

Table 3. List of the 227 organisms which were investigated for evolutionary conservation of intracellular metabolites found in *E. coli* (see the main text). We integrated the organisms from LIGAND database (<http://www.genome.ad.jp/ligand/>), and dropped some organisms due to their insufficient annotations.

Eukaryotes

Category		Species	No. of available metabolites	No. of available reactions
Animals	Insects	<i>Drosophila melanogaster</i>	906	882
	Nematodes	<i>Caenorhabditis elegans</i>	929	871
Plants	Dicotyledons	<i>Arabidopsis thaliana</i>	1043	996
	Red alga	<i>Cyanidioschyzon merolae</i>	821	758
Fungi	Ascomycetes	<i>Saccharomyces cerevisiae</i>	928	960
		<i>Ashbya gossypii</i> (<i>Eremothecium gossypii</i>)	873	867
		<i>Candida albicans</i>	1220	1235
		<i>Schizosaccharomyces pombe</i>	824	815
	Basidiomycetes	<i>Cryptococcus neoformans</i> JEC21	282	172
	Microsporidian	<i>Encephalitozoon cuniculi</i>	262	192
Protists	Protozoa	<i>Plasmodium falciparum</i>	544	478
		<i>Cryptosporidium parvum</i>	312	246
		<i>Cryptosporidium hominis</i>	354	258

Prokaryotes

Category		Species	No. of available metabolites	No. of available reactions
Gamma/Enterobacteria		<i>Yersinia pestis</i> CO92	992	1012
		<i>Yersinia pestis</i> KIM	970	972
		<i>Yersinia pestis</i> Mediaevails	954	976
		<i>Yersinia pseudotuberculosis</i>	1017	1037
		<i>Shigella flexneri</i> 301	1031	1060
		<i>Shigella flexneri</i> 2457T	1016	1041
		<i>Erwinia carotovora</i>	1020	1066
		<i>Photobacterium luminescens</i>	991	989
		<i>Buchnera aphidicola</i> APS	476	391
		<i>Buchnera aphidicola</i> Sg	466	375
		<i>Buchnera aphidicola</i> Bp	431	349
		<i>Wigglesworthia brevipalpis</i>	463	393
		<i>Blochmannia floridanus</i>	528	451
		<i>Haemophilus influenzae</i>	735	697
		<i>Haemophilus ducreyi</i>	576	522
		<i>Pasteurella multocida</i>	783	779
		<i>Mannheimia succiniciproducens</i>	812	815
		<i>Xylella fastidiosa</i> 9a5c	706	636
		<i>Xylella fastidiosa</i> Temecula1	734	660
		<i>Xanthomonas campestris</i>	960	929
		<i>Xanthomonas axonopodis</i>	953	915
		<i>Xanthomonas oryzae</i>	737	601
		<i>Vibrio cholerae</i>	921	922
		<i>Vibrio vulnificus</i> CMCP6	955	986
		<i>Vibrio vulnificus</i> YJ016	977	1008
		<i>Vibrio parahaemolyticus</i>	961	979

Proteobacteria	Gamma/Others	Vibrio fischeri	972	982
		Photobacterium profundum	988	1016
		Pseudomonas aeruginosa	1013	991
		Pseudomonas putida	977	951
		Pseudomonas syringae	966	927
		Acinetobacter sp. ADP1	991	927
		Shewanella oneidensis	910	891
		Idiomarina loihiensis	812	774
		Coxiella burnetii	646	581
		Legionella pneumophila Philadelphia 1	789	703
		Legionella pneumophila Lens	834	788
		Legionella pneumophila Paris	842	798
		Methylococcus capsulatus	787	726
		Francisella tularensis	805	748
	Beta	Neisseria meningitidis MC58 (serogroup B)	704	625
		Neisseria meningitidis Z2491 (serogroup A)	704	631
		Neisseria gonorrhoeae	559	446
		Chromobacterium violaceum	1071	1073
		Ralstonia solanacearum GMI1000	1094	1042
		Burkholderia mallei	893	792
		Burkholderia pseudomallei	834	733
		Bordetella pertussis	904	827
		Bordetella parapertussis	934	859
		Bordetella bronchiseptica	970	894
		Nitrosomonas europaea	832	748
	Azoarcus sp. EbN1	912	856	
	Epsilon	Helicobacter pylori 26695	593	478
		Helicobacter pylori J99	590	475
		Helicobacter hepaticus	582	517
		Wolinella succinogenes	573	512
Campylobacter jejuni NCTC11168		578	506	
Campylobacter jejuni RM1221		577	503	
Delta	Geobacter sulfurreducens	719	659	
	Desulfovibrio vulgaris Hildenborough	716	638	
	Bdellovibrio bacteriovorus	860	780	
	Desulfotalea psychrophila	704	635	
Alpha	Rickettsia prowazekii	396	289	
	Rickettsia typhi	422	327	
	Rickettsia conorii	414	305	
	Wolbachia wMel	395	314	
	Anaplasma marginale	469	367	
	Ehrlichia ruminantium Welgevonden (South Africa)	397	324	
	Mesorhizobium loti	1124	1110	
	Sinorhizobium meliloti	1156	1134	
	Agrobacterium tumefaciens C58 (UWash/Dupont)	1059	1017	
	Agrobacterium tumefaciens C58 (Cereon)	1059	1016	
	Brucella melitensis	1034	989	
	Brucella suis	959	880	
	Bradyrhizobium japonicum	1156	1120	
	Rhodopseudomonas palustris CGA009	1103	1043	
	Bartonella henselae	627	520	

		Bartonella quintana	582	469
		Caulobacter crescentus	936	853
		Silicibacter pomeroyi	1015	960
		Zymomonas mobilis	767	667
		Gluconobacter oxydans	844	771
Firmicutes	Bacillales	Bacillus subtilis	985	994
		Bacillus halodurans	962	942
		Bacillus anthracis Ames	973	959
		Bacillus anthracis Ames 0581	983	961
		Bacillus anthracis A2012	971	945
		Bacillus anthracis Sterne	974	964
		Bacillus cereus ATCC 14579	1004	1001
		Bacillus cereus ATCC 10987	1004	985
		Bacillus cereus ZK	1031	1043
		Bacillus thuringiensis	1009	1032
		Bacillus licheniformis ATCC 14580	974	989
		Bacillus licheniformis DSM13	985	1003
		Bacillus clausii	994	1014
		Oceanobacillus iheyensis	959	921
		Geobacillus kaustophilus	971	954
		Staphylococcus aureus N315	811	775
		Staphylococcus aureus Mu50	807	775
		Staphylococcus aureus MW2	811	774
		Staphylococcus aureus MRSA252	821	788
		Staphylococcus aureus MSSA476	819	784
		Staphylococcus aureus COL	815	781
		Staphylococcus epidermidis ATCC 12228	767	734
		Staphylococcus epidermidis RP62A	767	737
		Listeria monocytogenes EGD-e	753	742
	Listeria monocytogenes F2365	741	730	
	Listeria innocua	727	719	
	Lactobacillales	Lactococcus lactis	700	679
		Streptococcus pyogenes SF370	588	514
		Streptococcus pyogenes MGAS8232	589	520
		Streptococcus pyogenes MGAS315	591	520
		Streptococcus pyogenes SSI-1	588	518
		Streptococcus pyogenes MGAS10394	685	640
Streptococcus pneumoniae TIGR4		674	646	
Streptococcus pneumoniae R6		686	662	
Streptococcus agalactiae 2603		636	583	
Streptococcus agalactiae NEM316		643	592	
Streptococcus mutans		671	640	
Streptococcus thermophilus CNRZ1066		644	598	
Streptococcus thermophilus LMG18311		644	599	
Lactobacillus plantarum		811	789	
Lactobacillus johnsonii		489	448	
Lactobacillus acidophilus		581	532	
Enterococcus faecalis		673	633	
Clostridia		Clostridium acetobutylicum	787	748
	Clostridium perfringens	786	740	
	Clostridium tetani E88	766	661	

	Mollicutes	<i>Thermoanaerobacter tengcongensis</i>	692	656
		<i>Mycoplasma genitalium</i>	284	215
		<i>Mycoplasma pneumoniae</i>	299	229
		<i>Mycoplasma pulmonis</i>	301	235
		<i>Mycoplasma penetrans</i>	390	290
		<i>Mycoplasma gallisepticum</i>	316	238
		<i>Mycoplasma mycoides</i>	347	284
		<i>Mycoplasma mobile</i>	353	289
		<i>Mycoplasma hyopneumoniae</i>	296	216
		<i>Ureaplasma urealyticum</i>	238	177
		<i>Phytolasma</i> sp. onion yellows	205	163
		<i>Mesoplasma florum</i>	303	255
Actinobacteria	<i>Mycobacterium tuberculosis</i> H37Rv	966	894	
	<i>Mycobacterium tuberculosis</i> CDC1551	970	895	
	<i>Mycobacterium bovis</i>	1002	935	
	<i>Mycobacterium leprae</i>	726	663	
	<i>Mycobacterium avium</i> paratuberculosis	971	901	
	<i>Corynebacterium glutamicum</i> (Kitasato)	895	839	
	<i>Corynebacterium glutamicum</i> (Bielefeld)	868	807	
	<i>Corynebacterium efficiens</i>	841	791	
	<i>Nocardia farcinica</i>	1000	916	
	<i>Corynebacterium diphtheriae</i>	769	723	
	<i>Streptomyces coelicolor</i>	1045	971	
	<i>Streptomyces avermitilis</i>	1016	990	
	<i>Tropheryma whipplei</i> Twist	452	365	
	<i>Tropheryma whipplei</i> TW08/27	455	368	
	<i>Leifsonia xyli xyli</i> CTCB07	692	635	
	<i>Propionibacterium acnes</i>	821	807	
	<i>Bifidobacterium longum</i>	653	583	
	<i>Symbiobacterium thermophilum</i>	718	653	
Fusobacteria	<i>Fusobacterium nucleatum</i>	729	605	
Planctomyces	<i>Rhodopirellula baltica</i>	956	900	
Chlamydia	<i>Chlamydia trachomatis</i>	417	326	
	<i>Chlamydia muridarum</i>	415	326	
	<i>Chlamydophila pneumoniae</i> CWL029	425	347	
	<i>Chlamydophila pneumoniae</i> AR39	424	346	
	<i>Chlamydophila pneumoniae</i> J138	425	348	
	<i>Chlamydophila pneumoniae</i> TW183	425	348	
	<i>Chlamydophila caviae</i>	432	338	
	<i>Chlamydophila abortus</i>	266	191	
	<i>Parachlamydia</i> sp. UWE25	464	385	
Spirochete	<i>Borrelia burgdorferi</i>	349	279	
	<i>Borrelia garinii</i>	317	250	
	<i>Treponema pallidum</i>	370	310	
	<i>Treponema denticola</i>	590	510	
	<i>Leptospira interrogans</i> serovar lai	926	811	
	<i>Leptospira interrogans</i> serovar Copenhageni	891	777	
	<i>Synechocystis</i> sp. PCC6803	812	729	
	<i>Synechococcus</i> sp. WH8102	772	691	
	<i>Synechococcus</i> sp. PCC6301	765	662	
	<i>Thermosynechococcus elongatus</i>	715	637	

Cyanobacteria		Gloeobacter violaceus	784	702
		Anabaena sp. PCC7120	841	762
		Prochlorococcus marinus SS120	719	621
		Prochlorococcus marinus MED4	715	630
		Prochlorococcus marinus MIT9313	746	648
Bacteroid		Bacteroides thetaiotaomicron	744	738
		Bacteroides fragilis NCTC9343	615	515
		Porphyromonas gingivalis	585	497
Green sulfur bacteria	Chlorobium tepidum	711	610	
Green nonsulfur bacteria	Dehalococcoides ethenogenes	473	382	
Deinococcus–Thermus		Deinococcus radiodurans	850	820
		Thermus thermophilus HB27	863	831
		Thermus thermophilus HB8	840	811
Hyperthermophilic bacteria		Aquifex aeolicus	641	550
		Thermotoga maritima	661	638
Archaea	Euryarchaeota	Methanococcus jannaschii	513	392
		Methanococcus maripaludis	537	419
		Methanosarcina acetivorans	642	530
		Methanosarcina mazei	674	548
		Methanobacterium thermoautotrophicum	538	414
		Methanopyrus kandleri	474	344
		Archaeoglobus fulgidus	633	481
		Halobacterium sp. NRC-1	577	486
		Haloarcula marismortui	840	747
		Thermoplasma acidophilum	610	497
		Thermoplasma volcanium	609	494
		Picrophilus torridus	773	662
		Pyrococcus horikoshii	492	365
		Pyrococcus abyssi	548	421
		Pyrococcus furiosus	575	456
	Thermococcus kodakaraensis	540	415	
	Crenarchaeota	Aeropyrum pernix	586	460
		Sulfolobus solfataricus	776	617
		Sulfolobus tokodaii	696	553
		Pyrobaculum aerophilum	656	526