SUPPLEMENTARY MATERIAL

ADDITONAL FILE 2 - ADDITIONAL FIGURES

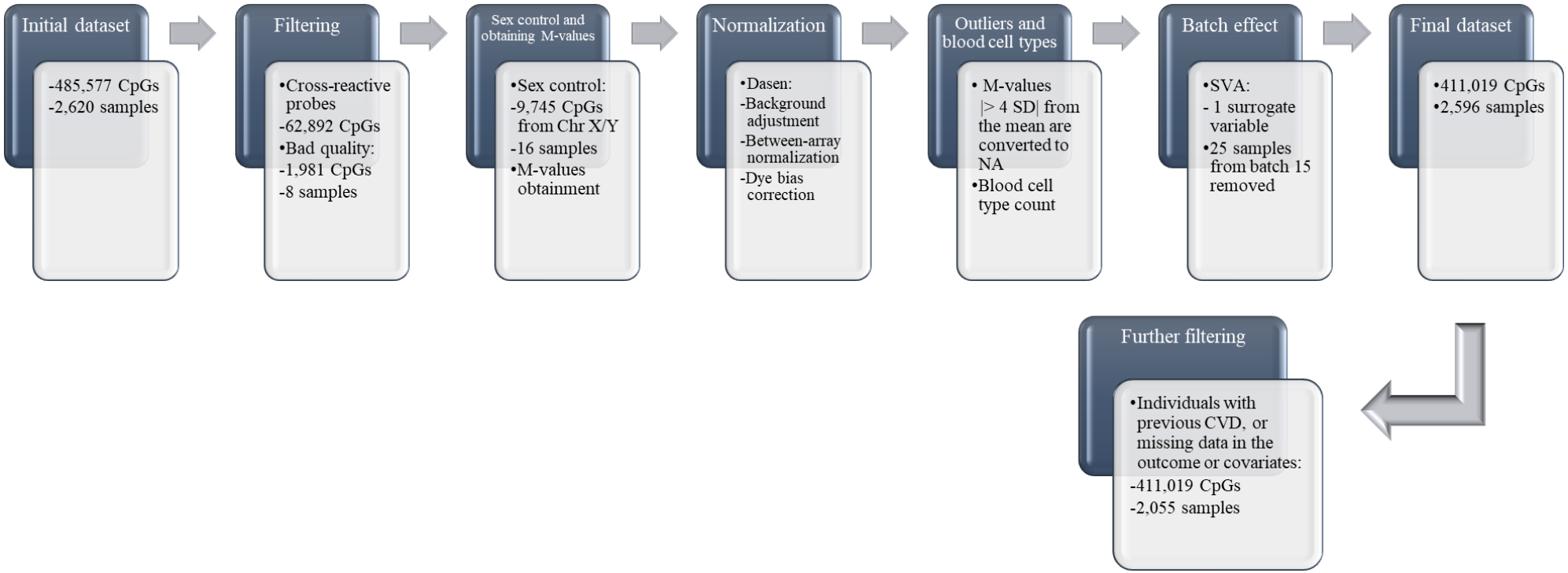


Figure S1. Quality control steps of the DNA methylation data. This flowchart indicates all the steps followed from the initial raw data until the final dataset used for all the *MOFA2* analyses.

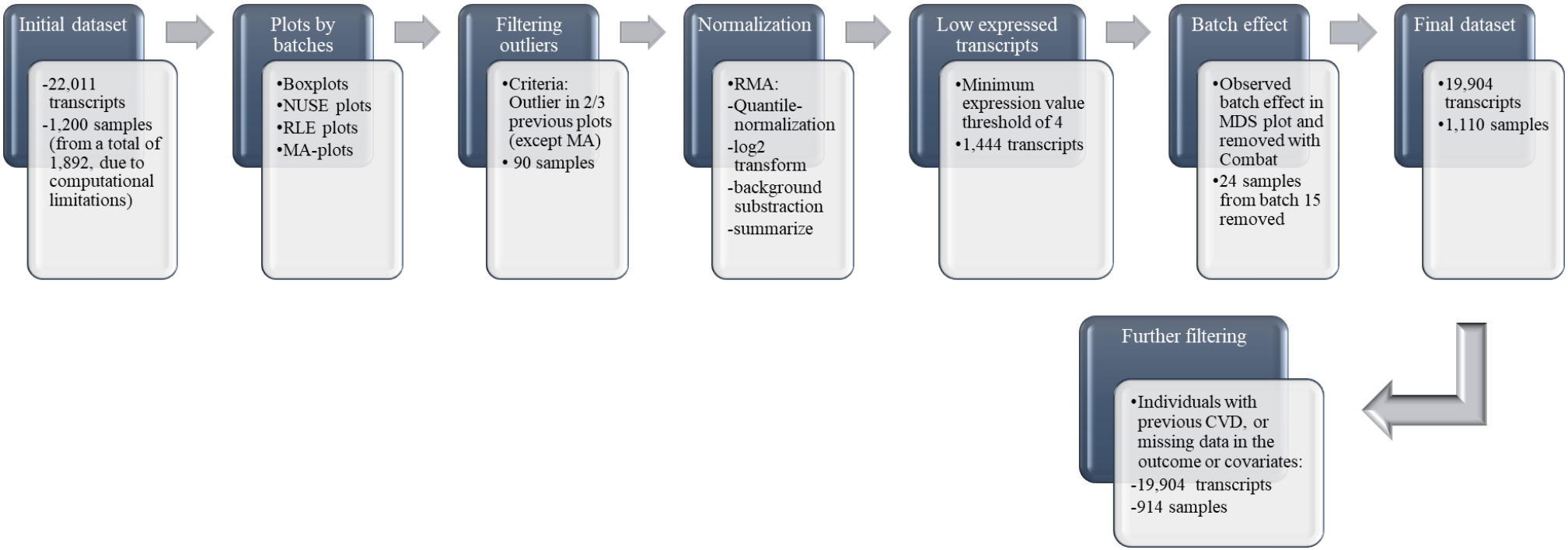
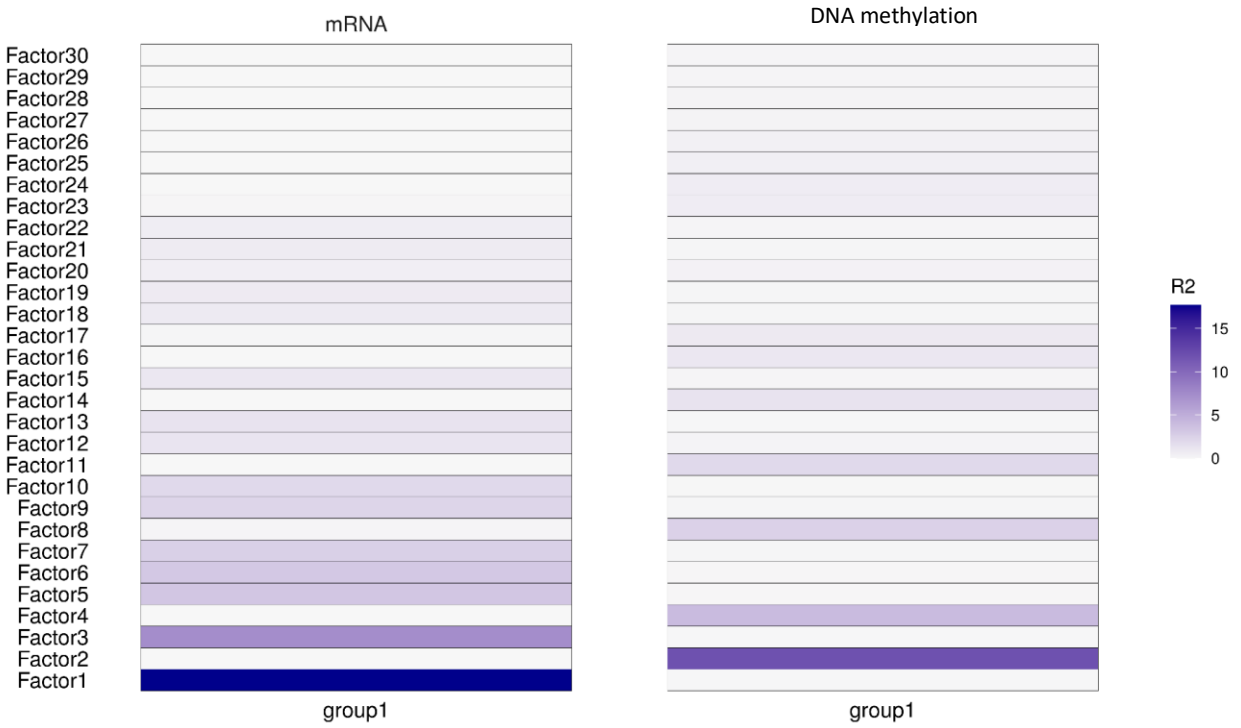


Figure S2. Quality control steps of the gene expression data. This flowchart indicates all the steps followed from the initial raw data until the final dataset used for all the *MOFA2* analyses.

A



B

Factor	DNA methylation	Gene expression
1	$7.52 \cdot 10^{-2}$	17.68
2	11.93	$5.25 \cdot 10^{-7}$
3	$6.99 \cdot 10^{-2}$	7.41
4	4.10	$5.19 \cdot 10^{-7}$
5	0.11	3.36
6	0.11	3.22
7	0.14	2.67
8	2.56	0.22
9	0.16	2.30
10	$9.58 \cdot 10^{-2}$	2.04
11	2.07	$4.37 \cdot 10^{-7}$
12	0.24	1.27
13	$6.74 \cdot 10^{-2}$	1.37
14	1.37	$1.68 \cdot 10^{-3}$
15	0.20	1.09
16	1.10	$1.63 \cdot 10^{-2}$
17	0.94	0.16
18	0.14	0.87
19	0.14	0.85
20	0.41	0.58
21	0.17	0.8
22	0.18	0.69
23	0.76	0.1
24	0.71	$3.87 \cdot 10^{-6}$
25	0.56	$1.12 \cdot 10^{-6}$
26	0.45	$4.76 \cdot 10^{-3}$
27	0.29	$1.24 \cdot 10^{-4}$
28	0.26	$3.70 \cdot 10^{-6}$
29	0.22	$6.22 \cdot 10^{-6}$
30	0.19	$3.02 \cdot 10^{-6}$
Total	**29.38**	**45.28**
	74.66	

Figure S3. Variance (R^2) explained by all factors in each omic data. (A) Shows the variance in a bluish colour. The more intense it is the more variance is explained by the factor in a specific omic. Group1 refers to the complete group of individuals analysed, i.e., 914 for gene expression and 2055 for DNA methylation. **(B)** Shows the specific percentage values of variance and the total variance explained in each omic.

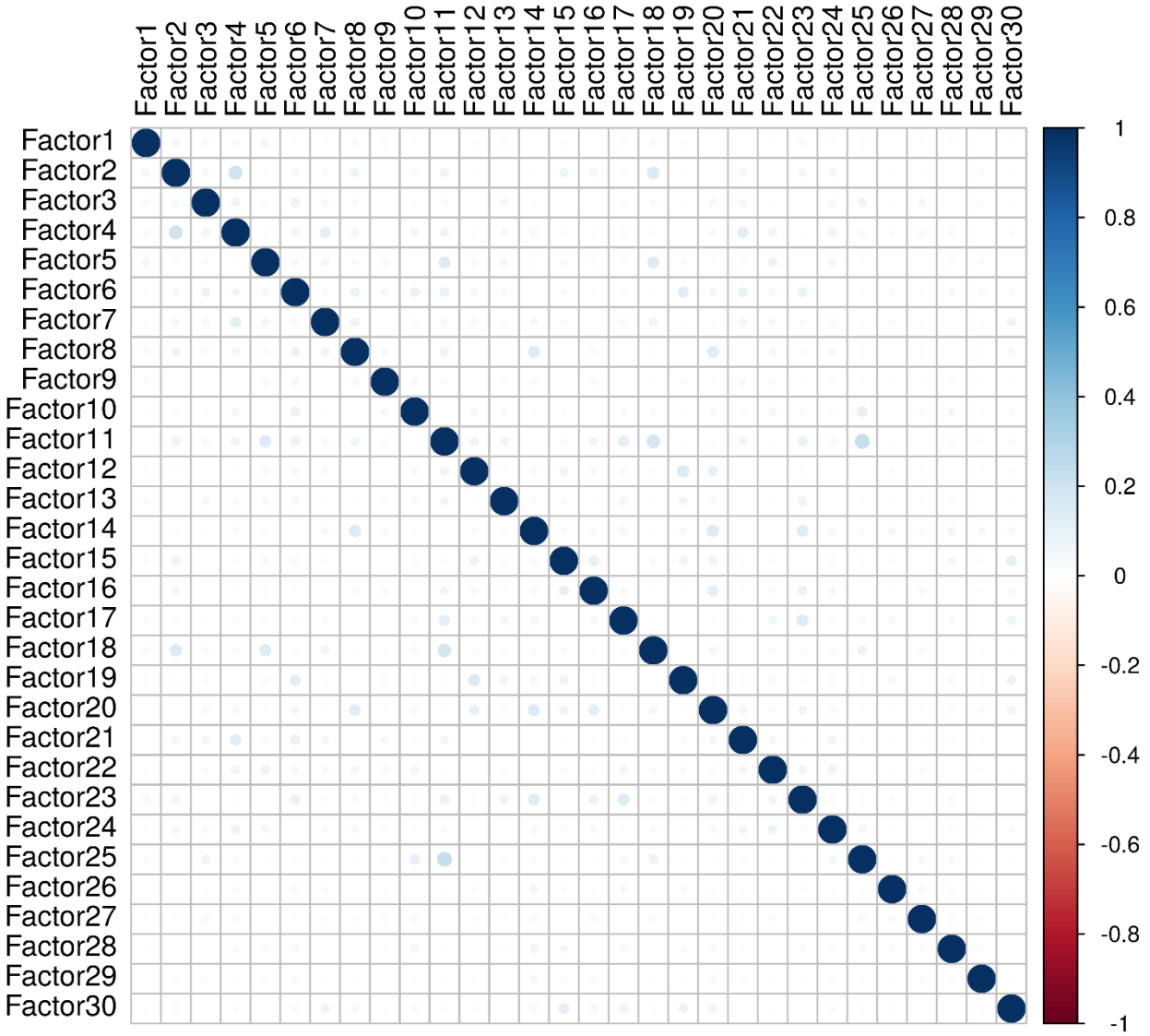
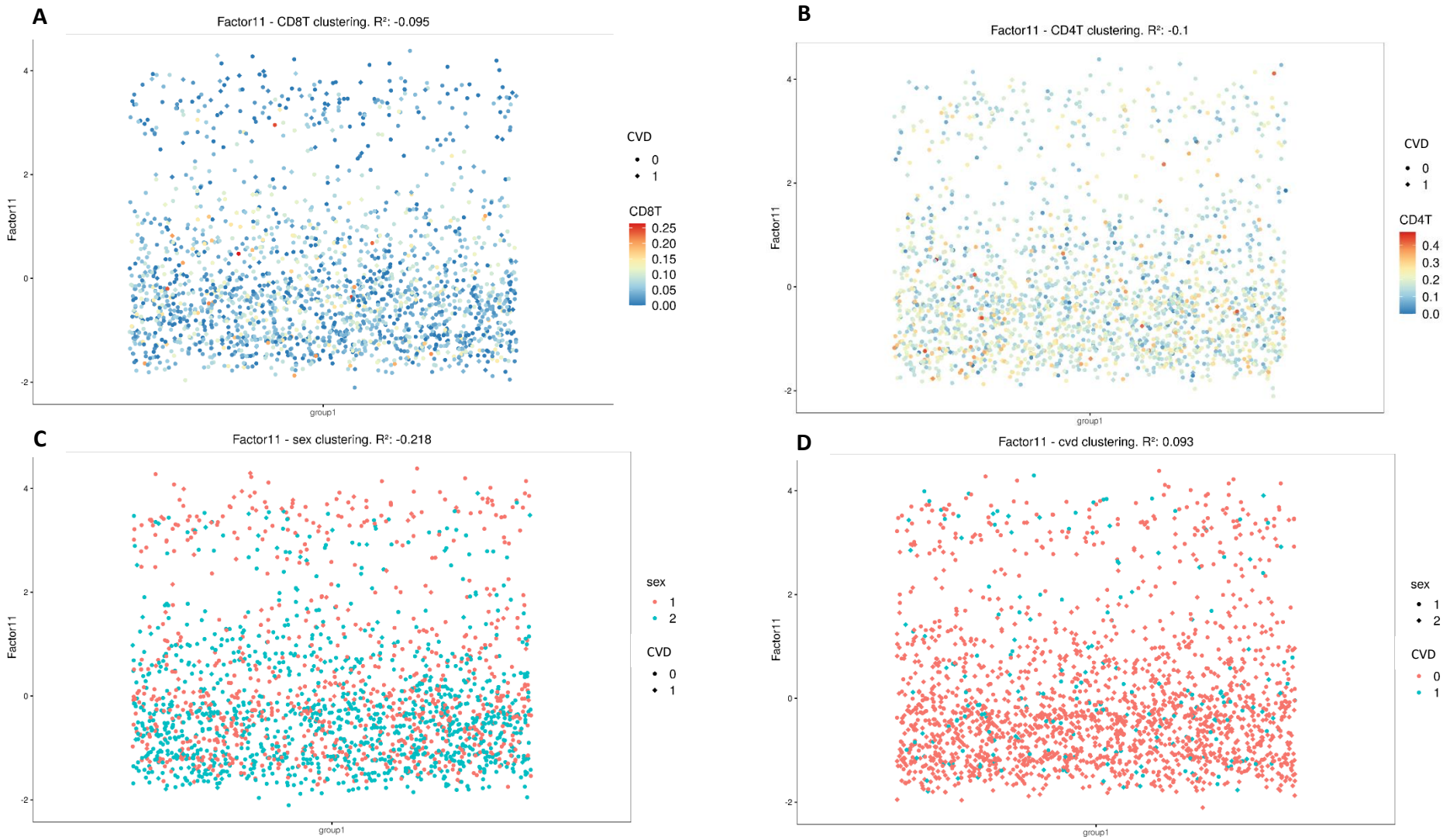
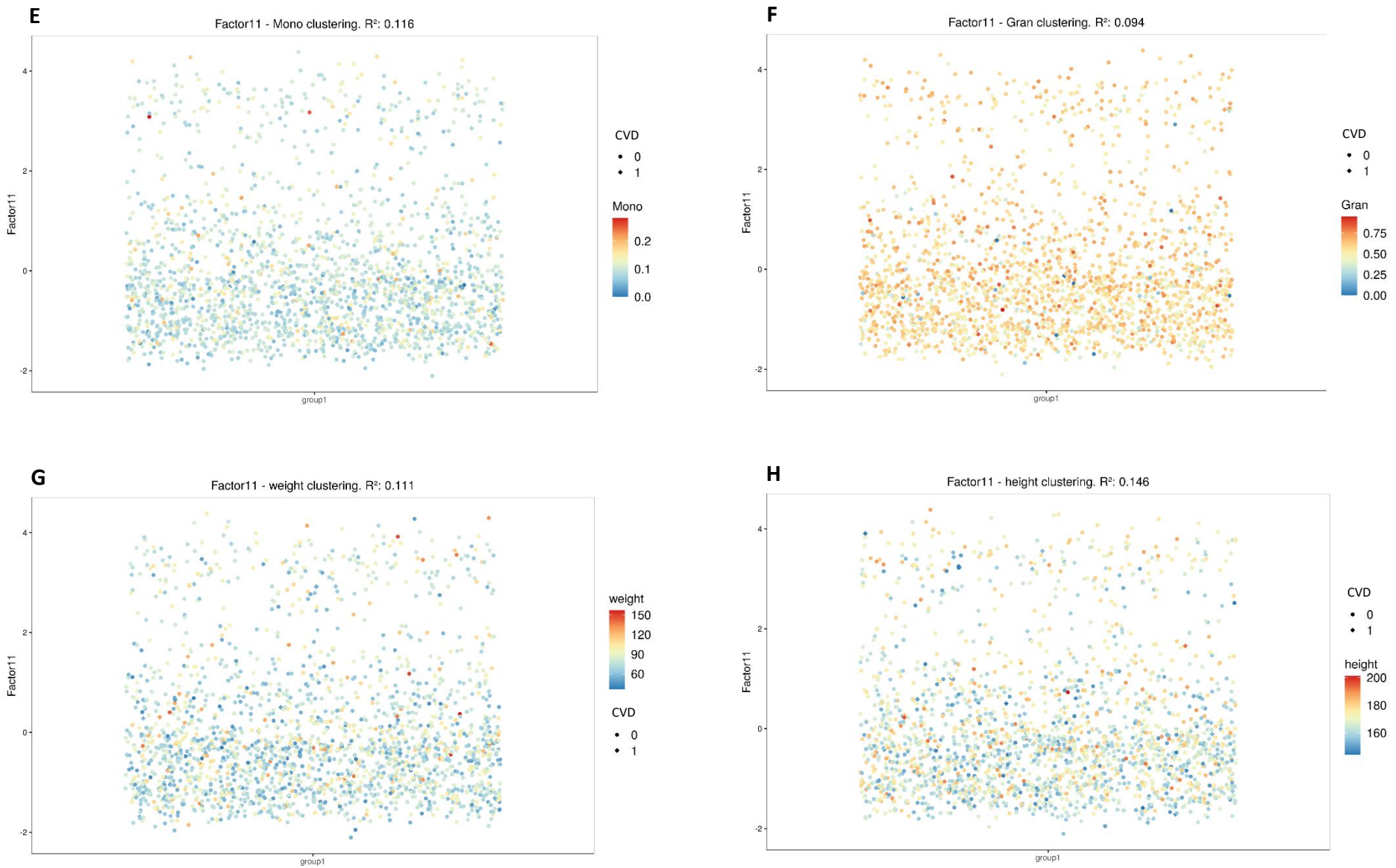


Figure S4. Correlations between factors. Correlation coefficients are represented in a colour scale from reddish for negative correlations to bluish for positive correlations. Values are below 0.20, indicating that factors are capturing unique sources of variation in the data set.


A
Factor11 - CD8T clustering. R²: -0.095
Factor11
group1
CVD
0
1
CD8T
0.25
0.20
0.15
0.10
0.05
0.00
B
Factor11 - CD4T clustering. R²: -0.1
Factor11
group1
CVD
0
1
CD4T
0.4
0.3
0.2
0.1
0.0
C
Factor11 - sex clustering. R²: -0.218
Factor11
group1
sex
1
2
CVD
0
1
D
Factor11 - cvd clustering. R²: 0.093
Factor11
group1
sex
1
2
CVD
0
1


E
Factor11 - Mono clustering. R²: 0.116
Factor11
group1
CVD
0
1
Mono
0.2
0.1
0.0
F
Factor11 - Gran clustering. R²: 0.094
Factor11
group1
CVD
0
1
Gran
0.75
0.50
0.25
0.00
G
Factor11 - weight clustering. R²: 0.111
Factor11
group1
weight
150
120
90
60
CVD
0
1
H
Factor11 - height clustering. R²: 0.146
Factor11
group1
CVD
0
1
height
200
180
160

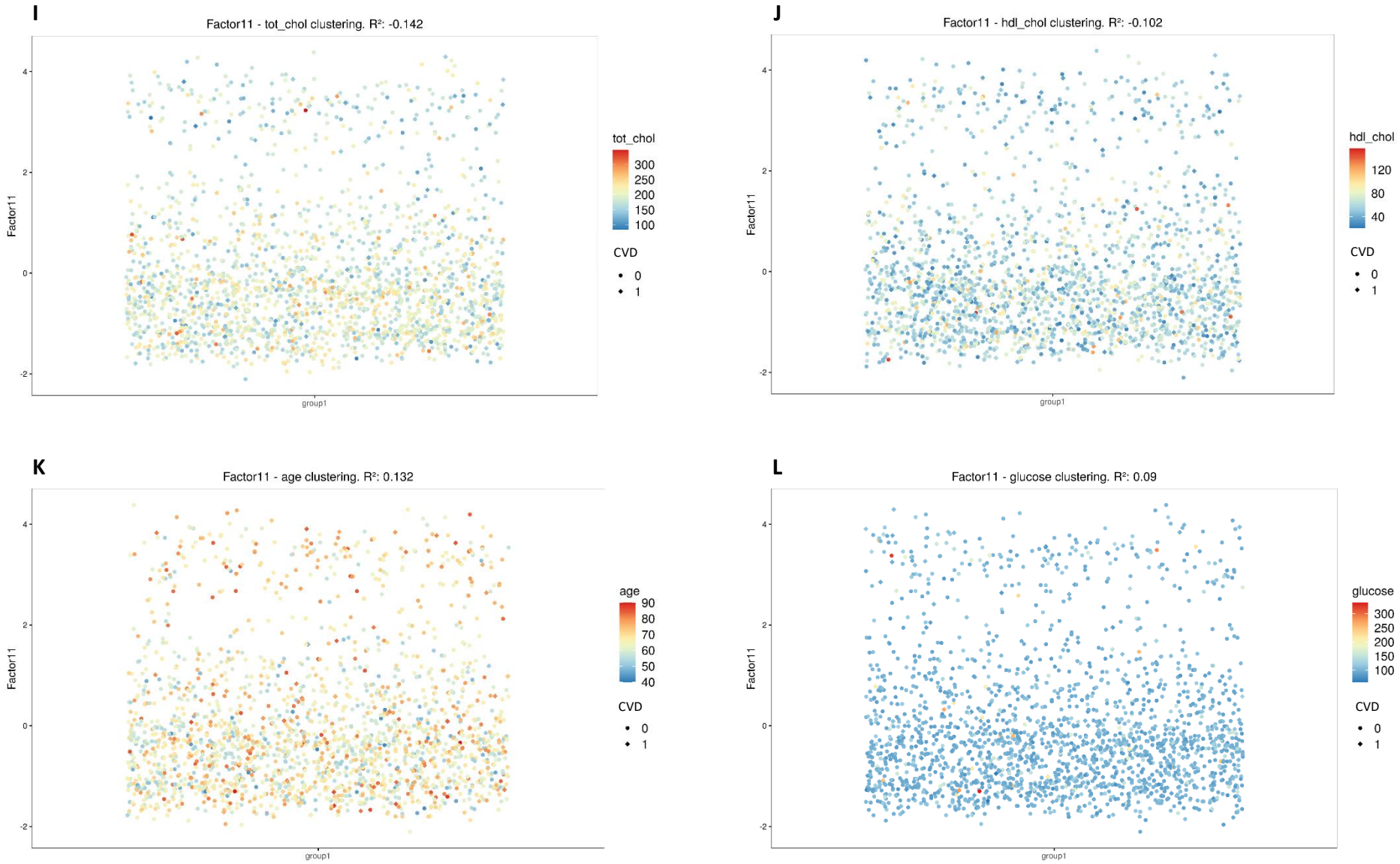
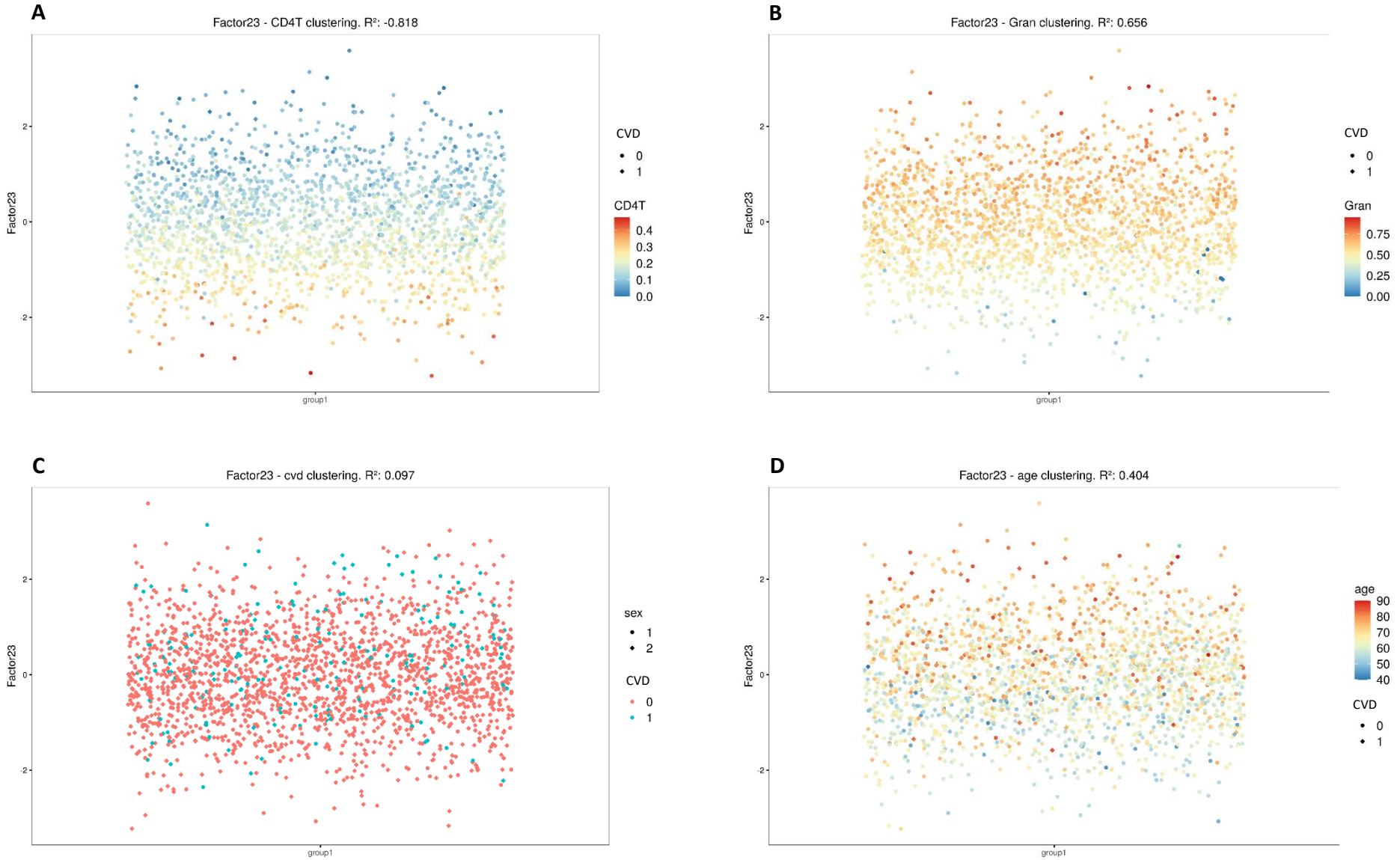
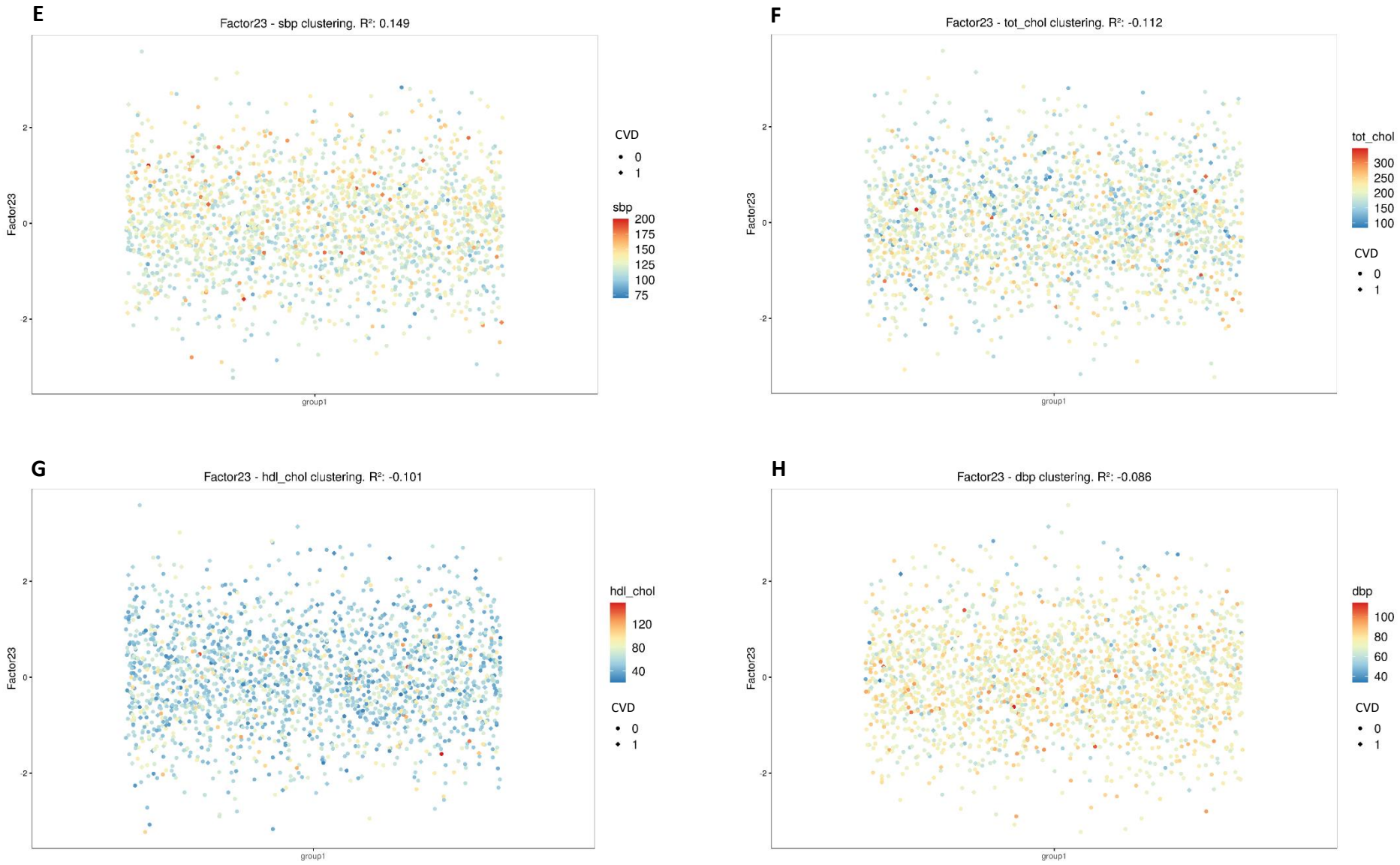


Figure S6. Clustering plots of factor 11. Dots are shaped by cardiovascular disease (CVD) incidence (except for CVD, shaped by sex) and coloured by the different covariates: **(A)** $CD8^+$ T cells, **(B)** $CD4^+$ T cells, **(C)** sex (1 = Male, 2 = Female), **(D)** CVD, **(E)** Monocytes, **(F)** Granulocytes, **(G)** weight, **(H)** height, **(I)** total cholesterol, **(J)** HDL-C, **(K)** age and **(L)** glucose. The colour scale for quantitative covariates ranges from bluish for low values to reddish for higher values. The correlation between the factor 11 and each variable is also showed in its respective plot.


A
Factor23 - CD4T clustering. R²: -0.818
Factor23
group1
CVD
0
1
CD4T
0.4
0.3
0.2
0.1
0.0
B
Factor23 - Gran clustering. R²: 0.656
Factor23
group1
CVD
0
1
Gran
0.75
0.50
0.25
0.00
C
Factor23 - cvd clustering. R²: 0.097
Factor23
group1
sex
1
2
CVD
0
1
D
Factor23 - age clustering. R²: 0.404
Factor23
group1
age
90
80
70
60
50
40
CVD
0
1


E
Factor23 - sbp clustering. R²: 0.149
Factor23
group1
CVD
0
1
sbp
200
175
150
125
100
75
F
Factor23 - tot_chol clustering. R²: -0.112
Factor23
group1
tot_chol
300
250
200
150
100
CVD
0
1
G
Factor23 - hdl_chol clustering. R²: -0.101
Factor23
group1
hdl_chol
120
80
40
CVD
0
1
H
Factor23 - dbp clustering. R²: -0.086
Factor23
group1
dbp
100
80
60
40
CVD
0
1

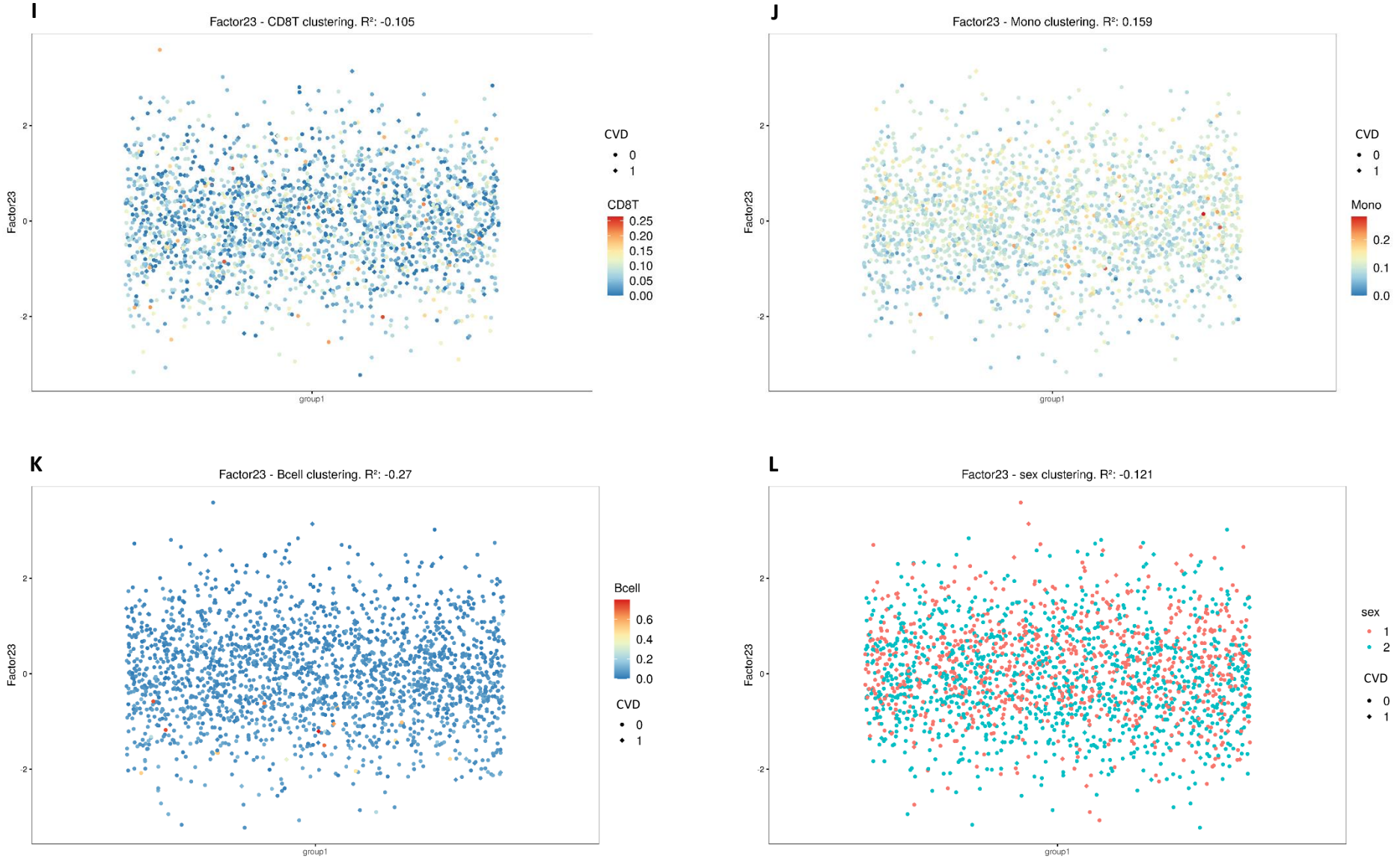


Figure S7. Clustering plots of factor 23. Dots are shaped by cardiovascular disease (CVD) incidence (except for CVD, shaped by sex) and coloured by the different covariates: **(A)** $CD4^+$ T cells, **(B)** Granulocytes, **(C)** CVD, **(D)** age, **(E)** SBP, **(F)** total cholesterol, **(G)** HDL-C, **(H)** DBP, **(I)** $CD8^+$ T cells, **(J)** Monocytes, **(K)** B cells and **(L)** sex. The colour scale for quantitative covariates ranges from bluish for low values to reddish for higher values. The correlation between the factor 23 and each variable is also showed in its respective plot.

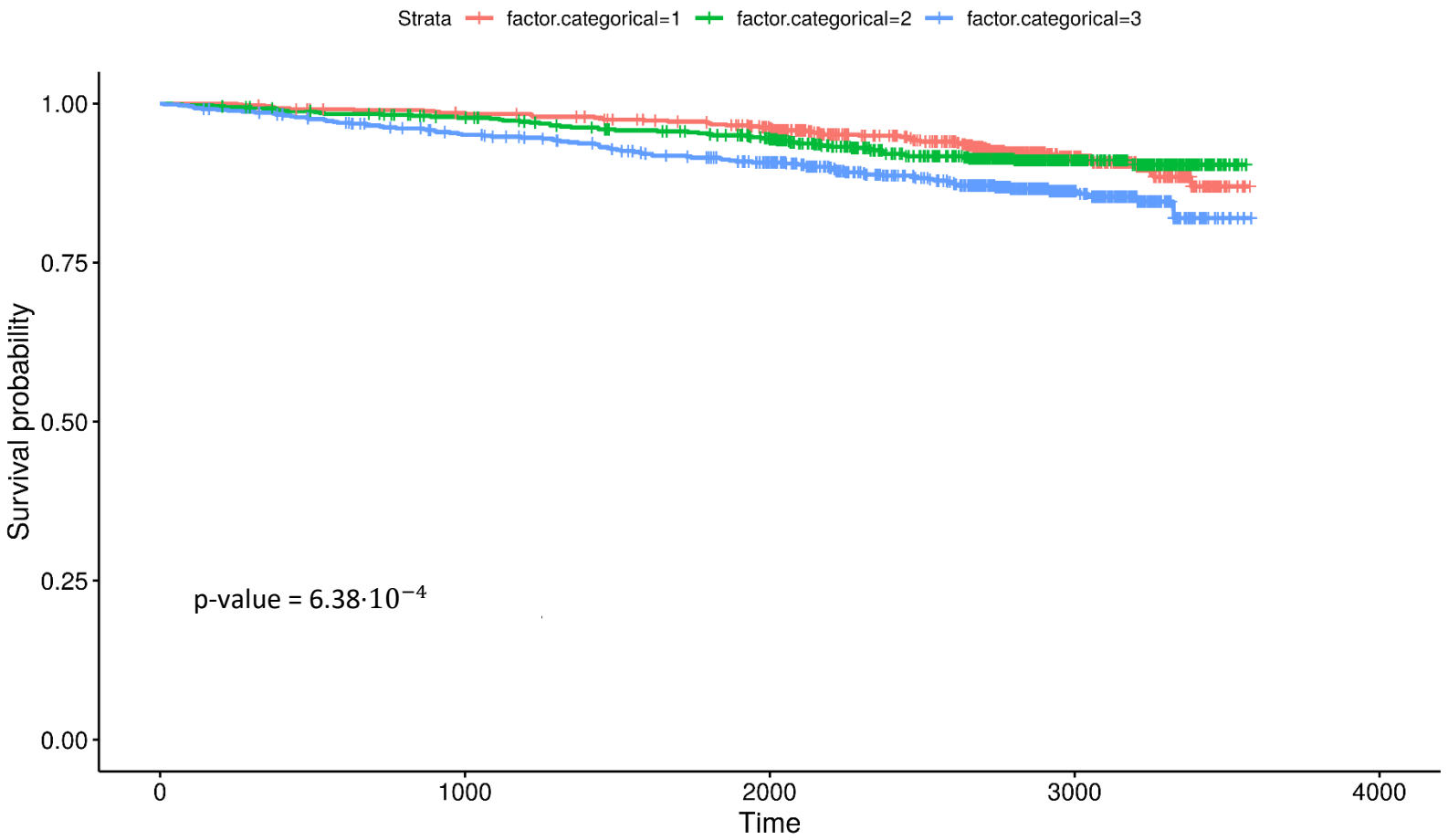


Figure S8. Kaplan-Meier curves for the association between Factor 11 and cardiovascular risk (CVR). Factor values have been transformed into a categorical variable by tertiles. Tertiles are showed in red (first tertile), green (second tertile) and blue (third tertile).

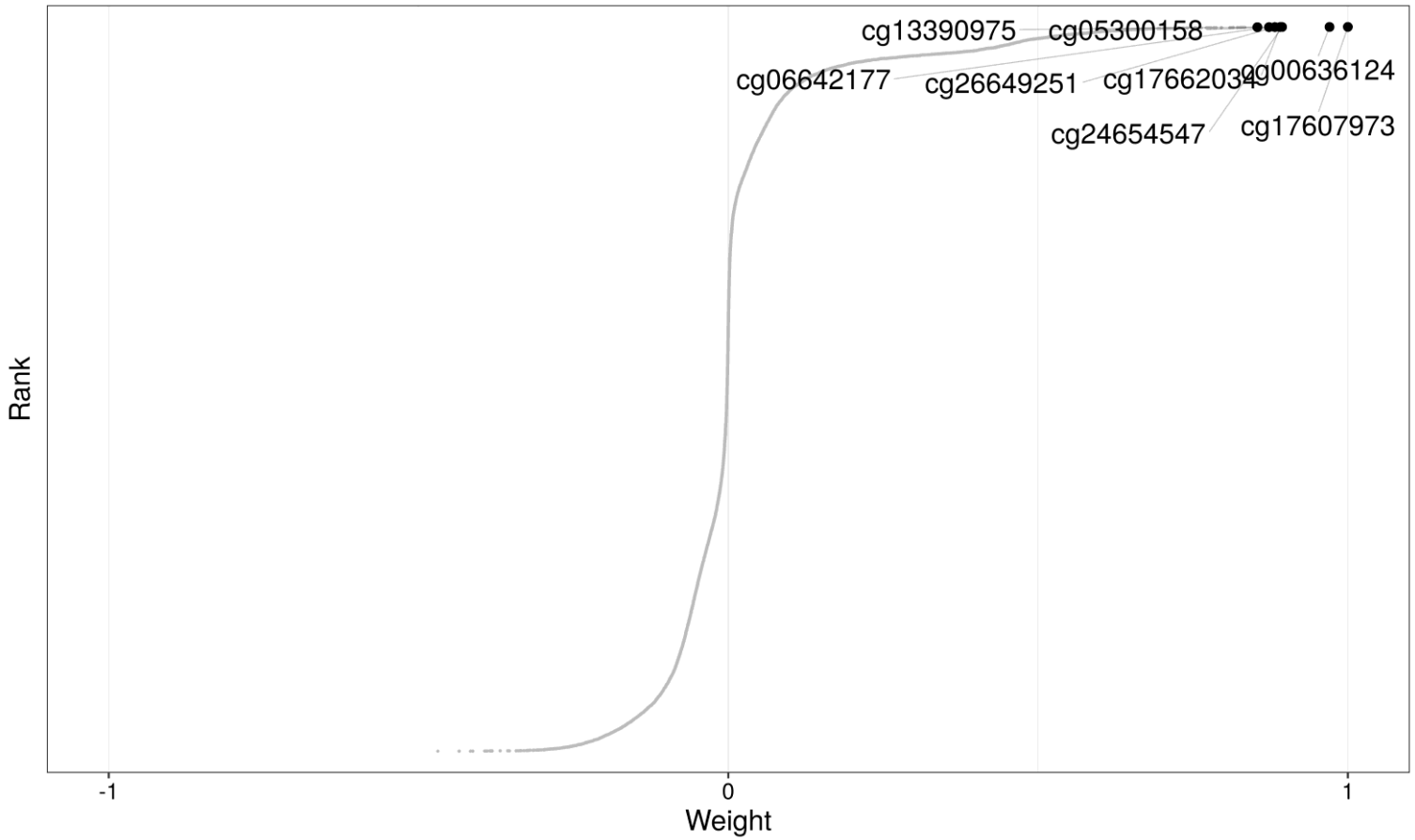


Figure S9. Overall features loading weights from Factor 11. Values range from -1 to 1. Features associated with the factor have larger absolute values, whereas features with no association are expected to have values close to zero. A positive weight indicates higher levels of that feature in samples with positive factor values, and vice versa.

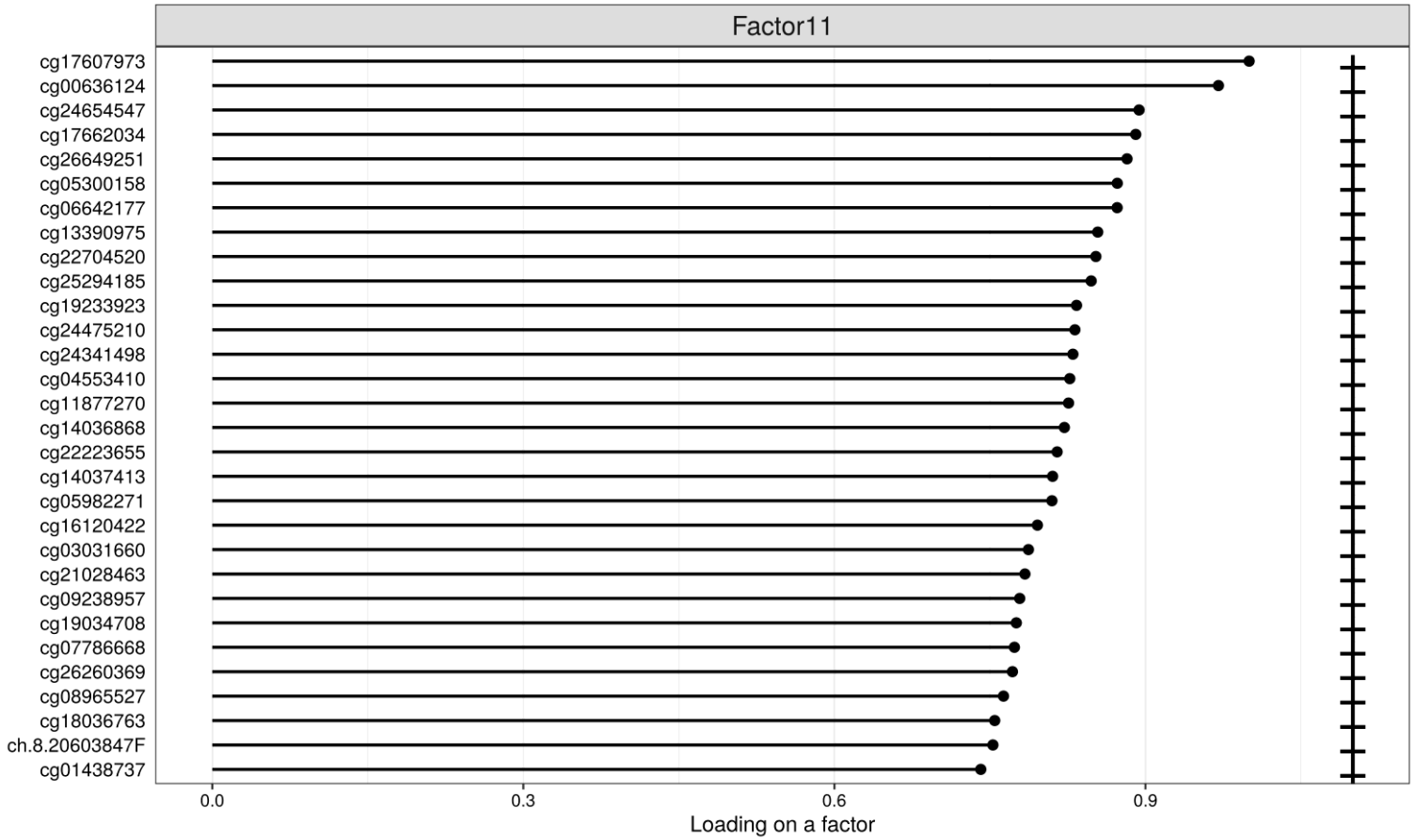


Figure S10. Top 30 features loading weights from Factor 11. Values ranges from 0 to 1 in absolute scale. Features associated with the factor have larger absolute values. A positive weight indicates higher levels of that feature in samples with positive factor values, and vice versa. In this factor, the top 30 CpGs only have positive weights.

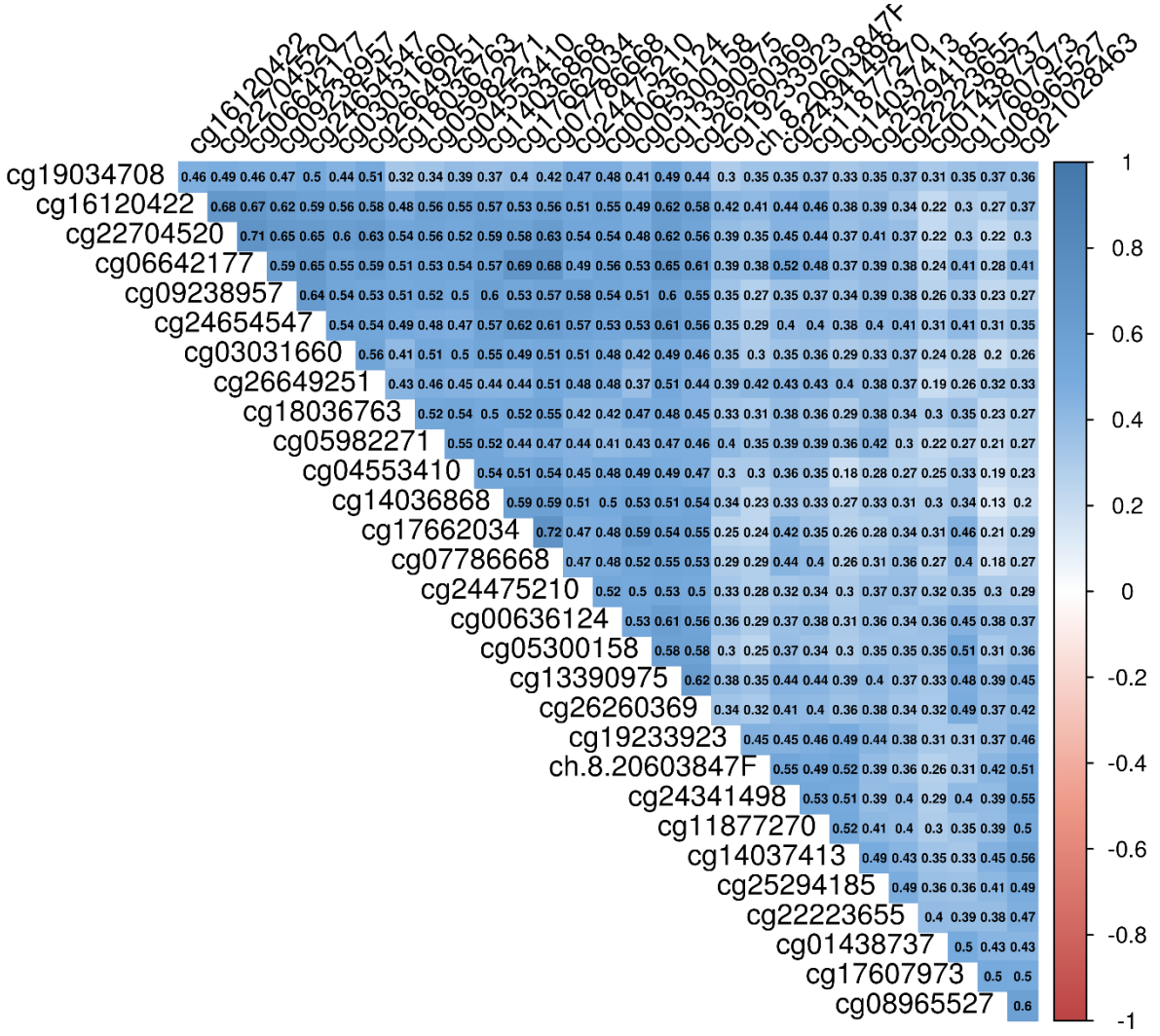


Figure S11. Correlations between top 30 CpGs and the highest weight from Factor 11. Correlation coefficients are represented in a colour scale from reddish for negative correlations to bluish for positive correlations Correlation coefficient ranges from 0.2 to 0.7.