

Using *In Vivo* Intact Structure for System-wide Quantitative Analysis of Changes in Proteins

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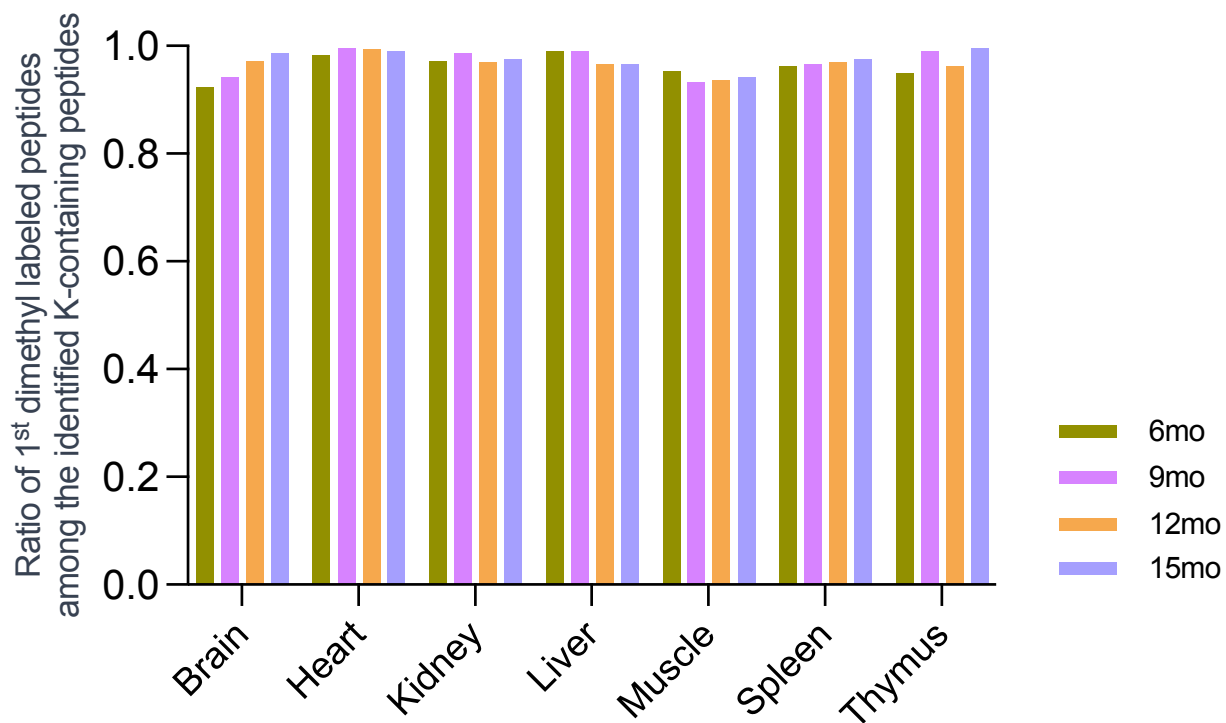
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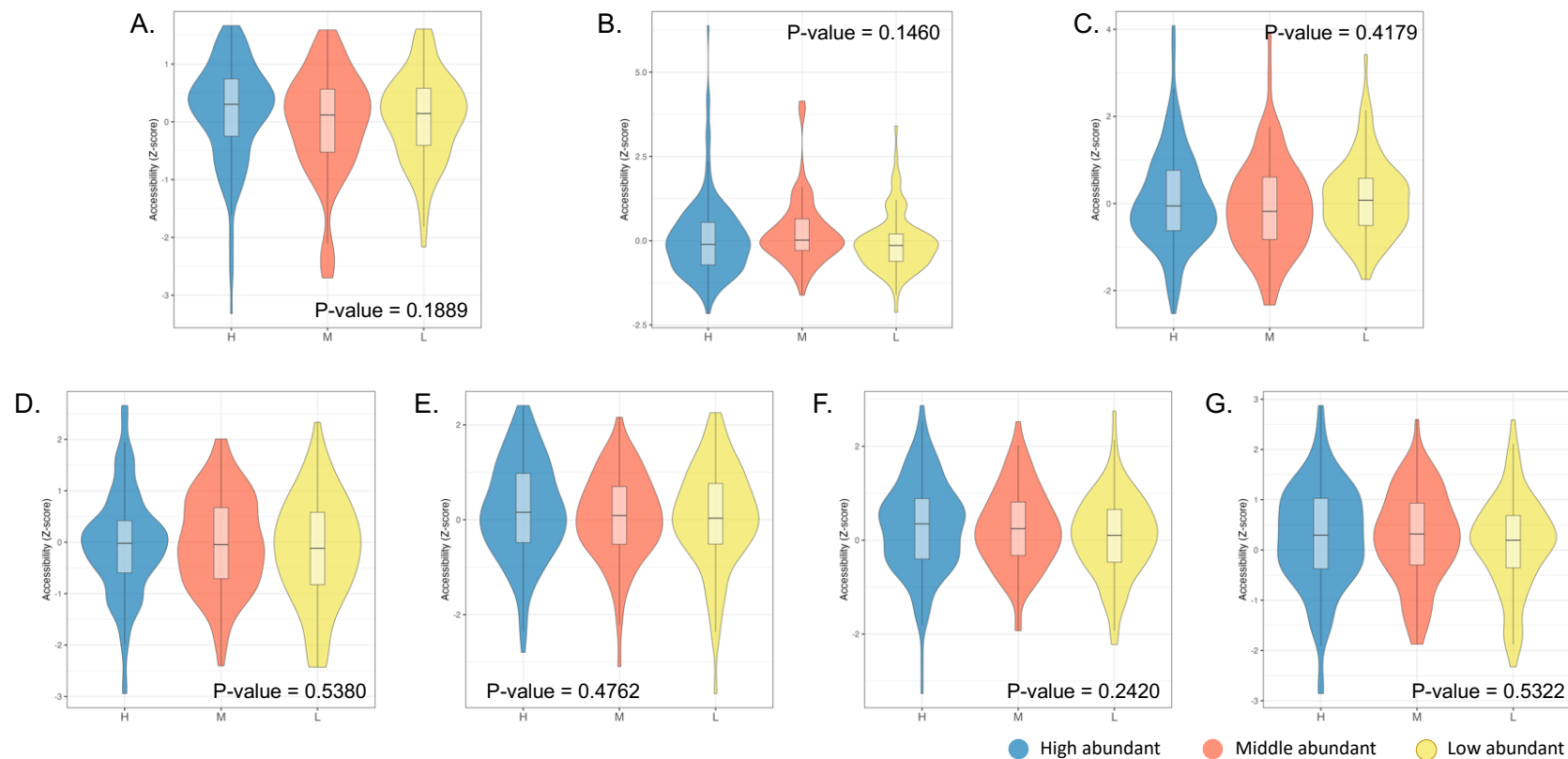
³Neurodegeneration New Medicines Center, The Scripps Research Institute, La Jolla, CA 92037, United States

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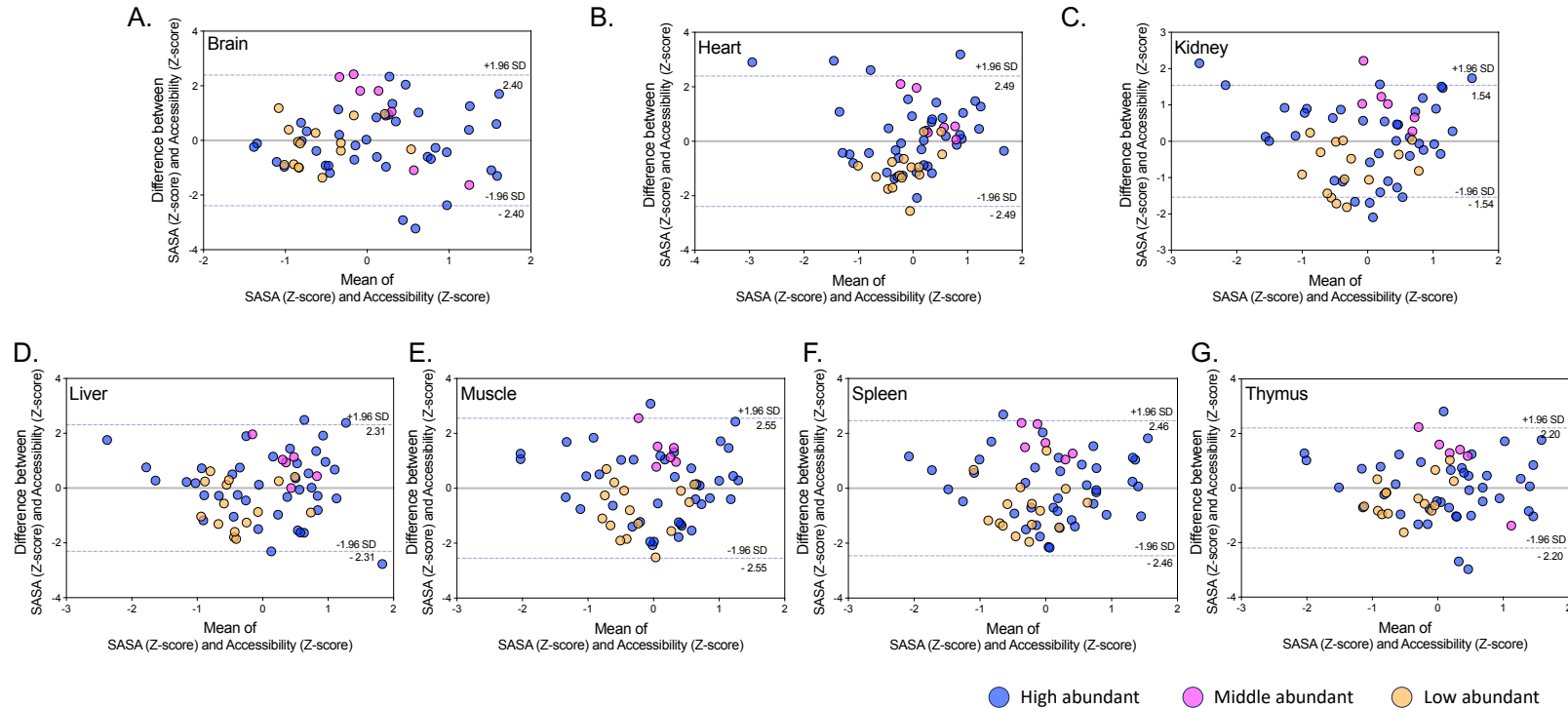
Supplementary Figures



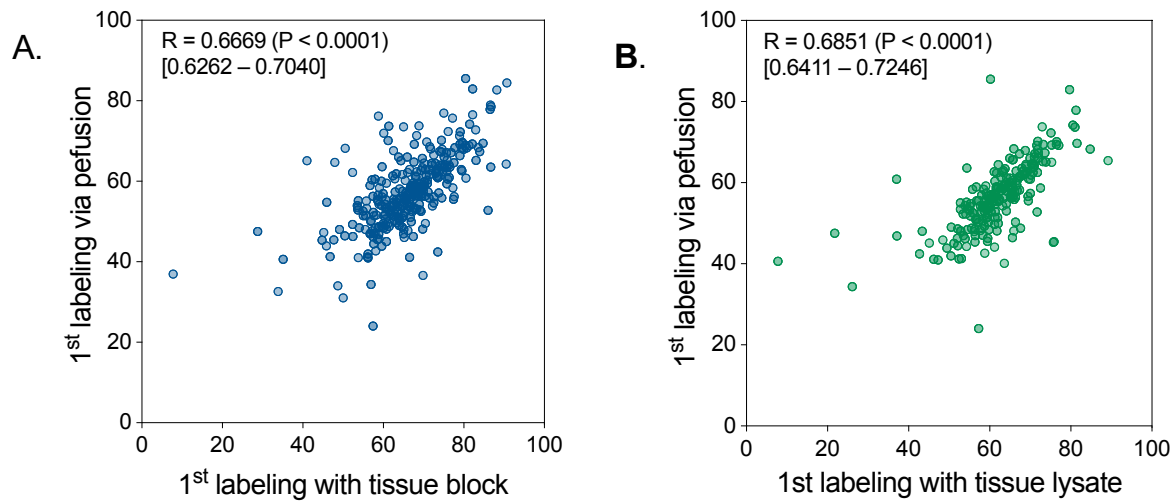
Supplementary Figure 1 Proportion of the first dimethyl labeled peptides. The number of dimethyl-labeled peptides was compared to the number of the lysine-containing peptides separately at each age. Four proportions per tissue were tested with Chi-square test. All comparisons in proportions were observed to be insignificantly different. P-values from Chi-square test were Brain = 0.1139, Heart = 0.9617, Kidney = 0.9313, Liver = 0.5891, Muscle = 0.9245, Spleen = 0.9587, Thymus = 0.1655. Source data are provided as a Source Data file.



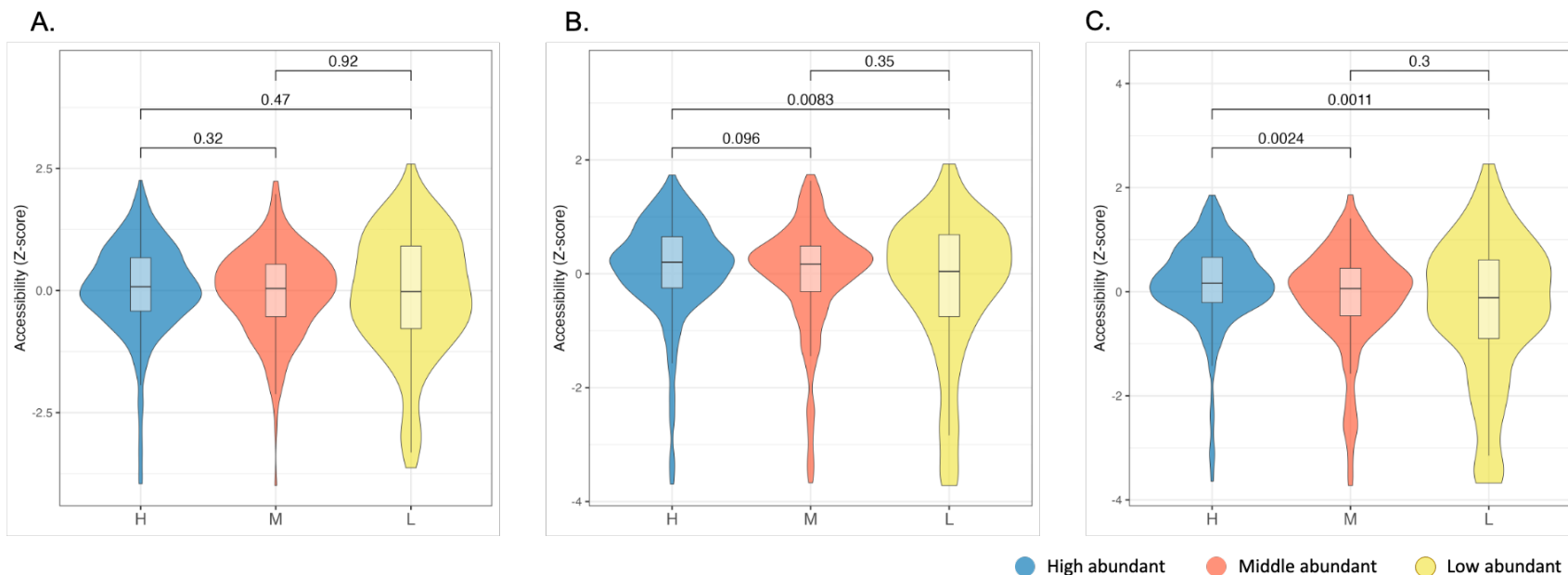
Supplementary Figure 2 Assessment of the influence of the protein abundance. To assess the effect of the protein abundance on the labeling efficiency, the accessibility values for the 328 labeled peptides were distributed according to groups where corresponding proteins were included. The differences in the accessibility were tested using ANOVA and P-values of all comparison that were observed to be more than 0.5. A: Brain, B: Heart, C: Kidney, D: Liver, E: Muscle, F: Spleen, and G: Thymus. Source data are provided as a Source Data file.



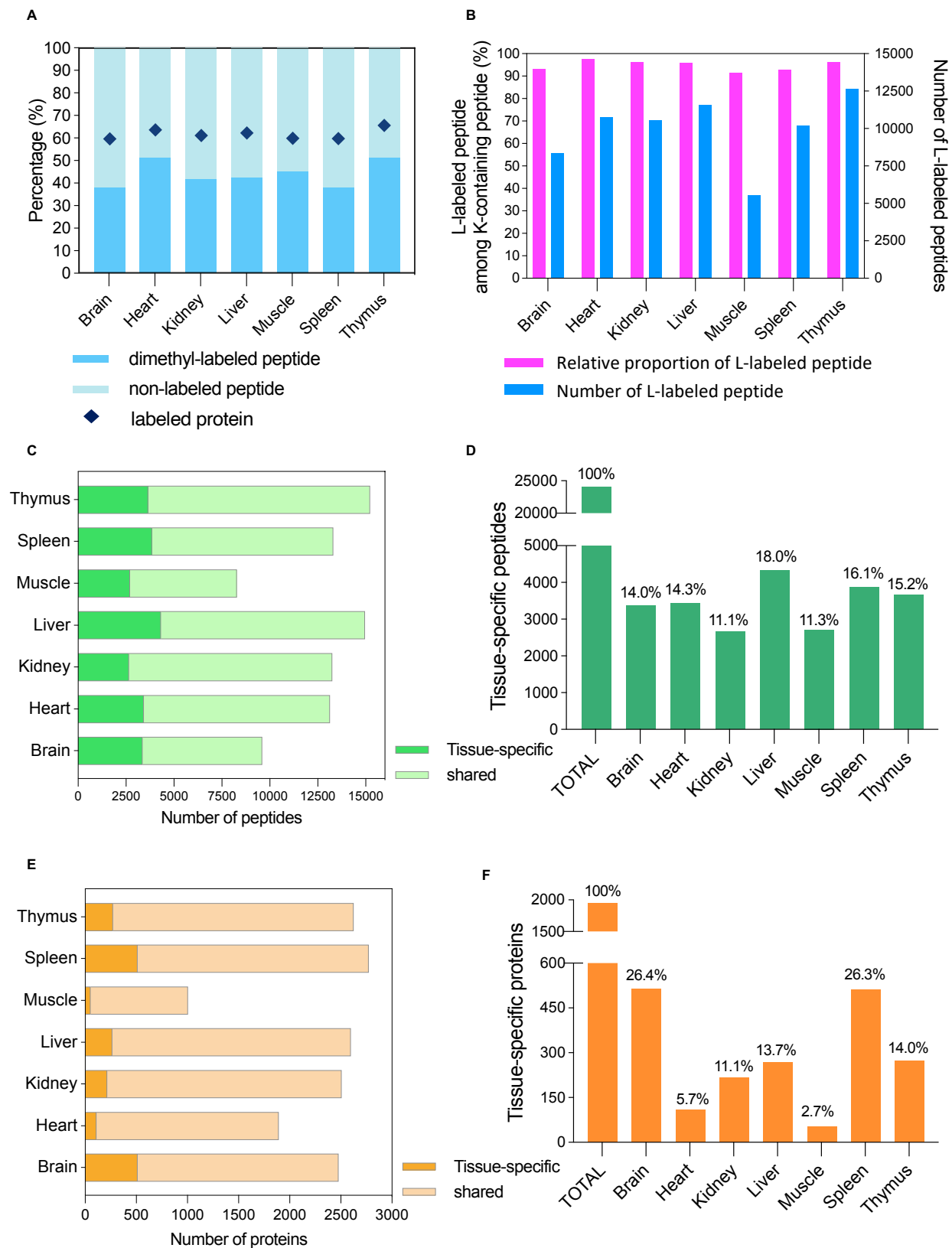
Supplementary Figure 3 Agreement with the structures determined by in vivo CPP and Crystal structures. Accessibility from dimethylation through perfusion and SASA values from crystal structures were transformed into z-scores for Bland-Altman plot. To calculate SASA value, PDB files from 11 housekeeping proteins were obtained from PDB database: Adk, Aldh4a1, Calr, Got2, Gpi, Hsp90ab1, Npm1, Pdla4, Sod1, Uba1, Vcp. Dotted line indicates ± 1.96 standard deviation representing 95% confidential interval. Solid line indicates overall bias of two measurements. A: Brain, B: Heart, C: Kidney, D: Liver, E: Muscle, F: Spleen, and G: Thymus Source data are provided as a Source Data file.



Supplementary Figure 4 Correlation of the accessibility values from different sample statuses. Mice brain samples were used for the correlation analysis between distinct processes in the initial labeling. Two mice were used, and the samples were analyzed in technical duplicates. Labeled peptides that were quantified in 3 out of 4 measurements were selected for this analysis, then 786 (A) and 624 (B) labeled peptides were used in each pair of methods. Two coefficients of correlation were not significantly different based on the Fisher r-to-z transformation (P-value = 0.4886). Source data are provided as a Source Data file.

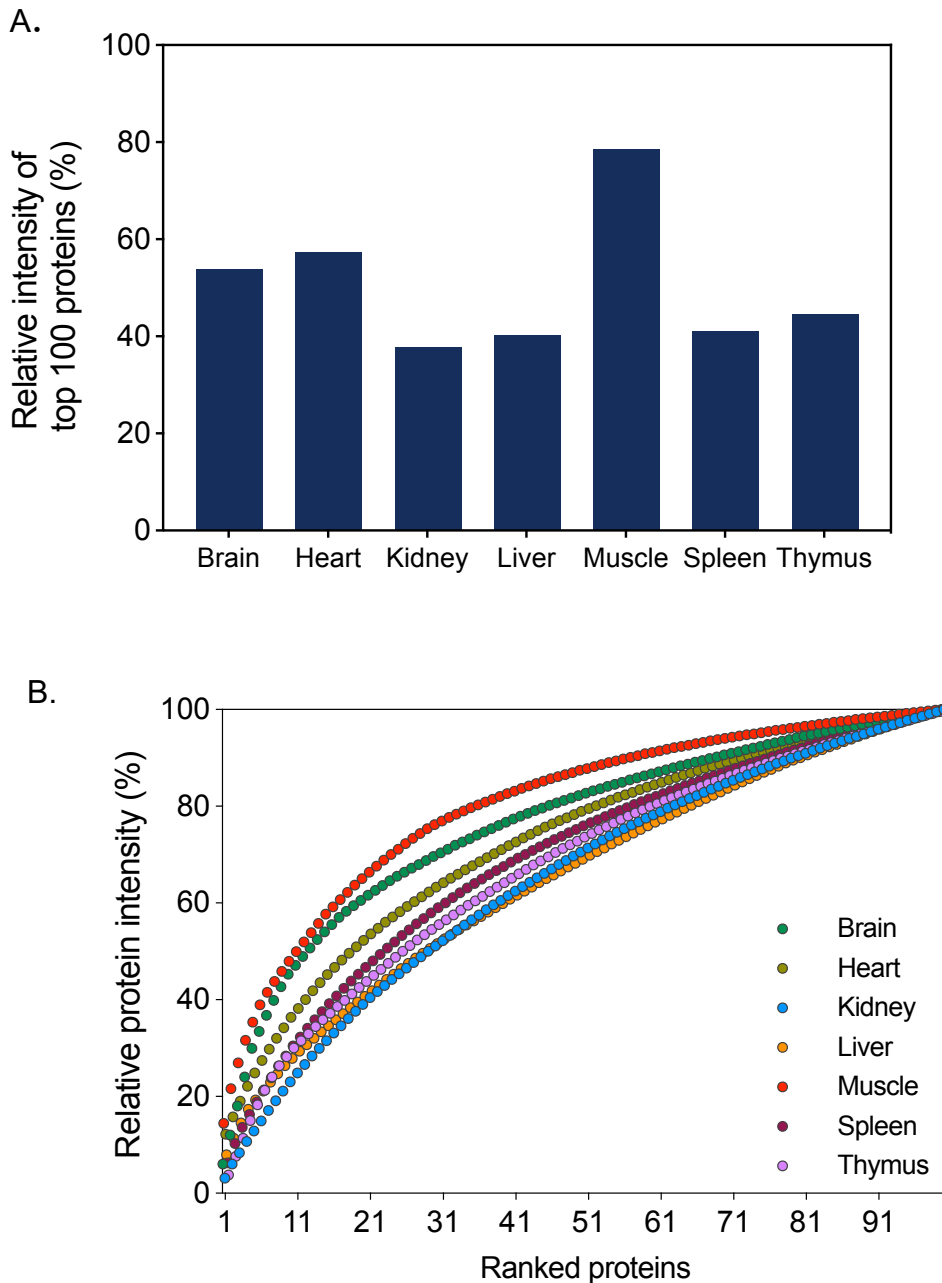


Supplementary Figure 5 Influence of protein abundance depending on sample status on labeling. All identified proteins were categorized into three groups (High, middle, and low) based on their protein abundance for each distinct process. Labeled peptides were then distributed according to the abundance of their corresponding proteins. The distribution of accessibility was tested using ANOVA, and post-hoc analyses were conducted using the Tukey method. A: 1st labeling through perfusion, B: 1st labeling with tissue block, and C: 1st labeling with tissue lysate. Source data are provided as a Source Data file.

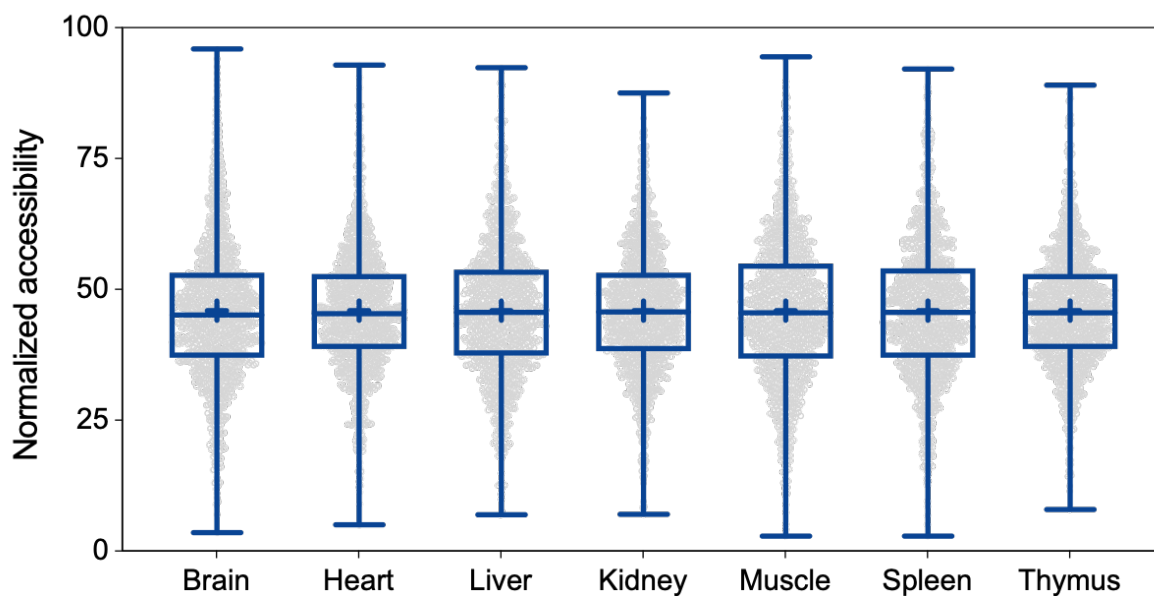


Supplementary Figure 6 Labeling efficiency of the 1st labeling via perfusion

(A) All the labeled peptides (light, heavy or both light and heavy) were counted as identified peptides for each tissue sample. The proportions of identified peptides that were labeled ranged from 38.01% (n = 8,758) in brain to 51.20% (n = 10,779) in heart (blue). Diamonds indicate the relative proportion of proteins that were labeled. (B) The proportions of lysine-containing peptides that were light-labeled were determined for each tissue. The proportions ranged from 91.5% (n = 5,583) in muscle to 97.5% (n = 10,745) in heart (pink). All tissue samples showed a labeling efficiency of more than 90% for labeling via the perfusion method, while the number of light-labeled peptides were variable (blue). (C and E) The tissue-specific labeled peptides (C)/proteins (E) (green/orange) and shared peptides/proteins (pale green/pale orange) were determined for each tissue sample. (D and F) These bar graphs represent the contribution of each tissue to the total number of tissue-specific labeled peptides (D)/proteins (F). Source data are provided as a Source Data file.



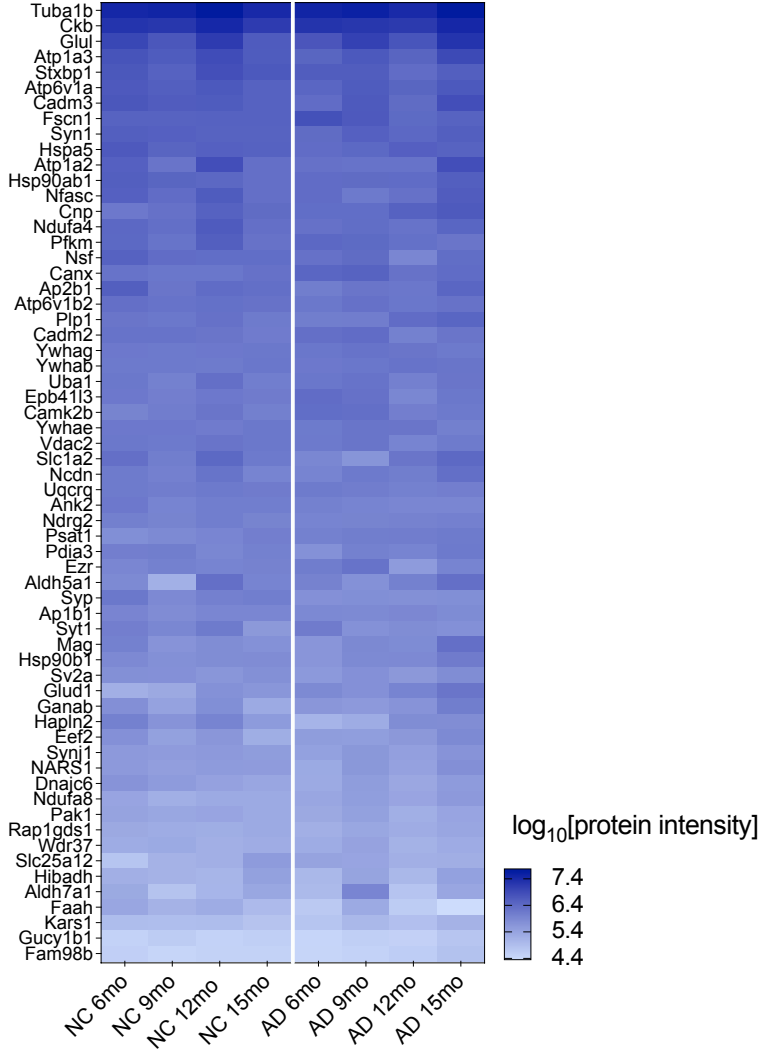
Supplementary Figure 7 Abundance of the 100 most abundant proteins in each tissue. (A) Relative abundance of the 100 most abundant proteins in each tissue. Abundance calculation was based on protein intensity relative to the overall intensity. The sum of intensity of the top100 proteins contributed over 78.6% to the total intensity in muscle tissue. (B) Accumulation of top 100-protein abundance in the mouse tissues. Accumulations of protein mass are plotted for 7 tissues. Proteins are ranked by their intensity. Source data are provided as a Source Data file.



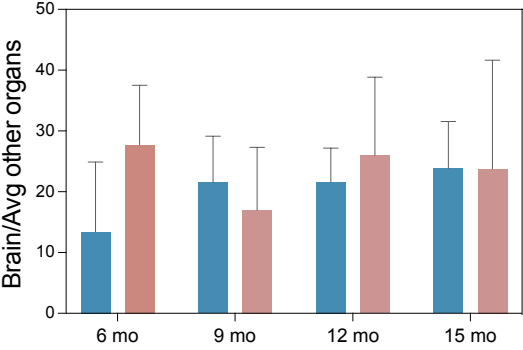
Supplementary Figure 8 Normalized accessibility.

The accessibility values of the peptides that were detected from all 7 tissues were quantile-normalized to identify the distribution of the values across 7 tissues. Source data are provided as a Source Data file.

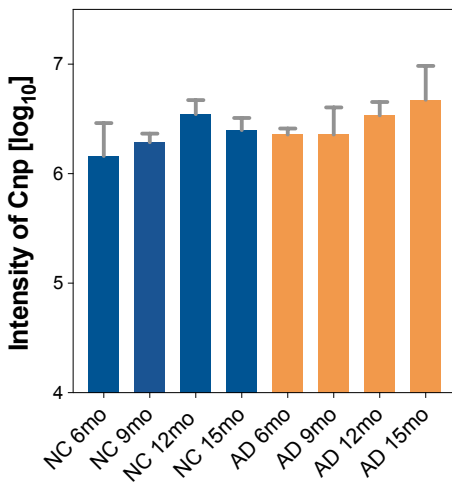
A.



B.

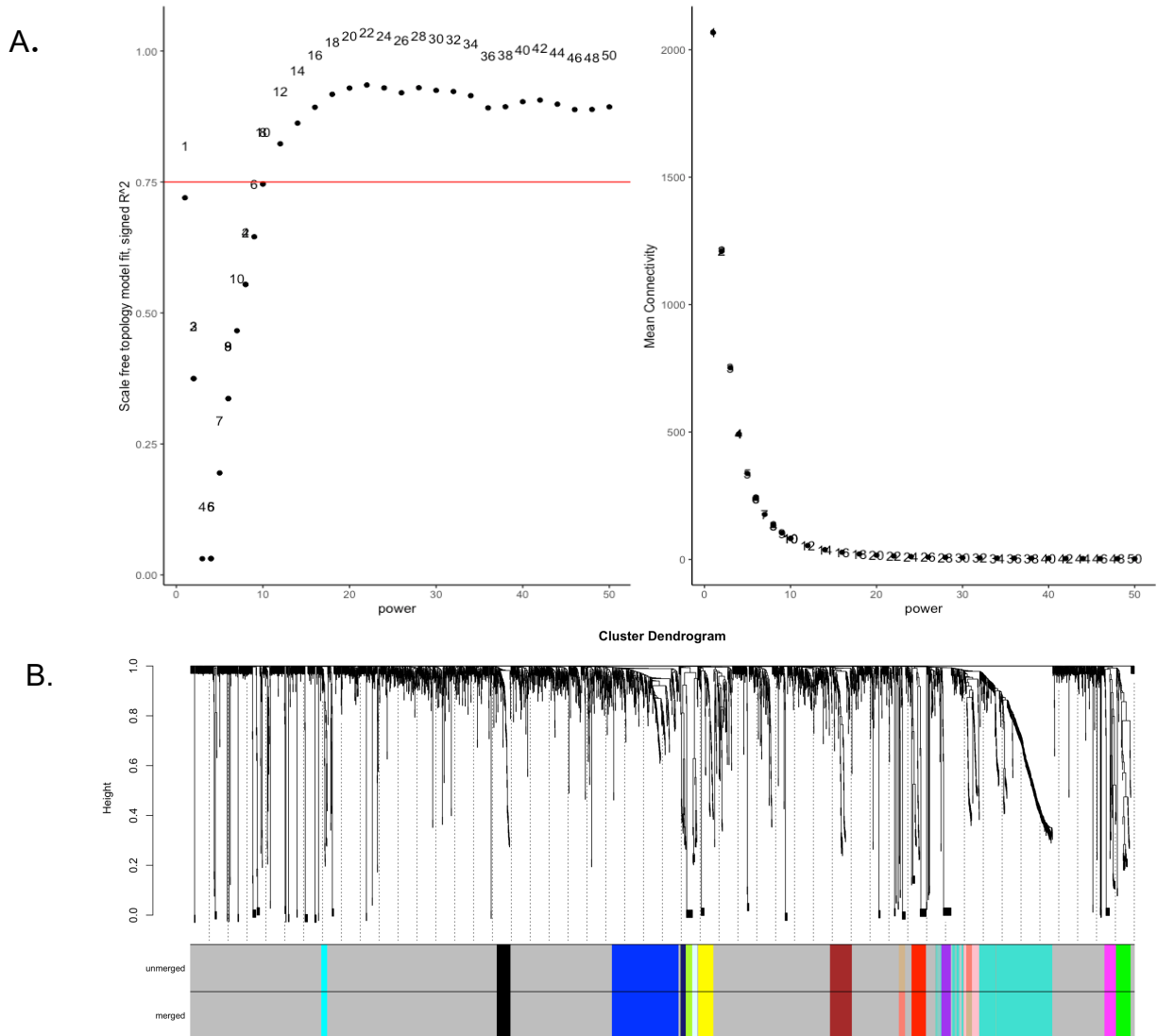


C.



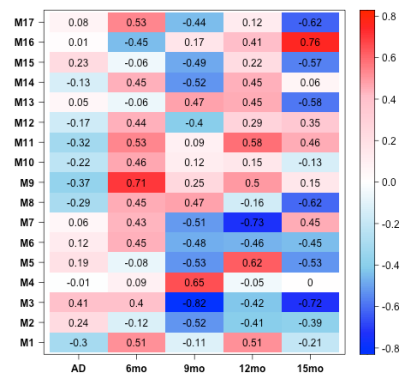
Supplementary Figure 9 Abundance levels of brain proteins

(A) Sixty proteins were known to be enriched in human brain. Protein abundance was derived by summing the top3 peptides. The values were transformed in logarithm. The protein intensity did not exhibit an obvious pattern of NC and AD, nor as progressing AD. (B) Cnp was highly expressed in the brain compared to averaged abundance of Cnp in the other 6 tissues. Blue bar indicates NC, pink bar indicates AD (C). The intensity of protein Cnp did not exhibit significant changes between NC and AD, nor among the time points of NC and AD. Source data are provided as a Source Data file.



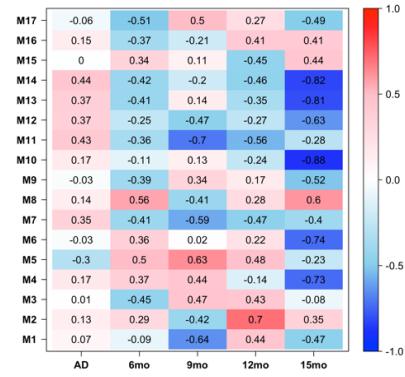
Supplementary Figure 10 Modularization of protein co-expression. A brain dataset shown representatively. Soft threshold power was determined using the `pickSoftThreshold()` function in the WGCNA package. The threshold value was selected when R^2 reaches a plateau over 0.75, indicating that the network has achieved a scale-free topology (A). The cluster dendrogram (upper) and the co-expression modules (lower) were generated by hierarchical clustering (B). The branches of the dendrogram represent individual proteins. The height indicates the Euclidean distance. Each module that contains weighted co-expressed proteins is displayed with a distinct color.

A.



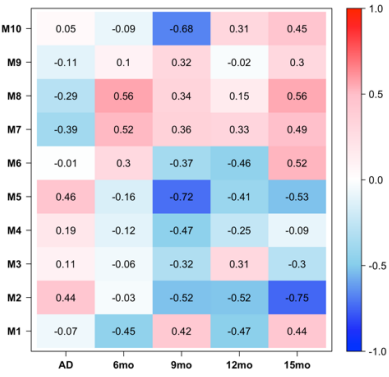
Brain

B.



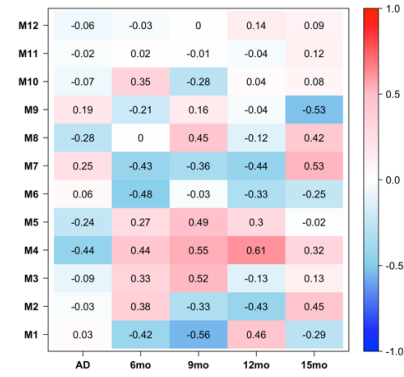
Kidney

C.



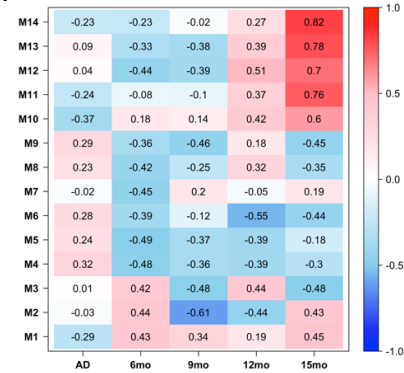
Muscle

D.



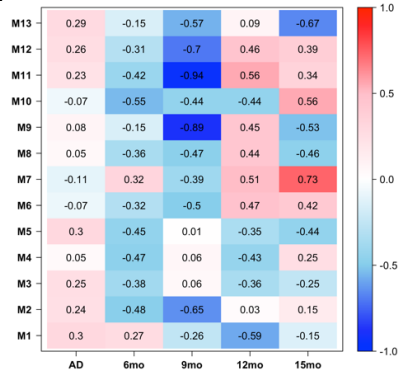
Spleen

E.



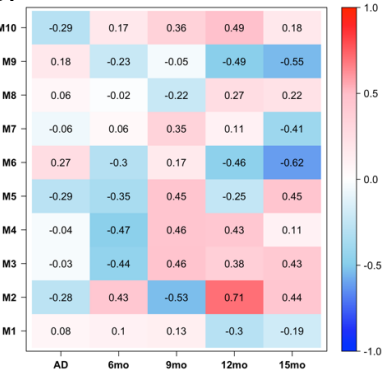
Heart

F.



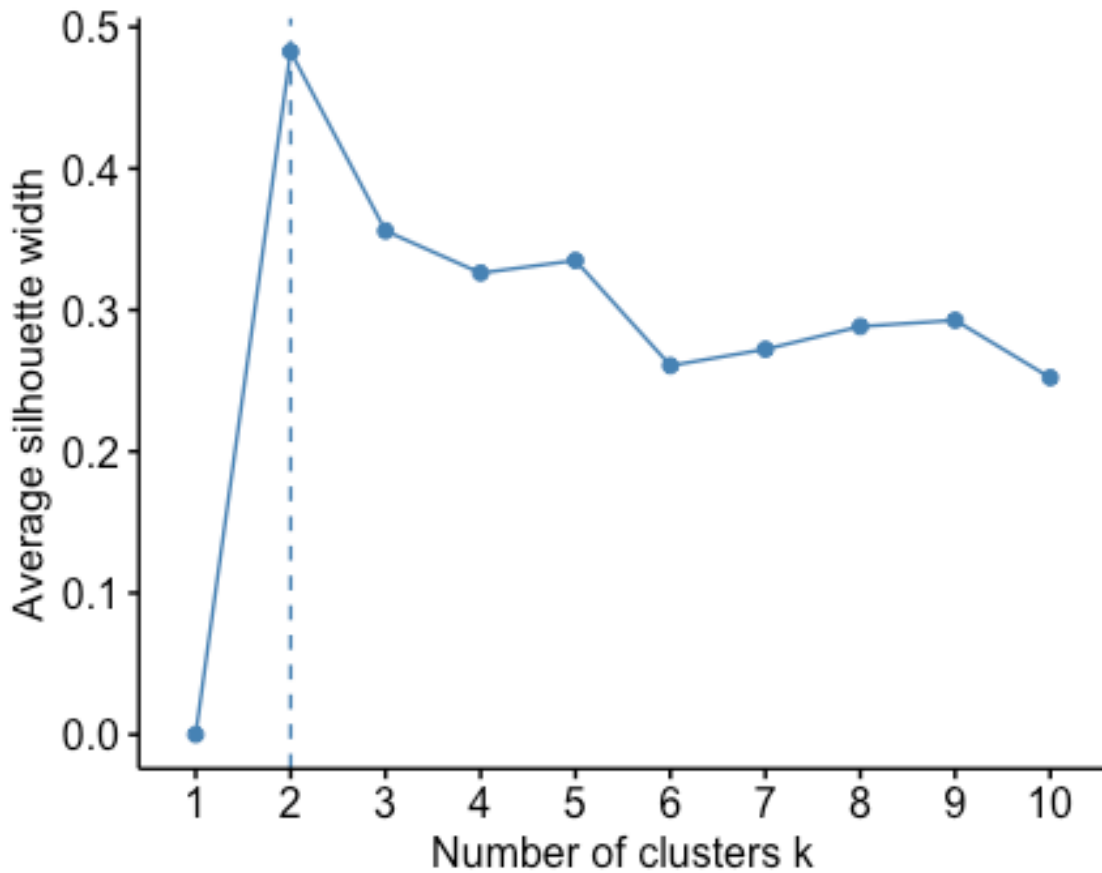
Liver

G.

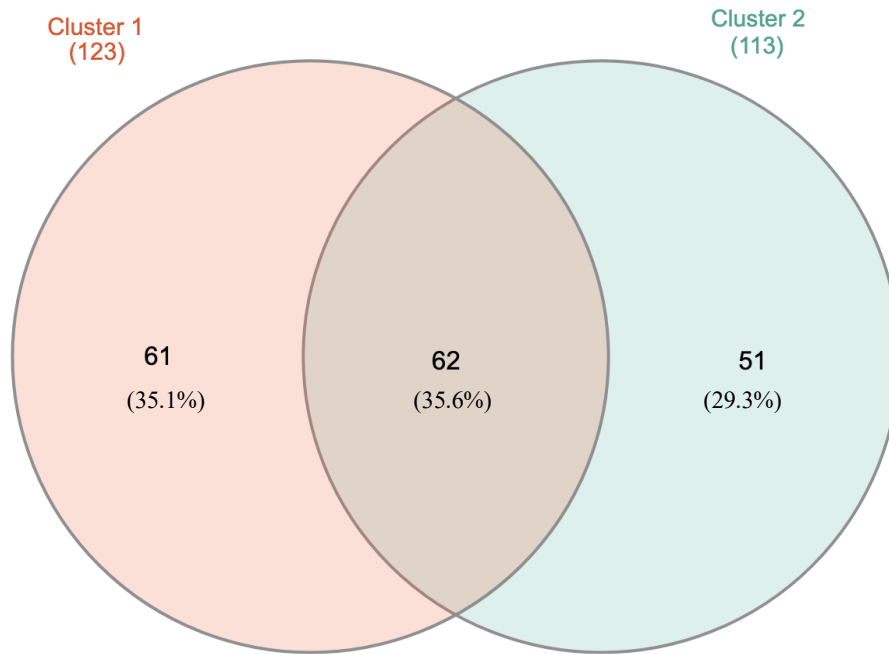


Thymus

Supplementary Figure 11 Relationship between module and traits in brain (A), kidney (B), muscle (C), spleen (D), heart (E), liver (F), and thymus (G). In the first column of each heatmap, the correlation was calculated with all samples, and in the next four columns, the correlations were calculated with samples sub-divided by age.

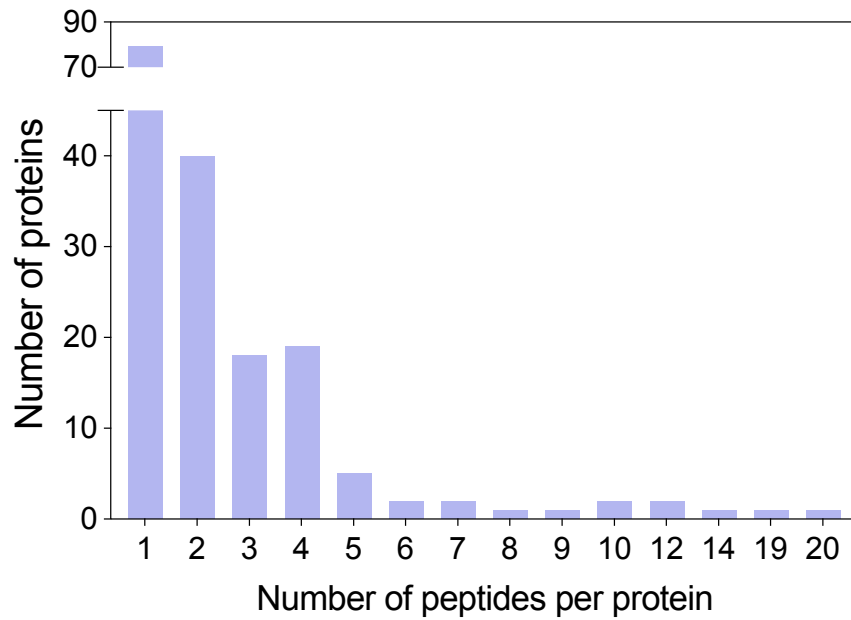


Supplementary Figure 12 Optimization of the number of clusters in unsupervised machine learning algorithms for the brain dataset. The number of clusters was determined in K-means clustering by evaluating the quality of the clustering results for different values of k (the number of clusters). The silhouette score (silhouette width) measures how similar the data is to its own cluster compared to other clusters. A score close to 1 indicates that the data is well-matched to its own cluster. The k value that showed the highest score was selected per each tissue dataset and was determined to be 2 in the brain dataset.



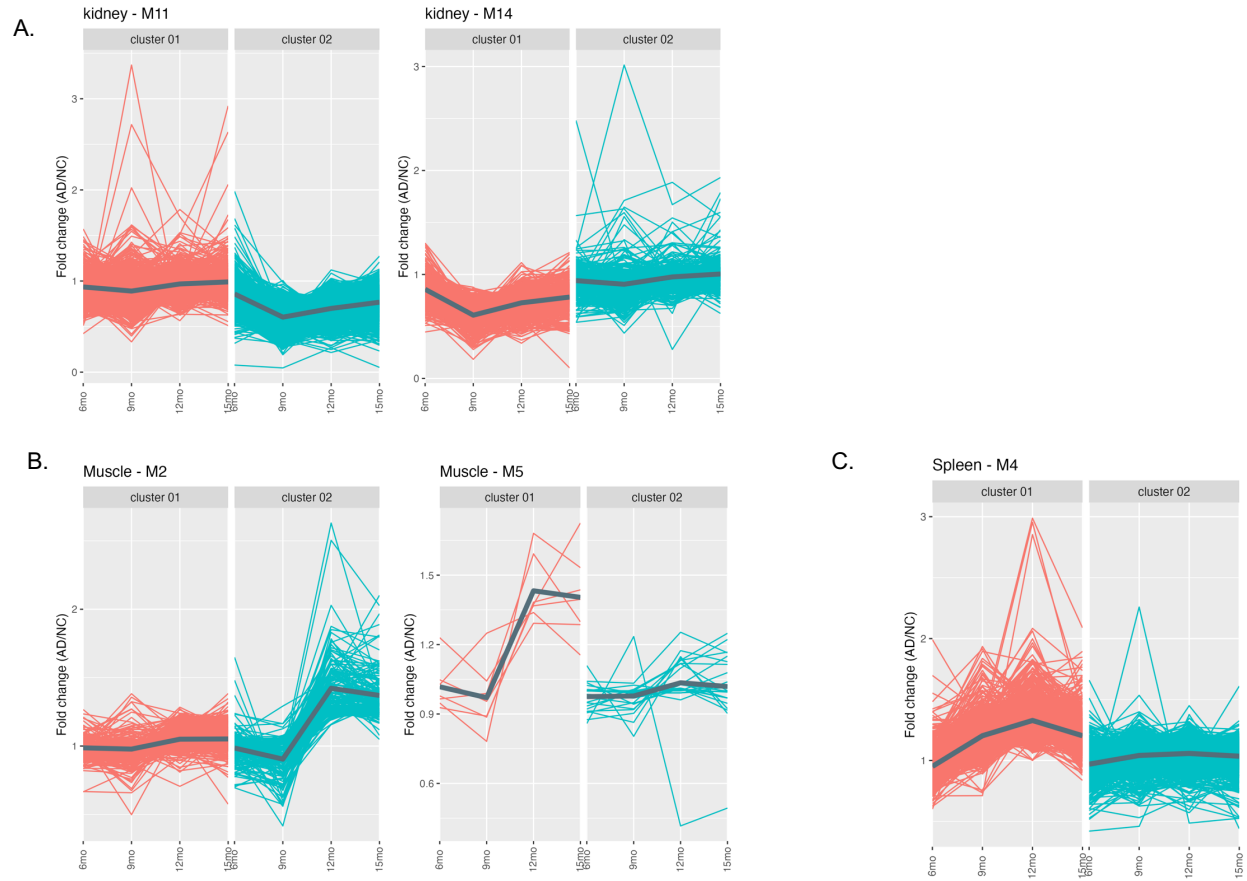
Supplementary Figure 13 Overlapped proteins between two clusters in module 3 (M3) of brain.

One hundred seventy-four of the 289 proteins of M3 were labeled with dimethylation, and the labeled peptides were clustered into two clusters. All the labeled peptides of 61 proteins were clustered into cluster 1; all the labeled peptides of 51 proteins were clustered into cluster 2.



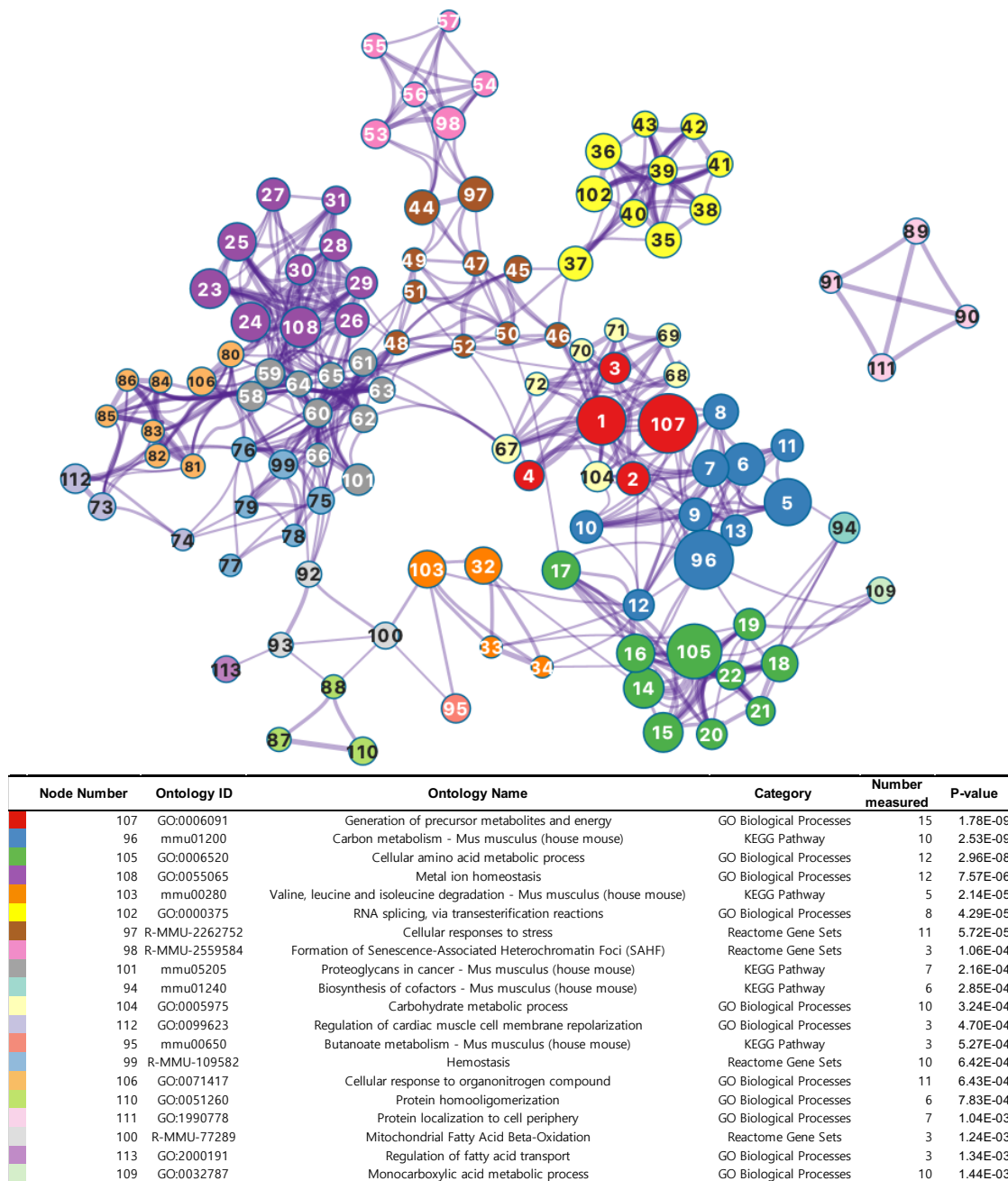
Supplementary Figure 14 Frequency of labeled peptides per proteins in M3.

Map1a showed the highest number of labeled peptides ($n = 20$) per protein. Pkg1 and Mdh1 each contained 19 labeled peptides. 79 proteins included a single labeled peptide. Source data are provided as a Source Data file.

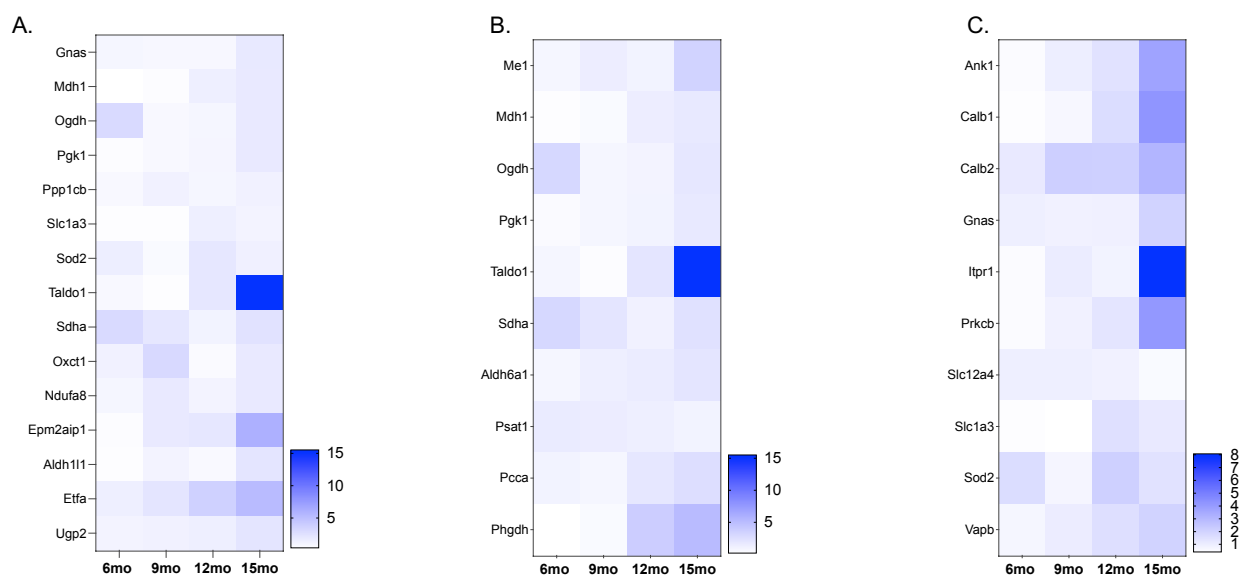


Supplementary Figure 15 Clusters of the labeled peptides based on the fold-change of the accessibility for Kidney (A), Muscle (B), and Spleen (C).

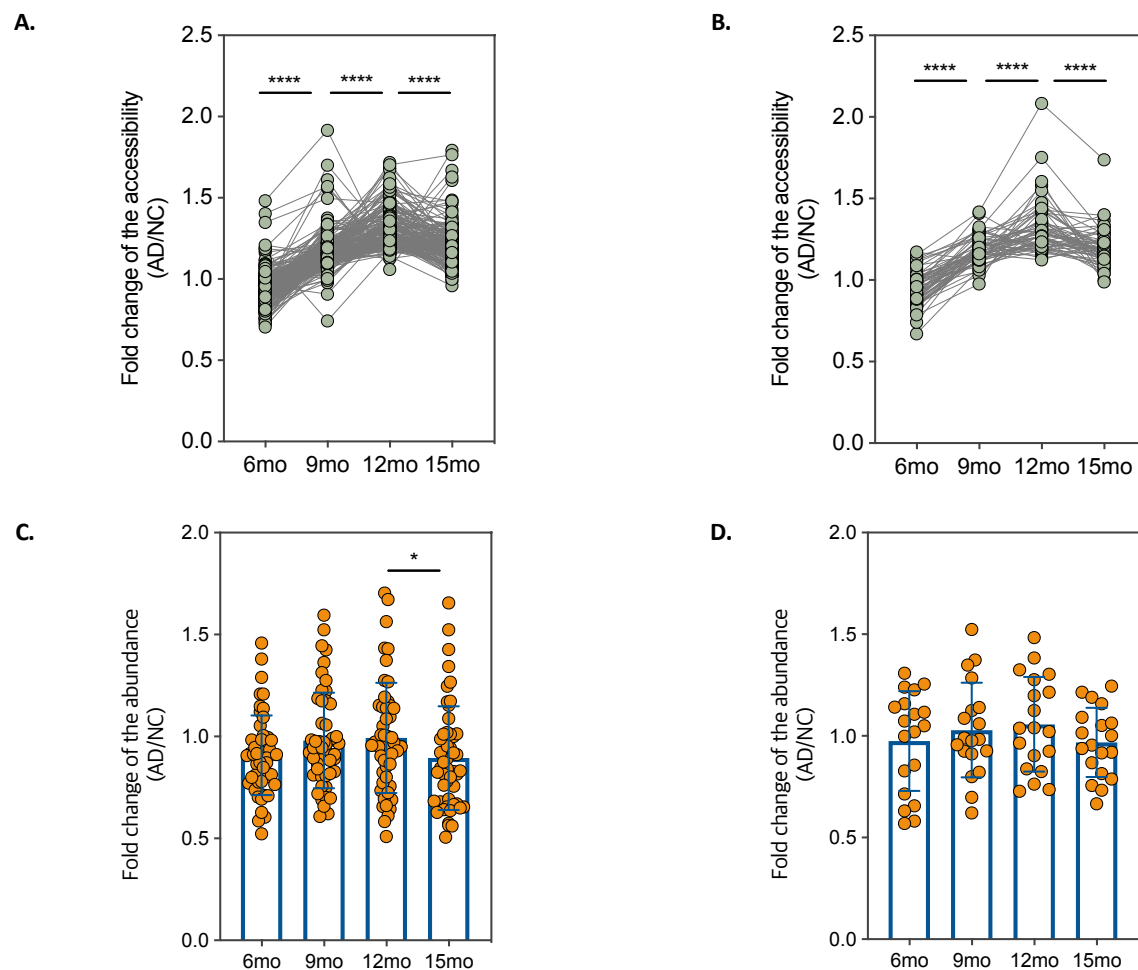
In the results of WGCNA analysis, two modules of kidney (M11 and M14), muscle (M2 and M5) and one module (M4) of spleen showed significant correlations with AD trait. Following that, the labeled peptides mapped to proteins in those modules were clustered by K-means clustering. For muscle, only 32 labeled peptides that mapped to 17 proteins were included in module 5 (M5), 7 peptides showed alterations in the fold-change of accessibility. GO enrichment analysis was not conducted with proteins of M5 due to the small number of peptides to be analyzed. Source data are provided as a Source Data file.



Supplementary Figure 16 Ontology network of brain constructed by structurally changing proteins, and representative terms. Ontology networks were constructed using the proteins that harbored changed peptides in accessibility (cluster 1 of K-means clustering). Each node indicates the individual terms, and the node size represents the significance. All terms with the *P*-value less than 0.5 were enriched. The color reflects the membership of the clusters. The lower table presents the details of the representative nodes for each cluster.



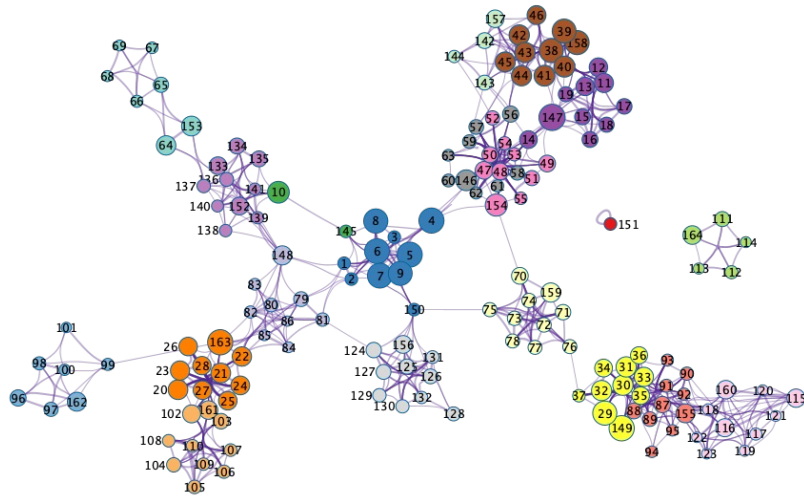
Supplementary Figure 17 Altered abundance of proteins. Heatmaps were plotted with the fold-change of the abundance, which is the value of protein abundance in AD divided by that in NC to correct for an age effect; node 107 (A), node 96 (B), and node 108 (C).



Supplementary Figure 18 Structural changes that precede expression changes in spleen.

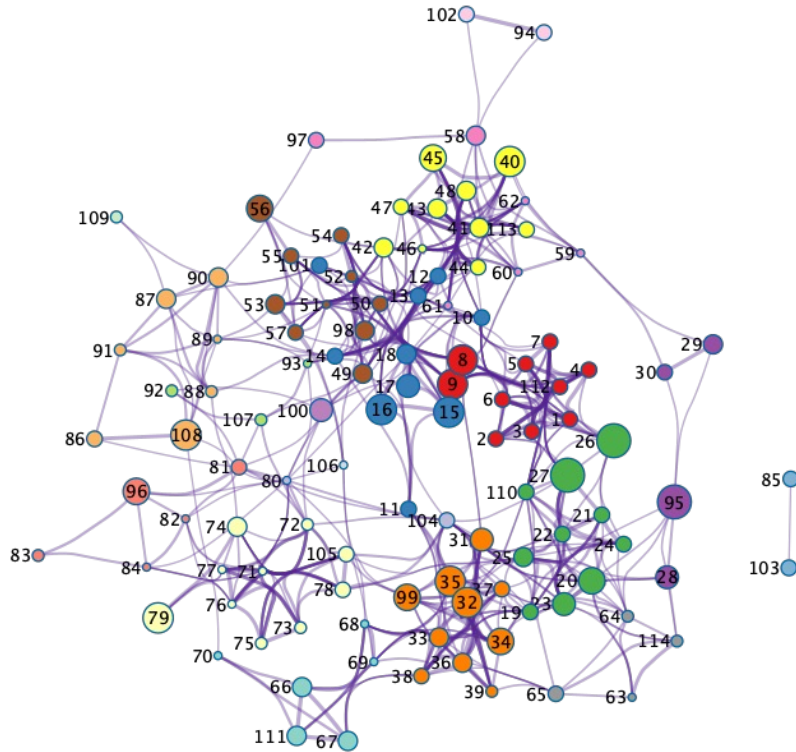
Fold changes of the accessibility (A, B) and fold change of the protein abundance (C, D) for neutrophil degranulation (A, C) and carbon metabolism (B, D). Source data are provided as a Source Data file. * $p < 0.05$, **** $p < 0.0001$

A.



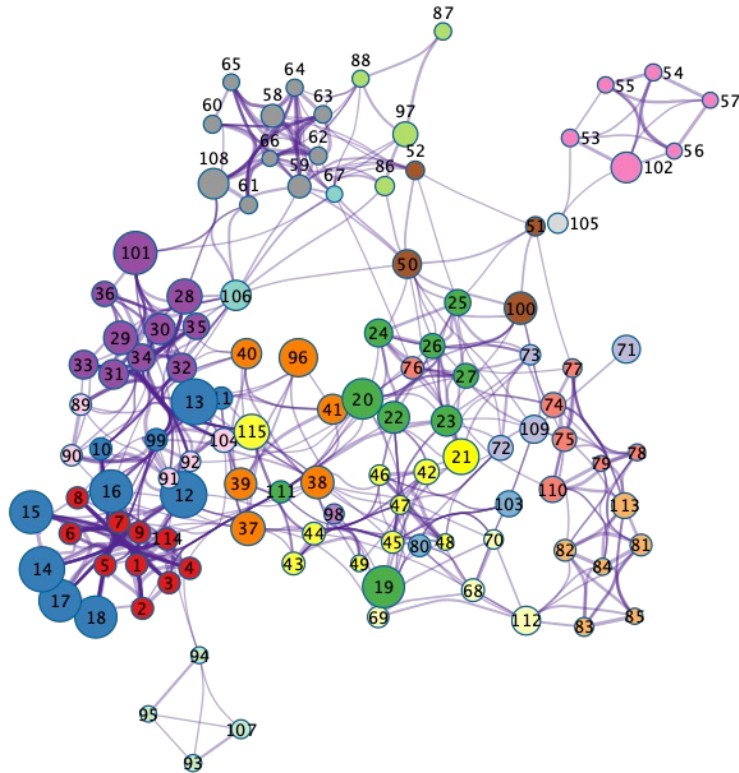
Node Number	Ontology ID	Ontology Name	Category	Number measured	P-value
151	R-MMU-6798695	Neutrophil degranulation	Reactome Gene Sets	52	1.69E+24
150	R-MMU-8953854	Metabolism of RNA	Reactome Gene Sets	45	2.79E+16
145	R-MMU-1280218	Adaptive Immune System	Reactome Gene Sets	44	9.50E+13
147	mmu01200	Carbon metabolism - Mus musculus (house mouse)	KEGG Pathway	19	4.11E+12
163	GO:0006457	protein folding	GO Biological Processes	21	9.63E+11
149	R-MMU-109582	Hemostasis	Reactome Gene Sets	35	8.76E+11
158	GO:0009117	nucleotide metabolic process	GO Biological Processes	34	1.73E+11
154	GO:0006520	amino acid metabolic process	GO Biological Processes	23	7.93E+09
146	WP662	Amino acid metabolism	WikiPathways	14	1.02E+09
153	R-MMU-194315	Signaling by Rho GTPases	Reactome Gene Sets	32	2.10E+08
159	GO:0006518	peptide metabolic process	GO Biological Processes	31	8.61E+07
148	R-MMU-3371497	HSP90 chaperone cycle for steroid hormone receptors (SHR) in the presence of ligand	Reactome Gene Sets	10	7.60E+07
155	GO:0007229	integrin-mediated signaling pathway	GO Biological Processes	12	5.78E+07
162	GO:0048524	positive regulation of viral process	GO Biological Processes	11	5.72E+07
164	GO:0010035	response to inorganic substance	GO Biological Processes	29	3.62E+07
161	GO:1903829	positive regulation of protein localization	GO Biological Processes	29	3.62E+07
160	GO:2000147	positive regulation of cell motility	GO Biological Processes	32	2.79E+07
156	WP310	mRNA processing	WikiPathways	26	1.05E+07
152	R-MMU-437239	Recycling pathway of L1	Reactome Gene Sets	8	9.26E+06
157	GO:0009112	nucleobase metabolic process	GO Biological Processes	8	7.31E+06

B.



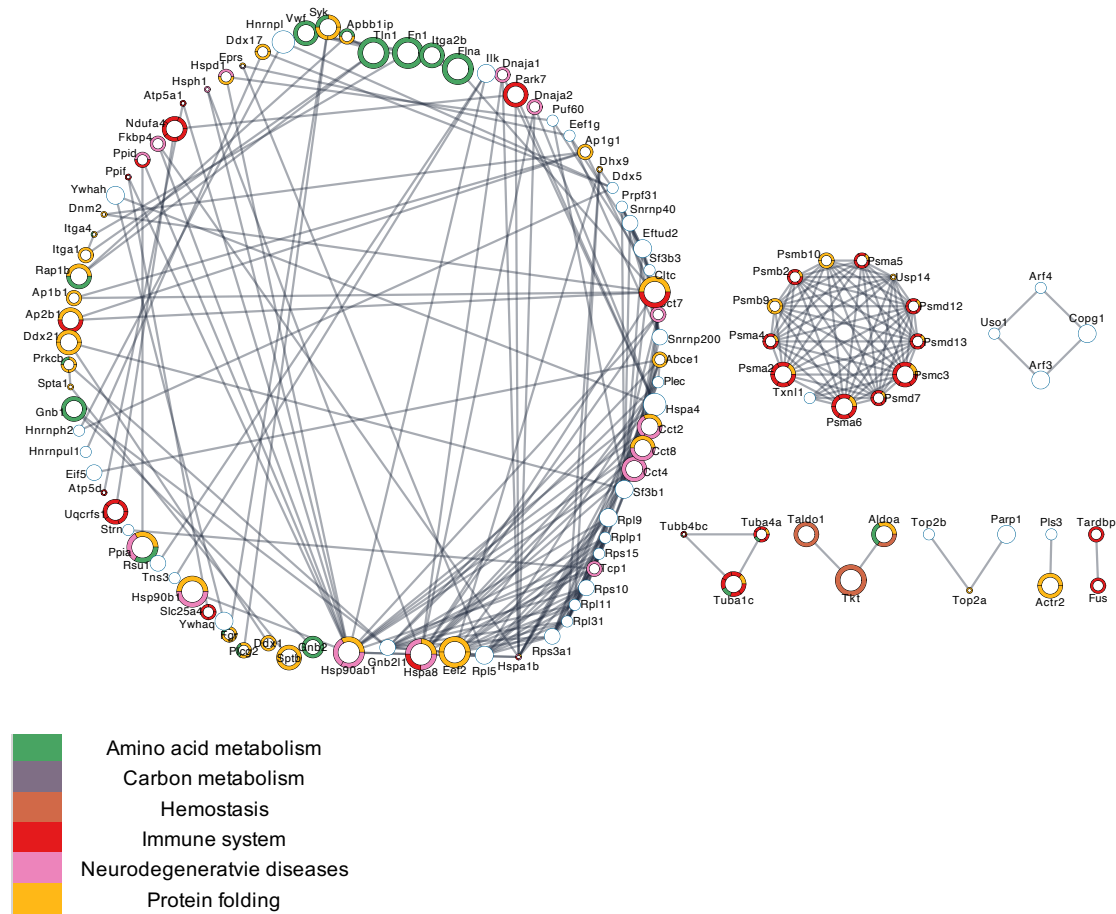
	Node Number	Ontology ID	Ontology Name	Category	Number measured	P-value
	112	GO:0006163	purine nucleotide metabolic process	GO Biological Processes	27	1.33E-21
	101	R-MMU-556833	Metabolism of lipids	Reactome Gene Sets	25	3.83E-16
	110	GO:0006091	generation of precursor metabolites and energy	GO Biological Processes	20	2.03E-15
	95	WP662	Amino acid metabolism	WikiPathways	10	7.81E-11
	99	mmu00010	Glycolysis / Gluconeogenesis - Mus musculus (house mouse)	KEGG Pathway	8	2.18E-09
	113	GO:0044282	small molecule catabolic process	GO Biological Processes	13	1.73E-08
	98	WP1269	Fatty acid beta-oxidation	WikiPathways	6	2.13E-08
	97	mmu00650	Butanoate metabolism - Mus musculus (house mouse)	KEGG Pathway	5	2.63E-07
	114	GO:0072350	tricarboxylic acid metabolic process	GO Biological Processes	4	9.25E-07
	111	GO:0046496	nicotinamide nucleotide metabolic process	GO Biological Processes	6	1.78E-06
	105	MMU-536251	Signaling by Retinoic Acid	Reactome Gene Sets	5	2.60E-06
	104	mmu00620	Pyruvate metabolism - Mus musculus (house mouse)	KEGG Pathway	5	3.30E-06
	96	R-MMU-211859	Biological oxidations	Reactome Gene Sets	8	1.08E-05
	103	MMU-679869	Neutrophil degranulation	Reactome Gene Sets	12	1.86E-05
	108	GO:0006066	alcohol metabolic process	GO Biological Processes	9	2.71E-05
	107	mmu00380	Tryptophan metabolism - Mus musculus (house mouse)	KEGG Pathway	4	1.58E-04
	102	R-MMU-196849	Metabolism of water-soluble vitamins and cofactors	Reactome Gene Sets	5	2.60E-04
	106	MMU-897922	Triglyceride metabolism	Reactome Gene Sets	3	2.60E-04
	100	R-MMU-71291	Metabolism of amino acids and derivatives	Reactome Gene Sets	7	3.39E-04
	109	GO:0042180	cellular ketone metabolic process	GO Biological Processes	4	1.08E-03

C.

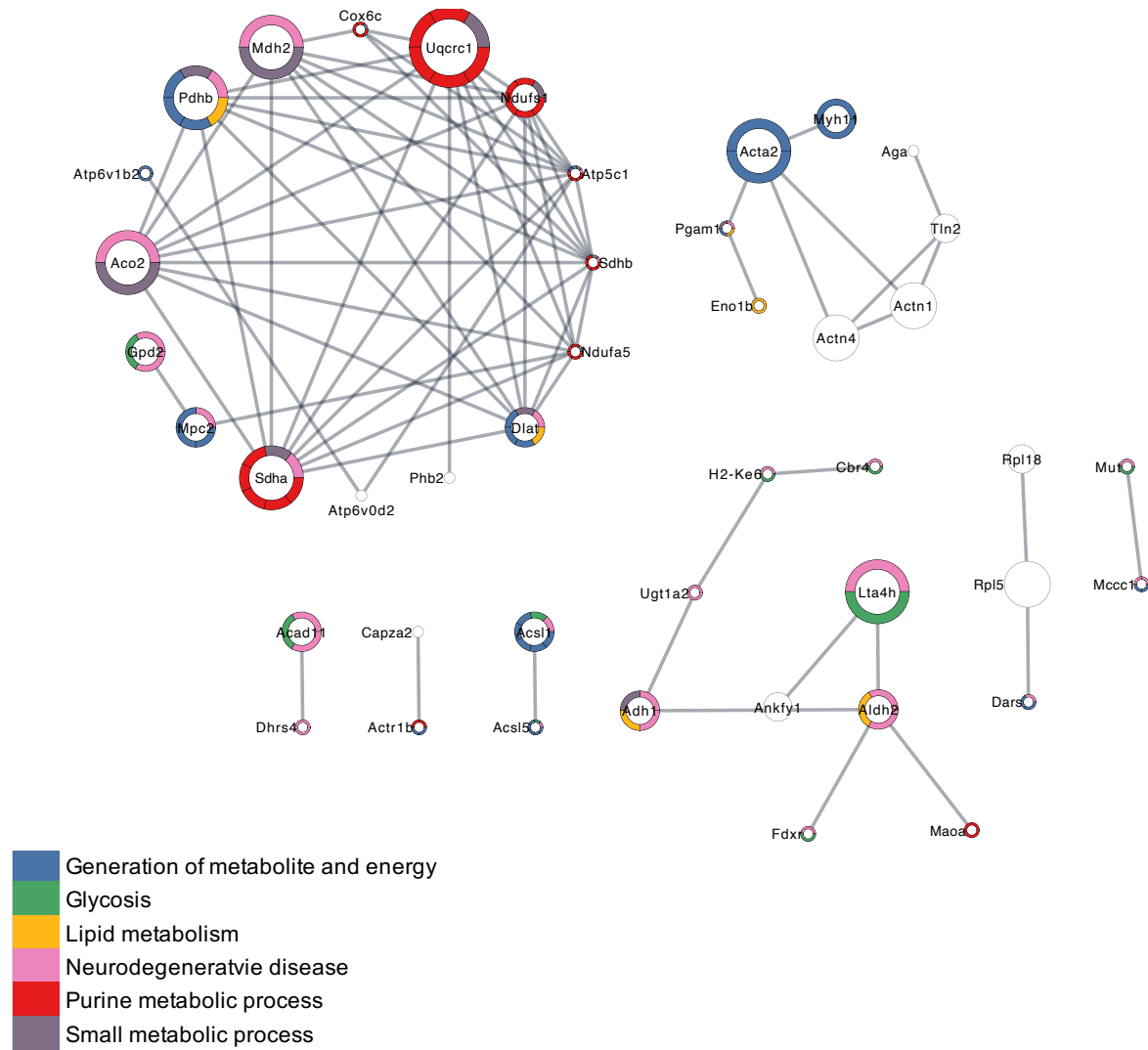


Node Number	Ontology ID	Ontology Name	Category	Number measured	P-value
114	GO:0072521	purine-containing compound metabolic process	GO Biological Processes	23	1.69E-17
99	mmu01200	Carbon metabolism - Mus musculus (house mouse)	KEGG Pathway	13	1.19E-14
111	GO:0032787	monocarboxylic acid metabolic process	GO Biological Processes	18	7.12E-11
101	mmu00010	Glycolysis / Gluconeogenesis - Mus musculus (house mouse)	KEGG Pathway	8	7.87E-10
96	WP662	Amino acid metabolism	WikiPathways	8	1.44E-08
115	GO:0044283	small molecule biosynthetic process	GO Biological Processes	13	8.78E-08
100	WP1269	Fatty acid beta-oxidation	WikiPathways	5	4.68E-07
102	R-MMU-2132295	MHC class II antigen presentation	Reactome Gene Sets	7	1.30E-06
108	R-MMU-5362517	Signaling by Retinoic Acid	Reactome Gene Sets	5	1.39E-06
106	mmu00620	Pyruvate metabolism - Mus musculus (house mouse)	KEGG Pathway	5	1.76E-06
112	GO:0006730	one-carbon metabolic process	GO Biological Processes	4	4.19E-06
109	mmu00280	ine, leucine and isoleucine degradation - Mus musculus (house mou	KEGG Pathway	5	6.47E-06
110	GO:0015908	fatty acid transport	GO Biological Processes	5	1.79E-05
103	R-MMU-71291	Metabolism of amino acids and derivatives	Reactome Gene Sets	8	1.99E-05
113	GO:0015849	organic acid transport	GO Biological Processes	8	2.50E-05
97	R-MMU-211859	Biological oxidations	Reactome Gene Sets	7	4.04E-05
104	GO:0006734	NADH metabolic process	GO Biological Processes	3	6.15E-05
105	R-MMU-6798695	Neutrophil degranulation	Reactome Gene Sets	9	6.82E-04
98	mmu01240	Biosynthesis of cofactors - Mus musculus (house mouse)	KEGG Pathway	5	6.93E-04
107	R-MMU-9013405	RHOD GTPase cycle	Reactome Gene Sets	3	1.41E-03

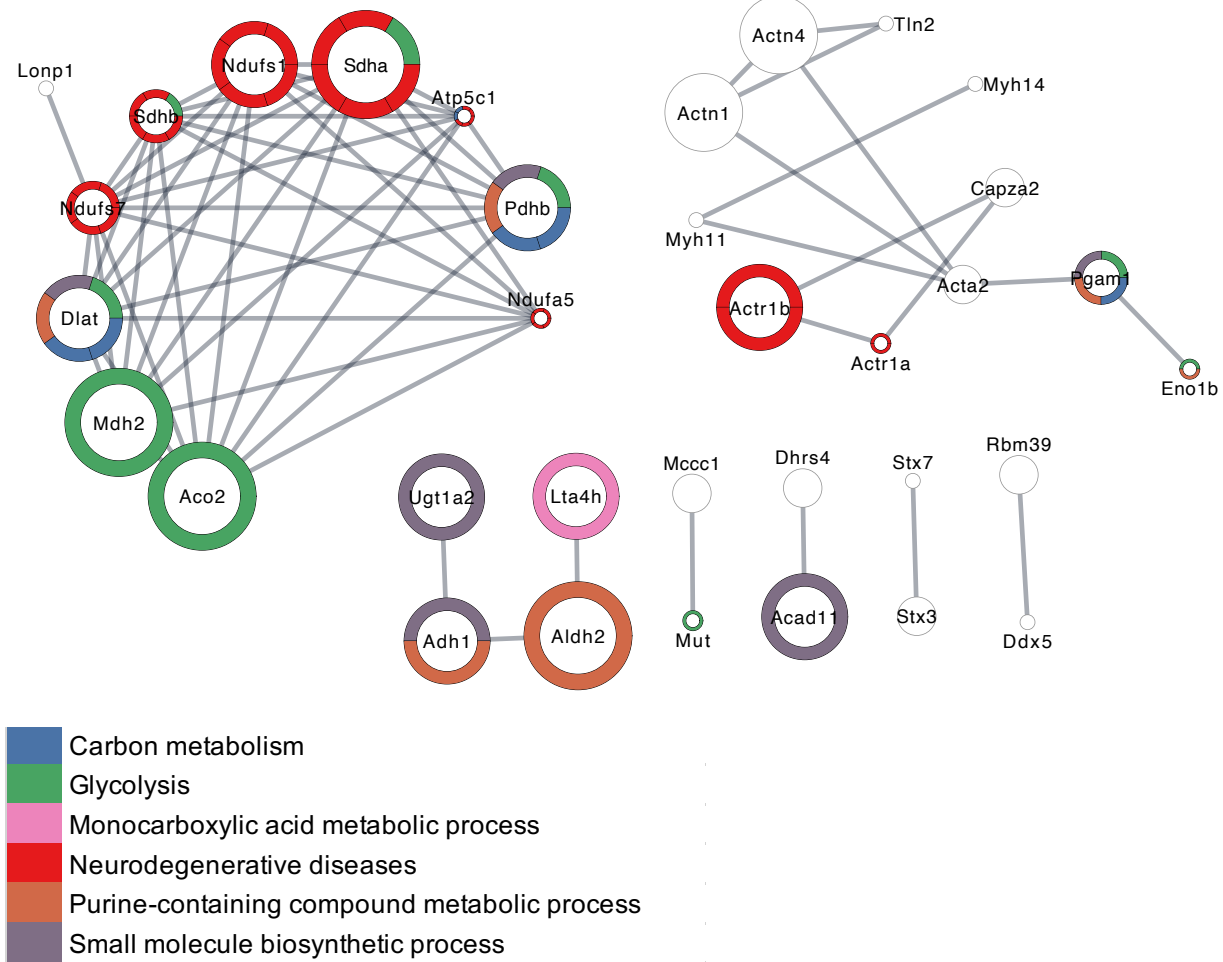
A.



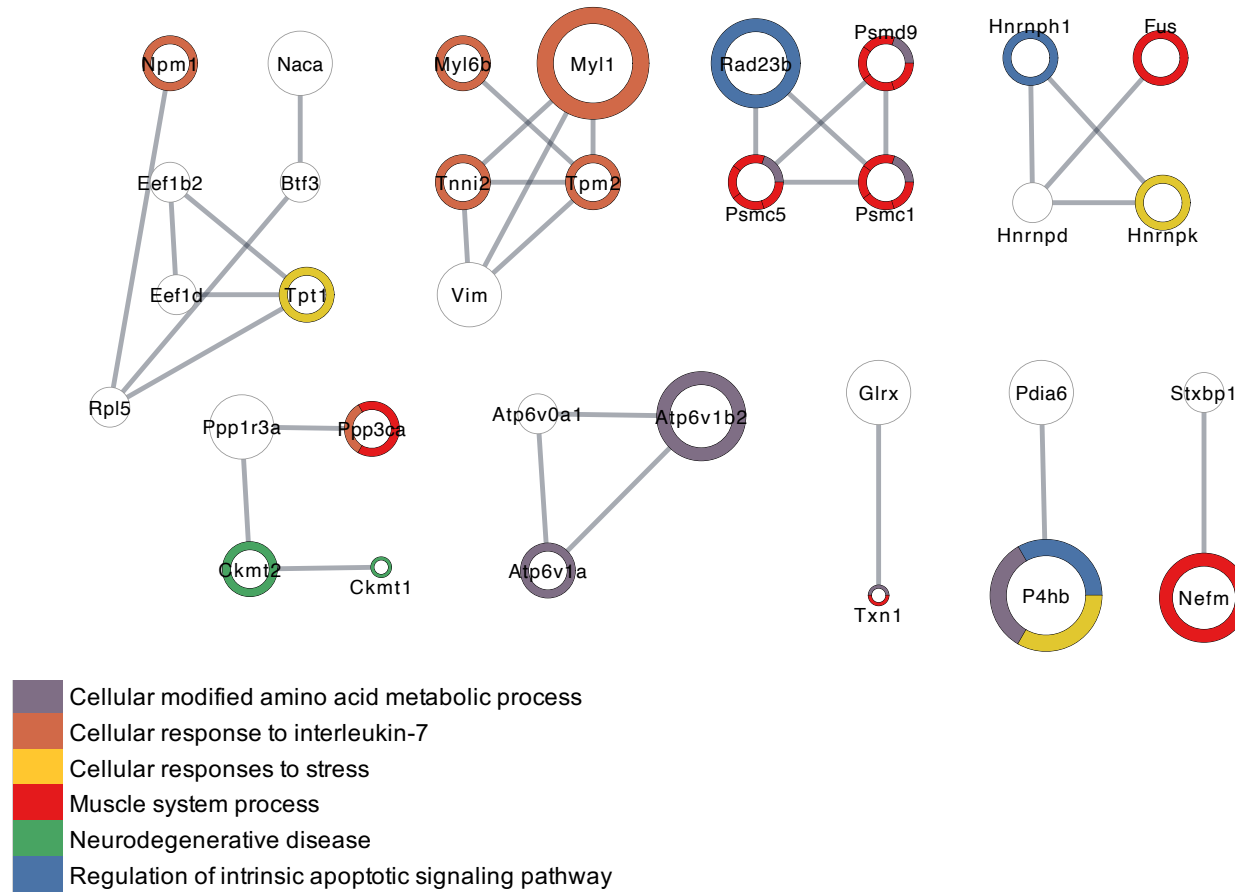
B.



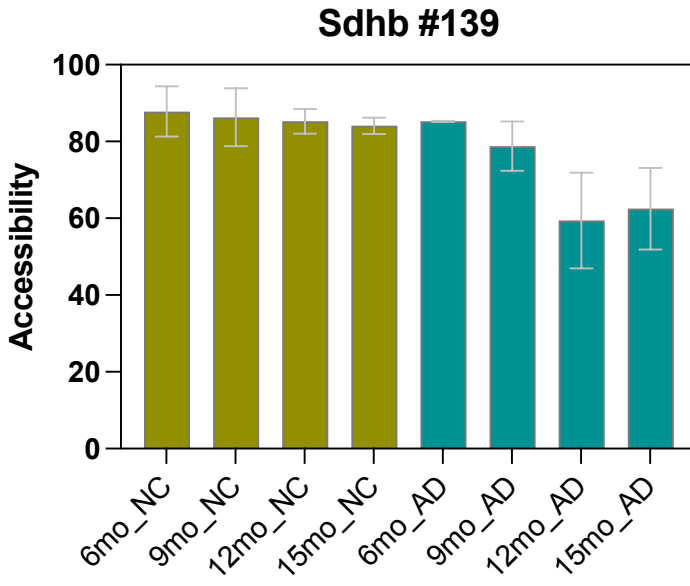
C.



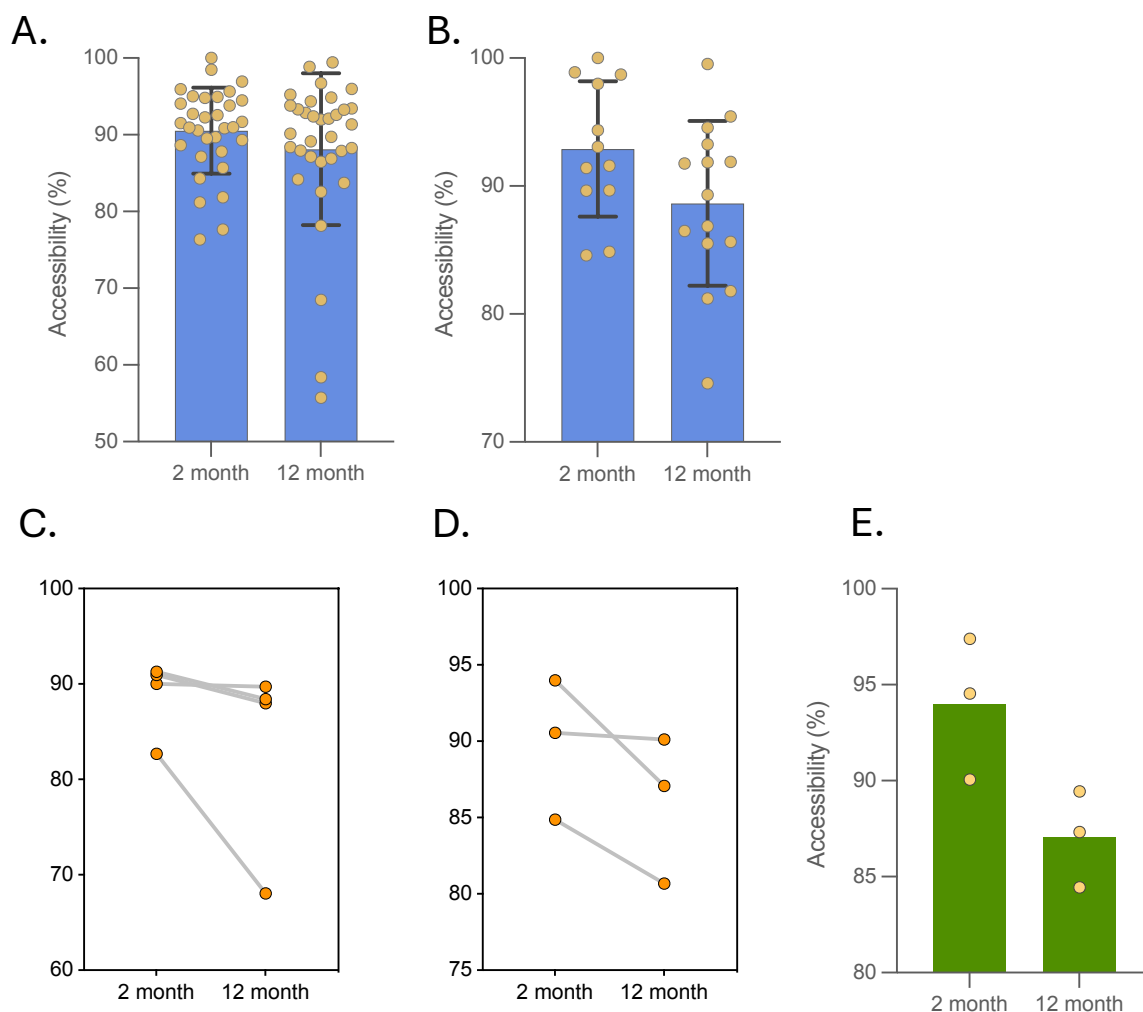
D.



Supplementary Figure 20 Physical interactions of proteins and their associated functions for spleen (A), M11 of kidney (B), M13 of kidney (C), and muscle (D). The ring color of the node indicates the terms that the protein is associated with. The size of node represents the number of significantly changed lysine sites. Source data are provided as a Source Data file.



Supplementary Figure 21 Distribution of the accessibility of lysine #139 of mitochondrial succinate dehydrogenase B A pattern of change in accessibility of lysine residue at position 139 showed a similar pattern to previous findings by Bamberger et. al³. Lysine residue at position 139 exhibited a significant decrease in the extent of its exposure as AD progression (Kruskal-Wallis, P-value = 0.0125), while the same residue did not show an alteration in its exposure during normal aging. Source data are provided as a Source Data file.



Supplementary Figure 22. Validation with 5XFAD model The accessibilities of 34 labeled peptides from 8 proteins enriched in carbon metabolism (A), and 15 labeled peptides from 9 proteins enriched in metal ion homeostasis (B) showed differences between 2- and 12-month-old mice. Four labeled peptides of Mag (C) and 3 labeled peptides of Map1a (D) showed a difference pattern in the accessibility between 2- and 12-month old mice. Each dot represents the averaged accessibility of three biological replicates per peptide. The accessibilities for FSKNYQDY of Plp1 were distributed (E). Each data point represents an individual mouse. Source data are provided as a Source Data file.

Supplementary Table 1. Correlation of biological replicates per 4 age groups.

	Brain-NC	Brain-AD	Heart-NC	Heart-AD	Kidney-NC	Kidney-AD	Liver-NC	Liver-AD	Muscle-NC	Muscle-AD	Spleen-NC	Spleen-AD	Thymus-NC	Thymus-AD	Average d NC	Average d AD
6 month	0.747	0.913	0.483	0.598	0.700	0.678	0.430	0.471	0.824	0.876	0.703	0.715	0.601	0.655	0.641	0.701
9 month	0.812	0.754	0.688	0.674	0.598	0.467	0.495	0.625	0.807	0.819	0.723	0.770	0.545	0.512	0.667	0.660
12 month	0.908	0.700	0.345	0.350	0.775	0.572	0.677	0.684	0.826	0.664	0.731	0.685	0.554	0.352	0.688	0.572
15 month	0.900	0.761	0.657	0.641	0.654	0.656	0.478	0.554	0.808	0.790	0.745	0.748	0.497	0.499	0.677	0.664
Average	0.842	0.782	0.543	0.566	0.682	0.593	0.520	0.583	0.816	0.787	0.726	0.730	0.549	0.505	0.668	0.649

Supplementary Table 2. Variability of the fold-change in other tissue relative to that in brain.

Genename		Atp5a1	Dlat	Eno1	Etfa	Gatd3	Gpi1	Ldha	Nit2	Nsf	Pdhb
Peptide		DDLKQAVAY	CIIVEKQEDI AAF	TAKGLF	ILETQKQF	AGTAEAIKAL	IIASKTF	GIQKELQF	QESKTLSPG DSFSTF	AAKIAEESNF PF	AKVLEDNSV PQVKDIIF
NC-AD P-value	Brain	0.003	0.002	0.013	0.001	0.002	0.031	0.000	0.001	0.001	0.000
	Heart	0.673	0.822	0.436	0.864	0.626	0.664	0.590	0.170	0.044	0.001
	Kidney	0.000	0.572	0.348	0.373	0.867	0.135	0.761	0.477	0.596	0.945
	Liver	0.015	0.039	0.002	0.002	0.003	0.007	0.002	0.021	0.019	0.036
	Muscle	0.010	0.037	0.013	0.003	0.004	0.002	0.003	0.007	0.037	0.003
	Spleen	0.436	0.001	0.035	0.023	0.030	0.280	0.043	0.719	0.221	0.421
	Thymus	0.920	0.478	1.000	0.691	0.786	0.021	0.555	0.044	0.298	0.389
Fold-change of the accessibility (6mo)	Brain	0.931	1.156	0.566	0.766	0.808	0.763	0.790	1.042	0.833	0.690
	Heart									1.146	1.340
	Kidney	0.705	0.833	1.254	0.757	0.787	1.148	0.975	0.854	0.779	0.818
	Liver	0.947									
	Muscle	0.897	0.910	0.855	0.802	0.942	0.895	0.967	0.899	0.719	0.748
	Spleen		1.691	0.744	0.986	1.114		0.851			
	Thymus						0.887		0.859		
Fold-change of the accessibility (9mo)	Brain	0.966	0.981	0.781	0.692	0.708	1.227	0.894	0.973	0.911	1.024
	Heart									1.058	2.008
	Kidney	1.040	1.063	0.966	0.748	0.802	0.666	0.872	1.091	1.021	0.583
	Liver	1.180									
	Muscle	0.748	0.905	0.857	0.986	0.941	1.033	1.026	0.974	0.585	0.843
	Spleen		0.847	1.300	0.948	1.186		0.995			
	Thymus						1.407		0.846		
Fold-change of the accessibility	Brain	0.918	0.938	0.477	0.810	0.655	0.811	0.693	1.012	0.751	0.866

(12mo)	Heart									0.942	0.731
	Kidney	0.974	1.131	0.586	0.669	0.676	0.820	0.634	0.936	1.093	0.884
	Liver	0.706									
	Muscle	1.130	1.049	1.425	1.235	1.280	1.010	1.214	1.177	1.130	1.116
	Spleen		1.033	1.264	1.221	1.243		1.097			
	Thymus						0.741		0.979		
Fold-change of the accessibility (15mo)	Brain	0.805	0.914	0.807	0.745	0.579	0.849	0.648	1.052	0.715	0.597
	Heart									1.050	0.958
	Kidney	0.850	0.978	0.671	0.704	0.747	0.859	0.678	0.821	0.726	0.929
	Liver	0.397									
	Muscle	0.960	0.936	1.156	1.114	1.015	1.088	1.120	1.146	1.283	1.226
	Spleen		3.091	1.167	0.992	1.304		1.224			
	Thymus						0.519		1.162		

Supplementary Table 3. List of the enriched terms in the ontology network for brain dataset.

Node label	Canonical Name	Category	Description	Hits	LogP*
1	GO:0015980	GO Biological Processes	energy derivation by oxidation of organic compounds	Gnas, Mdh1, Ogdh, Ppp1cb, Slc1a3, Sod2, Sdha, Ndufa8, Epm2aip1, Etfa, Ugp2	-6.58
2	GO:0045333	GO Biological Processes	cellular respiration	Mdh1, Ogdh, Slc1a3, Sod2, Sdha, Ndufa8, Etfa	-4.02
3	GO:0022904	GO Biological Processes	respiratory electron transport chain	Slc1a3, Sod2, Sdha, Ndufa8, Etfa	-3.69
4	GO:0022900	GO Biological Processes	electron transport chain	Slc1a3, Sod2, Sdha, Ndufa8, Etfa	-3.46
5	GO:0043648	GO Biological Processes	dicarboxylic acid metabolic process	Adss, Me1, Mdh1, Ogdh, Nit2, Sdha, Aldh1l1	-6.23
6	GO:0055086	GO Biological Processes	nucleobase-containing small molecule metabolic process	Adss, Ak4, Mdh1, Ogdh, Pgc1, Taldo1, Pycr1, Cmpk1, Sdha, Dmac2l, Ndufa8, Aldh6a1, Aldh1l1, Ugp2	-5.43
7	WP434	WikiPathways	TCA cycle	Mdh1, Ogdh, Pdk2, Sdha	-4.50
8	R-MMU-1428517	Reactome Gene Sets	The citric acid (TCA) cycle and respiratory electron transport	Me1, Ogdh, Pdk2, Sdha, Dmac2l, Ndufa8, Etfa	-4.25
9	GO:0009117	GO Biological Processes	nucleotide metabolic process	Adss, Ak4, Mdh1, Ogdh, Pgc1, Taldo1, Cmpk1, Sdha, Dmac2l, Ndufa8, Aldh1l1	-3.90
10	GO:0006753	GO Biological Processes	nucleoside phosphate metabolic process	Adss, Ak4, Mdh1, Ogdh, Pgc1, Taldo1, Cmpk1, Sdha, Dmac2l, Ndufa8, Aldh1l1	-3.84
11	R-MMU-71406	Reactome Gene Sets	Pyruvate metabolism and Citric Acid (TCA) cycle	Me1, Ogdh, Pdk2, Sdha	-3.77
12	WP662	WikiPathways	Amino acid metabolism	Bcat1, Hadh, Mdh1, Ogdh, Sdha	-3.58
13	GO:0009141	GO Biological Processes	nucleoside triphosphate metabolic process	Ak4, Ogdh, Pgc1, Cmpk1, Sdha, Dmac2l, Ndufa8	-3.58
14	mmu01230	KEGG Pathway	Biosynthesis of amino acids - Mus musculus (house mouse)	Bcat1, Pgc1, Taldo1, Pycr1, Psat1, Phgdh	-5.14
15	GO:1901605	GO Biological Processes	alpha-amino acid metabolic process	Adss, Bcat1, Tst, Nit2, Pycr1, Aldh6a1, Psat1, Phgdh	-5.03
16	mmu00270	KEGG Pathway	Cysteine and methionine metabolism - Mus musculus (house mouse)	Bcat1, Mdh1, Tst, Psat1, Phgdh	-4.78
17	R-MMU-71291	Reactome Gene Sets	Metabolism of amino acids and derivatives	Bcat1, Ogdh, Psma2, Tst, Psma6, Pycr1, Aldh6a1, Psat1, Phgdh	-4.78
18	GO:0008652	GO Biological Processes	cellular amino acid biosynthetic process	Bcat1, Slc1a3, Pycr1, Psat1, Phgdh	-4.52
19	GO:0044283	GO Biological Processes	small molecule biosynthetic process	Bcat1, Ephx1, Mif, Mdh1, Pgc1, Plp1, Slc1a3, Pycr1, Psat1, Phgdh	-3.72
20	GO:1901607	GO Biological Processes	alpha-amino acid biosynthetic process	Bcat1, Pycr1, Psat1, Phgdh	-3.54
21	GO:0046394	GO Biological Processes	carboxylic acid biosynthetic process	Bcat1, Mif, Plp1, Slc1a3, Pycr1, Psat1, Phgdh	-3.26
22	GO:0016053	GO Biological Processes	organic acid biosynthetic process	Bcat1, Mif, Plp1, Slc1a3, Pycr1, Psat1, Phgdh	-3.25
23	GO:0055080	GO Biological Processes	cation homeostasis	Ank1, Calb1, Calb2, Gnas, Itpr1, Pdk2, Prkcb, Slc12a4, Slc1a3, Sod2, Vapb, Fis1, Immt	-5.03
24	GO:0098771	GO Biological Processes	inorganic ion homeostasis	Ank1, Calb1, Calb2, Gnas, Itpr1, Pdk2, Prkcb, Slc12a4, Slc1a3, Sod2, Vapb, Fis1, Immt	-4.91
25	GO:0050801	GO Biological Processes	ion homeostasis	Ank1, Calb1, Calb2, Gnas, Itpr1, Pdk2, Prkcb, Slc12a4, Slc1a3, Sod2, Vapb, Fis1, Immt	-4.80
26	GO:0055074	GO Biological Processes	calcium ion homeostasis	Calb1, Calb2, Gnas, Itpr1, Prkcb, Vapb, Fis1, Immt	-4.10

27	GO:0070050	GO Biological Processes	neuron cellular homeostasis	Calb1, Calb2, Map1a, Immt	-3.93
28	GO:0006874	GO Biological Processes	cellular calcium ion homeostasis	Calb1, Calb2, Itpr1, Prkcb, Vapb, Fis1, Immt	-3.72
29	GO:0072507	GO Biological Processes	divalent inorganic cation homeostasis	Calb1, Calb2, Gnas, Itpr1, Prkcb, Vapb, Fis1, Immt	-3.71
30	GO:0072503	GO Biological Processes	cellular divalent inorganic cation homeostasis	Calb1, Calb2, Itpr1, Prkcb, Vapb, Fis1, Immt	-3.41
31	GO:0006875	GO Biological Processes	cellular metal ion homeostasis	Calb1, Calb2, Itpr1, Prkcb, Slc1a3, Vapb, Fis1, Immt	-3.11
32	GO:0044282	GO Biological Processes	small molecule catabolic process	Bcat1, Hadh, Pgk1, Bpnt1, Pycrl, Oxct1, Aldh6a1, Aldh1l1, Etfa, Inpp5a	-4.60
33	GO:0046395	GO Biological Processes	carboxylic acid catabolic process	Bcat1, Hadh, Aldh6a1, Aldh1l1, Etfa	-2.13
34	GO:0016054	GO Biological Processes	organic acid catabolic process	Bcat1, Hadh, Aldh6a1, Aldh1l1, Etfa	-2.11
35	GO:0000377	GO Biological Processes	RNA splicing, via transesterification reactions with bulged adenosine as nucleophile	Srsf3, Strap, Prpf19, Hnrnpa2b1, Psip1, Srsf7, Hnrnpa3, Nova1	-4.37
36	GO:0000398	GO Biological Processes	mRNA splicing, via spliceosome	Srsf3, Strap, Prpf19, Hnrnpa2b1, Psip1, Srsf7, Hnrnpa3, Nova1	-4.37
37	mmu05014	KEGG Pathway	Amyotrophic lateral sclerosis - Mus musculus (house mouse)	Psma2, Srsf3, Map2k6, Psma6, Hnrnpa2b1, Vapb, Sdha, Ndufa8, Srsf7, Hnrnpa3	-4.17
38	GO:0050684	GO Biological Processes	regulation of mRNA processing	Srsf3, Prpf19, Hnrnpa2b1, Sltm, Srsf7, Nova1	-3.52
39	GO:0048024	GO Biological Processes	regulation of mRNA splicing, via spliceosome	Srsf3, Prpf19, Hnrnpa2b1, Srsf7, Nova1	-3.21
40	GO:0008380	GO Biological Processes	RNA splicing	Srsf3, Strap, Prpf19, Hnrnpa2b1, Psip1, Srsf7, Hnrnpa3, Nova1	-3.03
41	GO:0050657	GO Biological Processes	nucleic acid transport	Srsf3, Tst, Hnrnpa2b1, Srsf7, Hnrnpa3	-2.76
42	GO:0050658	GO Biological Processes	RNA transport	Srsf3, Tst, Hnrnpa2b1, Srsf7, Hnrnpa3	-2.76
43	GO:0051236	GO Biological Processes	establishment of RNA localization	Srsf3, Tst, Hnrnpa2b1, Srsf7, Hnrnpa3	-2.73
44	R-MMU-8953897	Reactome Gene Sets	Cellular responses to stimuli	Lmn1b1, Psma2, Sod2, Stip1, Map2k6, Psma6, Cul3, H1f4, Lamtor3, H1f1, Blvra	-4.22
45	mmu05020	KEGG Pathway	Prion disease - Mus musculus (house mouse)	Fyn, Itpr1, Psma2, Stip1, Psma6, Sdha, Ndufa8	-2.97
46	mmu05016	KEGG Pathway	Huntington disease - Mus musculus (house mouse)	Itpr1, Psma2, Slc1a3, Sod2, Psma6, Sdha, Ndufa8	-2.68
47	R-MMU-9711123	Reactome Gene Sets	Cellular response to chemical stress	Psma2, Sod2, Psma6, Cul3, Blvra	-2.63
48	R-MMU-983705	Reactome Gene Sets	Signaling by the B Cell Receptor (BCR)	Itpr1, Prkcb, Psma2, Psma6	-2.54
49	R-MMU-5673001	Reactome Gene Sets	RAF/MAP kinase cascade	Fyn, Ppp1cb, Psma2, Psma6, Cul3, Lamtor3	-2.34
50	R-MMU-4641258	Reactome Gene Sets	Degradation of DVL	Psma2, Psma6, Cul3	-2.33
51	R-MMU-1280218	Reactome Gene Sets	Adaptive Immune System	Ctsd, Fyn, Itpr1, Prkcb, Psma2, Arih2, Psma6, Cul3, Ubr4, Dnm3	-2.33
52	mmu05012	KEGG Pathway	Parkinson disease - Mus musculus (house mouse)	Gnas, Itpr1, Psma2, Psma6, Sdha, Ndufa8	-2.32
53	R-MMU-2559586	Reactome Gene Sets	DNA Damage/Telomere Stress Induced Senescence	Lmn1b1, H1f4, H1f1	-3.28
54	R-MMU-2559583	Reactome Gene Sets	Cellular Senescence	Lmn1b1, Map2k6, H1f4, H1f1	-2.68
55	GO:0045910	GO Biological Processes	negative regulation of DNA recombination	H1f4, Terf2ip, H1f1	-2.57
56	R-MMU-75153	Reactome Gene Sets	Apoptotic execution phase	Lmn1b1, H1f4, H1f1	-2.55
57	GO:0006338	GO Biological Processes	chromatin remodeling	Gnas, Lmn1b1, H1f4, H1f1, Actl6b, Dek	-2.02
58	mmu04730	KEGG Pathway	Long-term depression - Mus musculus (house mouse)	Gnas, Gnaz, Itpr1, Prkcb	-3.36

59	mmu04961	KEGG Pathway	Endocrine and other factor-regulated calcium reabsorption - Mus musculus (house mouse)	Calb1, Gnas, Prkcb, Dnm3	-3.34
60	mmu04935	KEGG Pathway	Growth hormone synthesis, secretion and action - Mus musculus (house mouse)	Crk, Gnas, Itpr1, Prkcb, Map2k6	-3.19
61	mmu04611	KEGG Pathway	Platelet activation - Mus musculus (house mouse)	Fyn, Gnas, Itpr1, Ppp1cb, Arhgef12	-3.06
62	mmu04750	KEGG Pathway	Inflammatory mediator regulation of TRP channels - Mus musculus (house mouse)	Gnas, Itpr1, Prkcb, Ppp1cb, Map2k6	-3.03
63	mmu04270	KEGG Pathway	Vascular smooth muscle contraction - Mus musculus (house mouse)	Gnas, Itpr1, Prkcb, Ppp1cb, Arhgef12	-2.79
64	WP232	WikiPathways	G protein signaling pathways	Gnas, Gnaz, Itpr1, Prkcb	-2.72
65	mmu04912	KEGG Pathway	GnRH signaling pathway - Mus musculus (house mouse)	Gnas, Itpr1, Prkcb, Map2k6	-2.70
66	mmu05163	KEGG Pathway	Human cytomegalovirus infection - Mus musculus (house mouse)	Crk, Gnas, Itpr1, Prkcb, Map2k6, Arhgef12	-2.38
67	GO:0006112	GO Biological Processes	energy reserve metabolic process	Gnas, Ppp1cb, Epm2aip1, Ugp2	-3.18
68	GO:0044262	GO Biological Processes	cellular carbohydrate metabolic process	Ppp1cb, Bpnt1, Epm2aip1, Inpp5a, Ugp2	-2.61
69	GO:0005977	GO Biological Processes	glycogen metabolic process	Ppp1cb, Epm2aip1, Ugp2	-2.36
70	GO:0006073	GO Biological Processes	cellular glucan metabolic process	Ppp1cb, Epm2aip1, Ugp2	-2.36
71	GO:0044042	GO Biological Processes	glucan metabolic process	Ppp1cb, Epm2aip1, Ugp2	-2.33
72	GO:0016051	GO Biological Processes	carbohydrate biosynthetic process	Mdh1, Pkg1, Epm2aip1, Ugp2	-2.28
73	GO:0060306	GO Biological Processes	regulation of membrane repolarization	Snta1, Wdr1, Flna	-2.98
74	GO:0030029	GO Biological Processes	actin filament-based process	Crk, Snta1, Sptb, Wdr1, Cul3, Arhgef7, Anln, Flna, Flnb	-2.07
75	mmu04510	KEGG Pathway	Focal adhesion - Mus musculus (house mouse)	Crk, Fyn, Prkcb, Ppp1cb, Flna, Flnb	-2.91
76	R-MMU-76002	Reactome Gene Sets	Platelet activation, signaling and aggregation	Crk, Fyn, Itpr1, Prkcb, Wdr1, Flna	-2.49
77	GO:0043123	GO Biological Processes	positive regulation of I-kappaB kinase/NF-kappaB signaling	Fyn, Prkcb, Terf2ip, Alpk1	-2.16
78	WP407	WikiPathways	Kit receptor signaling pathway	Crk, Fyn, Prkcb	-2.14
79	mmu04010	KEGG Pathway	MAPK signaling pathway - Mus musculus (house mouse)	Crk, Prkcb, Map2k6, Lamtor3, Flna, Flnb	-2.10
80	GO:1901699	GO Biological Processes	cellular response to nitrogen compound	Crk, Fyn, Gnas, Gnaz, Itpr1, Pdk2, Srsf3, Slc1a3, Lamtor3, Fis1, Flna	-2.75
81	GO:1903350	GO Biological Processes	response to dopamine	Gnas, Gnaz, Flna	-2.47
82	GO:1903351	GO Biological Processes	cellular response to dopamine	Gnas, Gnaz, Flna	-2.47
83	GO:0071868	GO Biological Processes	cellular response to monoamine stimulus	Gnas, Gnaz, Flna	-2.19
84	GO:0071870	GO Biological Processes	cellular response to catecholamine stimulus	Gnas, Gnaz, Flna	-2.19
85	GO:0071867	GO Biological Processes	response to monoamine	Gnas, Gnaz, Flna	-2.14
86	GO:0071869	GO Biological Processes	response to catecholamine	Gnas, Gnaz, Flna	-2.14
87	GO:0051259	GO Biological Processes	protein complex oligomerization	Ehd1, Mif, Me1, Sod2, Acot13, Ehd4	-2.45
88	GO:0051289	GO Biological Processes	protein homotetramerization	Me1, Sod2, Acot13	-2.42
89	GO:0072659	GO Biological Processes	protein localization to plasma membrane	Ank1, Ehd1, Ehd4, Flna, Prepl, Fcho2	-2.74
90	GO:0051668	GO Biological Processes	localization within membrane	Ank1, Crk, Ehd1, Lmnb1, Clip1, Ehd4, Flna, Prepl, Fcho2	-2.30

91	GO:0072657	GO Biological Processes	protein localization to membrane	Ank1, Crk, Ehd1, Clip1, Ehd4, Flna, Prepl, Fcho2	-2.15
92	GO:0120161	GO Biological Processes	regulation of cold-induced thermogenesis	Gnas, Hadh, Map2k6, Acot13, Nova1	-2.75
93	GO:0120163	GO Biological Processes	negative regulation of cold-induced thermogenesis	Map2k6, Acot13, Nova1	-2.57
94	mmu01240	KEGG Pathway	Biosynthesis of cofactors - Mus musculus (house mouse)	Adss, Ak4, Bcat1, Cmpk1, Psat1, Ugp2	-3.55
95	mmu00650	KEGG Pathway	Butanoate metabolism - Mus musculus (house mouse)	Hadh, Oxct1, Bdh1	-3.28
96	mmu01200	KEGG Pathway	Carbon metabolism - Mus musculus (house mouse)	Me1, Mdh1, Ogdh, Pkg1, Taldo1, Sdha, Aldh6a1, Psat1, Pcca, Phgdh	-8.60
97	R-MMU-2262752	Reactome Gene Sets	Cellular responses to stress	Lmn1b, Psma2, Sod2, Stip1, Map2k6, Psma6, Cul3, H1f4, Lamtor3, H1f1, Blvra	-4.24
98	R-MMU-2559584	Reactome Gene Sets	Formation of Senescence-Associated Heterochromatin Foci (SAHF)	Lmn1b, H1f4, H1f1	-3.98
99	R-MMU-109582	Reactome Gene Sets	Hemostasis	Crk, Ehd1, Fyn, Gnas, Itpr1, Mif, Prkcb, Serpinb6a, Wdr1, Flna	-3.19
100	R-MMU-77289	Reactome Gene Sets	Mitochondrial Fatty Acid Beta-Oxidation	Hadh, Acot13, Pcca	-2.91
101	mmu05205	KEGG Pathway	Proteoglycans in cancer - Mus musculus (house mouse)	Ank1, Itpr1, Prkcb, Ppp1cb, Arhgef12, Flna, Flnb	-3.67
102	GO:0000375	GO Biological Processes	RNA splicing, via transesterification reactions	Srsf3, Strap, Prpf19, Hnrnpa2b1, Psp1, Srsf7, Hnrnpa3, Nova1	-4.37
103	mmu00280	KEGG Pathway	Valine, leucine and isoleucine degradation - Mus musculus (house mouse)	Bcat1, Hadh, Oxct1, Aldh6a1, Pcca	-4.67
104	GO:0005975	GO Biological Processes	carbohydrate metabolic process	Mdh1, Ogdh, Pdk2, Pkg1, Ppp1cb, Taldo1, Bpnt1, Epm2aip1, Inpp5a, Ugp2	-3.49
105	GO:0006520	GO Biological Processes	cellular amino acid metabolic process	Adss, Bcat1, Hars, Slc1a3, Tst, Nit2, Pycrl, Aldh6a1, Psat1, Etfa, Phgdh, lars2	-7.53
106	GO:0071417	GO Biological Processes	cellular response to organonitrogen compound	Crk, Fyn, Gnas, Gnaz, Itpr1, Pdk2, Srsf3, Slc1a3, Lamtor3, Fis1, Flna	-3.19
107	GO:0006091	GO Biological Processes	generation of precursor metabolites and energy	Gnas, Mdh1, Ogdh, Pkg1, Ppp1cb, Slc1a3, Sod2, Taldo1, Sdha, Oxct1, Ndufa8, Epm2aip1, Aldh1l1, Etfa, Ugp2	-8.75
108	GO:0055065	GO Biological Processes	metal ion homeostasis	Ank1, Calb1, Calb2, Gnas, Itpr1, Prkcb, Slc12a4, Slc1a3, Sod2, Vapb, Fis1, Immt	-5.12
109	GO:0032787	GO Biological Processes	monocarboxylic acid metabolic process	Ephx1, Hadh, Mif, Me1, Ogdh, Pkg1, Plp1, Slc1a3, Etfa, Phgdh	-2.84
110	GO:0051260	GO Biological Processes	protein homooligomerization	Ehd1, Mif, Me1, Sod2, Acot13, Ehd4	-3.11
111	GO:1990778	GO Biological Processes	protein localization to cell periphery	Ank1, Ehd1, Clip1, Ehd4, Flna, Prepl, Fcho2	-2.98
112	GO:0099623	GO Biological Processes	regulation of cardiac muscle cell membrane repolarization	Snta1, Wdr1, Flna	-3.33
113	GO:2000191	GO Biological Processes	regulation of fatty acid transport	Mif, Map2k6, Fis1	-2.87

*P-values were calculated based on Hypergeometric test.

Supplementary Table4. List of the lysine site sthat significantly changed in the accessibility in brain, spleen, kidney, and muscle

Gene name	Peptidesequene	Duplicated lysine sites between the different peptide seuenes (*)	Number of the significant changed lysine sites per protein	Organ
Psat1	DYKVQAGNNSLY	*	6	Brain
Psat1	KVQAGNNSLY	*	6	Brain
Psat1	SSIKSQMIY		6	Brain
Psat1	EIQKQLL		6	Brain
Psat1	TKIPDPSTW		6	Brain
Psat1	DFVPDVKGAVL		6	Brain
Psat1	LSRPVDVSKF		6	Brain
Wdr1	AVCDASKVVTVF		5	Brain
Wdr1	IASGDISGKL	*	5	Brain
Wdr1	SGQGTVVKL	*	5	Brain
Wdr1	TLRDYSGQGTVVKL	*	5	Brain
Wdr1	EAKGPVTDVAY		5	Brain
Wdr1	FEGPPFKF	*	5	Brain
Plp1	NAFPGKVCGSNLL		5	Brain
Plp1	GDYKTTICGKGL	*	5	Brain
Plp1	KTTCGKGL	*	5	Brain
Plp1	TTCQSIAPFSKTSASIGSL		5	Brain
Plp1	SICKTAEF		5	Brain
Plp1	FSKNYQDY		5	Brain
Mag	STLSPELGGKY		4	Brain
Mag	CVVKSNPEPSVAF		4	Brain
Mag	VLREAVAKSLY	*	4	Brain
Mag	VLREAVAKSL	*	4	Brain
Mag	YFNSPYPKNYPPVVF		4	Brain
Lmnb1	QIELGKF		4	Brain
Lmnb1	SNLQKESRACL		4	Brain
Lmnb1	KEELEQTY		4	Brain
Lmnb1	VLKAGQTVTVW		4	Brain
Sdha	SYVDIKTGKVTL		4	Brain
Sdha	KHVNGQDQIVPGLY		4	Brain
Sdha	DTVKGSDWLGDQDAIHY		4	Brain
Sdha	AGVDVTKEPIVPLTVHY		4	Brain
Etfa	NVAPVSDIIEIKSPDTF		3	Brain
Etfa	ILETQKQF		3	Brain
Etfa	KGLLPEELTPL		3	Brain
Flnb	DASKVTASGPGLSAY		3	Brain
Flnb	AGDAIPKSPF		3	Brain
Flnb	GGDPIPKSPF		3	Brain
Hnrnpa3	DDHDTVDKIVVQKY		3	Brain
Hnrnpa3	GKIETIEVM		3	Brain
Hnrnpa3	VGGIKEDTEEY		3	Brain
Ogdh	GLHESDLDKVF		3	Brain
Ogdh	VCKVAAEW		3	Brain
Ogdh	IVFTPKSLL		3	Brain
Ehd1	LIPDNRKLF		2	Brain
Ehd1	LQTQDFSKE		2	Brain
Ppp1cb	KTFTDCF		2	Brain
Ppp1cb	GADVVSKE	*	2	Brain
Ppp1cb	TFGADVVSKE	*	2	Brain
Sod2	VNNLNATEEKYHEAL	*	2	Brain
Sod2	VNNLNATEEKY	*	2	Brain
Sod2	TNLSPKGGGEPKGELL		2	Brain
Dnm3	ELPQIAVVGGQSAGKSSVL		2	Brain
Dnm3	VLQLVTSKAEY		2	Brain
Gnaz	ALTGPAESKGEITPELL		2	Brain
Gnaz	TFKELTF		2	Brain
Phgdh	MGTELNGKTL		2	Brain
Phgdh	AGSPKGTIQVVTQGTSL		2	Brain
Hadh	ESLVDFCKTL		1	Brain
Cul3	TVNDQFTSKL		1	Brain
Fis1	QSEQAAGSVSKSTQFEY		1	Brain
Hnrnpa2b1	DDHDPVDKIVLQKY		1	Brain
Prpf19	TKVTDETSKCSL		1	Brain
Taldo1	AADAIKL		1	Brain

Adss	KELPVNAQNY		1	Brain
Ank1	LLKNGASPNEVSSNGTTPL		1	Brain
Ehd4	KSISIIDSPGIL		1	Brain
Gnas	TSGIFETKF		1	Brain
Iars2	VTEPKSVF		1	Brain
Itpr1	SAQKQFW		1	Brain
Map2k6	VKLILGD		1	Brain
Mrps7	ADPVISKF		1	Brain
Ndufa8	DQCVLDKLGW		1	Brain
Pma2	SPSGKLVQIEY		1	Brain
Pma6	KCDPAGYY		1	Brain
Rpl30	SGNNIELGTACGKY		1	Brain
Sptb	AALEKPTTL		1	Brain
Srsf3	VGNLGNNGNKTELERAF		1	Brain
Srsf7	VGNLGTGAGKGELERAF		1	Brain
Tagln	ALGSLAVTKNDGNY		1	Brain
Terf2ip	LLGNAPVSPSSQKL		1	Brain
Abce1	GLVGTNGIGKSTAL		1	Spleen
Actl6a	VLQQGIVKSPL		1	Spleen
Actr2	TLPDGRRIKVGGERF		3	Spleen
Actr2	DYTFGPEKL		3	Spleen
Actr2	NIDTRNCKIL		3	Spleen
Adh5	YIPQCGECKF		3	Spleen
Adh5	CLNPKTNL		3	Spleen
Adh5	KAGDTVIPL		3	Spleen
Adk	FGCIGIDKFGEIL		2	Spleen
Adk	LIQEPHKAATF	*	2	Spleen
Adk	LIQEPHKAATFF	*	2	Spleen
Adss2	VRFIEDELQIPVKW		1	Spleen
Aldh2	KLGPALATGNVVVM		3	Spleen
Aldh2	KTIEEVVGRANDSKY		3	Spleen
Aldh2	KVAEQTPL		3	Spleen
Aldh9a1	ELGGKSPL		1	Spleen
Aldoa	VTEKVLAAVY		3	Spleen
Aldoa	LSGGQSEEEASINLNAINKCPL		3	Spleen
Aldoa	SDIAHRIVAPGKGIL		3	Spleen
Ap1b1	QAYETILKN		1	Spleen
Ap1g1	VFQAAVPKTF		1	Spleen
Ap2b1	TAIVKLF		2	Spleen
Ap2b1	GCIRVDKITEY		2	Spleen
Apbb1ip	FLEKEERY		1	Spleen
Arf3	ANKQDLPNAM		4	Spleen
Arf3	VGLDAAGKTTILY		4	Spleen
Arf3	KLGEIVTTIPTIGF		4	Spleen
Arf3	KLKLGEIVTTIPTIGF		4	Spleen
Arf4	LFANKQDLPNAM		1	Spleen
Atp5f1a	YKGIRPAINVGL	*	4	Spleen
Atp5f1a	IIGDRQTGKTSIAIDTIINQKRF		4	Spleen
Atp5f1a	IYDDLKQAVAY		4	Spleen
Atp5f1a	KAPGIIPRISVREPM		4	Spleen
Atp5f1a	KGIRPAINVGL	*	4	Spleen
Atp5f1d	FDSANVKQVDVPTLTGAF		1	Spleen
Axl	FLEEPEDKAVPANTPF		1	Spleen
Bgn	SRVPAGLPDLKLL		1	Spleen
Bgn	ISKNHLEIPPNLPSLVEL		2	Spleen
Cad	VDPNARPLAPEVSIKTPRVF		2	Spleen
Cad	GIGRSFEEAFQKAL		2	Spleen
Cct2	IANTGMDTDKIKIF		3	Spleen
Cct2	IGAIAIGDLVKSTL		3	Spleen
Cct2	KAGADEERAETARLSSF		3	Spleen
Cct4	KIDDVVNTR		2	Spleen
Cct4	SAPKTDMDNQIVVSDY		2	Spleen
Cct7	DATNILNKL		1	Spleen
Cct8	AENSGVKANEVISKLY		2	Spleen
Cct8	VINRLEKLF		2	Spleen
Cfl1	AEKLGGSAVISL		4	Spleen
Cfl1	TGIKHEL		4	Spleen
Cfl1	VKMLPDKDCRY		4	Spleen
Cfl1	EEVKDRCTL		4	Spleen
Cltc	AETGQVQKIVLY		10	Spleen
Cltc	SRVNIPKVL		10	Spleen

Cltc	STDELVAEVEKRNRL		10	Spleen
Cltc	SVDRKVSQPIEGHAASF		10	Spleen
Cltc	VKEAIDSIKADDPSSY		10	Spleen
Cltc	DAAKLLY		10	Spleen
Cltc	FIQVMKEY		10	Spleen
Cltc	IKADDPSSY		10	Spleen
Cltc	LVRKDPPELW		10	Spleen
Cltc	SEAAKVAANAPKGIL		10	Spleen
Cnn2	SIGPDFQKGLKDGVL		1	Spleen
Copg1	TLEPSEKPF		2	Spleen
Copg1	DLKSVPL		2	Spleen
Ctsa	SRFLNKEPY		2	Spleen
Ctsa	FVESQNDPKNSPVVL	*	2	Spleen
Ctsa	FVESQNDPKNSPVVLW	*	2	Spleen
Ctsc	AQGCDGGFPYLIAGKY	*	1	Spleen
Ctsc	LIAGKY	*	1	Spleen
Ctsd	TLCKGGCEAIVDTGTSL	*	6	Spleen
Ctsd	TLCKGGCEAIVDTGTSL	*	6	Spleen
Ctsd	GEATKQPGIVF		6	Spleen
Ctsd	ILKVSQGGKTICL		6	Spleen
Ctsd	LKLGKKNY		6	Spleen
Ctsd	MIPCEKVSSLPTVY		6	Spleen
Ctsd	QKAIGAVPL		6	Spleen
Ddx1	IDNPKLRELL		1	Spleen
Ddx17	AQQVQQVADDYGKCSRL		1	Spleen
Ddx21	LFPIQAKTF		2	Spleen
Ddx21	QLAQVEQKAGIKF		2	Spleen
Ddx5	SGLDMVGVAQTGSGKTL		1	Spleen
Dnaja1	EVLADSKKRELY		1	Spleen
Dnaja2	KIGLVEALCGF		1	Spleen
Dync1h1	AGRSNLPDNLKKLF		2	Spleen
Dync1h1	SIITKDLF		2	Spleen
Eef1g	KALIAAQY		1	Spleen
Eef2	SVIAHVDHKGSTL		14	Spleen
Eef2	SVSPVVRVAVEAKNPADLPKLVEGL		14	Spleen
Eef2	ATKEGALCEENMRGVRF		14	Spleen
Eef2	VCKAGIIASARAGETRF		14	Spleen
Eef2	CFGPDGTGPNILTDITKGVQY	*	14	Spleen
Eef2	EWDVAEARKIW		14	Spleen
Eef2	FDPANGKF	*	14	Spleen
Eef2	FVVKAYLPVNESF		14	Spleen
Eef2	GDRYFDPANGKF	*	14	Spleen
Eef2	GPDGTGPNILTDITKGVQY	*	14	Spleen
Eef2	ILDPIFKVF		14	Spleen
Eef2	ISKMVPTSDKGRFY		14	Spleen
Eef2	LKPIQRTIL		14	Spleen
Eef2	LNEIKDSVVAGF		14	Spleen
Eef2	LVKTGTITTF		14	Spleen
Eef2	MKARPFDPGLAEDIDKGEVSARQEL		14	Spleen
Eftud2	TIKAFIPIDSF		2	Spleen
Eftud2	KILDAVVAQEPL		2	Spleen
Eif4a1	DVIAQAQSGTGKTATF		2	Spleen
Eif4a1	KDQIYDIF		2	Spleen
Eprs1	ELKGVPVRL		2	Spleen
Eprs1	NKVAAQGEVVRKL		2	Spleen
Ezr	VDNKGFPPTWL		1	Spleen
Fen1	TASEAKKLPQEF		2	Spleen
Fen1	IADVAPSAIRENDIKSY		2	Spleen
Fgr	LLTAPCTTTKPTQL		1	Spleen
Fkbp4	LKPSYAF		1	Spleen
Flna	TVKYTPCGAGSY		24	Spleen
Flna	VKYNDQHHPGSPF		24	Spleen
Flna	TVKYIPVQQGPVGVNVTY		24	Spleen
Flna	LISIKYGGPY		24	Spleen
Flna	IKYGGDEIPFSPY		24	Spleen
Flna	TVTIKY		24	Spleen
Flna	TVSSLQESGLKVNQPASF		24	Spleen
Flna	KVNQPASF	*	24	Spleen
Flna	RVNVGAGSHPNKVKVY		24	Spleen
Flna	SVTIDGPSKVKMDCQCEPEGY		24	Spleen
Flna	EVKVGTECGNQKVRW		24	Spleen

Flna	KVGSAADIPINISEDL		24	Spleen
Flna	KVEYTPY		24	Spleen
Flna	GPVAKTGL		24	Spleen
Flna	AGQHIAKSPF		24	Spleen
Flna	GGDHIPKSPF		24	Spleen
Flna	GPGLEGGIVGKSADF		24	Spleen
Flna	GGQVPVPNFPSKL		24	Spleen
Flna	TVDAKHAGKAPL		24	Spleen
Flna	KGQHVPGPSF		24	Spleen
Flna	IINIKFADQHVPGSPF		24	Spleen
Flna	LIDVKF		24	Spleen
Flna	DNKDGSCSVEYIPYEAGTY		24	Spleen
Flna	QVDTSKAGVAPL		24	Spleen
Flna	AIAVEGPSKAEISFEDRKDGSCGVAY		24	Spleen
Fn1	TVPGSKSTATINNIKPGADY		7	Spleen
Fn1	VAVKGNQQSPKATGVF		7	Spleen
Fn1	CGTTQNYDADQKF		7	Spleen
Fn1	KEINLSPDSSSVIVSGLM		7	Spleen
Fn1	KFSQVTPTSF		7	Spleen
Fn1	NAPEPSHITKY		7	Spleen
Fn1	NVGPLASKYPL		7	Spleen
Fus	SGNPIKVSF		1	Spleen
Gnb1	VSGACDASAKLW		2	Spleen
Gnb1	DALKADRAGVL		2	Spleen
Got1	EALKTPGTW		1	Spleen
H2-D1	TAADMAAQITRRKW		1	Spleen
Hadha	RQGKVIIVVKDGPFGFY		1	Spleen
Hcls1	GIQKDRVDKSAVGF		2	Spleen
Hcls1	KKTTPIEAASSGARGL		2	Spleen
Hibch	ALKKPSAEDVAGVLESY		2	Spleen
Hibch	ILNNAIASCQKPY		2	Spleen
Hnrnph2	FSDCKIQNGTSGVRF	*	1	Spleen
Hnrnph2	SDCKIQNGTSGVRF	*	1	Spleen
Hnrnpl	TLKLCF		6	Spleen
Hnrnpl	CLYGNVEKVKF		6	Spleen
Hnrnpl	DSKSDALETL		6	Spleen
Hnrnpl	KDFSESNNRF		6	Spleen
Hnrnpl	KNPNGPYPY		6	Spleen
Hnrnpl	NVCVSKQPAIMPGQSY		6	Spleen
Hnrnpul1	KQEAPPSFLPPEASQL		1	Spleen
Hnrnpul2	VGLPGSGKTQW		3	Spleen
Hnrnpul2	KAENGQFEFGQT		3	Spleen
Hnrnpul2	NFGQKEEPFFPPPEEF		3	Spleen
Hsp90ab1	TVRADHGEPIGRGTKVIL		7	Spleen
Hsp90ab1	CVQQLKEF		7	Spleen
Hsp90ab1	ESLTDPSKLDSGKEL		7	Spleen
Hsp90ab1	HLKEDQTEY		7	Spleen
Hsp90ab1	ISNASDALDKIRY		7	Spleen
Hsp90ab1	ITGESKEQVANSAF		7	Spleen
Hsp90ab1	LQQSKIL		7	Spleen
Hsp90b1	TREELVKNLGTIAKSGTSEF		13	Spleen
Hsp90b1	VKGVVDSDDLPLNVSRETL	*	13	Spleen
Hsp90b1	VKNLGTIAKSGTSEF	*	13	Spleen
Hsp90b1	CIQALPEFDGKRF		13	Spleen
Hsp90b1	FMAGSSRKEAESSPF		13	Spleen
Hsp90b1	GTNIKLGVIEDHSNRTRL		13	Spleen
Hsp90b1	ISNASDALDKIRL		13	Spleen
Hsp90b1	KLIINSLY		13	Spleen
Hsp90b1	LELDTIKNL		13	Spleen
Hsp90b1	LLPDTKAY		13	Spleen
Hsp90b1	MAGSSRKEAESSPF		13	Spleen
Hsp90b1	NFVKGVVDSDDLPL	*	13	Spleen
Hsp90b1	NFVKGVVDSDDLPLNVSRETL	*	13	Spleen
Hsp90b1	QNVAKEGVKF		13	Spleen
Hsp90b1	QTGKDISTNY	*	13	Spleen
Hsp90b1	QTGKDISTNYY	*	13	Spleen
Hspa4	SPAFKVREF		5	Spleen
Hspa4	TGIKVTY		5	Spleen
Hspa4	EELGKQIQQY		5	Spleen
Hspa4	FGKELSTTL		5	Spleen
Hspa4	MKVISSF		5	Spleen

Hspa8	TIEDGIFEVKSTAGDTHLGGEDF		11	Spleen
Hspa8	VLTKMKEIAEAY		11	Spleen
Hspa8	VVNDAGRPKVQVEY		11	Spleen
Hspa8	GLDKKVGAEARNVL		11	Spleen
Hspa8	IGRRFDDAVVQSDMKHWPF		11	Spleen
Hspa8	KGETKSFYPEEVSSM		11	Spleen
Hspa8	LGKTVTNAVVTVPAYF		11	Spleen
Hspa8	NDSQRQATKDAGTIAGL		11	Spleen
Hspa8	QHGKVEIIANDQGNRTTPSY		11	Spleen
Hspa8	RGTLDPVEKALRDAKL		11	Spleen
Hspd1	FINTSKGQKCEFQDAY		1	Spleen
Hspg2	KLTVPSQNSSF		2	Spleen
Hspg2	SFLPLPTIKDAY		2	Spleen
Ilf2	KILPTLEAVAAL		2	Spleen
Ilf2	KRNQDLAPNSAEQASIL		2	Spleen
Ilk	VVDQSQAVKF		3	Spleen
Ilk	KADINAVNEHGNVPLHY		3	Spleen
Ilk	QGNDIVVKVL		3	Spleen
Itga1	TVQQYENEEGKW		1	Spleen
Itga2b	CSTQPSPKVDW		2	Spleen
Itga2b	KTGQGLGASVVSWS		2	Spleen
Itgax	GFPDLKTL		1	Spleen
Lap3	TRQVIDCQLADVNNLGKY		2	Spleen
Lap3	NPKVIINAATL		2	Spleen
Ldha	GIQKELQF		4	Spleen
Ldha	IIPNIVKY		4	Spleen
Ldha	KDQLIVNLL		4	Spleen
Ldha	KFIIPNIVKY		4	Spleen
Napsa	VIKILQSDVGL		2	Spleen
Napsa	DIPKPAGPLW		2	Spleen
Ndufa4	GQAKKHPSLIPLF		2	Spleen
Ndufa4	NKLGPNQY		2	Spleen
Nme1	FTGLVKY		1	Spleen
Park7	SYSESERVEKDGIL		3	Spleen
Park7	GCKVTTHPL		3	Spleen
Park7	ICPDTSLEDKTQGPY		3	Spleen
Parp1	SLLSAEDKEAL		4	Spleen
Parp1	SVTSAPTAVNSSAPADKPL		4	Spleen
Parp1	FADMVSKSANY		4	Spleen
Parp1	GALLPCKECSGQLVF		4	Spleen
Pebp1	KGNDISSGTVLSDYVGSPPSGTGL	*	1	Spleen
Pebp1	LVVNMKGNDISSGTVL	*	1	Spleen
Pepd	GVIDVDTGKSTL		1	Spleen
Pfn1	AAVPGKTF	*	3	Spleen
Pfn1	AAVPGKTFVSITPAEVGVLVGKDRSSF	*	3	Spleen
Pfn1	TMDLRTKSTGGAPTF	*	3	Spleen
Pfn1	VSITPAEVGVLVGKDRSSFF		3	Spleen
Pfn1	DLRTKSTGGAPTF	*	3	Spleen
Phgdh	AGSPKGTIQVVTQGTSL		3	Spleen
Phgdh	MGTELNKTL		3	Spleen
Phgdh	QVVGRAGTGVDNVLEAATRKGIL		3	Spleen
Plcg2	KTTVVNDNGLSPVWAPTQEKVTF		1	Spleen
Plec	VIDPIKGL		1	Spleen
Pls3	AVELGKNPAKF		1	Spleen
Ppia	ELFADKVPKTAENF		6	Spleen
Ppia	FICTAKTEW		6	Spleen
Ppia	GEKFEDENF		6	Spleen
Ppia	GKVKEGMNIVEAMERF		6	Spleen
Ppia	ILKHTGPGIL		6	Spleen
Ppia	LDGKHVVF		6	Spleen
Ppid	FITTVPTPHLDGKHVVF		1	Spleen
Prkar1a	AALAKAIEKNVLF		2	Spleen
Prkar1a	VRKVIPKDY		2	Spleen
Prkcb	ALPGKPPFLTQL		1	Spleen
Prpf31	SKRFPELESVLPNAL		1	Spleen
Psm2	ALAAVAGGAPSVGIKAANGVVL		2	Spleen
Psm2	SPSGKLVIQIEY		2	Spleen
Psm4	SAEKVEIATL		1	Spleen
Psm5	SGLIADAKTL		1	Spleen
Psm6	KATAAGVKQTESTSF		2	Spleen
Psm6	KCDPAGYY		2	Spleen

Psmb10	IAPKIY		1	Spleen
Psmb2	SVRVIDKDGIIHNLENIAPFKRDS		1	Spleen
Psmb9	AAANVVKNISY		1	Spleen
Psmc3	ENLGIQPPKGV		2	Spleen
Psmc3	IDELDAIGTKRF		2	Spleen
Psmc12	VEEITDLPVKL		1	Spleen
Psmc13	LGCVDIKDLPVSEQQERAF		1	Spleen
Psmc7	VIIDVKPKDLGLPTEAY		1	Spleen
Ptk2b	VVPVDVEKEDVRIL		1	Spleen
Puf60	VASVHQDLSDDDIKSVF		1	Spleen
Pum2	ISAAPGAEAKY		1	Spleen
Qdpr	IQVVTTDGKTELTPAYF		1	Spleen
Rab7a	KTLDSWRDEF		1	Spleen
Rack1	DLNEGKHL		2	Spleen
Rack1	LCAATGPSIKIW		2	Spleen
Rap1b	VQGIFVEKYDPTIEDSY		3	Spleen
Rap1b	VVLGSGGVGKSAL		3	Spleen
Rap1b	ESSAKSKINVNEIFY	*	3	Spleen
Rap1b	LESSAKSKINVNEIFY	*	3	Spleen
Rpl11	FQKKYDGIILPGK		1	Spleen
Rpl31	AKGIRNVPY		1	Spleen
Rpl5	GALKGAVDGG		4	Spleen
Rpl5	GMDKIYEGQVEVNGGEY		4	Spleen
Rpl5	LDAGLARTTTGNKVF		4	Spleen
Rpl5	SIPHSTKRFPGYDSEKFE		4	Spleen
Rpl9	SNQTVDIPENVEITLKGRTVIVKGPRGTL		2	Spleen
Rpl9	LDGIYVSEKGTVQQADE		2	Spleen
Rplp1	IKAAGVSVPEFWPGLF		1	Spleen
Rps15	NQVEIKPEMIGHY		1	Spleen
Rps3a	VRTTQGTKIASDGL		3	Spleen
Rps3a	DVKAPAMF		3	Spleen
Rps3a	NIRNIGKTL		3	Spleen
S100a11	SGKDGNNNTQLSKTEF		1	Spleen
Serpina1c	KKPFDPENTTEAEF		1	Spleen
Sf3b1	VKVIDRILY		2	Spleen
Sf3b1	IKTEILPPFF		2	Spleen
Sf3b3	YFPVKNVIDGDLCEQF		1	Spleen
Slc25a4	AADVGKGSQREF		1	Spleen
Snmp200	VHLFPKLEL		1	Spleen
Sptb	AALEKPTTL		3	Spleen
Sptb	KGLQDALQGQEL		3	Spleen
Sptb	SAGHPEGEQIIRLQGQVDKQY		3	Spleen
Strn	IASAGADALAKVFF		1	Spleen
Syk	SYKPDGLL		2	Spleen
Syk	TVPCQKIG AQM		2	Spleen
Synpo2	LLTDAPNPNSKGV		1	Spleen
Taldo1	AADAIKL		3	Spleen
Taldo1	KKIPGRVSTVEDARL		3	Spleen
Taldo1	RNTGEIKAL		3	Spleen
Tardbp	CQYGEVVDVFIPKPF		1	Spleen
Tcp1	AAASIANIVKSSF		1	Spleen
Tkt	AANTKGICF		5	Spleen
Tkt	TGKYFDKASY		5	Spleen
Tkt	GIDKDAIVQAVKGL		5	Spleen
Tkt	GWHTIIVDGHVSVEELCKAF		5	Spleen
Tkt	KLDNLVAIF		5	Spleen
Tln1	AAVGAASKTL	*	15	Spleen
Tln1	ALLDQTKTL	*	15	Spleen
Tln1	TLAAVGAASKTL	*	15	Spleen
Tln1	RVDEKTKEVIQEW		15	Spleen
Tln1	STDPASP NLKSQL		15	Spleen
Tln1	VTKSNTSPEELGPLANQL		15	Spleen
Tln1	SLTNIKRW		15	Spleen
Tln1	RAVGDAASKRLL		15	Spleen
Tln1	TLQKPNPDLKQQL	*	15	Spleen
Tln1	QKPNPDLKQQL	*	15	Spleen
Tln1	SLKISIGNVVKTM		15	Spleen
Tln1	LQAAKGLAGAVSEL		15	Spleen
Tln1	KFLPSELRDEH		15	Spleen
Tln1	VQSAKEVANSTANL		15	Spleen
Tln1	DLKDFLPKEY		15	Spleen

Tln1	VAAAKASVPTIQDQASAM		15	Spleen
Tln1	VLKAKSVAQRTEDSGLQTQVIAAATQCAL	*	15	Spleen
Tln1	KAKSVAQRTEDSGLQTQVIAAATQCAL	*	15	Spleen
Tln1	VRTAKAIAVTVQEM		15	Spleen
Tmed9	VEQVEIQKEQNY		2	Spleen
Tmed9	VEVKDPEDKVIL		2	Spleen
Tns3	LIECTPKGVRL		1	Spleen
Top2b	KGTIQELGQNQY		1	Spleen
Tuba1c	APVISAEEKAY	*	2	Spleen
Tuba1c	ATYAPVISAEEKAY	*	2	Spleen
Tuba1c	ITGKEDAANNY		2	Spleen
Tuba4a	TIGKEIIDPVLDRIKRL		1	Spleen
Tubb4b	YNEATGGKYVPRAVL		1	Spleen
Txn1	SNKYPQAVF		1	Spleen
Ube2h	KVRVDLPDKYPF		1	Spleen
Uqcrfs1	AAKNVVSQF		2	Spleen
Uqcrfs1	LQGAVPAASEPPVLDVKRPF		2	Spleen
Uso1	KQLGPPVQIIL		1	Spleen
Usp5	ASFPDYLVIQIKKF		3	Spleen
Usp5	QNAPTDPDQFSTQVAKL		3	Spleen
Usp5	RFLVEEKIKCL		3	Spleen
Vwf	AFNGAQSKEEVL		2	Spleen
Vwf	QLQLSPKTF		2	Spleen
Ywhah	LAEVASGEKKNSVVEASEAAY		2	Spleen
Ywhah	LIKNCNDF		2	Spleen
Ywhaq	KAVTEQGAEL		3	Spleen
Ywhaq	LAEVACGDDRKQTIENSQGAY		3	Spleen
Ywhaq	LIANATNPESKVF		3	Spleen
Acad11	AGDKSLSNVIAHEISHSW		1	Kidney(M11)
Acads	AKAIANECQANF		2	Kidney(M11)
Acads	AGVDVTKEPIVLPVTVHY		2	Kidney(M11)
Acly	ALESPKGRGTVL		1	Kidney(M11)
Aco1	SKAFDSGIIPMEF		2	Kidney(M11)
Aco1	ARLCDKTTPTGW		2	Kidney(M11)
Aco2	SLVDAMNGKEGVVECSF		2	Kidney(M11)
Aco2	SLVIIPKNW		2	Kidney(M11)
Acox2	ASVAVANKL		1	Kidney(M11)
Acsl1	TLKYPIEHGIITNW		1	Kidney(M11)
Acta2	VCDNGSGLCKAGF		4	Kidney(M11)
Acta2	VTAKEEDLSSF		4	Kidney(M11)
Acta2	TYTAEVSVPKEL		4	Kidney(M11)
Acta2	TRDAKGISQEQMNEF		4	Kidney(M11)
Actn1	CITKFGIEAF		3	Kidney(M11)
Actn1	CTSATESEVTRGKNIL		3	Kidney(M11)
Actn1	YGPPGCGKTL		3	Kidney(M11)
Actn4	DFIVKGSCF		4	Kidney(M11)
Actn4	DIAHTPGVAADLSHIETRANVKGY		4	Kidney(M11)
Actn4	DAAQPGKRFF		4	Kidney(M11)
Actn4	DGGALVQVQKW		4	Kidney(M11)
Adh1	EINFNTLQTKL		1	Kidney(M11)
Aldh2	ESRIQEVDAQMLRDICSKY		1	Kidney(M11)
Ankfy1	FYGPPGCGKTL		1	Kidney(M11)
Bdh1	GALKGAVDGGL		2	Kidney(M11)
Bdh1	GAPLTKL		2	Kidney(M11)
Ckmt1	GCLEQAEKGYEEW		2	Kidney(M11)
Ckmt1	GATECINPDYSKPIQEV		2	Kidney(M11)
Crot	GDKRIIDTPISEMGE		1	Kidney(M11)
Dlat	GHLDDPANQEIERGKTY		1	Kidney(M11)
Fabp4	GIHNEVSKIVQTY		2	Kidney(M11)
Fabp4	GLESEVAQHAKTY		2	Kidney(M11)
Fbp1	GVLGPTIKGY		2	Kidney(M11)
Fbp1	IAPEKIENIY		2	Kidney(M11)
Gcdh	IDAGSRYETEKNNAGY		1	Kidney(M11)
Gpd2	ILPSQPGLVHPKGDEAELY		1	Kidney(M11)
Lta4h	KEVAELAEICIGSGL		3	Kidney(M11)
Lta4h	ITPFTNGDKIGCF		3	Kidney(M11)
Lta4h	ISQCTPKVDFFPDQDLATL		3	Kidney(M11)
Mdh2	KHVNGQDQIVPGLY		4	Kidney(M11)
Mdh2	KIIRALSEIAGITLPY		4	Kidney(M11)
Mdh2	KLEAPDADELPRSDFDPGQDITY		4	Kidney(M11)
Mdh2	KLVSSNFDDY		4	Kidney(M11)

Mpc2	KMSGSGRELGEY		1	Kidney(M11)
Myh11	KPARVILQDFTGVPAVDF		1	Kidney(M11)
Ndufs1	KSTLPDADREREAIL		1	Kidney(M11)
Ntn4	KVAEQTPLTALY		1	Kidney(M11)
Pdha	LEKPITM		2	Kidney(M11)
Pdha	KYPIEHGIITNW		2	Kidney(M11)
Rpl18	LIKNGALVNAATAGAQETPL		1	Kidney(M11)
Rpl5	LNKQAPQTVHLPSETLDVF		1	Kidney(M11)
Sdha	MERYAPVAKDL		3	Kidney(M11)
Sdha	NAHIKGLLETIASDVVSL		3	Kidney(M11)
Sdha	NAIRSLGSEQIAKW		3	Kidney(M11)
Tln2	NHFDKDHGGALGPEEF		1	Kidney(M11)
Uqcrc1	QHPPKDSGQRVDVSPTSQRL		5	Kidney(M11)
Uqcrc1	QHLEQAEKGYYEEW		5	Kidney(M11)
Uqcrc1	QEGCEKISQLY		5	Kidney(M11)
Uqcrc1	NRDGSYDMQIDNKSF		5	Kidney(M11)
Uqcrc1	QGPDAAPGALDYKSF		5	Kidney(M11)
Vcp	SAIRDGEAPDPEDPSRKIY		3	Kidney(M11)
Vcp	QWLTPEQTSKGQHPY		3	Kidney(M11)
Vcp	RTTPPQADAKSQLF		3	Kidney(M11)
Acad11	ALIAEETGKCF		2	Kidney(M14)
Acad11	SIGFPVAKPL		2	Kidney(M14)
Acads	AEKELVPIAAQL		4	Kidney(M14)
Acads	TKLQNIQF	*	4	Kidney(M14)
Acads	GAPLTKLQNIQF	*	4	Kidney(M14)
Acads	GIAQASLDCAVKY		4	Kidney(M14)
Acads	LGPILKF		4	Kidney(M14)
Acly	TLLNPKGRIW		2	Kidney(M14)
Acly	DYAKTIL		2	Kidney(M14)
Aco1	AAPSEKLY	*	9	Kidney(M14)
Aco1	AWNPKSTY		8	Kidney(M14)
Aco1	DLQPPKSIVDAY		8	Kidney(M14)
Aco1	IKSPPFESL		8	Kidney(M14)
Aco1	IKTSLSPGSGVVTY		8	Kidney(M14)
Aco1	IVLAGKEY		8	Kidney(M14)
Aco1	LLGIKAVL		8	Kidney(M14)
Aco1	LVKKNDIENILNW		8	Kidney(M14)
Aco1	NALAAPSEKLY	*	8	Kidney(M14)
Aco2	ADPSDYNKIHPVDKL	*	14	Kidney(M14)
Aco2	SKTGRTDIANLAEF		14	Kidney(M14)
Aco2	TFADPSDYNKIHPVDKL	*	14	Kidney(M14)
Aco2	TLSEKIVY		14	Kidney(M14)
Aco2	TSPKDVIL		14	Kidney(M14)
Aco2	TVKGGTGAIVEY		14	Kidney(M14)
Aco2	DGKDLEDLQIL		14	Kidney(M14)
Aco2	ELKCPKIVIGVKL		14	Kidney(M14)
Aco2	GGRAIITKSF		14	Kidney(M14)
Aco2	GHLDDPANQEIERGKTY		14	Kidney(M14)
Aco2	GHLDDPANQEIERGKTYL		14	Kidney(M14)
Aco2	KDHLVPDPGCQY		14	Kidney(M14)
Aco2	KFNPETDFL		14	Kidney(M14)
Aco2	KLEAPDADELPRSDFPQGDTY		14	Kidney(M14)
Aco2	LATAGAKY	*	14	Kidney(M14)
Aco2	NFLATAGAKY	*	14	Kidney(M14)
Acx2	EWAQKSPANTQENPAY	*	2	Kidney(M14)
Acx2	EWAQKSPANTQENPAYKKY	*	2	Kidney(M14)
Acx2	IRKDAILLDAF		2	Kidney(M14)
Acta2	KCDIDIRKDLY		1	Kidney(M14)
Actn1	TTITPQEINGKW		5	Kidney(M14)
Actn1	DAEDIVGTARPDEKAIMTY		5	Kidney(M14)
Actn1	ETATLSEIKALL		5	Kidney(M14)
Actn1	KATLPDADKERLAIL		5	Kidney(M14)
Actn1	KPKIDQLECDHQLIQEAL		5	Kidney(M14)
Actn4	AGDKNFITAEEL		9	Kidney(M14)
Actn4	TRDAKGISQEQMQEF		9	Kidney(M14)
Actn4	DSHNVNTRCQKICDQW		9	Kidney(M14)
Actn4	ETATLSDIKAL		9	Kidney(M14)
Actn4	IFDNKHTNY		9	Kidney(M14)
Actn4	KNVNVQNF		9	Kidney(M14)
Actn4	KQRDYETATLSDIKAL		9	Kidney(M14)
Actn4	QGPDAAPGALDYKSF		9	Kidney(M14)

Actn4	TTVTPQIINSKW		9	Kidney(M14)
Actr1b	VYSKDQLQTF		2	Kidney(M14)
Actr1b	LSINPQKDEALETEKVQY		2	Kidney(M14)
Adh1	EKINEAFDLL		2	Kidney(M14)
Adh1	KSKDSVPKLVADF		2	Kidney(M14)
Aldh11i	AAGNTVVIKPAQVTPL		9	Kidney(M14)
Aldh11i	TALKFAEL		9	Kidney(M14)
Aldh11i	TLTKKEPVGVCGIVIPW		9	Kidney(M14)
Aldh11i	TRDINKALY		9	Kidney(M14)
Aldh11i	VSDKLQAGTVF		9	Kidney(M14)
Aldh11i	ELGGKSPL		9	Kidney(M14)
Aldh11i	GKDLGEAALNEY		9	Kidney(M14)
Aldh11i	LQKECDVLPDDTVSTLY		9	Kidney(M14)
Aldh11i	NKTDVAAPF		9	Kidney(M14)
Aldh2	AALETLDNGKPY		6	Kidney(M14)
Aldh2	AGWADKY		6	Kidney(M14)
Aldh2	GYIKSGQQEGAKL		6	Kidney(M14)
Aldh2	HGKTIPIDGDF		6	Kidney(M14)
Aldh2	KLGPALATGNVVVM		6	Kidney(M14)
Aldh2	KVAEQTPL		6	Kidney(M14)
Aldh8a1	DKAGVPPGVINIVF		3	Kidney(M14)
Aldh8a1	IGGKFLPCNSY		3	Kidney(M14)
Aldh8a1	KVGVPSPDSANM	*	3	Kidney(M14)
Aldh8a1	KVGVPSPDSANMGAL	*	3	Kidney(M14)
Arf4	DVGGQDKIRPL	*	2	Kidney(M14)
Arf4	DVGGQDKIRPLW	*	2	Kidney(M14)
Arf4	LFANKQDLPNAM		2	Kidney(M14)
Asl	TLKGLPSTY	*	4	Kidney(M14)
Asl	VGAVDPIMEKF	*	4	Kidney(M14)
Asl	GGRFVGAVDPIMEKF	*	4	Kidney(M14)
Asl	KGLPSTY	*	4	Kidney(M14)
Asl	NVDVQGSKAY		4	Kidney(M14)
Asl	QGLDKVAEEW		4	Kidney(M14)
Atp6v1b2	AIGKDVQAM		4	Kidney(M14)
Atp6v1b2	TLPDGTRSGQVL		4	Kidney(M14)
Atp6v1b2	EGTSGIDAKKTSCEF		4	Kidney(M14)
Atp6v1b2	EVSGSKAVVQVF		4	Kidney(M14)
Bdh1	GVKVSVEPGNF		1	Kidney(M14)
Capza2	TVSNEVQTAKEF		1	Kidney(M14)
Ckmt1	IKTVGMVAGDEETY		2	Kidney(M14)
Ckmt1	LFDKPV SPL		2	Kidney(M14)
Crot	KAASDLQIAASTF		1	Kidney(M14)
Ctsb	TKKGLVSGGVY		1	Kidney(M14)
Cyb5b	RLEEVAKRNSAEETW		1	Kidney(M14)
Dhrs4	NVSKTALL		1	Kidney(M14)
Dlat	ACLKVPEANSSW		3	Kidney(M14)
Dlat	AIGASEDKLIPADNEKGFVDASVM		3	Kidney(M14)
Dlat	CIIVEKQEDIAAF		3	Kidney(M14)
Fabp4	KNTEISF		1	Kidney(M14)
Fbp1	AKDFDPAINEY		4	Kidney(M14)
Fbp1	VMEKAGGLATTGDKDIL		4	Kidney(M14)
Fbp1	GIAGSTNVTGDQVKKL	*	4	Kidney(M14)
Fbp1	GIAGSTNVTGDQVKKLDIL	*	4	Kidney(M14)
Fbp1	LQRKKFPPDGSAFY		4	Kidney(M14)
Gcdh	TLSGTKTW		2	Kidney(M14)
Gcdh	LPGLAKGELL		2	Kidney(M14)
Gpd2	TLKNTPEFDIL		1	Kidney(M14)
Lgmn	KGVLKDYTGEDVTPENF		1	Kidney(M14)
Lta4h	SYQSVTTDDWKSF		2	Kidney(M14)
Lta4h	TAEVSVPKEL		2	Kidney(M14)
Mccc1	TGTIEKVF		1	Kidney(M14)
Mdh2	SLVDAMNGKEGVVECSF		9	Kidney(M14)
Mdh2	VQSKETECTYF		9	Kidney(M14)
Mdh2	EKNLGIGKITPF		9	Kidney(M14)
Mdh2	GIGKITPF		9	Kidney(M14)
Mdh2	ISQCTPKVDFFPQDQLATL		9	Kidney(M14)
Mdh2	KGLDPARVNVPIGGHAGKTIPL		9	Kidney(M14)
Mdh2	KNSPLVSRL		9	Kidney(M14)
Mdh2	LLKNSPL		9	Kidney(M14)
Mdh2	NPNKIFGVTTTL		9	Kidney(M14)
Ndufs1	AKCVKAVTEGAQAVEEPSIC		4	Kidney(M14)

Ndufs1	VNTEGRAQQTKVAVTPPGLAREDW		4	Kidney(M14)
Ndufs1	LLGADGGCITRQDLPKDCF		4	Kidney(M14)
Ndufs1	RYDHLGDSPKIL		4	Kidney(M14)
Ndufs7	VVTKLDDLINW		1	Kidney(M14)
Oxct1	TDPVEAVKDIPNGATL	*	7	Kidney(M14)
Oxct1	TDPVEAVKDIPNGATLL	*	7	Kidney(M14)
Oxct1	TDPVEAVKDIPNGATLLVGGF	*	7	Kidney(M14)
Oxct1	TSTGYGTLVQEGGSPIKY	*	7	Kidney(M14)
Oxct1	VQEGGSPIKY	*	7	Kidney(M14)
Oxct1	YTDPVEAVKDIPNGATL	*	7	Kidney(M14)
Oxct1	YTDPVEAVKDIPNGATLL	*	7	Kidney(M14)
Oxct1	EGLTVDDIKKSTGCDF	*	7	Kidney(M14)
Oxct1	GTLVQEGGSPIKY	*	7	Kidney(M14)
Oxct1	KADRAGNVIF	*	7	Kidney(M14)
Oxct1	KDEADADLINAGKETVTVLPGASFF	*	7	Kidney(M14)
Oxct1	KTGVKDLTAVSNNAGVDNF		7	Kidney(M14)
Oxct1	NKDGSAIAASKPREVREF	*	7	Kidney(M14)
Pdhb	AKVLEDNSVPQVKDIIF		4	Kidney(M14)
Pdhb	SKEGIECEVINL		4	Kidney(M14)
Pdhb	ELPAEAQSKDF		4	Kidney(M14)
Pdhb	NFSMQAIDQVINSAAKTY		4	Kidney(M14)
Pgam1	ADLTEDQLPSCESLKDITIARALPF		1	Kidney(M14)
Rbm39	SDSECAKKALEQLNGF		1	Kidney(M14)
Scly	IAGLGKAADLVSENCETY		2	Kidney(M14)
Scly	IGGKPKQDIIF		2	Kidney(M14)
Sdha	SIAESCRPGDKVPSIKANAGEESVM		8	Kidney(M14)
Sdha	SYVDIKTGKVTL		8	Kidney(M14)
Sdha	DTVKGSDWLGQDAIHY		8	Kidney(M14)
Sdha	DYSKPIQGQKKPF		8	Kidney(M14)
Sdha	IFAGVDVTKEPIPVLPVHY		8	Kidney(M14)
Sdha	KHVNGQDQIVPGLY		8	Kidney(M14)
Sdha	MERYAPVAKDL		8	Kidney(M14)
Sdha	RVGSVLQEGCEKISQLY		8	Kidney(M14)
Sdha	VIKDLVPDLNPF		1	Kidney(M14)
Stx3	TSGIIDSQISKQAL		1	Kidney(M14)
Ugt1a2	AFPTYKKEEY		3	Kidney(M14)
Ugt1a2	VKWLPQNDLL		3	Kidney(M14)
Ugt1a2	IGGINCVTKKPL		3	Kidney(M14)
Vcp	AKAIANECQANF	*	7	Kidney(M14)
Vcp	AQIKEMVELPL		7	Kidney(M14)
Vcp	YGPPGCGKTL	*	7	Kidney(M14)
Vcp	YGPPGCGKTLL	*	7	Kidney(M14)
Vcp	IPLPDEKSRVAIL		7	Kidney(M14)
Vcp	ISIKGPELL		7	Kidney(M14)
Vcp	KAIGVKPPRGIL		7	Kidney(M14)
Vcp	KVVETDPSPY		7	Kidney(M14)
Vcp	LAKAIANECQANF	*	7	Kidney(M14)
Vcp	LYGPPGTGKTL	*	7	Kidney(M14)
Acadm	AQRALDEATKY		5	Muscle
Acadm	AREEIIPVAPEYDKSGEYPFPL		5	Muscle
Acadm	GFNTEYVPEKL		5	Muscle
Acadm	SFELTEQQKEF		5	Muscle
Acadm	YASIAKAF		5	Muscle
Ahcy	KVADIGLAAW		1	Muscle
Akr1b3	VVIPKSVTPVRIAENL		4	Muscle
Akr1b3	KPAVNQIECHPY		4	Muscle
Akr1b3	LTQEKLEIY		4	Muscle
Akr1b3	QNEKEVGVAL		4	Muscle
Aldh1a1	LSDLGGCIKAL		1	Muscle
Apoa1	KSNPTLNEY		1	Muscle
Atic	VTGTIGEGEDLVKW		2	Muscle
Atic	SVSDKTGLVEF		2	Muscle
Atp6v0a1	SFEHIREGKFDE		1	Muscle
Atp6v1a	EFIPSKNL		1	Muscle
Atp6v1b2	VILDHVKFPRYAEIVHL		2	Muscle
Atp6v1b2	TRKDHADVSNQLY		2	Muscle
Bola1	AIQAKTPAQW		1	Muscle
Btf3	NNPKVQASLAANTF		1	Muscle
Ckb	AELRAKCTPSGF		1	Muscle
Ckmt2	ADLFDPVIKL		1	Muscle
Dnpep	TAFEEAIPKSF		1	Muscle

Eef1b2	GSSKLVPVGY		1	Muscle
Eef1d	GASKLVPVGY		1	Muscle
Fabp3	TRELVDGKLIL		1	Muscle
Fus	SGNPIKVSF		1	Muscle
Glrx	KQIGALQL		2	Muscle
Glrx	IKPTCPY		2	Muscle
Hdgf	EIENNPTVKASGY		1	Muscle
Hnmpd	VGGLSPDTPEEKIREY		1	Muscle
Hnrnph1	VVKVRGLPW		1	Muscle
Hnrnpk	LLQNSVKQY		1	Muscle
Lgals1	KVRGEVASDAKSF		4	Muscle
Lgals1	NLKPGECL		4	Muscle
Lgals1	KIKCVAFE		4	Muscle
Lgals1	VLNLGKDSNNL		4	Muscle
Mif	TQQLAQATGKPAQY		1	Muscle
Myl1	GTNPNTNAEVKKVL	*	8	Muscle
Myl1	RALGTNPNTNAEVKKVL	*	8	Muscle
Myl1	GNPSNEEMNAKKIEF		8	Muscle
Myl1	DRTGECKITL	*	8	Muscle
Myl1	FDRTGECKITL	*	8	Muscle
Myl1	LFDRTGECKITL	*	8	Muscle
Myl1	SAIKIEF		8	Muscle
Myl1	EAFVKHIMSV	*	8	Muscle
Myl1	VKHIMSV	*	8	Muscle
Myl1	SKEQQEDFKEAF	*	8	Muscle
Myl1	SKEQQEDFKEAFL	*	8	Muscle
Myl1	SADQIADFKEAF	*	8	Muscle
Myl1	SADQIADFKEAFL	*	8	Muscle
Myl1	MQAISNNKDQGGYEDF		8	Muscle
Myl6b	DRVGDGKILY		1	Muscle
Naca	VTQVPASQKTGL		3	Muscle
Naca	SNTSPVKGVPISAL		3	Muscle
Naca	SQTVGPKETSLEGATAVPL		3	Muscle
Nefm	KRSALAPRLAY		2	Muscle
Nefm	RKLLEGEETRF		2	Muscle
Nme2	FPGLVKY		3	Muscle
Nme2	GETNPADSKPGTIRGDF		3	Muscle
Nme2	FKPEELIDY		3	Muscle
Npm1	EGSPIKVTL		1	Muscle
Nutf2	LLKNINDAW		1	Muscle
P4hb	FLPKSVSDY	*	6	Muscle
P4hb	LFLPKSVSDY	*	6	Muscle
P4hb	SQEVPEWDKQPVKVL		6	Muscle
P4hb	VIEFTEQTAPKIF		6	Muscle
P4hb	GVRGYPTIKFF		6	Muscle
P4hb	GVRGYPTIKF		6	Muscle
P4hb	QLDKDGVVLF		6	Muscle
Pdia6	GVQGFPPTIKIF		2	Muscle
Pdia6	GIKGFPPTIKIF		2	Muscle
Pebp1	AGVTVDELGKVL		4	Muscle
Pebp1	SCDEPILSNKSGDNRGKF		4	Muscle
Pebp1	DGLDPGKLY		4	Muscle
Pebp1	LVVNMKGNDISSGTVL		4	Muscle
Ppp1r3a	SLVSVKEF		2	Muscle
Ppp1r3a	GLSSLADHGITEKAQAVTAY		2	Muscle
Ppp3ca	RKSQTTGFPSLITIF		1	Muscle
Psmc1	LAKAVANQTSATF		1	Muscle
Psmc5	VVDVDKNIDINDVTPNCRVAL		1	Muscle
Psmc9	QSVQNVGTVVQHSEKPL		1	Muscle
Pvalb	AAADSFHKKF		1	Muscle
Rad23b	KTLQQQTF		2	Muscle
Rad23b	FACEKNENLAANF		2	Muscle
Rpl5	GALKGAVDGGL		1	Muscle
S100a6	TIGSKLQDAEIAL		1	Muscle
Sod1	KGDGPVQGTIHF		2	Muscle
Sod1	EQKASGEPVVL		2	Muscle
Stxbp1	KEYPAVRY		1	Muscle
Tnni2	SEVQELCKQL		1	Muscle
Tpm2	KAISEELDNALNDITSL		1	Muscle
Tpt1	MTGAEEQIKHIL		1	Muscle
Tubb1	SVMPSPKVSDTVVEPY		1	Muscle

Txn	QEALAAAGDKLVVDF		2	Muscle
Txn	SGANKEKLEASITEYA		2	Muscle
Uchl3	LLFPITEKY		1	Muscle
Vim	ADLSEAANRRNDALRQAKQESNEY		3	Muscle
Vim	ESVAAKNLQEAEW		3	Muscle
Vim	RKLLEGEESRISLPLPTF		3	Muscle
Ybx3	GFINRNDTKEDVF		1	Muscle
Ywhag	RYLAEVATGEKRATVVESSEKAY		4	Muscle
Ywhag	KNVVGARRSSW		4	Muscle
Ywhag	LIKNCSETQY		4	Muscle
Ywhag	VDREQLVQKARLAEQAERY	*	4	Muscle
Ywhag	VQKARLAEQAERY	*	4	Muscle

Supplementary Table 5. List of the enriched terms in the ontology network for spleen dataset

Node label	Canonical Name	Category	Description	Hits	LogP*
1	R-MMU-2262752	Reactome Gene Sets	Cellular responses to stress	Prdx3,Dync1h1,Fkbp4,Hmox1,Hspa8,Dnaja1,Hsph1,Hspa1b,Hsp90ab1,Lmnb1,Psmb9,Psmd7,Ncf2,Ndufa4,P4hb,Pma2,Psmb10,Psmc3,Rbbp4,Prdx2,Tuba4a,Tuba1c,Psmd13,Pma4,Pma5,Pma6,Psmb2,Nup210,Prdx5,Dnaj a2,Psmd12,Rpa1,Tubb4b,Nup214,Nup54	-13.36
2	R-MMU-8953897	Reactome Gene Sets	Cellular responses to stimuli	Prdx3,Dync1h1,Fkbp4,Hmox1,Hspa8,Dnaja1,Hsph1,Hspa1b,Hsp90ab1,Lmnb1,Psmb9,Psmd7,Ncf2,Ndufa4,P4hb,Pma2,Psmb10,Psmc3,Rbbp4,Prdx2,Tuba4a,Tuba1c,Psmd13,Pma4,Pma5,Pma6,Psmb2,Nup210,Prdx5,Dnaj a2,Psmd12,Rpa1,Tubb4b,Nup214,Nup54	-13.27
3	R-MMU-450531	Reactome Gene Sets	Regulation of mRNA stability by proteins that bind AU-rich elements	Anp32a,Hspa8,Hspa1b,Psmb9,Psmd7,Prkcd,Pma2,Psmb10,Psmc3,Psmd13,Pma4,Pma5,Pma6,Psmb2,Psmd12,Nup214,Tnpo1	-13.14
4	R-MMU-71291	Reactome Gene Sets	Metabolism of amino acids and derivatives	Ass1,Ckb,Gls,Got1,Psmb9,Slc3a2,Psmd7,Ogdh,Pma2,Psmb10,Psmc3,Srm,Psmd13,Pma4,Pma5,Pma6,Psmb2,Aldh9a1,Psmd12,Psat1,Qdpr,Acat1,Hibch,Cps1,Phgdh	-11.86
5	R-MMU-4086400	Reactome Gene Sets	PCP/CE pathway	Ap2a2,Psmb9,Psmd7,Pfn1,Prkcb,Pma2,Psmb10,Psmc3,Psmd13,Pma4,Pma5,Pma6,Psmb2,Psmd12,Cltc,Ap2b1	-11.81
6	R-MMU-8852276	Reactome Gene Sets	The role of G2E1 in G2/M progression after G2 checkpoint	Hsp90ab1,Psmb9,Psmd7,Pma2,Psmb10,Psmc3,Tuba4a,Tuba1c,Psmd13,Pma4,Pma5,Pma6,Psmb2,Psmd12,Tubb4b	-11.67
7	WP519	WikiPathways	Proteasome degradation	Psmb9,Psmd7,Pma2,Psmb10,Psmc3,Rpn2,Uba1,Psmd13,Pma4,Pma5,Pma6,Psmb2,Psmd12	-11.63
8	R-MMU-3858494	Reactome Gene Sets	Beta-catenin independent WNT signaling	Ap2a2,Gnb1,Gnb2,Psmb9,Psmd7,Pfn1,Prkcb,Pma2,Psmb10,Psmc3,Psmd13,Pma4,Pma5,Pma6,Psmb2,Psmd12,Cltc,Ap2b1	-11.26
9	R-MMU-450408	Reactome Gene Sets	AUF1 (hnRNP D0) binds and destabilizes mRNA	Hspa8,Hspa1b,Psmb9,Psmd7,Pma2,Psmb10,Psmc3,Psmd13,Pma4,Pma5,Pma6,Psmb2,Psmd12	-11.07
10	R-MMU-2132295	Reactome Gene Sets	MHC class II antigen presentation	Ap1b1,Ap1g1,Ap2a2,Ctsc,Ctsd,Ctsh,Dync1h1,Dnm2,Ctsa,Rab7,Sec23a,Tuba4a,Tuba1c,Cltc,Ap2b1,Tubb4b	-9.67
11	GO:0072524	GO Biological Processes	pyridine-containing compound metabolic process	Ldha,Ncf2,Ogdh,Pnp,Prps1,Taldo1,Tkt,Prdx5,Nampt,Pgls,Pgd,Naxe	-7.88
12	GO:0046496	GO Biological Processes	nicotinamide nucleotide metabolic process	Ldha,Ncf2,Ogdh,Prps1,Taldo1,Tkt,Prdx5,Nampt,Pgls,Pgd,Naxe	-7.55
13	GO:0019362	GO Biological Processes	pyridine nucleotide metabolic process	Ldha,Ncf2,Ogdh,Prps1,Taldo1,Tkt,Prdx5,Nampt,Pgls,Pgd,Naxe	-7.42
14	mmu01230	KEGG Pathway	Biosynthesis of amino acids - Mus musculus (house mouse)	Aldoa,Ass1,Cs,Got1,Prps1,Taldo1,Tkt,Psat1,Shmt2,Cps1,Phgdh	-6.99
15	GO:0006098	GO Biological Processes	pentose-phosphate shunt	Prps1,Taldo1,Tkt,Pgls,Pgd	-5.78
16	R-MMU-71336	Reactome Gene Sets	Pentose phosphate pathway	Prps1,Taldo1,Tkt,Pgls,Pgd	-5.78
17	WP63	WikiPathways	Pentose phosphate pathway	Taldo1,Tkt,Pgls,Pgd	-5.55
18	GO:0006740	GO Biological Processes	NADPH regeneration	Prps1,Taldo1,Tkt,Pgls,Pgd	-5.27
19	GO:0006739	GO Biological Processes	NADP metabolic process	Ncf2,Prps1,Taldo1,Tkt,Prdx5,Pgls,Pgd	-5.25
20	GO:1904851	GO Biological Processes	positive regulation of establishment of protein localization to telomere	Cct2,Cct4,Cct6a,Cct7,Cct8,Tcp1	-8.32
21	R-MMU-390471	Reactome Gene Sets	Association of Tric/CCT with target proteins during biosynthesis	Cct2,Cct4,Cct6a,Cct7,Cct8,Tcp1	-8.32
22	GO:0061077	GO Biological Processes	chaperone-mediated protein folding	Cct2,Cct4,Cct6a,Cct7,Cct8,Fkbp4,Hspa8,Hsph1,Hspa1b,Tcp1,Ppid	-8.05
23	GO:0070203	GO Biological Processes	regulation of establishment of protein localization to telomere	Cct2,Cct4,Cct6a,Cct7,Cct8,Tcp1	-7.98
24	GO:0070202	GO Biological Processes	regulation of establishment of protein localization to chromosome	Cct2,Cct4,Cct6a,Cct7,Cct8,Tcp1	-7.69

25	CORUM:132	CORUM	CCT complex (chaperonin containing TCP1 complex)	Cct2,Cct4,Cct7,Cct8,Tcp1	-7.53
26	CORUM:51	CORUM	CCT complex (chaperonin containing TCP1 complex)	Cct2,Cct4,Cct7,Cct8,Tcp1	-7.53
27	CORUM:52	CORUM	CCT complex (chaperonin containing TCP1 complex)	Cct2,Cct4,Cct7,Cct8,Tcp1	-7.53
28	GO:1904816	GO Biological Processes	positive regulation of protein localization to chromosome, telomeric region	Cct2,Cct4,Cct6a,Cct7,Cct8,Tcp1	-7.42
29	R-MMU-76002	Reactome Gene Sets	Platelet activation, signaling and aggregation	Aldoa,Rhob,Cd9,Fn1,Gnb1,Gnb2,Itga2b,Prkcb,Prkcd,Lgals3bp,Serpina1c,Stxbp3,Syk,Tln1,Tuba4a,Vav1,Vwf,Apbb1ip,Ola1,Tmx3,Fgg,Flna,Rap1b,Plcg2	-11.17
30	R-MMU-354194	Reactome Gene Sets	GRB2:SOS provides linkage to MAPK signaling for Integrins	Fn1,Itga2b,Tln1,Vwf,Apbb1ip,Fgg,Rap1b	-8.63
31	R-MMU-372708	Reactome Gene Sets	p130Cas linkage to MAPK signaling for integrins	Fn1,Itga2b,Tln1,Vwf,Apbb1ip,Fgg,Rap1b	-8.63
32	R-MMU-76005	Reactome Gene Sets	Response to elevated platelet cytosolic Ca2+	Aldoa,Cd9,Fn1,Itga2b,Prkcb,Lgals3bp,Serpina1c,Stxbp3,Tln1,Tuba4a,Vwf,Ola1,Tmx3,Fgg,Flna	-8.60
33	R-MMU-354192	Reactome Gene Sets	Integrin signaling	Fn1,Itga2b,Syk,Tln1,Vwf,Apbb1ip,Fgg,Rap1b	-7.94
34	R-MMU-114608	Reactome Gene Sets	Platelet degranulation	Aldoa,Cd9,Fn1,Itga2b,Lgals3bp,Serpina1c,Tln1,Tuba4a,Vwf,Ola1,Tmx3,Fgg,Flna	-7.00
35	R-MMU-76009	Reactome Gene Sets	Platelet Aggregation (Plug Formation)	Fn1,Itga2b,Syk,Tln1,Vwf,Apbb1ip,Fgg,Rap1b	-6.86
36	R-MMU-5674135	Reactome Gene Sets	MAP2K and MAPK activation	Fn1,Itga2b,Tln1,Vwf,Pebp1,Apbb1ip,Fgg,Rap1b	-6.58
37	mmu04611	KEGG Pathway	Platelet activation - Mus musculus (house mouse)	Itga2b,Syk,Tln1,Vwf,Apbb1ip,Fgg,Myk,Rap1b,Plcg2	-3.51
38	GO:0055086	GO Biological Processes	nucleobase-containing small molecule metabolic process	Adk,Parp1,Adss,Aldoa,Atp5a1,Cs,Hspa8,Ldha,Ncf2,Nme1,Ogdh,Pnp,Prps1,Rrm1,Taldo1,Tkt,Xdh,Impdh2,Prdx5,Ak3,Park7,Nampt,Atp5d,Pgls,Paics,Ola1,Cad,Shmt2,Mthfd1,Pgd,Acat1,Cps1,Gmps,Pfas,Naxe,Gars	-11.15
39	GO:0006753	GO Biological Processes	nucleoside phosphate metabolic process	Adk,Parp1,Adss,Aldoa,Atp5a1,Cs,Hspa8,Ldha,Ncf2,Nme1,Ogdh,Pnp,Prps1,Rrm1,Taldo1,Tkt,Xdh,Impdh2,Prdx5,Ak3,Park7,Nampt,Atp5d,Pgls,Paics,Ola1,Cad,Mthfd1,Pgd,Acat1,Gmps,Pfas,Naxe,Gars	-11.07
40	GO:0006163	GO Biological Processes	purine nucleotide metabolic process	Adk,Parp1,Adss,Aldoa,Atp5a1,Cs,Hspa8,Ldha,Ncf2,Nme1,Ogdh,Pnp,Prps1,Taldo1,Tkt,Xdh,Impdh2,Prdx5,Ak3,Nampt,Atp5d,Pgls,Paics,Ola1,Mthfd1,Pgd,Acat1,Gmps,Pfas	-9.22
41	GO:0072521	GO Biological Processes	purine-containing compound metabolic process	Adk,Parp1,Adss,Aldoa,Atp5a1,Cs,Hspa8,Ldha,Ncf2,Nme1,Ogdh,Pnp,Prps1,Taldo1,Tkt,Xdh,Impdh2,Prdx5,Ak3,Nampt,Atp5d,Pgls,Paics,Ola1,Shmt2,Mthfd1,Pgd,Acat1,Gmps,Pfas	-9.07
42	GO:0009161	GO Biological Processes	ribonucleoside monophosphate metabolic process	Adk,Adss,Pnp,Prps1,Xdh,Impdh2,Ak3,Paics,Cad,Gmps,Pfas	-8.80
43	GO:0009123	GO Biological Processes	nucleoside monophosphate metabolic process	Adk,Adss,Nme1,Pnp,Prps1,Xdh,Impdh2,Ak3,Paics,Cad,Gmps,Pfas	-8.71
44	GO:0009124	GO Biological Processes	nucleoside monophosphate biosynthetic process	Adk,Adss,Nme1,Pnp,Prps1,Impdh2,Paics,Cad,Gmps,Pfas	-8.65
45	GO:0009156	GO Biological Processes	ribonucleoside monophosphate biosynthetic process	Adk,Adss,Pnp,Prps1,Impdh2,Paics,Cad,Gmps,Pfas	-8.51
46	GO:0009167	GO Biological Processes	purine ribonucleoside monophosphate metabolic process	Adk,Adss,Pnp,Xdh,Impdh2,Ak3,Paics,Gmps,Pfas	-7.81
47	GO:1901605	GO Biological Processes	alpha-amino acid metabolic process	Adss,Ass1,Gls,Got1,Cad,Psat1,Shmt2,Mthfd1,Sephs1,Qdpr,Acat1,Hibch,Cps1,Gmps,Phgdh,Pfas	-6.98
48	GO:1901607	GO Biological Processes	alpha-amino acid biosynthetic process	Ass1,Gls,Got1,Cad,Psat1,Shmt2,Mthfd1,Sephs1,Phgdh	-6.37
49	GO:0044283	GO Biological Processes	small molecule biosynthetic process	Adk,Aldoa,Asah1,Ass1,Gba,Gls,Got1,Gsto1,Ldha,Pnp,Prps1,Syk,Ggt5,Park7,Pgp,Cad,Psat1,Shmt2,Mthfd1,Sephs1,Pgd,Qdpr,Plcg2,Phgdh	-6.34
50	GO:0008652	GO Biological Processes	amino acid biosynthetic process	Ass1,Gls,Got1,Cad,Psat1,Shmt2,Mthfd1,Sephs1,Phgdh	-5.86

51	GO:0009070	GO Biological Processes	serine family amino acid biosynthetic process	Psat1,Shmt2,Mthfd1,Sephs1,Phgdh	-5.27
52	GO:0006564	GO Biological Processes	L-serine biosynthetic process	Psat1,Shmt2,Phgdh	-4.71
53	GO:0046394	GO Biological Processes	carboxylic acid biosynthetic process	Ass1,Gls,Got1,Gsto1,Ldha,Syk,Ggt5,Park7,Cad,Psat1,Shmt2,Mthfd1,Sephs1,Phgdh	-4.02
54	GO:0016053	GO Biological Processes	organic acid biosynthetic process	Ass1,Gls,Got1,Gsto1,Ldha,Syk,Ggt5,Park7,Cad,Psat1,Shmt2,Mthfd1,Sephs1,Phgdh	-3.97
55	GO:0009069	GO Biological Processes	serine family amino acid metabolic process	Psat1,Shmt2,Mthfd1,Sephs1,Phgdh	-3.52
56	GO:0006541	GO Biological Processes	glutamine metabolic process	Gls,Cad,Cps1,Gmps,Phgdh,Pfas	-5.97
57	GO:0009064	GO Biological Processes	glutamine family amino acid metabolic process	Ass1,Gls,Got1,Cad,Cps1,Gmps,Phgdh,Pfas	-5.04
58	GO:0043648	GO Biological Processes	dicarboxylic acid metabolic process	Adss,Ass1,Cs,Gls,Got1,Ogdh,Me2,Shmt2,Mthfd1	-4.70
59	mmu00250	KEGG Pathway	Alanine, aspartate and glutamate metabolism - Mus musculus (house mouse)	Adss,Ass1,Gls,Got1,Cad,Cps1	-4.31
60	GO:0006531	GO Biological Processes	aspartate metabolic process	Adss,Ass1,Got1	-3.78
61	mmu00220	KEGG Pathway	Arginine biosynthesis - Mus musculus (house mouse)	Ass1,Gls,Got1,Cps1	-3.48
62	GO:0009066	GO Biological Processes	aspartate family amino acid metabolic process	Adss,Ass1,Got1,Mthfd1,Phgdh	-3.34
63	GO:0043650	GO Biological Processes	dicarboxylic acid biosynthetic process	Gls,Got1,Mthfd1	-3.01
64	R-MMU-9716542	Reactome Gene Sets	Signaling by Rho GTPases, Miro GTPases and RHOBTB3	Rhob,Arhgdib,Cct2,Cct6a,Cct7,Ckb,Dync1h1,Hsp90ab1,Lmnb1,Ncf2,Pfn1,Prkcb,Prkcd,Plk2b,Rab7,Swap70,Tuba4a,Tuba1c,Vav1,Ywhah,Ywhaq,Esyt1,Txn11,Fmnl1,Actr2,Cltc,Arhgap45,Dock8,Shmt2,Rbm39,Flna,Tubb4b	-8.05
65	R-MMU-9012999	Reactome Gene Sets	RHO GTPase cycle	Rhob,Arhgdib,Cct2,Cct6a,Cct7,Ckb,Hsp90ab1,Lmnb1,Ncf2,Plk2b,Rab7,Swap70,Vav1,Esyt1,Txn11,Fmnl1,Cltc,Arhgap45,Dock8,Shmt2,Rbm39	-5.30
66	R-MMU-9013149	Reactome Gene Sets	RAC1 GTPase cycle	Arhgdib,Ncf2,Rab7,Swap70,Vav1,Esyt1,Fmnl1,Arhgap45,Dock8,Rbm39	-3.28
67	R-MMU-9013408	Reactome Gene Sets	RHOG GTPase cycle	Arhgdib,Rab7,Vav1,Esyt1,Shmt2,Rbm39	-2.93
68	R-MMU-9013404	Reactome Gene Sets	RAC2 GTPase cycle	Ncf2,Rab7,Swap70,Vav1,Esyt1,Rbm39	-2.57
69	R-MMU-9013423	Reactome Gene Sets	RAC3 GTPase cycle	Arhgdib,Ncf2,Rab7,Swap70,Esyt1,Rbm39	-2.44
70	GO:0043604	GO Biological Processes	amide biosynthetic process	Asah1,Ass1,Eef2,Eif4a1,Gba,Rack1,Rpl9,Rps15,Rps3a1,Sars,Vars,Ggt5,Abce1,Vapa,Rplp1,Rpl11,Rps10,Eef1g,lars,Eprs,Acat1,Tars,Rpl31,Eif5,Cps1,Gars,Rpl5	-6.32
71	GO:0002181	GO Biological Processes	cytoplasmic translation	Eif4a1,Rpl9,Rps15,Rps3a1,Sars,Rplp1,Rpl11,Rps10,Rpl31,Eif5,Rpl5	-5.44
72	GO:0043043	GO Biological Processes	peptide biosynthetic process	Eef2,Eif4a1,Rack1,Rpl9,Rps15,Rps3a1,Sars,Vars,Ggt5,Abce1,Rplp1,Rpl11,Rps10,Eef1g,lars,Eprs,Tars,Rpl31,Eif5,Gars,Rpl5	-4.83
73	R-MMU-72706	Reactome Gene Sets	GTP hydrolysis and joining of the 60S ribosomal subunit	Eif4a1,Rpl9,Rps15,Rps3a1,Rplp1,Rpl11,Rps10,Rpl31,Eif5,Rpl5	-4.74
74	GO:0006412	GO Biological Processes	translation	Eef2,Eif4a1,Rack1,Rpl9,Rps15,Rps3a1,Sars,Vars,Abce1,Rplp1,Rpl11,Rps10,Eef1g,lars,Eprs,Tars,Rpl31,Eif5,Gars,Rpl5	-4.69
75	R-MMU-975956	Reactome Gene Sets	Nonsense Mediated Decay (NMD) independent of the Exon Junction Complex (EJC)	Upf1,Rpl9,Rps15,Rps3a1,Rplp1,Rpl11,Rps10,Rpl31,Rpl5	-4.58
76	mmu05171	KEGG Pathway	Coronavirus disease - COVID-19 - Mus musculus (house mouse)	C4b,Prkcb,Rpl9,Rps15,Rps3a1,Syk,Vwf,Rplp1,Rpl11,Rps10,Fgg,Rpl31,Rigi,Plcg2,Rpl5	-4.57
77	R-MMU-72613	Reactome Gene Sets	Eukaryotic Translation Initiation	Eif4a1,Rpl9,Rps15,Rps3a1,Rplp1,Rpl11,Rps10,Rpl31,Eif5,Rpl5	-4.50

78	R-MMU-72737	Reactome Gene Sets	Cap-dependent Translation Initiation	Eif4a1,Rpl9,Rps15,Rps3a1,Rplp1,Rpl11,Rps10,Rpl31,Eif5,Rpl5	-4.50
79	R-MMU-3371556	Reactome Gene Sets	Cellular response to heat stress	Fkbp4,Hspa8,Hsph1,Hspa1b,Hsp90ab1,Nup210,Rpa1,Nup214,Nup54	-5.08
80	R-MMU-3371568	Reactome Gene Sets	Attenuation phase	Fkbp4,Hspa8,Hspa1b,Hsp90ab1	-4.27
81	R-MMU-3371453	Reactome Gene Sets	Regulation of HSF1-mediated heat shock response	Hspa8,Hsph1,Hspa1b,Nup210,Rpa1,Nup214,Nup54	-4.09
82	R-MMU-3371571	Reactome Gene Sets	HSF1-dependent transactivation	Fkbp4,Hspa8,Hspa1b,Hsp90ab1	-3.31
83	mmu04612	KEGG Pathway	Antigen processing and presentation - Mus musculus (house mouse)	H2-Aa,H2-D1,Hspa8,Hspa1b,Hsp90ab1,Hspa4,Tapbp	-3.04
84	GO:0051084	GO Biological Processes	'de novo' post-translational protein folding	Cct2,Hspa8,Hsph1,Hspa1b	-2.45
85	GO:0006458	GO Biological Processes	'de novo' protein folding	Cct2,Hspa8,Hsph1,Hspa1b	-2.40
86	mmu04915	KEGG Pathway	Estrogen signaling pathway - Mus musculus (house mouse)	Ctsd,Fkbp4,Hspa8,Hspa1b,Hsp90ab1,Prkcd,Hsp90b1	-2.08
87	WP85	WikiPathways	Focal adhesion	Rhob,Col4a2,Fgr,Fn1,Ilk,Itga2b,Itga4,Itgax,Thbs1,Tln1,Vav1,Vwf,Myk,Flna,Rap1b	-6.13
88	R-MMU-216083	Reactome Gene Sets	Integrin cell surface interactions	Col18a1,Col4a2,Fn1,Itga2b,Itga4,Itgax,Vwf,Fgg,Itga1	-5.74
89	mmu04510	KEGG Pathway	Focal adhesion - Mus musculus (house mouse)	Col4a2,Fn1,Ilk,Itga2b,Itga4,Prkcb,Thbs1,Tln1,Vav1,Vwf,Myk,Itga1,Flna,Rap1b	-4.99
90	GO:0031589	GO Biological Processes	cell-substrate adhesion	Coro1a,Fn1,Ilk,Itga2b,Itga4,Itgax,Ptk2b,Thy1,Vwf,Axl,Fgg,Itga1	-4.01
91	mmu04512	KEGG Pathway	ECM-receptor interaction - Mus musculus (house mouse)	Col4a2,Fn1,Hspg2,Itga2b,Itga4,Thbs1,Vwf,Itga1	-3.87
92	GO:0007160	GO Biological Processes	cell-matrix adhesion	Fn1,Ilk,Itga2b,Itga4,Itgax,Ptk2b,Thy1,Fgg,Itga1	-3.34
93	R-MMU-1474244	Reactome Gene Sets	Extracellular matrix organization	Bgn,Col18a1,Col4a2,Ctsd,Fn1,Itga2b,Itga4,Itgax,P4hb,Vwf,Fgg,Itga1	-3.17
94	mmu04640	KEGG Pathway	Hematopoietic cell lineage - Mus musculus (house mouse)	Cd5,Cd9,Csf1r,H2-Aa,Itga2b,Itga4,Itga1	-2.93
95	mmu04151	KEGG Pathway	PI3K-Akt signaling pathway - Mus musculus (house mouse)	Col4a2,Csf1r,Fn1,Gnb1,Gnb2,Hsp90ab1,Itga2b,Itga4,Syk,Thbs1,Hsp90b1,Vwf,Ywhah,Ywhaq,Itga1	-2.84
96	GO:0050792	GO Biological Processes	regulation of viral process	Bsg,Ddb1,Ddx5,Dhx9,Ly6e,P4hb,Pfn1,Rab7,Top2a,Top2b,Axl,Ppid,Gsn,Ifi209,Ppia	-5.95
97	GO:1903900	GO Biological Processes	regulation of viral life cycle	Bsg,Ddb1,Ddx5,Ly6e,P4hb,Top2a,Top2b,Axl,Ppid,Gsn,Ifi209,Ppia	-4.65
98	GO:0045070	GO Biological Processes	positive regulation of viral genome replication	Ddb1,Top2a,Top2b,Ppid,Ppia	-3.92
99	GO:0018208	GO Biological Processes	peptidyl-proline modification	P4hb,Prdx4,Ppid,Ppif,Ppia	-3.29
100	GO:0045069	GO Biological Processes	regulation of viral genome replication	Ddb1,Ddx5,Top2a,Top2b,Ppid,Ifi209,Ppia	-2.78
101	GO:0000413	GO Biological Processes	protein peptidyl-prolyl isomerization	Ppid,Ppif,Ppia	-2.16
102	GO:1904951	GO Biological Processes	positive regulation of establishment of protein localization	Anxa7,Bsg,Cct2,Cct4,Cct6a,Cct7,Cct8,Rack1,Hcfc1,Hcls1,Hsp90ab1,Prkcb,Prkcd,Prkar1a,Tcp1,Ezr,Ppid,Ipo5,Fgg,Sri,Flna,Tardbp,Ppia	-7.16
103	GO:0070201	GO Biological Processes	regulation of establishment of protein localization	Anxa7,Bsg,Cct2,Cct4,Cct6a,Cct7,Cct8,Ctsd,Rack1,Hcfc1,Hcls1,Dnaja1,Hsp90ab1,Gbp4,Prkcb,Prkcd,Prkar1a,Tcp1,Ezr,Park7,Ppid,Ipo5,Fgg,Sri,Flna,Tardbp,Ppia,Nup54	-5.53
104	GO:0046822	GO Biological Processes	regulation of nucleocytoplasmic transport	Dhx9,Hcls1,Hsp90ab1,Gbp4,Prkcd,Park7,Ipo5,Flna,Nup214,Tardbp,Nup54	-4.73

105	GO:0042306	GO Biological Processes	regulation of protein import into nucleus	Hcls1,Hsp90ab1,Gbp4,Prkcd,Ipo5,Flna,Tardbp,Nup54	-4.21
106	GO:0051222	GO Biological Processes	positive regulation of protein transport	Anxa7,Bsg,Rack1,Hcfc1,Hcls1,Hsp90ab1,Prkcb,Prkcd,Prkar1a,Ezr,Ppid,Ipo5,Fgg,Sri,Flna,Tardbp,Ppia	-4.01
107	GO:1900182	GO Biological Processes	positive regulation of protein localization to nucleus	Parp1,Hcls1,Hsp90ab1,Prkcd,Park7,Ipo5,Flna,Tardbp	-3.61
108	GO:0042307	GO Biological Processes	positive regulation of protein import into nucleus	Hcls1,Hsp90ab1,Prkcd,Ipo5,Flna,Tardbp	-3.55
109	GO:0046824	GO Biological Processes	positive regulation of nucleocytoplasmic transport	Dhx9,Hcls1,Hsp90ab1,Prkcd,Ipo5,Flna,Tardbp	-3.52
110	GO:1900180	GO Biological Processes	regulation of protein localization to nucleus	Parp1,Hcls1,Hsp90ab1,Gbp4,Prkcd,Park7,Ipo5,Flna,Tardbp,Nup54	-3.43
111	GO:0010038	GO Biological Processes	response to metal ion	Anxa11,Anxa7,Ass1,Fn1,Hmox1,Serpina1c,Serpina1d,Thbs1,Xdh,Park7,Fgg,Ppif,Myk,Gsn,Wnk1,Fus,Plcg2,Cpne1	-5.20
112	GO:0051592	GO Biological Processes	response to calcium ion	Anxa11,Anxa7,Thbs1,Fgg,Ppif,Myk,Wnk1,Fus,Plcg2,Cpne1	-3.92
113	GO:0071277	GO Biological Processes	cellular response to calcium ion	Ppif,Myk,Wnk1,Fus,Plcg2,Cpne1	-2.57
114	GO:0071248	GO Biological Processes	cellular response to metal ion	Fn1,Hmox1,Ppif,Myk,Gsn,Wnk1,Fus,Plcg2,Cpne1	-2.48
115	GO:0030335	GO Biological Processes	positive regulation of cell migration	Aldoa,Rhob,Atp5a1,Bsg,Coro1a,Col18a1,Csf1r,Ctsh,F3,Fgr,Fn1,Rack1,Hmox1,Ilk,Itga2b,Itga4,Itgax,Pfn1,Ptk2b,Ptpcr,Ptpj,S100a11,Swap70,Thbs1,Thy1,Dock8,Myk,Synpo2,Flna,Wnk1,Plcg2	-7.35
116	GO:0040017	GO Biological Processes	positive regulation of locomotion	Aldoa,Rhob,Atp5a1,Bsg,Cf1,Coro1a,Col18a1,Csf1r,Ctsh,F3,Fgr,Fn1,Rack1,Hmox1,Ilk,Itga2b,Itga4,Itgax,Pfn1,Ptk2b,Ptpcr,Ptpj,S100a11,Swap70,Thbs1,Thy1,Dock8,Myk,Synpo2,Flna,Wnk1,Plcg2	-7.18
117	GO:0010634	GO Biological Processes	positive regulation of epithelial cell migration	Rhob,Atp5a1,Bsg,Col18a1,Ctsh,Hmox1,Pfn1,Ptk2b,Thbs1,Plcg2	-3.30
118	GO:0001525	GO Biological Processes	angiogenesis	Rhob,Bsg,Col18a1,Col4a2,Fn1,Hmox1,Hspg2,Itga2b,Ptk2b,Syk,Thbs1,Thy1,Flna,Naxe	-2.64
119	GO:0010595	GO Biological Processes	positive regulation of endothelial cell migration	Rhob,Atp5a1,Bsg,Col18a1,Hmox1,Ptk2b,Thbs1	-2.52
120	GO:0045766	GO Biological Processes	positive regulation of angiogenesis	Rhob,Ctsh,F3,Hmox1,Itgax,Prkcb,Ptk2b,Thbs1,Erap1	-2.39
121	GO:1904018	GO Biological Processes	positive regulation of vasculature development	Rhob,Ctsh,F3,Hmox1,Itgax,Prkcb,Ptk2b,Thbs1,Erap1	-2.39
122	GO:0048514	GO Biological Processes	blood vessel morphogenesis	Rhob,Bsg,Col18a1,Col4a2,Fn1,Hmox1,Hspg2,Itga2b,Ptk2b,Ptpj,Syk,Thbs1,Thy1,Myk,Flna,Naxe	-2.24
123	GO:0035239	GO Biological Processes	tube morphogenesis	Rhob,Bsg,Cf1,Col18a1,Col4a2,Ctsh,Dlg1,Fn1,Hmox1,Hspg2,Ilk,Itga2b,Pfn1,Ptk2b,Ptpj,Syk,Thbs1,Thy1,Ctsz,Myk,Mthfd1,Flna,Naxe	-2.22
124	R-MMU-72203	Reactome Gene Sets	Processing of Capped Intron-Containing Pre-mRNA	Dhx9,Hnrnp1,Hspa8,Eftud2,Nup210,Hnrnp2,Hnrnp1,Snmp40,Puf60,Prpf31,Hnrnpf,Sf3b3,Rbm39,Nup214,Fus,Nup54,Snmp200	-5.42
125	R-MMU-72163	Reactome Gene Sets	mRNA Splicing - Major Pathway	Dhx9,Hnrnp1,Hspa8,Eftud2,Hnrnp2,Hnrnp1,Snmp40,Puf60,Prpf31,Hnrnpf,Sf3b3,Rbm39,Fus,Snmp200	-5.22
126	GO:0008380	GO Biological Processes	RNA splicing	Ddx5,Dhx9,Celf2,Hspa8,Eftud2,Hnrnp1,Snmp40,Ddx17,Puf60,Prpf31,Sfpq,Sf3b1,Hnrnpf,Sf3b3,Ddx1,Rbm39,Tardbp,Fus,Snmp200	-5.07
127	R-MMU-72172	Reactome Gene Sets	mRNA Splicing	Dhx9,Hnrnp1,Hspa8,Eftud2,Hnrnp2,Hnrnp1,Snmp40,Puf60,Prpf31,Hnrnpf,Sf3b3,Rbm39,Fus,Snmp200	-5.06
128	GO:0000380	GO Biological Processes	alternative mRNA splicing, via spliceosome	Ddx5,Dhx9,Ddx17,Puf60,Sfpq	-4.53
129	mmu03040	KEGG Pathway	Spliceosome - Mus musculus (house mouse)	Ddx5,Hspa8,Hspa1b,Eftud2,Snmp40,Puf60,Prpf31,Sf3b1,Sf3b3,Fus,Snmp200	-4.19
130	GO:0043484	GO Biological Processes	regulation of RNA splicing	Ddx5,Celf2,Hnrnp1,Hspa8,Hnrnp2,Hnrnp1,Ddx17,Puf60,Hnrnpf,Sf3b3,Rbm39,Fus	-4.04
131	GO:0006397	GO Biological Processes	mRNA processing	Ddx5,Dhx9,Celf2,Hnrnp1,Hspa8,Eftud2,Hnrnp1,Snmp40,Ddx17,Puf60,Prpf31,Sfpq,Sf3b1,Hnrnpf,Sf3b3,Ddx1,Rbm39,Tardbp,Snmp200	-3.72

132	GO:0000375	GO Biological Processes	RNA splicing, via transesterification reactions	Ddx5,Dhx9,Celf2,Hspa8,Eftud2,Ddx17,Puf60,Prpf31,Sfpq,Sf3b1,Sf3b3,Snrm p200	-3.43
133	R-MMU-373760	Reactome Gene Sets	L1CAM interactions	Ap2a2,Dnm2,Iitga2b,Spta1,Tuba4a,Tuba1c,Ezr,Cltc,Ap2b1,Tubb4b	-6.96
134	R-MMU-422475	Reactome Gene Sets	Axon guidance	Ap2a2,Rhob,Col4a2,Dnm2,Hsp90ab1,Iitga2b,Pfn1,Ptpcr,Spta1,Tln1,Tuba4a,Tuba1c,Ezr,Actr2,Cltc,Ap2b1,Tubb4b	-5.81
135	R-MMU-9675108	Reactome Gene Sets	Nervous system development	Ap2a2,Rhob,Col4a2,Dnm2,Hsp90ab1,Iitga2b,Pfn1,Ptpcr,Spta1,Tln1,Tuba4a,Tuba1c,Ezr,Actr2,Cltc,Ap2b1,Tubb4b	-5.79
136	mmu05132	KEGG Pathway	Salmonella infection - Mus musculus (house mouse)	Rhob,Dync1h1,Dnm2,Hsp90ab1,Kpna4,Pfn1,Ptpcr,Rab7,Hsp90b1,Tuba4a,Tuba1c,Tubb5,Actr2,Flna,Tubb4b	-4.47
137	R-MMU-195258	Reactome Gene Sets	RHO GTPase Effectors	Rhob,Dync1h1,Ncf2,Pfn1,Prkcb,Prkcd,Tuba4a,Tuba1c,Ywhah,Ywhaq,Fmnl 1,Actr2,Flna,Tubb4b	-4.18
138	mmu04145	KEGG Pathway	Phagosome - Mus musculus (house mouse)	Coro1a,Dync1h1,H2-Aa,H2-D1,Ncf2,Rab7,Thbs1,Tuba4a,Tuba1c,Tubb5,Tubb4b	-3.50
139	R-MMU-9646399	Reactome Gene Sets	Aggrephagy	Dync1h1,Tuba4a,Tuba1c,Park7,Tubb4b	-3.40
140	R-MMU-190828	Reactome Gene Sets	Gap junction trafficking	Dnm2,Tuba4a,Tuba1c,Cltc,Tubb4b	-3.24
141	R-MMU-157858	Reactome Gene Sets	Gap junction trafficking and regulation	Dnm2,Tuba4a,Tuba1c,Cltc,Tubb4b	-3.14
142	GO:0006144	GO Biological Processes	purine nucleobase metabolic process	Adk,Pnp,Prps1,Xdh,Paics,Shmt2	-5.72
143	GO:0046112	GO Biological Processes	nucleobase biosynthetic process	Prps1,Paics,Cad,Shmt2,Cps1	-5.12
144	GO:0009113	GO Biological Processes	purine nucleobase biosynthetic process	Prps1,Paics,Shmt2	-3.41
145	R-MMU-1280218	Reactome Gene Sets	Adaptive Immune System	Ap1b1,Ap1g1,Ap2a2,Ctsc,Ctsd,Ctsh,Dync1h1,Dnm2,Iitga4,Psmb9,Psmd7,Ncf2,Prkcb,Ctsa,Psma2,Psmb10,Psmd3,Ptpcr,Ptpj,Rab7,Sec23a,Siglec1,Syk,Tabbp,Tuba4a,Tuba1c,Uba1,Ube2h,Vav1,Xdh,Psma4,Psma5,Psma6,Psmb2,Psmd12,Cltc,Herc4,Trem1,Ap2b1,Erap1,Rap1b,Tubb4b,Plcg2	-13.98
146	WP662	WikiPathways	Amino acid metabolism	Adh5,Ass1,Cs,Gls,Got1,Ldha,Ogdh,Srm,Vars,Cad,Iars,Eprs,Hibch,Cps1	-9.01
147	mmu01200	KEGG Pathway	Carbon metabolism - Mus musculus (house mouse)	Adh5,Aldoa,Cs,Esd,Got1,Ogdh,Prps1,Taldo1,Tkt,Pgls,Pgp,Me2,Psat1,Shmt 2,Pgd,Acat1,Hibch,Cps1,Phgdh	-12.61
148	R-MMU-3371497	Reactome Gene Sets	HSP90 chaperone cycle for steroid hormone receptors (SHR) in the presence of ligand	Dync1h1,Fkbp4,Hspa8,Dnaja1,Hspa1b,Hsp90ab1,Tuba4a,Tuba1c,Dnaja2,Tubb4b	-7.88
149	R-MMU-109582	Reactome Gene Sets	Hemostasis	Aldoa,Rhob,Cd9,F3,Fgr,Fn1,Gnb1,Gnb2,Iitga2b,Iitga4,Iitgax,Prkcb,Prkcd,Lgal s3bp,Prkar1a,Serpina1c,Stxbp3,Syk,Tln1,Tuba4a,Tuba1c,Vav1,Vwf,Atp2a3,Apbb1p,Ak3,Ola1,Tmx3,Dock8,Fgg,Sri,Flna,Rap1b,Tubb4b,Plcg2	-11.94
150	R-MMU-8953854	Reactome Gene Sets	Metabolism of RNA	Anp32a,Dhx9,Eif4a1,Hnrnp1,Hspa8,Hspa1b,Psmb9,Psmd7,Prkcd,Psma2,Psmb10,Psmd3,Upf1,Rpl9,Rps15,Rps3a1,Eftud2,Supt5,Psmd13,Psma4,Psma5,Psma6,Psmb2,Nup210,Rpl1,Ddx21,Hnrnp2,Hnrnp13,Snrnp40,Psmd12,Rpl11,Rps10,Puf60,Prpf31,Cnot2,Hnrnpf,Sf3b3,Rpl31,Rbm39,Nup214,Fus,Tnpo1,Nup54,Snrnp200,Rpl5	-16.45
151	R-MMU-6798695	Reactome Gene Sets	Neutrophil degranulation	Aldoa,Ap2a2,Asah1,Cct2,Cct8,Cnn2,Ctsc,Ctsd,Ctsh,Dync1h1,Eef2,Fgr,Hex b,Hp,Hspa8,Hspa1b,Hsp90ab1,Kpnb1,Iitgax,Psmd7,Pirb,Prkcd,Pnp,Ctsa,Psma2,Psmd3,Ptpcr,Ptpj,Rab7,S100a11,Serpina1c,Tubb5,Impdh2,Psmd13,Psma5,Vat1,Gyg,Vapa,Prdx4,Ctsz,Serpina1a,Actr2,Psmd12,Ilf2,Arhgap45,Pygb,Rap1b,Tubb4b,Gsn,Cpne1,Ppia,Creg1	-24.23
152	R-MMU-437239	Reactome Gene Sets	Recycling pathway of L1	Ap2a2,Dnm2,Tuba4a,Tuba1c,Ezr,Cltc,Ap2b1,Tubb4b	-6.97
153	R-MMU-194315	Reactome Gene Sets	Signaling by Rho GTPases	Rhob,Arhgdib,Cct2,Cct6a,Cct7,Ckb,Dync1h1,Hsp90ab1,Lmn1b,Ncf2,Pfn1,Prkcb,Prkcd,Ptk2b,Rab7,Swap70,Tuba4a,Tuba1c,Vav1,Ywhah,Ywhaq,Esy1,Txn1,Fmnl1,Actr2,Cltc,Arhgap45,Dock8,Shmt2,Rbm39,Flna,Tubb4b	-8.32
154	GO:0006520	GO Biological Processes	amino acid metabolic process	Adss,Ass1,Gls,Got1,Sars,Vars,Ggt5,Cad,Iars,Psat1,Eprs,Shmt2,Mthf11,Sephs1,Qdpr,Acat1,Tars,Hibch,Cps1,Gmps,Phgdh,Pfas,Gars	-9.90

155	GO:0007229	GO Biological Processes	integrin-mediated signaling pathway	Fgr,Fn1,Ilk,Itga2b,Itga4,Itgax,Itk2b,Syk,Thy1,Tln1,Vav1,Itga1	-7.76
156	WP310	WikiPathways	mRNA processing	Slc25a4,Ddx5,Dhx9,Celf2,Hnrnp1,Rpl9,Eftud2,Supt5,G3bp1,Ddx21,Hnrnp12,Park7,Hnrnp11,Snrnp40,Rpl11,Puf60,Sfpq,Pum2,Sf3b1,Hnrnpf,Sf3b3,Ddx1,Rbm39,Rnpep,Tardbp,Fus	-7.02
157	GO:0009112	GO Biological Processes	nucleobase metabolic process	Adk,Pnp,Prps1,Xdh,Paics,Cad,Shmt2,Cps1	-6.86
158	GO:0009117	GO Biological Processes	nucleotide metabolic process	Adk,Parp1,Adss,Aldoa,Atp5a1,Cs,Hspa8,Ldha,Ncf2,Nme1,Ogdh,Pnp,Prps1,Rrm1,Taldo1,Tkt,Xdh,Impdh2,Prdx5,Ak3,Park7,Nampt,Atp5d,Pgls,Paics,Ola1,Cad,Mthfd1,Pgd,Acat1,Gmps,Pfas,Naxe,Gars	-11.24
159	GO:0006518	GO Biological Processes	peptide metabolic process	Tpp1,Ctsh,Eef2,Eif4a1,Rack1,Gstt2,Gsto1,P4hb,Rpl9,Rps15,Rps3a1,Sars,Tapbp,Hsp90b1,Vars,Ggt5,Abce1,Rplp1,Park7,Rpl11,Rps10,Eef1g,Erap1,Iars,Eprs,Tars,Clic1,Rpl31,Eif5,Gars,Rpl5	-7.93
160	GO:2000147	GO Biological Processes	positive regulation of cell motility	Aldoa,Rhob,Atp5a1,Bsg,Cfl1,Coro1a,Col18a1,Csf1r,Ctsh,F3,Fgr,Fn1,Rack1,Hmox1,Ilk,Itga2b,Itga4,Itgax,Pfn1,Ptk2b,Ptpcr,Ptpj,S100a11,Swap70,Thbs1,Thy1,Dock8,Mylk,Synpo2,Flna,Wnk1,Plcg2	-7.44
161	GO:1903829	GO Biological Processes	positive regulation of protein localization	Parp1,Anxa7,Bsg,Cct2,Cct4,Cct6a,Cct7,Cct8,Cfl1,Dlg1,Rack1,Hcfc1,Hcls1,Hsp90ab1,Prkcb,Prkcd,Prkar1a,Tcp1,Ezr,Park7,Ppid,Ipo5,Ap2b1,Snx27,Fgg,Sri,Flna,Tardbp,Ppia	-7.56
162	GO:0048524	GO Biological Processes	positive regulation of viral process	Bsg,Ddb1,Dhx9,P4hb,Pfn1,Rab7,Top2a,Top2b,Axl,Ppid,Ppia	-7.76
163	GO:0006457	GO Biological Processes	protein folding	Cct2,Cct4,Cct6a,Cct7,Cct8,Fkbp4,Hspa8,Dnaja1,Hsph1,Hspd1,Hspa1b,Hsp90ab1,Hspa4,P4hb,Tcp1,Hsp90b1,Prdx4,Dnaja2,Ppid,Ppif,Ppia	-11.98
164	GO:0010035	GO Biological Processes	response to inorganic substance	Parp1,Anxa11,Anxa7,Prdx3,Rhob,Ass1,Cfl1,Fn1,Hmox1,Kpna4,Prkcd,Plec,Ptk2b,Serpina1c,Serpina1d,Prdx2,Thbs1,Xdh,Axl,Park7,Fgg,Ppif,Mylk,Cps1,Gsn,Wnk1,Fus,Plcg2,Cpne1	-7.56

* P-values were calculated based on Hypergeometric test.

Supplementary Table 6. List of the enriched terms in the ontology network for M11 of kidney dataset.

Nod e label	Canonical Name	Category	Description	Hits	LogP ⁺
1	GO:0072521	GO Biological Processes	purine-containing compound metabolic process	Atp5c1,Atp6v1b2,Eno1,Acs1,Fdxr,Gpd2,Mdh2,Mmut ,Pgam1,Acs3,Ak3,Mlycd,Sdha,Sdhb,Ndufa5,Pdhb, Mpc2,Crot,Shpk,Acly,Aldh111,Hmgcs1,Ndufs1,Dlat,V cp,Gcdh,Acs15	-20.01
2	GO:0009117	GO Biological Processes	nucleotide metabolic process	Atp5c1,Atp6v1b2,Eno1,Acs1,Fdxr,Gpd2,Mdh2,Mmut ,Pgam1,Acs3,Ak3,Mlycd,Sdha,Sdhb,Ndufa5,Pdhb, Mpc2,Crot,Shpk,Acly,Aldh111,Hmgcs1,Ndufs1,Dlat,V cp,Gcdh,Acs15	-19.56
3	GO:0006753	GO Biological Processes	nucleoside phosphate metabolic process	Atp5c1,Atp6v1b2,Eno1,Acs1,Fdxr,Gpd2,Mdh2,Mmut ,Pgam1,Acs3,Ak3,Mlycd,Sdha,Sdhb,Ndufa5,Pdhb, Mpc2,Crot,Shpk,Acly,Aldh111,Hmgcs1,Ndufs1,Dlat,V cp,Gcdh,Acs15	-19.41
4	GO:0055086	GO Biological Processes	nucleobase-containing small molecule metabolic process	Atp5c1,Atp6v1b2,Eno1,Acs1,Fdxr,Gpd2,Mdh2,Mmut ,Pgam1,Acs3,Gnpda1,Ak3,Mlycd,Sdha,Sdhb,Ndufa 5,Pdhb,Mpc2,Crot,Shpk,Acly,Aldh111,Hmgcs1,Ndufs 1,Dlat,Vcp,Gcdh,Acs15	-19.40
5	GO:0009150	GO Biological Processes	purine ribonucleotide metabolic process	Atp5c1,Atp6v1b2,Eno1,Acs1,Mmut,Pgam1,Acs3,A k3,Mlycd,Sdha,Sdhb,Ndufa5,Pdhb,Mpc2,Crot,Acly,H mgcs1,Ndufs1,Dlat,Vcp,Gcdh,Acs15	-16.86
6	GO:0009259	GO Biological Processes	ribonucleotide metabolic process	Atp5c1,Atp6v1b2,Eno1,Acs1,Mmut,Pgam1,Acs3,A k3,Mlycd,Sdha,Sdhb,Ndufa5,Pdhb,Mpc2,Crot,Acly,H mgcs1,Ndufs1,Dlat,Vcp,Gcdh,Acs15	-16.39
7	GO:0019693	GO Biological Processes	ribose phosphate metabolic process	Atp5c1,Atp6v1b2,Eno1,Acs1,Mmut,Pgam1,Acs3,A k3,Mlycd,Sdha,Sdhb,Ndufa5,Pdhb,Mpc2,Crot,Acly,H mgcs1,Ndufs1,Dlat,Vcp,Gcdh,Acs15	-16.13
8	GO:0035384	GO Biological Processes	thioester biosynthetic process	Acs1,Mmut,Mlycd,Pdhb,Mpc2,Acly,Dlat,Gcdh,Acs15	-14.79
9	GO:0071616	GO Biological Processes	acyl-CoA biosynthetic process	Acs1,Mmut,Mlycd,Pdhb,Mpc2,Acly,Dlat,Gcdh,Acs15	-14.79
10	GO:0032787	GO Biological Processes	monocarboxylic acid metabolic process	Acads,Adh1,Fabp4,Eno1,Acs1,Hsd17b8,Mmut,Pga m1,Acs3,Ugt1a2,Mlycd,Pdhb,Mpc2,Crot,Acox2,Aca d11,Acly,Thns12,Cbr4,Dlat,Aldh8a1,Gcdh,Acs15	-13.96
11	GO:0044283	GO Biological Processes	small molecule biosynthetic process	Eno1,Fbp1,Fdxr,Gpd2,Hsd17b8,Lta4h,Mdh2,Pgam1, Acs3,Spr,Gnpda1,Mlycd,Dhcr24,Acly,Asl,Hmgcs1,T hns12,Cbr4,Aldh8a1	-12.03
12	R-MMU-8978868	Reactome Gene Sets	Fatty acid metabolism	Acads,Cyp4b1,Acs1,Hsd17b8,Lta4h,Mmut,Mlycd,Cr ot,Acox2,Acad11,Acly,Cbr4,Acs15	-11.51
13	GO:0006631	GO Biological Processes	fatty acid metabolic process	Acads,Fabp4,Acs1,Hsd17b8,Mmut,Acs3,Mlycd,Cr ot,Acox2,Acad11,Acly,Thns12,Cbr4,Gcdh,Acs15	-8.92
14	GO:0008610	GO Biological Processes	lipid biosynthetic process	Acs1,Hsd17b8,Hsd3b4,Acs3,Mlycd,Dhcr24,Acly,H mgcs1,Thns12,Cbr4,Aldh8a1,Gcdh,Acs15	-5.39
15	GO:0046394	GO Biological Processes	carboxylic acid biosynthetic process	Hsd17b8,Lta4h,Acs3,Mlycd,Acly,Asl,Thns12,Cbr4,AI dh8a1	-5.23
16	GO:0016053	GO Biological Processes	organic acid biosynthetic process	Hsd17b8,Lta4h,Acs3,Mlycd,Acly,Asl,Thns12,Cbr4,AI dh8a1	-5.19
17	GO:0072330	GO Biological Processes	monocarboxylic acid biosynthetic process	Hsd17b8,Acs3,Mlycd,Acly,Thns12,Cbr4,Aldh8a1	-4.78
18	GO:0006633	GO Biological Processes	fatty acid biosynthetic process	Hsd17b8,Acs3,Mlycd,Acly,Thns12,Cbr4	-4.52
19	mmu01200	KEGG Pathway	Carbon metabolism - Mus musculus (house mouse)	Acads,Aco1,Aco2,Eno1,Fbp1,Mdh2,Mmut,Pgam1,Sd ha,Sdhb,Pdhb,Dlat	-11.78
20	mmu00020	KEGG Pathway	Citrate cycle (TCA cycle) - Mus musculus (house mouse)	Aco1,Aco2,Mdh2,Sdha,Sdhb,Pdhb,Acly,Dlat	-11.39
21	GO:0009060	GO Biological Processes	aerobic respiration	Aco1,Aco2,Atp5c1,Cox6c,Mdh2,Uqcr1,Sdha,Sdhb, Ndufa5,Pdhb,Ndufs1,Dlat	-10.57
22	GO:0045333	GO Biological Processes	cellular respiration	Aco1,Aco2,Atp5c1,Cox6c,Mdh2,Uqcr1,Sdha,Sdhb, Ndufa5,Pdhb,Ndufs1,Dlat	-9.52
23	GO:0006099	GO Biological Processes	tricarboxylic acid cycle	Aco1,Aco2,Mdh2,Sdha,Sdhb,Pdhb,Dlat	-9.47
24	GO:0015980	GO Biological Processes	energy derivation by oxidation of organic compounds	Aco1,Aco2,Atp5c1,Cox6c,Mdh2,Uqcr1,Sdha,Sdhb, Ndufa5,Pdhb,Ndufs1,Dlat	-7.96
25	WP434	WikiPathways	TCA cycle	Aco2,Mdh2,Sdha,Sdhb,Pdhb,Dlat	-7.93
26	GO:0046034	GO Biological Processes	ATP metabolic process	Atp5c1,Atp6v1b2,Eno1,Pgam1,Ak3,Sdha,Sdhb,Nduf a5,Ndufs1,Vcp	-7.87

27	R-MMU-1428517	Reactome Gene Sets	The citric acid (TCA) cycle and respiratory electron transport	Aco2,Atp5c1,Mdh2,Uqcrc1,Sdha,Sdhb,Ndufa5,Pdhb,Ndufs1,Dlat	-7.80
28	GO:0043648	GO Biological Processes	dicarboxylic acid metabolic process	Mdh2,Prodh,Sdha,Sdhb,Acly,Aldh1l1,Asl	-6.40
29	GO:0006520	GO Biological Processes	amino acid metabolic process	Mmut,Prodh,Spr,Asl,Dars,Thnsl2	-2.62
30	GO:1901605	GO Biological Processes	alpha-amino acid metabolic process	Mmut,Prodh,Spr,Asl,Thnsl2	-2.57
31	WP157	WikiPathways	Glycolysis and gluconeogenesis	Eno1,Fbp1,Mdh2,Pgam1,Pdhb,Mpc2,Dlat	-8.20
32	GO:0019318	GO Biological Processes	hexose metabolic process	Eno1,Fbp1,Gpd2,Mdh2,Pgam1,Gnpda1,Pdhb,Dlat,Galm	-6.56
33	GO:0019319	GO Biological Processes	hexose biosynthetic process	Eno1,Fbp1,Gpd2,Mdh2,Pgam1,Gnpda1	-6.52
34	GO:0006006	GO Biological Processes	glucose metabolic process	Eno1,Fbp1,Gpd2,Mdh2,Pgam1,Pdhb,Dlat,Galm	-6.26
35	GO:0005996	GO Biological Processes	monosaccharide metabolic process	Eno1,Fbp1,Gpd2,Mdh2,Pgam1,Gnpda1,Pdhb,Dlat,Galm	-6.19
36	GO:0046364	GO Biological Processes	monosaccharide biosynthetic process	Eno1,Fbp1,Gpd2,Mdh2,Pgam1,Gnpda1	-6.15
37	GO:0005975	GO Biological Processes	carbohydrate metabolic process	Eno1,Fbp1,Gpd2,Gk,Mdh2,Pgam1,Slc3a1,Gnpda1,Pdhb,Shpk,Dlat,Galm	-5.50
38	GO:0006094	GO Biological Processes	gluconeogenesis	Eno1,Fbp1,Gpd2,Mdh2,Pgam1	-5.29
39	R-MMU-70263	Reactome Gene Sets	Gluconeogenesis	Eno1,Fbp1,Mdh2,Pgam1	-4.54
40	GO:0016054	GO Biological Processes	organic acid catabolic process	Acads,Prodh,Gnpda1,Crot,Acox2,Acad11,Aldh1l1,Thnsl2,Gcdh	-5.69
41	GO:0019395	GO Biological Processes	fatty acid oxidation	Acads,Mlycd,Crot,Acox2,Acad11,Gcdh	-5.34
42	mmu04146	KEGG Pathway	Peroxisome - Mus musculus (house mouse)	Acs1,Dhrs4,Mlycd,Crot,Acox2,Acs15	-5.22
43	GO:0034440	GO Biological Processes	lipid oxidation	Acads,Mlycd,Crot,Acox2,Acad11,Gcdh	-5.14
44	GO:0006635	GO Biological Processes	fatty acid beta-oxidation	Acads,Crot,Acox2,Acad11,Gcdh	-4.92
45	GO:0046395	GO Biological Processes	carboxylic acid catabolic process	Acads,Prodh,Gnpda1,Crot,Acox2,Acad11,Aldh1l1,Gcdh	-4.77
46	GO:0033539	GO Biological Processes	fatty acid beta-oxidation using acyl-CoA dehydrogenase	Acads,Acad11,Gcdh	-4.53
47	GO:0009062	GO Biological Processes	fatty acid catabolic process	Acads,Crot,Acox2,Acad11,Gcdh	-4.10
48	GO:0030258	GO Biological Processes	lipid modification	Acads,Mlycd,Crot,Acox2,Acad11,Gcdh	-3.59
49	mmu00071	KEGG Pathway	Fatty acid degradation - Mus musculus (house mouse)	Acads,Adh1,Aldh2,Acs1,Gcdh,Acs15	-6.52
50	R-MMU-75105	Reactome Gene Sets	Fatty acyl-CoA biosynthesis	Acs1,Hsd17b8,Acly,Cbr4,Acs15	-6.12
51	GO:0046949	GO Biological Processes	fatty-acyl-CoA biosynthetic process	Acs1,Gcdh,Acs15	-5.86
52	mmu00061	KEGG Pathway	Fatty acid biosynthesis - Mus musculus (house mouse)	Acs1,Hsd17b8,Cbr4,Acs15	-5.59
53	mmu03320	KEGG Pathway	PPAR signaling pathway - Mus musculus (house mouse)	Fabp4,Acs1,Gk,Acox2,Hmgcs1,Acs15	-5.14
54	mmu01212	KEGG Pathway	Fatty acid metabolism - Mus musculus (house mouse)	Acads,Acs1,Hsd17b8,Cbr4,Acs15	-4.74
55	GO:0015908	GO Biological Processes	fatty acid transport	Fabp4,Acs1,Crot,Slc5a8,Acs15	-4.48
56	GO:0015849	GO Biological Processes	organic acid transport	Fabp4,Sfxn1,Acs1,Slc3a1,Mpc2,Crot,Slc5a8,Acs15	-4.20
57	WP2316	WikiPathways	PPAR signaling pathway	Fabp4,Acs1,Gk,Acox2,Acs15	-4.15

58	mmu00280	KEGG Pathway	Valine, leucine and isoleucine degradation - Mus musculus (house mouse)	Acads,Aldh2,Mmut,Oxct1,Mcccc1,Hmgcs1	-6.28
59	GO:0046459	GO Biological Processes	short-chain fatty acid metabolic process	Acads,Mmut,Thnsl2	-4.22
60	mmu00640	KEGG Pathway	Propanoate metabolism - Mus musculus (house mouse)	Acads,Mmut,Mlycd	-3.25
61	mmu00410	KEGG Pathway	beta-Alanine metabolism - Mus musculus (house mouse)	Acads,Aldh2,Mlycd	-3.21
62	R-MMU-77289	Reactome Gene Sets	Mitochondrial Fatty Acid Beta-Oxidation	Acads,Mmut,Acad11	-3.06
63	GO:0006101	GO Biological Processes	citrate metabolic process	Aco1,Aco2,Acly	-5.56
64	mmu00630	KEGG Pathway	Glyoxylate and dicarboxylate metabolism - Mus musculus (house mouse)	Aco1,Aco2,Mdh2,Mmut	-4.64
65	mmu01230	KEGG Pathway	Biosynthesis of amino acids - Mus musculus (house mouse)	Aco1,Aco2,Eno1,Pgam1,Asl	-4.23
66	GO:0019362	GO Biological Processes	pyridine nucleotide metabolic process	Fdxr,Gpd2,Mdh2,Shpk,Aldh1l1,Vcp	-5.68
67	GO:0072524	GO Biological Processes	pyridine-containing compound metabolic process	Fdxr,Gpd2,Mdh2,Shpk,Aldh1l1,Vcp	-5.38
68	GO:0006734	GO Biological Processes	NADH metabolic process	Gpd2,Mdh2,Vcp	-4.05
69	GO:0019674	GO Biological Processes	NAD metabolic process	Gpd2,Mdh2,Vcp	-3.06
70	GO:0006739	GO Biological Processes	NADP metabolic process	Fdxr,Shpk,Aldh1l1	-2.89
71	R-MMU-5365859	Reactome Gene Sets	RA biosynthesis pathway	Adh1,Dhrs4,Aldh8a1	-3.76
72	GO:0006081	GO Biological Processes	cellular aldehyde metabolic process	Adh1,Aldh2,Dhrs4,Aldh8a1	-3.68
73	GO:0006721	GO Biological Processes	terpenoid metabolic process	Adh1,Dhrs4,Hmgcs1,Aldh8a1	-3.28
74	GO:0042445	GO Biological Processes	hormone metabolic process	Adh1,Ctsb,Hsd17b8,Hsd3b4,Selenom,Aldh8a1	-3.16
75	GO:0006720	GO Biological Processes	isoprenoid metabolic process	Adh1,Dhrs4,Hmgcs1,Aldh8a1	-2.86
76	GO:0001523	GO Biological Processes	retinoid metabolic process	Adh1,Dhrs4,Aldh8a1	-2.38
77	GO:0016101	GO Biological Processes	diterpenoid metabolic process	Adh1,Dhrs4,Aldh8a1	-2.34
78	R-MMU-9006931	Reactome Gene Sets	Signaling by Nuclear Receptors	Adh1,Dhrs4,Pdxb,Dlat,Aldh8a1	-2.31
79	GO:0010817	GO Biological Processes	regulation of hormone levels	Adh1,Ctsb,Hsd17b8,Hsd3b4,Oxct1,Mpc2,Selenom,Tarabp,Aldh8a1	-2.24
80	GO:0045471	GO Biological Processes	response to ethanol	Adh1,Aldh2,Gk	-2.04
81	R-MMU-211945	Reactome Gene Sets	Phase I - Functionalization of compounds	Adh1,Aldh2,Cyp4b1,Fdxr,Maoa	-3.72
82	mmu00982	KEGG Pathway	Drug metabolism - cytochrome P450 - Mus musculus (house mouse)	Adh1,Maoa,Ugt1a2	-2.21
83	WP1251	WikiPathways	Metapathway biotransformation	Cyp4b1,Ugt1a2,Sult1c2,Akr7a5	-2.19
84	mmu00980	KEGG Pathway	Metabolism of xenobiotics by cytochrome P450 - Mus musculus (house mouse)	Adh1,Ugt1a2,Akr7a5	-2.18
85	R-MMU-2132295	Reactome Gene Sets	MHC class II antigen presentation	Capza2,Ctsb,Rab7,Sar1b,Actr1b	-3.39
86	GO:1901615	GO Biological Processes	organic hydroxy compound metabolic process	Aco2,Adh1,Ctsb,Fdxr,Gk,Maoa,Spr,Shpk,Dhcr24,Hmgcs1,Cbr4	-4.54
87	R-MMU-8957322	Reactome Gene Sets	Metabolism of steroids	Fdxr,Hsd3b4,Osblp3,Dhcr24,Acox2,Hmgcs1	-4.26

88	GO:0006694	GO Biological Processes	steroid biosynthetic process	Hsd17b8,Hsd3b4,Dhcr24,Hmgcs1	-2.63
89	WP4346	WikiPathways	Cholesterol metabolism with Bloch and Kandutsch-Russell pathways	Acs1,Dhcr24,Hmgcs1	-2.59
90	GO:0008202	GO Biological Processes	steroid metabolic process	Fdxr,Hsd17b8,Hsd3b4,Bdh1,Dhcr24,Hmgcs1	-2.46
91	GO:1902652	GO Biological Processes	secondary alcohol metabolic process	Aco2,Fdxr,Dhcr24,Hmgcs1	-2.23
92	mmu00330	KEGG Pathway	Arginine and proline metabolism - Mus musculus (house mouse)	Aldh2,Ckmt1,Maoa,Prodh	-3.74
93	WP79	WikiPathways	Tryptophan metabolism	Aldh2,Dhcr24,Gcdh	-2.77
94	R-MMU-196854	Reactome Gene Sets	Metabolism of vitamins and cofactors	Mmut,Nfs1,Mccc1,Aldh1l1,Slc5a8	-2.73
95	WP662	WikiPathways	Amino acid metabolism	Aco2,Adh1,Maoa,Mdh2,Mmut,Prodh,Sdha,Mccc1,Acly,Asl	-10.11
96	R-MMU-211859	Reactome Gene Sets	Biological oxidations	Adh1,Aldh2,Cyp4b1,Fdxr,Maoa,Ugt1a2,Sult1c2,Akr7a5	-4.97
97	mmu00650	KEGG Pathway	Butanoate metabolism - Mus musculus (house mouse)	Acads,Acs3,Oxct1,Bdh1,Hmgcs1	-6.58
98	WP1269	WikiPathways	Fatty acid beta-oxidation	Acads,Acs1,Gpd2,Gk,Gcdh,Acs15	-7.67
99	mmu00010	KEGG Pathway	Glycolysis / Gluconeogenesis - Mus musculus (house mouse)	Adh1,Aldh2,Eno1,Fbp1,Pgam1,Pdhb,Dlat,Galm	-8.66
100	R-MMU-71291	Reactome Gene Sets	Metabolism of amino acids and derivatives	Ckmt1,Prodh,Pdhb,Mccc1,Asl,Dlat,Gcdh	-3.47
101	R-MMU-556833	Reactome Gene Sets	Metabolism of lipids	Acads,Fabp4,Cyp4b1,Acs1,Fdxr,Gpd2,Gk,Hsd17b8,Hsd3b4,Lta4h,Mmut,Mlycd,Oxct1,Slc44a2,Osbpl3,Bdh1,Crot,Dhcr24,Acox2,Acad11,Acly,Hmgcs1,Cbr4,Cpne1,Acs15	-15.42
102	R-MMU-196849	Reactome Gene Sets	Metabolism of water-soluble vitamins and cofactors	Mmut,Nfs1,Mccc1,Aldh1l1,Slc5a8	-3.59
103	R-MMU-6798695	Reactome Gene Sets	Neutrophil degranulation	Aga,Ctsb,Lta4h,Pgam1,Rab7,Tspan14,Snap29,Slc44a2,Acly,Actr1b,Cpne1,Vcp	-4.73
104	mmu00620	KEGG Pathway	Pyruvate metabolism - Mus musculus (house mouse)	Adh1,Aldh2,Mdh2,Pdhb,Dlat	-5.48
105	R-MMU-5362517	Reactome Gene Sets	Signaling by Retinoic Acid	Adh1,Dhrs4,Pdhb,Dlat,Aldh8a1	-5.58
106	R-MMU-8979227	Reactome Gene Sets	Triglyceride metabolism	Fabp4,Gpd2,Gk	-3.58
107	mmu00380	KEGG Pathway	Tryptophan metabolism - Mus musculus (house mouse)	Aldh2,Maoa,Aldh8a1,Gcdh	-3.80
108	GO:0006066	GO Biological Processes	alcohol metabolic process	Aco2,Adh1,Fdxr,Gk,Spr,Shpk,Dhcr24,Hmgcs1,Cbr4	-4.57
109	GO:0042180	GO Biological Processes	cellular ketone metabolic process	Fdxr,Hsd3b4,Oxct1,Cbr4	-2.97
110	GO:0006091	GO Biological Processes	generation of precursor metabolites and energy	Aco1,Aco2,Adh1,Atp5c1,Cox6c,Eno1,Mdh2,Pgam1,Uqcrc1,Gnpda1,Sdha,Oxct1,Sdhb,Ndufa5,Pdhb,Crot,Shpk,Aldh1l1,Ndufs1,Dlat	-14.69
111	GO:0046496	GO Biological Processes	nicotinamide nucleotide metabolic process	Fdxr,Gpd2,Mdh2,Shpk,Aldh1l1,Vcp	-5.75
112	GO:0006163	GO Biological Processes	purine nucleotide metabolic process	Atp5c1,Atp6v1b2,Eno1,Acs1,Fdxr,Gpd2,Mdh2,Mmut,Pgam1,Acs3,Ak3,Mlycd,Sdha,Sdhb,Ndufa5,Pdhb,Mpc2,Crot,Shpk,Acly,Aldh1l1,Hmgcs1,Ndufs1,Dlat,Vcp,Gcdh,Acs15	-20.88
113	GO:0044282	GO Biological Processes	small molecule catabolic process	Acads,Adh1,Eno1,Prodh,Gnpda1,Oxct1,Crot,Acox2,Acad11,Aldh1l1,Thns12,Gcdh,Galm	-7.76
114	GO:0072350	GO Biological Processes	tricarboxylic acid metabolic process	Aco1,Aco2,Acly,Asl	-6.03

* P-values were calculated based on Hypergeometric test.

Supplementary Table 7. List of the enriched terms in the ontology network for M14 of kidney dataset.

Nod e label	Canonical Name	Category	Description	Hits	LogP*
1	GO:0009117	GO Biological Processes	nucleotide metabolic process	Atp5c1,Atp6v1b2,Eno1,Acs1,Gpd2,Mdh2,Mmut,Pgam1,Acs3,Shmt1,Ak3,Sdha,Sdhb,Ndufa5,Pdhb,Crot,Ndufs7,Acly,Aldh1l1,Ndufs1,Dlat,Vcp,Gcdh	-16.40
2	GO:0006163	GO Biological Processes	purine nucleotide metabolic process	Atp5c1,Atp6v1b2,Eno1,Acs1,Gpd2,Mdh2,Mmut,Pgam1,Acs3,Ak3,Sdha,Sdhb,Ndufa5,Pdhb,Crot,Ndufs7,Acly,Aldh1l1,Ndufs1,Dlat,Vcp,Gcdh	-16.32
3	GO:0006753	GO Biological Processes	nucleoside phosphate metabolic process	Atp5c1,Atp6v1b2,Eno1,Acs1,Gpd2,Mdh2,Mmut,Pgam1,Acs3,Shmt1,Ak3,Sdha,Sdhb,Ndufa5,Pdhb,Crot,Ndufs7,Acly,Aldh1l1,Ndufs1,Dlat,Vcp,Gcdh	-16.26
4	GO:0055086	GO Biological Processes	nucleobase-containing small molecule metabolic process	Atp5c1,Atp6v1b2,Eno1,Acs1,Gpd2,Mdh2,Mmut,Pgam1,Acs3,Shmt1,Ak3,Sdha,Sdhb,Ndufa5,Pdhb,Crot,Ndufs7,Acly,Aldh1l1,Ndufs1,Dlat,Vcp,Gcdh	-15.31
5	GO:0009150	GO Biological Processes	purine ribonucleotide metabolic process	Atp5c1,Atp6v1b2,Eno1,Acs1,Mmut,Pgam1,Acs3,Ak3,Sdha,Sdhb,Ndufa5,Pdhb,Crot,Ndufs7,Acly,Ndufs1,Dlat,Vcp,Gcdh	-14.47
6	GO:0009259	GO Biological Processes	ribonucleotide metabolic process	Atp5c1,Atp6v1b2,Eno1,Acs1,Mmut,Pgam1,Acs3,Ak3,Sdha,Sdhb,Ndufa5,Pdhb,Crot,Ndufs7,Acly,Ndufs1,Dlat,Vcp,Gcdh	-14.06
7	GO:0019693	GO Biological Processes	ribose phosphate metabolic process	Atp5c1,Atp6v1b2,Eno1,Acs1,Mmut,Pgam1,Acs3,Ak3,Sdha,Sdhb,Ndufa5,Pdhb,Crot,Ndufs7,Acly,Ndufs1,Dlat,Vcp,Gcdh	-13.84
8	GO:0072522	GO Biological Processes	purine-containing compound biosynthetic process	Atp5c1,Acs1,Mmut,Shmt1,Ak3,Sdha,Sdhb,Ndufa5,Pdhb,Ndufs7,Acly,Ndufs1,Dlat,Gcdh	-12.22
9	GO:0009152	GO Biological Processes	purine ribonucleotide biosynthetic process	Atp5c1,Acs1,Mmut,Ak3,Sdha,Sdhb,Ndufa5,Pdhb,Ndufs7,Acly,Ndufs1,Dlat,Gcdh	-11.97
10	GO:0006091	GO Biological Processes	generation of precursor metabolites and energy	Aco1,Aco2,Adh1,Atp5c1,Eno1,Mdh2,Pgam1,Sdha,Oxct1,Sdhb,Ndufa5,Pdhb,Crot,Ndufs7,Aldh1l1,Ndufs1,Dlat	-12.31
11	mmu00020	KEGG Pathway	Citrate cycle (TCA cycle) - Mus musculus (house mouse)	Aco1,Aco2,Mdh2,Sdha,Sdhb,Pdhb,Acly,Dlat	-11.84
12	GO:0009060	GO Biological Processes	aerobic respiration	Aco1,Aco2,Atp5c1,Mdh2,Sdha,Sdhb,Ndufa5,Pdhb,Ndufs7,Ndufs1,Dlat	-9.92
13	GO:0006099	GO Biological Processes	tricarboxylic acid cycle	Aco1,Aco2,Mdh2,Sdha,Sdhb,Pdhb,Dlat	-9.86
14	GO:0046034	GO Biological Processes	ATP metabolic process	Atp5c1,Atp6v1b2,Eno1,Pgam1,Ak3,Sdha,Sdhb,Ndufa5,Ndufs7,Ndufs1,Vcp	-9.65
15	GO:0009205	GO Biological Processes	purine ribonucleoside triphosphate metabolic process	Atp5c1,Atp6v1b2,Eno1,Pgam1,Ak3,Sdha,Sdhb,Ndufa5,Ndufs7,Ndufs1,Vcp	-9.01
16	GO:0045333	GO Biological Processes	cellular respiration	Aco1,Aco2,Atp5c1,Mdh2,Sdha,Sdhb,Ndufa5,Pdhb,Ndufs7,Ndufs1,Dlat	-8.96
17	GO:0009144	GO Biological Processes	purine nucleoside triphosphate metabolic process	Atp5c1,Atp6v1b2,Eno1,Pgam1,Ak3,Sdha,Sdhb,Ndufa5,Ndufs7,Ndufs1,Vcp	-8.87
18	GO:0009199	GO Biological Processes	ribonucleoside triphosphate metabolic process	Atp5c1,Atp6v1b2,Eno1,Pgam1,Ak3,Sdha,Sdhb,Ndufa5,Ndufs7,Ndufs1,Vcp	-8.84
19	R-MMU-556833	Reactome Gene Sets	Metabolism of lipids	Acads,Fabp4,Cyp4b1,Acs1,Gpd2,Gk,Hsd3b4,Lta4h,Mmut,Oxct1,Sumf2,Slc44a2,Bdh1,Crot,Acox2,Acad11,Acly	-8.81
20	GO:0044282	GO Biological Processes	small molecule catabolic process	Acads,Adh1,Eno1,Shmt1,Scly,Oxct1,Crot,Acox2,Acad11,Aldh1l1,Thnsl2,Gcdh,Galm	-8.44
21	R-MMU-8978868	Reactome Gene Sets	Fatty acid metabolism	Acads,Cyp4b1,Acs1,Lta4h,Mmut,Crot,Acox2,Acad11,Acly	-7.20
22	GO:0016054	GO Biological Processes	organic acid catabolic process	Acads,Shmt1,Scly,Crot,Acox2,Acad11,Aldh1l1,Thnsl2,Gcdh	-6.16
23	GO:0006631	GO Biological Processes	fatty acid metabolic process	Acads,Fabp4,Acs1,Mmut,Acs3,Crot,Acox2,Acad11,Acly,Thnsl2,Gcdh	-5.88
24	GO:0006635	GO Biological Processes	fatty acid beta-oxidation	Acads,Crot,Acox2,Acad11,Gcdh	-5.19
25	GO:0033539	GO Biological Processes	fatty acid beta-oxidation using acyl-CoA dehydrogenase	Acads,Acad11,Gcdh	-4.69
26	GO:0019395	GO Biological Processes	fatty acid oxidation	Acads,Crot,Acox2,Acad11,Gcdh	-4.41
27	GO:0009062	GO Biological Processes	fatty acid catabolic process	Acads,Crot,Acox2,Acad11,Gcdh	-4.36
28	WP157	WikiPathways	Glycolysis and gluconeogenesis	Eno1,Fbp1,Mdh2,Pgam1,Pdhb,Dlat	-7.01
29	GO:0006006	GO Biological Processes	glucose metabolic process	Eno1,Fbp1,Gpd2,Mdh2,Pgam1,Pdhb,Dlat,Galm	-6.68
30	GO:0019318	GO Biological Processes	hexose metabolic process	Eno1,Fbp1,Gpd2,Mdh2,Pgam1,Pdhb,Dlat,Galm	-5.92

31	GO:0005996	GO Biological Processes	monosaccharide metabolic process	Eno1,Fbp1,Gpd2,Mdh2,Pgam1,Pdhb,Dlat,Galm	-5.59
32	GO:0006094	GO Biological Processes	gluconeogenesis	Eno1,Fbp1,Gpd2,Mdh2,Pgam1	-5.56
33	GO:0019319	GO Biological Processes	hexose biosynthetic process	Eno1,Fbp1,Gpd2,Mdh2,Pgam1	-5.39
34	GO:0046364	GO Biological Processes	monosaccharide biosynthetic process	Eno1,Fbp1,Gpd2,Mdh2,Pgam1	-5.08
35	R-MMU-70263	Reactome Gene Sets	Gluconeogenesis	Eno1,Fbp1,Mdh2,Pgam1	-4.75
36	GO:0005975	GO Biological Processes	carbohydrate metabolic process	Eno1,Fbp1,Gpd2,Gk,Mdh2,Pgam1,Slc3a1,Pdhb,Dlat,Galm	-4.47
37	GO:0043648	GO Biological Processes	dicarboxylic acid metabolic process	Mdh2,Shmt1,Sdha,Sdhb,Acly,Aldh111,Asl	-6.78
38	mmu00630	KEGG Pathway	Glyoxylate and dicarboxylate metabolism - Mus musculus (house mouse)	Aco1,Aco2,Mdh2,Mmut,Shmt1	-6.47
39	GO:0072350	GO Biological Processes	tricarboxylic acid metabolic process	Aco1,Aco2,Acly,Asl	-6.26
40	mmu01230	KEGG Pathway	Biosynthesis of amino acids - Mus musculus (house mouse)	Aco1,Aco2,Eno1,Pgam1,Shmt1,Asl	-5.76
41	GO:0006101	GO Biological Processes	citrate metabolic process	Aco1,Aco2,Acly	-5.73
42	GO:0009071	GO Biological Processes	serine family amino acid catabolic process	Shmt1,Scly,Thnsl2	-4.48
43	GO:0046394	GO Biological Processes	carboxylic acid biosynthetic process	Lta4h,Acs3,Shmt1,Acly,Asl,Thnsl2,Aldh8a1	-3.84
44	GO:0016053	GO Biological Processes	organic acid biosynthetic process	Lta4h,Acs3,Shmt1,Acly,Asl,Thnsl2,Aldh8a1	-3.81
45	GO:1901605	GO Biological Processes	alpha-amino acid metabolic process	Mmut,Shmt1,Spr,Scly,Asl,Thnsl2	-3.70
46	GO:0009069	GO Biological Processes	serine family amino acid metabolic process	Shmt1,Scly,Thnsl2	-3.25
47	GO:0006520	GO Biological Processes	amino acid metabolic process	Mmut,Shmt1,Spr,Scly,Asl,Thnsl2	-2.91
48	GO:1901606	GO Biological Processes	alpha-amino acid catabolic process	Shmt1,Scly,Thnsl2	-2.25
49	GO:0072330	GO Biological Processes	monocarboxylic acid biosynthetic process	Acs3,Acly,Thnsl2,Aldh8a1	-2.25
50	mmu00071	KEGG Pathway	Fatty acid degradation - Mus musculus (house mouse)	Acads,Adh1,Aldh2,Acs1,Gcdh	-5.39
51	GO:1901568	GO Biological Processes	fatty acid derivative metabolic process	Acs1,Oxct1,Gcdh	-2.99
52	mmu00380	KEGG Pathway	Tryptophan metabolism - Mus musculus (house mouse)	Aldh2,Aldh8a1,Gcdh	-2.75
53	R-MMU-1280218	Reactome Gene Sets	Adaptive Immune System	Capza2,Cd36,Ctsb,Lgmn,Rab7,Actr1a,Sar1b,Fbxo22,Actr1b	-2.48
54	R-MMU-199977	Reactome Gene Sets	ER to Golgi Anterograde Transport	Arf4,Capza2,Actr1a,Sar1b	-2.36
55	R-MMU-446203	Reactome Gene Sets	Asparagine N-linked glycosylation	Arf4,Capza2,Actr1a,Sar1b,Vcp	-2.18
56	R-MMU-948021	Reactome Gene Sets	Transport to the Golgi and subsequent modification	Arf4,Capza2,Actr1a,Sar1b	-2.09
57	R-MMU-6807878	Reactome Gene Sets	COPI-mediated anterograde transport	Arf4,Capza2,Actr1a	-2.07
58	R-MMU-5365859	Reactome Gene Sets	RA biosynthesis pathway	Adh1,Dhrs4,Aldh8a1	-3.93
59	GO:0006081	GO Biological Processes	cellular aldehyde metabolic process	Adh1,Aldh2,Dhrs4,Aldh8a1	-3.89
60	GO:0042445	GO Biological Processes	hormone metabolic process	Adh1,Ctsb,Hsd3b4,Selenom,Aldh8a1	-2.60
61	R-MMU-9006931	Reactome Gene Sets	Signaling by Nuclear Receptors	Adh1,Dhrs4,Pdhb,Dlat,Aldh8a1	-2.55
62	GO:0001523	GO Biological Processes	retinoid metabolic process	Adh1,Dhrs4,Aldh8a1	-2.53
63	GO:0016101	GO Biological Processes	diterpenoid metabolic process	Adh1,Dhrs4,Aldh8a1	-2.49
64	GO:0006721	GO Biological Processes	terpenoid metabolic process	Adh1,Dhrs4,Aldh8a1	-2.36
65	GO:0120254	GO Biological Processes	olefinic compound metabolic process	Adh1,Hsd3b4,Dhrs4,Aldh8a1	-2.25
66	GO:0006720	GO Biological Processes	isoprenoid metabolic process	Adh1,Dhrs4,Aldh8a1	-2.05

67	GO:0045471	GO Biological Processes	response to ethanol	Adh1,Aldh2,Gk	-2.19
68	R-MMU-196849	Reactome Gene Sets	Metabolism of water-soluble vitamins and cofactors	Mmut,Shmt1,Mccc1,Aldh111,Slc5a8	-3.84
69	GO:0042558	GO Biological Processes	pteridine-containing compound metabolic process	Shmt1,Spr,Aldh111	-3.45
70	R-MMU-196854	Reactome Gene Sets	Metabolism of vitamins and cofactors	Mmut,Shmt1,Mccc1,Aldh111,Slc5a8	-2.98
71	mmu00650	KEGG Pathway	Butanoate metabolism - Mus musculus (house mouse)	Acads,Acsn3,Oxct1,Bdh1	-5.16
72	GO:0046459	GO Biological Processes	short-chain fatty acid metabolic process	Acads,Mmut,Thnsl2	-4.38
73	R-MMU-77289	Reactome Gene Sets	Mitochondrial Fatty Acid Beta-Oxidation	Acads,Mmut,Acad11	-3.22
74	WP2316	WikiPathways	PPAR signaling pathway	Fabp4,Cd36,Acs1,Gk,Acox2	-4.41
75	mmu03320	KEGG Pathway	PPAR signaling pathway - Mus musculus (house mouse)	Fabp4,Cd36,Acs1,Gk,Acox2	-4.24
76	R-MMU-8979227	Reactome Gene Sets	Triglyceride metabolism	Fabp4,Gpd2,Gk	-3.75
77	GO:0015909	GO Biological Processes	long-chain fatty acid transport	Fabp4,Cd36,Acs1	-2.80
78	GO:0006869	GO Biological Processes	lipid transport	Fabp4,Cd36,Acs1,Crot,Selenom,Slc5a8	-2.32
79	GO:0010876	GO Biological Processes	lipid localization	Fabp4,Cd36,Acs1,Crot,Selenom,Slc5a8	-2.10
80	GO:0006575	GO Biological Processes	cellular modified amino acid metabolic process	Ckmt1,Ctsb,Shmt1,Crot,Aldh111,Asl	-3.68
81	GO:1905039	GO Biological Processes	carboxylic acid transmembrane transport	Cd36,Sfxn1,Slc3a1,Sfxn3,Slc5a8	-3.60
82	GO:1903825	GO Biological Processes	organic acid transmembrane transport	Cd36,Sfxn1,Slc3a1,Sfxn3,Slc5a8	-3.58
83	GO:0015804	GO Biological Processes	neutral amino acid transport	Sfxn1,Slc3a1,Sfxn3	-2.85
84	GO:0046942	GO Biological Processes	carboxylic acid transport	Cd36,Sfxn1,Slc3a1,Sfxn3,Slc5a8	-2.39
85	GO:0003333	GO Biological Processes	amino acid transmembrane transport	Sfxn1,Slc3a1,Sfxn3	-2.13
86	R-MMU-211945	Reactome Gene Sets	Phase I - Functionalization of compounds	Adh1,Aldh2,Cyp4b1,Cyb5b	-2.91
87	WP1251	WikiPathways	Metapathway biotransformation	Cyp4b1,Ugt1a2,Sult1c2,Akr7a5	-2.38
88	mmu00980	KEGG Pathway	Metabolism of xenobiotics by cytochrome P450 - Mus musculus (house mouse)	Adh1,Ugt1a2,Akr7a5	-2.33
89	GO:0046496	GO Biological Processes	nicotinamide nucleotide metabolic process	Gpd2,Mdh2,Aldh111,Vcp	-3.51
90	GO:0019362	GO Biological Processes	pyridine nucleotide metabolic process	Gpd2,Mdh2,Aldh111,Vcp	-3.47
91	GO:0072524	GO Biological Processes	pyridine-containing compound metabolic process	Gpd2,Mdh2,Aldh111,Vcp	-3.27
92	GO:0019674	GO Biological Processes	NAD metabolic process	Gpd2,Mdh2,Vcp	-3.22
93	R-MMU-9013408	Reactome Gene Sets	RHOG GTPase cycle	Rab7,Ndufa5,Rbm39	-2.40
94	GO:0008333	GO Biological Processes	endosome to lysosome transport	Rab7,Stx7,Vcp	-2.33
95	GO:0022406	GO Biological Processes	membrane docking	Rab7,Stx3,Stx7	-2.19
96	WP662	WikiPathways	Amino acid metabolism	Aco2,Adh1,Mdh2,Mmut,Sdha,Mccc1,Acly,Asl	-7.84
97	R-MMU-211859	Reactome Gene Sets	Biological oxidations	Adh1,Aldh2,Cyp4b1,Ugt1a2,Cyb5b,Sult1c2,Akr7a5	-4.39
98	mmu01240	KEGG Pathway	Biosynthesis of cofactors - Mus musculus (house mouse)	Aldh2,Shmt1,Spr,Ugt1a2,Ak3	-3.16
99	mmu01200	KEGG Pathway	Carbon metabolism - Mus musculus (house mouse)	Acads,Aco1,Aco2,Eno1,Fbp1,Mdh2,Mmut,Pgam1,Shmt1,Sdha,Sdhb,Pdhb,Dlat	-13.93
100	WP1269	WikiPathways	Fatty acid beta-oxidation	Acads,Acs1,Gpd2,Gk,Gcdh	-6.33
101	mmu00010	KEGG Pathway	Glycolysis / Gluconeogenesis - Mus musculus (house mouse)	Adh1,Aldh2,Eno1,Fbp1,Pgam1,Pdhb,Dlat,Galm	-9.10

102	R-MMU-2132295	Reactome Gene Sets	MHC class II antigen presentation	Capza2,Ctsb,Lgmn,Rab7,Actr1a,Sar1b,Actr1b	-5.89
103	R-MMU-71291	Reactome Gene Sets	Metabolism of amino acids and derivatives	Ckmt1,Shmt1,Scly,Pdhb,Mccc1,Asl,Dlat,Gcdh	-4.70
104	GO:0006734	GO Biological Processes	NADH metabolic process	Gpd2,Mdh2,Vcp	-4.21
105	R-MMU-6798695	Reactome Gene Sets	Neutrophil degranulation	Cd36,Ctsb,Lta4h,Pgam1,Rab7,Slc44a2,Acly,Actr1b,Vcp	-3.17
106	mmu00620	KEGG Pathway	Pyruvate metabolism - Mus musculus (house mouse)	Adh1,Aldh2,Mdh2,Pdhb,Dlat	-5.75
107	R-MMU-9013405	Reactome Gene Sets	RHOD GTPase cycle	Rab7,Actn1,Rbm39	-2.85
108	R-MMU-5362517	Reactome Gene Sets	Signaling by Retinoic Acid	Adh1,Dhrs4,Pdhb,Dlat,Aldh8a1	-5.86
109	mmu00280	KEGG Pathway	Valine, leucine and isoleucine degradation - Mus musculus (house mouse)	Acads,Aldh2,Mmut,Oxct1,Mccc1	-5.19
110	GO:0015908	GO Biological Processes	fatty acid transport	Fabp4,Cd36,Acs1,Crot,Slc5a8	-4.75
111	GO:0032787	GO Biological Processes	monocarboxylic acid metabolic process	Acads,Adh1,Fabp4,Eno1,Acs1,Mmut,Pgam1,Acsm3,Ugt1a2,Pdhb,Crot,Acox2,Acad11,Acly,Thnsl2,Dlat,Aldh8a1,Gcdh	-10.15
112	GO:0006730	GO Biological Processes	one-carbon metabolic process	Sfxn1,Shmt1,Sfxn3,Aldh1l1	-5.38
113	GO:0015849	GO Biological Processes	organic acid transport	Fabp4,Cd36,Sfxn1,Acs1,Slc3a1,Crot,Sfxn3,Slc5a8	-4.60
114	GO:0072521	GO Biological Processes	purine-containing compound metabolic process	Atp5c1,Atp6v1b2,Eno1,Acs1,Gpd2,Mdh2,Mmut,Pgam1,Acsm3,Shmt1,Ak3,Sdha,Sdhb,Ndufa5,Pdhb,Crot,Ndufs7,Acly,Aldh1l1,Ndufs1,Dlat,Vcp,Gcdh	-16.77
115	GO:0044283	GO Biological Processes	small molecule biosynthetic process	Eno1,Fbp1,Gpd2,Lta4h,Mdh2,Pgam1,Acsm3,Shmt1,Spr,Acly,Asl,Thnsl2,Aldh8a1	-7.06

* P-values were calculated based on Hypergeometric test.

Supplementary Table 8. List of the enriched terms in the ontology network for muscle dataset

Nod e label	Canonical Name	Category	Description	Hits	LogP*
1	GO:0098761	GO Biological Processes	cellular response to interleukin-7	Hdgf,P4hb,Rad23b,Hnrnp1,Atic	-8.50
2	GO:0006599	GO Biological Processes	phosphagen metabolic process	Ckb,Ckmt1,Ckmt2	-6.75
3	GO:0006603	GO Biological Processes	phosphocreatine metabolic process	Ckb,Ckmt1,Ckmt2	-6.75
4	GO:0042396	GO Biological Processes	phosphagen biosynthetic process	Ckb,Ckmt1,Ckmt2	-6.75
5	GO:0046314	GO Biological Processes	phosphocreatine biosynthetic process	Ckb,Ckmt1,Ckmt2	-6.75
6	GO:0042398	GO Biological Processes	cellular modified amino acid biosynthetic process	Acadm,Ckb,Ckmt1,Ckmt2,Atic	-6.74
7	R-MMU-71291	Reactome Gene Sets	Metabolism of amino acids and derivatives	Ass1,Ckb,Ckmt1,Psmc1,Psmc5,Psmd9,Ckmt2,Ahcy	-5.50
8	R-MMU-71288	Reactome Gene Sets	Creatine metabolism	Ckb,Ckmt1,Ckmt2	-5.43
9	GO:0090407	GO Biological Processes	organophosphate biosynthetic process	Apoa1,Ckb,Ckmt1,Nme2,Impa1,Ckmt2,Atic,Ndufs6	-3.54
10	mmu00330	KEGG Pathway	Arginine and proline metabolism - Mus musculus (house mouse)	Ckb,Ckmt1,Ckmt2	-3.01
11	mmu04721	KEGG Pathway	Synaptic vesicle cycle - Mus musculus (house mouse)	Atp6v1a,Atp6v1b2,Atp6v0a1,Slc1a3,Stxbp1	-5.07
12	GO:0019725	GO Biological Processes	cellular homeostasis	Atp1b1,Atp6v1a,Atp6v1b2,Atp6v0a1,Ckb,Npm1,Ppp3ca,Nptn,Slc1a3,Sod1,Txn1	-4.53
13	GO:0097401	GO Biological Processes	synaptic vesicle lumen acidification	Atp6v1a,Atp6v1b2,Atp6v0a1	-4.45
14	GO:1902600	GO Biological Processes	proton transmembrane transport	Atp1b1,Atp6v1a,Atp6v1b2,Atp6v0a1	-3.98
15	mmu04966	KEGG Pathway	Collecting duct acid secretion - Mus musculus (house mouse)	Atp6v1a,Atp6v1b2,Atp6v0a1	-3.91
16	R-MMU-77387	Reactome Gene Sets	Insulin receptor recycling	Atp6v1a,Atp6v1b2,Atp6v0a1	-3.82
17	R-MMU-917977	Reactome Gene Sets	Transferrin endocytosis and recycling	Atp6v1a,Atp6v1b2,Atp6v0a1	-3.73
18	GO:0006873	GO Biological Processes	cellular monoatomic ion homeostasis	Atp1b1,Atp6v1a,Atp6v1b2,Atp6v0a1,Ckb,Nptn,Slc1a3,Sod1	-3.70
19	GO:0055082	GO Biological Processes	cellular chemical homeostasis	Atp1b1,Atp6v1a,Atp6v1b2,Atp6v0a1,Ckb,Ppp3ca,Nptn,Slc1a3,Sod1	-3.69
20	R-MMU-8953897	Reactome Gene Sets	Cellular responses to stimuli	Apoa1,Atp6v1a,Atp6v1b2,P4hb,Psmc1,Psmc5,Sod1,Txn1,Psmd9,Tubb1	-5.39
21	mmu05014	KEGG Pathway	Amyotrophic lateral sclerosis - Mus musculus (house mouse)	Nefm,Ppp3ca,Psmc1,Psmc5,Sod1,Psmd9,Fus,Ndufs6,Tubb1	-5.16
22	R-MMU-9711123	Reactome Gene Sets	Cellular response to chemical stress	P4hb,Psmc1,Psmc5,Sod1,Txn1,Psmd9	-4.68
23	mmu05012	KEGG Pathway	Parkinson disease - Mus musculus (house mouse)	Psmc1,Psmc5,Sod1,Txn1,Psmd9,Ndufs6,Tubb1	-4.34
24	mmu05022	KEGG Pathway	Pathways of neurodegeneration - multiple diseases - Mus musculus (house mouse)	Nefm,Ppp3ca,Psmc1,Psmc5,Sod1,Psmd9,Fus,Ndufs6,Tubb1	-4.32
25	R-MMU-450408	Reactome Gene Sets	AUF1 (hnRNP D0) binds and destabilizes mRNA	Hnrnpd,Psmc1,Psmc5,Psmd9	-4.31
26	mmu05020	KEGG Pathway	Prion disease - Mus musculus (house mouse)	Ppp3ca,Psmc1,Psmc5,Sod1,Psmd9,Ndufs6,Tubb1	-4.29
27	R-MMU-5358346	Reactome Gene Sets	Hedgehog ligand biogenesis	P4hb,Psmc1,Psmc5,Psmd9	-4.10
28	R-MMU-382551	Reactome Gene Sets	Transport of small molecules	Apoa1,Atp1b1,Atp6v1a,Atp6v1b2,Atp6v0a1,P4hb,Psmc1,Psmc5,Slc1a3,Psmd9	-4.00
29	R-MMU-390522	Reactome Gene Sets	Striated Muscle Contraction	Myl1,Tnni2,Tpm2,Vim	-5.29
30	R-MMU-397014	Reactome Gene Sets	Muscle contraction	Atp1b1,Myl1,Tnni2,Tpm2,Vim,Myl6b	-4.72
31	GO:0006936	GO Biological Processes	muscle contraction	Atp1b1,Myl1,Tnni2,Tpm2,Myl6b,Ndufs6	-4.09
32	GO:0090257	GO Biological Processes	regulation of muscle system process	Atp1b1,Ppp3ca,Sod1,Tnni2,Cmya5	-2.60
33	GO:0044057	GO Biological Processes	regulation of system process	Apoa1,Atp1b1,Hnrnpk,Ppp3ca,Sod1,Tnni2,Pebp1,Cmya5	-2.57
34	GO:0060047	GO Biological Processes	heart contraction	Atp1b1,Myl1,Sod1	-2.35

35	GO:0006941	GO Biological Processes	striated muscle contraction	Atp1b1,Myl1,Tnni2	-2.17
36	GO:0003015	GO Biological Processes	heart process	Atp1b1,Myl1,Sod1	-2.15
37	GO:1901796	GO Biological Processes	regulation of signal transduction by p53 class mediator	Hnrmpk,Mif,Npm1,Rpl5	-3.60
38	GO:0080135	GO Biological Processes	regulation of cellular response to stress	Hnrmpk,Mif,Npm1,P4hb,Sod1,Tpt1,Txn1,Ybx3,Pdia6,Fus	-3.53
39	GO:1902229	GO Biological Processes	regulation of intrinsic apoptotic signaling pathway in response to DNA damage	Hnrmpk,Mif,Tpt1	-3.46
40	GO:2001233	GO Biological Processes	regulation of apoptotic signaling pathway	Hnrmpk,Mif,P4hb,Sod1,Tpt1,Ybx3	-2.38
41	GO:2001020	GO Biological Processes	regulation of response to DNA damage stimulus	Hnrmpk,Mif,Npm1,Tpt1,Fus	-2.27
42	GO:2001243	GO Biological Processes	negative regulation of intrinsic apoptotic signaling pathway	Mif,Tpt1,Ybx3	-2.25
43	R-MMU-381426	Reactome Gene Sets	Regulation of Insulin-like Growth Factor (IGF) transport and uptake by Insulin-like Growth Factor Binding Proteins (IGFBPs)	Ahsg,Apoa1,Lgals1,P4hb,Pdia6	-4.14
44	R-MMU-15869	Reactome Gene Sets	Metabolism of nucleotides	Nme2,Txn1,Glrx,Atic	-3.43
45	GO:1903201	GO Biological Processes	regulation of oxidative stress-induced cell death	P4hb,Sod1,Txn1	-2.54
46	GO:1900407	GO Biological Processes	regulation of cellular response to oxidative stress	P4hb,Sod1,Txn1	-2.38
47	GO:1902882	GO Biological Processes	regulation of response to oxidative stress	P4hb,Sod1,Txn1	-2.26
48	GO:0032892	GO Biological Processes	positive regulation of organic acid transport	Fabp3,Mif,Stxbp1	-2.76
49	WP2316	WikiPathways	PPAR signaling pathway	Acadm,Apoa1,Fabp3	-2.49
50	GO:0032890	GO Biological Processes	regulation of organic acid transport	Fabp3,Mif,Stxbp1	-2.25
51	GO:0032370	GO Biological Processes	positive regulation of lipid transport	Apoa1,Fabp3,Mif	-2.12
52	R-MMU-8953854	Reactome Gene Sets	Metabolism of RNA	Hnrmpd,Hnrmpk,Psmc1,Psmc5,Hnrnph1,Psmc9,Fus,Rpl5	-2.91
53	GO:0045727	GO Biological Processes	positive regulation of translation	Hnrmpd,Npm1,Vim,Rpl5	-2.79
54	GO:0043488	GO Biological Processes	regulation of mRNA stability	Hnrmpd,Npm1,Vim,Fus	-2.56
55	GO:0034250	GO Biological Processes	positive regulation of amide metabolic process	Hnrmpd,Npm1,Vim,Rpl5	-2.49
56	GO:0043487	GO Biological Processes	regulation of RNA stability	Hnrmpd,Npm1,Vim,Fus	-2.42
57	GO:0061013	GO Biological Processes	regulation of mRNA catabolic process	Hnrmpd,Npm1,Vim,Fus	-2.36
58	GO:0043484	GO Biological Processes	regulation of RNA splicing	Hnrmpk,Npm1,Hnrnph1,Fus	-2.34
59	GO:1903311	GO Biological Processes	regulation of mRNA metabolic process	Hnrmpd,Hnrmpk,Npm1,Vim,Fus	-2.30
60	R-MMU-72163	Reactome Gene Sets	mRNA Splicing - Major Pathway	Hnrmpd,Hnrmpk,Hnrnph1,Fus	-2.29
61	GO:0010038	GO Biological Processes	response to metal ion	Ass1,Hnrmpd,Ppp3ca,Sod1,Fus	-2.31
62	GO:1901215	GO Biological Processes	negative regulation of neuron death	Hdgf,Npm1,Psmc1,Sod1,Stxbp1	-2.50
63	GO:0031647	GO Biological Processes	regulation of protein stability	Apoa1,Atp1b1,Npm1,Stxbp1,Rpl5	-2.29
64	GO:0043524	GO Biological Processes	negative regulation of neuron apoptotic process	Hdgf,Npm1,Sod1,Stxbp1	-2.22
65	GO:0008406	GO Biological Processes	gonad development	Ahsg,Hnrmpk,Sod1,Serpinb6a,Ybx3	-2.82
66	GO:0045137	GO Biological Processes	development of primary sexual characteristics	Ahsg,Hnrmpk,Sod1,Serpinb6a,Ybx3	-2.79
67	R-MMU-109582	Reactome Gene Sets	Hemostasis	Ahsg,Apoa1,F3,Mif,Sod1,Serpinb6a,Tubb1	-2.71
68	GO:0007548	GO Biological Processes	sex differentiation	Ahsg,Hnrmpk,Sod1,Serpinb6a,Ybx3	-2.30
69	GO:0050766	GO Biological Processes	positive regulation of phagocytosis	Ahsg,Apoa1,Sod1	-2.29
70	GO:0048608	GO Biological Processes	reproductive structure development	Ahsg,Hnrmpk,Sod1,Serpinb6a,Ybx3	-2.27
71	R-MMU-114608	Reactome Gene Sets	Platelet degranulation	Ahsg,Apoa1,Sod1	-2.07

72	R-MMU-76005	Reactome Gene Sets	Response to elevated platelet cytosolic Ca2+	Ahsg,Apoa1,Sod1	-2.02
73	GO:0006970	GO Biological Processes	response to osmotic stress	Akr1b3,Serpinb6a,Ybx3	-2.38
74	GO:0071214	GO Biological Processes	cellular response to abiotic stimulus	Akr1b3,Npm1,Serpinb6a,Ybx3,Eef1d	-2.13
75	GO:0104004	GO Biological Processes	cellular response to environmental stimulus	Akr1b3,Npm1,Serpinb6a,Ybx3,Eef1d	-2.13
76	GO:0034504	GO Biological Processes	protein localization to nucleus	Hdgf,Ppp3ca,Txn1,Nutf2	-2.26
77	GO:0046394	GO Biological Processes	carboxylic acid biosynthetic process	Aldh1a1,Akr1b3,Ass1,Mif,Slc1a3	-2.71
78	GO:0016053	GO Biological Processes	organic acid biosynthetic process	Aldh1a1,Akr1b3,Ass1,Mif,Slc1a3	-2.69
79	GO:0044283	GO Biological Processes	small molecule biosynthetic process	Aldh1a1,Akr1b3,Apoa1,Ass1,Mif,Slc1a3	-2.34
80	WP662	WikiPathways	Amino acid metabolism	Acadm,Aldh1a1,Ass1	-2.30
81	GO:0045471	GO Biological Processes	response to ethanol	Aldh1a1,Sod1,Eef1b2	-2.49
82	GO:0005975	GO Biological Processes	carbohydrate metabolic process	Acadm,Aldh1a1,Akr1b3,Impa1,Glo1,Ppp1r3a	-2.31
83	GO:0044282	GO Biological Processes	small molecule catabolic process	Acadm,Aldh1a1,Impa1,Glo1,Ahcy	-2.18
84	R-MMU-2262752	Reactome Gene Sets	Cellular responses to stress	Apoa1,Atp6v1a,Atp6v1b2,P4hb,Psmc1,Psmc5,Sod1,Txn1,Psmd9,Tubb1	-5.42
85	R-MMU-3299685	Reactome Gene Sets	Detoxification of Reactive Oxygen Species	P4hb,Sod1,Txn1	-3.65
86	R-MMU-499943	Reactome Gene Sets	Interconversion of nucleotide di- and triphosphates	Nme2,Txn1,GlrX	-3.91
87	mmu03320	KEGG Pathway	PPAR signaling pathway - Mus musculus (house mouse)	Acadm,Apoa1,Fabp3,Plin4	-3.52
88	R-MMU-8957275	Reactome Gene Sets	Post-translational protein phosphorylation	Ahsg,Apoa1,Lgals1,P4hb,Pdia6	-4.24
89	GO:0008652	GO Biological Processes	amino acid biosynthetic process	Aldh1a1,Ass1,Slc1a3	-2.80
90	GO:0044262	GO Biological Processes	cellular carbohydrate metabolic process	Acadm,Akr1b3,Impa1,Ppp1r3a	-2.70
91	GO:0006575	GO Biological Processes	cellular modified amino acid metabolic process	Acadm,Ass1,Ckb,Ckmt1,Sod1,Ckmt2,Atic,Glo1,Ahcy	-7.69
92	GO:0071470	GO Biological Processes	cellular response to osmotic stress	Akr1b3,Serpinb6a,Ybx3	-2.94
93	GO:1901657	GO Biological Processes	glycosyl compound metabolic process	Akr1b3,Atic,Ahcy	-2.63
94	GO:0003012	GO Biological Processes	muscle system process	Atp1b1,Myl1,Ppp3ca,Sod1,Tnni2,Tpm2,Myl6b,Ndufs6	-5.39
95	GO:1903312	GO Biological Processes	negative regulation of mRNA metabolic process	Hnrnpd,Hnrnpk,Npm1,Fus	-3.45
96	GO:1903828	GO Biological Processes	negative regulation of protein localization	Naca,Ppp3ca,Txn1,Psmd9,Btf3	-2.81
97	GO:0050821	GO Biological Processes	protein stabilization	Apoa1,Atp1b1,Npm1,Stxbp1,Rpl5	-3.17
98	GO:2001242	GO Biological Processes	regulation of intrinsic apoptotic signaling pathway	Hnrnpk,Mif,P4hb,Sod1,Tpt1,Ybx3	-4.31
99	GO:0061458	GO Biological Processes	reproductive system development	Ahsg,Hnrnpk,Sod1,Serpinb6a,Ybx3,Ndufs6	-3.01
100	GO:0097305	GO Biological Processes	response to alcohol	Aldh1a1,Hnrnpd,Hnrnpk,Sod1,Eef1b2	-2.72
101	GO:0010035	GO Biological Processes	response to inorganic substance	Akr1b3,Ass1,Hnrnpd,Ppp3ca,Slc1a3,Sod1,Txn1,Fus	-3.26
102	GO:0098760	GO Biological Processes	response to interleukin-7	Hdgf,P4hb,Rad23b,Hnrnp1,Atic	-8.50
103	GO:0016188	GO Biological Processes	synaptic vesicle maturation	Atp6v1a,Atp6v1b2,Atp6v0a1,Stxbp1	-5.53

* P-values were calculated based on Hypergeometric test.

Supplementary Notes

Validation for the utility of CPP via perfusion

We sought to assess the utility of dimethyl labeling through perfusion by labeling a mouse model. To demonstrate that the efficiency of dimethyl labeling via perfusion was independent of aging, we counted the number of lysine (K)-containing peptides that were labeled in the 1st labeling step in normal mice, and determined what proportion of the K-containing peptides were dimethyl labeled in the first step. We hypothesized that the proteostasis process may decline with age, thus affecting lysine accessibility due to the increased presence of misfolded protein molecules. Therefore, to assess the age-caused influence on the labeling efficiency we only considered the number of K-containing peptides that were dimethyl-labeled. In all 7 tissues, more than 90% of the lysine-containing peptides were shown to be dimethylated at the lysine residue in all age groups (6mo, 9mo, 12mo, and 15mo), and the proportion of the labeled peptide among K-containing peptides were not significantly different across all ages for all tissues (Chi-square test, P-values > 0.05) (Supplementary Figure 1). Based on the consistent proportions of the labeled peptides across ages in all 7 tissues, we concluded that vascular variability did not influence the dimethyl labeling.

Next, we used housekeeping proteins to investigate the impact of protein abundance on dimethyl labeling for all 7 tissues of the normal mice aged 6mo. Based on the Housekeeping and Reference Transcript Atlas (<https://housekeeping.unicamp.br>)¹, 143 housekeeping proteins were quantified in all of 7 tissues in our datasets, which were divided into three groups (High, Middle, Low) by protein abundance. For brain, heart, kidney, liver, spleen, and thymus, the accessibility values exhibited a wider distribution as protein abundance increased. This resulted in irregularly higher variability, which did not differ significantly among 3 groups (based on protein abundance exhibiting P-values > 0.05 (ANOVA)) for all 7 tissues (Supplementary Figure 2). The results suggest that protein abundance did not impact labeling efficiency, as the labeling reagent distributed evenly through the micro-blood vessels, uniformly exposing proteins to labeling reagents independent of protein abundance.

We also sought to assess how closely dimethyl labeling through perfusion matches results from a more conventional approach for determining protein structure using crystal structures. We chose 61 peptides from 11 housekeeping proteins (Adk, Aldh4a1, Calr, Got2, Gpi, Hsp90ab1, Npm1, Pdla4, Sod1n, Uba1, Vcp), whose crystal structures have been revealed empirically, and 3 or more labeled peptides per protein were quantified across all 7 tissues in our dataset. We then compared the accessibility values that were determined by dimethylation through perfusion with Solvent Accessible Surface Area (SASA) values derived from crystal structures². There were no peptides located in an intrinsically disordered region. Due to the differences in units and the magnitude of ranges of values, we transformed the accessibility (%) and SASA (Å) into z-scores. We found that two measurements agreed well with most values distributed within ± 1.96 standard deviation (95% confidence interval) for all 7 tissues (Supplementary Figure 3). Additionally, no specific bias based on protein abundance was observed, and there was no systematic bias for all seven tissues. By comparing dimethyl labeling through perfusion with a conventional approach, we demonstrated that our new dimethyl-

labeling approach for quantifying the accessibility was reliable and provides a viable alternative for structure determination.

Lastly, we compared the patterns of dimethyl labeling using 3 different approaches for the first labeling step: labeling through perfusion, labeling with tissue block, and labeling with tissue lysate. We analyzed brain tissue samples from 2 normal mice in technical duplicates. We selected the labeled peptides that were quantified in 3 or more of 4 measurements. First, dimethyl labeling through perfusion was compared with the method we validated in a previous study³, which is to dimethyl label proteins at the tissue block. Good correlation ($R = 0.67$) was observed between labeling performed in tissue blocks and labeling through perfusion, using 786 labeled peptides (Supplementary Figure 4A). Labeling through perfusion also showed good correlation with labeling with tissue lysates after tissue homogenization ($R = 0.69$), using 624 labeled peptides (Supplementary Figure 4B). These two coefficient correlations were not statistically different with a P-value of 0.4886. When looking at the accessibility distribution of all quantified peptides under each condition, a trend of decreasing accessibility with lower protein abundance was observed in 1st labeling with tissue lysate. There was also a slightly different pattern of the accessibility between high abundant proteins and low abundant proteins in 1st labeling with tissue block. Unlike the two other labeling techniques, 1st labeling via perfusion showed a consistent accessibility distribution across protein abundance (Supplementary Figures 5A-C). From the results, we inferred that distribution of the reagent solution for labeling through microvascular pathways allowed proteins to be uniformly dimethylated, independent of protein abundance. This contrasts with tissue block labeling, where efficiency might vary based on protein abundance in specific tissue areas with limited access to the label. While tissue lysate has uniform access to label, the protein structures would be perturbed during homogenization, which influences protein interactions or protein structures. The ratio of proteins responding to physiological perturbation may vary depending on the protein concentration, thus leading to different distributions of accessibility as the protein abundance changes.

Overall, the efficiency of dimethyl labeling through perfusion was demonstrated to be robust in vascular conditions that may differ due to aging. The perfusion-based approach allowed proteins to be labeled efficiently and uniformly independent of protein abundance. The reliability of dimethyl labeling through perfusion makes it well suited for quantitatively assessing subtle structural alterations in proteins.

Dimethylation pattern encoding tissue-specific protein conformation

With the aim of identifying the tissue-specific pattern of dimethylation, we compared the dimethylation of proteins across multiple tissues. Of a total of 23,039 peptides detected in the brain, 39.0% of peptides ($n = 8,974$) harbored lysine sites, and 8,758 of the 8,974 peptides were labeled with light- or heavy-dimethyl modifications (or both) (Supplementary Figure 6A). Of a total of 4,295 detected proteins in brain, 2,565 (59.7%) proteins were modified with dimethyl. The proportion of labeled proteins in all 7 tissues showed an even distribution, ranging from 59.7% to 65.7%. This suggests that, despite the potentially distinctive tissue-specific structures, the reagents were distributed uniformly across the mouse organs. Among the 8,974 lysine-containing peptides in brain, 8,368 were light-dimethyl labeled through perfusion, indicating a high labeling efficiency (93.2%), while 606 peptides (6.8%) were not labeled with light-dimethyl tags (Supplementary Figure 6B). Among the 606 peptides that were not light-dimethylated,

390 were solely heavy-dimethylated and 216 were not labeled with either light- or heavy-dimethyl tags. Heart showed the highest efficiency of light-dimethylation, 10,745 peptides (97.5%) of 11,018 K-containing peptides. We presume that the high light-labeling efficiency of heart is due to the extended time that reagent remained in heart before being circulated to other organs. Labeling efficiency was high and consistent across all organs, ranging from 91.5% in muscle to 97.5% in heart, with a standard deviation for all organs of 2.3%. The average of the first labeling efficiency in all 7 tissues was 94.8%. Thus, we confirmed that the first labeling via perfusion was efficient, which provided a valid basis for subsequent comparisons cross tissues.

We then plotted the dimethylation pattern in each tissue. The liver had the second highest number of identified labeled peptides ($n = 14,962$) but the highest number of tissue-specific labeled peptides ($n = 4,321$), accounting for 18% of all 24,026 tissue-specific labeled peptides (Supplementary Figures 6C and S6D). The kidney had the lowest number (11.1%, $n = 2,664$) of labeled tissue-specific peptides but ranked third lowest in the number of labeled tissue-specific proteins (11.1%, $n = 216$) (Supplementary Figure 6F). Muscle-specific proteins represented a small proportion (2.7%, $n = 53$ out of a total of 1,947) of tissue-specific proteins (Supplementary Figures 6E and 6F). However, the presence of highly abundant proteins in muscle may have affected the identification of lower abundance proteins. The top 100 muscle proteins accounted for 78.6% of all identified muscle proteins, while the top 100 proteins in the kidney and heart accounted for 37.8% and 57.5% of the identified proteins, respectively (Supplementary Figure 7A). Myosin regulatory light chain 11 (Myl11), the most abundant protein in muscle, contributed 11.3% of the total muscle protein mass, and the top 12 proteins in muscle represented more than half of the mass of the top 100 proteins (Supplementary Figure 7B). In conclusion, the labeling data provides tissue-specific protein information, which is valuable for understanding the physiological changes associated with disease in each tissue.

Validation with different AD mouse model

To validate the findings of this study, we used a different AD mouse model (5XFAD) at 2 and 12 months of age. This mouse model expresses human APP and PSEN1 transgenes with a total of five AD-linked mutation and rapidly develops amyloid pathology, with extracellular amyloid deposition beginning around 2 months. With the APP NL-F model, we highlighted the structural changes of protein communities enriched in carbon metabolism, and metal ion homeostasis. These proteins exhibited a decreased pattern in the accessibility as AD progressed (Figure 6). With the 5XFAD model, we focused on the same peptides identified in the APP NL-F model. Proteins enriched in carbon metabolism and metal ion homeostasis showed a different trend in the accessibility between two-month and twelve-month old mice; the accessibility on average decreased by 2.7% for carbon metabolism and 4.6% metal ion homeostasis as AD progressed (Supplementary Figures 22A and 22B). Although the P-value did not reach statistical significance (P-value = 0.2287 for carbon metabolism, P-value = 0.0775 for metal ion homeostasis), the effect size as measured by Cohen's d were large ($d = 0.30211$ for carbon metabolism and $d = 0.720492$ for metal ion homeostasis). Additionally, Mag and Map1a, which were highlighted in the APP NL-F model as they are highly expressed in neuronal cells and showed accessibility changes for the multiple peptides (Figures 5F

and 5H), exhibited decreased accessibility by an average of 5.8% and 4.3%, respectively (Supplementary Figures 22C and 22D). For Plp1, the lysine residue of FSKNYQDY showed a greater decrease in the accessibility in AD compared to normal control in the APP NL-F model (Figure 7C). The 5XFAD model also showed a similar pattern for this labeled peptide, with the accessibility in 12-months-old mice decreased by 7.4% (Supplementary Figure 22E). While the p-value did not reach statistical significance (P -value > 0.05), indicating no observable difference between the groups based on traditional hypothesis testing, the effect sizes measured by Cohen's d were substantial: 0.6 (Mag), 0.8 (Map1a), and 2.1 (Plp1). The discrepancy between statistical significance and effect size suggests that the limited sample size may have reduced the statistical power of the test, preventing the detection of a significant difference. Despite the non-significant p-value, the large effect sizes highlight potentially meaningful differences between the groups. This underscores that traditional significance testing may not capture substantial differences when sample sizes are limited. Therefore, while the statistical evidence based on P-value for a difference is weak, the magnitude of the effects indicates that the observed differences might be practically meaningful.

Supplementary References

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