

Varied doses and chemical forms of selenium supplementation differentially affect mouse intestinal physiology

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Supplementary materials

Materials and Methods

Fecal metabolomic analysis

Sample collection and metabolite extraction

Fresh fecal samples were collected in a 1.5-ml tube, immediately frozen in liquid nitrogen, and then stored at $-80\text{ }^{\circ}\text{C}$. The fecal samples

(60 mg) were mixed with 600- μ L pre-cooled mixture of methanol and ultra-pure water (4:1, v/v) and subjected to ice-based sonication (500 W; 6 s on, 6 s off) for 10 min to extract metabolites. After incubation at -20 °C for 30 min, the samples were centrifuged at 13000 rpm for 15 min and the supernatant (0.2 mL) was collected for liquid chromatography-mass spectrometry (LC-MS) analysis. Quality control (QC) samples were prepared by pooling the aliquots of all samples.

LC-MS conditions

The following parameters were used for LC-MS analysis. Each sample (3 μ L) was injected and separated on an Acquity BEH C18 column (100 mm \times 2.1 mm i.d., 1.7 μ m; Waters, Milford, USA). The mobile phase A was 0.1% formic acid in water, and the mobile phase B was 0.1% formic acid in acetonitrile (ACN). The column was maintained at 45 °C, and the following solvent gradient was used: 5% B–25% B over 0–1.5 min, 25% B–100% B over 1.5–10.0 min, 100% B–100% B over 10.0–13.0 min, 100% B–5% B over 13.0–13.5 min, and 13.5–14.5 min holding at 5% B at a flow rate of 0.40 mL/min. The MS data were collected in a positive or negative ion mode. The gas temperature was set at 350 °C with a gas flow of 45 L/h, and data were collected from 50 to 1,000 m/z with a mass resolution of 30000.

Data processing and quality control settings

The parameters of XCMS were the same as previously described.¹

The variables present in at least 80% of the mice of either group were extracted, and the variables with a retention time of <0.5 min (near to the dead time) were excluded owing to the high degree of ion suppression. Variables with <30% relative standard deviation in QC samples were then retained for further multivariate data analysis. The result was a three-dimensional matrix, including retention time, m/z, sample names, and normalized ion intensities.

Jejunal proteomic analysis

Protein extraction

The collected jejunum samples were immediately stored at $-80\text{ }^{\circ}\text{C}$ until the use for protein extraction. The lysis buffer (1% sodium deoxycholate, 8 M urea, and protease inhibitor) was added to the tissue samples at a ratio of 15:1. After homogenizing, the samples were kept on ice for 30 min, centrifuged at $16000\times g$ for 30 min, and the supernatants were collected.

Protein sample preparation and iTRAQ labeling

The extracted protein (100 μg in each sample) was reduced, alkylated, hydrolysis, and labeled with iTRAQ reagents as per the instruction manual (Applied Biosystems, USA). The labeled peptides were then pooled and dried using a rotary vacuum concentrator (Christ RVC 2-25, Christ, Germany). Each sample was labeled with one of eight

iTRAQ reagents. The iTRAQ experiment was performed with six replicates (three biological replicates \times two mechanical replicates in MS runs). Notably, each tube contained a mixture of jejunum tissues from three individuals, thus providing information of nine mice from each group (the Se-D, 0.15-SeL, 0.40-SeL, 0.15-SeM, and 0.40-SeM groups). Equal volumes of aliquots from 15 samples were mixed and labeled with 121 (Fig. 1) and served as an intermediate to interact the samples in three separate 8-plex iTRAQ labeling sets.

LC/LC–MS/MS analysis

The peptides were separated by high-pH reversed-phase liquid chromatography (RPLC, Waters ACQUITY UPLC) with ACQUITY UPLC BEH C18 Column 1.7 μm , 2.1 mm \times 150 mm (Waters, USA). The solvents A and B were 2% ACN (adjusted to pH 10 by ammonia) and 80% ACN (adjusted to pH 10 by ammonia), respectively. The gradient elution was performed as follows: t = 0–2 min, 0% B; t = 17 min, 3.8% B; t = 35 min, 24% B; t = 38 min, 30% B; t = 39 min, 43% B; t = 40 min, 100% B; t = 46 min, 0% B; t = 66 min, stop. LC-MS/MS analyses of all of the collected fractions were performed using an EASY-nLC 1200 system (Thermo Scientific) connected to a Q Exactive mass spectrometer (Thermo Fisher Scientific, USA). A peptide sample was loaded onto the C18 column (75 μm \times 25 cm, Thermo, USA). The solvents A and B used for separation were 2% ACN containing 0.1% formic acid and 80% ACN

containing 0.1% formic acid, respectively. The gradient elution was performed as follows: t = 0, 0% B; t=1, 5% B; t = 63, 23% B; t = 88, 48% B; t = 89, 100% B; t = 95, 100% B; t = 100, 0% B; t = 120, 0% B.

The Q Exactive mass spectrometer was operated in the data-dependent mode to switch automatically between MS and MS/MS acquisition modes. Survey full-scan MS spectra (m/z 350 to 1300) were acquired with a mass resolution of 70 K, followed by MS/MS scans with a resolution of 17.5 K.

References

1. Y. Xiao, Q. Zhai, G. Wang, X. Liu, J. Zhao, F. Tian, H. Zhang, and W. Chen, Metabolomics analysis reveals heavy metal copper-induced cytotoxicity in HT-29 human colon cancer cells, *RSC Adv.*, 2016, **6**, 78445-78456.

Figures

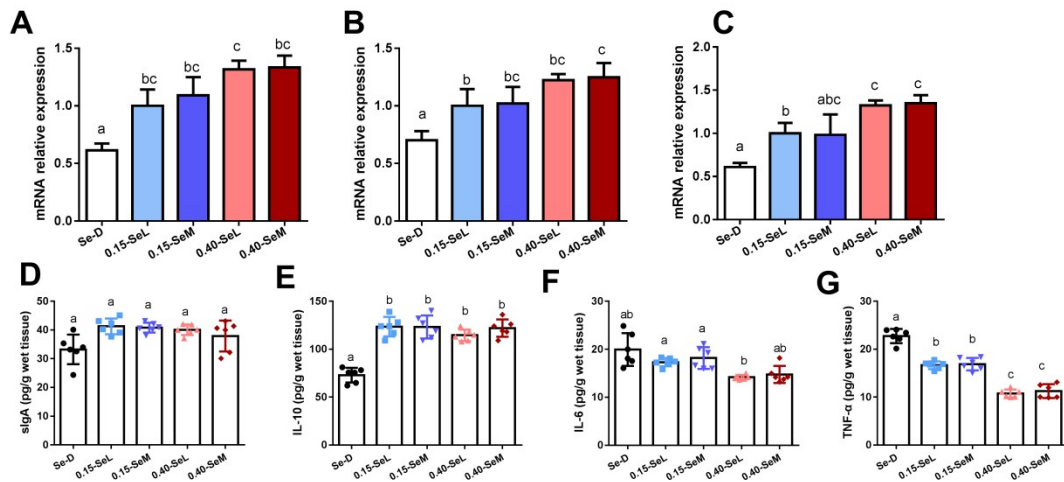


Fig. S1 Effects of different Se supplementations on the intestinal barrier and immune responses in the colon of normal mice. (A–C) mRNA expression levels of ZO-1 (A), occludin (B), and claudin-1 (C) in the colon of the mice. (D–G) Immune responses-related biomarkers, including sIgA (D), IL-10 (E), IL-6 (F), and TNF- α (G), in the colon of the mice. Values are the mean \pm SD of six mice per group. Significant differences ($P < 0.05$) between the groups are indicated with different letters above the bars.

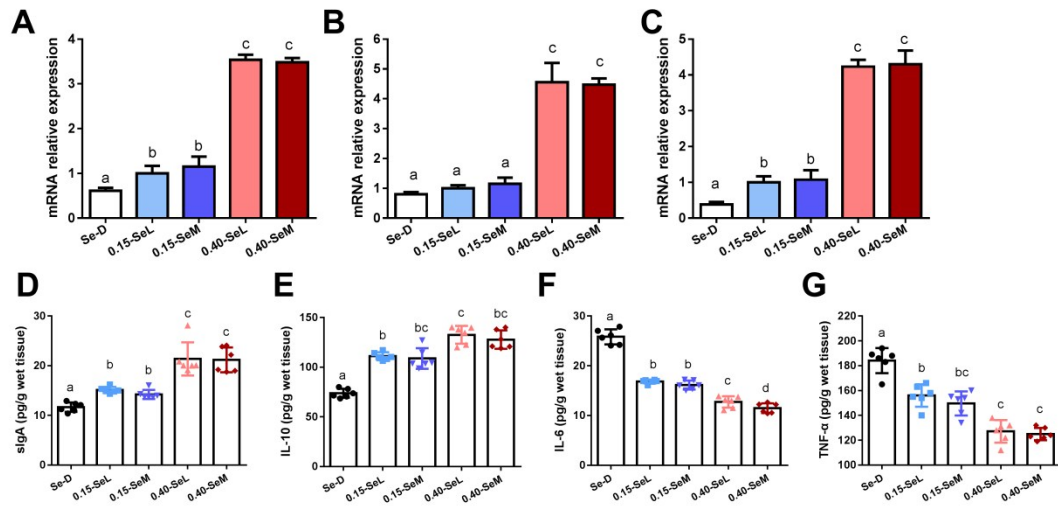


Fig. S2 Effects of different Se supplementations on the intestinal barrier and immune responses in the colon of DSS-treated mice. (A–C) mRNA expression levels of ZO-1 (A), occludin (B), and claudin-1 (C) in the colon of the mice. (D–G) Immune responses-related biomarkers including sIgA (D), IL-10 (E), IL-6 (F), and TNF- α (G), in the colon of the mice. Values are the mean \pm SD of six mice per group. Significant differences ($P < 0.05$) between the groups are indicated with different letters above the bars.

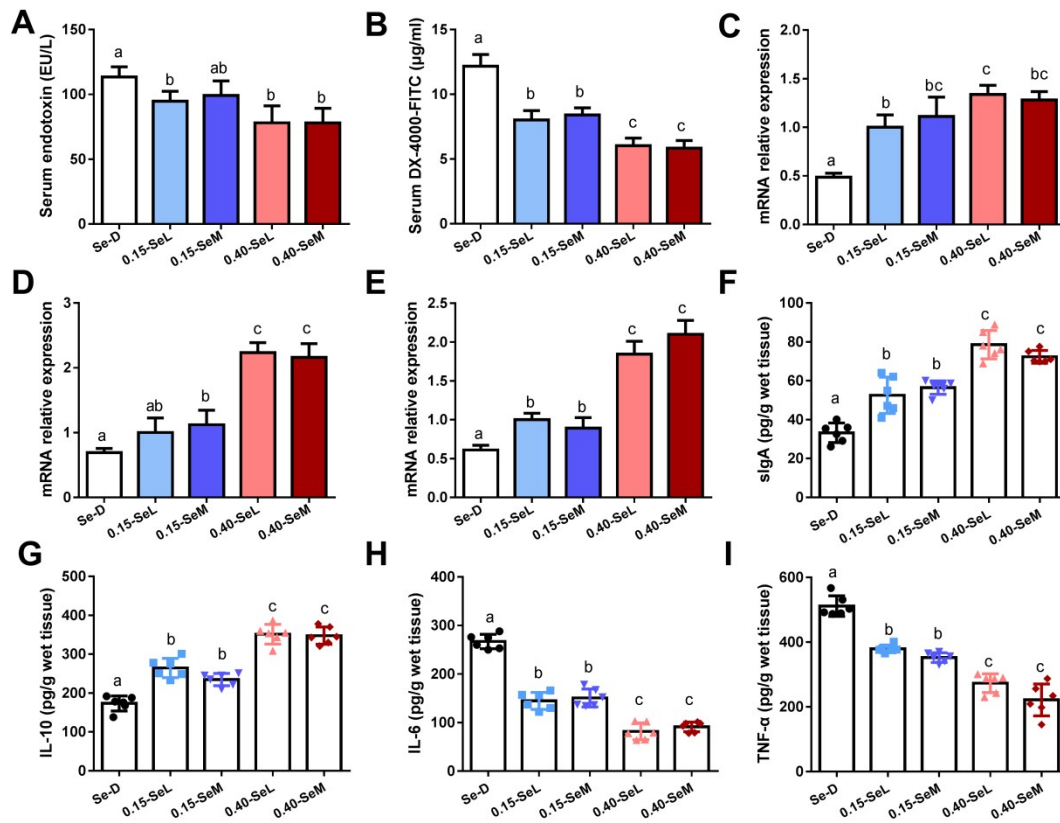


Fig. S3 Effects of different Se supplementations on the intestinal barrier and immune responses in the jejunum of ST-treated mice. (A) Serum endotoxin levels in the mice ($n = 8$). (B) Serum DX-4000-FITC levels in the mice ($n = 8$). (C–E) mRNA expression levels of ZO-1 (C), occludin (D), and claudin-1 (E) in the jejunum of the mice. (F–I) Immune response-related biomarkers, including sIgA (F), IL-10 (G), IL-6 (H), and TNF- α (I), in the jejunum of the mice ($n = 6$). Values are the mean \pm SD of six or eight mice per group. Significant differences ($P < 0.05$) between the groups are indicated with different letters above the bars.

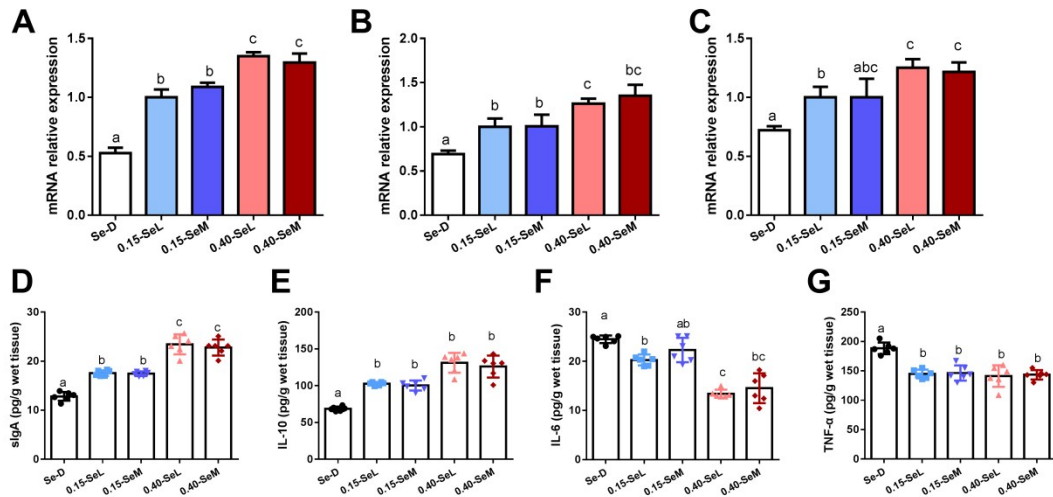


Fig. S4 Effects of different Se supplementations on the intestinal barrier and immune responses in the colon of ST-treated mice. (A–C) mRNA expression levels of ZO-1 (A), occludin (B), and claudin-1 (C) in the colon of the mice. (D–G) Immune response-related biomarkers, including sIgA (D), IL-10 (E), IL-6 (F), and TNF- α (G) in the colon of the mice. Values are the mean \pm SD of six mice per group. Significant differences ($P < 0.05$) between the groups are indicated with different letters above the bars.

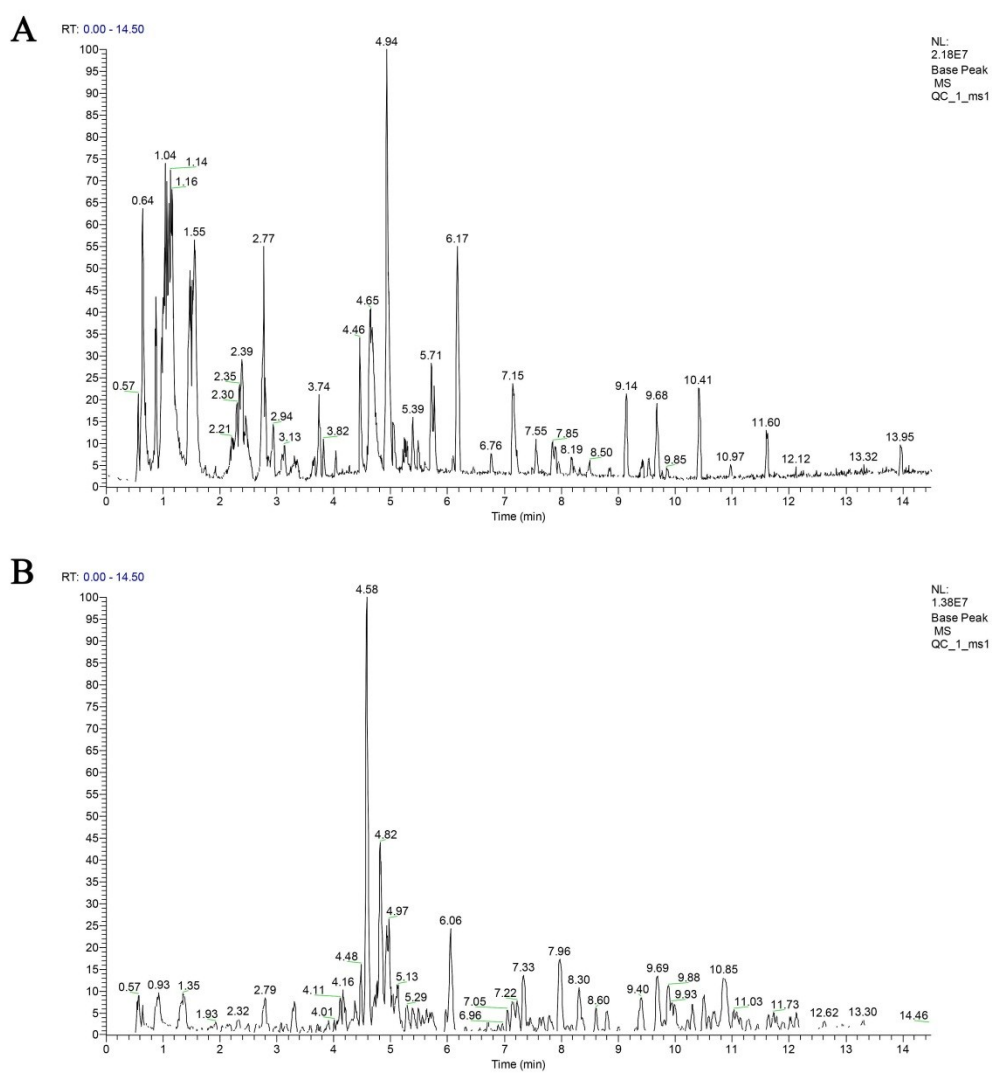


Fig. S5 Representational base peak intensity (BPI) chromatograms derived for the fecal metabolomic analysis by UPLC/MS under positive (A) and negative (B) ion modes.

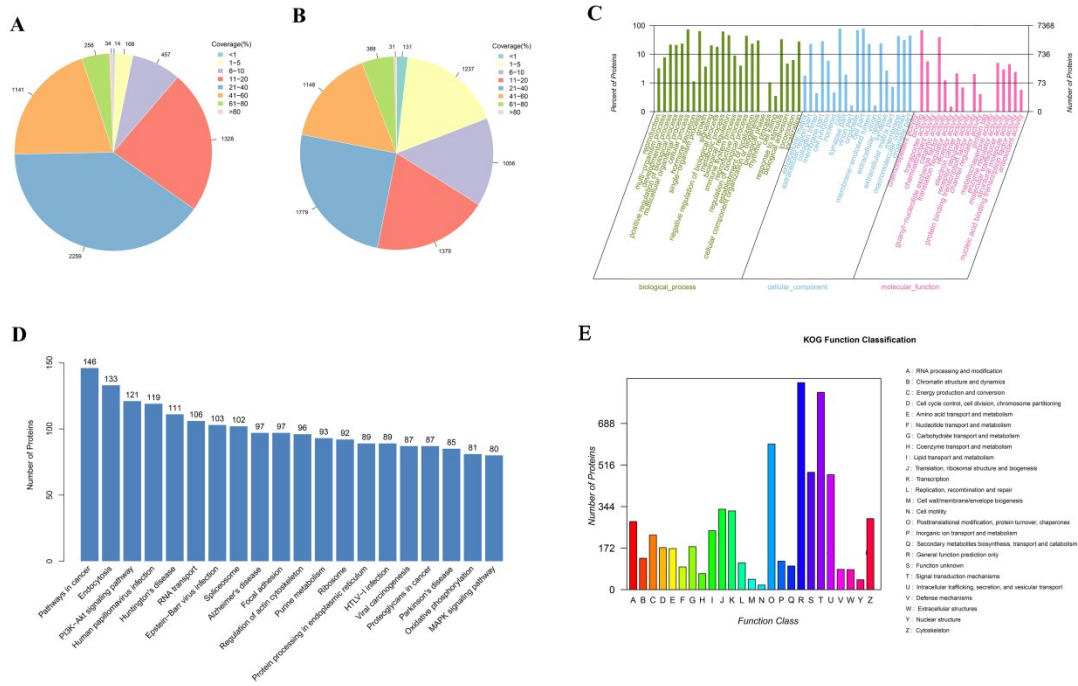


Fig. S6 Function overview of all of the proteins identified in the jejunal proteomic analysis. (A and B) Protein coverage in the first MS run (A) and the second MS run (B). (C–E) GO (C), KEGG (D) and KOG (E) analyses of all 4446 proteins identified in the different Se supplementation groups.

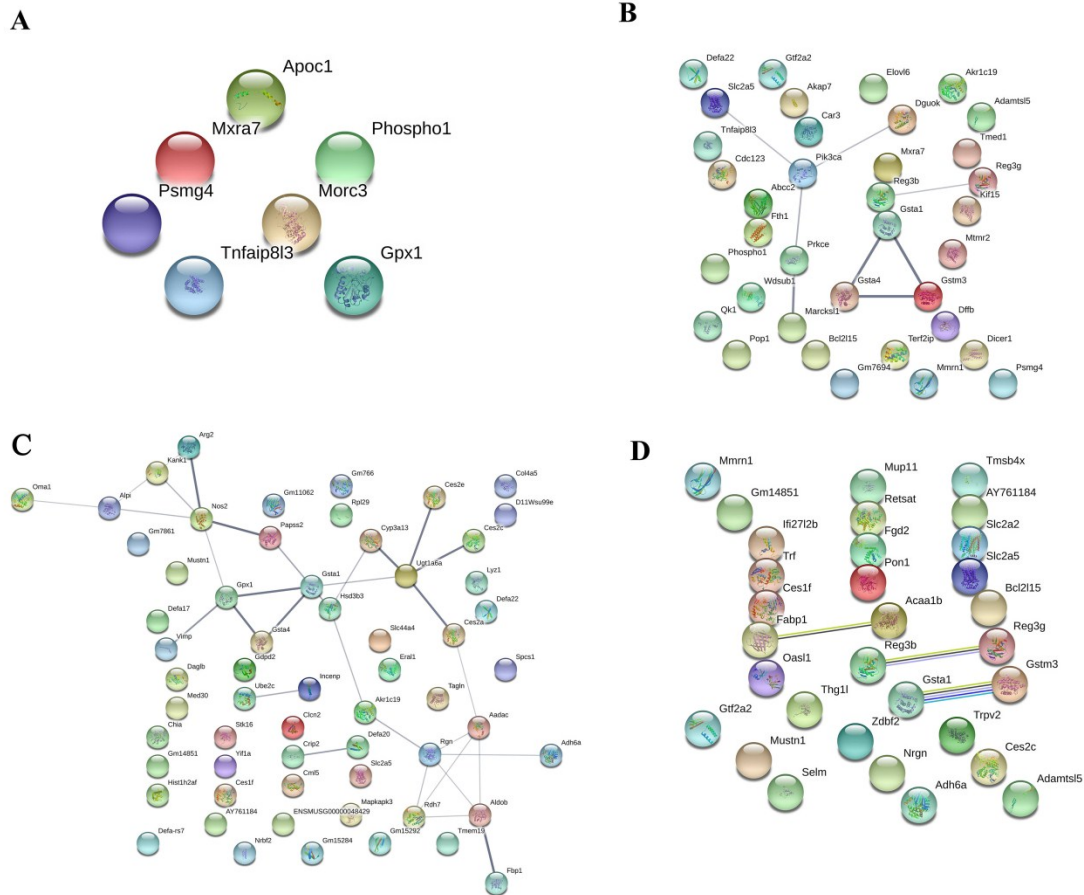


Fig. S7 Protein–protein interaction networks for the Se-D/0.15-SeL (A), 0.40-SeL/0.15-SeL(B), Se-D/0.15-SeM (C), and 0.40-SeM/0.40-SeL (D) comparisons. The networks were constructed based on the differentially expressed proteins using the string tool. Edges represent protein–protein associations. These associations are meant to be specific and meaningful, i.e., proteins jointly contribute to a shared function. The meaning of different line colors is as follows: —, from curated databases; —, experimentally determined; —, gene neighborhood; —, gene fusions; —, gene co-occurrence; —, text mining; —, co-expression; —, protein homology.

Tables

Table S1 Effects of different Se supplementations on the body weight of mice

Body weight (g)	
Se-D	23.15 ± 0.69
0.15-SeL	24.87 ± 1.22
0.15-SeM	24.89 ± 1.71
0.40-SeL	25.10 ± 1.01
0.40-SeM	24.33 ± 0.59

Values are the mean ± SD of 15 mice per group.

Table S2 Significantly altered fecal metabolites in the Se-D/0.15-SeL comparison

Super-pathway	Sub-pathway	Metabolites	VIP value	FC ^a	P value ^b
Bile acid metabolism		Bilirubin	1.11198	4.745319	0.037719
		12alpha-Hydroxy-5beta-cholesterol-3-en-24-oic Acid	4.2154	2.022339	0.045407
		glycochenodeoxycholic acid 7-sulfate	1.40734	0.467824	0.002994
		Glycocholic acid 3-glucuronide	2.39999	0.018521	0.006336
Neurosubstances		Serotonin	1.13435	0.39575	1.5E-06
		Ecgonine methyl ester	6.51579	0.197386	1.03E-05
		Nervonic acid	6.56631	4.09234	0.000712
		Melatonin	1.92426	0.331674	2.73E-05
Vitamins	Vitamin D	4,4-difluorovitamin D3 / 4,4-difluorocholecalciferol	2.70592	4.830988	0.000162
		24,24-difluoro-1alpha,25-dihydroxy-26,27-dimethylvitamin D3 / 24,24-difluoro-1alpha,25-dihydroxy-26,27-dimethylcholecalciferol	2.10573	3.648916	0.000719
		26,26,26-trifluoro-25-hydroxy-27-norvitamin D3 / 26,26,26-trifluoro-25-hydroxy-27-norcholecalciferol	1.00309	2.286718	2.21E-06
	Vitamin B6	Pyridoxamine	1.41104	0.263022	0.000448
Amino acids	Lysine	Epsilon-(gamma-Glutamyl)-lysine	2.38557	0.269455	0.00184
	Histidine	N-palmitoyl histidine	1.01284	0.473089	0.044666
	Tryptophan metabolism	Indoleacetic acid	1.41296	0.427967	0.0096
	Isoleucine	N-oleoyl isoleucine	1.18324	0.409617	0.00013
	Tryptophan metabolism	Indolelactic acid	3.43422	0.402127	1.89E-06
	Histidine	L-Histidine	1.52805	0.257568	0.003078
	Sulfur containing amino acids	N-oleoyl methionine	1.08236	4.554149	0.003284
		5-Methyltetrahydrofolic acid	3.60857	0.130514	0.005641
Glycine	N-oleoyl glycine	1.03021	2.649554	0.000279	

	Arginine biosynthesis	N-Acetylmethionine	2.12362	0.253828	3.4E-07
	Homoserine	N-(3S-hydroxy-butanoyl)-homoserine lactone	2.89208	0.198993	0.001318
		N-butanoyl-homoserine lactone	5.76281	0.400755	6.3E-07
		N-heptanoyl-homoserine lactone	7.59261	0.161339	0.00208
Fatty acids	Long chain unsaturated fatty acids and their derivatives	Lesquerolic acid	8.89117	0.436771	0.004373
		22-tricosenoic acid	7.76763	4.504038	0.000119
		24-hydroxy-10Z-tetracosenoic acid	8.60159	2.808366	0.000986
		2-propyl-9Z-octadecenoic Acid	3.26708	6.7815	8.63E-05
		Mycolipenic acid (C25)	9.34617	3.653569	0.000737
		28:3(5Z,9Z,21Z)	1.45931	2.062528	2.07E-05
		25:2(5Z,9Z)(23Me)	2.56801	3.173515	0.004754
		6-bromo-docosa-5E,9Z-dienoic acid	1.2372	0.342756	0.008136
	Long chain saturated fatty acids and their derivatives	12-bromo-octadecanoic acid	1.43854	0.381267	1.31E-06
		2-hydroxy-tricosanoic acid	3.38175	4.029593	9.95E-05
		Heptadecanoic acid	6.13827	3.398736	8.1E-05
		24-hydroxy-tetracosanoic acid	4.51481	3.185718	0.00083
		Pristanic acid	3.7659	2.835295	0.003092
		2-oxo-tricosanoic acid	1.05847	2.68558	0.02811
		Pentadecanoic acid	1.82315	2.297082	0.00514
	Medium chain fatty acids and their derivatives	9R,10S-dihydroxy-stearic acid	4.27656	2.07132	0.000126
		N-(6-aminohexanoyl)-6-aminohexanoic acid	6.29186	0.135088	0.000545
5-oxo-7-octenoic acid		2.50475	0.419555	0.023825	
Diprotic acids and their derivatives	2-amino-8-oxo-9,10-epoxy-decanoic acid	9.71078	0.128726	1.77E-05	
	Eicosanedioic acid	1.2935	7.745093	7.84E-05	
Carbohydrate metabolism		5-Hydroxy-7,8-dimethoxyflavanone 5-rhamnoside	1.30968	0.342789	0.026159
		dihydrophaseic acid 4-O-beta-D-glucoside	2.13498	2.427102	0.009372
Antibiotics	Antibiotics	10-Deoxymethymycin	2.53523	3.62771	0.001756
Alkanes/ Hydrocarbons		6Z,9Z-Docosadiene	1.89508	6.124374	6.88E-05
		9,10-Epoxy-3Z,6Z-tricosadiene	2.76506	3.86578	0.001263
Alcohols		Nitenin	1.16588	14.96872	1.25E-07
		2,6,8,12-Tetramethyl-2,4-tridecadien-1-ol	3.19284	3.405357	9.61E-05
		6Z-Heneicosen-11-ol	4.9172	3.378709	0.000101
		Panaxydol chlorohydrine	1.16224	2.908549	0.005501
		11Z-eicosen-1-ol	1.17022	2.353323	0.022243
		9-pentadecen-1-ol	9.26866	2.131542	0.000147
		6-Ketoestriol	1.0418	0.015055	0.003897
Aldehydes		2-dodecenal	2.85319	9.697252	3.39E-05
		10Z-Nonadecenal	1.41385	2.823455	0.003212
		2-decene-4,6,8-trien-1-al	1.46591	0.262492	0.001964
Lipid metabolism	Lipid biosynthesis	Dodecanoylcarnitine	4.33506	2.253399	4.7E-05
	Glycerophospholipids metabolism	PA(13:0/20:3(8Z,11Z,14Z))	1.59048	4.693227	7.44E-07

		PE(14:0/20:1(11Z))	4.20449	2.440155	0.000628
		PC(15:0/18:3(6Z,9Z,12Z))	1.13902	2.397449	0.00973
		PS(16:0/16:0)	1.32945	2.283652	0.01178
		PE(14:0/P-18:0)	1.01992	2.160331	0.000106
		PG(13:0/22:0)	1.11037	2.086772	0.0098
		CPA(18:0)	1.14	0.492719	0.009228
		PC(P-17:0/0:0)	2.15012	0.474005	0.000155
		PS(O-16:0/18:2(9Z,12Z))	2.74271	0.430267	1.49E-05
		PA(22:1(11Z)/0:0)	1.46916	0.417669	0.014856
		PE(O-16:0/15:0)	3.09194	0.407563	6.83E-05
		PG(O-18:0/20:3(8Z,11Z,14Z))	1.67542	0.404793	0.000989
		LysoPC(P-18:0)	2.09968	0.394092	0.002952
		PC(O-14:0/15:0)	8.75641	0.381714	3.62E-05
		PG(22:6(4Z,7Z,10Z,13Z,16Z,19Z)/22:6(4Z,7Z,10Z,13Z,16Z,19Z))	2.29949	0.38032	0.006239
		PS(15:0/0:0)	1.40393	0.371359	4.74E-05
		PI(O-16:0/0:0)	5.982	0.367007	0.000117
		PC(O-16:0/0:0)	5.83258	0.341182	0.007486
		PG(10:0/10:0)	2.05919	0.280087	5.58E-05
		PG(O-16:0/19:1(9Z))	1.03657	0.246507	0.000655
		PI(16:0/0:0)	1.00255	0.22227	8.69E-06
		PI(13:0/20:5(5Z,8Z,11Z,14Z,17Z))	1.19969	0.20191	0.000199
		PG(O-16:0/17:2(9Z,12Z))	1.52326	0.156852	0.008711
		PC(O-14:0/16:0)	4.12867	0.325234	0.000118
	Cholesterol	Cholest-5-ene	2.68411	2.774294	0.000687
		24-norcholesterol	1.50111	2.072878	0.000222
		15,20-dihydroxycholest-4,14-dien-3,16-dione	1.67285	2.067256	0.001343
		cholesteryl beta-D-glucoside	2.30224	0.335648	0.004005
	Isoprenoids	Gibberellin A20	1.9875	2.019044	2.58E-05
		Gibberellin A9	1.94777	0.022024	0.000181
		Ngaione (-)	1.46783	2.01645	2.78E-07
		20:2(5Z,9Z)(11Me,15Me,19Me)	1.42664	10.46879	0.000186
	Glycerolipids	DG(17:2(9Z,12Z)/22:5(7Z,10Z,13Z,16Z,19Z)/0:0)[iso2]	1.22941	3.943995	0.000146
		DG(17:2(9Z,12Z)/22:4(7Z,10Z,13Z,16Z)/0:0)[iso2]	3.09315	2.136885	0.000166
	Sphingolipids/ sphingosine	Cer(d18:0/14:0)	1.2145	13.27052	6.62E-06
		Cer(d18:0/15:0)	2.47798	6.446123	3.42E-05
		Cer(d18:1/14:0)/N-myristoylsphingosine	1.51562	3.079244	0.00064
		C19 Sphingosine-1-phosphate	1.89247	0.485883	0.001837
		C16 Sphinganine-1-phosphate	3.59881	0.278316	0.002839
		Cer(d16:1/17:0)	3.55825	2.734519	0.001128
		Cer(d18:0/h17:0)	6.58307	2.564602	1.3E-05
		Cer(d18:2/14:0)	1.20976	0.436225	0.001242

		Cer(t18:0/16:0)	4.95114	3.262675	1.8E-05
	Phosphocholine	PC(O-14:0/O-1:0)	1.89092	0.474855	0.037794
		PC(O-18:0/O-2:0)	1.23818	0.484419	0.006597
		PC(O-16:0/O-1:0)	1.91994	0.392796	0.001452
		PC(O-8:0/O-8:0)	2.18348	0.332826	0.008113
	Steroids/ Sterols	3-O-(Rhaa1-4(Rhaa1-2)Glc)-26-O-(Glc)-(25R)-furost-5-en-3beta,22,26-triol	1.75721	0.159756	0.00476
		Campestanol	2.60135	11.07493	0.000625
		Campesterol	1.48666	8.934155	8.87E-08
		1,3,5(10)-estratrien-17-one-3,7,8-triol	1.86366	0.01813	0.000404
		Tetrahydrodeoxycorticosterone	1.83304	2.171491	0.01987
		6beta-hydroxytestosterone	1.24158	0.013943	4.68E-07
Incretions		Androsterone sulfate	1.55082	2.884155	1.78E-06
		Nandrolone	1.42475	6.006259	0.001427
Ketones		3-Geranyl-4,2',4',6'-tetrahydroxy-5-prenyldihydrochalcone	1.65874	24.35876	6.77E-06
		2-Pyrrolidinone	1.12122	0.473508	4.39E-08
		Grandiflorone	1.36872	0.02504	0.000146
		Distemonanthin	1.11748	0.014495	0.009956
Esters		(Z)-5-Dodecenyl (Z)-5-dodecenoate	2.01674	9.420365	5E-05
		(E,E)-3,7,11-Trimethyl-2,6,10-dodecatrienyl decanoate	2.54595	10.77435	6.47E-05
Others	Diphenyl ethers, biphenyls, dibenzyls and stilbenes	Batatasin IV	1.04961	0.289258	0.011858
	Amines	N,N-(2,2-dihydroxy-ethyl) arachidonoyl amine	1.13419	20.53557	0.04273
	Antioxidants	Gambiriin C	1.04196	2.013454	0.011259
		Pandaroside B	1.90952	2.414363	0.001172
		punaglandin 6	1.02293	0.018538	0.012134

^aThe difference in the abundance of each metabolite is expressed as the ratio of its average content in the Se-D group and in the 0.15-SeL group (Se-D/0.15-SeL). A ratio of >1 indicates that the corresponding metabolite had higher abundance in the Se-D group, whereas a ratio of <1 indicates that the corresponding metabolite has lower abundance in the Se-D group. ^bDifferences in metabolite abundances between the Se-D and 0.15-SeL groups were analyzed using one-way analysis of variance, followed by the Tukey's post hoc test. $P < 0.05$ was considered as significant.

Table S3 Significantly altered fecal metabolites in the 0.40-SeL/0.15-SeL comparison

Super-pathway	Sub-pathway	Metabolites	VIP value	FC ^a	P value ^b
Bile acid metabolism		Bilirubin	1.08297	2.458061	0.016425
		Chenodeoxycholic acid	1.19666	3.887948	0.013919
		24-Nor-5beta-chol-22-ene-3alpha,6alpha-diol	3.17098	3.377215	0.018269
		3alpha,7alpha,12alpha-trihydroxy-27-carboxymethyl-5beta-cholestan-26-oic acid	1.5037	3.365941	0.020076
		24-Nor-5beta-cholane-3alpha,12alpha,23-triol	3.82275	3.408076	0.02382
		3alpha,7alpha,12alpha-trihydroxy-5alpha-cholan-24-yl sulfate	1.00305	0.074988	0.01217
		Sulfolithocholic acid	3.59121	0.00108	0.00873
		glycochenodeoxycholic acid 7-sulfate	3.03942	0.061459	3.12E-09

Vitamins	Vitamin D	26,26,26-trifluoro-25-hydroxy-27-norvitamin D3 / 26,26,26-trifluoro-25-hydroxy-27-norcholecalciferol	1.76064	0.30828	0.000804
		EB 1213	1.09812	2.235743	0.004502
		1alpha,25-dihydroxy-21-nor-20-oxavitamin D3 / 1alpha,25-dihydroxy-21-nor-20-oxacholecalciferol	2.71579	3.213566	0.032692
Amino acids	Tryptophan metabolism	Indoleacetic acid	2.15971	0.351225	0.002943
	Serine	N-(3-(15-methyl-hexadecanoyloxy)-13-methyl-tetradecanoyl)-L-serine	1.13968	0.402032	0.002639
	Histidine	N-palmitoyl histidine	1.39359	0.453366	0.031709
Fatty acids	Long chain unsaturated fatty acids and its derivates	14,15-DiHETrE	1.95475	2.281614	0.000662
		6-bromo-tricosa-5E,9Z-dienoic acid	1.07012	0.336338	0.002261
		9,13-dihydroxy-10-ethoxy-11-octadecenoic acid	1.17065	0.435093	0.041427
	Medium chain fatty acids and their derivates	N-(6-aminohexanoyl)-6-aminohexanoic acid	4.50026	3.442128	0.04882
	Diprotic acids and their derivates	2-hydroxy-decanedioic acid	3.73184	0.05955	0.044194
		Pimelic acid	1.29148	0.07723	0.012374
	Short chain fatty acid and their derivatives	Mevalonic acid	2.22795	0.339121	0.004308
Lipid metabolism	Cholesterol and derivatives	Cholesterol glucuronide	1.42708	6.74064	5.02E-08
	Phosphocholine	PC(O-16:0/O-2:0)	1.27788	0.268227	0.001154
		PC(8:0/0:0)	1.60281	0.21713	0.003671
		PC(16:0/2:0)	2.71234	2.750722	0.006302
		PC(O-14:0/O-1:0)	3.07215	0.345473	0.007596
		PC(O-8:0/O-8:0)	2.4164	0.488431	0.047821
	Glycerophospholipids	PG(16:1(9Z)/22:2(13Z,16Z))	1.78403	2.509152	1.1E-08
		PS(16:0/16:0)	2.06037	2.047363	3.02E-07
		PG(18:0/18:1(11Z))	7.14413	2.767204	9.96E-07
		PG(14:0/20:3(8Z,11Z,14Z))	1.38747	2.94259	1.18E-06
		PS(16:0/18:1(9Z))	7.00115	3.430207	1.81E-06
		PG(18:0/0:0)	3.5555	0.340466	2.51E-06
		PI(12:0/19:0)	1.63818	4.183373	2.69E-06
		PS(O-16:0/18:3(9Z,12Z,15Z))	2.58142	7.489005	3.13E-06
		PE(14:0/P-18:0)	1.56137	2.437515	5.65E-06
		PA(22:0/12:0)	2.31638	2.13532	6.84E-06
		PG(20:2(11Z,14Z)/0:0)	2.48212	7.221531	7.08E-06
		PA(16:0/18:1(11Z))	1.35756	16.44603	9.35E-06
		PI(18:4(6Z,9Z,12Z,15Z)/20:5(5Z,8Z,11Z,14Z,17Z))	1.19926	2.47979	1.18E-05
		PE(16:1(9Z)/P-18:1(11Z))	2.85638	3.373724	1.68E-05
		PE(14:0/20:1(11Z))	6.21779	2.562148	1.75E-05
		PE(14:0/20:3(5Z,8Z,11Z))	2.11651	4.412098	1.98E-05
		PC(15:0/20:1(11Z))	1.22482	2.317441	2.32E-05
		PS(16:0/20:4(5Z,8Z,11Z,14Z))	1.2354	4.698771	2.93E-05
		PC(15:0/18:3(6Z,9Z,12Z))	2.01545	2.936664	0.000164
		PE(16:0/22:6(4Z,7Z,10Z,13Z,16Z,19Z))	1.15709	2.843547	0.0003

		PE(18:2(9Z,12Z)/0:0)	1.1296	0.410319	0.000306
		PA(P-16:0/15:1(9Z))	1.63355	3.272371	0.000356
		PI(20:5(5Z,8Z,11Z,14Z,17Z)/0:0)	1.06734	0.312122	0.001015
		PS(22:1(11Z)/0:0)	1.77188	0.343688	0.001422
		PG(16:0/20:4(5Z,8Z,11Z,14Z))	1.03493	2.040321	0.001545
		PG(O-16:0/20:2(11Z,14Z))	1.43067	2.057013	0.001902
		PI(18:4(6Z,9Z,12Z,15Z)/0:0)	7.07601	0.33405	0.007722
		PG(10:0/10:0)	2.43747	2.075134	0.029753
		PG(O-16:0/17:2(9Z,12Z))	1.72249	0.29128	0.030238
	Glycerolipids	DG(17:2(9Z,12Z)/22:4(7Z,10Z,13Z,16Z)/0:0)[iso2]	5.6121	2.865126	2.27E-06
		DG(17:2(9Z,12Z)/22:5(7Z,10Z,13Z,16Z,19Z)/0:0)[iso2]	1.83968	4.337038	3E-06
		DG(14:0/20:3(5Z,8Z,11Z)/0:0)	1.11385	2.638215	0.000495
		DG(18:1(11Z)/22:6(4Z,7Z,10Z,13Z,16Z,19Z)/0:0)	1.51081	74.24566	0.000644
		DG(14:0/20:2(11Z,14Z)/0:0)	1.08354	2.11338	0.008679
		DG(17:2(9Z,12Z)/22:6(4Z,7Z,10Z,13Z,16Z,19Z)/0:0)[iso2]	1.34784	0.016105	0.008883
		MGDG(16:0/18:2(9Z,12Z))	1.07381	2.018792	0.018195
		DG(12:0/12:0/0:0)[iso2]	1.08678	153.9806	0.0223
	Isoprenoids	Loganin	2.65788	0.288176	0.000326
		Rhodoxanthin	1.62266	2.926133	0.000683
		(-)-Jolkinol B	1.32317	0.052775	0.007286
		(+)-Dysideapalaunic acid	1.33455	3.639304	0.016737
		Chamazulene	2.63312	2.187569	0.04359
		Gibberellin A9	2.58016	0.010884	0.000161
	Steroids/Sterols	6beta-hydroxytestosterone	1.6196	0.02154	5.53E-07
		Xeniasterol-b	1.34143	2.245727	4.13E-06
		Estriol	1.41698	0.008738	0.000205
		27-nor-campestan-3beta,4beta,5alpha,6alpha,7beta,8beta,14alpha,15alpha,24-nonol	2.56422	4.118123	0.000394
		1,3,5(10)-estratrien-17-one-3,7,8-triol	2.44022	0.020739	0.000414
		Hydrocortisone cypionate	4.41987	0.354596	0.000816
		16-a-Hydroxypregnenolone	1.50838	2.559452	0.001003
		Tetrahydrodeoxycorticosterone	3.49644	2.707549	0.001215
		2-deoxyecdysone 22-phosphate	1.34993	3.820382	0.00209
		3-O-(Galb)-(25R)-12-oxo-5alpha-spirostan-3beta-ol	1.65956	2.596219	0.008336
		Fludrocortisone	1.44792	0.001575	0.016053
	Sphingolipids/ sphingosine	Prosafrinine	2.56955	2.036356	0.001061
Nucleic acid metabolism	Pyrimidine metabolism	Thymidine	1.02049	0.090325	1.74E-05
	Purine metabolism	Adenosine	2.7713	0.415298	4.16E-05
		Adenine	3.97607	0.360246	0.00407
Incretions		L-Thyronine	1.05446	4.177319	2.26E-05
		Nandrolone	1.08422	2.48015	0.001398
		C22-PGF4alpha	2.07767	3.37504	0.002451

		11-deoxy-16,16-dimethyl-PGE2	2.11617	2.137295	0.000311
		1a,1b-dihomo-PGE2	3.21462	2.893371	0.002157
Ketones		Denticulaflavonol	15.3186	0.341953	2.98E-05
		Grandiflorone	1.77779	0.019568	0.000137
		3beta,4beta,5-Trimethoxy-4'-hydroxy- (6:7)-2,2-dimethylpyranoflavan	4.49618	10.62155	0.002796
		Flemiphyllin	1.4848	0.310648	0.002891
		8,8-Dimethyl-2-phenyl-4H,8H-benzo[1,2-b:3,4-b']dipyrans-4-one	1.11657	0.163325	0.00602
		Repensol3,7,9-Trihydroxycoumestan	1.36235	0.43457	0.006667
		Epothilone B	1.28482	3.747531	0.007136
Carbohydrate metabolism		L-Malic acid	3.11298	0.345209	0.014738
		Collettiside I	1.75132	2.727368	0.007184
Antibiotics	Antibiotics	Azithromycin	1.03926	0.103445	0.000165
Others	Alkanes/ Hydrocarbons	14S-Methyl-1-octadecene	1.52161	2.010568	0.014926
		all-trans-heptaprenyl diphosphate	4.37249	2.973273	0.000124
		Rolliniastatin-1	1.72134	2.989453	0.041589
		Pyridinoline	3.95487	0.286546	5.37E-08
		Ibuprofen	1.33037	0.410886	0.000365
		Eugenol	3.15307	2.09968	0.000954

^aThe difference in the abundance of each metabolite is expressed as the ratio of its average content in the 0.40-SeL group and in the 0.15-SeL group (0.40-SeL/0.15-SeL). A ratio of >1 indicates that the corresponding metabolite had higher abundance in the 0.40-SeL group, whereas a ratio of <1 indicates that the corresponding metabolite has lower abundance in the 0.40-SeL group. ^bDifferences in metabolite abundances between the 0.40-SeL and 0.15-SeL groups were analyzed using one-way analysis of variance, followed by the Tukey's post hoc test. $P < 0.05$ was considered as significant.

Table S4 Significantly altered fecal metabolites in the Se-D/0.15-SeM comparison

Super-pathway	Sub-pathway	Metabolites	VIP value	FC ^a	P value ^b
Bile acid metabolism		Chenodeoxycholic acid glycine conjugate	1.51285	0.476466	0.032429
		Sulfolithocholic acid	3.92342	26.63791	0.000842
		Tauroursodeoxycholic acid	1.26087	0.237499	2.53E-09
		Bilirubin	1.01558	4.271931	0.042908
		L-Carnitine	1.48519	2.441368	1.51E-05
		Glycocholic acid 3-glucuronide	3.41026	0.011692	9.39E-15
Neurosubstances		4-Acetamidobutanoic acid	1.40817	2.95161	0.04105
		Escitalopram	1.56893	0.08739	8.5E-06
		Melatonin	1.36749	0.43562	5.6E-06
		Ecgonine methyl ester	4.20657	0.32494	2.7E-08
		Nervonic acid	7.30779	223.1153	1.16E-05
		N-stearoyl GABA	1.51419	0.282118	1.12E-07
		Arachidonoyl Serotonin	1.55344	2.176414	5.22E-08
Vitamins	Vitamin D and its derivatives	(17E)-1alpha,25-dihydroxy-26,27-dimethyl-17,20,22,22,23,23-hexadehydro-24a-homovitamin D3 / (17E)-1alpha,25-dihydroxy-26,27-dimethyl-17,20,22,22,23,23-hexadehydro-24a-homocholecalciferol	1.24422	0.391733	0.00393
		1alpha-hydroxy-24-methylsulfonyl-25,26,27-trinorvitamin D3 / 1alpha-hydroxy-24-methylsulfonyl-	1.61722	2.008662	8.67E-08

		25,26,27-trinorcholecalciferol			
		24,24-difluoro-1alpha,25-dihydroxy-26,27-dimethylvitamin D3 / 24,24-difluoro-1alpha,25-dihydroxy-26,27-dimethylcholecalciferol	2.42068	223.2241	3.81E-06
		24,25-Dihydroxyvitamin D	1.67867	2.245452	0.002819
		26,26,26,27,27,27-hexafluoro-1alpha-hydroxyvitamin D3 / 26,26,26,27,27,27-hexafluoro-1alpha-hydroxycholecalciferol	2.10718	0.486232	0.008562
		26,26,26-trifluoro-25-hydroxy-27-norvitamin D3 / 26,26,26-trifluoro-25-hydroxy-27-norcholecalciferol	1.28119	0.363562	0.001774
		4,4-difluorovitamin D3 / 4,4-difluorocholecalciferol	2.80543	38.91997	5.73E-06
Amino acids	Homoserine	N-(3S-hydroxy-butanoyl)-homoserine lactone	1.58598	0.378397	0.000823
		N-butanoyl-lhomoserine lactone	4.11693	0.476125	8.43E-06
		N-heptanoyl-homoserine lactone	3.57278	0.45242	1.39E-06
	Sulfur-containing amino acids	5-Methyltetrahydrofolic acid	3.28058	0.12541	0.00282
	Lysine	Epsilon-(gamma-Glutamyl)-lysine	1.39232	0.459528	0.000539
	Tryptophan metabolism	Indolelactic acid	2.42811	0.464381	0.000119
	Aspartic acid	L-Aspartic acid	2.10404	0.372443	6.59E-07
	Histidine	L-Histidine	1.94249	0.190876	3.76E-08
	Arginine	N-a-Acetyl-L-arginine	2.35978	0.429777	0.005641
	Arginine biosynthesis	N-Acetylmethionine	1.52921	0.32129	2.97E-06
	Glycine	N-stearoyl glycine	1.26753	0.303104	0.005873
		Isoleucine	N-oleoyl isoleucine	1.79024	0.203193
Carbohydrate metabolism		D-Xylose	1.29348	3.757102	8.23E-07
		Tuberonic acid glucoside	1.04322	0.286434	1.03E-08
		Fumaric acid	1.8847	0.373672	1.4E-05
		24Z-ethylidene-cholest-5-en-3beta-ol 3-O-beta-D-glucopyranoside	2.56334	0.300462	0.001362
		stigmast-5-en-3beta-ol 3-O-beta-D-glucopyranoside	4.3085	0.19313	0.019449
		Collettiside I	1.07039	0.409336	0.013867
		convallatoxin	1.30237	7.713719	4.61E-08
Nucleic acid metabolism	Pyrimidine metabolism	Thymine	2.43521	2.044122	0.000472
	Purine metabolism	Adenine	2.03822	2.032476	0.043829
		Adenosine	1.22361	2.373011	0.007951
		Xanthine	2.65497	3.030454	1.45E-05
Fatty acids	Medium chain fatty acids and their derivates	N-(6-aminohexanoyl)-6-aminohexanoic acid	3.43884	0.321762	1.07E-07
		2-amino-8-oxo-9,10-epoxy-decanoic acid	6.15581	0.238345	8.08E-10
	Long chain unsaturated fatty acids and their derivates	2-propyl-9Z-octadecenoic Acid	3.28469	264.6699	8.04E-06
		7,9,13,17-tetramethyl-7S,14S-dihydroxy-2E,4E,8E,10E,12E,16-octadecaheptaenoic acid	1.03026	3.810446	0.003208
		16-bromo-9E-hexadecenoic acid	1.19216	27.03482	0.000373
		22-tricosenoic acid	8.25461	133.6564	1.43E-06
		24-hydroxy-10Z-tetracosenoic acid	8.01133	3.182757	0.000567
		25:2(5Z,9Z)(23Me)	3.16577	231.5704	3.83E-05

		3E,5E-tridecadienoic acid	3.86685	2.181473	1.14E-07
		6-bromo-docosa-5E,9Z-dienoic acid	1.48979	0.274924	6.51E-06
		9,13-dihydroxy-10-ethoxy-11-octadecenoic acid	1.19264	2.80324	0.000108
		9-hexacosenoic acid	3.88443	41.51341	0.009512
		Lesquerolic acid	12.744	0.279808	1.07E-05
		Mycolipenic acid (C25)	10.6047	81.79125	5.27E-06
	Long chain saturated fatty acids and their derivates	9R,10S-dihydroxy-stearic acid	3.91542	2.039498	0.000208
		12-bromo-octadecanoic acid	1.29127	0.367813	2.1E-07
		15-hydroxy-pentadecanoic acid	1.89218	2.610553	2.62E-06
		20-oxo-heneicosanoic acid	3.05452	2.134339	0.00799
		24-hydroxy-tetracosanoic acid	4.42964	4.783347	0.000187
		2-hydroxy-tricosanoic acid	3.36299	8.204516	1.1E-05
		3-bromohexadecanoic acid	1.99935	3.394409	4.89E-06
		3-hydroxy-eicosanoic acid	1.04145	0.434255	0.003332
		Heptadecanoic acid	4.29624	2.094429	0.003457
		Pentadecanoic acid	1.73755	2.840238	0.001728
	Diprotic acid and their derivatives	2-hydroxy-decanedioic acid	1.01118	3.800817	0.023452
		Eicosanedioic acid	1.26437	37.22752	1.65E-05
		Heneicosanedioic acid	1.65907	2.193262	0.010956
		Hexacosanedioic acid	1.03894	2.534165	0.012001
	Short chain fatty acid and their derivatives	Hydroxypropionic acid	1.58132	2.600682	0.003772
		4-Guanidinobutanoic acid	1.1526	2.921946	0.001674
		3-O-(alpha-L-arabinopyranosyl-(1->6)-beta-D-glucopyranosyl) butyl 3S-hydroxybutanoate	1.4572	0.113013	3.86E-06
Lipid metabolism	Cholesterol and derivatives	Cholesterol glucuronide	1.50907	0.303193	0.000402
		24-norcholesterol	1.62072	3.154935	2.84E-06
		7-Dehydrocholesterol	4.16527	2.014309	2.03E-06
		Cholest-5-ene	3.40571	151.1536	6.3E-09
		cholesteryl beta-D-glucoside	3.13711	0.220244	7.12E-06
		ecdysone 25-O-D-glucopyranoside	1.56044	0.026715	0.030173
	Lysophospholipid	LysoPC(20:0)	1.22355	0.464634	0.001324
		LysoPC(22:0)	1.07541	0.235347	9.97E-08
		LysoPC(P-18:0)	1.97157	0.340696	0.00332
		LysoPC(P-18:1(9Z))	1.90433	0.45288	0.022305
	Glycerophosphates	PA(12:0/12:0)	1.38459	0.34183	0.001193
		PA(13:0/18:4(6Z,9Z,12Z,15Z))	1.09736	2.374589	8.31E-08
		PA(13:0/20:3(8Z,11Z,14Z))	1.66837	105.1573	2.15E-10
		PA(O-16:0/12:0)	1.31156	2.825885	0.020691
		PA(P-16:0/14:1(9Z))	2.25008	2.218962	0.031652
	Glycerophosphocholines	PC(10:0/10:0)	2.78479	0.307512	0.008677
		PC(15:0/18:3(6Z,9Z,12Z))	1.05435	2.687711	0.003103
		PC(16:0/2:0)	1.12363	0.38546	0.008072

	PC(4:0/4:0)	1.48298	2.023942	1.67E-09
	PC(6:0/0:0)	1.04525	0.291782	5.11E-06
	PC(8:0/0:0)	1.28244	4.507191	8.67E-05
	PC(9:0/0:0)	1.84122	5.285621	6.42E-05
	PC(O-14:0/15:0)	13.4395	0.185339	5.42E-07
	PC(O-14:0/16:0)	5.97736	0.160269	2.32E-05
	PC(O-16:0/0:0)	4.92324	0.327681	0.01017
	PC(P-17:0/0:0)	3.27697	0.270812	3.21E-09
	PC(P-19:1(12Z)/0:0)	1.40214	0.40143	7.9E-07
	PC(O-16:0/O-1:0)	3.27968	0.18922	2.65E-08
	PC(O-18:0/O-2:0)	1.99337	0.293378	1.23E-06
	PC(O-18:1(9Z)/O-1:0)	1.01305	0.119464	2.44E-16
	PC(O-8:0/O-8:0)	1.68984	0.347959	0.013595
Glycerophosphoethanolamines	PE(14:0/20:1(11Z))	3.28265	2.067292	0.002507
	PE(18:4(6Z,9Z,12Z,15Z)/18:4(6Z,9Z,12Z,15Z))	1.19765	2.343079	0.031017
	PE(O-16:0/14:0)	1.02774	0.260694	4.91E-05
	PE(O-16:0/15:0)	5.78097	0.140236	6.6E-06
Glycerophosphoglycerols	PG(10:0/10:0)	2.24491	0.212055	7.75E-06
	PG(16:1(9Z)/22:2(13Z,16Z))	1.12813	0.346039	0.000397
	PG(20:2(11Z,14Z)/0:0)	1.15136	0.143676	7.09E-05
	PG(22:6(4Z,7Z,10Z,13Z,16Z,19Z)/0:0)	1.657	0.416546	2.35E-10
	PG(22:6(4Z,7Z,10Z,13Z,16Z,19Z)/22:6(4Z,7Z,10Z,13Z,16Z,19Z))	2.75306	0.26133	0.00202
	PG(O-16:0/17:2(9Z,12Z))	1.26308	0.200057	0.000141
	PG(O-16:0/20:1(11Z))	1.44994	0.364076	4.78E-06
	PG(O-16:0/20:2(11Z,14Z))	1.18306	0.281006	6.29E-07
	PG(O-18:0/20:3(8Z,11Z,14Z))	2.14475	0.289553	1.51E-06
	PG(O-20:0/0:0)	1.1837	0.427089	0.00033
	PG(P-20:0/0:0)	3.52799	0.240855	2.9E-07
Glycerophosphoinositols	PI(16:0/0:0)	1.06745	0.169251	1.24E-06
	PI(18:4(6Z,9Z,12Z,15Z)/0:0)	2.79354	2.138101	0.03241
	PI(22:2(13Z,16Z)/0:0)	1.85259	3.0903	0.000282
	PI(O-16:0/0:0)	8.07426	0.225936	2.04E-07
	PI(O-16:0/16:1(9Z))	1.52967	0.178632	3.68E-05
Glycerophosphoserines	PS(14:1(9Z)/22:6(4Z,7Z,10Z,13Z,16Z,19Z))	1.11057	2.475111	0.045703
	PS(15:0/0:0)	1.02726	0.417823	0.00223
	PS(15:0/22:2(13Z,16Z))	2.04239	0.481339	0.008709
	PS(O-16:0/18:2(9Z,12Z))	3.93155	0.242425	7.25E-08
	PS(P-20:0/17:2(9Z,12Z))	1.4295	0.301035	1.41E-05
	CPA(18:0)	1.30219	0.423639	0.000526
Diacylglycerols	DG(15:0/18:3(6Z,9Z,12Z)/0:0)	1.7421	2.230961	0.003317
	DG(17:2(9Z,12Z)/22:4(7Z,10Z,13Z,16Z)/0:0)[iso2]	2.75846	2.271019	8.54E-05

		DG(17:2(9Z,12Z)/22:5(7Z,10Z,13Z,16Z,19Z)/0:0)[iso2]	1.05893	3.999539	0.000178	
Isoprenoids		20:2(5Z,9Z)(11Me,15Me,19Me)	1.36032	117.1252	5.95E-05	
		4-oxo-Retinoic acid	1.28998	2.312699	0.000284	
		C25:4 Highly branched isoprenoid A	1.16329	0.398792	1.64E-05	
		Gibberellin A9	1.66937	0.022096	0.000163	
		Moronic acid	1.46605	2.789352	0.00223	
		Rhodoxanthin	1.05423	7.60183	0.00016	
Steroids/ Sterols		29-demethylgeodisterol-O-sulfite	2.6649	11.83113	0.024001	
		3-O-(Galb)-(25R)-12-oxo-5alpha-spirostan-3beta-ol	1.41856	0.272145	0.00081	
		3-O-(Rhaa 1-4(Rhaa 1-2)Glc)-26-O-(Glc)-(25R)-furost-5-en-3beta,22,26-triol	2.32149	0.098371	6.84E-06	
		Campestanol	2.41991	9.722291	0.000762	
		cyasterone	1.23612	0.495401	0.003568	
		Theonellasterol D	2.28727	2.743582	0.008416	
		19-Hydroxyandrost-4-ene-3,17-dione	1.39549	2.149774	0.003882	
		6beta-hydroxytestosterone	1.0598	0.012658	2.21E-05	
		Fludrocortisone	1.47565	55.85572	0.001407	
		1,3,5(10)-estratrien-17-one-3,7,8-triol	1.50954	0.021883	5.52E-05	
		Ximaosteroid C	1.61306	0.494979	0.005481	
	Sphingolipids/ sphingosine		(3'-sulfo)Galbeta-Cer(d18:1/16:0(2OH))	1.0114	0.363995	1.05E-05
		(4E,6E,d14:2) sphingosine	1.11479	0.083007	0.000181	
		C16 Sphinganine-1-phosphate	4.8912	0.195409	2.89E-12	
		Obscuraminol A	1.09294	2.745768	5.13E-07	
		Phytosphingosine	1.37166	0.39726	0.00104	
		Prosafrinine	1.6407	2.146507	0.000603	
		Cer(d16:1/17:0)	2.49776	2.122916	0.014313	
		Cer(d18:0/13:0)	1.18199	0.318654	5.2E-08	
		Cer(d18:0/14:0)	1.50966	0.099343	3.18E-07	
		Cer(d18:0/15:0)	2.10072	5.637528	5.05E-05	
		Cer(d18:0/h17:0)	6.06897	2.587865	2.93E-06	
		Cer(d18:1/14:0)	1.24812	2.916059	0.001756	
		Cer(d18:2/14:0)	1.59714	0.289542	2.06E-06	
		Cer(d18:2/16:0)	1.3032	0.304232	1.48E-05	
		Cer(t18:0/16:0)	4.5425	3.296807	1.2E-05	
Acyl carnitine/lipid biosynthesis			Dodecanoylcarnitine	3.80777	2.142821	4.12E-05
			Isobutyryl-L-carnitine	1.0355	2.388871	0.015755
		L-Palmitoylcarnitine	3.17695	0.446867	0.017235	
Incretions		Nandrolone	1.10202	4.074855	0.003431	
		Tetranor-PGEM-d6	3.61457	2.056475	2.21E-05	
		Androsterone sulfate	1.21593	2.14206	1.68E-05	
Antibiotics		Glycyrrhetic acid	1.14791	2.66517	0.00779	
		10-Deoxymethymycin	2.89236	89.63038	2.41E-05	

Amines		N,N-(2,2-dihydroxy-ethyl) arachidonoyl amine	1.07743	25.37584	0.040999
		N-Oleylethanolamine	2.45581	0.412021	0.015505
Ketones		3-Geranyl-4,2',4',6'-tetrahydroxy-5-prenyldihydrochalcone	1.50858	2687.155	3.75E-06
		Desmosdumotin C	1.07441	0.000672	0.021118
		Grandiflorone	1.31381	0.021586	3.7E-05
		Isocordoin	1.43148	0.1224	3.38E-08
		Lophirone E	1.08086	581.3657	0.042539
Aldehydes		2-decene-4,6,8-triyn-1-al	1.03212	0.338198	0.005342
		2-dodecenal	2.70565	349.2531	7.02E-06
Alcohols		3,7,11-Trimethyl-6E,10-dodecadien-1-ol	3.2097	3.926297	0.002934
		6Z-Heneicosen-11-ol	4.89917	5.955072	8.72E-06
		9-pentadecen-1-ol	8.65895	2.343414	9.5E-05
		Gummiferol	1.09118	6.924574	0.002354
		Panaxydol chlorohydrine	1.02533	3.086127	0.003992
		Nitenin	1.05613	59.42946	4.12E-08
		6-Ketoestriol	1.61583	0.007046	2.99E-08
Esters		Epothilone A	4.36586	0.346651	3.07E-09
		(E,E)-3,7,11-Trimethyl-2,6,10-dodecatrienyl decanoate	2.4257	96.07922	2.01E-05
		(Z)-5-Dodecenyl (Z)-5-dodecenoate	1.94152	739.5735	9.88E-06
Alkanes/ Hydrocarbons		9,10-Epoxy-3Z,6Z-tricosadiene	2.53064	4.18538	0.001043
		14S-Methyl-1-octadecene	1.16088	2.612936	0.000367
		6Z,9Z-Docosadiene	1.92092	602.6862	3.75E-06
Others	Ethers	3'-O-methylbatatasin III	1.95069	2.270517	0.010383
		Pyridinoline	2.25639	2.035763	3.37E-06
		Pandaroside B	1.74333	2.749691	0.000284
		Atenolol	1.73398	0.11659	2.7E-06
		Scilliroside	2.05118	2.719489	0.006231
		punaglandin 6	1.05865	0.01531	0.00138

^aThe difference in the abundance of each metabolite is expressed as the ratio of its average content in the Se-D group and in the 0.15-SeM group (Se-D/0.15-SeM). A ratio of >1 indicates that the corresponding metabolite had higher abundance in the Se-D group, whereas a ratio of <1 indicates that the corresponding metabolite has lower abundance in the Se-D group. ^bDifferences in metabolite abundances between the Se-D and 0.15-SeM groups were analyzed using one-way analysis of variance, followed by the Tukey's post hoc test. $P < 0.05$ was considered as significant.

Table S5 Significantly altered fecal metabolites in the 0.40-SeM/0.15-SeM comparison

Super-pathway	Sub-pathway	Metabolites	VIP value	FC ^a	P value ^b
Bile acid metabolism	Bile acid metabolism	glycochenodeoxycholic acid 7-sulfate	1.39184	0.274189	0.00032
		ponasterone A	1.76251	2.22668	0.000214
		Glycocholic acid 3-glucuronide	2.95388	0.43708	5.22E-07
Neurosubstances		5-Hydroxy-L-tryptophan	3.1321	2.674812	1.31E-06
		Escitalopram	1.40917	0.417351	0.002265

		Pregnenolone sulfate	1.19279	2.048167	0.000161	
		Ecgonine methyl ester	2.23635	0.351039	0.023194	
Vitamins	Vitamin B6 and its derivatives	4-Pyridoxic acid	3.04365	0.486049	0.000939	
	Vitamin H and its derivatives	Biotin	1.22612	0.265059	0.037365	
	Vitamin D2 and its derivatives	7-Dehydrocholesterol-3-sulfate ester	5.06783	2.635881	7.88E-05	
	Vitamin D3 and its derivatives		(22E)-26,26,26,27,27,27-hexafluoro-25-hydroxy-22,23-didehydrovitamin D3 / (22E)-26,26,26,27,27,27-hexafluoro-25-hydroxy-22,23-didehydrocholecalciferol	5.37945	0.361466	0.00243
			(23R,25R)-25-hydroxyvitamin D3 26,23-lactone / (23R,25R)-25-hydroxycholecalciferol 26,23-lactone	2.63078	3.776422	0.00048
			(23S)-1alpha-hydroxy-25,27-didehydrovitamin D3 26,23-lactone	2.73971	0.471401	0.008969
			(6RS)-6,19-epidioxy-24,24-difluoro-25-hydroxy-6,19-dihydrovitamin D3 / (6RS)-6,19-epidioxy-24,24-difluoro-25-hydroxy-6,19-dihydrocholecalciferol	1.20118	14.65293	9.15E-05
			1,25-dihydroxy-2,4-dinor-1,3-secovitamin D3 / 1,25-dihydroxy-2,4-dinor-1,3-secocholecalciferol	2.04387	2.231559	0.000664
			1alpha,25-dihydroxy-21-nor-20-oxavitamin D3 / 1alpha,25-dihydroxy-21-nor-20-oxacholecalciferol	1.88511	2.35564	0.005949
			1alpha,25-dihydroxy-25,25-diphenyl-26,27-dinorvitamin D3 / 1alpha,25-dihydroxy-25,25-diphenyl-26,27-dinorcholecalciferol	1.80107	2.588921	7.32E-06
			1alpha,25-dihydroxy-2beta-(6-hydroxyhexyl)vitamin D3 / 1alpha,25-dihydroxy-2beta-(6-hydroxyhexyl)cholecalciferol	1.16158	23.10517	0.00038
			1alpha-hydroxy-2beta-(4-hydroxybutoxy)vitamin D3 / 1alpha-hydroxy-2beta-(4-hydroxybutoxy)cholecalciferol	1.74648	22.58923	6.25E-05
			24,24-Difluoro-1,25,26-trihydroxyvitamin D3	1.19319	2.626957	0.000151
	24,24-difluoro-1alpha,25-dihydroxy-26,27-dimethyl-24a-homovitamin D3 / 24,24-difluoro-1alpha,25-dihydroxy-26,27-dimethyl-24a-homocholecalciferol	1.33195	0.384979	6.33E-06		
	26,27-diethyl-1alpha,25-dihydroxy-20,21-methano-23-oxavitamin D3 / 26,27-diethyl-1alpha,25-dihydroxy-20,21-methano-23-oxacholecalciferol	1.12078	5.267158	0.000826		
Fatty acids	Medium chain fatty acids and their derivatives	10-undecynoic acid	1.87866	5.036351	3.19E-05	
		2,6-nonadienoic acid	3.16804	2.548586	1.3E-07	
		2E,4E,8Z,10E-dodecatetraenoic acid	2.69952	4.683978	1.26E-06	
		2-hydroxy-10-undecenoic acid	5.93091	5.792366	1.23E-06	
		5-oxo-7-octenoic acid	2.83596	0.281451	0.014799	
		9-hydroxy-5Z-nonenoic acid	1.44308	5.195959	4.06E-06	
		9-oxo-2E-decenoic acid	1.68978	5.468252	0.010675	

		formyl 2E,4E,6Z-decatrienoate	1.34307	3.839562	3.13E-06
		5-hydroperoxy-7-[3,5-epidioxy-2-(2-octenyl)-cyclopentyl]-6-heptenoic acid	1.26263	4364.57	0.004231
		9,12-dioxo-dodecanoic acid	5.76685	5.885062	9.45E-07
		methyl 8-[2-(2-formyl-vinyl)-3-hydroxy-5-oxo-cyclopentyl]-octanoate	1.42795	2.347081	8.5E-05
		2-hydroxy pelargonic acid	3.60671	10.21506	1.27E-07
		3-O-(2-O-(2E-decenoyl)-alpha-L-rhamnopyranosyl)-3-hydroxydecanoic acid	2.03902	14.74886	2.72E-06
		3-O-alpha-L-rhamnopyranosyl-3-hydroxydecanoic acid	2.25881	2.640501	2.35E-07
		3,6-dioxo-decanoic acid	2.19732	6.094899	3.9E-06
		Pelargonic acid	1.49568	2.641251	7.24E-07
		Sebacic acid	1.03068	3.508608	1.53E-06
		N-(6-aminohexanoyl)-6-aminohexanoic acid	6.0325	5.131858	0.001035
	Long chain unsaturated fatty acids and their derivatives	methyl 9,10-epoxy-12,15-octadecadienoate	1.97342	2.583436	0.033802
		methyl 9,12-dihydroxy-13-oxo-10-octadecenoate	4.39168	17.11936	0.000717
		12S-hydroxy-16-heptadecynoic acid	1.99028	2.808387	2.29E-05
		10-hydroxy-2E-decenoic acid	1.70331	3.221949	0.000118
		10-nitro-9E-octadecenoic acid	1.30045	13.79857	3.96E-05
		11-hydroperoxy-12,13-epoxy-9-octadecenoic acid	13.9255	7.466856	5.59E-07
		12,13-dihydroxy-11-methoxy-9-octadecenoic acid	1.32385	4.574064	4.78E-05
		12-oxo-14,18-dihydroxy-9Z,13E,15Z-octadecatrienoic acid	6.06167	3.535304	4.77E-07
		13-keto-9Z,11E,15Z-octadecatrienoic acid	14.1017	3.264298	1.12E-06
		24:3(15Z,18Z,21Z)	2.26397	0.315339	3.58E-05
		7-oxo-11E,13-Tetradecadienoic acid	2.20703	2.379941	4.83E-06
		8,12-dihydroxy-9-chloro-5Z,10Z,14Z,17Z-eicosatetraenoic acid	1.12989	0.223427	1.34E-05
		8-hydroxy-13Z-octadecene-9,11-diynoic acid	3.79683	2.337949	2.91E-07
		9,10,13-TriHOME	4.72744	4.391364	0.001232
		9,10-DHOME	4.74896	2.364995	0.000421
		9,12,13-TriHOME	2.41816	28.41526	4.32E-07
		9S-HpOTrE	8.29206	3.708413	4.45E-07
	Long chain saturated fatty acids and their derivatives	10-oxo-nonadecanoic acid	6.9923	2.411156	0.005163
		Pristanic acid	3.09847	2.063572	0.016631
		13-hydroxy-tridecanoic acid	2.30041	11.99126	3.82E-09
		14-hydroxy-heneicosanoic acid	1.46201	0.396476	0.000377
		17-hydroxy-heptadecanoic acid	6.46418	6.666473	0.002548
		18-hydroxy-9S,10R-dihydroxy-stearic acid	6.07809	5.579911	0.001818
		20-oxo-heneicosanoic acid	3.2229	0.351562	0.000603
		9R,10S-dihydroxy-stearic acid	1.40147	3.316757	3.77E-05

		Heptadecanoic acid	2.45507	2.845595	2.58E-06
		Pentadecanoic acid	1.61025	2.339282	0.005221
		Sativic acid	3.26826	12.5606	7.13E-07
	Diprotic acid and their derivatives	Undecanedioic acid	1.45439	2.694848	0.001575
		2-methyl-tridecanedioic acid	1.4195	20.19946	2E-08
		3-hydroxy-tetradecanedioic acid	3.0375	2.998576	5.47E-06
		2-methyl-hexadecanedioic acid	5.10095	3.617884	5.54E-05
		3-hydroxy-dodecanedioic acid	4.22283	4.711392	5.96E-07
		9,10-dihydroxy-Octadecanedioic acid	3.28376	7.145032	4.53E-10
		Azelaic acid	2.98324	4.259401	8.12E-05
		Dodecanedioic acid	1.48551	2.661637	0.005538
		Eicosanedioic acid	1.04058	22.42105	0.045419
		Heneicosanedioic acid	1.77873	0.337802	0.000341
		Hexacosanedioic acid	1.15313	0.194729	0.000106
	Short chain fatty acids and their derivatives	Propionylcarnitine	2.80363	5.156399	7.61E-06
		3-O-(alpha-L-arabinopyranosyl-(1->6)-beta-D-glucopyranosyl) butyl 3S-hydroxybutanoate	1.30971	0.46107	0.001597
		4-Guanidinobutanoic acid	1.35904	3.614156	3.82E-08
		N-arachidonoyl GABA	1.31617	0.459002	0.009853
		Butyric acid	1.227	10.57198	3.16E-05
		Hydroxypropionic acid	1.56172	2.508874	0.019257
Aldehydes	Aldehydes	2-decene-4,6,8-triyn-1-al	1.44699	0.276092	0.001695
		3,7-Dimethyl-8,11-dioxo-2E,6E,9E-dodecatrienal	3.01251	7.584885	0.002221
		10Z-Nonadecenal	1.23773	2.123758	0.018867
		Sorbaldehyde	1.11236	5.347953	0.000159
Nucleic acid metabolism		Adenine	2.29564	0.302591	0.004776
		Uric acid	1.03177	0.213765	2.89E-05
		Inosine	1.52592	2.312746	0.004559
		Thymidine	3.27502	2.273618	0.001763
		Adenosine	1.67522	2.393845	0.001912
Ketones		Isocordoin	1.35401	0.402362	6.89E-05
		Piperaduncin A	2.23194	0.274542	9.57E-07
		Piperaduncin B	1.48247	0.340539	8.67E-08
		2-Geranyl-3,4,2',4'-tetrahydroxydihydrochalcone	1.0598	0.301054	0.009292
		alpha,4,2'-Trihydroxy-4-O-geranyldihydrochalcone	1.11874	2.127727	0.01915
		Denticulaflavonol	3.29932	0.402993	0.00137
		Ulexone B	1.42724	0.415636	0.046744
		Lespedeol A	1.02031	2.85974	0.000197
		cis-Jasmone	2.04388	5.583376	1.15E-06
Alcohols		3,5-Di-O-methyl-8-prenylafzelechin-4beta-ol	4.36129	0.47497	0.045876
		Dryopterin	1.63308	0.258039	0.001722

		3,4,7-Trihydroxy-5,4'-dimethoxy-6,8-dimethylflavan	1.18992	3.031596	2.41E-07
Amides		Capsaicin	2.12392	22.59326	0.000462
		N-Oleoylethanolamine	2.537	0.491345	0.025048
Esters		2,6Z-Nonadien-4-olide	1.53381	5.104719	2.58E-05
		phorbol 13-acetate 12-myristate	4.49669	131.4075	9.55E-07
Incretions		Zearalenone	1.03545	0.361257	0.025758
		3b,17b-Dihydroxyetiocholane	5.32934	3.404629	0.003914
		15R-PGE2 methyl ester, 15-acetate	1.66788	4.663334	8.95E-07
		1a,1b-dihomo-PGE2	1.80148	0.48111	0.001435
		2,3-Dinor-6-keto-prostaglandin F1 a	1.15125	2.075251	5.72E-06
		Norepinephrine sulfate	1.02463	8.103244	0.02678
		Prostaglandin F1a	3.02952	3.465786	1.57E-07
		11-dehydro-2,3-dinor-TXB2	1.75557	5.236511	9.48E-07
		Jasmonic acid	4.09825	5.289132	7.91E-07
		Prostaglandin D3	1.08306	2.867618	5.72E-07
		Tetranor-PGF1alpha	1.01318	2.6909	6.29E-06
		9-deoxy-9-methylene-PGE2	1.05845	5.772397	0.000122
		18-Oxocortisol	2.21108	5.144901	3.33E-08
		Nandrolone	1.50247	3.678347	3.61E-05
		Androsterone	1.79868	2.541592	0.003409
Carbohydrate metabolism		L-Malic acid	3.46073	3.562484	0.007878
		(-)-menthyl beta-D-glucoside	2.75843	2.688984	2.37E-07
Lipid metabolism	Lipid biosynthesis	Stearoylcarnitine	1.02253	14.00904	0.001189
	Diacylglycerols	DG(14:1(9Z)/18:3(6Z,9Z,12Z)/0:0)	1.30819	7.660168	0.002433
		DG(15:0/18:3(6Z,9Z,12Z)/0:0)	1.08585	66.4905	0.000139
		DG(15:0/20:3(5Z,8Z,11Z)/0:0)	1.3073	2.351588	0.008105
		DG(15:0/20:4(5Z,8Z,11Z,14Z)/0:0)	1.79862	4.072392	0.018504
		DG(15:0/20:5(5Z,8Z,11Z,14Z,17Z)/0:0)	3.02358	3.17541	0.021071
	Glycerophosphocholine	LysoPC(P-18:0)	1.04603	0.24615	0.000956
	Glycerophospholipids	PA(13:0/18:4(6Z,9Z,12Z,15Z))	1.47294	2.461601	1.18E-10
		PA(16:0/0:0)	3.27287	0.447462	1.38E-06
		PA(17:0/0:0)	1.71381	5.564419	8.26E-06
		PA(20:0/0:0)	6.65211	0.453672	0.001773
		PA(O-16:0/12:0)	1.35878	0.157242	0.00023
		PA(P-16:0/14:1(9Z))	2.43238	0.372049	0.000399
		PC(O-16:0/0:0)	7.37947	0.19687	0.00193
		PE(14:0/20:3(5Z,8Z,11Z))	1.09718	2.351224	0.027181
PE(15:0/18:3(6Z,9Z,12Z))		1.51421	0.275268	1E-05	
PE(18:4(6Z,9Z,12Z,15Z)/18:4(6Z,9Z,12Z,15Z))		1.31934	0.323243	0.000189	
	PG(14:0/14:0)	3.10654	36.5033	9.44E-05	

		PG(16:1(9Z)/22:2(13Z,16Z))	1.12345	0.498495	0.003071
		PG(20:1(11Z)/0:0)	2.38064	2.0496	0.001477
		PG(22:6(4Z,7Z,10Z,13Z,16Z,19Z)/0:0)	1.18361	0.323964	0.026082
		PG(O-20:0/14:1(9Z))	2.17245	0.405598	1.08E-05
		PI(O-20:0/0:0)	1.59036	63.13903	0.001094
		PS(14:1(9Z)/20:5(5Z,8Z,11Z,14Z,17Z))	1.05458	0.298195	7.9E-06
		PS(14:1(9Z)/22:6(4Z,7Z,10Z,13Z,16Z,19Z))	1.28976	0.237165	0.00015
		2-(8-[3]-ladderane-octanyl)-sn-glycero-3-phosphocholine	1.83634	3.819344	0.000106
	Cholesterol	(25S)-5alpha-cholestan-3beta,6alpha,7beta,8beta,15alpha,16beta,26-heptol	5.40233	7.880885	1.48E-06
		15,20-dihydroxycholest-4,14-dien-3,16-dione	3.75972	3.833045	0.000455
		5alpha-cholestan-3beta,6alpha,8beta,15alpha,24S-triol	3.61778	0.334533	6.75E-05
		5alpha,9alpha-epidioxy-cholest-7-en-3beta,6alpha-diol	1.10061	0.321722	0.002184
		5alpha,6beta-dihydroxycholestanol	1.30117	0.437402	0.000102
		Cholest-5-ene	1.56938	31.07336	0.018112
	Phosphocholine	PC(O-16:0/O-1:0)	3.04969	0.468931	7.08E-05
		PC(O-16:0/O-2:0)	1.79686	0.407786	9.01E-05
		PC(O-18:0/O-2:0)	2.02848	0.47774	8.04E-05
		PC(O-8:0/O-8:0)	2.65647	0.181121	0.001716
		PC(P-15:0/0:0)	1.94635	2.503571	3.14E-06
	Isoprenoids	(-)-Fusidic acid	1.02097	0.155374	0.000953
		(-)-Jolkinol A	1.55147	2.495695	0.001935
		C25:2 6,7-Epoxy highly branched isoprenoid	1.26594	0.337396	9.95E-05
		C25:4 Highly branched isoprenoid A	1.04556	0.457068	2.69E-05
		Chamazulene	2.98647	2.737421	0.007051
		forskolin	3.38114	4.85845	1.4E-07
		gibberellin A17	1.87795	3.919063	0.001076
		Hemigossypol	1.03289	0.459242	0.000464
		Japonicumins A	2.87958	16.12562	0.000146
		Ketospirilloxanthin	1.72151	7.489274	0.000939
		Moronic acid	1.24728	0.335918	0.000568
	Terpenoids	Onocerin	1.06739	0.464906	0.00033
	Steroids/ Sterols	(20S,24S)-24-ethylthornasterol	1.46585	0.492038	0.000763
		1,3,5(10)-estratrien-17-one-3,7,8-triol	1.05074	0.423778	0.039574
		20,26-dihydroxyecdysone	4.05479	7.308466	1.14E-05
		22-deoxy-20,21-dihydroxyecdysone	8.36008	12.85633	3.08E-06
		3-O-(Rhaa1-4(Rhaa1-2)Glc)-26-O-(Glc)-25R-furost-5-en-3beta,22,26-triol	2.38434	0.312513	0.000233
		6alpha-Hydroxycasterone	2.57382	0.451054	4.59E-06
		6beta-hydroxytestosterone	2.51439	9.829817	0.000226
		cimicifoetiside B	1.63258	2.654956	0.002079

		Cucurbitacin C	1.17527	3.233139	6.53E-06
		Cucurbitacin D	3.77724	5.136351	1.53E-06
		Cucurbitacin F	1.0605	0.379701	0.000444
		Episceptrungenin	1.32346	2.316955	0.000187
		Kammogenin	5.29412	5.039512	6.08E-08
		Minabeolide-4	1.49096	4.611352	0.000471
		Stoloniferone F	1.03069	0.465241	0.002139
		Tetrahydrodeoxycorticosterone	1.87284	0.496163	0.002383
		Theonellasterol D	2.22177	2.039856	0.003984
Amino acid metabolism	Glycine derivatives	Isovalerylglycine	2.09032	0.330386	0.016698
		Nicotinuric acid	1.22354	0.267572	0.028315
		Hippuric acid	1.26224	0.275227	0.031193
	Arginine and proline metabolism	Creatinine	3.45053	0.32937	0.020922
		N-palmitoyl proline	1.12871	4.405075	0.027671
	Serine	N-(3-oxododecanoyl) homoserine lactone	1.73031	24.85566	0.00024
		Serratamic acid	1.44743	3.024756	5.95E-07
	Sulfur amino acid metabolism	5-Methyltetrahydrofolic acid	3.83094	0.280994	0.013244
	Lysine derivative	Homocitrulline	2.6318	5.531063	1.83E-09
pentapeptide	APGPR Enterostatin	1.00427	0.402019	0.008248	
Others	Phenols	p-Cresol sulfate	3.98782	0.39179	0.009265
		Epigallocatechin 5,3',5'-trimethyl ether 3-O-gallate	1.10019	0.056623	0.000471
		Coproporphyrin III	4.49746	0.306939	0.000353
		2R-HpOTrE	2.34593	5.965969	5.24E-05
		Rolliniastatin-1	2.72984	6.33468	0.000384
		Berberine	1.01593	5.435721	1.31E-06
		30,32-dihydroxy-2b-methyl-bishomohopane	1.51266	0.366162	0.000421
		Kynurenic acid	1.5162	0.354634	0.017425
		all-trans-heptaprenyl diphosphate	1.76779	0.360671	0.01502
		Atenolol	1.61144	0.398444	0.002468

^aThe difference in the abundance of each metabolite is expressed as the ratio of its average content in the 0.40-SeM group and in the 0.15-SeM group (0.40-SeM/0.15-SeM). A ratio of >1 indicates that the corresponding metabolite had higher abundance in the 0.40-SeM group, whereas a ratio of <1 indicates that the corresponding metabolite has lower abundance in the 0.40-SeM group. ^bDifferences in metabolite abundances between the 0.40-SeM and 0.15-SeM groups were analyzed using one-way analysis of variance, followed by the Tukey's post hoc test. $P < 0.05$ was considered as significant.

Table S6 Significantly altered fecal metabolites in the 0.15-SeM and 0.15-SeL comparison

Super-pathway	Sub-pathway	Metabolites	VIP value	FC ^a	P value ^b
Bile acid metabolism	Bile acid metabolism	(20S,22E)-3beta-Hydroxychole-5,16,22-trien-24-oic Acid	20.3042	0.499669	0.007718
		3alpha,7alpha,12alpha-trihydroxy-5alpha-cholan-24-yl sulfate	1.004	0.079772	0.012698
		Sulfolithocholic acid	3.4565	0.075366	0.014594
Neurosubstances	GABA derivative	12-HETE-GABA	7.59703	0.487429	0.004939

		Escitalopram	1.39545	2.044428	0.022871
		Nervonic acid	4.51618	0.018342	0.009229
Vitamins	Vitamin D	24,24-difluoro-1alpha,25-dihydroxy-26,27-dimethylvitamin D3 / 24,24-difluoro-1alpha,25-dihydroxy-26,27-dimethylcholecalciferol	1.56192	0.016346	0.009599
		24,25-Dihydroxyvitamin D	2.36412	0.464389	0.006392
		4,4-difluorovitamin D3 / 4,4-difluorocholecalciferol	1.48771	0.124126	0.012718
	Vitamin B6	Pyridoxamine	1.43986	0.47474	0.007479
Amino acids	Tryptophan metabolism	Indoleacetic acid	1.70765	0.490105	0.019732
	Homoserine	N-heptanoyl-homoserine lactone	8.04266	0.356614	0.013146
	isoleucine	N-oleoyl isoleucine	1.93878	2.0159	0.00223
Carbohydrate metabolism		24Z-ethylidene-cholest-5-en-3beta-ol 3-O-beta-D-glucopyranoside	3.45892	2.155823	0.001448
		2-O-(beta-D-galactopyranosyl-(1->6)-beta-D-galactopyranosyl) 2S,3R-dihydroxyundecanoic acid	1.02843	2.989993	5.56E-05
		Collettiside I	1.95715	3.134898	0.004241
		convallatoxin	1.3721	0.200266	0.000169
		D-Xylose	1.021	0.436381	0.025178
		Iokundjoside	1.19018	4.547486	0.000174
Nucleic acid metabolism		Adenosine	2.9959	0.32556	1.51E-06
		Uric acid	1.35464	0.454336	0.011001
Fatty acids	Long chain saturated fatty acids and their derivatives	15-hydroxy-pentadecanoic acid	1.7828	0.478506	0.037777
		3-bromohexadecanoic acid	1.81252	0.401048	0.021109
		2-hydroxy-tricosanoic acid	1.47773	0.491143	0.037373
	Long chain unsaturated fatty acids and their derivatives	16-bromo-9E-hexadecenoic acid	1.06182	0.072904	0.015058
		18-fluoro-9Z-octadecenoic acid	1.41743	0.342272	0.014041
		22-tricosenoic acid	4.73134	0.033699	0.009918
		25:2(5Z,9Z)(23Me)	2.26632	0.013704	0.009466
		28:2(5Z,9Z)(6Br)	1.11437	2.905645	0.004954
		2-propyl-9Z-octadecenoic Acid	1.5337	0.025622	0.011241
		8,12-dihydroxy-9-chloro-5Z,10Z,14Z,17Z-eicosatetraenoic acid	1.00786	2.218218	0.010311
		9,13-dihydroxy-10-ethoxy-11-octadecenoic acid	1.24003	0.416479	0.032661
		9-hexacosenoic acid	4.31862	0.04399	0.008244
		Hydroxyeicosatetraenoic acid	3.12705	2.159697	0.010994
	Mycolipenic acid (C25)	6.86281	0.04467	0.009242	
	Medium chain fatty acids and their derivatives	3-O-(2-O-(2E-decenoyl)-alpha-L-rhamnopyranosyl)-3-hydroxydecanoic acid	1.18888	3.069376	0.001826
		N-(6-aminohexanoyl)-6-aminohexanoic acid	6.05797	0.419839	0.011457
	Short chain fatty acid derivatives	11,11-Difluoro-9Z-dodecenyl acetate	1.12914	2.045574	0.000562
	Diprotic acid	2-hydroxy-decanedioic acid	4.24002	0.045162	0.041341
		Pimelic acid	1.36116	0.060191	0.011235
Lipid metabolism	Cholesterol and derivatives	Cholest-5-ene	2.42976	0.018354	0.00993
		Cholesterol glucuronide	2.169	2.89347	0.001736
	Lysophospholipid	LysoPC(22:0)	1.27504	2.053082	3.15E-05

		LysoPC(24:0)	1.19473	2.261584	2.46E-06
	Glycerophosphates	PA(18:0/18:1(9Z))	1.11835	0.431081	0.023524
		PA(22:1(11Z)/0:0)	1.99219	0.416601	0.011821
	Glycerophosphocholines	PC(11:0/0:0)	2.16009	0.46492	0.048111
		PC(12:0/0:0)	7.11034	0.465356	0.049884
		PC(8:0/0:0)	1.57615	0.244548	0.004823
		PC(9:0/0:0)	1.80698	0.330435	0.003907
		PC(O-14:0/15:0)	15.1294	2.059543	0.000102
		PC(O-14:0/16:0)	6.22912	2.029295	0.003134
		PC(O-16:0/O-1:0)	3.63589	2.075869	0.000154
		PC(O-18:1(9Z)/O-1:0)	1.15015	2.172964	1.53E-06
	Glycerophosphoethanolamines	PE(O-16:0/14:0)	1.40193	2.656529	0.0002
		PE(O-16:0/15:0)	7.33687	2.906254	0.000171
	Glycerophosphoglycerols	PG(16:1(9Z)/22:2(13Z,16Z))	1.73221	2.775226	0.000237
		PG(18:0/18:1(11Z))	5.56416	2.243027	0.000307
		PG(20:2(11Z,14Z)/0:0)	1.59875	3.884499	0.000259
		PG(21:0/0:0)	1.32784	3.215985	0.000983
		PG(22:1(11Z)/0:0)	2.78892	0.307749	0.002256
		PG(O-20:0/0:0)	1.69215	2.074906	0.000449
		PG(P-20:0/0:0)	4.68311	2.530474	6.18E-06
	Glycerophosphoinositols	PI(18:4(6Z,9Z,12Z,15Z)/0:0)	7.23333	0.276719	0.003496
	Isoprenoids	(-)-Jolkinol B	1.16872	0.148852	0.015719
		(11Z)-8,18-propano-retinal	8.38407	0.458676	0.008611
		Caesalpinin N	1.34069	3.084153	0.001289
	Steroids/ Sterols	27-nor-campestan-3beta,4beta,5alpha,6alpha,7beta,8beta,14alpha,15alpha,24-nonol	1.62497	2.553424	0.006492
		29-demethylgeodisterol-O-sulfite	2.67913	0.198664	0.008267
		3-O-(Galb)-(25R)-12-oxo-5alpha-spirostan-3beta-ol	2.09667	3.308359	0.001803
		Cucurbitacin D	2.40508	0.399089	0.002388
		Fludrocortisone	1.45689	0.03075	0.01909
	Sphingolipids/ sphingosine	(3'-sulfo)Galbeta-Cer(d18:1/16:0(2OH))	1.55514	2.526705	4.37E-06
		C16 Sulfatide	1.68028	2.298188	0.00011
		Cer(d18:0/14:0)	1.75815	2.591061	0.000283
		Obscuraminol A	1.32961	0.48544	7.12E-08
		Sphinganine-1-phosphocholine	1.09193	2.988506	2.14E-06
	Glycosyldiradylglycerols	MGDG(16:0/18:2(9Z,12Z))	1.70905	2.441004	7.63E-07
	Glycerophosphoserines	CPA(18:0)	1.20174	0.309212	0.024583
	Diacylglycerols	DG(17:2(9Z,12Z)/22:6(4Z,7Z,10Z,13Z,16Z,19Z)/0:0)[iso2]	1.42504	0.015226	0.008811
	Other	PT(18:0/18:1(9Z))	1.13333	2.496505	0.000464
Incretions		1(3)-glyceryl-PGF2alpha	1.05499	0.28607	0.024052
		18-Oxocortisol	1.09924	0.448452	0.022182
		Estrone	1.34977	0.208686	0.023191

Alcohols		11Z-eicosen-1-ol	2.52714	4.218534	0.010267
		3,7,11-Trimethyl-6E,10-dodecadien-1-ol	3.1878	0.432384	0.007761
		6-Ketoestriol	1.45009	2.136686	0.007277
Ketones		8,8-Dimethyl-2-phenyl-4H,8H-benzo[1,2-b:3,4-b']dipyran-4-one	1.01912	0.248429	0.012364
		Euchrenone b2	1.10955	0.004907	0.018047
		Isocordoin	1.38433	2.00039	0.00326
		Lophirone E	1.12243	0.004801	0.012627
Amines		N-Oleoylethanolamine	1.19278	2.14711	0.01479
Others	Antibiotics	10-Deoxymethymycin	1.93079	0.040474	0.009069
	Aldehydes	2-dodecenal	1.067	0.027766	0.011862
	Ester	phorbol 13-acetate 12-myristate	1.85483	0.033284	0.044236
	Antioxidant	Gambiriin C	1.76759	2.14935	2.36E-05
		Eugenol	3.23192	2.19116	0.001
		Atenolol	2.66546	7.930791	4.19E-06

^aThe difference in the abundance of each metabolite is expressed as the ratio of its average content in the 0.15-SeM group and in the 0.15-SeL group (0.15-SeM/0.15-SeL). A ratio of >1 indicates that the corresponding metabolite had higher abundance in the 0.15-SeM group, whereas a ratio of <1 indicates that the corresponding metabolite has lower abundance in the 0.15-SeM group. ^bDifferences in metabolite abundances between the 0.15-SeM and 0.15-SeL groups were analyzed using one-way analysis of variance, followed by the Tukey's post hoc test. $P < 0.05$ was considered as significant.

Table S7 Significantly altered fecal metabolites in the 0.4-SeM/0.4-SeL comparison

Super-pathway	Sub-pathway	Metabolites	VIP value	FC ^a	P value ^b
Bile acid metabolism		12alpha-Hydroxy-5beta-chol-3-en-24-oic Acid	6.47654	2.811598	0.000251
		27-Norcholestanehexol	1.11839	0.340178	6.22E-06
		3alpha,7alpha,12alpha-trihydroxy-27-carboxymethyl-5beta-cholestan-26-oic acid	1.02346	0.365031	0.031638
		Chenodeoxycholic acid glycine conjugate	3.01406	3.063198	0.002044
		Tauroursodeoxycholic acid	1.12574	2.049367	0.001417
Neurosubstances		12-HETE-GABA	6.29729	0.278152	0.003169
		5-Hydroxy-L-tryptophan	2.53347	2.543108	1.06E-05
		4-Acetamidobutanoic acid	1.69026	0.206727	0.014579
		Ecgonine methyl ester	2.20517	0.337182	0.006742
		Gabapentin	1.16537	0.254905	0.005073
		N-arachidonoyl GABA	1.64158	0.333583	0.001213
		N-docosahexaenoyl GABA	2.99481	2.839085	0.002546
		Norepinephrine sulfate	1.02108	14.64516	0.019446
Vitamins	Vitamin D	(17E)-1alpha,25-dihydroxy-26,27-dimethyl-17,20,22,22,23,23-hexadehydro-24a-homovitamin D3 / (17E)-1alpha,25-dihydroxy-26,27-dimethyl-17,20,22,22,23,23-hexadehydro-24a-homocholecalciferol	1.8254	2.778742	0.002759

		(22E)-26,26,26,27,27,27-hexafluoro-25-hydroxy-22,23-didehydrovitamin D3 / (22E)-26,26,26,27,27,27-hexafluoro-25-hydroxy-22,23-didehydrocholecalciferol	4.87512	0.30144	0.014411
		(23R,25R)-25-hydroxyvitamin D3 26,23-lactone / (23R,25R)-25-hydroxycholecalciferol 26,23-lactone	3.0928	10.22713	1.29E-05
		(23S)-1alpha-hydroxy-25,27-didehydrovitamin D3 26,23-lactone	2.7228	0.382753	0.019073
		1alpha,25-dihydroxy-19-nor-22-oxavitamin D3 / 1alpha,25-dihydroxy-19-nor-22-oxacholecalciferol	2.18005	0.355821	0.000427
		1alpha-hydroxy-2beta-(4-hydroxybutoxy)vitamin D3 / 1alpha-hydroxy-2beta-(4-hydroxybutoxy)cholecalciferol	1.0089	3.405688	0.008244
		24,24-difluoro-1alpha,25-dihydroxy-26,27-dimethyl-24a-homovitamin D3 / 24,24-difluoro-1alpha,25-dihydroxy-26,27-dimethyl-24a-homocholecalciferol	3.07961	0.494584	0.000193
		26,26,26-trifluoro-25-hydroxy-27-norvitamin D3 / 26,26,26-trifluoro-25-hydroxy-27-norcholecalciferol	1.78807	4.470322	9.2E-07
		C-9,11,21-Trisnor-17-methyl-1alpha,25-dihydroxyvitamin D3	1.25733	0.234061	9.49E-05
	Vitamin B6	4-Pyridoxic acid	1.06551	0.479468	0.027984
	Vitamin H	Biotin	1.28105	0.226647	0.02472
Amino acids	Glycine	Hippuric acid	1.24722	0.278489	0.017885
		4-Aminohippuric acid	1.27558	0.190354	0.004781
		Nicotinuric acid	1.34597	0.226602	0.017578
		Isovalerylglycine	2.24295	0.304888	0.002805
	Serine	Serratamic acid	1.30424	3.587943	7.93E-07
		N-(3-(15-methyl-hexadecanoyloxy)-13-methyl-tetradecanoyl)-L-serine	1.20051	3.639548	0.000124
		N-(3-oxododecanoyl) homoserine lactone	1.45963	5.72078	0.001265
	Phenylalanine	L-Aspartyl-L-phenylalanine	1.20904	0.405374	0.000159
	Pentapeptide	APGPR Enterostatin	1.59617	0.163574	0.003522
	Aspartic acid	N-oleoyl asparagine	1.18762	0.459977	1E-06
	Methionine	N-palmitoyl methionine	2.3864	0.44707	8.3E-07
	Arginine	L-Arginine	3.08161	0.384338	0.046818
	Tryptophan metabolism	Xanthurenic acid	4.06497	0.21178	0.00276
Lysine derivatives	Homocitrulline	1.92478	3.028259	1.68E-06	
Carbohydrate metabolism		(-)-menthyl beta-D-glucoside	2.01677	2.089462	8.78E-06
		L-Malic acid	3.87644	6.222569	0.001314
Nucleic acid metabolism		Adenosine	1.94461	2.763653	0.001697
		Cytosine	2.31303	0.402554	0.000289
		Thymidine	3.48431	2.892382	0.000365
		Uric acid	1.44402	0.110322	9.54E-09
Fatty acids	Long chain unsaturated fatty acids and their derivates	12S-hydroxy-16-heptadecynoic acid	1.31438	2.136076	0.001772
		11-hydroperoxy-12,13-epoxy-9-octadecenoic acid	8.29529	2.469887	0.002446
	Long chain unsaturated fatty acids and their derivates	12-oxo-14,18-dihydroxy-9Z,13E,15Z-octadecatrienoic acid	3.94919	2.177596	0.000264
		13-keto-9Z,11E,15Z-octadecatrienoic acid	9.08854	2.115562	0.000561

		14,15-DiHETrE	1.32509	0.467916	0.001187
		18-fluoro-9Z-octadecenoic acid	1.11917	0.201485	6.52E-06
		24:3(15Z,18Z,21Z)	2.51429	0.214741	6.91E-05
		28:3(5Z,9Z,21Z)	1.28701	2.207903	2.28E-05
		3E,5E-tridecadienoic acid	3.58926	0.460008	4.64E-05
		8,11,14-Eicosatrienoic acid	2.88509	0.483278	0.000175
		9,12,13-TriHOME	1.86826	8.135563	4.64E-06
		9S-HpOTrE	5.62679	2.35879	0.000159
		Eicosenoic acid	4.25078	3.038308	3.32E-07
		Vaccenic acid	2.38527	0.441766	1.08E-05
	Long chain saturated fatty acids and their derivates	13-hydroxy-tridecanoic acid	1.9042	6.896806	2.52E-08
		14-hydroxy-heneicosanoic acid	1.95845	0.21367	0.000176
		15-hydroxy-pentadecanoic acid	1.40014	0.437632	0.008687
		20-oxo-heneicosanoic acid	4.10972	0.216423	5.57E-05
		21-hydroxy-heneicosanoic acid	1.0506	0.499762	0.00087
		3-bromohexadecanoic acid	1.16056	0.368702	0.008375
		Heptadecanoic acid	4.04576	2.08861	0.006919
		Pristanic acid	3.95653	3.150009	0.002455
		Sativic acid	2.38836	4.879585	3.2E-05
	Medium chain fatty acids and their derivates	10-undecynoic acid	1.31045	3.054431	0.000601
		2,6-nonadienoic acid	2.41155	2.095623	6.97E-06
		2E,4E,8Z,10E-dodecatetraenoic acid	1.90781	2.817639	8.68E-05
		2-hydroxy-10-undecenoic acid	4.2052	3.245082	7.52E-05
		5-oxo-7-octenoic acid	2.6653	0.258704	0.009019
		2-hydroxy pelargonic acid	2.79336	5.608216	1.83E-06
		3,6-dioxo-decanoic acid	1.3678	2.49998	0.001064
		3-O-(2-O-(2E-decenoyl)-alpha-L-rhamnopyranosyl)-3-hydroxydecanoic acid	1.16241	2.77458	0.004235
		3-O-alpha-L-rhamnopyranosyl-3-hydroxydecanoic acid	1.69257	2.029412	7.85E-06
		3-O-alpha-L-rhamnopyranosyl-3-hydroxydecanoyl-3-hydroxydecanoic acid	1.00195	2.642189	0.000486
		9,12-dioxo-dodecanoic acid	4.04483	3.137825	9.51E-05
		methyl 8-[2-(2-formyl-vinyl)-3-hydroxy-5-oxo-cyclopentyl]-octanoate	1.26441	3.046238	1.37E-05
	Short chain fatty acid derivatives	Mevalonic acid	1.21463	2.200159	0.003354
	Diprotic acid and their derivatives	2-methyl-hexadecanedioic acid	3.15365	2.324072	0.006439
		2-methyl-tridecanedioic acid	1.19167	10.90055	4.57E-08
		3-hydroxy-dodecanedioic acid	2.8767	2.62862	0.000159
		3-hydroxy-tetradecanedioic acid	1.99426	2.152979	0.001907
		9,10-dihydroxy-Octadecanedioic acid	2.63023	4.413756	2.83E-08
		Azelaic acid	1.97039	2.560911	0.001882
		Dodecanedioic acid	1.19087	2.605516	0.005525
		Heneicosanedioic acid	2.26421	0.193885	0.000143

		Hexacosanedioic acid	1.43296	0.092231	0.000774
Lipid metabolism	Lipid biosynthesis	Hexanoylcarnitine	1.23262	0.355708	0.000265
		Isobutyryl-L-carnitine	1.12919	0.447748	0.001044
		L-Acetylcarnitine	13.1806	2.015422	0.000238
		Propionylcarnitine	1.55468	2.107986	0.00746
		Tiglylcarnitine	1.43487	0.189223	0.003377
	Cholesterol and derivatives	(25S)-5alpha-cholestan-3beta,6alpha,7beta,8beta,15alpha,16beta,26-heptol	3.6951	3.419886	0.00016
		15,20-dihydroxycholest-4,14-dien-3,16-dione	4.14582	6.696632	3.68E-05
		24-Hydroxycholesterol	1.66802	3.202702	0.000273
		3beta-hydroxy-4beta-methyl-5alpha-cholest-7-ene-4alpha-carbaldehyde	1.23662	0.394269	1.1E-07
		5alpha-cholestan-3beta,6alpha,8beta,15alpha,24S-triol	4.47277	0.197227	3.26E-05
		Herbasterol	1.40615	0.360264	0.000732
	Glycerophosphoglycerols	PG(13:0/0:0)	1.09173	0.380068	0.00109
		PG(13:0/22:0)	1.38256	3.309614	0.000173
		PG(15:0/0:0)	1.5836	0.450488	0.021966
		PG(18:0/0:0)	2.36958	2.681771	9.28E-06
		PG(18:1(9Z)/0:0)	2.07314	0.483077	0.015091
		PG(18:3(6Z,9Z,12Z)/0:0)	1.07152	3.864389	0.000324
		PG(20:2(11Z,14Z)/0:0)	1.33686	0.391506	0.000863
		PG(21:0/0:0)	1.76835	4.442165	2.08E-08
		PG(22:1(11Z)/0:0)	2.16681	0.243833	0.003308
		PG(O-16:0/17:2(9Z,12Z))	1.47788	4.138596	0.004399
		PG(P-16:0/0:0)	18.5157	0.447495	6.29E-06
	Diradylglycerols	DG(13:0/18:2(9Z,12Z)/0:0)[iso2]	2.27941	0.429562	2.93E-05
		DG(13:0/20:5(5Z,8Z,11Z,14Z,17Z)/0:0)[iso2]	2.80845	0.376806	1.09E-05
		DG(15:0/16:0/0:0)	1.01928	3.144933	0.000302
		DG(15:0/16:1(9Z)/0:0)	2.917	0.367112	4.99E-06
		DG(15:0/18:3(6Z,9Z,12Z)/0:0)	2.1665	0.313649	5.21E-06
		DG(17:2(9Z,12Z)/22:4(7Z,10Z,13Z,16Z)/0:0)[iso2]	3.61668	0.434258	5.42E-05
		DG(17:2(9Z,12Z)/22:5(7Z,10Z,13Z,16Z,19Z)/0:0)[iso2]	1.14697	0.33793	0.000166
	Glycerophosphates	PA(18:0/0:0)	5.45442	0.48253	0.015483
		PA(20:0/0:0)	5.29898	0.462234	0.007743
		PA(22:1(11Z)/0:0)	1.38586	0.34619	0.032327
PA(O-16:0/12:0)		1.9978	0.059234	0.000179	
PA(O-16:0/14:1(9Z))		1.03933	0.272106	7.79E-06	
PA(P-16:0/14:1(9Z))		3.87987	0.159681	5.26E-05	
PA(P-16:0/15:1(9Z))		1.15927	0.327589	0.000394	
PA(P-18:0/17:2(9Z,12Z))		1.18356	0.418858	0.001499	
Glycerophosphocholine	LysoPC(P-18:0)	1.32647	0.489958	0.04805	
	PC(12:0/12:0)	1.09621	0.035984	0.000124	

		PC(9:0/0:0)	1.87375	0.079881	0.00015
		PC(O-16:0/0:0)	4.03704	0.340236	0.028169
		PC(O-8:0/O-8:0)	1.3516	0.354695	0.023776
	Glycerophosphoethanolamines	PE(12:0/15:1(9Z))	1.0076	0.077228	0.000214
		PE(15:0/18:3(6Z,9Z,12Z))	1.05741	0.394374	2.57E-06
		PE(18:2(9Z,12Z)/0:0)	1.02192	3.338561	4.97E-05
		PE(18:4(6Z,9Z,12Z,15Z)/18:4(6Z,9Z,12Z,15Z))	1.67561	0.187594	7.31E-06
	Glycerophosphoserines	PS(12:0/15:0)	1.14042	0.050414	0.000174
		PS(14:1(9Z)/20:5(5Z,8Z,11Z,14Z,17Z))	1.98709	0.423466	6.26E-06
		PS(14:1(9Z)/22:6(4Z,7Z,10Z,13Z,16Z,19Z))	1.60736	0.122793	0.000208
		PS(15:0/22:2(13Z,16Z))	3.14225	2.542123	0.000565
		PS(O-16:0/18:3(9Z,12Z,15Z))	1.39079	0.390676	0.00101
	Steroids/ Sterols	(20S,24S)-24-ethylthornasterol	1.34409	0.470274	0.002317
		16-a-Hydroxypregnenolone	1.14055	0.328858	0.000572
		20,26-dihydroxyecdysone	2.43645	2.766946	0.003663
		22-deoxy-20,21-dihydroxyecdysone	5.34434	3.255316	0.001196
		27-nor-campestan-3beta,4beta,5alpha,6alpha,7beta,8beta,14alpha,15alpha,24-nonol	2.45186	0.246816	7.5E-06
		29-demethylgeodisterol-O-sulfite	2.08168	0.145391	0.024346
		6-deoxoteasterone	1.29031	2.727758	0.002682
		Campesterol	1.40358	8.100639	8.83E-11
		cimicifoetiside B	1.23711	2.4368	0.002422
		Cucurbitacin D	2.13648	2.156043	0.003738
		Hydrocortisone cypionate	3.49639	2.849681	4.59E-05
		Kammogenin	2.97614	2.066764	0.002048
		Minabeolide-4	1.65909	12.43375	3.05E-05
		Tetrahydrodeoxycorticosterone	2.73481	0.287802	0.000394
		Theonellasterol D	2.07082	2.004003	0.006766
		Xeniasterol-b	1.15751	0.263416	6.69E-09
		Ximaosteroid C	2.62136	2.664539	0.000658
	Isoprenoids	(-)-Fusidic acid	1.45586	0.066513	0.000103
		(-)-Jolkinol A	2.01034	6.091185	1.52E-05
		19-(3-methyl-butanoyloxy)-villanovane-13alpha,17-diol	1.13133	0.356608	4.54E-05
		5-(1-hydroxypropan-2-yl)isolongifol-4-ene	3.05805	0.386003	0.002457
		C25:2 6,7-Epoxy highly branched isoprenoid	1.56225	0.202187	2.62E-05
		forskolin	2.01101	2.128276	0.000927
		gibberellin A17	1.60981	4.673945	0.000654
		Japonicumins A	1.61946	3.127666	0.011503
		Ketospiriloxanthin	1.09233	3.854058	0.011617
		Moronic acid	1.44701	0.219209	0.000113
		Rhodoxanthin	1.59553	0.02089	1.4E-08

	Sphingolipids/ sphingosine	Cer(d18:0/13:0)	1.00904	2.12405	0.000745
		Cer(d18:0/14:0)	1.84458	6.890001	4.25E-06
		Sphinganine	11.2087	2.586811	0.000685
		Spisulosine	2.48007	2.49487	1.1E-05
	Glycosyldiradylglycerols	MGDG(18:5(3Z,6Z,9Z,12Z,15Z)/18:4(6Z,9Z,12Z,15Z))	3.56462	4.075042	0.001311
	Other	15-HETE-G	1.25366	0.455931	5.83E-06
Incretions		11-dehydro-2,3-dinor-TXB2	1.20414	2.782206	0.000117
		11-deoxy-16,16-dimethyl-PGE2	1.66029	0.380777	4.87E-05
		15R-PGE2 methyl ester, 15-acetate	1.15447	2.785809	0.000103
		18-Oxocortisol	1.3986	2.399231	0.000242
		1a,1b-dihomo-PGE2	2.44566	0.306106	0.001141
		3b,17b-Dihydroxyetiocholane	4.47233	2.708955	0.018512
		Androsterone	1.43509	2.137605	0.02097
		C22-PGF4alpha	1.61455	0.214107	0.000826
		Estrone	1.08339	0.098192	0.000909
		Jasmonic acid	2.88291	2.932751	7.8E-05
		Nandrolone	1.03861	2.186078	0.001422
		Prostaglandin F1a	2.1804	2.446682	1.68E-05
Amides		Anandamide (22:6, n-3)	1.27217	0.47385	0.0079
		Margaroyl-EA	3.77403	2.418226	5.91E-05
		Oleamide	4.08377	0.349365	8.67E-05
		Palmitoleoyl-EA	1.04008	0.18414	0.00063
Ketones		12-Tridecen-2-one	1.22552	2.194226	0.021471
		5,5'-Dihydroxy-3,6,7,2',4'-pentamethoxyflavone 5'-glucoside	1.44651	0.496222	2.14E-05
		cis-Jasmone	1.42912	3.02993	0.000104
		Repensol3,7,9-Trihydroxycoumestan	1.24551	3.263273	0.005993
		Ulexone B	1.2354	0.3917	0.039145
		zymosterol intermediate 1c	1.60358	0.472279	1.65E-07
Alkanes/ Hydrocarbons		2,4-Dimethyl-2E,4E-hexadien-1-ol	4.09094	0.268854	0.01521
		3,5-Di-O-methyl-8-prenylafzelechin-4beta-ol	3.97163	0.440696	0.026404
		3,7,11-Trimethyl-6E,10-dodecadien-1-ol	4.15307	0.147623	8.45E-05
		3Z,13Z-octadecadien-1-ol	5.46838	2.618402	0.000725
		Dryopterin	1.22795	0.352479	0.002114
		Falcarindiol	1.47493	2.772684	0.000165
		Hydroxytyrosol	1.70502	0.259461	0.011991
		14S-Methyl-1-octadecene	1.63874	0.262973	0.000258
		3Z,6Z,9Z-Octadecatriene	1.34764	2.531684	0.000564
		4Z,8Z-Heptadecadiene	1.27434	2.927974	0.000312
		6-Ethyl-4-methyl-3E,5E,7E-decatriene	1.01416	2.25116	0.019285
		7-Ethyl-3,11-dimethyl-1,3Z,6E,10-tridecatetraene	1.45864	2.709998	2.05E-05

Aldehydes	10Z-Nonadecenal	1.59361	3.405558	0.002801
	2-decene-4,6,8-triyn-1-al	1.06716	0.328586	0.001366
	Nonadecanal	1.18589	5.081851	4.2E-05
	4-Hydroxynonenal	1.41105	2.08862	9.2E-05
Phenols	p-Cresol sulfate	3.85549	0.384081	0.00495
	Thymol	1.25663	2.178806	0.000442
Antibiotics	Glycyrrhetic acid	1.40838	0.206781	1.76E-06
Esters	phorbol 13-acetate 12-myristate	2.54865	3.067039	0.002731
Alcohols	2,6,8,12-Tetramethyl-2,4-tridecadien-1-ol	2.24003	2.179889	0.006216
	11Z-eicosen-1-ol	1.38584	2.617502	0.048721
Others	20-acetoxy-clavulone I	1.51929	0.470837	5.35E-07
	2-Aminobenzoic acid	1.00218	0.299932	0.004482
	2R-HpOTrE	1.57856	3.307703	0.001589
	30,32-dihydroxy-2b-methyl-bishomohopane	2.17546	0.182189	7.66E-06
	31-hydroxy-32,35-anhydrobacteriohopanetetrol	4.24197	0.378775	1.14E-05
	all-trans-heptaprenyl diphosphate	3.78288	0.118924	3.71E-07
	Bufalin	2.84451	2.367503	0.001208
	Coproporphyrin III	6.02306	0.190126	1.6E-07
	Creatinine	3.75189	0.280939	0.008226
	Deoxy pyridinoline	2.12584	2.365123	0.000348
	Kynurenic acid	1.80473	0.274545	0.007071
	Onocerin	1.24831	0.337667	5.36E-06
	Protoporphyrin IX	1.08095	0.11919	0.003458

^aThe difference in the abundance of each metabolite is expressed as the ratio of its average content in the 0.40-SeM group and in the 0.40-SeL group (0.40-SeM/0.40-SeL). A ratio of >1 indicates that the corresponding metabolite had higher abundance in the 0.40-SeM group, whereas a ratio of <1 indicates that the corresponding metabolite has lower abundance in the 0.40-SeM group. ^bDifferences in metabolite abundances between the 0.40-SeM and 0.40-SeL groups were analyzed using one-way analysis of variance, followed by the Tukey's post hoc test. $P < 0.05$ was considered as significant.

Table S8 Differentially expressed proteins in the Se-D/0.15-SeL comparison

Accession ^a	Description ^b	FC ^c	P value ^d
B1Q450	HBB1; Hemoglobin beta chain subunit	1.98	0.0007
Q8CGP0	Hist3h2bb; Histone H2B type 3-B	1.25	0.0129
P11352	Gpx1; Glutathione peroxidase 1	0.75	0.0000
A0A075B5S2	Ighv7-1; Uncharacterized protein (Fragment)	0.61	0.0499
A0A0A6YXN4	Ighv1-18; Immunoglobulin heavy variable V1-18	0.81	0.0081
P34928	Apoc1; Apolipoprotein C-I	1.21	0.0073
I6L998	N/A; Uncharacterized protein	1.58	0.0414
Q3TBL6	Tnfaip8l3; Tumor necrosis factor alpha-induced protein 8-like protein 3	0.80	0.0015

A0A1E1GJG6	Wgn-scFv; Single-chain variable	0.67	0.0023
Q9CZH7	Mxra7; Matrix-remodeling-associated protein 7	0.83	0.0334
F7BJB9	Morc3; MORC family CW-type zinc finger protein 3	0.76	0.0422
X5J5N0	N/A; IgM heavy chain VDJ region	1.29	0.0294
Q924Q3	Ighm; VH186.2-D-J-C mu protein	0.62	0.0329
P0C7N9	Psmg4; Proteasome assembly chaperone 4	0.81	0.0011
E9PWN0	Lpin2; Phosphatidate phosphatase LPIN2	0.79	0.0467
Q8R2H9	Phospho1; Phosphoethanolamine/phosphocholine phosphatase	0.82	0.0256
G5E8C6	Vill; Villin-like protein	1.45	0.0081
E0CX47	Nxpe5; Neurexophilin and PC-esterase domain family, member 5	0.79	0.0403

^aThe accession ID of each protein in the Uniprot database. ^bThe gene name and protein description of each protein in the Uniprot database. ^cThe fold change value of each differentially expressed protein in the Se-D/0.15-SeL comparison. ^dDifferences in protein abundances between the Se-D and 0.15-SeL groups were analyzed using one-way analysis of variance, followed by the Tukey's post hoc test. $P < 0.05$ was considered as significant. The value 0 indicates $P < 0.0001$.

Table S9 Differentially expressed proteins in the 0.40-SeL/0.15-SeL comparison

Accession ^a	Description ^b	FC ^c	P value ^d
F6V2H5	Vill1; Villin-1 (Fragment)	0.79	0.0392
B1Q450	HBB1; Hemoglobin beta chain subunit	1.92	0.0081
P16015	Ca3; Carbonic anhydrase 3	1.31	0.0349
P19639	Gstm3; Glutathione S-transferase Mu 3	0.81	0.0023
Q3UKA4	Adh1; Alcohol dehydrogenase 1 (Class I), isoform CRA_c	0.81	0.0078
P13745	Gsta1; Glutathione S-transferase A1	0.74	0.0012
F6XWD4	Ppp1r12c; Protein phosphatase 1 regulatory subunit 12C (Fragment)	0.81	0.0340
G3X9Y6	Akr1c19; Aldo-keto reductase family 1, member C19	0.83	0.0002
P09528	Fth1; Ferritin heavy chain	0.82	0.0460
P24472	Gsta4; Glutathione S-transferase A4	0.79	0.0026
O09049	Reg3g; Regenerating islet-derived protein 3-gamma	1.49	0.0002
Q9D8L4	N/A; Uncharacterized protein	0.82	0.0418
Q8C1N8	Defa22; Alpha-defensin 22	1.53	0.0428
A0A075B5K2	Igkv9-124; Immunoglobulin kappa chain variable 9-124	0.57	0.0287
Q0PD10	Rab43; RIKEN cDNA 1810048P08, isoform CRA_c	0.79	0.0300
Q3UEN8	Cyp3a11; MCG15287	0.82	0.0291
Q08ED0	Bcl2l15; Bcl-2-like protein 15	1.27	0.0026
A0A075B5Y4	Ighv1-81; Immunoglobulin heavy variable 1-81	0.77	0.0066

Q9QX60	Dguok; Deoxyguanosine kinase, mitochondrial	0.81	0.0200
Q3UYR3	Cbfb; Putative uncharacterized protein (Fragment)	0.79	0.0230
P35230	Reg3b; Regenerating islet-derived protein 3-beta	1.82	0.0003
Q8VI47	Abcc2; Canalicular multispecific organic anion transporter 1	0.82	0.0499
A0A0G2JFE9	Ighv1-76; Immunoglobulin heavy variable 1-76 (Fragment)	0.79	0.0050
Q3TBL6	Tnfaip8l3; Tumor necrosis factor alpha-induced protein 8-like protein 3	0.82	0.0050
P28667	Marcks1l; MARCKS-related protein	0.81	0.0001
Q8K205	Pop1; Processing of 1, ribonuclease P/MRP family, (S. cerevisiae)	0.81	0.0495
A0A1E1GJG6	Wgn-scFv; Single-chain variable	0.65	0.0014
Q3UP47	Cfd; Complement factor D (Adipsin)	0.81	0.0041
P70410	Gnl2; Nucleolar GTP-binding protein 2 (Fragment)	0.83	0.0135
Q7TN79	Akap7; A-kinase anchor protein 7 isoform gamma	0.83	0.0002
J3QP43	Stum; Protein stum homolog	0.76	0.0029
Q920L5	Elovl6; Elongation of very long chain fatty acids protein 6	0.82	0.0062
D3Z689	Adamts15; ADAMTS-like 5	0.80	0.0445
P42337	Pik3ca; Phosphatidylinositol 4,5-bisphosphate 3-kinase catalytic subunit alpha isoform	0.78	0.0457
A5D6P2	Pard3; Par-3 (Partitioning defective 3) homolog (C. elegans)	0.81	0.0143
Q9CZH7	Mxra7; Matrix-remodeling-associated protein 7	0.82	0.0273
Q9QYS9	Qki; Protein quaking	0.82	0.0161
Q9WV38	Slc2a5; Solute carrier family 2, facilitated glucose transporter member 5	0.73	0.0032
A0A0B4J1I9	Igkv4-55; Immunoglobulin kappa variable 4-55 (Fragment)	0.78	0.0351
E9QAU9	Lrch3; Leucine-rich repeat and calponin homology domain-containing protein 3	0.79	0.0002
Q6P9L6	Kif15; Kinesin-like protein KIF15	0.80	0.0317
A0A0A0MQ99	Swi5; DNA repair protein SWI5 homolog	0.81	0.0376
Q8R418	Dicer1; Endoribonuclease Dicer	0.82	0.0184
P16054	Prkce; Protein kinase C epsilon type	0.82	0.0389
Q3UGB8	Der1l; Derlin	0.83	0.0460
Q91VL8	Terf2ip; Telomeric repeat-binding factor 2-interacting protein 1	0.78	0.0080
Q3V009	Tmed1; Transmembrane emp24 domain-containing protein 1	0.81	0.0044
Q924Q3	Ighm; VH186.2-D-J-C mu protein (Fragment)	0.60	0.0251
A0A0A6YXB7	Ssr2; Translocon-associated protein subunit beta	1.35	0.0314
P0C7N9	Psmg4; Proteasome assembly chaperone 4	0.81	0.0053
E9PWN0	Lpin2; Phosphatidate phosphatase LPIN2	0.72	0.0289
Q8CII2	Cdc123; Cell division cycle protein 123 homolog	0.83	0.0317
Q8R2H9	Phospho1; Phosphoethanolamine/phosphocholine	0.77	0.0182

	phosphatase		
Q5F2D0	Acs16; Putative uncharacterized protein	0.82	0.0011
Q3TV21	Fxn; Frataxin	0.79	0.0217
Q80ZM7	Gtf2a2; Transcription initiation factor IIA subunit 2	1.31	0.0152
J3QNH8	Gm7694; Uncharacterized protein	0.81	0.0499
B2RPV6	Mmrn1; Multimerin-1	0.80	0.0010
O54788	Dffb; DNA fragmentation factor subunit beta	0.83	0.0350
Q9D0I6	Wdsub1; WD repeat, SAM and U-box domain-containing protein 1	0.79	0.0094
E9QJT3	Sft2d3; Vesicle transport protein	0.83	0.0144
G5E8C6	Vill; Villin-like protein	2.00	0.0001
Q9Z2D1	Mtmr2; Myotubularin-related protein 2	0.78	0.0171
E0CX47	Nxpe5; Neurexophilin and PC-esterase domain family, member 5	0.79	0.0393
Q3TQY2	Dctn4; Putative uncharacterized protein	0.82	0.0199

^aThe accession ID of each protein in the Uniprot database. ^bThe gene name and protein description of each protein in the Uniprot database. ^cThe fold change value of each differentially expressed protein in the 0.40-SeL/0.15-SeL comparison. ^dDifferences in protein abundances between the 0.40-SeL and 0.15-SeL groups were analyzed using one-way analysis of variance, followed by the Tukey's post hoc test. $P < 0.05$ was considered as significant. The value 0 indicates $P < 0.0001$.

Table S10 Differentially expressed proteins in the Se-D/0.15-SeM comparison

Accession ^a	Description ^b	FC ^c	P value ^d
Q3UBP6	Actb; Putative uncharacterized protein	1.37	0.0005
O88428	Papss2; Bifunctional 3'-phosphoadenosine 5'-phosphosulfate synthase 2	1.50	0.0015
Q91Y97	Aldob; Fructose-bisphosphate aldolase B	1.23	0.0270
Q8BK48	Ces2e; Pyrethroid hydrolase Ces2e	1.21	0.0391
E9Q5Z6	Adh6a; Alcohol dehydrogenase 6A (class V)	1.29	0.0014
P37804	Tagln; Transgelin	0.81	0.0217
E9QA16	Cald1; Caldesmon 1	0.83	0.0231
Q4FJX4	Csrp1; Csrp1 protein	0.81	0.0185
A2AEX6	Fhl1; Four and a half LIM domains protein 1	0.83	0.0065
Q91WG0	Ces2c; Acylcarnitine hydrolase	1.24	0.0230
Q64464	Cyp3a13; Cytochrome P450 3A13	1.29	0.0026

A0A0J9YU79	Khk; Ketohekinase	1.22	0.0043
B1Q450	B1Q450; Hemoglobin beta chain subunit	2.39	0.0001
F8VPQ6	Alpi; Alkaline phosphatase	1.32	0.0328
E9Q1Q9	Khk; Ketohekinase	1.21	0.0106
E9QNA7	Sorbs1; Sorbin and SH3 domain	0.75	0.0100
Q91WU0	Sorbs1; Carboxylesterase 1F	1.21	0.0000
Q9QXD6	Fbp1; Fructose-1,6-bisphosphatase 1	1.26	0.0016
B9EK97	Itln1; Itln1 protein	0.77	0.0217
O08691	Arg2; Arginase-2, mitochondrial	1.24	0.0010
Q3UKA4	Adh1; Alcohol dehydrogenase 1 (Class I), isoform CRA_c	1.38	0.0000
O88451	Rdh7; Retinol dehydrogenase 7	1.23	0.0029
Q8QZR3	Ces2a; OS=Mus musculus GN=Ces2a PE=1 SV=1	1.24	0.0021
P13745	Gsta1; Glutathione S-transferase A1	1.34	0.0010
D3YYJ7	Mptx2; Pentaxin	0.75	0.0010
G3X9Y6	Akr1c19; Aldo-keto reductase family 1, member C19	1.23	0.0001
Q99PG0	Aadac; Arylacetamide deacetylase	1.22	0.0020
Q64435	Ugt1a6; UDP-glucuronosyltransferase 1-6	1.28	0.0074
Q8CGP0	Hist3h2bb; Histone H2B type 3-B	1.28	0.0116
P17897	Lyz1; Lysozyme C-1	0.73	0.0150
Q9WUD0	Q9WUD0; Cytochrome P450 2B10	1.32	0.0019
P24472	Gsta4; Glutathione S-transferase A4	1.28	0.0019
F6T2Z7	Cald1; Caldesmon 1 (Fragment)	0.80	0.0162
Q9DCT8	Crip2; Cysteine-rich protein 2	0.83	0.0023
B7ZWN4	Sult6b2; Sulfotransferase	1.42	0.0232
Q58E35	Rplp1; MCG10168	0.83	0.0021
P11352	Gpx1; Glutathione peroxidase 1	1.36	0.0000
Q8CGP5	Hist1h2af; Histone H2A type 1-F	0.76	0.0322
A0A0F7QZE4	HC; MAb 110 heavy chain	1.23	0.0037
D3YX03	Gm7849; Uncharacterized protein	0.79	0.0273
Q5ERJ0	Gm14851; CRS1C-2	0.69	0.0048
K3W4L7	Pbld1; Phenazine biosynthesis-like domain-containing protein 2	1.38	0.0019
Q9D8L4	N/A; Uncharacterized protein	1.25	0.0002
P29477	Nos2; Nitric oxide synthase, inducible	1.22	0.0180
P47915	Rpl29; 60S ribosomal protein L29	0.81	0.0026
W0UUX7	Ang4; Ribonuclease A a4	0.68	0.0014
Q8C1N8	Defa22; Alpha-defensin 22	0.59	0.0107
A0A075B5K2	Igkv9-124; Immunoglobulin kappa chain variable 9-124	1.23	0.0342
P28310	Defa3; Alpha-defensin 3	0.75	0.0037
Q3UEN8	Cyp3a11; MCG15287	1.37	0.0034
Q9D848	AY761184; CDNA sequence AY761184	0.81	0.0070

Q5G866	Defa23; Alpha-defensin 23	0.81	0.0300
Q45VN2	Defa20; Alpha-defensin 20	0.54	0.0272
B3VKY5	AY761184; CRS1C-6 (Fragment)	0.64	0.0491
A0A075B5R5	Ighv4-1; Immunoglobulin heavy variable 4-1 (Fragment)	0.78	0.0134
Q9D958	Spcs1; Signal peptidase complex subunit 1	0.83	0.0185
E9QPZ2	Defa30; Defensin, alpha, 30	0.69	0.0412
Q5DTK3	Prkci; Protein kinase C iota	1.22	0.0383
Q8BGX2	Timm29; Mitochondrial import inner membrane translocase subunit Tim29	1.24	0.0117
Q64374	Rgn; Regucalcin	1.26	0.0002
P03987	N/A; Ig gamma-3 chain C region	1.21	0.0013
Q545M7	Pvalb; Parvalbumin, isoform CRA_a	1.40	0.0145
A0A0G2JFE9	Ighv1-76; Immunoglobulin heavy variable 1-76 (Fragment)	1.43	0.0347
I6L998	N/A; Uncharacterized protein	1.60	0.0230
Q3UMW7	Mapkapk3; MAP kinase-activated protein kinase 3	1.21	0.0003
Q9BCZ4	Selenos; Selenoprotein S	1.21	0.0058
A2RSF1	Commd1; COMM domain containing 1	1.23	0.0142
Q9D1C1	Ube2c; Ubiquitin-conjugating enzyme E2 C	1.24	0.0037
Q3UM95	Vipas39; Putative uncharacterized protein	1.27	0.0309
E9Q238	Kank1; KN motif and ankyrin repeat domains 1	1.33	0.0362
A2N1N1	N/A; B cell antigen receptor	1.42	0.0402
A4GE64	Ctnna3; Alpha-T-catenin	1.30	0.0392
P18531	Ighv3-6; Ig heavy chain V region 3-6	0.56	0.0051
Q9ESM6	Gdpd2; Glycerophosphoinositol inositolphosphodiesterase GDPD2	1.22	0.0238
A0A140T8P6	Igkv12-46; Immunoglobulin kappa variable 12-46 (Fragment)	1.39	0.0074
Q9CZU4	Eral1; GTPase Era, mitochondrial	1.23	0.0214
Q91XA9	Chia; Acidic mammalian chitinase	1.27	0.0305
Q91XB7	Yif1a; Protein YIF1A	1.21	0.0280
J3QP43	Stum; Protein stum homolog	1.27	0.0397
Q99JI1	Mustn1; Musculoskeletal embryonic nuclear protein 1	1.34	0.0321
A0A0A6YXZ4	Ighv1-62-2; Immunoglobulin heavy variable 1-62-2 (Fragment)	1.40	0.0091
Q3TWI2	Sardh; Putative uncharacterized protein	1.25	0.0452
Q9WV38	Slc2a5; Solute carrier family 2, facilitated glucose transporter member 5	1.31	0.0030
Q3UNJ7	B3gnt3; Hexosyltransferase	1.25	0.0203
Q91WC9	Daglb; Sn1-specific diacylglycerol lipase beta	1.26	0.0238
O88697	Stk16; Serine/threonine-protein kinase 16	1.23	0.0212
Q91W52	Tmem19; Transmembrane protein 19	1.21	0.0073

P26150	Hsd3b3; 3 beta-hydroxysteroid dehydrogenase/Delta 5-->4-isomerase type 3	1.23	0.0052
X5J5N0	N/A; IgM heavy chain VDJ region (Fragment)	1.28	0.0442
Q922F6	N/A; Putative uncharacterized protein (Fragment)	2.16	0.0265
Q9CQI9	Med30; Mediator of RNA polymerase II transcription subunit 30	1.41	0.0494
A0A0A6YXB7	Ssr2; Translocon-associated protein subunit beta	0.83	0.0163
Q9D8H7	Oma1; Metalloendopeptidase OMA1, mitochondrial	1.23	0.0234
Q91VA1	Slc44a4; Choline transporter-like protein 4	1.21	0.0472
Q3V2X3	Il1rap; Putative uncharacterized protein	1.25	0.0007
Q3TV21	Fxn; Frataxin	1.41	0.0044
F8VQ45	Tmc4; Transmembrane channel-like protein	1.24	0.0454
Q9R0A1	Clcn2; Chloride channel protein 2	1.22	0.0357
B2RSR2	Sec22a; SEC22 vesicle trafficking protein homologue A (S. cerevisiae)	1.25	0.0481
A2A6P4	Fam104a; Family with sequence similarity 104, member A	0.82	0.0208
B1ASK8	Ube2j2; Ubiquitin-conjugating enzyme E2 J2	1.21	0.0476
Q9WU62	Incenp; Inner centromere protein	1.28	0.0009
Q9QXS8	Cml5; Probable N-acetyltransferase CML5	1.22	0.0376
G5E8C6	Vill; Villin-like protein	1.73	0.0027
L7N231	Gm15292; Uncharacterized protein	0.77	0.0155
Q8VCQ3	Nrbf2; Nuclear receptor-binding factor 2	0.58	0.0283
Q148Z6	Gpr107; Expressed sequence AI790205	1.23	0.0317
A0A0C6E3V3	HC;HC protein	1.21	0.0301
Q63ZW6	Col4a5; Col4a5 protein	0.75	0.0211

^aThe accession ID of each protein in the Uniprot database. ^bThe gene name and protein description of each protein in the Uniprot database. ^cThe fold change value of each differentially expressed protein in the Se-D/0.15-SeM comparison. ^dDifferences in protein abundances between the Se-D and 0.15-SeM groups were analyzed using one-way analysis of variance, followed by the Tukey's post hoc test. $P < 0.05$ was considered as significant. The value 0 indicates $P < 0.0001$.

Table S11 Differentially expressed proteins in the 0.40-SeM/0.15-SeM comparison

Accession ^a	Description ^b	FC ^c	P value ^d
Q8BTM8	Flna; Filamin-A	0.81	0.0078
Q6URW6	Myh14; Myosin-14	1.20	0.0205
F8VQM5	Sis; Sucrase isomaltase (alpha-glucosidase)	1.29	0.0408

O08601	Mttp; Microsomal triglyceride transfer protein large subunit	1.37	0.0083
P62737	Acta2; Actin, aortic smooth muscle	0.72	0.0201
Q8VDN2	Atp1a1; Sodium/potassium-transporting ATPase subunit alpha-1	1.24	0.0027
Q64727	Vcl; Vinculin	0.82	0.0117
Q62468	Vill1; Villin-1	1.30	0.0194
Q3UQ44	Iqgap2; Ras GTPase-activating-like protein IQGAP2	1.20	0.0145
B1B1A8	Mylk; Myosin light chain kinase, smooth muscle	0.83	0.0295
O88329	Myo1a; Unconventional myosin-Ia	1.20	0.0357
Q3V0K9	Pls1; Plastin-1	1.33	0.0219
P31001	Des; Desmin	0.79	0.0134
O88428	Papss2; Bifunctional 3'-phosphoadenosine 5'-phosphosulfate synthase 2	1.45	0.0172
Q91Y97	Aldob; Fructose-bisphosphate aldolase B	1.37	0.0018
Q3TAN0	Cdh17; Putative uncharacterized protein	1.23	0.0202
P14824	Anxa6; Annexin A6	0.81	0.0120
Q8VC30	Tkfc; Triokinase/FMN cyclase	1.33	0.0029
P20152	Vim; Vimentin	0.78	0.0044
Q64521	Gpd2; Glycerol-3-phosphate dehydrogenase, mitochondrial	1.21	0.0021
P48678	Lmna; Prelamin-A/C	0.83	0.0042
Q3UQ71	Ephx2; Putative uncharacterized protein	1.33	0.0052
P08249	Mdh2; Malate dehydrogenase, mitochondrial	1.22	0.0041
Q3UKS0	Acs15; Putative uncharacterized protein	1.41	0.0033
Q9D312	Krt20; Keratin, type I cytoskeletal 20	1.32	0.0294
Q91W97	Hkdc1; Putative hexokinase HKDC1	1.24	0.0079
G3X925	Pklr; Pyruvate kinase	1.27	0.0098
B2RSN3	Tubb2b; Tubulin beta chain	0.83	0.0038
Q8BH64	Ehd2; EH domain-containing protein 2	0.79	0.0079
Q8BK48	Ces2e; Pyrethroid hydrolase Ces2e	1.33	0.0043
Q545N7	Ckmt1; Creatine kinase, mitochondrial 1, ubiquitous, isoform CRA_a	1.32	0.0086
P13707	Gpd1; Glycerol-3-phosphate dehydrogenase [NAD(+)], cytoplasmic	1.27	0.0023
A0A1B0GRV0	Bpnt1; 3'(2'),5'-bisphosphate nucleotidase 1	1.22	0.0003
Q69ZN0	Gda; MKIAA1258 protein (Fragment)	1.28	0.0110
Q6ZQM8	Ugt1a7c; UDP-glucuronosyltransferase 1-7C	1.26	0.0006

E9Q5Z6	Adh6a; Alcohol dehydrogenase 6A (class V)	1.45	0.0006
Q9DBM2	Ehhadh; Peroxisomal bifunctional enzyme	1.21	0.0016
P82198	Tgfbi; Transforming growth factor-beta-induced protein ig-h3	0.76	0.0056
P48036	Anxa5; Annexin A5	0.79	0.0155
Q9QWG7	Sult1b1; Sulfotransferase family cytosolic 1B member 1	1.29	0.0149
Q9JMH6	Txnrd1; Thioredoxin reductase 1, cytoplasmic	1.23	0.0000
P37804	Tagln; Transgelin	0.75	0.0060
E9QA16	Cald1; Caldesmon 1	0.79	0.0084
P12710	Fabp1; Fatty acid-binding protein, liver	1.37	0.0147
Q8BZF8	Pgm5; Phosphoglucomutase-like protein 5	0.79	0.0115
P14094	Atp1b1; Sodium/potassium-transporting ATPase subunit beta-1	1.30	0.0024
Q4FJX4	Csrp1; Csrp1 protein	0.74	0.0038
Q61391	Mme; Neprilysin	1.25	0.0137
A2AEX6	Fhl1; Four and a half LIM domains protein 1	0.79	0.0031
Q91WG0	Ces2c; Acylcarnitine hydrolase	1.34	0.0043
Q9CQ19	Myl9; Myosin regulatory light polypeptide 9	0.81	0.0071
Q64464	Cyp3a13; Cytochrome P450 3A13	1.43	0.0003
A0A0J9YU79	Khk; Ketohexokinase	1.21	0.0065
P19324	Serpinh1; Serpin H1	0.83	0.0148
P32020	Scp2; Non-specific lipid-transfer protein	1.24	0.0492
Q922Q1	Marc2; Mitochondrial amidoxime reducing component 2	1.23	0.0001
F8VPQ6	Alpi; Alkaline phosphatase	1.36	0.0085
E9Q1Q9	Khk; Ketohexokinase	1.30	0.0014
Q08091	Cnn1; Calponin-1	0.78	0.0045
Q63886	Ugt1a1; UDP-glucuronosyltransferase 1-1	1.22	0.0209
Q91WU0	Ces1f; Carboxylesterase 1F	1.26	0.0086
Q9QXD6	Fbp1; Fructose-1,6-bisphosphatase 1	1.28	0.0064
Q8BXX9	Clic5; Chloride intracellular channel protein 5	1.23	0.0178
Q148B1	Cyp2c65; Cytochrome P450, family 2, subfamily c, polypeptide 65	1.23	0.0119
B9EK97	Itn1; Itln1 protein	0.68	0.0037
Q61425	Hadh; Hydroxyacyl-coenzyme A dehydrogenase, mitochondrial	1.27	0.0053
Q8QZR5	Gpt; Alanine aminotransferase 1	1.30	0.0074

Q059R7	Rbp2; Retinol binding protein 2, cellular	1.42	0.0002
O54724	Cavin1; Polymerase I and transcript release factor	0.78	0.0042
A0A0R4IZY2	Cyp2d26; Cytochrome P450 2D26	1.30	0.0021
Q62009	Postn; Periostin	0.80	0.0224
P70441	Slc9a3r1; Na(+)/H(+) exchange regulatory cofactor NHE-RF1	1.31	0.0398
P28653	Bgn; Biglycan	0.83	0.0092
O08691	Arg2; Arginase-2, mitochondrial	1.32	0.0002
Q3UKA4	Adh1; Alcohol dehydrogenase 1 (Class I), isoform CRA_c	1.34	0.0042
Q3UKR1	Dcn; Decorin	0.73	0.0156
P51885	Lum; Lumican	0.74	0.0094
Q3TJD7	Pdlim7; PDZ and LIM domain protein 7	0.80	0.0116
O55222	Ilk; Integrin-linked protein kinase	0.79	0.0113
Q99L04	Dhrs1; Dehydrogenase/reductase SDR family member 1	1.27	0.0002
Q3UZZ6	Sult1d1; Sulfotransferase 1 family member D1	1.23	0.0181
O88451	Rdh7; Retinol dehydrogenase 7	1.23	0.0014
Q8K154	Ugt2b34; UDP-glucuronosyltransferase	1.22	0.0088
Q3U687	Ifit1b12; Interferon-induced protein with tetratricopeptide repeats 1B-like 2	1.29	0.0198
Q9EPC1	Parva; Alpha-parvin	0.80	0.0074
P13745	Gsta1; Glutathione S-transferase A1	1.34	0.0239
Q8CCA7	Slc5a1; Putative uncharacterized protein	1.42	0.0252
Q3V0B5	Lmod1; Putative uncharacterized protein	0.83	0.0075
A6H6K1	Aspn; Aspn protein	0.76	0.0052
P16045	Lgals1; Galectin-1	0.78	0.0049
Q8BWQ1	Ugt2a3; UDP-glucuronosyltransferase 2A3	1.21	0.0143
D3YYJ7	Mptx2; Pentaxin	0.70	0.0002
Q543S0	Prelp; Proline arginine-rich end leucine-rich repeat	0.80	0.0130
Q63918	Cavin2; Serum deprivation-response protein	0.79	0.0067
Q6DYE8	Enpp3; Ectonucleotide pyrophosphatase/phosphodiesterase family member 3	1.24	0.0192
Q99PG0	Aadac; Arylacetamide deacetylase	1.29	0.0005
O08738	Casp6; Caspase-6	1.23	0.0015
Q8R1Q7	Arg2; Arginase	1.21	0.0213

Q9JLT2	Treh; Trehalase	1.23	0.0109
Q3U0N0	Gzma; Putative uncharacterized protein	1.28	0.0214
Q62000	Ogn; Mimecan	0.75	0.0139
P17897	Lyz1; Lysozyme C-1	0.63	0.0027
P56389	Cda; Cytidine deaminase	1.23	0.0079
P49817	Cav1; Caveolin-1	0.79	0.0088
A0A0R4J111	Gpx2; Glutathione peroxidase	1.29	0.0008
Q9WUD0	Cyp2b10; Cytochrome P450 2B10	1.29	0.0050
Q9R092	Hsd17b6; 17-beta-hydroxysteroid dehydrogenase type 6	1.20	0.0089
Q3TQC7	Entpd5; Ectonucleoside triphosphate diphosphohydrolase 5	1.22	0.0353
P11087	Col1a1; Collagen alpha-1(I) chain	0.77	0.0110
Q9CRB6	Tppp3; Tubulin polymerization-promoting protein family member 3	0.81	0.0074
P24472	Gsta4; Glutathione S-transferase A4	1.22	0.0440
Q6YI28	2210407C18Rik; EP1	1.25	0.0060
F6T2Z7	Cald1; Caldesmon 1 (Fragment)	0.76	0.0067
Q9DCT8	Crip2; Cysteine-rich protein 2	0.81	0.0116
Q3U5N2	Ifit1; Putative uncharacterized protein	1.37	0.0310
Q3TU64	Col1a2; Putative uncharacterized protein	0.79	0.0085
Q8VBX5	Ppt1; Palmitoyl-protein thioesterase	0.81	0.0006
P97354	St3gal4; Gal beta 1,4(3) GlcNAc alpha 2,3-sialyltransferase	1.25	0.0046
Q8VC49	Ifi2712b; Interferon alpha-inducible protein 27-like protein 2B	1.35	0.0040
Q8C0N2	Gpat3; Glycerol-3-phosphate acyltransferase 3	1.21	0.0159
Q99LP6	Grpel1; GrpE protein homolog 1, mitochondrial	1.27	0.0068
P11352	Gpx1; Glutathione peroxidase 1	1.54	0.0000
Q8CFJ7	Slc25a45; Solute carrier family 25 member 45	1.24	0.0007
F7A8H6	Glutathione peroxidase	1.32	0.0000
Q3UZK0	Lpgat1; Putative uncharacterized protein (Fragment)	1.22	0.0019
P70677	Casp3; Caspase-3	1.24	0.0005
D3Z6F0	Ifit1b1; Interferon-induced protein with tetratricopeptide repeats 1B-like 1	1.37	0.0267
Q8CIW6	Slc26a6; Solute carrier family 26 member 6	1.21	0.0256
D3YX03	Gm7849; Uncharacterized protein	0.70	0.0029
Q5ERJ0	Gm14851; CRS1C-2	0.65	0.0019

G3X939	Slc9a3; Sodium/hydrogen exchanger 3	1.23	0.0033
Q80W94	Mogat2; 2-acylglycerol O-acyltransferase 2	1.32	0.0047
P40240	Cd9; CD9 antigen	0.80	0.0194
A0A1L1SUM8	St3gal4; CMP-N-acetylneuraminate-beta-galactosamide-alpha-2,3-sialyltransferase 4 (Fragment)	1.45	0.0027
Q9QZZ6	Dpt; Dermatopontin	0.77	0.0225
W0UUX7	Ang4; Ribonuclease A a4	0.65	0.0008
Q8C1N8	Defa22; Alpha-defensin 22	0.50	0.0019
Q78JN3	Eci3; Enoyl-CoA delta isomerase 3, peroxisomal	1.31	0.0087
Q3UEN8	Cyp3a11; MCG15287	1.25	0.0068
Q9D848	AY761184; CDNA sequence AY761184	0.72	0.0007
P14246	Slc2a2; Solute carrier family 2, facilitated glucose transporter member 2	1.44	0.0040
Q3UN27	Mmp7; Matrilysin	0.82	0.0104
Q8VI94	Oas1; 2'-5'-oligoadenylate synthase-like protein 1	1.31	0.0084
A2ARJ3	Tmem236; Transmembrane protein 236	1.26	0.0184
Q5G866	Defa23; Alpha-defensin 23	0.80	0.0312
P61226	Rap2b; Ras-related protein Rap-2b	0.81	0.0180
Q8C1E7	Tmem120a; Transmembrane protein 120A	1.21	0.0062
Q3KNZ2	Bco2; Beta-carotene 9', 10'-dioxygenase 2	1.22	0.0041
Q8K3K7	Agpat2; 1-acyl-sn-glycerol-3-phosphate acyltransferase beta	1.21	0.0175
Q9D115	Mcee; Methylmalonyl-CoA epimerase, mitochondrial	1.23	0.0300
Q45VN2	Defa20; Alpha-defensin 20	0.42	0.0062
B3VKY5	AY761184; CRS1C-6	0.51	0.0128
E9QM19	Tm6sf2; Transmembrane 6 superfamily member 2	1.25	0.0248
A0A140LIU4	Cox7a1; Cytochrome c oxidase subunit 7A1, mitochondrial	1.30	0.0117
Q64522	Hist2h2ab; Histone H2A type 2-B	0.79	0.0068
Q9DCZ1	Gmpr; GMP reductase 1	0.83	0.0369
P14069	S100a6; Protein S100-A6	0.80	0.0363
O09158	Cyp3a25; Cytochrome P450 3A25	1.31	0.0029
Q5F218	IgG1 TS1 VH; Gamma heavy chain variable region	1.58	0.0283
P34928	Apoc1; Apolipoprotein C-I	0.77	0.0033
Q497J1	Tmem86b; Lysoplasmalogenase	1.20	0.0137

Q5XK38	Hmgn2; Hmgn2 protein	0.82	0.0281
G5E897	Kdelc2; KDEL (Lys-Asp-Glu-Leu) containing 2, isoform CRA_b	0.79	0.0009
A0A0R4J003	Vip; VIP peptides	0.81	0.0490
Q78HU7	Gypc; Glycophorin-C	0.81	0.0182
Q5DTG2	Col3a1; MKIAA4231 protein (Fragment)	0.77	0.0170
P42337	Pik3ca; Phosphatidylinositol 4,5-bisphosphate 3-kinase catalytic subunit alpha isoform	0.82	0.0364
Q80SZ7	Gng5; Guanine nucleotide-binding protein G(I)/G(S)/G(O) subunit gamma-5	0.80	0.0081
P35576	G6pc; Glucose-6-phosphatase	1.34	0.0296
Q9WV38	Slc2a5; Solute carrier family 2, facilitated glucose transporter member 5	1.22	0.0238
Q8R0H4	Lypd8; RIKEN cDNA 2210415F13, isoform CRA_a	1.24	0.0053
Q9WVB0	Rbpms; RNA-binding protein with multiple splicing	0.81	0.0083
B1AWB9	Col5a1; Collagen, type V, alpha 1	0.83	0.0271
Q545V6	Sst; Putative uncharacterized protein	0.73	0.0101
Q3TBR1	Gskip; Putative uncharacterized protein	1.20	0.0004
Q9JHH9	Copz2; Coatamer subunit zeta-2	0.79	0.0047
Q62277	Syp; Synaptophysin	0.79	0.0357
P20491	Fcer1g; High affinity immunoglobulin epsilon receptor subunit gamma	0.78	0.0171
Q3UPR9	Sbson; Somatomedin-B and thrombospondin type-1 domain-containing protein	0.78	0.0460
Q8BTJ4	Enpp4; Bis(5'-adenosyl)-triphosphatase enpp4	0.82	0.0385
A0A0R4J097	Tgfr3; Transforming growth factor beta receptor type 3	0.77	0.0197
A0A1B0GRV7	Gm17949; Uncharacterized protein	1.22	0.0317
P0DN89	Tmem254a; Transmembrane protein 254	0.82	0.0416
O70303	Cideb; Cell death activator CIDE-B	1.21	0.0032
Q3UU11	Fkbp7; Peptidylprolyl isomerase	0.80	0.0143
Q99MV1	Tdrd1; Tudor domain-containing protein 1	0.79	0.0453
Q8R115	Tmem82; Transmembrane protein 82	1.30	0.0063
Q3UTR7	Agt; Angiotensinogen	0.80	0.0124
F7C0E4	Atxn7l1; Ataxin-7-like protein 1	1.74	0.0170
L7N231	Gm15292; Uncharacterized protein	0.71	0.0034
Q9Z2D1	Mtmr2; Myotubularin-related protein 2	0.79	0.0406

Q8VCQ3	Nrbf2; Nuclear receptor-binding factor 2	0.44	0.0163
Q14BV7	Acbd6; Acyl-Coenzyme A binding domain containing 6	0.74	0.0080
Q7TQA6	Tas2r38; Taste receptor type 2 member 38	0.76	0.0461

^aThe accession ID of each protein in the Uniprot database. ^bThe gene name and protein description of each protein in the Uniprot database. ^cThe fold change value of each differentially expressed protein in the 0.40-SeM/0.15-SeM comparison. ^dDifferences in protein abundances between the 0.40-SeM and 0.15-SeM groups were analyzed using one-way analysis of variance, followed by the Tukey's post hoc test. $P < 0.05$ was considered as significant. The value 0 indicates $P < 0.0001$.

Table S12 Differentially expressed proteins in the 0.15-SeM/0.15-SeL comparison

Accession ^a	Description ^b	FC ^c	P value ^d
A0A075B5Y4	Ighv1-81; Immunoglobulin heavy variable 1-81 (Fragment)	0.74	0.0020
A0A075B6A0	Ighm; Ig mu chain C region (Fragment)	0.83	0.0142
A0A087WPM0	Selenoh; Selenoprotein H	0.76	0.0213
A0A087WS16	Col6a3; Collagen, type VI, alpha 3	1.31	0.0340
A0A0A6YWH6	Ighv9-4; Immunoglobulin heavy variable 9-4 (Fragment)	0.67	0.0042
A0A0A6YXB7	Ssr2; Translocon-associated protein subunit beta	1.28	0.0073
A0A0C6E3V3	HC; HC protein	0.80	0.0262
A0A0G2JG52	Crybg1; Absent in melanoma 1	0.82	0.0088
A0A0J9YU79	Khk; Ketoheokinase	0.82	0.0138
A0A0R4J111	Gpx2; Glutathione peroxidase	0.76	0.0004
A0A0R4J119	Cyfip1; Cytoplasmic FMR1-interacting protein 1	0.80	0.0021
A0A0R4J138	Arsb; Arylsulfatase B	0.78	0.0067
A0A0R4J203	Dao; D-amino-acid oxidase	0.79	0.0091
A0A140LHQ9	Synm; Synemin	0.82	0.0023
A0A140T8P6	Igkv12-46; Immunoglobulin kappa variable 12-46 (Fragment)	0.83	0.0465
A0A1E1GJG6	Wgn-scFv; Single-chain variable	0.75	0.0182
A0JLQ7	Pcid2; Pcid2 protein (Fragment)	0.79	0.0336
A2AEX6	Fhl1; Four and a half LIM domains protein 1	1.21	0.0175
A2ARJ3	Tmem236; Transmembrane protein 236	0.81	0.0233
A2N1N1	N/A; B cell antigen receptor	0.62	0.0161
A6H6K1	Aspn; Aspn protein	1.23	0.0293
A8CA96	Tcea3; Tissue-specific transcription factor S-II	0.77	0.0035
B1Q450	HBB1; Hemoglobin beta chain subunit	0.83	0.0452
B2RTP7	Krt2; Krt2 protein	0.81	0.0092
B3VKY5	AY761184; CRS1C-6 (Fragment)	1.72	0.0310
B7ZWN4	Sult6b2; Sulfotransferase	0.67	0.0061
B9EK97	Itln1; Itln1 protein	1.35	0.0272
D3YX03	Gm7849; Q5ERJ0	1.31	0.0266

D3YYJ7	Mptx2; Pentaxin	1.46	0.0002
E0CX47	Nxpe5; Neurexophilin and PC-esterase domain family, member 5	0.68	0.0055
E9PVZ9	Eif4e1b; Eukaryotic translation initiation factor 4E type 1B	0.75	0.0149
E9PWN0	Lpin2; Phosphatidate phosphatase LPIN2	0.73	0.0260
E9Q0F0	Krt78; Keratin 78	0.78	0.0123
E9Q1Q9	Khk; Ketoheokinase	0.81	0.0134
E9Q5Z6	Adh6a; Alcohol dehydrogenase 6A (class V)	0.73	0.0083
F6T2Z7	Cald1; Caldesmon 1 (Fragment)	1.28	0.0222
F7A8H6	Glutathione peroxidase	0.75	0.0000
F8VPQ6	Alpi; Alkaline phosphatase	0.70	0.0273
F8VQ45	Tmc4; Transmembrane channel-like protein	0.80	0.0206
G3X939	Slc9a3; Sodium/hydrogen exchanger 3	0.82	0.0145
G3X9Y6	Akr1c19; Aldo-keto reductase family 1, member C19	0.83	0.0002
J3QNH8	Gm7694; Uncharacterized protein	0.79	0.0484
K3W4L7	Pbld1; Phenazine biosynthesis-like domain-containing protein 2	0.75	0.0027
L7N231	Gm15292; Uncharacterized protein	1.34	0.0245
O08691	Arg2; Arginase-2, mitochondrial	0.78	0.0031
O09158	Cyp3a25; Cytochrome P450 3A25	0.81	0.0489
O35242	Nsmaf; Protein FAN	0.81	0.0121
O54724	Cavin1; Polymerase I and transcript release factor	1.22	0.0459
O54750	Cyp2j6; Cytochrome P450 2J6	0.83	0.0068
O54788	Dffb; DNA fragmentation factor subunit beta	0.76	0.0006
O54909	Rdh16; Cis-retinol androgen dehydrogenase 1	0.81	0.0297
O88428	Papss2; Bifunctional 3'-phosphoadenosine 5'-phosphosulfate synthase 2	0.63	0.0223
O88451	Rdh7; Retinol dehydrogenase 7	0.82	0.0376
O88665	Brd7; Bromodomain-containing protein 7	0.82	0.0162
O89109	Kcnn4; Intermediate conductance calcium-activated potassium channel protein 4	0.80	0.0349
P04104	Krt1; Keratin, type II cytoskeletal 1	0.74	0.0162
P08882	Gzmc; Granzyme C	0.80	0.0331
P09528	Fth1; Ferritin heavy chain	0.80	0.0312
P11352	Gpx1; Glutathione peroxidase 1	0.55	0.0000
P13745	Gsta1; Glutathione S-transferase A1	0.73	0.0008
P16045	Lgals1; Galectin-1	1.22	0.0300
P17897	Lyz1; Lysozyme C-1	1.46	0.0128
P18531	Ighv3-6; Ig heavy chain V region 3-6	1.68	0.0067
P21956	Mfge8; Lactadherin	0.79	0.0019
P24472	Gsta4; Glutathione S-transferase A4	0.76	0.0015

P28310	Defa3; Alpha-defensin 3	2.25	0.0014
P32507	Nectin2; Nectin-2	0.82	0.0225
P37804	Tagln; Transgelin	1.28	0.0350
P49135	Ercc3; TFIIH basal transcription factor complex helicase XPB subunit	0.83	0.0500
P49817	Cav1; Caveolin-1	1.24	0.0332
P59108	Cpne2; Copine-2	0.81	0.0267
P62342	Selenot; Selenoprotein T	0.83	0.0001
P82198	Tgfb1; Transforming growth factor-beta-induced protein ig-h3	1.24	0.0214
P97364	Seps2; Selenide, water dikinase 2	0.82	0.0000
P97816	S100g; Protein S100-G	0.70	0.0289
Q059R7	Rbp2; Retinol binding protein 2, cellular	0.79	0.0272
Q0VEE6	Znf800; Zinc finger protein 800	0.80	0.0003
Q32P04	Krt5; Keratin 5	0.69	0.0191
Q3TBL6	Tnfaip8l3; Tumor necrosis factor alpha-induced protein 8-like protein 3	0.73	0.0001
Q3TCT4	Entpd7; Ectonucleoside triphosphate diphosphohydrolase 7	0.80	0.0084
Q3TI65	Mtfp1; Putative uncharacterized protein	0.83	0.0041
Q3TIR3	Ric8a; Synembryn-A	0.82	0.0215
Q3TV21	Fxn; Frataxin	0.78	0.0152
Q3UBP6	Actb; Putative uncharacterized protein	0.76	0.0010
Q3UEN8	Cyp3a11; MCG15287	0.76	0.0034
Q3UKA4	Adh1; Alcohol dehydrogenase 1 (Class I), isoform CRA_c	0.70	0.0000
Q3UMW7	Mapkapk3; MAP kinase-activated protein kinase 3	0.80	0.0050
Q3UN27	Mmp7; Matrilysin	1.21	0.0117
Q3UP47	Cfd; Complement factor D (Adipsin)	0.75	0.0004
Q3UV17	Krt76; Keratin, type II cytoskeletal 2 oral	0.78	0.0246
Q3UYR3	Cbfb; Putative uncharacterized protein (Fragment)	0.79	0.0205
Q3V009	Tmed1; Transmembrane emp24 domain-containing protein 1	0.82	0.0075
Q45VN2	Defa20; Alpha-defensin 20	2.57	0.0052
Q4FJX4	Csrp1; Csrp1 protein	1.28	0.0244
Q545M7	Pvalb; Parvalbumin, isoform CRA_a	0.78	0.0304
Q545Y5	Cd74; CD74 antigen (Invariant polypeptide of major histocompatibility complex, class II antigen-associated)	1.22	0.0490
Q5ERJ0	Gm14851; CRS1C-2	1.52	0.0043
Q62245	Sos1; Son of sevenless homolog 1	0.73	0.0385
Q63ZW6	Col4a5; Col4a5 protein	1.42	0.0197
Q64374	Rgn; Regucalcin	0.81	0.0005
Q64435	Col4a5; UDP-glucuronosyltransferase 1-6	0.79	0.0337

Q64464	Cyp3a13; Cytochrome P450 3A13	0.81	0.0396
Q6QI06	Rictor; Rapamycin-insensitive companion of mTOR	0.82	0.0166
Q8BGX2	Timm29; Mitochondrial import inner membrane translocase subunit Tim29	0.82	0.0044
Q8BLY2	Tarsl2; Probable threonine--tRNA ligase 2, cytoplasmic	0.82	0.0402
Q8BS35	Agmo; Alkylglycerol monooxygenase	0.82	0.0002
Q8BTM8	Flna; Filamin-A	1.20	0.0413
Q8BWQ1	Ugt2a3; UDP-glucuronosyltransferase 2A3	0.81	0.0429
Q8C1N8	Defa22; Alpha-defensin 22	2.25	0.0014
Q8CB77	Eloa; Elongin-A	0.82	0.0122
Q8CFA1	Irak2; Interleukin-1 receptor-associated kinase-like 2	0.81	0.0280
Q8CFJ7	Slc25a45; Solute carrier family 25 member 45	0.81	0.0081
Q8K0J2	B3gnt7; UDP-GlcNAc:betaGal beta-1,3-N-acetylglucosaminyltransferase 7	0.81	0.0146
Q8K205	Pop1; Processing of 1, ribonuclease P/MRP family, (S. cerevisiae)	0.77	0.0206
Q8R1J5	Fcgbp; Fcgbp protein (Fragment)	0.79	0.0485
Q8R1K1	Ubac2; Ubiquitin-associated domain-containing protein 2	0.68	0.0479
Q8R1N0	Znf830; Zinc finger protein 830	0.81	0.0088
Q8R1Q7	Arg2; Arginase	0.78	0.0173
Q8R2H9	Phospho1; Phosphoethanolamine/phosphocholine phosphatase	0.78	0.0232
Q8R418	Dicer1; Endoribonuclease Dicer	0.80	0.0083
Q8R4U7	Luzp1; Leucine zipper protein 1	0.78	0.0335
Q8R5A6	Tbc1d22a; TBC1 domain family member 22A	0.82	0.0148
Q8VCY3	Rdh16f2; cDNA sequence BC089597	0.77	0.0320
Q8VED5	Krt79; Keratin, type II cytoskeletal 79	0.71	0.0444
Q8VHC3	Selenom; Selenoprotein M	0.81	0.0077
Q91VL8	Terf2ip; Telomeric repeat-binding factor 2-interacting protein 1	0.80	0.0001
Q91WG0	Ces2c; Acylcarnitine hydrolase	0.80	0.0339
Q91Y97	Aldob; Fructose-bisphosphate aldolase B	0.78	0.0194
Q91Z58	N/A; Uncharacterized protein C6orf132 homolog	0.74	0.0419
Q91ZT5	Fgd4; FYVE, RhoGEF and PH domain-containing protein 4	0.81	0.0093
Q99L15	Acot1; Acot1 protein (Fragment)	0.83	0.0402
Q99PG0	Aadac; Arylacetamide deacetylase	0.78	0.0024
Q9BCZ4	Selenos; Selenoprotein S	0.81	0.0196
Q9CQ19	My19; Myosin regulatory light polypeptide 9	1.21	0.0376
Q9CYW4	Hdhd3; Haloacid dehalogenase-like hydrolase domain-containing protein 3	0.80	0.0052
Q9CZH7	Mxra7; Matrix-remodeling-associated protein 7	0.81	0.0059

Q9CZU4	Eral1; GTPase Era, mitochondrial	0.83	0.0018
Q9D848	AY761184; CDNA sequence AY761184	1.23	0.0082
Q9D869	Chp2; Calcineurin B homologous protein 2	0.82	0.0056
Q9D8L4	N/A; Uncharacterized protein	0.74	0.0066
Q9D958	Spcs1; Signal peptidase complex subunit 1	1.26	0.0262
Q9DCT8	Crip2; Cysteine-rich protein 2	1.23	0.0087
Q9ESM6	Gdpd2; Glycerophosphoinositol inositolphosphodiesterase GDPD2	0.78	0.0172
Q9JHJ3	Glmp; Glycosylated lysosomal membrane protein	0.83	0.0141
Q9JLI0	Akr1c12; Aldo-keto reductase	0.82	0.0013
Q9JMH6	Txnrd1; Thioredoxin reductase 1, cytoplasmic	0.79	0.0000
Q9QX60	Dguok; Deoxyguanosine kinase, mitochondrial	0.81	0.0249
Q9QXD6	Fbp1; Fructose-1,6-bisphosphatase 1	0.82	0.0046
Q9QY93	Dctpp1; dCTP pyrophosphatase 1	0.80	0.0003
Q9R092	Hsd17b6; 17-beta-hydroxysteroid dehydrogenase type 6	0.80	0.0185
Q9WUD0	Cyp2b10; Cytochrome P450 2B10	0.80	0.0305
Q9WV38	Slc2a5; Solute carrier family 2, facilitated glucose transporter member 5	0.72	0.0016
W0UUX7	Ang4; Ribonuclease A a4	1.48	0.0018

^aThe accession ID of each protein in the Uniprot database. ^bThe gene name and protein description of each protein in the Uniprot database. ^cThe fold change value of each differentially expressed protein in the 0.15-SeM/0.15-SeL comparison. ^dDifferences in protein abundances between the 0.15-SeM and 0.15-SeL groups were analyzed using one-way analysis of variance, followed by the Tukey's post hoc test. $P < 0.05$ was considered as significant. The value 0 indicates $P < 0.0001$.

Table S13 Differentially expressed proteins in the 0.40-SeM and 0.40-SeL comparison

Accession ^a	Description ^b	FC ^c	P value ^d
Q3UBP6	Actb; Putative uncharacterized protein	0.73	0.0002
Q921I1	Tf; Serotransferrin	1.21	0.0022
Q3UQ71	Ephx2; Putative uncharacterized protein	1.26	0.0137
Q3UKS0	Acs15; Putative uncharacterized protein	1.24	0.0206
E9Q5Z6	Adh6a; Alcohol dehydrogenase 6A (class V)	1.22	0.0063
P12710	Fabp1; Fatty acid-binding protein, liver	1.41	0.0050
Q91WG0	Ces2c; Acylcarnitine hydrolase	1.25	0.0011
B1Q450	HBB1; Hemoglobin beta chain subunit	0.39	0.0016
Q91WU0	Ces1f; Carboxylesterase 1F	1.20	0.0279
P19639	Gstm3; Glutathione S-transferase Mu 3	1.26	0.0054
Q059R7	Rbp2; Retinol binding protein 2, cellular	1.35	0.0004
Q8VCH0	Acaa1b; 3-ketoacyl-CoA thiolase B, peroxisomal	1.27	0.0307
A0A0R4IZY2	Cyp2d26; Cytochrome P450 2D26	1.23	0.0050

P13745	Gsta1; Glutathione S-transferase A1	1.31	0.0310
Q8CGP0	Hist3h2bb; Histone H2B type 3-B	0.71	0.0060
O09049	Reg3g; Regenerating islet-derived protein 3-gamma	0.73	0.0031
P04938	Mup11; Major urinary protein 11	1.20	0.0074
Q8VC49	Ifi2712b; Interferon alpha-inducible protein 27-like protein 2B	1.20	0.0240
Q64FW2	Retsat; All-trans-retinol 13,14-reductase	1.25	0.0047
Q8VHC3	Selenom; Selenoprotein M	0.80	0.0338
Q5ERJ0	Gm14851; CRS1C-2	0.82	0.0204
A0A075B5S2	Ighv7-1; Uncharacterized protein (Fragment)	0.53	0.0000
Q9D848	AY761184; CDNA sequence AY761184	0.82	0.0270
Q08ED0	Bcl2l15; Bcl-2-like protein 15	0.80	0.0150
P14246	Slc2a2; Solute carrier family 2, facilitated glucose transporter member 2	1.22	0.0405
Q8VI94	Oas1; 2'-5'-oligoadenylate synthase-like protein 1	1.21	0.0217
P01628	N/A; Ig kappa chain V-II region MOPC 511	0.59	0.0388
B3VKY5	AY761184; CRS1C-6 (Fragment)	0.82	0.0007
P35230	Reg3b; Regenerating islet-derived protein 3-beta	0.58	0.0014
A0A097PUD0	N/A; Anti-dectin-1 15E2 light chain	1.25	0.0301
P52430	Pon1; Serum paraoxonase/arylesterase 1	0.83	0.0055
P18531	Ighv3-6; Ig heavy chain V region 3-6	1.44	0.0311
Q8BY35	Fgd2; FYVE, RhoGEF and PH domain-containing protein 2	0.80	0.0425
A0A140T8P6	Igkv12-46; Immunoglobulin kappa variable 12-46 (Fragment)	0.72	0.0031
Q5DTG2	Col3a1; MKIAA4231 protein (Fragment)	0.80	0.0275
D3Z689	Adamts15; ADAMTS-like 5	1.23	0.0224
P20065	Tmsb4x; Thymosin beta-4	0.80	0.0245
Q99JI1	Mustn1; Musculoskeletal embryonic nuclear protein 1	0.76	0.0437
Q9WTR1	Trpv2; Transient receptor potential cation channel subfamily V member 2	0.73	0.0395
Q9WV38	Slc2a5; Solute carrier family 2, facilitated glucose transporter member 5	1.20	0.0437
A0A0B4J1I9	Igkv4-55; Immunoglobulin kappa variable 4-55 (Fragment)	1.41	0.0025
Q3UNJ7	B3gnt3; Hexosyltransferase	0.75	0.0248
Q9CY52	Thg1l; Probable tRNA(His) guanylyltransferase	0.82	0.0259
Q545V6	Sst; Putative uncharacterized protein	0.81	0.0070
Q922F6	N/A; Putative uncharacterized protein	0.48	0.0151
Q3TWR1	Traf2; Putative uncharacterized protein	0.81	0.0121
Q80ZM7	Gtf2a2; Transcription initiation factor IIA subunit 2	0.81	0.0427
A0A0R4J291	Fastkd5; FAST kinase domain-containing protein 5, mitochondrial	0.82	0.0344
B2RPV6	Mmrn1; Multimerin-1	1.21	0.0152
P60761	Nrgn; Neurogranin	0.79	0.0014

A0A1S6GWI2	Tmem258; Uncharacterized protein	0.81	0.0095
Q5SS00	Zdbf2; DBF4-type zinc finger-containing protein 2 homolog	0.81	0.0379
F8WGQ9	Kctd10; BTB/POZ domain-containing adapter for CUL3-mediated RhoA degradation protein 3	0.78	0.0162
G5E8C6	Vill; Villin-like protein	0.39	0.0002
F7C0E4	Atxn7l1; Ataxin-7-like protein 1 (Fragment)	1.44	0.0372

^aThe accession ID of each protein in the Uniprot database. ^bThe gene name and protein description of each protein in the Uniprot database. ^cThe fold change value of each differentially expressed protein in the 0.40-SeM/0.40-SeL comparison. ^dDifferences in protein abundances between the 0.40-SeM and 0.40-SeL groups were analyzed using one-way analysis of variance, followed by the Tukey's post hoc test. $P < 0.05$ was considered as significant. The value 0 indicates $P < 0.0001$.