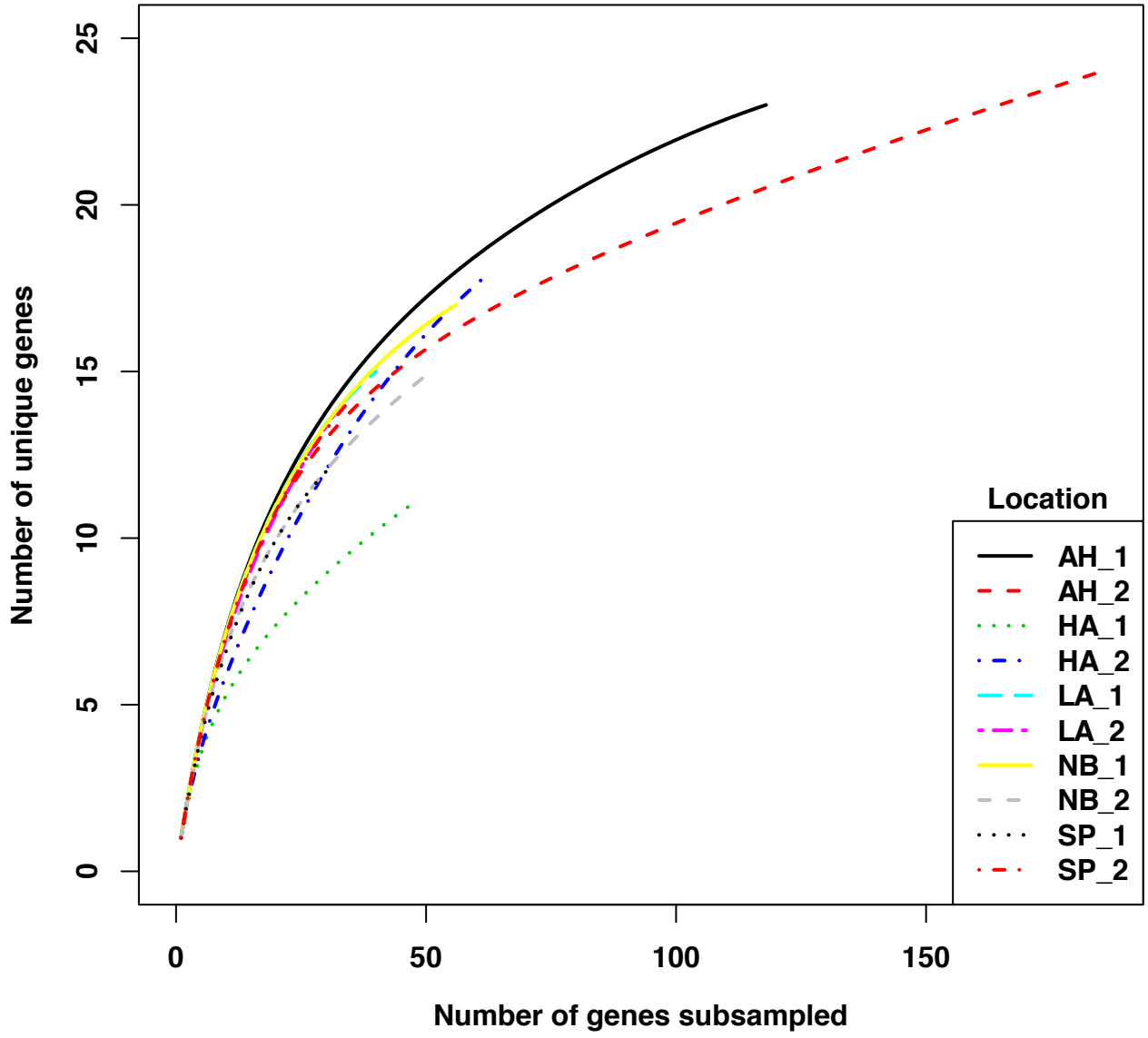

Fig. S1. Rarefaction curve of sequenced genes that conferred resistance to antibiotics across sample locations.

Table S1. The minimum inhibitory concentrations used for the antibiotic screens. The concentrations inhibited growth of E. cloni 10G cells (Lucigen, Middleton, WI) carrying empty pZE-21 plasmid.

Antibiotic	Natural/ synthetic	Minimum inhibitory concentration (ug/ml)	Antibiotic activity
Ampicillin	Semi-synthetic	60	Arrests cell wall synthesis
Tetracycline	Natural	8	Inhibits protein synthesis
Sulfadimethoxine	Synthetic	700	Inhibits folic acid synthesis
Nitrofurantoin	Synthetic	5	Damages intracellular macromolecules

Table S2. Statistical results for Kruskal-Wallis tests and permutational analysis of variance.

Model	Kruskal-Wallis $\chi 2$	Pseudo-F	d.f.	P-value
positive clone frequencies across sites	15.6	-	4	0.004*
positive clone frequency across antibiotics	9.1	-	3	0.03*
frequency of known AR genes across sites	7.4	-	4	0.1
frequency of known AR genes across antibiotics	6.7	-	3	0.08
composition of known AR genes across sites	-	4.1	4	0.01*
composition of known AR genes across antibiotics	-	4.6	3	0.009*
composition of gene functions across sites	-	3.6	4	0.004*
frequency of marine taxa across sites	7.6	-	4	0.1
frequency of marine taxa across antibiotics	5.2	-	3	0.2

Table S3. The abundance of previously uncharacterized AR genes across sample site and host organism . These are sequences that did not match sequences in the ARDB. Gene names are the top hit to the non-redundant database in GenBank.

Gene	Sample site					Host organism					Clones sequenced
	AH	HOT	LA	NB	SP	Non-marine	Marine	Eukaryote	Unknown	Virus	
(S)-2-hydroxy-acid oxidase	0	0	0	0	2	0	2	0	0	0	2
2-oxoglutarate dehydrogenase	0	1	0	1	0	1	1	0	0	0	2
3-alpha,7-alpha, 12-alpha-trihydroxy-5-beta-cholest-24-enoyl-CoAhydratase	1	0	0	0	0	1	0	0	0	0	1
3-hydroxyacyl-CoA dehydrogenase	2	0	0	0	0	0	2	0	0	0	2
3-isopropylmalate dehydratase	0	0	1	0	0	0	1	0	0	0	1
6-phosphofructokinase	0	0	1	0	0	0	1	0	0	0	1
ABC transporter	1	0	0	1	1	1	1	0	1	0	3
Acetyl/propionyl-CoA carboxylase	0	1	0	0	0	0	1	0	0	0	1
Acetylornithine aminotransferase	0	0	1	0	0	0	1	0	0	0	1
Acetyltransferase	1	0	0	0	0	0	1	0	0	0	1
Acyl-CoA thioesterase	0	1	0	0	0	0	0	0	1	0	1
Adenylate cyclase	0	0	1	0	0	1	0	0	0	0	1
Adenylate/Guanylate Cyclase	0	0	1	0	0	0	1	0	0	0	1
Alanyl-tRNA synthetase	0	0	0	5	0	0	5	0	0	0	5
Alcohol dehydrogenase	0	0	0	0	1	0	0	0	1	0	1
Aldehyde dehydrogenase	1	0	0	0	0	1	0	0	0	0	1
Alpha/beta fold family hydrolase	0	1	0	0	0	0	1	0	0	0	1
Amidotransferase	0	2	0	0	0	2	0	0	0	0	2
Ammonium transporter family protein	1	0	0	0	0	0	0	0	1	0	1
Ankyrin repeat protein	0	0	0	0	1	0	0	1	0	0	1
Anthranilate synthase	0	0	0	0	1	1	0	0	0	0	1
Arabinose efflux protein	0	0	0	0	1	0	0	0	1	0	1
Aspartate aminotransferase	0	1	0	0	0	0	1	0	0	0	1
Aspartate/ornithine carbamoyltransferase	0	0	1	0	0	0	0	0	1	0	1
ATP-dependent metalloprotease	0	0	0	8	0	8	0	0	0	0	8
Beta-carbonic anhydrase	9	0	0	0	0	0	0	0	9	0	9
Beta-ketoacyl synthase	0	0	1	0	0	0	1	0	0	0	1
Betaine aldehyde dehydrogenase	5	0	1	0	0	0	6	0	0	0	6
Bifunctional deaminase-reductase	1	0	0	0	0	0	0	0	1	0	1
Bifunctional dihydrofolate/folylpolyglutamate synthase	0	1	0	0	0	0	1	0	0	0	1
IMP cyclohydrolase	1	0	0	0	0	0	0	0	1	0	1
Carbonate dehydratase	0	0	1	0	0	0	1	0	0	0	1
Carboxyl transferase	0	0	1	0	0	0	1	0	0	0	1
Chaperonin	0	0	1	0	0	0	0	0	1	0	1
Choline dehydrogenase	0	0	0	0	7	0	7	0	0	0	7
Chromate transporter	1	0	0	0	0	1	0	0	0	0	1
Conserved hypothetical protein	11	1	1	0	0	8	3	0	2	0	13

Gene	Sample site					Host organism					Clones sequenced
	AH	HOT	LA	NB	SP	Non-marine	Marine	Eukaryote	Unknown	Virus	
Cysteine desulfurase	0	2	0	0	0	1	1	0	0	0	2
D-ala-D-ala dipeptidase	0	1	0	0	0	0	1	0	0	0	1
D-amino acid oxidase	0	1	0	0	0	0	1	0	0	0	1
DEAD/DEAH box helicase	1	0	0	0	0	0	1	0	0	0	1
Delta 1-pyrroline-5-carboxylate reductase	0	0	1	0	0	0	1	0	0	0	1
Diaminopimelate epimerase	1	0	0	0	0	1	0	0	0	0	1
Dienelactone hydrolase	0	0	0	1	0	1	0	0	0	0	1
Dihydrolipoamide dehydrogenase	0	0	0	0	2	0	0	0	2	0	2
Dihydroneopterin aldolase	0	0	0	1	0	1	0	0	0	0	1
Dihydroxy-acid dehydratase	0	0	0	0	1	0	1	0	0	0	1
DNA gyrase	0	1	0	0	0	0	1	0	0	0	1
DNA helicase	0	0	1	0	0	0	0	0	1	0	1
DNA mismatch	1	1	0	0	0	2	0	0	0	0	2
DNA polymerase III	3	0	0	1	0	1	3	0	0	0	4
DNA primase	1	0	0	0	0	0	1	0	0	0	1
DNA topoisomerase	0	1	0	0	0	0	1	0	0	0	1
DNA-binding protein	21	0	1	6	1	1	28	0	0	0	29
DNA-directed RNA polymerase	0	0	2	0	0	0	2	0	0	0	2
DSBA oxidoreductase	0	0	1	0	0	0	1	0	0	0	1
DSBA-like thioredoxin domain protein	1	0	0	0	0	0	1	0	0	0	1
Esterase	1	0	0	0	0	1	0	0	0	0	1
Exonuclease domain protein	0	2	0	0	0	2	0	0	0	0	2
FAD dependent oxidoreductase/aminomethyl transferase	0	0	1	0	0	0	0	0	1	0	1
FAD-binding domain protein	1	0	0	0	0	1	0	0	0	0	1
FAD/FMN-containing dehydrogenase	0	1	0	0	0	0	1	0	0	0	1
Ferrochelatase	1	0	0	0	0	0	1	0	0	0	1
FeS assembly ATPase SufC	0	0	0	0	1	0	1	0	0	0	1
FeS assembly protein SufB	0	1	0	0	0	0	1	0	0	0	1
FeS assembly protein SufD	0	2	0	0	0	0	2	0	0	0	2
Fmu	0	0	1	0	0	0	1	0	0	0	1
Formate dehydrogenase	1	0	0	0	0	0	1	0	0	0	1
Formate--tetrahydrofolate ligase	0	0	0	1	0	0	1	0	0	0	1
Fumarate reductase/succinate dehydrogenase	0	0	0	0	1	1	0	0	0	0	1
gag polyprotein	1	0	0	0	0	0	0	0	1	0	1
Gamma-glutamyl phosphate reductase	2	0	0	0	0	0	0	0	2	0	2
Glucokinase	0	0	1	0	0	1	0	0	0	0	1
Gluconolaconase	0	1	0	0	0	1	0	0	0	0	1
Glutamate synthase	1	0	0	0	0	1	0	0	0	0	1
Glycine dehydrogenase	1	0	1	0	0	1	1	0	0	0	2
Glycyl-tRNA synthetase	0	0	0	0	1	0	1	0	0	0	1
Glyoxylate reductase	1	0	0	0	0	0	0	0	1	0	1

Gene	Sample site					Host organism					Clones sequenced
	AH	HOT	LA	NB	SP	Non-marine	Marine	Eukaryote	Unknown	Virus	
GMC oxidoreductase	1	0	0	0	0	0	1	0	0	0	1
GP30.3 family protein	1	0	0	0	0	1	0	0	0	0	1
GTP cyclohydrolase	1	0	1	0	0	2	0	0	0	0	2
HlyD family secretion protein	1	0	0	0	0	0	1	0	0	0	1
Homoserine/homoserine lactone efflux protein	1	0	0	0	0	1	0	0	0	0	1
Hypothetical membrane protein	1	0	0	0	0	1	0	0	0	0	1
Hypothetical protein	30	31	6	17	5	10	22	45	4	8	89
Hypothetical transport protein	0	0	1	0	0	0	1	0	0	0	1
Inosine-5-monophosphate dehydrogenase	1	0	0	0	0	0	1	0	0	0	1
Integral membrane protein DUF6	1	0	0	0	0	0	1	0	0	0	1
Integrase catalytic region	2	0	0	0	0	2	0	0	0	0	2
Ion channel	0	0	0	0	1	0	0	1	0	0	1
IS1 transposase	0	0	0	0	1	1	0	0	0	0	1
Isocitrate dehydrogenase	1	0	0	0	1	1	0	0	1	0	2
Isoleucyl-tRNA synthetase	1	0	0	0	1	1	1	0	0	0	2
Ketol-acid reductoisomerase	9	0	1	1	0	0	4	0	7	0	11
L-sorbosone dehydrogenase	0	1	0	0	0	0	1	0	0	0	1
Leucyl-tRNA synthetase	1	0	0	1	0	0	2	0	0	0	2
Lon-B peptidase	0	0	0	0	1	0	1	0	0	0	1
Long-chain fatty-acid-CoA ligase	1	0	0	0	0	0	1	0	0	0	1
LrgB-like family	0	0	1	0	0	0	1	0	0	0	1
LysM domain-containing protein	0	1	0	0	0	0	1	0	0	0	1
Major facilitator family protein	6	0	1	2	0	6	2	0	1	0	9
Malate dehydrogenase	0	0	1	0	0	1	0	0	0	0	1
Mandelate racemase	4	0	0	0	0	0	0	0	4	0	4
MFS-type transporter	1	0	0	0	0	1	0	0	0	0	1
Molecular chaperone DnaK	0	1	0	0	0	0	1	0	0	0	1
Molybdenum cofactor biosynthesis protein A	0	0	0	0	1	0	1	0	0	0	1
N6-adenine-specific methylase	0	0	0	0	1	0	1	0	0	0	1
Na+/Ca2+-exchanging protein	1	0	0	0	0	1	0	0	0	0	1
NADPH-ferredoxin reductase	0	0	1	0	0	0	0	0	1	0	1
Nitrate reductase	0	0	0	0	1	0	1	0	0	0	1
Nitrite and sulfite reductase	0	0	1	0	0	1	0	0	0	0	1
Nitrogen regulatory protein PII	1	0	0	0	0	0	0	0	1	0	1
O-methyltransferase	0	0	0	0	1	0	1	0	0	0	1
Oligoendopeptidase F	0	0	0	0	1	1	0	0	0	0	1
Oligoribonuclease	1	0	0	0	0	0	1	0	0	0	1
Orphan protein	1	0	0	0	0	0	1	0	0	0	1
Outer membrane receptor	0	0	2	0	0	0	2	0	0	0	2
Oxidoreductase, GMC family protein	0	0	1	0	0	0	0	0	1	0	1

Gene	Sample site					Host organism					Clones sequenced
	AH	HOT	LA	NB	SP	Non-marine	Marine	Eukaryote	Unknown	Virus	
parB-like protein partition protein	0	0	0	1	0	1	0	0	0	0	1
Peptidase	2	0	0	0	0	1	1	0	0	0	2
Phage integrase	0	0	0	1	0	1	0	0	0	0	1
Phage tail fiber protein	0	0	0	1	0	1	0	0	0	0	1
Phenylacetic acid degradation protein	0	1	0	0	0	0	1	0	0	0	1
Phosphoenolpyruvate carboxylase	0	0	0	1	0	1	0	0	0	0	1
Phosphoglucomutase/phosphomannomutase	0	0	0	2	0	0	2	0	0	0	2
Phosphoglucosamine mutase	0	0	0	3	0	1	2	0	0	0	3
Phosphomethylpyrimidine kinase	0	0	0	1	0	1	0	0	0	0	1
Phosphoribosylamino-imidazole-carboxylase	5	0	0	0	0	0	0	5	0	0	5
Phosphoribosylanthranilate isomerase	0	0	0	0	1	1	0	0	0	0	1
Phosphoribosylformylglycinamidine synthase	0	0	0	1	0	0	1	0	0	0	1
Phosphoserine aminotransferase	0	0	0	1	0	0	1	0	0	0	1
Pleckstrin	0	0	0	1	0	0	0	1	0	0	1
Polyprenyl P-hydroxybenzoate and phenylacrylic acid decarboxylases	0	1	0	0	0	0	1	0	0	0	1
Porin	0	0	0	0	1	0	1	0	0	0	1
Porphobilinogen deaminase	1	0	0	0	0	1	0	0	0	0	1
Predicted protein	1	0	3	2	3	0	0	9	0	0	9
Probable oxidoreductase	0	0	0	0	1	0	1	0	0	0	1
Propionyl-CoA carboxylase	14	0	9	6	4	7	26	0	0	0	33
Protein-L-isoaspartate O-methyltransferase	1	0	0	0	0	0	1	0	0	0	1
Protocatechuate 4,5-dioxygenase	0	0	1	0	0	0	0	0	1	0	1
Putative Gingipain R	0	1	0	0	0	1	0	0	0	0	1
Pyridoxamine 5'-phosphate oxidase	1	0	0	0	0	1	0	0	0	0	1
Pyruvate decarboxylase	0	0	1	0	0	0	0	0	1	0	1
Quinolinate synthetase	0	1	0	0	0	0	1	0	0	0	1
Recombinase A	0	0	1	1	0	0	2	0	0	0	2
Recombination protein recR	6	0	0	0	0	0	6	0	0	0	6
RecX family transcriptional regulator	0	0	0	1	0	1	0	0	0	0	1
Resolvase	0	0	1	0	0	0	1	0	0	0	1
Ribose 5-phosphate isomerase A	0	0	0	1	0	0	0	0	1	0	1
Ribose-phosphate pyrophosphokinase	0	1	0	0	0	0	1	0	0	0	1

Gene	Sample site					Host organism					Clones sequenced
	AH	HOT	LA	NB	SP	Non-marine	Marine	Eukaryote	Unknown	Virus	
Ribosomal large subunit pseudouridine synthase D	0	1	0	0	0	0	1	0	0	0	1
rrf2 transcriptional regulator	0	0	1	0	0	0	1	0	0	0	1
Sarcosine oxidase	0	0	0	1	0	1	0	0	0	0	1
SecD export membrane protein	0	0	1	0	0	0	0	0	1	0	1
Secreted protein	2	0	0	0	0	0	2	0	0	0	2
Segregation and condensation protein A	1	0	0	0	0	0	1	0	0	0	1
Shikimate kinase I	1	0	0	0	0	1	0	0	0	0	1
Short chain dehydrogenase/reductase	0	0	1	0	0	0	1	0	0	0	1
Single-strand binding protein	1	0	0	0	0	0	0	0	1	0	1
Sodium-glucose/galactose cotransporter	0	1	0	0	0	0	1	0	0	0	1
Sodium/solute symporter	3	0	1	0	0	0	4	0	0	0	4
SRP	0	2	0	0	0	0	0	2	0	0	2
Succinyl-CoA synthetase	0	1	0	0	0	1	0	0	0	0	1
Superfamily II DNA and RNA helicase	0	0	0	1	0	1	0	0	0	0	1
Tetratricopeptide TPR_2	0	1	0	0	0	0	0	0	1	0	1
Thymidylate synthase	0	1	0	0	1	1	0	0	0	1	2
Transcription elongation factor NusA	0	0	0	0	1	0	1	0	0	0	1
Transcription-repair coupling factor	0	0	0	1	0	0	0	0	1	0	1
Transcriptional regulator	1	0	0	0	1	0	2	0	0	0	2
Transcriptional regulator, AraC	2	0	0	0	0	2	0	0	0	0	2
Transcriptional regulator, XRE	13	0	3	1	2	0	19	0	0	0	19
Transketolase	1	0	0	0	0	1	0	0	0	0	1
Translocator protein, LysE family	1	0	0	0	0	0	1	0	0	0	1
Transposase	1	0	1	0	0	2	0	0	0	0	2
Triose-phosphate isomerase	0	0	0	0	1	0	1	0	0	0	1
tRNA (uracil-5-)-methyltransferase	0	0	0	0	1	0	1	0	0	0	1
Two component transcriptional regulator	0	1	0	0	0	0	1	0	0	0	1
Type IIA topoisomerase	1	0	0	0	0	0	0	0	1	0	1
Uncharacterized protein	1	1	0	0	0	1	1	0	0	0	2
Unknown function	2	0	0	0	0	2	0	0	0	0	2
Valyl-tRNA synthetase	0	0	0	0	1	0	1	0	0	0	1
Total	204	71	63	74	54	105	232	64	56	9	466

Table S4. The number of hits to each previously known antibiotic resistance gene in marine taxa. Genes were identifed using the ARDB or described as resistance proteins in GenBank.

	Antibiotic resistance gene											
Taxa	bcr	bl2_tem1	bl2c_pse1	bl2d_oxa2	cml_e1	matE	MFS	pbp2	rosb	vanre	vansd	vanxd
Dinoroseobacter	9	0	0	0	1	0	0	0	0	0	0	0
Jannaschia	3	0	0	0	0	0	0	0	0	0	0	0
Marinobacter	0	0	0	0	0	1	0	0	0	0	0	0
Oceanobacter	1	0	0	0	0	0	0	0	0	0	0	0
Oceanospirillium	1	0	0	0	0	0	0	0	0	0	0	0
Octadecabacter	20	0	0	0	0	0	0	0	0	0	0	0
Pelagibacter	0	0	0	0	0	0	0	1	0	0	0	0
Photobacterium	0	0	2	0	0	0	0	0	0	0	0	0
Prochlorococcus	0	0	0	0	0	0	0	0	1	0	1	1
Puniceispirillium	0	0	0	0	0	0	0	0	0	1	0	0
Roseovarius	1	0	0	0	0	0	0	0	0	0	0	0
Shewanella	0	0	0	1	0	0	0	0	0	0	0	0
uncultured marine group II euryarchaeote	0	0	0	0	0	0	1	0	0	0	0	0
Vibrio	0	7	0	0	0	0	0	0	0	0	0	0
Total	35	7	2	1	1	1	1	1	1	1	1	1

Table S5. The number of hits to protein functional types in marine taxa.

	Gene function													
Taxa	Ligase	DNA binding	Oxido-reductase	Unknown	Regulation	Transferase	Transport	Hydrolase	Isomerase	Lyase	DNA repair	Receptor	Chaperone	RNA binding
Alcanivorax	0	0	0	0	0	1 (5)	0	0	0	0	0	0	0	0
Alteromonas	0	0	1 (3)	0	0	0	0	0	0	0	0	0	0	0
Cellulophaga	0	0	0	1 (4)	0	0	0	0	0	0	0	0	0	0
Dinoroseobacter	0	0	0	0	1 (4)	0	0	0	0	0	0	0	0	0
Erythrobacter	1 (2)	0	0	2 (7)	0	0	1 (7)	1 (8)	0	1 (12)	0	0	0	0
Glaciecola	0	0	0	0	0	0	0	0	0	1 (12)	0	0	0	0
Kordia	0	0	0	0	0	0	0	0	0	1 (12)	0	0	0	0
Leeuwenhoekiella	0	0	2 (6)	0	0	1 (5)	0	0	0	0	0	0	0	0
Loktanella	0	3 (8)	4 (11)	0	0	0	0	0	0	0	0	0	0	0
Lyngbya	0	0	0	0	0	0	0	1 (8)	0	0	0	0	0	0
Maribacter	0	0	0	1 (4)	0	0	0	0	0	0	0	0	0	0
marine γ-proteobacterium	0	0	6 (17)	3 (11)	0	1 (5)	1 (7)	1 (8)	0	1 (12)	0	0	0	0
Marinobacter	0	0	0	0	1 (4)	0	0	0	0	0	0	0	0	0
Marinomonas	1 (2)	0	0	0	0	0	0	0	0	1 (12)	0	0	0	0
Maritimibacter	0	0	0	0	0	0	0	0	0	0	1 (50)	0	0	0
Methylophaga	0	0	0	0	0	0	1 (7)	0	0	0	0	0	0	0
Microscilla	0	0	0	0	0	0	1 (7)	0	0	0	0	0	0	0
Moritella	0	0	0	0	0	0	1 (7)	0	0	0	0	0	0	0
Oceanicola	3 (7)	0	0	2 (7)	0	0	0	0	1 (11)	0	0	0	0	0
Oceanospirillum	0	1 (3)	1 (3)	0	0	0	0	0	0	0	0	0	0	0
Octadecabacter	0	0	0	1 (4)	3 (13)	0	0	1 (8)	0	0	0	0	0	0
Odyssella	0	0	0	0	0	0	0	0	1 (11)	0	0	0	0	0
Owenweeksia	0	0	0	0	0	0	0	0	0	0	0	2 (100)	0	0
Pelagibaca	0	3 (8)	0	0	0	0	0	0	0	0	0	0	0	0
Pelagibacter	3 (7)	0	2	4 (14)	1 (4)	5 (25)	2 (13)	1 (8)	2 (22)	2 (25)	0	0	0	0
Phaeobacter	1 (2)	0	0	0	0	1 (5)	0	0	0	0	0	0	0	0
Polaribacter	1 (2)	6 (17)	1 (3)	1 (4)	0	0	4 (27)	1 (8)	0	0	0	0	0	0
Prochlorococcus	1 (2)	0	2 (6)	2 (7)	0	2 (10)	1 (7)	2 (17)	0	0	0	0	1 (100)	0
Pseudoalteromonas	0	0	3 (8)	0	0	0	0	1 (8)	0	0	0	0	0	0
Puniceispirillum	2 (5)	0	1 (3)	0	0	2 (10)	0	1 (8)	0	0	0	0	0	0
Robiginitalea	0	0	1 (3)	0	0	0	0	0	0	0	0	0	0	0
Roseibium	0	0	0	0	0	0	0	0	2 (22)	0	0	0	0	0
Roseobacter	1	6 (17)	4 (11)	5 (18)	3 (13)	2 (10)	0	0	0	0	0	0	0	0
Roseovarius	9 (22)	7 (19)	5 (14)	0	0	0	0	0	0	0	1 (50)	0	0	0
Ruegeria	17 (41)	9 (25)	0	1 (4)	2 (9)	0	1 (7)	0	0	0	0	0	0	0
Ruthia	0	0	0	0	0	0	0	0	1 (11)	0	0	0	0	0
Shewanella	0	0	0	3 (11)	0	0	0	0	0	0	0	0	0	0
Silicibacter	0	0	0	0	11 (48)	0	0	0	0	0	0	0	0	1 (100)
Stappia	0	0	0	0	0	1 (5)	0	0	2 (22)	0	0	0	0	0
Sulfitobacter	1 (2)	1 (2)	0	0	0	0	0	0	0	0	0	0	0	0
Synechococcus	0	0	3 (8)	0	1 (4)	0	0	1 (8)	0	1 (12)	0	0	0	0
uncultured marine group II euryarchaeote	0	0	0	1 (4)	0	3 (15)	0	1 (8)	0	0	0	0	0	0
Vibrio	0	0	0	1 (4)	0	1 (5)	0	0	0	0	0	0	0	0
Zunongwangia	0	0	0	0	0	0	2 (13)	0	0	0	0	0	0	0
Total	41	36	36	28	23	20	15	12	9	8	2	2	1	1

Numbers in parentheses represent the percentage of that functional type that was found in each taxa

Table S6. Top hits to the ARDB and GenBank for genes cloned from *E. coli* genomic DNA, which conferred resistance in E. cloni 10G cells (Lucigen, Middleton, WI)

		ARDB hit			GenBank hit		
Clone	Antibiotic	Accession number	Description	Amino acid ID	Accession number	Description	Amino acid ID
Ecoli_1F	Amp	YP_002806354	bl1_ec	1	NP_757087	fumarate reductase subunit D	0.87
Ecoli_1R	Amp	-	-	-	NP_710018	outer membrane lipoprotein	0.99
Ecoli_2F	Amp	-	-	-	ZP_06656271	taurine dioxygenase	0.5
Ecoli_3F	Amp	YP_002806354	bl1_ec	1	ACT97394	AmpC beta-lactamase	1
Ecoli_3R	Amp	BAE78154	bl1_ec	1	3IXG	AmpC beta-lactamase	0.97
Ecoli_4F	Amp	YP_002806354	bl1_ec	0.96	ACT97394	AmpC beta-lactamase	0.97
Ecoli_4R	Amp	BAE78154	bl1_ec	0.99	3IWQ	AmpC beta-lactamase	0.82
Ecoli_5F	Amp	-	-	-	YP_217252	periplasmic nitrate reductase	0.6
Ecoli_5R	Amp	-	-	-	ZP_02901751	periplasmic nitrate reductase	0.96
Ecoli_6F	Amp	YP_002806354	bl1_ec	0.99	ACT97394	AmpC beta-lactamase	1
Ecoli_6R	Amp	ABS73653	ykkC	0.53	2ACO	outer membrane lipoprotein Blc	0.88
Ecoli_7F	Amp	ZP_04534300	bl1_ec	0.99	ACT97394	AmpC beta-lactamase	1
Ecoli_7R	Amp	BAE78154	bl1_ec	1	ZP_03069379	outer membrane lipoprotein Blc	1
Ecoli_8F	Amp	YP_002806354	bl1_ec	0.99	ACT97394	AmpC beta-lactamase	0.95
Ecoli_8R	Amp	BAE78154	bl1_ec	1	ACT97420	AmpC beta-lactamase	0.96
Ecoli_9F	Amp	YP_002806354	-	0.98	ACT97394	AmpC beta-lactamase	0.85
Ecoli_9R	Amp	-	-	-	NP_710018	outer membrane lipoprotein Blc	0.99
Ecoli_10F	Amp	ZP_04534300	bl1_ec	0.99	ACT97394	AmpC beta-lactamase	1
Ecoli_10R	Amp	ABS73653	ykkC	0.53	ZP_06664871	SMR family small multidrug resistance protein	0.87
Ecoli_11F	Amp	ZP_04534300	bl1_ec	0.98	ACT97394	AmpC beta-lactamase	1
Ecoli_11R	Amp	BAE78154	bl1_ec	1	3IXG	AmpC beta-lactamase	0.9
Ecoli_12F	Amp	YP_002806354	bl1_ec	1	ACT97394	AmpC beta-lactamase	1
Ecoli_12R	Amp	-	-	-	NP_757081	hypothetical protein	0.97
Ecoli_13F	Amp	-	-	-	CBI55270	unnamed protein product	0.48
Ecoli_13R	Amp	BAE78154	bl1_ec	1	ACT97394	AmpC beta-lactamase	1
Ecoli_14F	Amp	YP_002806354	bl1_ec	1	ACT97394	AmpC beta-lactamase	1
Ecoli_14R	Amp	ABS73653	ykkC	0.53	CAA49570	sugEL	0.9
Ecoli_15F	Amp	YP_002806354	bl1_ec	1	ACT97394	AmpC beta-lactamase	1

		ARDB hit			GenBank hit		
Clone	Antibiotic	Accession number	Description	Amino acid ID	Accession number	Description	Amino acid ID
Ecoli_16F	Amp	ZP_04534300	bl1_ec	0.99	ACT97394	AmpC beta-lactamase	0.99
Ecoli_16R	Amp	ABS73653	ykkC	0.53	ZP_03061458	ammonium compound-resistance protein SugE	0.89
Ecoli_17F	Amp	ZP_04534300	bl1_ec	0.99	ACT97394	AmpC beta-lactamase	1
Ecoli_17R	Amp	-	-	-	CAA49570	sugEL	0.93
Ecoli_18F	Amp	YP_002806354	bl1_ec	1	ACT97394	AmpC beta-lactamase	1
Ecoli_18R	Amp	-	-	-	NP_414589	potassium:proton antiporter	0.73
Ecoli_19F	Amp	YP_002806354	bl1_ec	0.98	NP_757087	fumarate reductase subunit D	0.87
Ecoli_19R	Amp	BAE78154	bl1_ec	1	ZP_03069379	outer membrane lipoprotein Blc	1
Ecoli_20F	Amp	-	-	-	NP_757087	fumarate reductase subunit D	0.87
Ecoli_20R	Amp	BAE78154	bl1_ec	1	3IWI	AmpC beta-lactamase	0.88
Ecoli_21F	Amp	YP_002806354	bl1_ec	0.72	NP_757087	fumarate reductase subunit D	0.87
Ecoli_21R	Amp	BAE78154	bl1_ec	1	ACT97648	outer membrane lipoprotein Blc	1
Ecoli_22F	Amp	YP_002806354	bl1_ec	1	ACT97394	AmpC beta-lactamase	1
Ecoli_22R	Amp	ABS73653	ykkC	0.53	NP_757085	outer membrane lipoprotein Blc	0.9
Ecoli_23F	Amp	YP_002806354	bl1_ec	1	ACT97394	AmpC beta-lactamase	0.93
Ecoli_23R	Amp	ABS73653	ykkC	0.51	ZP_03069379	outer membrane lipoprotein Blc	0.98
Ecoli_24F	Amp	YP_002806354	bl1_ec	1	ACT97394	AmpC beta-lactamase	0.99
Ecoli_24R	Amp	ABS73653	ykkC	0.53	ZP_03069379	outer membrane lipoprotein Blc	1
Ecoli_25F	Amp	YP_002806354	bl1_ec	1	ACT97394	AmpC beta-lactamase	1
Ecoli_25R	Amp	ABS73653	ykkC	0.53	CAA49570	sugEL	0.9
Ecoli_26F	Amp	YP_002806354	bl1_ec	1	ACT97394	AmpC beta-lactamase	1
Ecoli_26R	Amp	ZP_04534300	bl1_ec	0.99	CAA49570	sugEL	0.95
Ecoli_27F	Amp	-	-	-	ACT97394	AmpC beta-lactamase	1
Ecoli_27R	Amp	ABS73653	ykkC	0.53	NP_710018	outer membrane lipoprotein Blc	0.87
Ecoli_28F	Amp	ZP_04004609	bl1_ec	0.99	ACT97398	AmpC beta-lactamase	1
Ecoli_28R	Amp	ABS73653	ykkC	0.54	CAA49570	sugEL	0.9
Ecoli_29F	Amp	YP_002806354	bl1_ec	1	NP_757087	fumarate reductase subunit D	0.87
Ecoli_29R	Amp	BAE78154	bl1_ec	1	1I5Q	AmpC beta-lactamase	0.93
Ecoli_30F	Amp	YP_002806354	bl1_ec	1	ACT97394	AmpC beta-lactamase	1

		ARDB hit			GenBank hit		
Clone	Antibiotic	Accession number	Description	Amino acid ID	Accession number	Description	Amino acid ID
Ecoli_30R	Amp	-	-	-	ZP_03069379	outer membrane lipoprotein Blc	1
Ecoli_31F	Amp	ZP_04534300	bl1_ec	0.99	ACT97394	AmpC beta-lactamase	1
Ecoli_31R	Amp	ABS73653	ykkC	0.58	CAA49570	sugEL	0.94
Ecoli_32F	Amp	ZP_04534300	bl1_ec	0.99	ACT97394	AmpC beta-lactamase	1
Ecoli_32R	Amp	-	-	-	ZP_03069379	outer membrane lipoprotein Blc	1
Ecoli_33F	Amp	YP_002806354	bl1_ec	1	ACT97394	AmpC beta-lactamase	0.92
Ecoli_33R	Amp	-	-	-	NP_757081	hypothetical protein	0.98
Ecoli_34F	Tet	-	-	-	AP_002151	DNA-binding transcriptional repressor	1
Ecoli_34R	Tet	-	-	-	NP_757081	hypothetical protein	0.61
Ecoli_35F	Tet	-	-	-	ZP_06352119	putative helicase, ATP-dependent	0.86
Ecoli_35R	Tet	-	-	-	ZP_07244647	O-acetylserine/cysteine export protein EamA	0.96
Ecoli_36F	Tet	-	-	-	ZP_06352119	putative helicase, ATP-dependent	0.79
Ecoli_36R	Tet	-	-	-	ZP_02793228	hypothetical protein	0.94
Ecoli_37F	Tet	-	-	-	NP_414982	predicted multidrug transporter subunits of ABC superfamily	0.93
Ecoli_37R	Tet	YP_001453760	macB	0.51	AAB40205	multidrug resistance-like ATP-binding protein	1
Ecoli_38F	Tet	-	-	-	YP_539470	hypothetical protein	0.97
Ecoli_38R	Tet	-	-	-	ZP_07134808	oxidoreductase, aldo/keto reductase family protein	1
Ecoli_39F	Tet	-	-	-	NP_291009	right origin-binding protein	0.98
Ecoli_39R	Tet	-	-	-	NP_313380	phosphoglycerate mutase	1
Ecoli_40F	Tet	-	-	-	NP_291009	right origin-binding protein	1
Ecoli_40R	Tet	-	-	-	YP_001746852	hypothetical protein	0.93
Ecoli_41F	Tet	-	-	-	ZP_03064302	multiple antibiotic resistance protein MarR	0.99
Ecoli_41R	Tet	-	-	-	ZP_07244647	O-acetylserine/cysteine export protein EamA	1
Ecoli_42F	Tet	-	-	-	ZP_07124080	redox-sensitive transcriptional activator SoxR	1
Ecoli_42R	Tet	-	-	-	ZP_07169733	cyclic diguanylate phosphodiesterase	0.85
Ecoli_43F	Tet	-	-	-	ABF03767	Multiple antibiotic resistance protein marA	1

Clone	Antibiotic	ARDB hit			GenBank hit		
		Accession number	Description	Amino acid ID	Accession number	Description	Amino acid ID
Ecoli_43R	Tet	-	-	-	ZP_07244647	O-acetylserine/cysteine export protein EamA	0.93
Ecoli_44F	Tet	-	-	-	AP_002151	DNA-binding transcriptional repressor	1
Ecoli_44R	Tet	-	-	-	ZP_07244647	O-acetylserine/cysteine export protein EamA	1
Ecoli_45F	Tet	-	-	-	ZP_07124080	redox-sensitive transcriptional activator SoxR	1
Ecoli_45R	Tet	-	-	-	NP_291010	hypothetical protein	1
Ecoli_46F	Tet	-	-	-	NP_291009	right origin-binding protein	1
Ecoli_46R	Tet	-	-	-	YP_001746852	hypothetical protein	0.93
Ecoli_47F	Tet	-	-	-	NP_290695	DNA-binding transcriptional regulator SoxS	1
Ecoli_47R	Tet	-	-	-	YP_002415202	putative signal transduction protein	1
Ecoli_48F	Tet	-	-	-	ZP_07150143	DEAD/DEAH box helicase	0.93
Ecoli_48R	Tet	-	-	-	ZP_07244647	O-acetylserine/cysteine export protein EamA	1
Ecoli_49F	Tet	-	-	-	BAJ11987	DNA-binding transcriptional regulator	1
Ecoli_49R	Tet	-	-	-	ZP_07140304	cyclic diguanylate phosphodiesterase	1
Ecoli_50F	Tet	-	-	-	AP_002151	DNA-binding transcriptional repressor	1
Ecoli_50R	Tet	-	-	-	ZP_07244647	O-acetylserine/cysteine export protein EamA	1
Ecoli_51F	Tet	-	-	-	NP_291009	right origin-binding protein	1
Ecoli_51R	Tet	-	-	-	NP_313380	phosphoglycerate mutase	1
Ecoli_52F	Tet	-	-	-	AP_002151	DNA-binding transcriptional repressor	1
Ecoli_52R	Tet	-	-	-	ZP_07244647	O-acetylserine/cysteine export protein EamA	1
Ecoli_53F	Tet	-	-	-	AP_002151	DNA-binding transcriptional repressor	1
Ecoli_53R	Tet	-	-	-	ACT97580	major facilitator family transporter	0.87
Ecoli_54F	Tet	-	-	-	NP_291009	right origin-binding protein	1
Ecoli_54R	Tet	-	-	-	YP_001746852	hypothetical protein	0.93

		ARDB hit			GenBank hit		
Clone	Antibiotic	Accession number	Description	Amino acid ID	Accession number	Description	Amino acid ID
Ecoli_55F	Tet	-	-	-	NP_290695	DNA-binding transcriptional regulator SoxS	1
Ecoli_55R	Tet	-	-	-	ZP_07169733	cyclic diguanylate phosphodiesterase	0.89
Ecoli_56F	Tet	CAA45230	bcr	0.98	ZP_07150141	Bcr/CflA family protein	1
Ecoli_56R	Tet	-	-	-	ZP_07120164	hypothetical protein	0.98
Ecoli_57F	Tet	-	-	-	1JGS	Multiple Antibiotic Resistance Repressor, MarR	0.92
Ecoli_57R	Tet	-	-	-	ZP_07244647	O-acetylserine/cysteine export protein EamA	0.84
Ecoli_58R	Tet	-	-	-	CAM34292	non-ribosomal peptide synthetase	0.95
Ecoli_59F	Tet	-	-	-	ZP_07137802	transporter, major facilitator family protein	0.84
Ecoli_59R	Tet	-	-	-	ZP_07124391	putative 2-deoxy-D-gluconate 3-dehydrogenase	1
Ecoli_60F	Tet	-	-	-	NP_291009	right origin-binding protein	1
Ecoli_60R	Tet	-	-	-	ZP_03051554	phosphoglycerate mutase family protein	1
Ecoli_61F	Tet	-	-	-	ZP_07186351	integral membrane protein, PqiA family	0.89
Ecoli_61R	Tet	AAC32027	carA	0.51	EEF06825	ABC transporter family protein	0.96
Ecoli_62F	Tet	-	-	-	ZP_06990264	multiple antibiotic resistance protein marA	1
Ecoli_62R	Tet	-	-	-	ZP_07164887	transporter, major facilitator family protein	0.96
Ecoli_63F	Tet	-	-	-	ZP_07447277	multidrug transporter membrane	0.9
Ecoli_63R	Tet	YP_001453760	macB	0.5	YP_002291750	multidrug transporter membrane	0.94
Ecoli_64F	Tet	-	-	-	NP_291009	right origin-binding protein	1
Ecoli_64R	Tet	-	-	-	ZP_07096244	transglycosylase SLT domain protein	0.99
Ecoli_65F	Tet	-	-	-	ZP_07152972	cyclic diguanylate phosphodiesterase	0.99
Ecoli_65R	Tet	-	-	-	ZP_07140304	cyclic diguanylate phosphodiesterase	0.95
Ecoli_66F	Nit	-	-	-	BAI55489	tyrosine-protein kinase	1
Ecoli_66R	Nit	-	-	-	ZP_07174446	amylovoran export outer membrane protein AmsH	0.89
Ecoli_67F	Nit	-	-	-	YP_002406175	carbonic anhydrase	0.92

Clone	Antibiotic	ARDB hit			GenBank hit		
		Accession number	Description	Amino acid ID	Accession number	Description	Amino acid ID
Ecoli_67R	Nit	-	-	-	ZP_07246326	polysaccharide deacetylase	1
Ecoli_68F	Nit	-	-	-	ADA75118	electron transfer flavoprotein subunit ygcR	0.74
Ecoli_68R	Nit	-	-	-	ZP_07164409	FAD binding domain protein	0.97
Ecoli_69F	Nit	-	-	-	YP_539654	sensor kinase DpiB	0.99
Ecoli_69R	Nit	-	-	-	YP_003220624	sensory histidine kinase CitA	0.99
Ecoli_70F	Nit	-	-	-	NP_417429	dITP/XTP pyrophosphatase	1
Ecoli_70R	Nit	-	-	-	AAA69117	hypothetical protein	1
Ecoli_71F	Nit	-	-	-	ZP_06934414	hypothetical protein	1
Ecoli_71R	Nit	-	-	-	ZP_07219958	lipid A export permease/ATP-binding protein MsbA	0.98
Ecoli_72F	Nit	-	-	-	YP_851762	rare lipoprotein A	0.99
Ecoli_72R	Nit	ZP_03837173	pbp2	0.81	ZP_07098061	penicillin-binding protein 2	0.98
Ecoli_73F	Nit	-	-	-	ZP_03034036	cystathionine beta-lyase	1
Ecoli_73R	Nit	-	-	-	ZP_07210309	AraC-type transcriptional regulator	1
Ecoli_74F	Nit	-	-	-	P76119	Putative transposase yncI	0.9
Ecoli_74R	Nit	-	-	-	NP_415977	conserved protein	1
Ecoli_75F	Nit	-	-	-	CBK86782	Predicted P-loop-containing kinase	1
Ecoli_75R	Nit	-	-	-	ZP_06655296	RNA polymerase sigma-54 factor	0.86
Ecoli_76F	Nit	-	-	-	ZP_07134251	HtpX	1
Ecoli_76R	Nit	-	-	-	ZP_07165283	peptidase	0.87
Ecoli_77F	Nit	-	-	-	ZP_07134251	HtpX	1
Ecoli_77R	Nit	-	-	-	ZP_07165283	peptidase	0.87
Ecoli_78F	Nit	-	-	-	ZP_06939494	bifunctional chorismate mutase/prephenate dehydrogenase	1
Ecoli_78R	Nit	-	-	-	ZP_07446679	phospho-2-dehydro-3-deoxyheptonate aldolase	1
Ecoli_79F	Nit	-	-	-	ZP_04873264	pyruvate formate-lyase 2 activating enzyme	0.95
Ecoli_79R	Nit	-	-	-	ZP_04873263	formate acetyltransferase 2	0.92
Ecoli_80F	Nit	-	-	-	ZP_07162560	phenylacetic acid degradation protein PaaY	1
Ecoli_80R	Nit	-	-	-	ZP_07246949	autotransporter beta-domain protein	0.9

		ARDB hit			GenBank hit		
Clone	Antibiotic	Accession number	Description	Amino acid ID	Accession number	Description	Amino acid ID
Ecoli_81F	Nit	-	-	-	ZP_07246946	conserved hypothetical protein	1
Ecoli_81R	Nit	-	-	-	ZP_03032646	phosphatidate cytidylyltransferase	0.87
Ecoli_82F	Nit	-	-	-	ZP_04871366	yjgB	0.92
Ecoli_82R	Nit	-	-	-	ZP_07123836	oxidoreductase, zinc-binding dehydrogenase family protein	0.8
Ecoli_83F	Nit	-	-	-	ZP_07144257	argininosuccinate lyase	0.93
Ecoli_83R	Nit	-	-	-	ZP_03031412	acetylglutamate kinase	0.92
Ecoli_84F	Nit	-	-	-	YP_851762	rare lipoprotein A	0.99
Ecoli_84R	Nit	ZP_03837173	pbp2	0.81	ZP_07098061	penicillin-binding protein 2	1
Ecoli_85F	Nit	-	-	-	YP_001457423	zinc-binding dehydrogenase family oxidoreductase	1
Ecoli_85R	Nit	-	-	-	YP_001725984	ribonuclease I	0.96
Ecoli_86F	Nit	-	-	-	YP_542608	D-arabinose 5-phosphate isomerase	0.95
Ecoli_86R	Nit	-	-	-	NP_289772	3-deoxy-D-manno-octulosonate 8-phosphate phosphatase	1
Ecoli_87F	Nit	-	-	-	NP_414902	taurine dioxygenase	0.94
Ecoli_87R	Nit	-	-	-	NP_757099	hypothetical protein	0.8
Ecoli_88F	Nit	-	-	-	ZP_07186568	oxidoreductase, zinc-binding dehydrogenase family protein	0.95
Ecoli_88R	Nit	-	-	-	YP_003499223	sugar ABC transporter permease	0.81
Ecoli_89F	Nit	-	-	-	ZP_07151899	thiamine biosynthesis/tRNA modification protein ThiI	1
Ecoli_89R	Nit	-	-	-	AAA82704	ThiJ	0.98
Ecoli_90F	Nit	-	-	-	ZP_06934414	hypothetical protein	1
Ecoli_90R	Nit	-	-	-	ZP_07219958	lipid A export permease/ATP-binding protein MsbA	0.99
Ecoli_91F	Nit	-	-	-	ZP_04873017	ATPase family	1
Ecoli_91R	Nit	-	-	-	ZP_04873019	RbsP	0.89
Ecoli_92F	Nit	-	-	-	ZP_07190304	LysM domain protein	1
Ecoli_92R	Nit	-	-	-	1JF9	Selenocysteine Lyase	0.99
Ecoli_93F	Nit	-	-	-	YP_001725984	ribonuclease I	1
Ecoli_93R	Nit	-	-	-	ZP_06936990	Citrate carrier	0.95
Ecoli_94F	Nit	-	-	-	NP_311509	SsrA-binding protein	1
Ecoli_94R	Nit	-	-	-	ZP_07177633	GTP-binding protein TypA/BipA	1
Ecoli_95F	Nit	-	-	-	XP_002275926	hypothetical protein	0.48

Table S7. Genes cloned from *Synechococcus* WH8102 genomic DNA that conferred resistance in *E. coli*. Descriptions are top hits to GenBank.

Clone	Accession	Description	Amino acid ID
Syn_1F	NP_896696	Hypothetical protein	1.00
Syn_1R	NP_896697	Arylsulfatase regulatory protein	0.84
Syn_2F	NP_896101	Phosphoribosylformylglycinamidine synthase II	0.89
Syn_2R	NP_896102	Amidophosphoribosyltransferase	1.00
Syn_3F	NP_898541	Allantoate amidohydrolase	0.87
Syn_3R	NP_898540	Hypothetical protein	0.84
Syn_4F	NP_896191	Hypothetical protein	0.86
Syn_4R	NP_896190	DNA gyrase subunit B	0.92
Syn_5F	NP_898357	Transcriptional regulator	1.00
Syn_5R	NP_898362	NADH dehydrogenase subunit I	0.98
Syn_6F	NP_898613	Hypothetical protein	0.90
Syn_6R	NP_898615	Threonine synthase	0.94