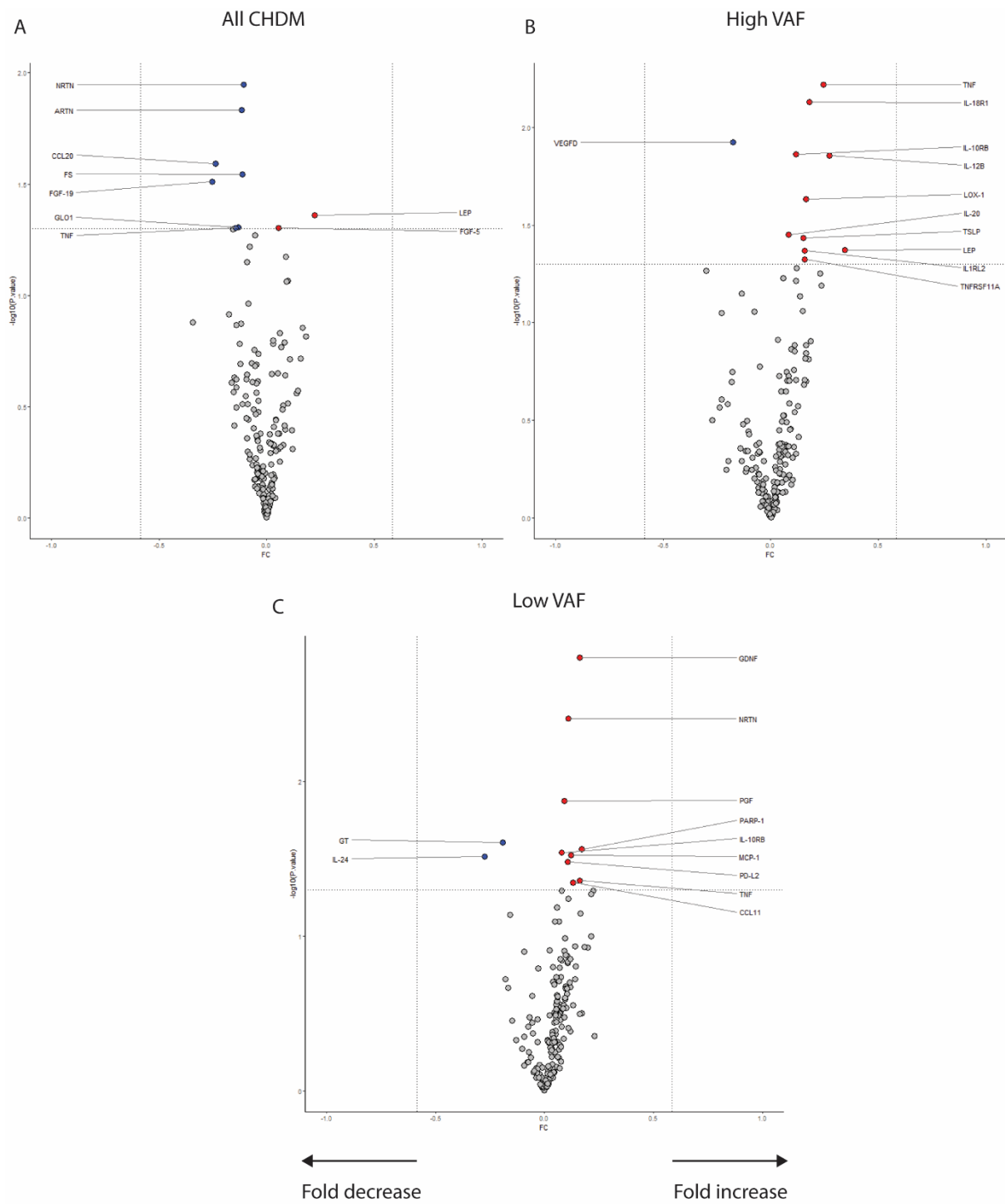
**Table S15. The association between targeted proteomic biomarkers and CHDM status of the entire study cohort.**

	<b>No CHDM (n=212)</b>	<b>All CHDM (n=85)</b>	<b>High VAF (n=33)</b>	<b>Low VAF (n=52)</b>	<b>Cor. VAF</b>
SLAMF7	3.6 (3.3-4.1)	3.5 (3.2-3.9)	3.6 (3.3-4)	3.4 (3-3.7)*	0.22
IL1RL2	4.5 (4.3-4.8)	4.6 (4.4-4.9)*	4.6 (4.3-4.8)	4.6 (4.4-4.9)	0.15
IL-27	6.5 (6.3-6.7)	6.4 (6.1-6.7)*	6.3 (6.1-6.7)	6.4 (6.1-6.6)	0.021
GH	8 (6.5-9.4)	7.3 (6.3-9.3)	7.9 (6.3-9.9)	7.2 (6.2-8.7)*	0.23
GLO1	5.6 (5.4-5.9)	5.5 (5.1-5.8)	5.4 (5.1-5.8)*	5.6 (5.2-5.9)	-0.21
AMBP	7.9 (7.9-8)	8 (7.8-8.1)	7.9 (7.8-8)	8 (7.9-8.1)*	-0.073
CCL3	6.7 (6.3-7)	6.7 (6.1-7)	6.4 (6.1-6.7)*	6.7 (6.4-7.1)	-0.26
TNFRSF13B	10 (9.8-10.3)	9.9 (9.7-10.1)*	10 (9.8-10.2)	9.9 (9.7-10.1)*	0.042
LEP	6.8 (6.2-7.4)	7.1 (6.5-7.5)*	7.1 (6.4-7.4)	7.2 (6.5-7.6)*	0.012
NEMO	5.8 (5.2-6.4)	5.7 (5-6.2)	5.5 (5-5.8)*	5.9 (5-6.4)	-0.21
VEGFD	8.1 (7.9-8.3)	8 (7.8-8.2)	8.1 (7.9-8.4)	8 (7.8-8.1)*	0.33
AXIN1	2.7 (2.3-3.2)	2.6 (2-3.2)	2.3 (2-3)*	2.7 (2.1-3.5)	-0.16
TSLP	0.6 (0.4-0.8)	0.6 (0.4-0.8)	0.5 (0.3-0.7)*	0.6 (0.4-0.8)	-0.14
MMP-1	9.7 (9-10.4)	9.6 (9-10.2)	9.4 (8.9-9.7)*	9.8 (9.2-10.5)	-0.23
CCL3.1	5.1 (4.9-5.5)	5.1 (4.8-5.4)	4.9 (4.8-5.2)*	5.2 (4.8-5.7)	-0.22
FGF-19	8.3 (7.7-8.9)	8 (7.4-8.5)*	8.1 (7.5-8.6)	7.9 (7.3-8.5)*	0.081
ST1A1	2.9 (2.3-3.5)	2.8 (2.1-3.4)	2.4 (2-3.1)*	2.9 (2.1-3.5)	-0.17

All data are given as median (interquartile ranges 1-3). \*indicates  $p < 0.05$  compared to No CHDM group.

Correlation is indicated with Spearman correlation coefficient.

**Figure S1. Volcano plots depicting increase and decrease in NPX (normalized protein expression) values of OLINK biomarkers measured in plasma with targeted proteomics.**



Differential expression of A) All CHDM, B) High VAF (VAF $\geq$ 2%) C) Low VAF (VAF<2%) groups compared to No CHDM group.