

Supplementary Table I. Organisms used in the study

Organism	# of protein-coding genes	# (%) of <i>E. coli</i> K12 protein-coding genes present in organism	Average percent identity of Present <i>E. coli</i> K12 proteins ^a	Average percent identity of Absent <i>E. coli</i> K12 proteins ^b	Pathogenicity	Motility
<i>Escherichia coli</i> O157:H7 EDL933	5324	3849 (92%)	97	20	Hamburger disease	Yes
<i>Escherichia coli</i> O157:H7	5341	3835 (92%)	96	20	Hamburger disease	Yes
<i>Escherichia coli</i> CFT073	5379	3689 (88%)	96	19	Urinary tract infections	Yes
<i>Shigella flexneri</i> 2a strain 2457T	4068	3304 (79%)	96	18	Shigellosis	No
<i>Shigella flexneri</i> 2a strain 301	4441	3355 (80%)	96	18	Shigellosis	No
<i>Salmonella paratyphi</i>	4092	3127 (75%)	86	19	Paratyphoid fever	Yes
<i>Salmonella typhimurium</i> LT2	4527	3246 (78%)	86	20	Gastroenteritis / Typhoid like disease in mice	Yes
<i>Salmonella typhi</i> strain CT18	4758	3162 (76%)	85	20	Typhoid fever	Yes
<i>Salmonella typhi</i> strain Ty2	4318	3140 (75%)	86	20	Typhoid fever	Yes

<i>Yersinia pestis</i> CO92	4067	2381 (57%)	71	20	Plague	No
<i>Yersinia pestis</i> KIM	4086	2375 (57%)	71	20	Plague	No
<i>Yersinia pestis</i> biovar Mediaevails	4142	2394 (57%)	71	20	Plague	No
<i>Yersinia</i> <i>pseudotuberculosis</i>	4038	2458 (59%)	72	20	Gastroenteritis and tuberculosis like infection	Yes
<i>Erwinia carotovora</i>	4472	2497 (60%)	71	20	Soft rot disease of potatoes	Yes
<i>Photorhabdus</i> <i>luminescens</i>	4683	2042 (49%)	69	19	Toxemia and septicemia in insects	Yes
<i>Vibrio cholerae</i>	3835	1568 (37%)	61	19	Cholerae	Yes
<i>Vibrio fischeri</i> ES114	3802	1540 (37%)	59	20	A symbiont in fish and squids. Is responsible for light generation	No
<i>Vibrio</i> <i>parahaemolyticus</i>	4832	1671 (40%)	60	20	food poisoning (gastroenteritis)	Yes
<i>Vibrio vulnificus</i> CMCP6	4488	1639 (39%)	59	20	Opportunistic pathogen. Causes gastroenteritis , wound infections, and primary septicemia.	Yes

<i>Photobacterium profundum</i> SS9		1731 (41%)	60	21	Non-pathogenic, A tractable model system for studies of low temperature and high pressure adaptation	Yes
<i>Pseudomonas aeruginosa</i>	5567	1475 (35%)	55	21	Opportunistic infections in immuno-compromised patients	Yes
<i>Pseudomonas fluorescens</i> Pf-5	6137	1427 (34%)	55	22	Nonpathogenic , inhabits soil, water and plant surface environments	Yes
<i>Pseudomonas putida</i> KT2440	5350	1363 (33%)	55	21	Non-pathogenic.	Yes
<i>Pseudomonas syringae</i>	5608	1350 (32%)	55	21	Plant pathogens	Yes
<i>Shewanella oneidensis</i>	4472	1369 (33%)	58	20	Rare opportunistic infections	Yes
<i>Haemophilus influenzae</i>	1657	1159 (28%)	60	17	Meningitis, septicemia, otitis media, sinusitis and chronic bronchitis	No
<i>Haemophilus ducreyi</i> 35000HP	1717	974 (23%)	60	16	Sexually-transmitted chancroid and enhances HIV transmission	No

<i>Xanthomonas campestris</i>	4181	978 (23%)	52	20	Black rot in plants	Yes
<i>Xanthomonas citri</i>	4427	981 (23%)	52	20	Plant pathogen. Affects citrus plants	?
<i>Xanthomonas oryzae</i> KACC10331	4637	819 (20%) ^l	53	19	Plant pathogen. Affects rice plants by causing leaf blight	No

^aAverage percent identity between the orthologous proteins found in the genome and their *E. coli* K12 counterparts.

^bAverage percent identity between the best hits that were found for in the genome for each *E. coli* K12 protein, for which no ortholog was identified

Supplementary Table 2. Association between the status of TFs and the status of their targets

Organism	Positive regulatory interactions						Negative regulatory interactions					
	TF ₋ ,tar ^a	TF ₋ ,tar ^b	TF ₊ ,tar ^c	TF ₊ ,tar ^d	p-value ^e	Phi ^f	TF ₋ ,tar ^a	TF ₋ ,tar ^b	TF ₊ ,tar ^c	TF ₊ ,tar ^d	p-value ^e	Phi ^f
<i>Escherichia coli</i> O157:H7 EDL933	17	5	79	1187	2.8e-36	0.35	12	11	12	687	2.9e-40	0.49
<i>Escherichia coli</i> O157:H7	9	5	76	1198	2.3e-18	0.24	22	5	16	679	4.8e-73	0.67
<i>Escherichia coli</i> CFT073	9	5	68	1206	2.2e-20	0.26	22	5	13	682	1.2e-79	0.7
<i>Shigella flexneri</i> 2a strain 2457T	29	106	153	1000	9.6e-3	0.07	23	9	55	635	5e-30	0.42
<i>Shigella flexneri</i> 2a strain 301	34	101	157	996	3.4e-4	0.1	23	10	54	635	2.4e-29	0.41
<i>Salmonella paratyphi</i>	54	39	160	1035	7.2e-29	0.31	28	11	49	634	4.8e-37	0.47
<i>Salmonella typhimurum</i> LT2	50	37	147	1054	1.1e-29	0.32	29	9	37	647	2.6e-49	0.55
<i>Salmonella typhi</i> strain CT18	52	37	149	1050	8.6e-31	0.32	28	9	49	636	1.6e-39	0.49
<i>Salmonella typhi</i> strain Ty2	53	36	151	1048	1.2e-31	0.33	28	9	48	637	4.1e-40	0.49
<i>Yersinia pestis</i> CO92	137	109	386	656	8.5e-08	0.15	49	23	153	497	1.4e-15	0.30
<i>Yersinia pestis</i> KIM	143	111	394	640	1.4e-07	0.15	50	30	164	478	8.8e-12	0.25
<i>Yersinia pestis</i> biovar Mediaevails	148	112	383	645	8.7e-09	0.16	53	31	170	468	1.1e-11	0.25
<i>Yersinia pseudotuberculosis</i>	150	111	385	642	4.9e-09	0.16	50	26	161	485	1.3e-13	0.28

<i>Erwinia carotovora</i>	107	65	321	795	4.4e-18	0.24	45	24	115	538	1.4e-19	0.34
<i>Photorhabdus luminescens</i>	163	85	515	525	4.4e-06	0.13	108	27	193	394	1.3e-23	0.37
<i>Vibrio cholerae</i>	338	109	507	334	3.5e-08	0.15	111	57	292	262	2.2e-3	0.11
<i>Vibrio fischeri</i> ES114	277	130	551	330	0.055	0.05	87	37	307	291	1.3e-4	0.14
<i>Vibrio parahaemolyticus</i>	263	137	517	371	0.011	0.07	64	53	290	315	0.18	0.05
<i>Vibrio vulnificus</i> CMCP6	282	124	501	381	1.5e-05	0.12	61	46	291	324	0.064	0.07
<i>Photobacterium profundum</i> SS9	254	106	539	389	3.6e-05	0.12	67	42	281	332	2.6e-3	0.11
<i>Pseudomonas aeruginosa</i>	310	144	475	359	6.9e-05	0.11	169	118	218	217	0.021	0.09
<i>Pseudomonas fluorescens</i> Pf-5	385	199	398	306	5.9e-4	0.1	224	143	160	195	1.7e-05	0.16
<i>Pseudomonas putida</i> KT2440	310	159	482	337	0.01	0.07	181	75	209	257	2.6e-11	0.25
<i>Pseudomonas syringae</i>	332	161	488	307	0.031	0.06	202	120	195	205	1.7e-4	0.14
<i>Shewanella oneidensis</i>	312	118	536	322	3.2e-4	0.1	168	83	237	234	1.8e-05	0.16
<i>Haemophilus influenzae</i>	416	87	526	259	5.6e-10	0.17	126	50	333	213	0.011	0.09
<i>Haemophilus ducreyi</i> 35000HP	504	88	525	171	1.5e-05	0.12	193	52	346	131	0.068	0.07
<i>Xanthomonas campestris</i>	499	147	501	141	0.73	-0.01	347	126	185	64	0.79	-0.01
<i>Xanthomonas citri</i>	484	143	507	154	0.83	0.01	341	127	191	63	0.5	-0.03

<i>Xanthomonas</i> <i>oryzae</i> KACC10331	521	112	531	124	0.57	0.02	384	97	195	46	0.73	-0.01
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^aNumber of positive or negative *E. coli* K12 regulatory interactions for which both the TF and its target are absent from this genome

^bNumber of positive or negative *E. coli* K12 regulatory interactions for which the TF is absent and its target is present.

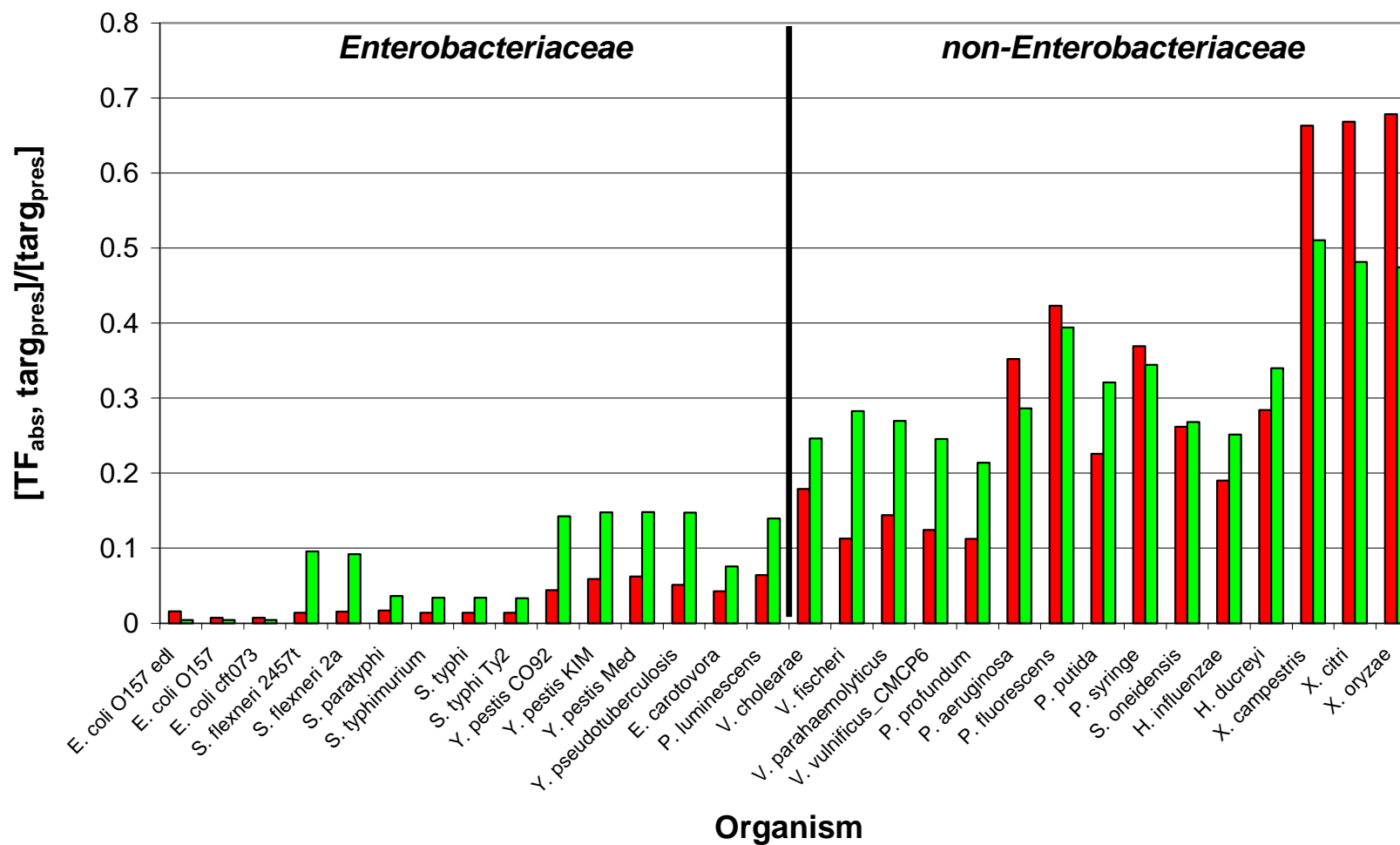
^cNumber of positive or negative *E. coli* K12 regulatory interactions for which the TF is present and its target is absent.

^dNumber of positive or negative *E. coli* K12 regulatory interactions for which both the TF and its target are present.

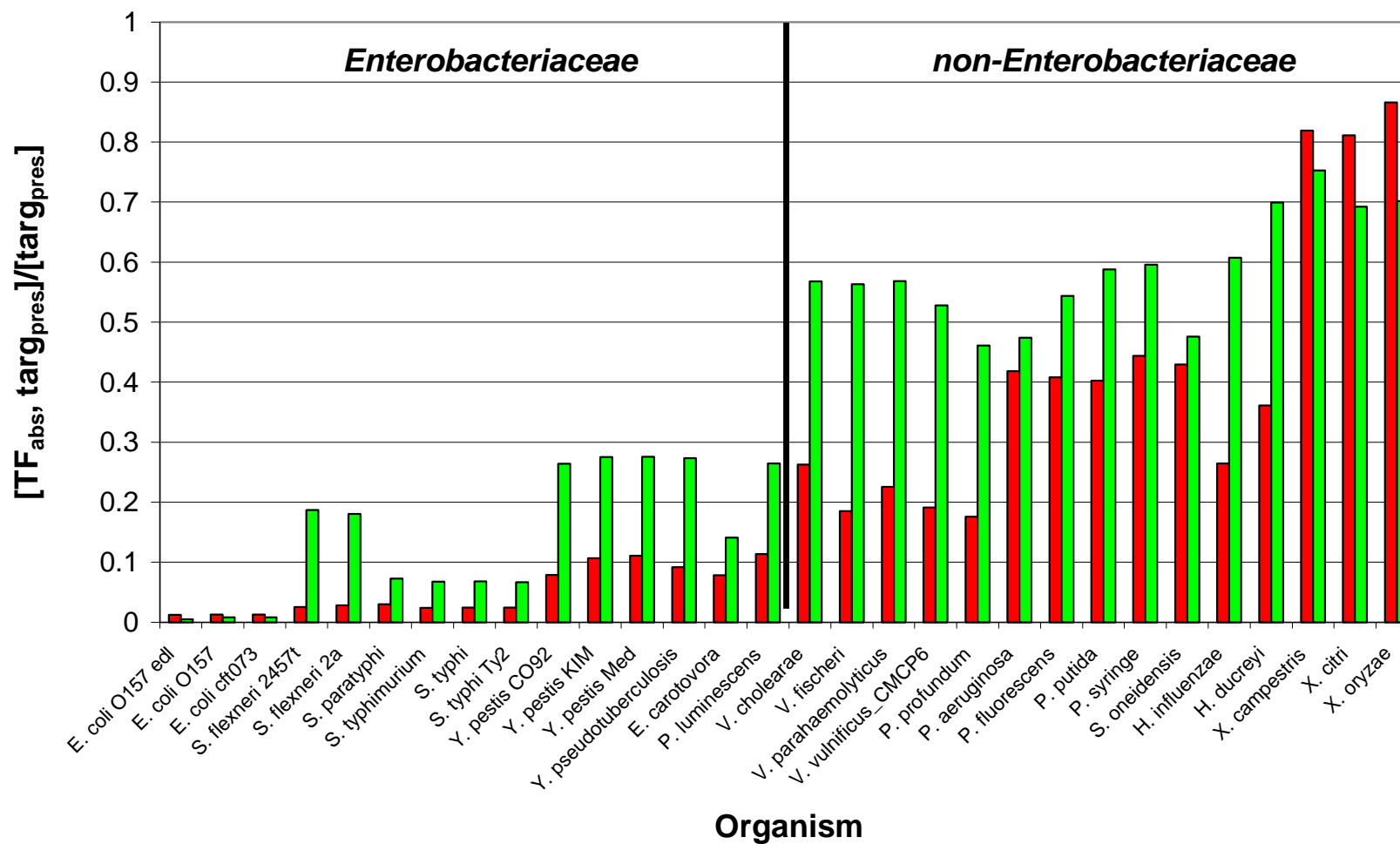
^eTwo-sided Pearson χ^2 test (df=1) was conducted to test the null hypothesis that the status of the targets (absent / present) and the status of the TFs are not associated. The p-values of the χ^2 test are listed. Rejection of the null hypothesis with $p \leq 0.01$ implied a statistical significant association.

^fThe *phi*-coefficient was calculated to measure the strength of the association between the status of the targets and the status of the TFs.

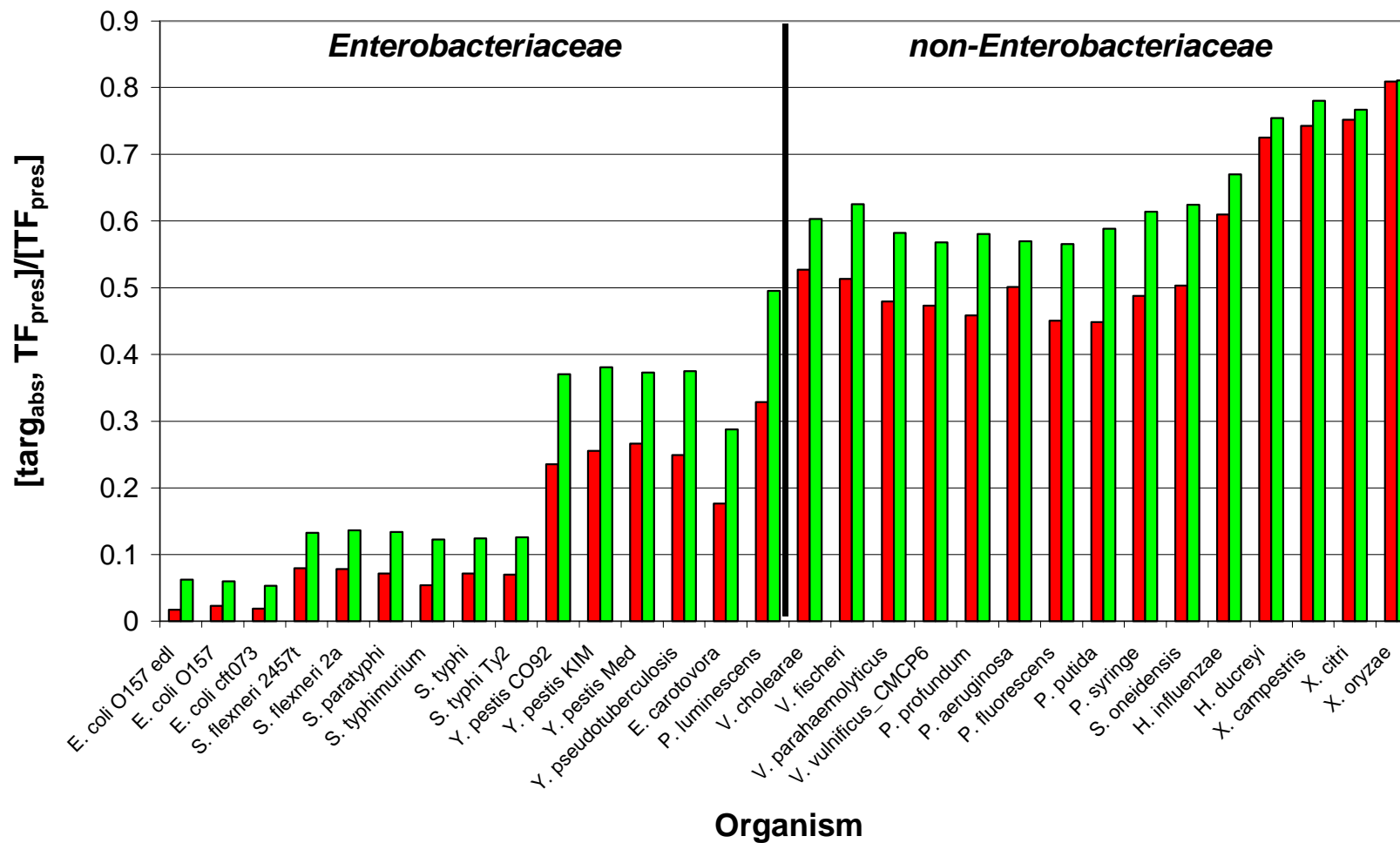
Supplementary Figure 1 (a)



Supplementary Figure 1 (b)



Supplementary Figure 2 (a)



Supplementary Figure 2 (b)

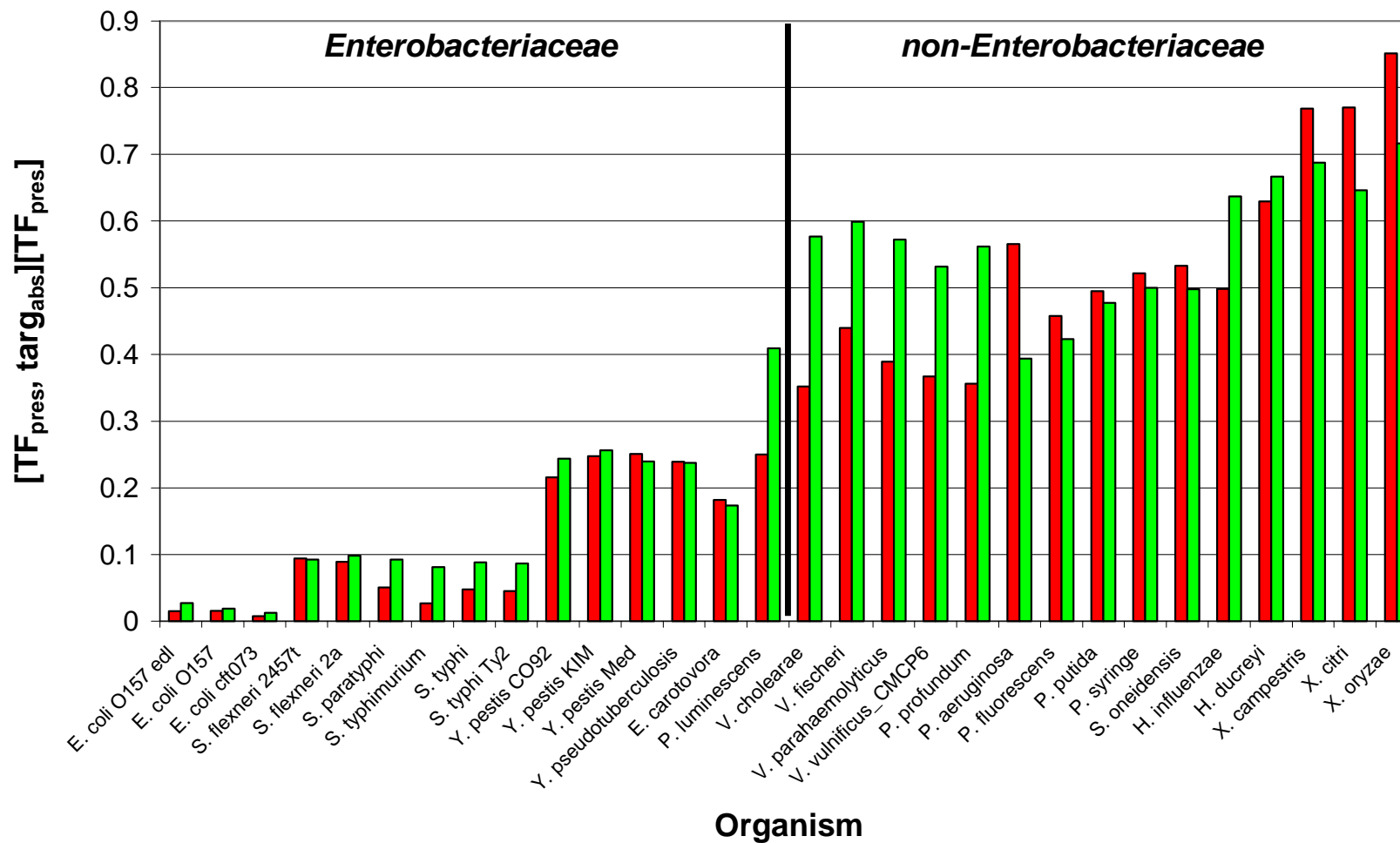


Figure legends

Supplementary Figure 1. Probability of a TF to be absent given that its targets are present. (a) Calculated for all positive (green bars) and negative (red bars) regulatory interactions. (b) Calculated after regulatory interactions mediated by global regulators were removed.

Supplementary Figure 2. Probability of target to be absent given its TF is present. (a) Calculated for all positive (green bars) and negative (red bars) regulatory interactions. (b) Calculated after regulatory interactions mediated by global regulators were removed.