Multiomics approach provides insight into altered choline metabolism and liver injury in patients with Glycogen storage disease type Ia

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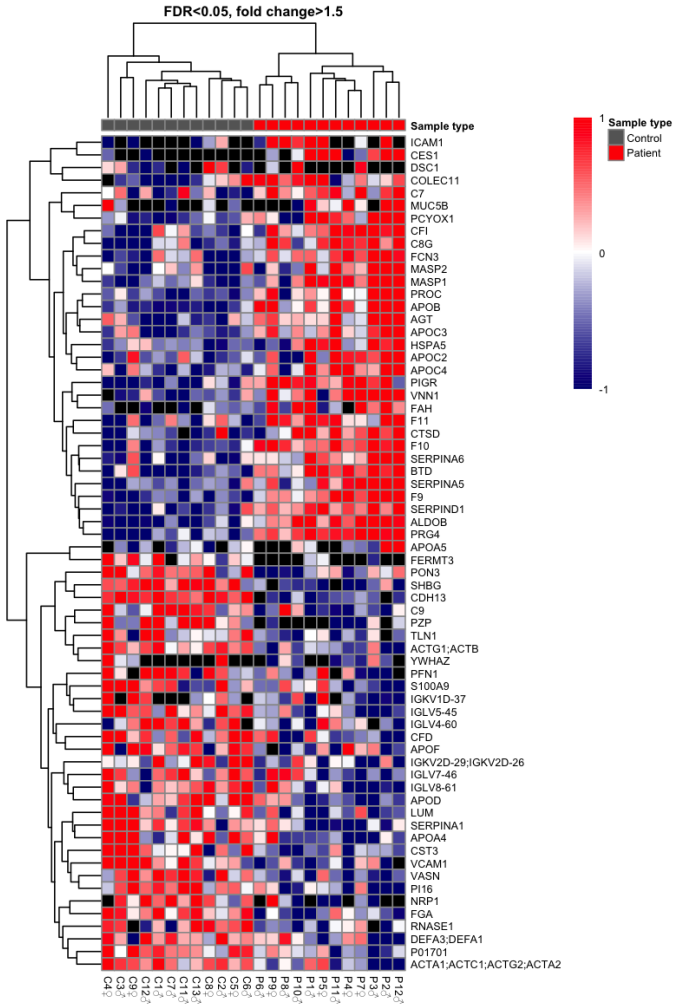
a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Sample type
Control
Patient
1
0
-1
ICAM1
CES1
DSC1
COLEC11
C7
MUC5B
PCYOX1
CFI
C8G
FCN3
MASP2
MASP1
PROC
APOB
AGT
APOC3
HSPA5
APOC2
APOC4
PIGR
VNN1
FAH
F11
CTSD
F10
SERPINA6
BTD
SERPINA5
F9
SERPIND1
ALDOB
PRG4
APOA5
FERMT3
PON3
SHBG
CDH13
C9
PZP
TLN1
ACTG1;ACTB
YWHAZ
PFN1
S100A9
IGKV1D-37
IGLV5-45
IGLV4-60
CFD
APOF
IGKV2D-29;IGKV2D-26
IGLV7-46
IGLV8-61
APOD
LUM
SERPINA1
APOA4
CST3
VCAM1
VASN
PI16
NRP1
FGA
RNASE1
DEFA3;DEFA1
P01701
ACTA1;ACTC1;ACTG2;ACTA2

b

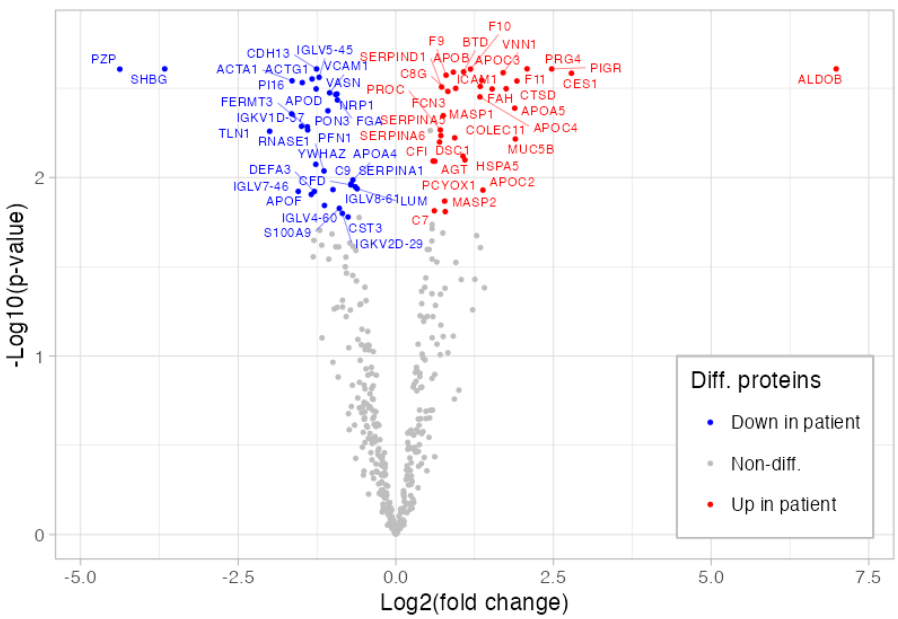
-Log10(p-value)
Log2(fold change)
Diff. proteins
Down in patient
Non-diff.
Up in patient
PZP
SHBG
CDH13
IGLV5-45
ACTA1
ACTG1
VCAM1
PI16
VASN
FERMT3
APOD
NRP1
IGKV1D-37
PON3
FGA
TLN1
RNASE1
PFN1
YWHAZ
APOA4
DEFA3
C9
SERPINA1
IGLV7-46
CFD
APOF
IGLV8-61
IGLV4-60
S100A9
CST3
IGKV2D-29
SERPIND1
C8G
PROC
SERPINA6
LUM
C7
F10
F9
BTD
VNN1
APOB
APOC3
PRG4
PIGR
ICAM1
F11
CES1
FAH
CTSD
FCN3
APOA5
MASP1
COLEC11
APOC4
CFI
DSC1
MUC5B
AGT
HSPA5
PCYOX1
APOC2
MASP2
ALDOB

Figure S1.

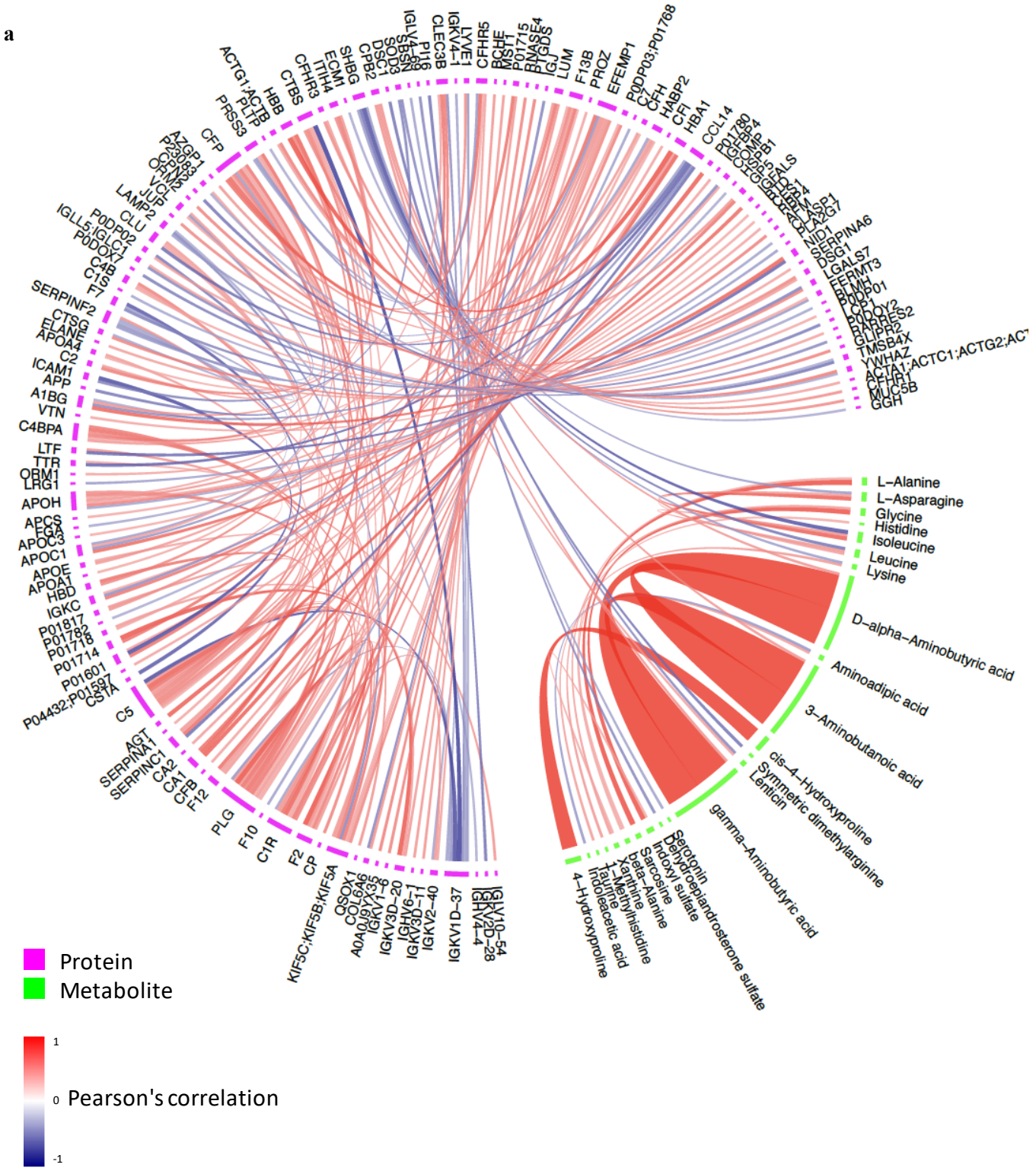
a
L-Alanine
L-Asparagine
Glycine
Histidine
Isoleucine
Leucine
Lysine
D-alpha-Aminobutyric acid
Aminoadipic acid
3-Aminobutanoic acid
cis-4-Hydroxyproline
Symmetric dimethylarginine
Lenticin
gamma-Aminobutyric acid
Serotonin
Dehydroepiandrosterone sulfate
Indoxyl sulfate
Sarcosine
beta-Alanine
Xanthine
1-Methylhistidine
Taurine
Indoleacetic acid
4-Hydroxyproline
Protein
Metabolite
1
0
Pearson's correlation
-1

Figure S2.

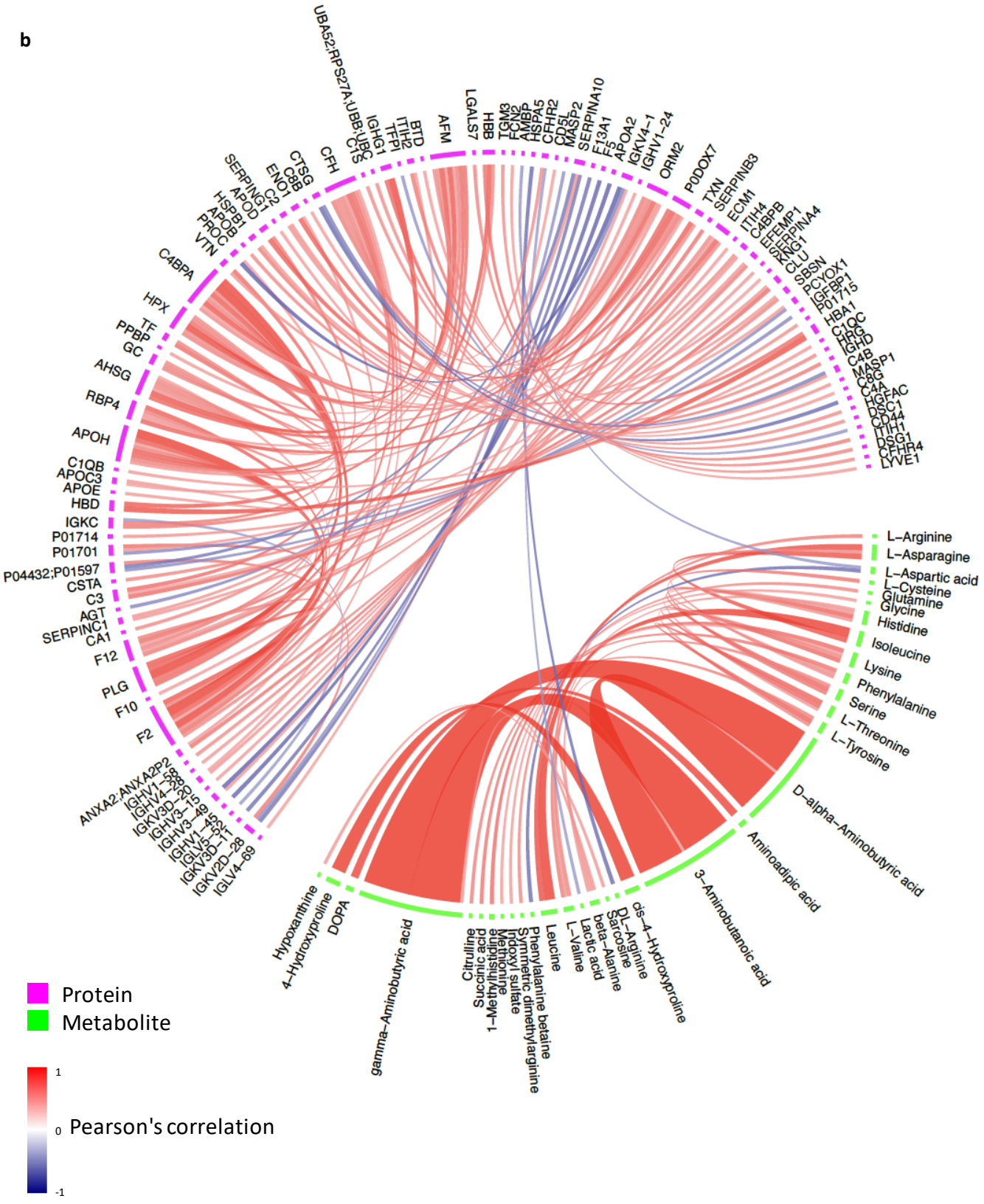
b
UBA52;RPS27A;UBB;UBC
CFH
CTSG
C8B
ENO1
C2
SERPING1
APOD
HSPB1
APOB
PROC
VTN
C4BPA
HPX
TF
PPBP
GC
AHSG
RBP4
APOH
C1QB
APOC3
APOE
HBD
IGKC
P01714
P01701
P04432;P01597
CSTA
C3
AGT
SERPINC1
CA1
F12
PLG
F10
F2
ANXA2;ANXA2P2
IGHV1–58
IGHV4–38
IGKV3D–20
IGHV3–15
IGHV3–49
IGHV1–45
IGLV5–52
IGKV3D–11
IGKV2D–28
IGLV4–69
CTS
IGHG1
TFPI
ITIH2
BTD
AFM
LGALS7
BHB
TGM3
FCN2
AMBP
HSPA5
CFHR2
CD5L
MASP2
SERPINA10
F13A1
F5
APOA2
IGKV4–1
IGHV1–24
ORM2
P0DOX7
TXN
SERPINB3
ECM1
ITIH4
C4BPB
EFEMP1
SERPINA4
KNG1
CLU
SBSN
PCYOX1
IGFBP1
P01715
HBA1
C1QC
HRG
IGHD
C4B
MASP1
C8G
C4A
HGFAC
DSC1
CD44
ITIH1
DSG1
CFHR4
LYVE1
L–Arginine
L–Asparagine
L–Aspartic acid
L–Cysteine
Glutamine
Glycine
Histidine
Isoleucine
Lysine
Phenylalanine
Serine
L–Threonine
L–Tyrosine
D–alpha–Aminobutyric acid
Aminoadipic acid
3–Aminobutanoic acid
cis–4–Hydroxyproline
DL–Arginine
Sarcosine
beta–Alanine
Lactic acid
L–Valine
Leucine
Phenylalanine betaine
Symmetric dimethylarginine
Indoxyl sulfate
Methionine
1–Methylhistidine
Succinic acid
Citrulline
gamma–Aminobutyric acid
DOPA
4–Hydroxyproline
Hypoxanthine
Protein
Metabolite
1
0
-1
Pearson's correlation

Figure S2.

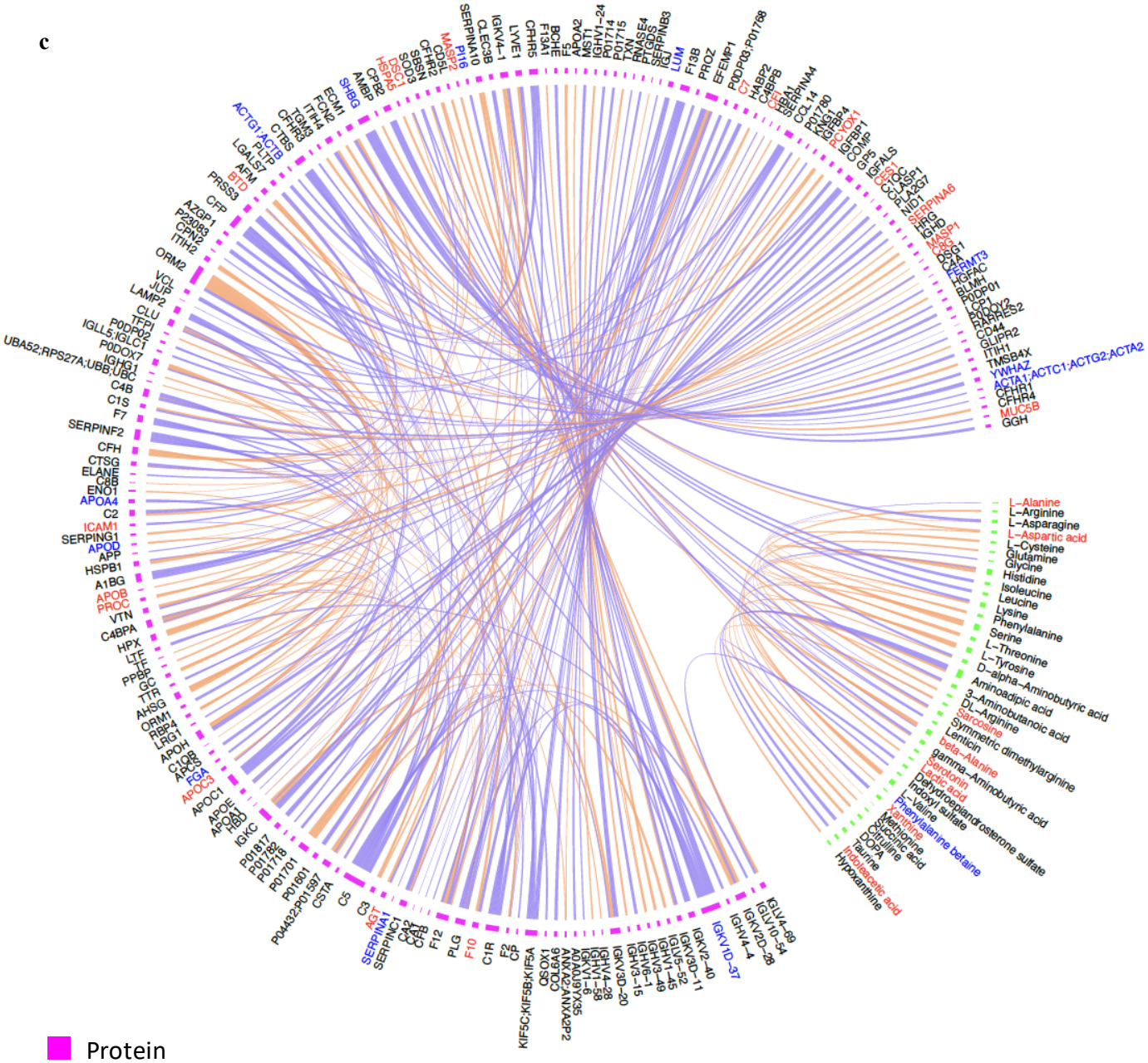
c
L–Alanine
L–Arginine
L–Asparagine
L–Aspartic acid
L–Cysteine
Glutamine
Glycine
Histidine
Isoleucine
Leucine
Lysine
Phenylalanine
Serine
L–Threonine
L–Tyrosine
D–alpha–Aminobutyric acid
Aminoadipic acid
3–Aminobutanoic acid
DL–Arginine
Sarcosine
Symmetric dimethylarginine
Lenticin
beta–Alanine
gamma–Aminobutyric acid
Serotonin
Lactic acid
Dehydroepiandrosterone sulfate
Indoxyl sulfate
L–Valine
Phenylalanine betaine
Xanthine
Methionine
Succinic acid
Citrulline
DOPA
Taurine
Indolelactic acid
Hypoxanthine
Protein
Metabolite
Significantly differential feature high in patient
Significantly differential feature low in patient
Gained correlation in patient
Lost correlation in patient

Figure S2.

SUPPLEMENTARY FIGURES LEGENDS

Figure S1. Serum proteomic profile of patients with GSDIa. A. Hierarchical clustering with heat map visualization of differential proteins for adj. $p<0.05$ and $|FC|>1.5$. Heatmap colour coding represents relative protein abundance: red and blue represent increased and decreased levels of each protein in patients compared to HC. **B.** Volcano plot of differential proteins for adj. $p<0.05$ and $|FC|>1.5$. Blue and red labelled dots refer to significantly decreased and increased proteins respectively in patients compared to HC. The corresponding tabular data are presented in Supplemental Table S1.

Figure S2. GSDIa and HC multiomics correlation analyses. A. All significant HC Pearson's correlations (adjusted p-value<0.1). Purple circular sectors correspond to proteins, green to metabolites. The width of the circular sectors is proportional to –Log(adj. p). A colour scale between red and blue shows positive and negative correlations in HCs. **B.** All significant patient Pearson's correlations (adjusted p-value<0.1). Purple circular sectors correspond to proteins, green to metabolites. The width of the circular sectors is proportional to –Log(adj. p). A colour scale between red and blue shows positive and negative correlations in patients with GSDIa. **C.** All lost or gained significant Pearson's correlations between patients and HCs (adjusted p-value<0.1). The width of the circular sectors is proportional to |corr. coeff. patient – corr. coeff. HC|. Purple circular sectors correspond to proteins, green to metabolites. The orange and purple colours indicate gained and lost correlations in patients. Gained correlations are those (positive or negative) significant only in patients, lost correlations are those (positive or negative) significant in the HC and non-significant in patients. Molecules highlighted in red are significantly increased in patients, those highlighted in blue are decreased. The corresponding tabular data are presented in Supplemental Table S3.