



Figure S1. The synthetic pathway of proline (A) and ectoine(B).

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Table S1. Genes related to osmotic regulation.

	Gene name	Annotation
Kdp-type systems	KdpD	Osmosensitive K ⁺ channel histidine kinase KdpD
Trk-type systems	TrkA	Trk system potassium uptake protein TrkA
	TrkB	Trk system potassium uptake protein TrkB
	KTRD	potassium uptake protein, integral membrane component, KtrD
Kef-type systems	VGSC	K ⁺ transporter
	KefA	Potassium efflux system KefA protein
Na ⁺ efflux systems	ABC-2.P	Na ⁺ efflux ABC transporter permease
	ABC-2.A	Na ⁺ efflux ABC transporter ATP-binding protein
	MnhA	monovalent cation/H ⁺ antiporter subunit A
	NhaC	Na ⁽⁺⁾ /H ⁽⁺⁾ antiporter NhaC
Glycine betaine	ProW	Glycine/betaine ABC transporter
	OpuD	Glycine betaine transporter
	ProX	Glycine betaine ABC transporter substrate-binding protein
	OpuC	Glycine/betaine ABC transporter substrate-binding protein
	OpuA	Proline/glycine betaine ABC transporter ATP-binding protein
	ProV	Glycine betaine ABC transporter ATP-binding protein
	OpuD	Glycine betaine transporter
	TC.BCT	Choline/glycine betaine transporter
	ProX	Proline/glycine betaine ABC transporter substrate-binding protein
	OpuA	Proline/glycine betaine ABC transporter ATP-binding protein
	OpuC	Proline/glycine betaine ABC transporter substrate-binding protein
	OpuBD	Proline/glycine betaine ABC transporter permease
	GbsR	Betaine operon transcriptional regulator

	BetL	Glycine betaine transporter
	BetT	High-affinity choline uptake protein
Trehalose	ScrA	PTS system trehalose-specific transporter subunits IIBC
	TreR	GntR family transcriptional repressor of trehalose operon
	MalF	Trehalose/maltose transport system permease protein MalF
	TreB	PTS system, trehalose-specific IIB component
Proline	PutA	1-pyrroline-5-carboxylate dehydrogenase
	ProA	Gamma-glutamyl phosphate reductase
	ProB	Gamma-glutamyl kinase
	ProC	Pyrroline-5-carboxylate reductase
	ProDH	Proline dehydrogenase
Ectoine	LysC	Aspartate kinase
	Asd	Aspartate-semialdehyde dehydrogenase
	EctA	L-2,4-diaminobutyric acid acetyltransferase
	EctB	Diaminobutyrate--2-oxoglutarate aminotransferase
	EctC	L-ectoine synthase
	EctD	Ectoine hydroxylase

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9 **Table S2.** Changes in gene expression when cells cultured in minimal medium supplemented with
 10 different salt concentration. A: 5% NaCl; B: 15% NaCl.

ID	Fold change (B/A)	Log₂ (fold change B/A)	Annotation
Energy metabolism and cell composition related genes			
AVZ68_RS15870	1.354	0.438	Class D sortase
AVZ68_RS08620	1.396	0.482	ATP synthase subunit I
AVZ68_RS02695	1.362	0.445	Dehydrogenase
AVZ68_RS12750	1.375	0.459	Dehydratase
AVZ68_RS10070	1.376	0.460	Pyruvate dehydrogenase (Acetyl- transferring) E1 component subunit alpha
AVZ68_RS10205	1.414	0.499	Acetyltransferase
AVZ68_RS09995	1.421	0.507	Phenylacetate-CoA oxygenase
AVZ68_RS09310	1.349	0.432	Carboxyvinyl- carboxyphosphonate phosphorylmutase
AVZ68_RS10075	1.351	0.434	Alpha-ketoacid dehydrogenase subunit beta
AVZ68_RS13645	1.335	0.417	Tryptophan synthase subunit alpha
AVZ68_RS13735	1.307	0.386	4-hydroxy-tetrahydrodipicolinate reductase
AVZ68_RS07410	0.697	-0.521	Dihydroxy-acid dehydratase
AVZ68_RS16190	1.339	0.422	Cystathionine gamma-synthase
AVZ68_RS05885	0.618	-0.694	Cysteine synthase A
AVZ68_RS17040	1.311	0.390	Riboflavin synthase
AVZ68_RS17450	0.677	-0.562	Homoserine dehydrogenase
AVZ68_RS04500	1.351	0.434	Imidazoleglycerol-phosphate dehydratase

AVZ68_RS02555	1.327	0.408	Oxidoreductase
AVZ68_RS16190	1.339	0.422	Cystathionine gamma-synthase
AVZ68_RS17220	0.663	-0.593	Diaminobutyrate acetyltransferase
AVZ68_RS01095	1.313	0.393	Shikimate dehydrogenase
AVZ68_RS12315	1.477	0.562	6-carboxy-5,6,7,8-tetrahydropterin synthase
AVZ68_RS11800	1.489	0.574	D-ribose pyranase
AVZ68_RS10010	1.490	0.575	Ethyl tert-butyl ether degradation protein EthD
AVZ68_RS15940	1.343	0.425	Succinyl-CoA--3-ketoacid-CoA transferase
Transcription regulation related genes			
AVZ68_RS15265	0.552	-0.857	Translation elongation factor Tu
AVZ68_RS14025	0.625	-0.678	Elongation factor Ts
AVZ68_RS15260	0.573	-0.803	Elongation factor G
AVZ68_RS08040	0.649	-0.623	Transcriptional regulator Spx
Transport system related genes			
AVZ68_RS14670	0.577	-0.794	ABC transporter permease
AVZ68_RS09530	1.365	0.449	ABC transporter permease
AVZ68_RS19130	1.439	0.524	PTS mannitol transporter subunit IIA
AVZ68_RS19125	1.444	0.529	PTS ascorbate transporter subunit IIB
AVZ68_RS09555	1.376	0.460	ABC transporter substrate-binding protein
AVZ68_RS09560	1.359	0.443	Sugar ABC transporter permease
Central carbon metabolic pathways			
Glycolysis pathway			
AVZ68_RS06075	1.102	0.139	PTS glucose transporter subunit

			IIA
AVZ68_RS06265	1.005	0.007	Glucose-6-phosphate isomerase
AVZ68_RS08755	0.986	-0.0193	Fructose-1,6-bisphosphate aldolase, class II
AVZ68_RS04405	0.966	-0.049	Triose-phosphate isomerase
AVZ68_RS07125	1.031	0.044	Glyceraldehyde-3-phosphate dehydrogenase
AVZ68_RS04410	1.001	0.001	Phosphoglycerate kinase
AVZ68_RS04400	1.118	0.161	Phosphoglycerate mutase 2,3- diphosphoglycerate-independent
AVZ68_RS04395	1.018	0.026	Phosphopyruvate hydratase
AVZ68_RS07065	0.873	-0.195	Pyruvate kinase
TCA cycle			
AVZ68_RS07080	0.821	-0.284	Citrate synthase
AVZ68_RS05050	0.919	-0.121	Aconitate hydratase 1
AVZ68_RS07085	0.969	-0.045	Isocitrate dehydrogenase (NADP(+))
AVZ68_RS12235	0.902	-0.149	2-oxoglutarate dehydrogenase E1 component
AVZ68_RS12230	0.940	-0.089	Dihydrolipoamide succinyltransferase
AVZ68_RS11090	0.868	-0.204	Succinate--CoA ligase subunit beta
AVZ68_RS11085	0.888	-0.171	Succinate--CoA ligase subunit alpha
AVZ68_RS07320	0.909	-0.137	Succinate dehydrogenase flavoprotein subunit
AVZ68_RS07325	0.921	-0.119	Succinate dehydrogenase iron- sulfur subunit

AVZ68_RS07315	0.929	-0.107	Succinate dehydrogenase
AVZ68_RS12160	1.049	0.070	Fumarate hydratase
AVZ68_RS12155	0.912	-0.133	Fumarate hydratase
AVZ68_RS07090	0.928	-0.108	Malate dehydrogenase
Pentose phosphate pathway			
AVZ68_RS17575	0.880	-0.184	Glucose-6-phosphate dehydrogenase
AVZ68_RS17370	1.056	0.079	Ferredoxin--NADP(+) reductase
AVZ68_RS02745	1.085	0.118	Ribose 5-phosphate isomerase A
AVZ68_RS14625	0.910	-0.135	Ribose-phosphate pyrophosphokinase
AVZ68_RS11290	0.844	-0.245	Ribulose-phosphate 3-epimerase
AVZ68_RS05020	0.882	-0.181	Transketolase
AVZ68_RS08750	0.891	-0.166	Transaldolase
AVZ68_RS08755	0.986	-0.019	Fructose-1,6-bisphosphate aldolase, class II
Proline synthesis pathway			
AVZ68_RS06000	1.199	0.262	Glutamate 5-kinase
AVZ68_RS05995	1.156	0.209	Pyrroline-5-carboxylate reductase
AVZ68_RS10650	1.072	0.101	Pyrroline-5-carboxylate reductase
AVZ68_RS10170	1.053	0.074	L-glutamate gamma-semialdehyde dehydrogenase
AVZ68_RS10160	0.877	-0.189	Proline dehydrogenase
Ribosomal proteins			
AVZ68_RS07680	0.434	-1.203	50S ribosomal protein L21
AVZ68_RS15270	0.489	-1.031	30S ribosomal protein S10
AVZ68_RS06885	0.548	-0.867	30S ribosomal protein S4
AVZ68_RS14020	0.494	-1.016	30S ribosomal protein S2
AVZ68_RS07690	0.564	-0.827	50S ribosomal protein L27

AVZ68_RS15245	0.574	-0.801	50S ribosomal protein L7ae-like protein
AVZ68_RS15300	0.579	-0.786	50S ribosomal protein L22
AVZ68_RS15310	0.584	-0.776	50S ribosomal protein L16
AVZ68_RS15255	0.589	-0.764	30S ribosomal protein S7
AVZ68_RS15305	0.599	-0.739	30S ribosomal protein S3
AVZ68_RS15440	0.626	-0.675	50S ribosomal protein L13
AVZ68_RS15210	0.641	-0.641	50S ribosomal protein L11
AVZ68_RS11280	0.646	-0.629	50S ribosomal protein L28
AVZ68_RS11160	0.653	-0.616	50S ribosomal protein L19
AVZ68_RS13470	0.657	-0.606	30S ribosomal protein S6
AVZ68_RS00955	0.663	-0.593	30S ribosomal protein S21
AVZ68_RS15215	0.669	-0.578	50S ribosomal protein L1
AVZ68_RS15355	0.681	-0.554	50S ribosomal protein L18
AVZ68_RS14085	0.689	-0.538	50S ribosomal protein L7
AVZ68_RS15315	2.812	1.492	50S ribosomal protein L29
AVZ68_RS15080	1.396	0.481	Ribosomal-protein-alanine N-acetyltransferase

Hypothetical proteins

AVZ68_RS19570	0.376	-1.412	Hypothetical protein
AVZ68_RS07685	0.557	-0.844	Hypothetical protein
AVZ68_RS17715	0.573	-0.803	Hypothetical protein
AVZ68_RS03505	0.587	-0.768	Hypothetical protein
AVZ68_RS03920	0.596	-0.748	Hypothetical protein
AVZ68_RS01975	0.666	-0.587	Hypothetical protein
AVZ68_RS17440	0.670	-0.577	Homoserine kinase
AVZ68_RS12915	0.673	-0.571	Hypothetical protein
AVZ68_RS13995	0.678	-0.561	Hypothetical protein
AVZ68_RS12345	0.697	-0.519	Hypothetical protein

AVZ68_RS10825	1.304	0.383	Hypothetical protein
AVZ68_RS19190	1.307	0.386	Hypothetical protein
AVZ68_RS08320	1.314	0.394	Hypothetical protein
AVZ68_RS06550	1.319	0.399	Hypothetical protein
AVZ68_RS16015	1.319	0.401	Hypothetical protein
AVZ68_RS10395	1.325	0.406	Hypothetical protein
AVZ68_RS13350	1.336	0.418	Hypothetical protein
AVZ68_RS14995	1.342	0.425	Hypothetical protein
AVZ68_RS06740	1.348	0.431	Hypothetical protein
AVZ68_RS09365	1.379	0.464	Hypothetical protein
AVZ68_RS08245	1.379	0.464	Hypothetical protein
AVZ68_RS02490	1.398	0.483	Hypothetical protein
AVZ68_RS00025	1.401	0.487	Hypothetical protein
AVZ68_RS07135	1.410	0.496	Hypothetical protein
AVZ68_RS11095	1.414	0.499	Hypothetical protein
AVZ68_RS08025	1.429	0.516	Hypothetical protein
AVZ68_RS04385	1.447	0.533	Hypothetical protein
AVZ68_RS13795	1.455	0.541	Hypothetical protein
AVZ68_RS07970	1.465	0.551	Hypothetical protein
AVZ68_RS19825	1.471	0.556	Hypothetical protein
AVZ68_RS07815	1.477	0.562	Hypothetical protein
AVZ68_RS13895	1.571	0.652	Hypothetical protein
AVZ68_RS19810	1.594	0.673	Hypothetical protein
AVZ68_RS18560	1.616	0.693	Hypothetical protein
AVZ68_RS17485	1.634	0.708	Hypothetical protein
AVZ68_RS04635	1.638	0.712	Hypothetical protein
AVZ68_RS01115	1.648	0.721	Hypothetical protein
AVZ68_RS05210	1.711	0.775	Hypothetical protein
AVZ68_RS04055	1.847	0.885	YqzE family protein

AVZ68_RS06905	1.886	0.915	Hypothetical protein
AVZ68_RS19605	2.308	1.207	Hypothetical protein
AVZ68_RS04875	2.384	1.253	Hypothetical protein
AVZ68_RS16610	1.357	0.441	Hypothetical protein
AVZ68_RS16010	1.359	0.443	Hypothetical protein
AVZ68_RS19110	1.376	0.460	Hypothetical protein
AVZ68_RS07965	1.503	0.588	Hypothetical protein
AVZ68_RS10570	1.483	0.568	Hypothetical protein
AVZ68_RS04065	0.685	-0.546	Hypothetical protein

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14 **Table S3.** Significant metabolic differences when cells were cultured in TSB medium

15 supplemented with different salt concentration. A: metabolic cultured with 5% NaCl; B: metabolic

16 cultured with 10% NaCl; C: metabolic cultured with 15% NaCl.

Name	molecular weight	Log₂(fold change B/A)	Log₂(fold change C/A)	Log₂(fold change C/B)
Amino acids and derivatives				
L-Proline	115.0631	-1.803	-2.698	-0.717
L-Valine	117.0784	-1.719	-1.301	0.505
Pyroglutamic acid	129.0424	-0.687	-2.613	-1.925
L-Pyrrolysine	255.1578	2.484	1.040	-1.444
L-Leucine	131.0942	-1.932	-3.564	-1.632
L-Tyrosine	181.0736	-2.610	-3.301	-0.691
L-Tryptophan	204.0894	-1.865	-2.216	-0.351
Nitrotyrosine	226.0572	3.145	1.825	-1.321
L-Pyrrolysine	255.1578	2.484	1.040	-1.444
L-Glutamate	147.0526	-0.052	-2.189	-2.059
Cinnamic acid	148.0572	1.401	-1.672	-3.072
L-Histidine	155.0692	-1.721	-4.556	-2.836
Hydroxylysine	162.1001	-1.920	-4.194	-2.274
Citrulline	175.0964	3.877	0.137	-3.739
Ornithine	132.0976	-1.951	-3.707	-1.756
N ² -Acetyl-L-ornithine	174.1001	-2.074	-3.474	-1.401
N ^α -Acetyl-L-glutamine	188.0794	-5.802	-6.081	-0.279
Fatty acids and derivatives				
Stearamide	283.2869	-1.648	-0.576	1.072
Palmitic amide	255.2556	-1.332	-2.548	-0.522
Oleamide	281.2713	-1.959	-1.312	0.647
Octadecanedioic acid	314.2464	-0.385	0.072	0.458
Sphinganine	301.2972	-2.011	-2.745	-0.734

MG(0:0/15:0/0:0)	316.2623	-0.141	0.388	0.530
PIP(18:1(9Z)/18:1(11Z))	942.5168	-1.474	0.683	2.157
PIP(20:3(5Z,8Z,11Z)/16:0)	940.5033	2.082	3.347	1.265
LysoPE(0:0/18:1(11Z))	479.3022	-4.205	-1.414	2.792
LysoPE(0:0/15:0)	439.2687	-2.094	-1.039	1.055
LysoPE(0:0/16:0)	453.2846	-6.276	-2.809	3.467
LysoPE(0:0/16:1(9Z))	451.2704	1.834	2.020	0.186
Nucleotide and derivatives				
Guanosine	283.1315	-4.705	-5.194	-0.489
Thymine	126.0428	-0.453	-2.051	-1.598
Hypoxanthine	136.0392	1.146	-2.696	-3.842
Inosine	268.0815	1.203	0.283	-0.920
Riboflavin	376.1374	1.080	-1.130	-2.210
Dihydrouracil	114.0435	2.952	-0.634	-3.586
deoxyguanosine 5'- monophosphate (dGMP)	347.0623	1.221	-0.984	-2.205
Glycitin	446.1219	-3.112	-1.224	1.888
Flavine mononucleotide (FMN)	456.1051	3.745	0.142	-3.603
Flavin adenine dinucleotide (FAD)	785.1571	2.856	-0.385	-3.242
Organic acid				
Glucosaminic acid	195.0753	-0.442	-0.712	-0.27043
Succinic acid	118.0749	2.087	-2.032	-3.586
Gluconic acid	196.0586	1.872	0.956	-0.916
Malic acid	134.0221	-1.112	-4.824	-3.712
Phosphohydroxypyruvic acid	183.9778	-1.155	-0.732	0.423
Pantothenic Acid	219.1103	0.211	-4.294	-4.506

Phenylpyruvic acid	164.0479	0.287	-4.601	-4.888
D(-)- β -hydroxy butyric acid	104.0479	-0.035	-2.741	-2.706
L-2,4-diaminobutyric acid	118.0779	-1.103	-0.632	0.471
Glycocholic Acid	463.2074	-4.226	-6.168	-1.943
12-Ketodeoxycholic acid	390.0595	3.094	-1.674	-4.779
Taurochenodeoxycholic acid	499.3015	-4.489	-8.586	-4.097
N-Acetylmuramic acid	293.1118	0.992	-6.405	-7.397
Others				
D-Sorbitol	182.0706	-1.138	-0.622	0.516
Ectoine	142.0736	0.667	0.338	-0.321
Acetylcholine	145.1096	-2.962	-1.154	1.809
Pyridoxamine	168.0896	-3.160	-3.701	-0.540
Tyramine	137.0838	-3.434	-2.491	0.943
Lactaldehyde	74.0372	0.714	-3.067	-3.781
Hydrouracil	128.0582	1.235	-1.021	-2.256
Phenylacetaldehyde	120.057	-1.095	-0.516	0.578
Glycitein	284.0674	-3.034	-1.270	1.764
Spermidine	145.1576	0.515	1.854	1.339

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20 **Table S4.** Significant metabolic differences when cells were cultured in minimal medium

21 supplemented with different salt concentration. D: metabolic cultured with 5% NaCl; E: metabolic

22 cultured with 10% NaCl; F: metabolic cultured with 15% NaCl.

Name	molecular weight	Log ₂ (fold change E/D)	Log ₂ (fold change F/D)	Log ₂ (fold change F/E)
Amino acids and derivatives				
L-Proline	115.0631	0.543	1.509	1.011
L-Valine	117.0784	0.042	0.298	0.256
Pyroglutamic acid	129.0424	0.136	0.204	0.068
L-Pyrrolysine	255.1578	1.301	1.493	0.192
L-Leucine	131.0952	0.124	0.298	0.177
L-Aspartic Acid	133.0382	0.497	0.533	0.036
L-Tyrosine	181.0745	0.750	1.040	0.290
L-Tryptophan	204.0906	0.241	0.304	0.063
Nitrotyrosine	226.0572	0.814	0.957	0.1423
L-Pyrrolysine	255.1586	1.674	2.14	0.466
L-Glutamate	147.0538	-0.365	-0.739	-0.375
Cinnamic acid	148.0572	-0.397	-0.785	-0.388
L-Histidine	155.0703	-0.437	-0.786	-0.348
Hydroxylysine	162.1009	-1.004	-1.641	-0.637
Citrulline	175.0964	-0.136	-0.809	-0.674
Ornithine	132.0906	0.198	-0.287	-0.485
N ² -Acetyl-L-ornithine	174.1001	0.974	0.692	-0.282
N α -Acetyl-L-glutamine	188.0794	0.123	0.372	0.249
Fatty acids and derivatives				
Stearamide	283.2869	0.262	1.235	0.918
Palmitic amide	255.2558	0.168	0.490	0.322
Oleamide	281.2713	0.557	1.526	0.969
Octadecanedioic acid	314.2464	0.515	1.747	1.430

Sphinganine	301.2972	0.282	0.550	0.268
MG(0:0/15:0/0:0)	316.2623	-0.32	-0.184	0.136
PIP(18:1(9Z)/18:1(11Z))	942.5168	0.889	2.405	1.516
PIP(20:3(5Z,8Z,11Z)/16:0)	940.5033	0.935	1.797	0.862
LysoPE(0:0/18:1(11Z))	479.3022	0.517	1.588	0.386
LysoPE(0:0/14:0)	425.2548	-0.186	-1.228	-1.043
LysoPE(0:0/15:0)	439.2707	-0.401	-1.047	-0.734
LysoPE(0:0/16:0)	453.2863	-0.488	-1.202	-0.955
LysoPE(0:0/16:1(9Z))	451.2704	-2.013	-3.426	-1.412
LysoPE(0:0/22:6(4Z,7Z,10Z, ,13Z,16Z,19Z))	525.2866	-1.217	-3.468	-2.251
Nucleotide and derivatives				
Guanosine	283.1315	0.034	0.136	0.102
Thymine	126.0434	0.036	-0.346	-0.383
Xanthosine	284.0764	-0.892	-2.419	-1.526
XMP	364.0428	-1.328	-4.184	-2.856
Hypoxanthine	136.0392	-0.099	-0.340	-0.241
Inosine	268.0815	-0.746	-0.934	-0.188
Riboflavin	376.1388	-0.305	-0.996	-0.691
Dihydrouracil	114.0435	-1.191	-2.581	-1.39
deoxyguanosine 5'- monophosphate (dGMP)	347.0639	0.444	0.272	-0.172
Glycitin	446.1219	0.522	0.750	0.557
Flavine mononucleotide (FMN)	456.1051	-0.151	-0.251	-0.099
Flavin adenine dinucleotide (FAD)	785.1571	-0.737	-0.894	-0.157
Organic acid				
Glucosaminic acid	195.0753	0.221	1.342	1.121

Succinic acid	118.027	0.008	-0.49	-0.497
Gluconic acid	196.0586	0.698	-0.781	-1.479
Malic acid	134.0221	1.016	1.689	0.673
Phosphohydroxypyruvic acid	183.9778	-0.166	-0.181	-0.015
Pantothenic Acid	219.1103	-1.276	-2.258	-0.983
Phenylpyruvic acid	164.048	-0.354	-0.533	-0.179
Dehydroascorbic acid	174.0171	0.898	1.647	0.748
D(-)- β -hydroxy butyric acid	104.0479	-1.267	-1.163	0.104
L-2,4-diaminobutyric acid	118.0749	0.286	0.303	0.018
Cholic acid	408.2883	0.378	0.188	-0.191
Glycocholic Acid	463.2074	-0.132	0.402	0.534
12-Ketodeoxycholic acid	390.0595	1.094	1.651	1.43
Taurochenodeoxycholic acid	499.3015	0.775	-0.220	-0.995
Glycodeoxycholate	449.3146	0.712	1.099	0.229
N-Acetylmuramic acid	293.1118	4.244	2.008	-2.237
Others				
D-Sorbitol	182.0796	0.411	-1.567	-1.978
Ectoine	142.0736	0.378	0.932	-0.361
Pyridoxamine	168.0896	-0.133	-0.156	-0.023
Tyramine	137.0838	-0.338	-0.179	0.159
Lactaldehyde	74.0372	0.034	-0.396	-0.431
Hydrouracil	128.0582	0.098	0.379	0.282
Phenylacetaldehyde	120.057	0.567	0.638	0.159
Niacin	122.0323	0.236	0.672	0.436
Glycitein	284.0674	0.495	1.144	0.648
Tautomycin	766.4503	1.167	2.295	1.071

D-Pantethine	554.245	0.059	-1.633	-1.692
Spermidine	145.1576	1.163	1.871	0.709

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