A chemical counterpunch: *Chromobacterium violaceum* ATCC31532 produces violacein in response to translation-inhibiting antibiotics

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ABSTRACT

Bacterially produced antibiotics play important roles in microbial interactions and competition. Antibiosis can induce resistance mechanisms in target organisms and may induce other countermeasures as well. Here, we show that hygromycin A from *Streptomyces* sp. 2AW induces *Chromobacterium violaceum* ATCC31532 to produce the purple antibiotic violacein. Sublethal doses of other antibiotics that similarly target the polypeptide elongation step of translation likewise induced violacein production, unlike antibiotics with different targets. *C. violaceum* biofilm formation and virulence against *Drosophila melanogaster* were also induced by translation-inhibiting antibiotics, and we identified an antibiotic-induced response (*air*) two-component regulatory system that is required for these responses. Genetic analyses indicated a connection between the Air system, quorum-dependent signaling, and the negative regulator VioS, leading us to propose a model for induction of violacein production. This work suggests a novel mechanism of interspecies interaction in which a bacterium produces an antibiotic in response to inhibition by another bacterium.

KEYWORDS

Sub-lethal concentration antibiotics, two-component regulatory system, *Streptomyces*, microbe-microbe interactions, translation inhibition.

INTRODUCTION

In many microbial communities, diverse species contribute to complex functions that they cannot perform in isolation (Newman & Banfield, 2002). Community members also compete with each other (Ghoul & Mitri, 2016), in part through production of antibiotics—secondary metabolites that inhibit other community members. The ability for microorganisms to detect and respond to antibiotics is likely to be important for survival and competitiveness in complex communities.

Actinobacteria are prolific producers of secondary metabolites that affect development and secondary metabolism in target bacteria (Abrudan et al., 2015; Traxler & Kolter, 2015). Different classes of secreted secondary metabolites, such as siderophores, biosurfactants, and antibiotics modulate bacterial interactions. In several pathogenic bacteria, sublethal concentrations of antibiotics induce a global transcriptional response, which might be a stress response but might also indicate that antibiotics act as signal molecules (Fajardo & Martínez, 2008; Goh et al., 2002). A current challenge is to understand how bacteria transduce antibiotic exposure to a targeted transcriptional response. Evidence suggests that antibiotics typically elicit physiological responses through their inhibitory activity rather than by other means such as structural recognition (Boehm et al., 2009; Dörr et al., 2016). Cellular damage generated by bactericidal antibiotics can induce transcription of stress-response genes, but it is less clear how bacteriostatic antibiotics elicit transcriptional changes. The concept of "competition sensing" suggests that some microbes may have evolved the ability to detect a hazard signal using established stress responses and respond by up-regulating production of toxins and antibiotics (Cornforth & Foster, 2013).

Chromobacterium species are Gram-negative β-proteobacteria well known for production of violacein, a purple pigment with antimicrobial and anti-parasitic activities (Durán et al., 2011; Gillis & Logan, 2005). We discovered an inter-species interaction that triggers violacein production, in which *Streptomyces* sp. 2AW (Stulberg et al., 2016) induces the production of violacein in *Chromobacterium violaceum* ATCC31532. The work presented here demonstrates that production of violacein in *C. violaceum* ATCC31532 is regulated by ribosomal perturbation generated by bacteriostatic translation-inhibiting antibiotics and modulated by a previously unknown two-component regulatory system.

RESULTS

Hygromycin A stimulates production of violacein. We found that *Streptomyces* sp. 2AW induces the production of violacein by *C. violaceum* ATCC31532 when the bacteria are grown in close proximity (Figure 1A). Contact is not necessary, suggesting that a diffusible molecule produced by *Streptomyces* sp. 2AW is responsible for triggering the response. Partially purified hygromycin A from *Streptomyces* sp. 2AW at sublethal levels induces violacein production, as does another hygromycin A producing bacterium, *Streptomyces hygroscopicus* NRRL 2388 (Figure 1B-C). Mutations that attenuate or block hygromycin A production (Δ*hyg17 or* Δ*hyg8*, respectively (Palaniappan et al., 2009)) eliminated violacein induction by *S. hygroscopicus* (Figure 1C). Taken together these results indicate that hygromycin A is likely responsible for the ability of *Streptomyces* sp. 2AW to induce violacein production in *C. violaceum* ATCC31532.

Violacein production is induced by inhibitors of polypeptide elongation. We considered the alternative possibilities that violacein induction could be a response to: (i) the hygromycin A molecule specifically, (ii) hygromycin A's inhibition of translation, or (iii) sublethal antibiosis more generally. To distinguish among these three alternatives, we evaluated diverse classes of antibiotics, including those that block various steps in translation and others that have different cellular targets (Figure supplement 1). Of the twenty antibiotics tested, seven induced violacein production in *C. violaceum* ATCC31532, including blasticidin S, spectinomycin, hygromycin B, apramycin, tetracycline, erythromycin, and chloramphenicol (Figure 2A, Figure supplement 1). These antibiotics share two characteristics with hygromycin A: they inhibit growth of *C. violaceum* ATCC31532, and they block polypeptide elongation during translation, although they belong to different chemical families and inhibit translation by binding to different sites in the ribosomal region responsible for polypeptide elongation. Other antibiotics, including several that block different steps in translation (e.g., kasugamycin, puromycin, and kanamycin), did not induce violacein (Figure supplement 1).

To explore whether induction of violacein production is a response to the inhibition of polypeptide elongation, we subjected *C. violaceum* ATCC31532 to cold shock. Sudden decreases in temperature can inhibit polypeptide elongation by generating secondary structures in mRNA (Horn, Hofweber, Kremer, & Kalbitzer, 2007), and previous studies indicated parallels in responses between translation-inhibiting antibiotics and cold-shock (VanBogelen & Neidhardt, 1990). We found that rapid transfer of exponential phase broth cultures from 28°C to 16°C induced violacein production in *C. violaceum* ATCC31532 (Figure 2A).

106 **The Air two-component regulatory system is required for the response to**
107 **translation inhibition.** To identify elements that participate in transducing the stimulus
108 of translation inhibition into the response of induced violacein production, we screened
109 random transposon mutants for loss of this ability. Because hygromycin A is not
110 commercially available, we screened responses to sublethal concentrations of
111 tetracycline, another strong inducer of violacein production (Figure 2A). Mutants were
112 selected for further characterization if the screen revealed at least two independent
113 mutants with transposon insertions in the same gene. To test the role of these genes in the
114 regulatory response to disruption of polypeptide elongation, we further evaluated each
115 mutant's violacein production when treated with spectinomycin, erythromycin, or cold
116 shock induction at 16°C. We identified five genes that, when disrupted, decrease
117 violacein production in response to each of these stimuli (Figure 2B). We also identified
118 mutants with altered responses to a subset of treatments (Figure supplement 2).
119
120 *Mutants with similar responses to inhibitors of polypeptide elongation.* Strains
121 with mutations in a three-gene cluster encoding a putative two-component regulatory
122 system do not respond to the three antibiotics tested or to cold shock (Figure 2B). We
123 designated this cluster the antibiotic-induced response (*air*) system, composed of genes
124 that encode proteins predicted to serve as a sensor histidine kinase (AirS), a response
125 regulator (AirR), and an oxidoreductase molybdopterin-binding domain (OxMoco)
126 (IPR036374) protein (AirM). The *airS* and *airM* genes appear to be organized in an
127 operon. In many two-component regulatory systems the sensor and response regulator
128 genes are co-transcribed. However, in this system *airMS* and *airR* are convergently

129 transcribed (Figure 3A-B). Notably, three other sensor histidine kinase genes in the
130 genome are similarly arranged near genes encoding an OxMoco domain. Similar systems
131 are also observed in other *Chromobacterium* and *Burkholderia* spp. (Figure supplement
132 3). To determine whether *airM* is essential for induction of violacein production, or if the
133 phenotype of the *airM* transposon mutant reflects a polar effect on *airS*, we deleted the
134 *airMS* operon and then complemented with *airS* or with *airMS*. Complementation with
135 *airMS* restored the response to tetracycline whereas supplying *airS* alone did not (Figure
136 3C), suggesting that *airM* provides an important functional role for the two-component
137 regulatory system.

138 In addition to the mutants with insertions disrupting the *air* system, we identified
139 strains containing transposon insertions in a phosphoenolpyruvate synthase gene (*ppsA*;
140 CLV04_1656) and a putative long chain fatty-acid CoA ligase gene (*fadD2*;
141 CLV04_3834) that likewise display attenuated violacein induction in response to
142 tetracycline or other conditions that inhibit polypeptide elongation (Figure 2B).

143

144 *Mutants with antibiotic-specific affects*. We also identified several mutants that
145 failed to induce violacein production but only for a specific subset of antibiotics (Figure
146 supplement 2A). Upon examination, these mutants, including the recently described *cdeR*
147 (CLV04_2412) transcriptional repressor of the *cdeAB-oprM* multidrug efflux pump
148 (Evans et al., 2018), had simply become more resistant to the respective antibiotic, and at
149 higher doses violacein induction was still evident (Figure supplement 4).

150 In addition, strains with mutations in a transcriptional regulator of the GntR
151 family (CLV04_3464) and in an ABC transporter (CLV04_3178), showed a more

pronounced induction of violacein in response to the presence of tetracycline, erythromycin, or spectinomycin. Strains with mutations in a putative enoyl-CoA hydratase (*fadB2*; CLV04_1011) likewise showed greater induction of violacein in the presence of the three antibiotics and to the cold shock induction at 16°C, but these mutants also had a higher basal level of violacein production even in the absence of these stimuli (Figure supplement 2B).

Additional responses to sub-lethal concentrations of antibiotics. Sublethal concentrations of tetracycline induced other phenotypes besides violacein production in *C. violaceum* ATCC31532. For example, *C. violaceum* ATCC31532 produced biofilms on glass in response to sublethal tetracycline concentrations in an *air*-dependent manner (Figure supplement 5). We also tested *C. violaceum* ATCC31532 in an oral infection assay with *Drosophila melanogaster,* which was of interest because of the strain's close phylogenetic association with *C. subtsugae*, an insect pathogen (Figure supplement 6). *C. violaceum* ATCC31532 killed *D. melanogaster* in the presence of tetracycline, but not in its absence, and this tetracycline-induced virulence required the *air* system (Figure 4).

Violacein expression is under control of the CviI/CviR quorum sensing system, and it is negatively regulated by *vioS*, an otherwise uncharacterized regulator (Devescovi et al., 2017; Swem et al., 2009). We tested biofilm formation and insecticidal activity in a *vioS* mutant, which produces violacein constitutively, and in a *vioS cviI* double mutant, which does not produce violacein. Both biofilm production and insecticidal activity are expressed in the *vioS* mutant and not in the *vioS cviI* double mutant, indicating that they

174 are regulated by the CviI/CviR quorum sensing system and repressed by VioS (Figure 4,
175 Figure supplement 5).
176
177 **Transcriptional changes in response to sublethal concentrations of**
178 **antibiotics.** To understand better the physiological response to sub-lethal concentrations
179 of antibiotics and the role of the *air* system in it, we used global RNA sequencing
180 analysis. *C. violaceum* ATCC31532 wild type and *airR* mutant were grown both with no
181 antibiotics and challenged separately with tetracycline and spectinomycin, and RNA
182 pools were subjected to RNA-sequencing analysis. Each antibiotic induced a distinct but
183 overlapping transcriptional response in the wild type (Figure supplement 7A). Using
184 Clusters of Orthologous Groups (COG) categories, we analyzed the 640 genes that
185 responded similarly to both antibiotics (Table supplement 1). Motility genes were
186 enriched among genes that were down-regulated in response to tetracycline and
187 spectinomycin (Figure supplement 7B). Genes that involved in translation, ribosomal
188 structure and biogenesis, and secondary metabolite biosynthesis, transport, and
189 catabolism were enriched among those up-regulated in response to both antibiotics
190 (Figure supplement 7B).
191 A comparison of the WT transcriptional response with the *airR* mutant response
192 identified 83 genes that were differentially regulated, suggesting they were directly or
193 indirectly modulated by the *air* system. These transcripts included the violacein gene
194 cluster and two other gene clusters encoding secondary metabolite biosynthetic pathways
195 (Table supplement 1). Other differentially expressed genes fell in several functional
196 categories with no distinct pattern.

Some genes that were described above as being identified in the transposon-mutant screen for altered violacein-induction responses were also found to be regulated in response to tetracycline and spectinomycin. For example, disruption of a gene that encodes a MarR family transcriptional regulator (CLV04_1869) resulted in loss of violacein induction specifically in response to tetracycline (Figure supplement 2), and this gene was upregulated in response to both spectinomycin and tetracycline (Table supplement 2). In contrast, disruption of *fadB2*, with a predicted function of an enoyl-CoA hydratase, resulted in a stronger up-regulation of violacein production but also higher background expression (Figure supplement 2), and this gene was down-regulated in response to both spectinomycin and tetracycline (Table supplement 2).

Mechanisms of violacein induction in response to inhibitors of polypeptide elongation. Two known regulators of violacein production, *vioS* and *cviR*, were differentially expressed in the presence of either tetracycline or spectinomycin (Table supplement 1). VioS represses violacein production (Devescovi et al., 2017; McClean et al., 1997; Swem et al., 2009), and CviR is the pheromone-sensing transcriptional activator of a quorum-dependent regulatory system that activates violacein production (Stauff & Bassler, 2011; Swem et al., 2009). The RNA-seq results for these genes of interest were corroborated and expanded using targeted q-RT-PCR (Figure 5A). Transcription of *vioS* is down-regulated by sub-lethal levels of tetracycline in the wild type and in the *airR* mutant, whereas *cviR* is up-regulated in the presence of tetracycline but only in wild-type and not in the *airR* mutant (Figure 5A). The apparent requirement of *airR* for *cviR* induction was confirmed by complementing the *airR* mutant with *airR in*

220 *trans* (Figure 5A). Thus, *airR* is required for the induction of *cviR* expression in response
221 to tetracycline.

222 Devescovi et al. recently showed that VioS is sufficient to inhibit expression of
223 the transcriptional promoter upstream of the violacein biosynthetic gene cluster, and
224 counteracts activation of this promoter by CviR/N-hexanoyl-L-homoserine lactone (C6-
225 HSL) in *E. coli* (Devescovi et al., 2017). Although the mechanism of *vioS*-mediated
226 inhibition of the *vioA* promoter is not known, the data suggest that VioS and CviR-AHL
227 compete for the *vioA* promoter, or that VioS binds the CviR-AHL complex, thereby
228 blocking its activity. These observations suggest that conditions favoring CviR levels
229 over VioS levels would favor violacein production. We therefore hypothesized that the
230 induction of violacein by sublethal concentration of antibiotics resulted from two
231 independent mechanisms, decreased *vioS* expression and increased *cviR* expression
232 mediated by the *air* system (Figure 5B).

233 We drew three predictions from this model (Figure 5B): (A) increasing the levels
234 of the violacein activator CviR would bypass repression by VioS; (B) constitutive
235 overexpression of *vioS* would block violacein induction by translation-inhibiting
236 antibiotics; and (C) the *air* system would mediate the violacein-induction response to
237 translation-inhibiting antibiotics even in the absence of *vioS*. We validated predictions A
238 and B, as follows. Overexpression of *cviR* induces violacein with no antibiotics added,
239 while overexpression of *cviI*, the quorum sensing autoinducer synthase, does not induce
240 violacein production (Figure 5C). This observation suggests that under these conditions,
241 the quorum-dependent response is limited by CviR levels but not by the autoinducer

levels. Also, constitutive overexpression of *vioS* blocks violacein induction in the presence of translation-inhibiting antibiotics (Figure 5D-E).

To test prediction C, we first generated the *vioS airMS* double mutant. Unexpectedly, this double mutant produced less violacein than the *vioS* single mutant without tetracycline (Figure 5F), and without impacting growth fitness (Figure 5G). The results suggested some activity of the Air system even in the absence of tetracycline. Consistent with this possibility, comparison between the wild type and *airR* mutant RNA-seq data in the absence of antibiotics showed that the *air* system affected regulation of at least 15 genes (Table supplement 3). Thus, the *air* system appears to have some activity even without a translation-inhibition signal. Importantly, the data in Figure 5F show that the *air* system modulates violacein production independently of VioS as we predicted above.

DISCUSSION

In this study, we examined an inter-bacterial interaction mediated by sublethal levels of antibiotics. We found that *C. violaceum* ATCC31532 produces violacein in response to sublethal levels of hygromycin A released from *Streptomyces* sp. 2AW, and in response to other structurally diverse bacteriostatic antibiotics that inhibit the elongation step of translation. Genetic analysis in *C. violaceum* ATCC31532 revealed a newly described two-component regulatory complex, the *air* system, that participates in the regulation of violacein production as well as virulence and biofilm production, all of which are regulated by the CviI/CviR quorum sensing system. Transcriptomic analysis of the wild type and *airR* mutant showed antibiotic-mediated down-regulation of *vioS* and

up-regulation of *cviR*, revealing a mechanism in which VioS repression of violacein is overcome. This new inter-bacterial competition mechanism differs from the previously identified competition strategy of acyl-homoserine lactone-dependent eavesdropping (Chandler, Heilmann, Mittler, & Greenberg, 2012), and suggest that *C. violaceum* ATCC31532 can sense and respond to other members of the microbial community in part by using transcriptional regulators that detect inhibitory effects of secondary metabolites produced by their neighbors.

The idea that antibiotics serve as signals in microbial communities (Fajardo & Martínez, 2008) is supported by our findings that sublethal levels of hygromycin A produced by *Streptomyces sp.* 2AW induce violacein production by *C. violaceum* ATCC31532 when the bacteria grow in close proximity. Further experiments are required to determine whether hygromycin A plays a signaling role in natural communities. As observed in human pathogenic bacteria, sub-lethal concentrations of antibiotics in *C. violaceum* ATCC31532 also influence social behavior such as pathogenesis, biofilm formation, quorum sensing, and secondary metabolite production (Andersson & Hughes, 2014). In those systems, it appears that antibiotics function as signals through cellular damage caused by the inducing antibiotic and detected by general stress response networks (Cornforth & Foster, 2013). *C. violaceum* ATCC31532 produces violacein only in response to inhibitors of the polypeptide elongation step of translation. Recently, Liu et al. reported a similar phenomenon in which translation-inhibitors induce sliding motility in *Bacillus subtilis* (Y. Liu, Kyle, & Straight, 2018). *C. violaceum* ATCC31532 also produces violacein in response to cold shock, providing another example of the long-known parallel between responses to translation-inhibiting antibiotics and cold-shock

(VanBogelen & Neidhardt, 1990). These findings suggest that the activity of the antibiotics, in this case inhibition of the polypeptide elongation step of translation, creates a cellular stress that initiates a signaling cascade.

The *air* system consists of a two-component regulatory system, a sensor (AirS) and a response regulator (AirR), and an oxidoreductase molybdopterin-binding protein (AirM), an unexpected element based on prototypical two-component regulators. In a broad database analysis, we found *airM*-like genes associated with two-component regulatory systems mainly in β-proteobacteria, but the *air* system is the first identified with an associated function. The *air* system is puzzling because a predicted membrane sensor, AirS, detects a cytoplasmic perturbation of ribosome activity. We hypothesize that the perturbation of actively translating ribosomes would create several cellular changes detected by the *air* system. We cannot infer the nature of the signal detected by AirS, since there is no annotation of known sensor domains in the AirS sequence. The predicted function of AirM, an oxidoreductase protein, suggests that the signal might involve oxidative change. This is compatible with the observed up-regulation of the NADH ubiquinone oxidoreductase complex, although expression of oxidative stress pathways did not appear to change (data not shown).

Another potential signal could be alteration in the lipid composition of the membrane. Our genetic screen identified two genes, a long chain fatty-acid CoA ligase (*fadB2*) and an enoyl-CoA hydratase (*fadD2*), that are homologs of genes that participate in fatty acid catabolism (Fujita, Matsuoka, & Hirooka, 2007). Enoyl-CoA hydratase is down-regulated by sublethal concentrations of tetracycline and spectinomycin, and the loss-of-function mutant produces violacein without exposure to antibiotics. The long

311 chain fatty-acid CoA might scavenge phospholipids associated with the membrane, and
312 the down-regulation of the enoyl-CoA hydratase mediated by antibiotics could change
313 the pool of saturated and unsaturated acyls-CoA, thereby altering the composition of the
314 new phospholipids added to the membrane.

315 The *air* system is needed for maximum violacein production without sublethal
316 concentration of tetracycline in a mutant lacking the negative regulator *vioS*, indicating
317 that the system is active without antibiotic stress and may have a housekeeping function.
318 This is supported by the differential gene expression of several genes mediated by the *air*
319 system without antibiotics. In addition, the presence of a third element in this two-
320 component system may indicate that the *air* system integrates multiple signals of
321 different cellular pathways, as has been shown in other two-component regulatory
322 systems with auxiliary elements (Buelow & Raivio, 2010). We hypothesized that *C.*
323 *violaceum* ATCC31532 co-opts a preexisting signaling network to integrate a response
324 generated by the ribosome perturbation. This could expand the model of "competition
325 sensing", whereby bacteria adapt not only to general stress response networks, but also
326 transcriptional modulators, such as two-component regulatory systems that respond to
327 any physiological response generated by antibiotics. The ribosome is one of the most
328 common targets for antibiotics (Wilson, 2014), and being able to sense inhibition of its
329 function rather than detecting each antibiotic independently might enable *C. violaceum*
330 ATCC31532 to have a single response to many competitors rather than separate
331 responses to individual species.

332 Our discovery of *C. violaceum's* antibiotic production in response to antibiosis
333 was facilitated by the fact that this "chemical counterpunch" (i.e., violacein) is purple.

334 With this fortuity in mind, a central question arising from the current study is whether
335 similar phenomena are widespread but less visible. It seems likely that microbial
336 communities possess less obvious but equally important emergent forms of chemical
337 competition. New approaches and technologies (Chodkowski & Shade, 2017; Harn,
338 Powers, Shank, & Jojic, 2015) have poised the field for a more comprehensive approach
339 to discovering chemically mediated responses underpin microbial interactions.
340

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348

349 **COMPETING INTEREST**

350 We declare that we have no significant competing financial, professional, or
351 personal interests that might have influenced the performance or presentation of the work
352 described in this manuscript.
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MATERIALS AND METHODS

Bacterial strains and culture conditions. *Streptomyces sp.* 2AW (Schloss et al., 2010), *Streptomyces hygroscopicus* NRRL2388 (Palaniappan et al., 2009), *Chromobacterium violaceum* ATCC31532 WT, *C. violaceum* ATCC31532 *vioS* (Cv017)(McClean et al., 1997), *C. violaceum* ATCC31532 *vioS cviI* (Cv026)(McClean et al., 1997) and *C. violaceum* ATCC12472 were cultured in LB (10 g L^{-1} tryptone; 5 g L^{-1} yeast extract; 10 g L^{-1} NaCl). *S. hygroscopicus* NRRL 2388 and the corresponding mutants were a gift from Kevin Reynolds at Portland State University. Antibiotics were obtained from Sigma (St. Louis, MO, USA) (ceftazidime, chloramphenicol, erythromycin, fusidic acid, hygromycin B, nalidixic acid, paromomycin, piperacillin, polymyxin B, puromycin, tetracycline, trimethoprim, vancomycin); from RPI (Mt Prospect IL, USA) (apramycin, blasticidin S, rifampicin, spectinomycin); from American Bio (Natick, MA, USA) (kanamycin); from MP Biomedicals (Santa Ana, CA, USA) (streptomycin); and from Enzo Life Sciences (Farmingdale, NY, USA) (kasugamycin).

Inter-species interaction assay. *Streptomyces sp.* 2AW and *S. hygroscopicus* NRRL2388 were spotted on LB plates and incubated for 3-5 d when 5-10 µL of *C. violaceum* ATCC31532 liquid culture grown for 16 h at 28°C were spotted on two different positions on the plates. Plates were incubated at 28°C until violacein production in *C. violaceum* ATCC31232 was observed.

379 **Violacein induction assay.** Fractions of a methanol extract from *Streptomyces sp.*
380 2AW grown on solid media (Stulberg et al., 2016) were directly tested against *C.*
381 *violaceum* ATCC31532. Each fraction was spotted on LB plates, and then 100 µL of *C.*
382 *violaceum* ATCC31532 liquid cultures grown to an OD_{600} ~ 4.0 at 28°C were spread
383 over the plates. Plates were incubated for two days at 28°C. The following antibiotics
384 were evaluated by directly spotting 10 µL of stock solution on LB plates: apramycin (100
385 µg mL^{-1}), blasticidin S (25 µg mL^{-1}), ceftazidime (20 µg mL^{-1}), chloramphenicol (34 µg
386 mL^{-1}), erythromycin (50 µg mL^{-1}), fusidic acid (10 µg mL^{-1}), hygromycin B (50 µg mL^{-1}),
387 kanamycin (50 µg mL^{-1}), kasugamycin (10 µg mL^{-1}), nalidixic acid (10 µg mL^{-1}),
388 paromomycin (10 µg mL^{-1}), piperacillin (50 µg mL^{-1}), polymyxin B (50 µg mL^{-1}),
389 puromycin (25 µg mL^{-1}), rifampicin (20 µg mL^{-1}), spectinomycin (50 µg mL^{-1}),
390 streptomycin (100 µg mL^{-1}), tetracycline (10 µg mL^{-1}), trimethoprim (5 µg mL^{-1}), and
391 vancomycin (10 µg mL^{-1}).
392
393 ***C. violaceum* ATCC31532 transposon mutagenesis and genetic screen for**
394 **mutants defective in violacein production**. pSAM_BT21 was generated from
395 pSAM_BT20 (Sivakumar et al., 2019) by interchanging the ampicillin-resistance gene
396 with a kanamycin resistance cassette amplified from pENTR/D-TOPO using primers
397 KanTopo_MluIFor/KanTopo_MluIRev (Table supplement 4), and inserted in the MluI
398 site. *C. violaceum* ATCC31532 and *E. coli* S17-1λpir with pSAM_BT21 with kanamycin
399 (50 µg mL^{-1}) were first grown individually for 16 h at 28°C and 37°C, respectively, with

agitation. Cells were washed and resuspended in fresh medium to an OD_{600} of 2.0. One volume of *E. coli* S17-1λpir with pSAM_BT21 was mixed with two volumes of *C. violaceum* ATCC31532. Cells were harvested (6,000 × *g*, 6 min), resuspended in 100 µL of fresh medium, and spotted on LB plates. The conjugation mixture was incubated at 28°C for 6 h, then scraped and resuspended in 2.5 mL of LB. 100 µL aliquots were plated on LB containing gentamicin (50 µg mL^{-1}), ampicillin (200 µg mL^{-1}) and tetracycline (0.125 µg mL^{-1}) for selection of *C. violaceum* ATCC31532 transconjugants defective in violacein production. Plates were incubated for two days at 28°C.

For each mutant, 1 mL of liquid culture grown for 16 h was harvested (6,000 × *g*, 6 min), and cells were resuspended in 400 µL of TE (10 µM Tris HCl pH 7.4; 1 µM EDTA pH 8.0). Samples were boiled for 6 min, centrifuged (6,000 × *g*, 6 min), and 2 µL of supernatant was used as a template for DNA amplification. Transposon locations were determined by arbitrarily primed PCR (Goodman et al., 2009), which consisted of a nested PCR using first-round primer GenPATseq1 and either AR1A or AR1B and second round primer GenPATseq2 and AR2 (Table supplement 4). PCR products of the second round were purified by gel extraction (QIAquick Gel Extraction Kit; QIAGEN) and then sequenced using primer GenPATseq2. PCR sequencing was performed by the DNA Analysis Facility on Science Hill at Yale University.

Assay for violacein production in response to antibiotics and cold shock. Violacein production by mutants identified as defective for violacein induction in response to tetracycline (0.125 µg mL^{-1}) was evaluated in the presence of spectinomycin

(2 μg mL^{-1}), erythromycin (2 μg mL^{-1}), and in liquid cultures at 16°C and 28°C. Dose-dependent response of violacein production to tetracycline (0.25 – 4 μg mL^{-1}), spectinomycin (4 – 64 μg mL^{-1}), and erythromycin (2 – 16 μg mL^{-1}) was evaluated in several mutants on LB plates. The response to these antibiotics and cold shock was evaluated visually based on the purple color of violacein.

Chromosomal deletion of the *airMS* operon. The *airMS* operon was deleted by allelic exchange and replaced with a chloramphenicol-resistance cassette. The *airMS* deletion cassette was constructed by a modified version of overlap extension (OE) PCR (Ho, Hunt, Horton, Pullen, & Pease, 1989). Fragments 1 kb upstream and 1 kb downstream of the *airMS* operon were amplified using primers MuCv0535/6_Afor and MuCv0535/6_Arev, or MuCv0535/6_Bfor and MuCv0535/6_Brev, respectively (Table supplement 4). The resulting products had overlapping homology and further amplification with primers MuCv0535/6_Afor and MuCv0535/6_Brev resulted in a single combined product of approximately 2 kb representing a fusion of the upstream and downstream sequences. This PCR product was cloned into pENTR/D-TOPO, generating pairMS_ENTR. Primers MuCv0535/6_Arev and MuCv0535/6_Bfor were designed to introduce a SphI site in the overlapping region to allow introduction of a selectable resistance gene. A chloramphenicol-resistance cassette was amplified from pACYC184 using primers pACYC184Cm_For/pACYC184Cm_Rev, which contain SphI sites in the 5' region, and cloned into pENTR/D-TOPO, generating pCm_ENTR. The chloramphenicol cassette was recovered from pCm_ENTR using SphI, and cloned

444 between the upstream and downstream region of the *airMS* operon. A *mob* element was
445 recovered from pmob_ENTR (Lozano et al., 2019) using AscI, and cloned into an AscI
446 site in the pENTR backbone, generating pairMS_Cm_mob_ENTR. Conjugation mixtures
447 of *C. violaceum* ATCC31532 and *E. coli* S17-1λpir carrying the
448 pairMS_Cm_mob_ENTR vector were prepared following the procedure for generating
449 transposon mutants. Double recombinant *C. violaceum* ATCC31532 transconjugants
450 were selected based on their ability to grow on chloramphenicol (34 μg mL^{-1}) and
451 screened for the inability to grow on kanamycin (50 μg mL^{-1}). The *airMS* deletion
452 mutant was confirmed by PCR using MuCv0535/6_Afor and MuCv0535/6_Brev, and by
453 evaluating violacein production in the presence of tetracycline. The same methodology
454 was used to delete *airMS* in the *C. violaceum* ATCC31532 *vioS* mutant.
455
456 **Complementation and overexpression assays.** The broad-host-range expression
457 and arabinose-inducible vector pJN105 was modified by introduction of the
458 chloramphenicol-resistance cassette recovered from pCm_ENTR into the SphI site,
459 generating pJN105Cm. *airS* was amplified using primers CV0536_For and
460 CV0536_Rev. *airMS* was amplified using primers CV0535/6_For and CV0536_Rev.
461 *airR* was amplified using primers CviR_For and CviR_Rev. *vioS* was amplified using
462 primers CV1055_For and CV1055_Rev. *cviI* was amplified using primers CviI_For and
463 CviI_Rev, and *cviR* was amplified using primers CviR_For and CviR_Rev. For all these
464 genes, a XbaI site in the 5' region was added to the forward primer, and a SacI site in the
465 5' region was added to the reverse primer, for a directional integration of each gene in
466 front of the *araBAD* promoter in pJN105Cm. Plasmids were transferred to the

467 corresponding host using the same conjugation protocol used for generating the
468 transposon mutants. Genes under control of the *araBAD* promoter were induced with
469 arabinose (0.05 – 1 mg mL^{-1}).

470

471 ***Drosophila melanogaster* oral infection assay.** *Canton-S* (*Cs*) flies (wolbachia
472 free) were used as standard wild-type lines. *Drosophila* stocks were maintained at 25°C
473 on cornmeal medium (8 g L^{-1} agar; 80 g L^{-1} polenta; 40 g L^{-1} yeast; 40 g L^{-1} sucrose;
474 53.6 ml L^{-1} moldex). *C. violaceum* strains were streaked from frozen glycerol stocks onto
475 LB plates and incubated at 28°C overnight. Isolated colonies were then inoculated into
476 LB medium and cultured at 28°C for 20 h. Cultures were centrifuged (4,000 *rpm*, 20 min,
477 4°C). The supernatant was decanted, the pellets were resuspended in the remaining
478 liquid, and the concentration of the cultures were adjusted to OD_{600} = 200
479 (approximately 100X concentration of the original overnight culture). For antibiotic
480 treatment, tetracycline (2.5 µg mL^{-1}) was added to concentrated cultures immediately
481 before feeding to flies.

482 Adult female flies were starved in empty vials for 2 h at 29°C. Paper filters were
483 placed on top of food medium and 150 µL of a 1:1 mixture of the concentrated pellet
484 (OD_{600} = 200) and 2.5% sucrose was added; for the sucrose-negative control, LB was
485 substituted for the bacterial pellet. The starved flies were transferred into the infection
486 vials and kept at 29°C. Survival was assessed at 2 h post-infection to account for any
487 infection-independent mortality. The number of dead flies per vial was recorded twice

488 per day for approximately five days after infection. Potential differences in survival
489 between treatments were analyzed for significance with Kaplan Meier Survival Analysis
490 using Graphpad Prism software.
491
492 **Phylogenetic analysis.** *Chromobacterium* spp. genomes were recovered from the
493 NCBI database, June 2017 (Table supplement 5). Phylogenomic reconstruction was
494 accomplished using the phylogenetic and molecular evolutionary (PhaME) analysis
495 software (Ahmed, Lo, Li, Davenport, & Chain, 2015). PhaME identified SNPs from the
496 core genome alignments, and the phylogenetic relationships were inferred by maximum
497 likelihood using FastTree.
498
499 **RNAseq analysis.** *C. violaceum* ATCC31532 WT and *airR* mutant were grown
500 without antibiotics, with tetracycline (0.125 µg mL^{-1}) or with spectinomycin (2 µg mL^{-1})
501 in 5 mL of LB at 28°C with agitation in duplicate. RNA samples were prepared from 250
502 µL of cells grown to an OD_{600} ~ 3.2. Cultures were mixed with 750 µL of TRIzol and
503 incubated at 65°C for 10 min. Samples were frozen at -80°C for 10 min and thawed at
504 room temperature for 15 min. Chloroform (200 µL) was added, the samples were shaken
505 and incubated at room temperature for 3 min and centrifuged (12,000 × *g*, 15 min, 4°C).
506 The aqueous phase was recovered, mixed with 500 µL of isopropanol, incubated at room
507 temperature for 10 min, and centrifuged (12,000 × *g*, 10 min, 4°C). The pellet was
508 washed with 1 mL of 75% ethanol, and air-dried for 10 minutes, resuspended with 50 µL
509 of RNase-free water, and finally incubated at 60°C for 15 min. DNA was removed from 5
510 µg of total RNA using the TURBO DNase kit (Invitrogen, Carlsbad, CA, USA).

511 RNA samples were treated with Ribo-Zero rRNA removal kit (Illumina, San
512 Diego, CA, USA), cDNA libraries were constructed with an average size between 150 bp
513 and 200 bp, and they were sequenced in Illumina HiSeq2500 paired-end 2x75 platform.
514 Library preparation and sequencing were performed by the Yale Center for Genome
515 Analysis. Low quality sequences were trimmed using Trimmomatic (Bolger, Lohse, &
516 Usadel, 2014). Mapped reads and estimated gene expression levels were calculated using
517 RSEM with a transcript list of ORFs recovered from *C. violaceum* ATCC31532 genome
518 (GenBank assembly accession GCA_002865685.1) (B. Li & Dewey, 2011). Differential
519 expression was assessed using limma (Ritchie et al., 2015) using "voom" function to
520 model the mean-variance relationship from read counts converted to log2-counts-per-
521 million (logCPM). Genes that were not appreciably expressed (transcripts per million
522 (TPM) < 5) were discarded, as recommended (Ritchie et al., 2015). Genes with an
523 adjusted P value < 0.01 were identified as being differentially expressed.
524 Genes were identified as having a generalized response to inhibition of
525 translational elongation if they were differentially expressed in WT in the presence of
526 tetracycline and in the presence of spectinomycin, relative to no antibiotic (Table
527 supplement 1). Genes for which the response to translational inhibition is mediated,
528 directly or indirectly, by the *air* system were identified if they were not differentially
529 expressed in response to tetracycline or streptomycin in the *airR* mutant background (but
530 were in WT), or if these genes are differentially expressed when compare WT against
531 *airR* in the presence of both antibiotics (Table supplement 6).
532

533 **Quantitative RT-PCR.** Quantitative reverse-transcriptase PCR was used to
534 validate the differential gene expression detected for *vioS* and *cviR* in the RNA-Seq
535 analysis. Primers used are listed in Table supplement 4. *C. violaceum* ATCC31532 WT
536 pJN105Cm, *airR* pJN105Cm, and *airR* pJN105Cm_airR were grown with
537 chloramphenicol (34 µg mL^{-1}), and with or without tetracycline (0.125 µg mL^{-1}) in
538 triplicate as reported above. Total RNA was recovered and DNAase treated in the same
539 manner as the RNA recovered for RNA-seq analysis. Two hundred nanograms of DNase-
540 treated RNA was reverse transcribed into cDNA using SuperScript™ III First-Strand
541 Synthesis System (Invitrogen). Quantitative PCR was carried out in a 10-µL volume
542 using PowerUp SYBR Green Master Mix (Applied biosystems) with 1 µL of cDNA and
543 200 nM PCR primers. These reactions were performed using the CFX96 Real-Time
544 System (Bio-Rad) using the following cycling parameters: 50°C for 10 min, 95°C for 5
545 min, followed by 40 cycles of 95°C for 10 sec and 60°C for 30 sec. Reverse
546 transcriptase-minus (RT-minus) template PCRs were included as negative controls to
547 confirm the absence of genomic DNA contamination. Tenfold serially diluted DNA
548 standard curves were included on every plate. Melting curve analysis were done to verify
549 the specificity of the PCR products. Expression levels under each condition were
550 normalized to the *dnaG* housekeeping gene, and the Pfaffl method was used to calculate
551 fold change in gene expression (Pfaffl, 2001). Differences between groups were tested for
552 statistical significance (Student's t-test) using GraphPadPrism 7 software.
553
554 **Characterization of *C. violaceum* ATCC31532 *vioS airR*.** *C. violaceum*
555 ATCC31532 *vioS* pJN105Cm, *vioS airMS* pJN105Cm, and *vioS airMS*

556 pJN105Cm_airMS were grown with chloramphenicol (34 µg mL^{-1}) and arabinose (0.2
557 mg mL^{-1}), with agitation for two days at 28°C. Samples were withdrawn periodically to
558 evaluate bacterial growth by serial dilution and plating in LB, and to quantify violacein
559 production. Violacein was quantified by a crude violacein extraction (Z. Liu et al., 2013).
560 One-mL aliquots of cultures of each strain were centrifuged (14,000 × *g*, 20 min), and
561 cells were resuspended in 1 mL of ethanol to dissolve violacein. Supernatants were
562 recovered after centrifugation (12,000 × *g*, 10 min), and transferred to 96-well plates.
563 Violacein concentration was determined spectrophotometrically at 575 nm in a Synergy
564 HT plate reader (BioTek).
565
566 **FIGURES AND TABLES**
567
568 **Figure 1.** Violacein production by *C. violaceum* ATCC31532 (Cv31532) is induced by
569 antibiotics produced by *Streptomyces* spp. (A) *C. violaceum* ATCC31532 growth with
570 *Streptomyces* sp. 2AW (2AW). (B) HPLC fractions of methanol extract from
571 *Streptomyces* sp. 2AW culture spotted on solid medium spread with *C. violaceum*
572 ATCC31532. (C) *C. violaceum* ATCC31532 growth with *S. hygroscopicus* NRRL 2388
573 (NRRL2388) wild type (WT) and two mutants with reduced (Δ*hyg17*) or abolished
574 (Δ*hyg8*) hygromycin A production.
575
576 **Figure 2.** Genes involved in induction of violacein production. (A) Violacein production
577 in response to several inducers in *C. violaceum* ATCC31532 wild type (WT). (B) *C.*
578 *violaceum* ATCC31532 mutants affected in violacein production in response to all

579 inducers tested. NA, No Antibiotic. Tet, Tetracycline. Spec, Spectinomycin. Ery,
580 Erythromycin.
581
582 **Figure 3.** Antibiotic-induced response system. Two-component regulatory system
583 identified by mutant analysis. (A) Gene organization; (B) Functional domains in
584 predicted proteins. SP, signal peptide; OxMoco, oxidoreductase molybdopterin-binding
585 domain superfamily (IPR036374); TM, transmembrane domain; NC, non-cytoplasmic
586 domain; HisK, signal transduction histidine kinase, dimerization/phosphoacceptor
587 domain superfamily (IPR036097); HATPase, histidine kinase/HSP90-like ATPase
588 superfamily (IPR036890); REC, CheY-like phosphoacceptor receiver domain
589 (IPR001789); BetR, beta-proteobacterial transcriptional regulator (IPR013975). (C)
590 Production of violacein in wild type (WT) carrying an empty vector and in *airMS* mutant
591 with empty vector or vector carrying *airS* or *airMS*. **** $P \leq 0.0001$; ns, not significant
592 ($P > 0.05$).
593
594 **Figure 4.** Insecticidal activity of *C. violaceum* ATCC31532 is enhanced by tetracycline.
595 Insecticidal activity of *C. violaceum* against *Drosophila melanogaster* with and without a
596 sublethal concentration of tetracycline. *C. violaceum* ATCC31332 (CvATCC31532) wild
597 type (WT), *airS*, *vioS* and *vioS cviI* mutants, and *C. violaceum* ATCC12472
598 (CvATCC12472) wild type (WT) were evaluated. Tet, Tetracycline.
599
600 **Figure 5.** A sublethal concentration of tetracycline bypasses *vioS* repression of violacein
601 production mediated by differential expression of *vioS* and *cviR*. (A) mRNA levels of

602 *vioS* and *cviR* from *C. violaceum* ATCC31532 wild type (WT) carrying an empty vector,
603 an *airR* mutant carrying an empty vector, and an *airR* mutant carrying a wild-type copy
604 of *airR* in the presence and absence of tetracycline. ** $P \leq 0.01$; **** $P \leq 0.001$; **** P
605 ≤ 0.0001; ns, no significant ($P > 0.05$). (B) Proposed model for violacein induction by
606 translation inhibitors. (C) Overexpression of *cviI* and *cviR* under arabinose regulation.
607 (D) Overexpression of *vioS* under arabinose regulation in the presence of a sublethal
608 concentration of tetracycline. (E) Complementation of *vioS* mutant with *vioS* gene under
609 regulation by arabinose, with and without tetracycline. (F) Violacein production by *vioS*
610 and *vioS airMS* mutant. (G) Growth of *vioS* mutant and *vioS airMS* mutant. Symbol
611 legend applies to both (F) and (G).
612
613 **Figure supplement 1.** Profile of *C. violaceum* ATCC31532 violacein production in
614 response to structurally diverse antibiotics. Antibiotics are classified by cellular target.
615
616 **Figure supplement 2.** Additional genes involved in induction of violacein production by
617 several inducers. (A) *C. violaceum* ATCC31532 mutants with a disrupted violacein
618 production in response to some of the inducers tested. (B) *C. violaceum* ATCC31532
619 mutants with increased violacein production in response to some of the inducers tested.
620 NA, No Antibiotic. Tet, Tetracycline. Spec, Spectinomycin. Ery, Erythromycin. *
621 Transposons in promotor.
622

623 **Figure supplement 3.** Other pair genes that encode oxidoreductase molybdopterin-
624 binding domain (OxMoco)(IPR036374) proteins next to a sensor histidine kinases in
625 *Chromobacterium* and *Burkholderia* spp genomes.
626
627 **Figure supplement 4.** Dose-dependent violacein production in two antibiotic-resistant
628 mutants. Survival and violacein production of *C. violaceum* ATCC31532 wild type (WT),
629 mutant in a SAM-dependent methyltransferase (CLV04_2730), and mutant in *cdeR*, a
630 transcriptional repressor of the *cdeAB-oprM* multidrug efflux pump system
631 (CLV04_2412) with (A) no antibiotic; (B) Erythromycin (μg mL^{-1}); (C) Tetracycline (μg
632 mL^{-1}); (D) Spectinomycin (μg.mL^{-1}).
633
634 **Figure supplement 5.** *C. violaceum* ATCC31532 biofilm formation on glass in response
635 to a sublethal concentration of tetracycline. Biofilm formation by *C. violaceum*
636 ATCC31532 wild type (WT), *vioA*, *airS*, *airR*, *vioS,* and *vioS cviI* mutants without
637 antibiotics, or in the presence of tetracycline (0.25 μg.mL^{-1}). Violacein mutant, *vioA*, was
638 used as a control for a biofilm visualization without violacein pigmentation. Arrow
639 indicates the location of the biofilm.
640
641 **Figure supplement 6.** Phylogenetic relatedness of several *Chromobacterium* spp.
642 Highlight in red *C. violaceum* ATCC31532.
643
644 **Figure supplement 7.** Transcriptome analysis of *C. violaceum* ATCC31532 in the
645 presence and absence of a sublethal concentration of translation inhibitors. The analysis

646 indicates change in expression from the baseline condition with no antibiotics. (A) Venn
647 diagram of gene differentially expressed by *C. violaceum* ATCC31532 wild type (WT) in
648 streptomycin or tetracycline. (B) COG classification of the differentially genes expressed
649 in streptomycin and tetracycline.
650
651 **Table supplement 1.** Genes expressed differentially in response to streptomycin and
652 tetracycline.
653
654 **Table supplement 2.** Differential gene expression values of the genes identified in the
655 genetic screen.
656
657 **Table supplement 3.** Genes differentially expressed between *C. violaceum* ATCC31532
658 WT and *airR* mutant in the absence of antibiotics.
659
660 **Table supplement 4.** Primers used in this study.
661
662 **Table supplement 5.** *Chromobacterium* spp. genomes used for phylogenetic
663 reconstruction.
664
665 **Table supplement 6.** Genes expressed differentially in response to streptomycin and
666 tetracycline that are modulated by *airR*.
667

668 **REFERENCES**

669 Abrudan, M. I., Smakman, F., Grimbergen, A. J., Westhoff, S., Miller, E. L., van Wezel,
670 G. P., & Rozen, D. E. (2015). Socially mediated induction and suppression of
671 antibiosis during bacterial coexistence. *Proceedings of the National Academy of*
672 *Sciences of the United States of America*, *112*(35), 11054–11059.
673 http://doi.org/10.1073/pnas.1504076112
674 Ahmed, S. A., Lo, C.-C., Li, P.-E., Davenport, K. W., & Chain, P. S. G. (2015). From
675 raw reads to trees: Whole genome SNP phylogenetics across the tree of life. *bioRxiv*,
676 032250. http://doi.org/10.1101/032250
677 Andersson, D. I., & Hughes, D. (2014). Microbiological effects of sublethal levels of
678 antibiotics. *Nature Reviews. Microbiology*, *12*(7), 465–478.
679 http://doi.org/10.1038/nrmicro3270
680 Boehm, A., Steiner, S., Zaehringer, F., Casanova, A., Hamburger, F., Ritz, D., et al.
681 (2009). Second messenger signalling governs *Escherichia coli* biofilm induction
682 upon ribosomal stress. *Molecular Microbiology*, *72*(6), 1500–1516.
683 http://doi.org/10.1111/j.1365-2958.2009.06739.x
684 Bolger, A. M., Lohse, M., & Usadel, B. (2014). Trimmomatic: a flexible trimmer for
685 Illumina sequence data. *Bioinformatics*, *30*(15), 2114–2120.
686 http://doi.org/10.1093/bioinformatics/btu170
687 Buelow, D. R., & Raivio, T. L. (2010). Three (and more) component regulatory systems -
688 auxiliary regulators of bacterial histidine kinases. *Molecular Microbiology*, *75*(3),
689 547–566. http://doi.org/10.1111/j.1365-2958.2009.06982.x
690 Chandler, J. R., Heilmann, S., Mittler, J. E., & Greenberg, E. P. (2012). Acyl-homoserine
691 lactone-dependent eavesdropping promotes competition in a laboratory co-culture
692 model. *The ISME Journal*, *6*(12), 2219–2228. http://doi.org/10.1038/ismej.2012.69
693 Chodkowski, J. L., & Shade, A. (2017). A synthetic community system for probing
694 microbial interactions driven by exometabolites. *mSystems*, *2*(6), 375.
695 http://doi.org/10.1128/mSystems.00129-17
696 Cornforth, D. M., & Foster, K. R. (2013). Competition sensing: the social side of
697 bacterial stress responses. *Nature Reviews. Microbiology*, *11*(4), 285–293.
698 http://doi.org/10.1038/nrmicro2977

699 Devescovi, G., Kojic, M., Covaceuszach, S., Cámara, M., Williams, P., Bertani, I., et al.
700 (2017). Negative regulation of violacein biosynthesis in *Chromobacterium*
701 *violaceum*. *Frontiers in Microbiology*, *8*(12), 349.
702 http://doi.org/10.3389/fmicb.2017.00349
703 Dörr, T., Alvarez, L., Delgado, F., Davis, B. M., Cava, F., & Waldor, M. K. (2016). A
704 cell wall damage response mediated by a sensor kinase/response regulator pair
705 enables beta-lactam tolerance. *Proceedings of the National Academy of Sciences of*
706 *the United States of America*, *113*(2), 404–409.
707 http://doi.org/10.1073/pnas.1520333113
708 Durán, M., Ponezi, A. N., Faljoni-Alario, A., Teixeira, M. F. S., Justo, G. Z., & Durán, N.
709 (2011). Potential applications of violacein: a microbial pigment. *Medicinal Chemistry*
710 *Research*, *21*(7), 1524–1532. http://doi.org/10.1007/s00044-011-9654-9
711 Evans, K. C., Benomar, S., Camuy-Vélez, L. A., Nasseri, E. B., Wang, X.,
712 Neuenswander, B., & Chandler, J. R. (2018). Quorum-sensing control of antibiotic
713 resistance stabilizes cooperation in *Chromobacterium violaceum*. *The ISME Journal*,
714 *12*(5), 1263–1272. http://doi.org/10.1038/s41396-018-0047-7
715 Fajardo, A., & Martínez, J. L. (2008). Antibiotics as signals that trigger specific bacterial
716 responses. *Current Opinion in Microbiology*, *11*(2), 161–167.
717 http://doi.org/10.1016/j.mib.2008.02.006
718 Fujita, Y., Matsuoka, H., & Hirooka, K. (2007). Regulation of fatty acid metabolism in
719 bacteria. *Molecular Microbiology*, *66*(4), 829–839. http://doi.org/10.1111/j.1365-
720 2958.2007.05947.x
721 Ghoul, M., & Mitri, S. (2016). The ecology and evolution of microbial competition.
722 *Trends in Microbiology*, *24*(10), 833–845. http://doi.org/10.1016/j.tim.2016.06.011
723 Gillis, M., & Logan, N. A. (2005). Chromobacterium Bergonzini 1881, 153 [AL]. In D. J.
724 Brenner, N. R. Krieg, J. T. Staley, & G. M. Garrity (Eds.), *Bergeys Manual of*
725 *Systematic Bacteriology* (2nd ed., Vol. 2, pp. 824–827). New York: Springer.
726 Goh, E.-B., Yim, G., Tsui, W., McClure, J., Surette, M. G., & Davies, J. (2002).
727 Transcriptional modulation of bacterial gene expression by subinhibitory
728 concentrations of antibiotics. *Proceedings of the National Academy of Sciences of the*
729 *United States of America*, *99*(26), 17025–17030.

http://doi.org/10.1073/pnas.252607699

Goodman, A. L., McNulty, N. P., Zhao, Y., Leip, D., Mitra, R. D., Lozupone, C. A., et al. (2009). Identifying genetic determinants needed to establish a human gut symbiont in its habitat. *Cell Host & Microbe*, *6*(3), 279–289. http://doi.org/10.1016/j.chom.2009.08.003

Harn, Y.-C., Powers, M. J., Shank, E. A., & Jojic, V. (2015). Deconvolving molecular signatures of interactions between microbial colonies. *Bioinformatics*, *31*(12), i142–50. http://doi.org/10.1093/bioinformatics/btv251

Ho, S. N., Hunt, H. D., Horton, R. M., Pullen, J. K., & Pease, L. R. (1989). Site-directed mutagenesis by overlap extension using the polymerase chain reaction. *Gene*, *77*(1), 51–59.

Horn, G., Hofweber, R., Kremer, W., & Kalbitzer, H. R. (2007). Structure and function of bacterial cold shock proteins. *Cell Mol Life Sci*, *64*(12), 1457–1470. http://doi.org/10.1007/s00018-007-6388-4

Li, B., & Dewey, C. N. (2011). RSEM: accurate transcript quantification from RNA-Seq data with or without a reference genome. *BMC Bioinformatics*, *12*(1), 323. http://doi.org/10.1186/1471-2105-12-323

Liu, Y., Kyle, S., & Straight, P. D. (2018). Antibiotic stimulation of a *Bacillus subtilis* migratory response. *mSphere*, *3*(1), e00586–17. http://doi.org/10.1128/mSphere.00586-17

Liu, Z., Wang, W., Zhu, Y., Gong, Q., Yu, W., & Lu, X. (2013). Antibiotics at subinhibitory concentrations improve the quorum sensing behavior of *Chromobacterium violaceum*. *FEMS Microbiology Letters*, *341*(1), 37–44. http://doi.org/10.1111/1574-6968.12086

Lozano, G. L., Park, H. B., Bravo, J. I., Armstrong, E. A., Denu, J. M., Stabb, E. V., et al. (2019). Bacterial analogs of plant tetrahydropyridine alkaloids mediate microbial interactions in a rhizosphere model system. *Applied and Environmental Microbiology*, AEM.03058–18. http://doi.org/10.1128/AEM.03058-18

McClean, K. H., Winson, M. K., Fish, L., Taylor, A., Chhabra, S. R., Camara, M., et al. (1997). Quorum sensing and *Chromobacterium violaceum*: exploitation of violacein production and inhibition for the detection of N-acylhomoserine lactones.

Microbiology, *143 (Pt 12)*(12), 3703–3711. http://doi.org/10.1099/00221287-143-12-3703

Newman, D. K., & Banfield, J. F. (2002). Geomicrobiology: how molecular-scale interactions underpin biogeochemical systems. *Science*, *296*(5570), 1071–1077. http://doi.org/10.1126/science.1010716

Palaniappan, N., Dhote, V., Ayers, S., Starosta, A. L., Wilson, D. N., & Reynolds, K. A. (2009). Biosynthesis of the aminocyclitol subunit of hygromycin A in *Streptomyces hygroscopicus* NRRL 2388. *Chemistry & Biology*, *16*(11), 1180–1189. http://doi.org/10.1016/j.chembiol.2009.10.013

Pfaffl, M. W. (2001). A new mathematical model for relative quantification in real-time RT-PCR. *Nucleic Acids Research*, *29*(9), e45.

Ritchie, M. E., Phipson, B., Wu, D., Hu, Y., Law, C. W., Shi, W., & Smyth, G. K. (2015). limma powers differential expression analyses for RNA-sequencing and microarray studies. *Nucleic Acids Research*, *43*(7), e47–e47. http://doi.org/10.1093/nar/gkv007

Schloss, P. D., Allen, H. K., Klimowicz, A. K., Mlot, C., Gross, J. A., Savengsuksa, S., et al. (2010). Psychrotrophic strain of *Janthinobacterium lividum* from a cold Alaskan soil produces prodigiosin. *DNA and Cell Biology*, *29*(9), 533–541. http://doi.org/10.1089/dna.2010.1020

Sivakumar, R., Ranjani, J., Vishnu, U. S., Jayashree, S., Lozano, G. L., Miles, J., et al. (2019). Evaluation of INSeq to identify genes essential for *Pseudomonas aeruginosa* PGPR2 corn root colonization. *G3 (Bethesda, Md.)*, *9*(3), 651–661. http://doi.org/10.1534/g3.118.200928

Stauff, D. L., & Bassler, B. L. (2011). Quorum sensing in *Chromobacterium violaceum*: DNA recognition and gene regulation by the CviR receptor. *Journal of Bacteriology*, *193*(15), 3871–3878. http://doi.org/10.1128/JB.05125-11

Stulberg, E. R., Lozano, G. L., Morin, J. B., Park, H., Baraban, E. G., Mlot, C., et al. (2016). Genomic and secondary metabolite analyses of *Streptomyces* sp. 2aw provide insight into the evolution of the cycloheximide pathway. *Frontiers in Microbiology*, *7*(R56), 573. http://doi.org/10.3389/fmicb.2016.00573

Swem, L. R., Swem, D. L., O'Loughlin, C. T., Gatmaitan, R., Zhao, B., Ulrich, S. M., &

792 Bassler, B. L. (2009). A quorum-sensing antagonist targets both membrane-bound
793 and cytoplasmic receptors and controls bacterial pathogenicity. *Molecular Cell*,
794 *35*(2), 143–153. http://doi.org/10.1016/j.molcel.2009.05.029
795 Traxler, M. F., & Kolter, R. (2015). Natural products in soil microbe interactions and
796 evolution. *Natural Product Reports*, *32*(7), 956–970.
797 http://doi.org/10.1039/c5np00013k
798 VanBogelen, R. A., & Neidhardt, F. C. (1990). Ribosomes as sensors of heat and cold
799 shock in *Escherichia coli*. *Proceedings of the National Academy of Sciences of the*
800 *United States of America*, *87*(15), 5589–5593.
801 Wilson, D. N. (2014). Ribosome-targeting antibiotics and mechanisms of bacterial
802 resistance. *Nature Reviews. Microbiology*, *12*(1), 35–48.
803 http://doi.org/10.1038/nrmicro3155
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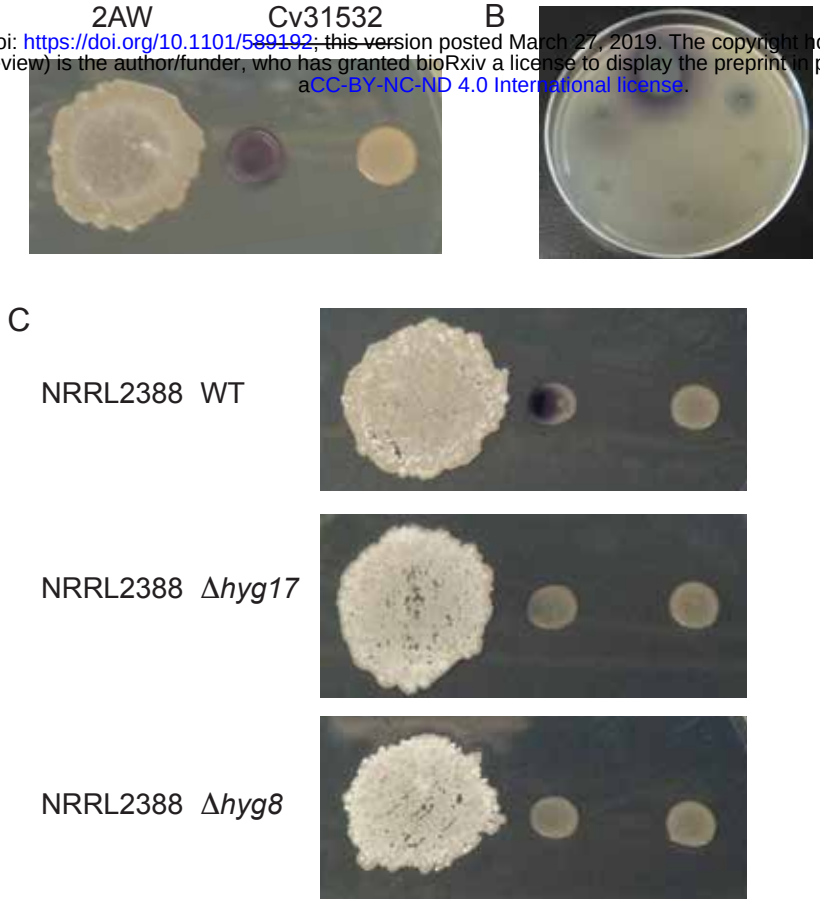


Figure 1. Violacein production by *C. violaceum* ATCC31532 (Cv31532) is induced by antibiotics produced by *Streptomyces spp.* (A) *C. violaceum* ATCC31532 growth with *Streptomyces sp.* 2AW (2AW). (B) HPLC fractions of methanol extract from *Streptomyces sp.* 2AW culture spotted on solid medium spread with *C. violaceum* ATCC31532. (C) *C. violaceum* ATCC31532 growth with *S. hygroscopicus* NRRL 2388 (NRRL2388) wild type (WT) and two mutants with reduced (*Δhyg17*) or abolished (*Δhyg8*) hygromycin A production.

A

	NA	Tet	Spec	Ery	28°C	16°C
WT						

B

Mutated genes

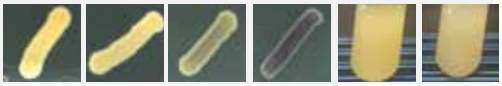
Gene ID	Predicted Function	Class	Name	NA	Tet	Spec	Ery	28°C	16°C
CLV04_2302	Oxidoreductase molybdopterin binding domain protein	Signaling	*airM*						
CLV04_2301	Sensor histidine kinase	Signaling	*airS*						
CLV04_2300	Response regulator	Signaling	*airR*						
CLV04_3834	Long chain fatty-acid CoA ligase	Others	*fadD2*						
CLV04_1656	Phosphoenolpyruvate synthase	Metabolism	*ppsA*						

Figure 2. Genes involved in induction of violacein production. (A) Violacein production in response to several inducers in *C. violaceum* ATCC31532 wild type (WT). (B) *C. violaceum* ATCC31532 mutants affected in violacein production in response to all inducers tested. NA, No Antibiotic. Tet, Tetracycline. Spec, Spectinomycin. Ery, Erythromycin.

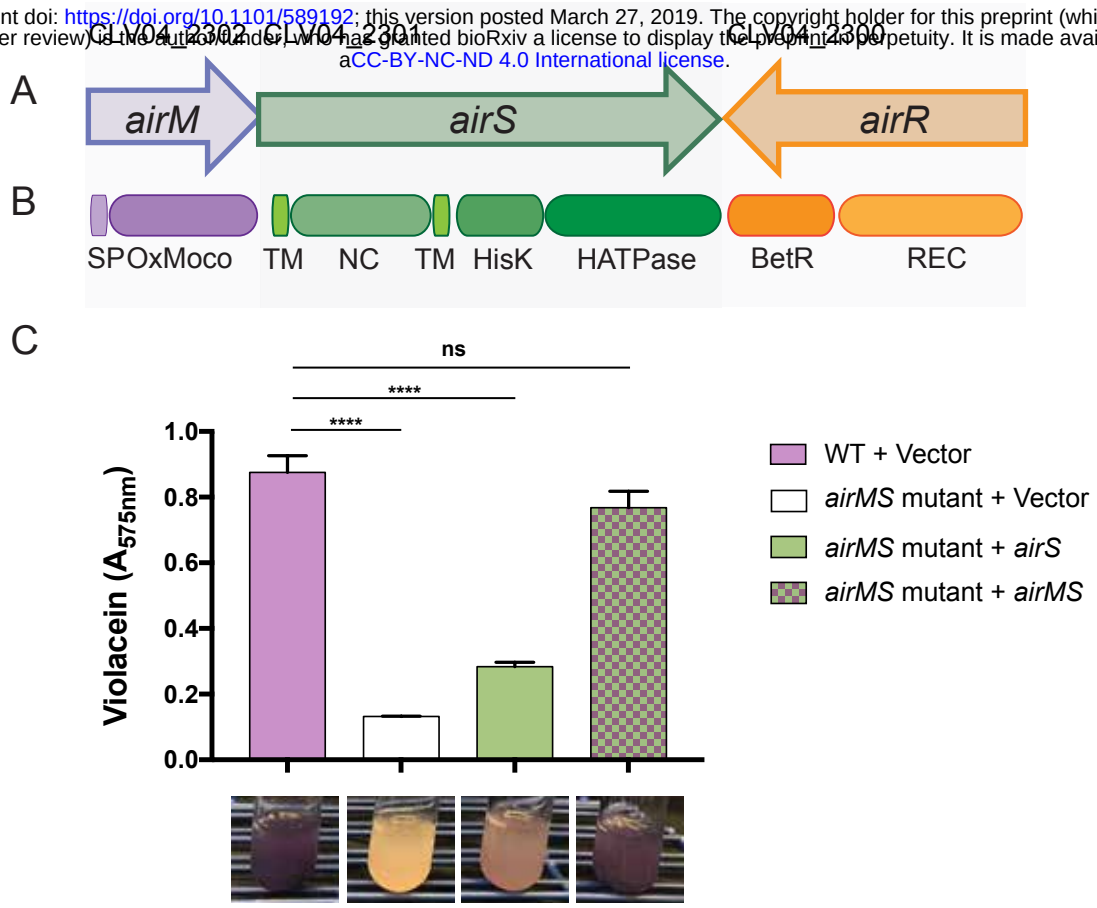


Figure 3. Antibiotic-induced response system. Two-component regulatory system identified by mutant analysis. (A) Gene organization; (B) Functional domains in predicted proteins. SP, signal peptide; OxMoco, oxidoreductase molybdopterin-binding domain superfamily (IPR036374); TM, transmembrane domain; NC, non-cytoplasmic domain; HisK, signal transduction histidine kinase, dimerization/phosphoacceptor domain superfamily (IPR036097); HATPase, histidine kinase/HSP90-like ATPase superfamily (IPR036890); REC, CheY-like phosphoacceptor receiver domain (IPR001789); BetR, beta-proteobacterial transcriptional regulator (IPR013975). (C) Production of violacein in wild type (WT) carrying an empty vector and in *airMS* mutant with empty vector or vector carrying *airS* or *airMS*. **** $P \leq 0.0001$; ns, no significant ($P > 0.05$).

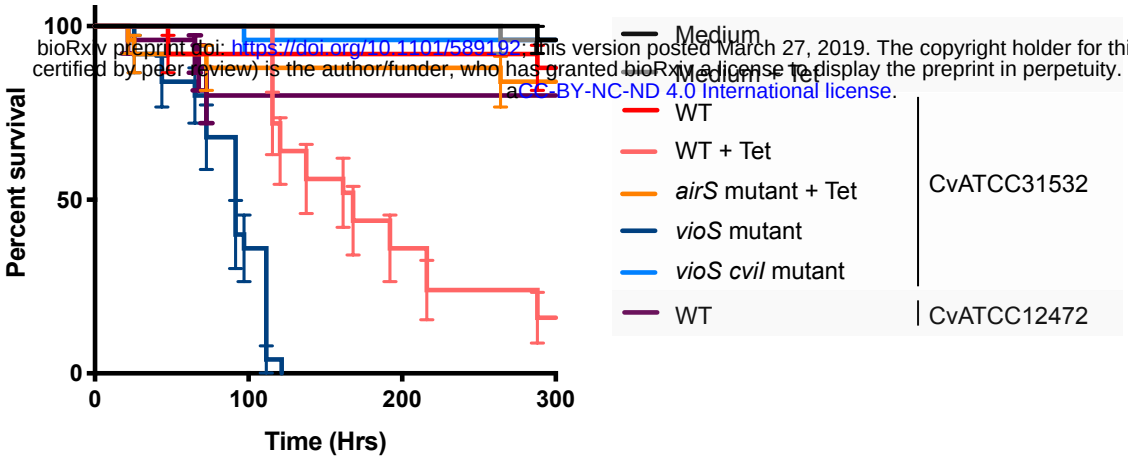


Figure 4. Insecticidal activity of *C. violaceum* ATCC31532 is enhanced by tetracycline. Insecticidal activity of *C. violaceum* against *Drosophila melanogaster* in response to a sublethal concentration of tetracycline. *C. violaceum* ATCC31332 (CvATCC31532) wild type (WT), *airS*, *vioS*, *vioS cviI* mutants, and *C. violaceum* ATCC12472 (CvATCC12472) wild type (WT) were evaluated. Tet, Tetracycline.

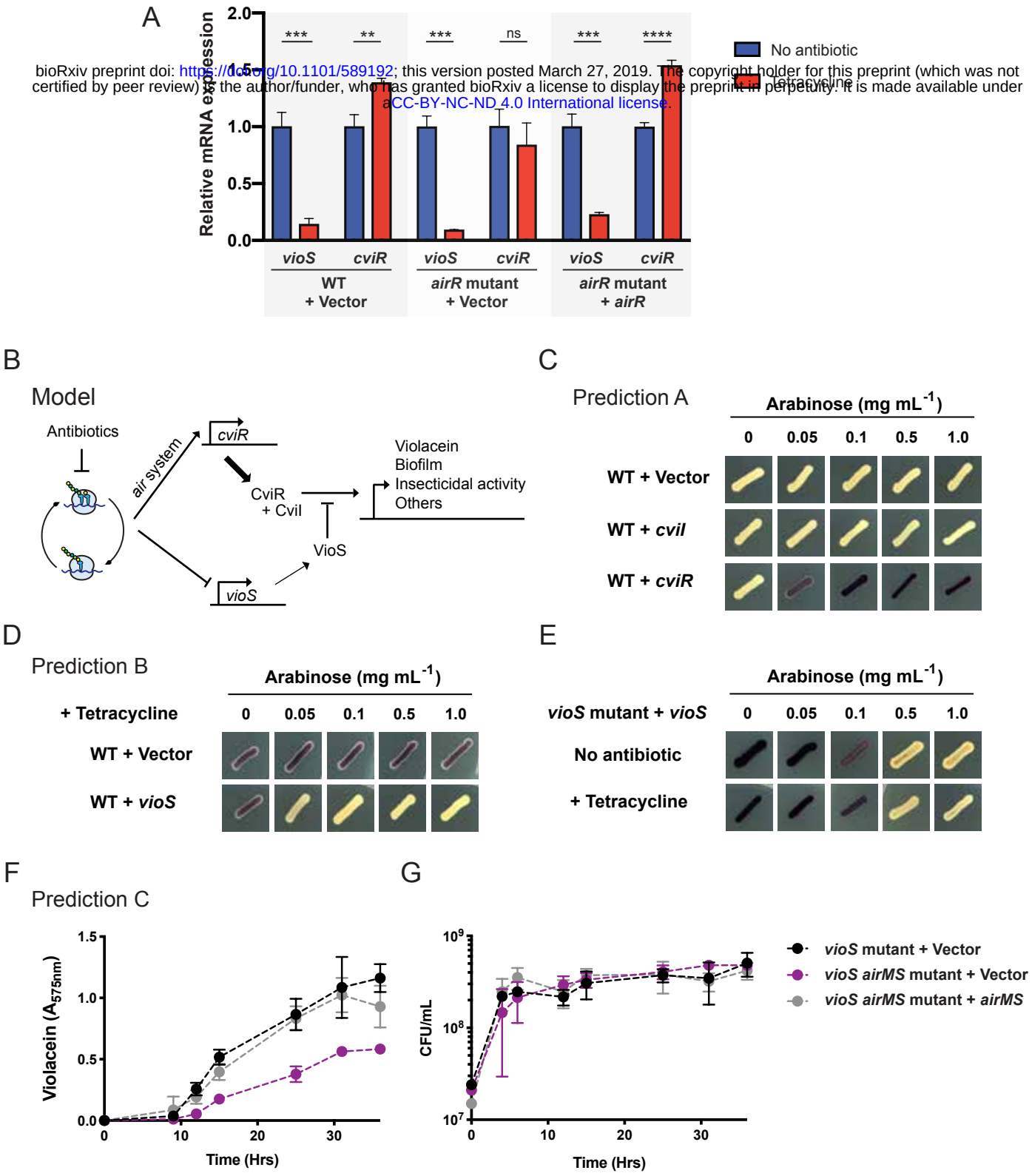
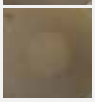
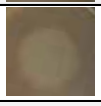
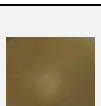
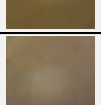
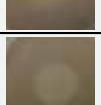
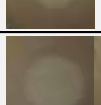
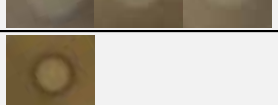
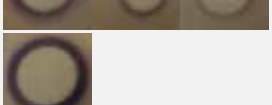
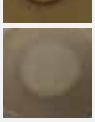


Figure 5. A sublethal concentration of tetracycline bypasses *vioS* repression of violacein production mediated by differential expression of *vioS* and *cviR*. (A) mRNA levels of *vioS* and *cviR* from *C. violaceum* ATCC31532 wild type (WT) carrying an empty vector, and *airR* mutant carrying an empty vector, and *airR* mutant carrying a wild-type copy of *airR* in the presence and absence of tetracycline. ** $P \leq 0.01$; **** $P \leq 0.001$; **** $P \leq 0.0001$; ns, no significant ($P > 0.05$). (B) Propose model for violacein induction by translation inhibitors. (C) Overexpression of *cviI* and *cviR* under arabinose regulation. (D) Overexpression of *vioS* under arabinose regulation in the presence of sublethal concentration of tetracycline. (E) Complementation of *vioS* mutant with *vioS* gene under regulation by arabisone, with and without tetracycline. (F) Violacein production by *vioS* and *vioS airMS* mutants. (E) Growth of *vioS* and *vioS airMS* mutants. Symbol legend applies to both (F) and (G).

Target	Antibiotic	Mode of Action	References	Activity
Membrane	Polymyxin B	bind to destabilizes cell membrane.	Yu et al., 2015	
Cell Wall	Ceftazidime	blocks bacterial cell wall synthesis by inhibiting penicillin-binding protein 3.	Hayes & Orr, 1983	
	Piperacillin	blocks bacterial cell wall synthesis by inhibiting penicillin-binding proteins.	Mitsuyama et al., 1987	
	Vancomycin	blocks bacterial cell wall synthesis by binding to the D-Ala-D-Ala end of the peptide preventing transglycosylation and transpeptidation of peptidoglycan precursors.	Barna & Williams, 1984	
RNA Synthesis	Rifampicin	inhibits transcription by binding to the RNA polymerase.	Wehrli, 1983	
DNA Replication	Nalidixic acid	inhibits DNA synthesis by blocking DNA gyrase activity.	Sugino et al., 1977	
Metabolism	Trimethoprim	binds to dihydrofolate reductase blocking the reduction of dihydrofolate to tetrahydrofolate, the last essential step for thymidine biosynthesis.	Gleckman et al., 1981	
Protein Synthesis				
Translation initiation	Kasugamycin	interacts with the mRNA-ribosome complex blocking the path of the 5'-UTR of the mRNA upstream of the start codon, thereby interfering with initiation of tRNA binding to the P-site.	Schluenzen et al., 2006; Schuwirth et al., 2006	
Ribosome subunit recycling	Fusidic acid	binds with the elongation factor G and inhibits ribosome disassembly activity by the elongation factor G with recycling factor complex after translation completes.	Savelsbergh et al., 2009	
Premature chain termination	Puromycin	inhibits protein synthesis by competing with aminoacyl-tRNAs, causing premature release of polypeptide from ribosome.	Darken, 1964	
Mistranslation induction	Kanamycin, Paromomycin, Streptomycin	bind to the A-site in the decoding center of the 30S subunit, interfering with the recognition of cognate tRNA by rRNA resulting in insertion of incorrect amino acids into polypeptides.	Kotra et al, 2000; Davies, 1964	
Elongation and Termination	Blasticidin S	blocks translation by bending the CCA end of the P-site tRNA toward the A site, thereby inhibiting peptidyl-tRNA hydrolysis by release factors and with lower activity peptide bond formation.	Svidritskiy et al., 2013	
Elongation	Spectinomycin, Hygromycin B, Apramycin	bind at the decoding center of the 30S subunit, inhibiting translocation of mRNA and tRNAs.	Borovinskaya et al., 2008; Borovinskaya et al., 2007; Perzynski et al., 1979	
	Tetracycline	binds to 30S subunit, interfering with the bind of aminoacyl-tRNA to the A site of the ribosomal complex.	Chopra & Roberts, 2001	
	Erythromycin	binds in the 50S subunit adjacent to the peptidyl-transferase center within the ribosomal exit tunnel blocking passage of newly polypeptide thought the exit tunnel interrupting elongation.	Kannan & Mankin, 2011	
	Chloramphenicol	binds in the 50S subunit at the peptidyl-transferase center overlapping with the aminoacyl moiety of the tRNA and inhibiting peptide-bond formation.	Bulkley et al., 2010; Dunkle et al., 2010	

References

- Barna, J. C.; Williams, D. H. Annu. Rev. Microbiol. 1984, 38 (1), 339.
- Borovinskaya, M. A.; Shoji, S.; Holton, J. M.; Fredrick, K.; Cate, J. H. D. ACS Chem. Biol. 2007, 2 (8), 545.
- Borovinskaya, M. A.; Shoji, S.; Fredrick, K.; Cate, J. H. D. RNA 2008, 14 (8), 1590.
- Bulkley, D.; Innis, C. A.; Blaha, G.; Steitz, T. A. Proc. Natl. Acad. Sci. U.S.A. 2010, 107 (40), 17158.
- Chopra, I.; Roberts, M. Microbiol. Mol. Biol. Rev. 2001, 65 (2), 232.
- Darken, M. A. Pharmacol. Rev. 1964, 16, 223.
- Davies, J. E. Proc. Natl. Acad. Sci. U.S.A. 1964, 51 (4), 659.
- Dunkle, J. A.; Xiong, L.; Mankin, A. S.; Cate, J. H. D. Proc. Natl. Acad. Sci. U.S.A. 2010, 107 (40), 17152.
- Gleckman, R.; Blagg, N.; Joubert, D. W. Pharmacotherapy 1981, 1 (1), 14.
- Hayes, M. V.; Orr, D. C. J. Antimicrob. Chemother. 1983, 12 (2), 119.
- Kannan, K.; Mankin, A. S. Ann. N. Y. Acad. Sci. 2011, 1241 (1), 33.
- Kotra, L. P.; Haddad, J.; Mobashery, S. Antimicrob Agents Chemother 2000, 44 (12), 3249.
- Mitsuyama, J.; Takahata, M.; Yasuda, T.; Saikawa, I. The Journal of Antibiotics 1987, 40 (6), 868.
- Perzynski, S.; Cannon, M.; Cundliffe, E.; Chahwala, S. B.; Davies, J. Eur. J. Biochem. 1979, 99 (3), 623.
- Savelsbergh, A.; Rodnina, M. V.; Wintermeyer, W. RNA 2009, 15 (5), 772.
- Schluenzen, F.; Takemoto, C.; Wilson, D. N.; Kaminishi, T.; Harms, J. M.; Hanawa-Suetsugu, K.; Szaflarski, W.; Kawazoe, M.; Shirouzu, M.; Shirouzo, M.; Nierhaus, K. H.; Yokoyama, S.; Fucini, P. Nat. Struct. Mol. Biol. 2006, 13 (10), 871.
- Schuwirth, B. S.; Day, J. M.; Hau, C. W.; Janssen, G. R.; Dahlberg, A. E.; Cate, J. H. D.; Vila-Sanjurjo, A. Nat. Struct. Mol. Biol. 2006, 13 (10), 879.
- Sugino, A.; Peebles, C. L.; Kreuzer, K. N.; Cozzarelli, N. R. Proc. Natl. Acad. Sci. U.S.A. 1977, 74 (11), 4767.
- Svidritskiy, E.; Ling, C.; Ermolenko, D. N.; Korostelev, A. A. Proc. Natl. Acad. Sci. U.S.A. 2013, 110 (30), 12283.
- Wehrli, W. Rev. Infect. Dis. 1983, 5 Suppl 3, S407.
- Yu, Z.; Qin, W.; Lin, J.; Fang, S.; Qiu, J. Biomed Res Int 2015, 2015 (6), 679109.

Figure supplement 1. Profile of *C. violaceum* ATCC31532 violacein production in response to structurally diverse antibiotics. Antibiotics are classified by cellular target.

					NA	Tet	Spec	Ery	28°C	16°C
	WT									
	Mutated genes									
A	Gene ID	Predicted Function	Class	Name	NA	Tet	Spec	Ery	28°C	16°C
	CLV04_2730	SAM-dependent methyltransferase	Others							
	CLV04_2412	Transcriptional repressor of *cdeAB-oprM* drug exporter	Signaling	*cdeR*						
	CLV04_1292	Phosphoglyceromutase	Metabolism	*pgm*						
	CLV04_2695	Phosphoglycerate kinase	Metabolism	*pgk*						
	CLV04_1869*	MarR family transcriptional regulator	Signaling							
B	CLV04_3464	GntR family transcriptional regulator	Signaling							
	CLV04_3178	Multidrug ABC transporter ATP-binding protein	Others							
	CLV04_1011	Enoyl-CoA hydratase	Others	*fadB2*						

Figure supplement 2. Additional genes involved in induction of violacein production by several inducers. (A) *C. violaceum* ATCC31532 mutants with a disrupted violacein production in response to some of the inducers tested. (B) *C. violaceum* ATCC31532 mutants with increased violacein production in response to some of the inducers tested. NA, No Antibiotic. Tet, Tetracycline. Spec, Spectinomycin. Ery, Erythromycin. * Transposons in promotor.

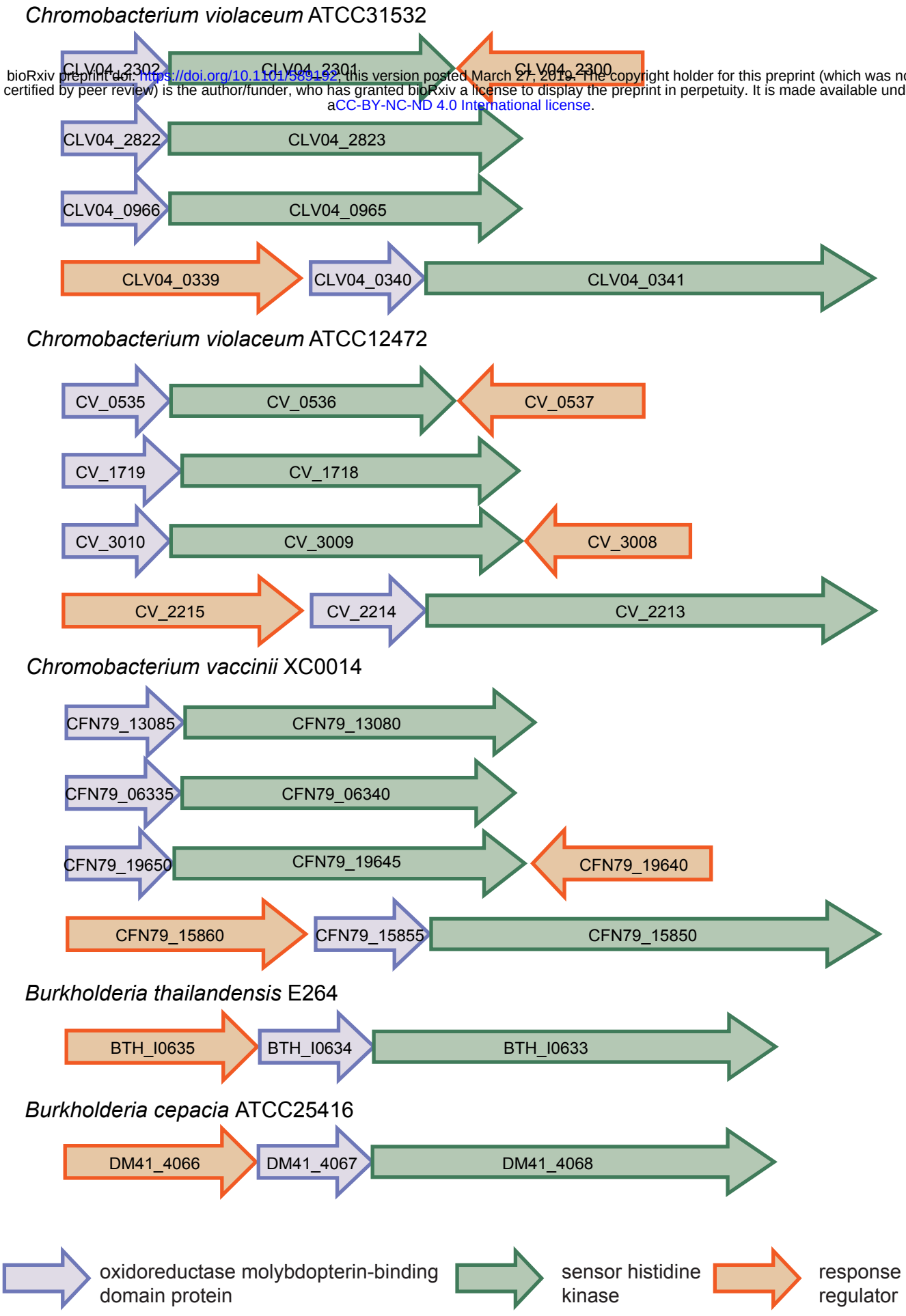


Figure supplement 3. Other pair genes that encode oxidoreductase molybdopterin-binding domain (OxMoco)(IPR036374) proteins next to a sensor histidine kinases in *Chromobacterium* and *Burkholderia* spp genomes.

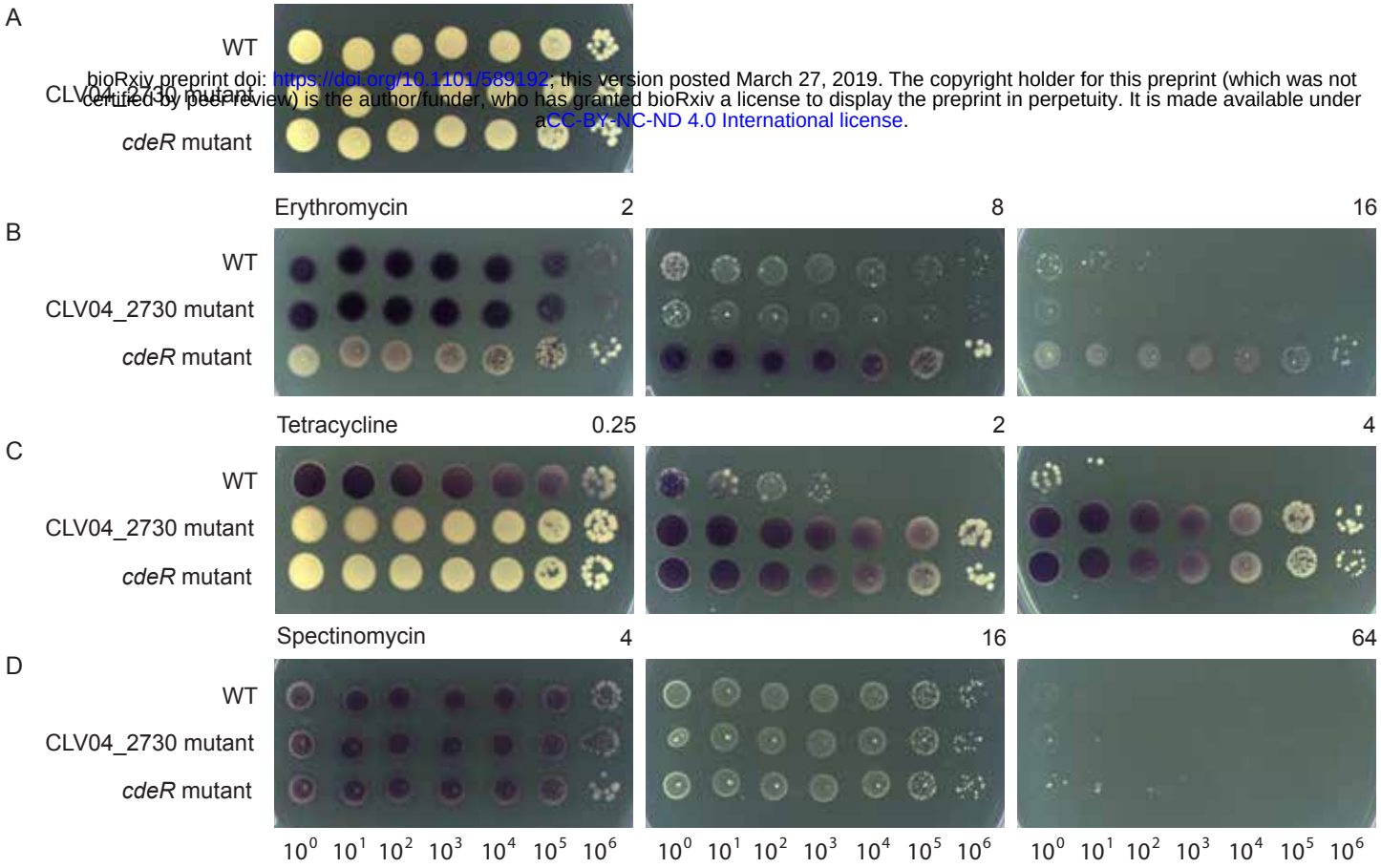


Figure supplement 4. Dose-dependent violacein production in two antibiotic-resistant mutants. Survival and violacein production of *C. violaceum* ATCC31532 wild type (WT), mutant in a SAM-dependent methyltransferase (CLV04_2730), and mutant in *cdeR*, a transcriptional repressor of the *cdeAB-oprM* multidrug efflux pump system (CLV04_2412) with (A) no antibiotic; (B) Erythromycin (µg ml-1); (C) Tetracycline (µg ml-1); (D) Spectinomycin (µg ml-1).

Figure supplement 5. *C. violaceum* ATCC31532 biofilm formation on glass in response to a sublethal concentration of tetracycline. Biofilm formation by *C. violaceum* ATCC31532 wild type (WT), *vioA*, *airS*, *airR*, *vioS,* and *vioS cviI* mutants without antibiotics, or in the presence of tetracycline (0.25 µg ml-1). Violacein mutant, *vioA*, was used as a control for a biofilm visualization without violacein pigmentation. Arrow indicates the location of the biofilm.

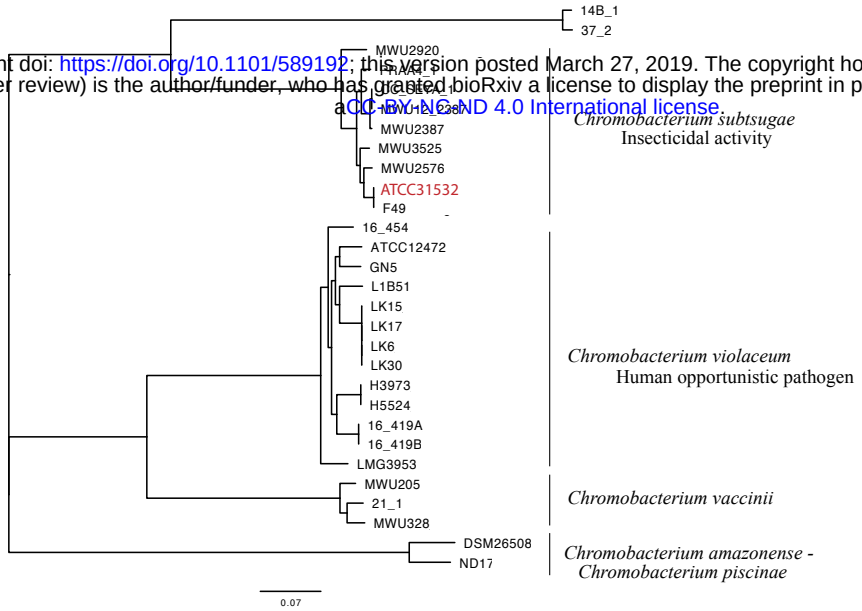
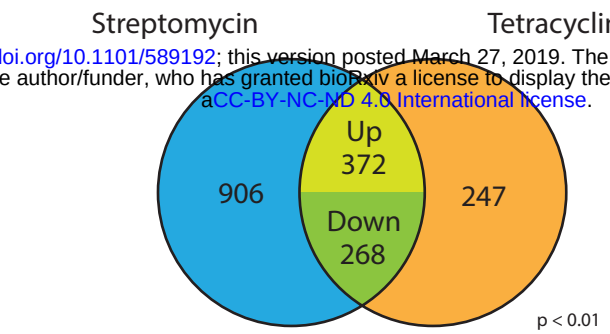
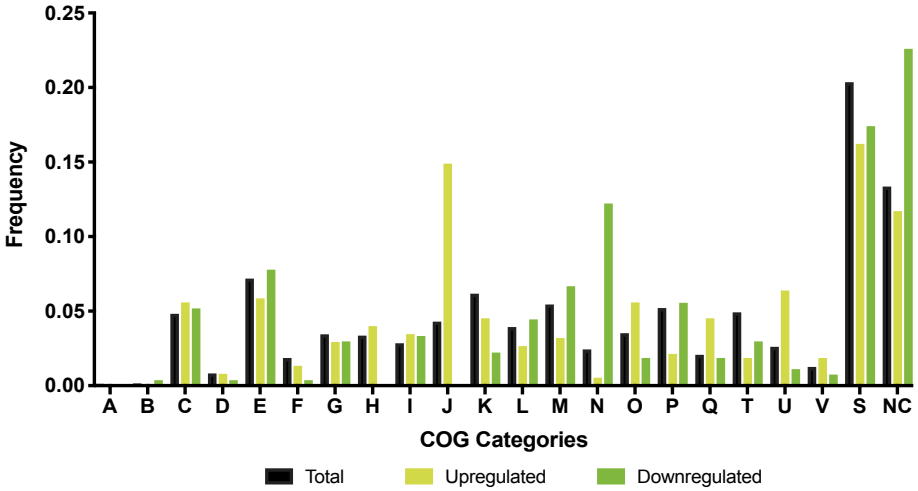


Figure supplement 6. Phylogenetic relatedness of several *Chromobacterium* spp. Highlight in red *C. violaceum* ATCC31532.

A



B



A	RNA processing and modification
B	Chromatin Structure and dynamics
C	Energy production and conversion
D	Cell cycle control, cell division, chromosome partitioning
E	Amino Acid transport and metabolism
F	Nucleotide transport and metabolism
G	Carbohydrate transport and metabolism
H	Coenzyme transport and metabolism
I	Lipid transport and metabolism
J	Translation, ribosomal structure and biogenesis
K	Transcription
L	Replication, recombination and repair
M	Cell wall/membrane/envelop biogenesis
N	Cell motility
O	Posttranslational modification, protein turnover, chaperones
P	Inorganic ion transport and metabolism
Q	Secondary metabolites biosynthesis, transport and catabolism
T	Signal transduction mechanisms
U	Intracellular trafficking, secretion, and vesicular transport
V	Defense mechanisms
S	Function Unknown
NC	Not classification

Figure supplement 7. Transcriptome analysis of *C. violaceum* ATCC31532 in the presence and absence of a sublethal concentration of translation inhibitors. The analysis indicates change in expression from the baseline condition with no antibiotics. (A) Venn diagram of gene differentially expressed by *C. violaceum* ATCC31532 wild type (WT) in streptomycin or tetracycline. (B) COG classification of the differentially genes expressed in streptomycin and tetracycline.

Table supplement 1. Genes expressed differentially in response to streptomycin and tetracycline.

				WT No Antibiotic VS Spectinomycin		WT No Antibiotic VS Tetracycline	
Gene ID	Predicted Function	COGs ID	COG Category	Log_2(Fold change)	P Value	Log_2(Fold change)	P Value
Genes downregulated by translation inhibition							
CLV04_0046	hypothetical protein			0.83	7.2E-03	1.12	1.8E-03
CLV04_0067	long-chain fatty acid transport protein	COG2067	I	1.89	3.4E-07	1.02	2.4E-04
CLV04_0075	uncharacterized protein DUF946		S	0.84	4.6E-03	1.41	2.0E-04
CLV04_0107	dienelactone hydrolase	COG0412	Q	0.62	9.0E-04	0.79	2.1E-04
CLV04_0173	amino acid/amide ABC transporter substrate-binding protein (HAAT family)	COG0683	E	2.39	5.8E-07	1.27	4.4E-04
CLV04_0203	TcdB toxin-like protein		S	1.68	2.6E-07	0.88	2.6E-04
CLV04_0282	Fe-Mn family superoxide dismutase	COG0605	P	1.35	2.4E-06	1.37	4.4E-06
CLV04_0414	gamma-glutamyl-gamma-aminobutyraldehyde dehydrogenase	COG1012	C	2.74	3.1E-07	1.58	1.3E-04
CLV04_0421	uncharacterized protein DUF3141		S	2.18	5.1E-07	1.67	1.5E-05
CLV04_0427	RHS repeat-associated protein	COG3209	M	1.08	3.6E-04	1.42	7.6E-05
CLV04_0428	hypothetical protein			2.92	4.9E-06	4.04	9.8E-07
CLV04_0444	hypothetical protein			1.62	6.1E-03	2.40	8.8E-04
CLV04_0447	hypothetical protein	COG1574	S	2.47	2.5E-07	1.31	1.1E-04
CLV04_0475	hypothetical protein	COG3558	S	2.10	2.5E-06	2.44	1.6E-06
CLV04_0491	hypothetical protein			0.87	4.8E-03	1.32	4.1E-04
CLV04_0506	DNA polymerase V	COG0389	L	1.72	3.7E-06	0.88	1.5E-03
CLV04_0521	hypothetical protein			1.73	1.9E-03	3.02	8.9E-05
CLV04_0555	Protein of unknown function (DUF3037)		S	1.54	1.1E-04	2.22	7.3E-06
CLV04_0563	hypothetical protein			1.09	5.8E-04	2.06	7.0E-06
CLV04_0572	hypothetical protein			2.04	2.4E-03	2.52	9.3E-04
CLV04_0604	hypothetical protein			0.95	6.5E-03	1.28	1.3E-03
CLV04_0667	hypothetical protein			1.32	1.6E-03	2.12	8.8E-05
CLV04_0668	wobble nucleotide-excising tRNase	COG4694		1.76	3.7E-03	3.01	1.1E-04
CLV04_0680	hypothetical protein			1.35	4.5E-05	0.73	6.9E-03
CLV04_0754	aspartate semialdehyde dehydrogenase	COG0136	E	1.48	1.5E-06	1.46	3.6E-06
CLV04_0757	3-isopropylmalate dehydrogenase	COG0473	E	0.69	3.0E-04	0.49	6.6E-03
CLV04_0762	3-isopropylmalate dehydratase large subunit	COG0065	E	0.96	1.2E-04	0.59	7.2E-03
CLV04_0769	acetyl-CoA acetyltransferase	COG0183	I	1.03	4.9E-04	0.80	5.0E-03
CLV04_0791	peroxiredoxin Q/BCP	COG1225	O	0.57	4.5E-03	0.93	1.9E-04
CLV04_0792	PhoH-like ATPase	COG1875	T	2.60	5.3E-08	1.53	2.0E-05
CLV04_0793	Ca2+-binding RTX toxin-like protein	COG2931	Q	2.78	5.8E-09	2.58	5.9E-08
CLV04_0796	ATP-binding cassette, subfamily B, HlyB/CyaB	COG2274	V	1.61	1.1E-05	1.19	2.5E-04
CLV04_0800	Ca2+-binding RTX toxin-like protein	COG2931	Q	2.84	3.9E-05	2.21	4.7E-04
CLV04_0828	flagellar hook-associated protein 3 FlgL	COG1344	N	1.64	2.7E-07	1.05	4.3E-05
CLV04_0829	flagellar hook-associated protein 1 FlgK	COG1256	N	1.88	1.5E-07	1.24	1.8E-05
CLV04_0830	flagellar protein FlgJ	COG1705	N	2.24	1.6E-06	1.41	1.7E-04
CLV04_0831	flagellar P-ring protein precursor FlgI	COG1706	N	1.62	3.4E-07	1.07	3.4E-05
CLV04_0832	flagellar L-ring protein precursor FlgH	COG2063	N	2.53	5.9E-08	1.65	5.0E-06
CLV04_0833	flagellar basal-body rod protein FlgG	COG4786	N	2.46	3.6E-07	1.48	5.0E-05
CLV04_0834	flagellar basal-body rod protein FlgF	COG4787	N	3.13	4.2E-08	1.72	1.2E-05
CLV04_0835	flagellar hook protein FlgE	COG1749	N	3.59	5.9E-09	1.75	1.1E-05
CLV04_0836	flagellar basal-body rod modification protein FlgD	COG1843	N	2.80	3.1E-07	1.35	3.3E-04
CLV04_0837	flagellar basal-body rod protein FlgC	COG1558	N	1.73	3.2E-06	1.25	1.0E-04
CLV04_0838	flagellar basal-body rod protein FlgB	COG1815	N	2.31	5.9E-06	1.52	3.1E-04

CLV04_0870	acyl dehydratase	COG2030	I	1.30	1.7E-04	1.06	1.4E-03
CLV04_0893	hypothetical protein			3.37	5.6E-09	1.67	4.1E-06
CLV04_0945	flagellar FliL protein		S	1.02	3.9E-03	2.39	1.5E-05
CLV04_0946	flagellar hook-length control protein FliK	COG3144	N	1.33	4.1E-04	2.61	3.3E-06
CLV04_0947	hypothetical protein			1.50	7.6E-04	2.85	1.4E-05
CLV04_0948	flagellar protein FliS	COG1516	N	1.21	2.5E-03	3.32	2.6E-06
CLV04_0950	flagellar export protein FliJ			2.00	1.4E-04	2.41	6.7E-05
CLV04_0951	flagellum-specific ATP synthase	COG1157	N, U	1.84	2.5E-04	2.06	1.9E-04
CLV04_0952	flagellar assembly protein FliH	COG1317	N	1.74	4.1E-05	2.27	1.0E-05
CLV04_0953	flagellar motor switch protein FliG	COG1536	N	1.38	4.3E-04	2.03	4.1E-05
CLV04_0954	flagellar M-ring protein FliF	COG1766	N	1.44	1.3E-03	2.13	1.4E-04
CLV04_0959	flagellar biosynthetic protein FliQ	COG1987	N	1.41	8.4E-04	1.09	7.2E-03
CLV04_0967	flagellin	COG1344	N	2.73	4.0E-06	3.97	2.3E-07
CLV04_0970	ribose-binding protein	COG1879	G	0.75	3.2E-04	0.72	7.3E-04
CLV04_1011	short chain enoyl-CoA hydratase	COG1024	I	2.93	8.6E-08	2.53	6.5E-07
CLV04_1084	flagellar hook-length control protein FliK		N	2.37	1.6E-05	1.34	2.4E-03
CLV04_1115	hypothetical protein			0.65	9.1E-04	0.54	5.7E-03
CLV04_1172	transcriptional regulator	COG0229	O	1.44	2.0E-05	1.17	2.1E-04
CLV04_1174	hypothetical protein			1.96	3.3E-05	2.31	1.7E-05
CLV04_1175	hypothetical protein			0.97	4.1E-03	1.75	6.2E-05
CLV04_1176	putative metal-binding integral membrane protein DUF2182		S	1.59	1.4E-05	2.38	1.0E-06
CLV04_1203	microbial collagenase		S	1.24	1.1E-05	0.99	1.5E-04
CLV04_1228	cation/acetate symporter	COG4147	S	1.75	1.1E-05	1.35	2.1E-04
CLV04_1229	acetyl-coenzyme A synthetase	COG0365	I	1.37	8.7E-06	0.84	1.2E-03
CLV04_1247	malate synthase	COG2225	C	2.27	6.9E-06	1.47	5.4E-04
CLV04_1248	putative secreted protein	COG3471	S	1.68	3.3E-06	1.68	7.2E-06
CLV04_1290	acyl-coenzyme A thioesterase PaaI-like protein			1.45	9.8E-05	1.13	1.2E-03
CLV04_1297	polyphosphate kinase	COG0855	P	0.51	3.7E-03	0.63	1.3E-03
CLV04_1314	phasin family protein		S	2.53	1.3E-04	3.30	2.2E-05
CLV04_1365	putative porin		M	1.43	1.7E-06	0.80	7.4E-04
CLV04_1390	two-component system chemotaxis sensor kinase CheA	COG0643	T	1.17	9.4E-07	0.46	6.0E-03
CLV04_1399	enolase	COG0148	G	1.34	2.8E-06	0.99	1.0E-04
CLV04_1420	hypothetical protein			1.32	4.4E-05	0.89	2.0E-03
CLV04_1442	LysR family transcriptional regulator		K	0.69	5.5E-03	0.68	9.2E-03
CLV04_1459	hypothetical protein	COG3220	S	0.93	2.3E-04	0.64	6.1E-03
CLV04_1505	catalase	COG0753	P	3.46	1.9E-08	3.62	5.9E-08
CLV04_1515	acetoin utilization deacetylase AcuC-like enzyme	COG0123	B, Q	2.51	4.1E-04	1.92	3.7E-03
CLV04_1532	3-oxoacyl-[acyl-carrier-protein] reductase		I	1.75	3.7E-06	2.95	7.0E-08
CLV04_1545	L-glutamine synthetase	COG0174	E	2.88	7.9E-09	1.99	7.2E-07
CLV04_1576	putative acetyltransferase	COG0454	K	1.01	1.0E-03	1.12	8.1E-04
CLV04_1613	isocitrate dehydrogenase	COG2838	C	1.66	2.1E-07	0.71	1.2E-03
CLV04_1714	uncharacterized protein (TIGR02646 family)			3.50	5.2E-07	4.67	1.9E-07
CLV04_1715	putative ATP-binding protein involved in virulence	COG3950	S	2.32	2.0E-04	3.38	1.4E-05
CLV04_1716	retron-type reverse transcriptase	COG3344	L	1.67	1.2E-03	2.60	6.7E-05
CLV04_1718	hypothetical protein			1.43	3.4E-05	2.19	2.0E-06
CLV04_1789	acyl-CoA dehydrogenase	COG1960	I	1.07	7.8E-06	0.51	6.6E-03
CLV04_1843	flagellin	COG1344	N	2.08	9.9E-05	3.16	3.6E-06
CLV04_1882	crotonobetainyl-CoA:carnitine CoA-transferase CaiB-like acyl-CoA transferase	COG1804	C	1.73	9.9E-08	0.60	2.3E-03
CLV04_1893	DHA2 family multidrug resistance protein		P	1.37	3.0E-05	0.92	1.2E-03
CLV04_1940	DDE family transposase	COG3039	L	1.00	5.1E-03	1.37	1.1E-03
CLV04_1941	hypothetical protein			1.28	1.2E-04	1.80	1.4E-05

CLV04_1942	MAC/Perforin domain-containing protein			1.00	2.8E-03	1.38	4.8E-04
CLV04_1946	hypothetical protein			1.20	4.8E-04	1.23	6.8E-04
CLV04_1949	TetR family transcriptional regulator		K	0.67	3.1E-03	1.15	8.3E-05
CLV04_1950	hypothetical protein			1.93	8.7E-04	3.33	2.1E-05
CLV04_1951	hypothetical protein			1.40	7.5E-03	2.81	6.6E-05
CLV04_1957	allosteric NADP-dependent malic enzyme	COG0280, COG0281	C	1.45	7.0E-08	0.72	1.2E-04
CLV04_2008	amino acid ABC transporter substrate-binding protein (PAAT family)		G	2.82	4.5E-08	2.88	8.8E-08
CLV04_2015	hypothetical protein			2.08	5.4E-04	3.27	3.3E-05
CLV04_2037	hypothetical protein			2.06	8.9E-06	2.18	1.2E-05
CLV04_2127	D-mannose binding lectin		M	1.15	1.7E-04	2.30	1.1E-06
CLV04_2128	hypothetical protein			1.12	2.1E-03	3.00	1.9E-06
CLV04_2131	VCBS repeat-containing protein		S	1.78	2.5E-06	3.06	8.2E-08
CLV04_2145	hypothetical protein	COG2910	S	1.05	5.6E-05	1.41	9.5E-06
CLV04_2161	amino acid ABC transporter substrate-binding protein (PAAT family)		E	1.31	1.1E-05	1.17	5.6E-05
CLV04_2163	3-hydroxybutyrate dehydrogenase		C	0.85	1.6E-03	1.32	7.3E-05
CLV04_2164	NTE family protein	COG1752	S	1.57	4.8E-05	1.39	2.7E-04
CLV04_2167	glutamine--fructose-6-phosphate transaminase	COG0449	M	1.55	5.1E-05	1.17	9.1E-04
CLV04_2200	uncharacterized protein (TIGR04141 family)			3.39	1.9E-07	3.77	2.2E-07
CLV04_2202	vioS			4.00	5.2E-08	2.98	2.0E-06
CLV04_2252	ferritin-like protein			1.73	3.4E-05	1.24	7.7E-04
CLV04_2286	chitin-binding protein	COG3397	G	3.49	1.5E-04	2.66	1.5E-03
CLV04_2316	hypothetical protein			1.66	1.9E-03	2.57	1.6E-04
CLV04_2396	hypothetical protein			0.80	1.1E-03	1.36	2.8E-05
CLV04_2455	aspartate carbamoyltransferase	COG0540	F	1.13	5.5E-03	1.55	1.2E-03
CLV04_2474	phage tail sheath gpL-like	COG4386	S	4.73	1.8E-07	4.18	9.3E-07
CLV04_2475	hypothetical protein			2.64	4.3E-06	3.55	1.1E-06
CLV04_2476	hypothetical protein			2.59	5.8E-05	3.47	1.5E-05
CLV04_2477	prophage DNA circulation protein	COG4228	L	2.51	5.7E-06	2.65	8.3E-06
CLV04_2478	prophage tail gpP-like protein	COG4379	S	2.38	1.0E-04	1.55	2.9E-03
CLV04_2480	phage gp46-like protein	COG4381	S	1.74	4.1E-05	1.36	4.8E-04
CLV04_2481	putative phage protein gp47/JayE	COG3299	S	2.71	9.3E-06	1.90	2.6E-04
CLV04_2482	uncharacterized protein YmfQ (DUF2313 family)	COG3778	S	2.14	7.8E-05	2.05	1.9E-04
CLV04_2483	short tail fiber-like protein		S	3.46	2.3E-08	3.25	8.8E-08
CLV04_2484	virus tail fiber assembly protein lambda gpK		S	3.00	1.4E-06	3.48	1.1E-06
CLV04_2485	hypothetical protein		S	1.51	3.0E-05	1.75	1.6E-05
CLV04_2486	microcystin-dependent protein		S	1.96	5.0E-07	2.09	6.9E-07
CLV04_2520	glutathione S-transferase	COG0625	O	1.73	1.2E-06	1.12	1.4E-04
CLV04_2527	hypothetical protein			2.17	3.0E-06	1.53	9.8E-05
CLV04_2671	glutathione S-transferase		O	0.62	2.4E-03	0.57	6.5E-03
CLV04_2672	secreted protein		S	0.67	2.1E-03	0.75	1.6E-03
CLV04_2693	fructose-bisphosphate aldolase	COG0191	G	1.38	7.0E-06	1.01	2.4E-04
CLV04_2708	L-glutamate ABC transporter membrane protein /L-aspartate ABC transporter membrane protein	COG0765	E	1.99	1.6E-05	1.21	1.4E-03
CLV04_2710	L-glutamate-binding protein /L-aspartate-binding protein	COG0834	P	2.23	1.3E-07	1.85	1.7E-06
CLV04_2737	nucleoside-specific channel-forming protein Tsx		M	0.53	3.7E-03	0.77	4.0E-04
CLV04_2782	methyl-accepting chemotaxis sensory transducer with Cache sensor	COG0840	T	0.73	8.5E-04	0.62	4.2E-03
CLV04_2805	methyltransferase family protein		S	0.98	8.1E-03	1.20	3.8E-03
CLV04_2809	DNA sulfur modification protein DndD	COG0419	L	1.01	5.3E-03	1.52	5.9E-04
CLV04_2810	DNA sulfur modification protein DndE		L	1.83	2.9E-04	2.99	1.2E-05
CLV04_2811	hypothetical protein			2.37	1.3E-04	3.94	3.0E-06
CLV04_2812	DndB-like DNA-sulfur modification-associated protein			1.69	7.4E-04	2.97	9.0E-06
CLV04_2813	restriction system protein	COG1715	V	1.35	4.6E-03	2.56	6.8E-05

CLV04_2882	cell division protein FtsZ	COG0206	D	1.36	2.2E-07	0.90	2.6E-05
CLV04_2883	UDP-3-O-[3-hydroxymyristoyl] N-acetylglucosamine deacetylase	COG0774	M	1.00	1.7E-06	0.83	2.1E-05
CLV04_2907	hypothetical protein			2.02	1.1E-06	3.15	5.9E-08
CLV04_2923	methyl-accepting chemotaxis sensory transducer with Cache sensor	COG0840	P	1.25	5.1E-05	0.82	2.4E-03
CLV04_2968	starvation-inducible DNA-binding protein	COG0783	P	1.67	9.5E-05	1.21	2.1E-03
CLV04_3091	hypothetical protein			1.85	5.8E-05	1.88	9.2E-05
CLV04_3131	hypothetical protein			1.94	3.8E-04	1.27	8.9E-03
CLV04_3144	putative spermidine/putrescine transport system substrate-binding protein	COG0687	G	0.80	6.2E-04	0.91	3.7E-04
CLV04_3211	glutamate synthase (NADPH) large subunit	COG0067, COG0069	E	2.38	2.4E-06	1.71	8.6E-05
CLV04_3212	glutamate synthase (NADPH) small subunit	COG0493	E	1.90	7.3E-06	1.61	5.6E-05
CLV04_3213	lipopolysaccharide/colanic/teichoic acid biosynthesis glycosyltransferase	COG2148	M	3.42	4.2E-07	4.88	8.8E-08
CLV04_3214	polysaccharide biosynthesis protein	COG1086	M	2.39	2.7E-06	3.34	3.5E-07
CLV04_3215	uncharacterized protein DUF1792	COG1442	M	2.64	5.6E-07	4.06	5.9E-08
CLV04_3216	GT2 family glycosyltransferase	COG1216	M	2.87	3.0E-06	4.56	2.2E-07
CLV04_3217	O-antigen/teichoic acid export membrane protein			3.35	4.8E-07	4.91	8.4E-08
CLV04_3218	polysaccharide deacetylase	COG0726	G	3.01	2.4E-06	4.75	2.2E-07
CLV04_3219	hypothetical protein			3.66	1.8E-06	5.36	2.3E-07
CLV04_3220	hypothetical protein			3.22	1.8E-06	4.97	1.8E-07
CLV04_3221	glycosyl transferase-like sugar-binding protein	COG3774	M	2.80	2.6E-05	4.28	1.4E-06
CLV04_3222	hypothetical protein			3.43	2.8E-06	4.97	3.5E-07
CLV04_3223	nucleoside-diphosphate-sugar epimerase	COG0451	M	2.75	4.2E-07	4.18	5.9E-08
CLV04_3224	glycosyltransferase involved in cell wall biosynthesis		M	3.27	1.3E-06	4.57	2.2E-07
CLV04_3225	methionyl-tRNA formyltransferase	COG0223	M	3.25	7.4E-06	2.97	3.4E-05
CLV04_3226	hypothetical protein			1.10	4.1E-04	0.83	4.7E-03
CLV04_3227	glycosyl transferase family 2	COG0463	M	1.03	5.3E-06	0.45	7.5E-03
CLV04_3295	CobQ/CobB/MinD/ParA family nucleotide binding protein		U	1.11	5.6E-03	2.08	1.4E-04
CLV04_3341	addiction module HigA family antidote	COG3093	S	1.75	4.5E-04	3.04	5.9E-06
CLV04_3342	proteic killer suppression protein	COG3549	S	1.40	3.4E-03	2.46	1.0E-04
CLV04_3343	integrase	COG0582	L	0.80	3.3E-04	1.01	8.9E-05
CLV04_3357	phosphate ABC transporter substrate-binding protein (PhoT family)	COG0226	P	2.24	8.4E-06	1.44	7.4E-04
CLV04_3391	hypothetical protein			0.84	4.4E-03	1.22	5.2E-04
CLV04_3449	hypothetical protein			1.81	3.6E-05	3.04	1.4E-06
CLV04_3455	DNA polymerase-3 subunit epsilon	COG0322, COG0847	L	0.83	8.3E-04	0.81	1.7E-03
CLV04_3487	hypothetical protein			1.31	1.2E-03	2.43	2.0E-05
CLV04_3488	HTH-type transcriptional regulator/antitoxin HigA	COG5499	K	1.70	6.3E-05	3.11	1.0E-06
CLV04_3489	mRNA interferase HigB	COG4680	S	2.23	5.4E-05	4.22	9.3E-07
CLV04_3492	malate dehydrogenase (NAD)	COG0039	C	1.62	1.3E-05	1.02	1.3E-03
CLV04_3576	aryl-alcohol dehydrogenase-like predicted oxidoreductase	COG0667	C	1.20	8.9E-05	0.75	6.0E-03
CLV04_3590	Cd2+/Zn2+-exporting ATPase	COG2217	P	1.57	1.1E-04	1.58	1.9E-04
CLV04_3680	spermidine export protein MdtJ	COG2076	P	1.28	3.7E-05	0.98	6.6E-04
CLV04_3686	hypothetical protein		S	1.02	1.5E-03	1.06	1.8E-03
CLV04_3691	carboxypeptidase Taq	COG2317	E	1.34	1.6E-04	0.83	7.4E-03
CLV04_3763	phasin family protein		S	2.88	3.8E-07	3.46	1.8E-07
CLV04_3772	glycosyl hydrolase family 101		S	0.53	8.1E-03	1.03	1.1E-04
CLV04_3788	serine transporter	COG0814	E	1.96	2.7E-05	1.61	2.4E-04
CLV04_3806	beta-alanine--pyruvate transaminase	COG0161	E	2.21	1.2E-07	1.67	3.3E-06
CLV04_3807	methylmalonate-semialdehyde dehydrogenase [acylating]	COG1012	I	2.78	8.6E-09	2.12	2.7E-07
CLV04_3808	acetyltransferase (GNAT) family protein	COG3153	S	1.00	2.3E-04	1.00	4.0E-04
CLV04_3895	acetate kinase	COG0282	C	1.79	1.5E-04	1.26	3.0E-03
CLV04_3908	amino acid/amide ABC transporter substrate-binding protein (HAAT family)	COG0683	E	2.66	2.2E-10	1.36	5.9E-07
CLV04_3922	hypothetical protein			0.70	6.0E-03	1.47	4.4E-05

CLV04_4020	isocitrate lyase	COG2224	C	2.08	2.6E-06	1.62	6.0E-05
CLV04_4028	hypothetical protein			1.59	2.5E-03	3.31	3.5E-05
CLV04_4045	hypothetical protein	COG3417	S	1.33	1.1E-03	1.78	2.4E-04
CLV04_4081	flagellar basal-body rod protein FlgB	COG1815	N	1.44	1.3E-03	2.91	1.5E-05
CLV04_4088	flagellar P-ring protein precursor FlgI	COG1706	N	1.90	1.4E-05	1.93	2.3E-05
CLV04_4168	putative serine protein kinase PrkA	COG2766	T	2.41	3.4E-07	2.06	3.5E-06
CLV04_4169	hypothetical protein	COG2718	S	1.61	8.4E-05	1.58	1.8E-04
CLV04_4170	stage V sporulation protein R	COG2719	S	1.86	1.4E-06	1.37	5.6E-05
CLV04_4181	3-hydroxypropanoate dehydrogenase	COG0778	C	1.21	1.2E-06	0.78	1.3E-04
CLV04_4236	4-hydroxy-tetrahydrodipicolinate synthase	COG0329	E	1.94	3.4E-05	1.03	5.2E-03
CLV04_4256	nicotinamidase-related amidase	COG1335	Q	1.57	6.1E-05	1.43	2.4E-04
CLV04_4266	methyl-accepting chemotaxis sensory transducer with Pas/Pac sensor		T	2.53	9.1E-07	1.13	1.2E-03
CLV04_4309	putrescine transport system substrate-binding protein	COG0687	G	2.72	7.8E-09	1.84	8.2E-07
CLV04_4310	putrescine transport system permease protein	COG1176	P	2.29	3.6E-07	1.41	4.6E-05
CLV04_4311	putrescine transport system permease protein	COG1177	P	2.34	7.3E-08	1.46	8.3E-06
CLV04_4312	uncharacterized protein DUF3138		S	5.01	1.2E-10	3.39	4.5E-08
CLV04_4319	iron complex outermembrane receptor protein		P	0.64	4.7E-03	0.70	4.1E-03
CLV04_4331	iron complex outermembrane receptor protein		P	2.54	2.3E-06	1.45	7.9E-04
CLV04_4337	deoxyribonuclease-1	COG2356	L	1.06	2.6E-03	0.95	8.4E-03
CLV04_4341	arginine decarboxylase	COG1982	E	1.83	3.6E-07	0.76	2.1E-03
Genes downregulated by translation inhibition moduladed by *air* system							
CLV04_0005	hypothetical protein			1.78	1.3E-04	1.86	1.7E-04
CLV04_0010	EAL domain-containing protein (putative c-di-GMP-specific phosphodiesterase class I)	COG2200	T	0.85	1.1E-03	0.67	8.3E-03
CLV04_0012	type 4 prepilin peptidase 1	COG1989	O	1.35	1.2E-04	1.70	3.5E-05
CLV04_0013	hypothetical protein			1.47	1.2E-04	1.10	1.7E-03
CLV04_0062	alcohol dehydrogenase	COG1454	C	2.63	2.1E-03	2.32	7.8E-03
CLV04_0330	L-lysine exporter family protein LysE/ArgO	COG1279	E	1.43	6.9E-05	1.48	1.0E-04
CLV04_0508	hypothetical protein			2.01	1.1E-05	1.36	4.1E-04
CLV04_0571	single-strand binding protein	COG0629	L	2.56	2.7E-05	1.80	5.8E-04
CLV04_0794	hypothetical protein	COG0438	M	1.06	4.2E-03	1.15	4.0E-03
CLV04_0827	succinylglutamate desuccinylase	COG2988	E	1.01	4.1E-04	0.72	6.7E-03
CLV04_0942	chemotaxis protein MotB	COG1360	N	0.92	6.8E-04	0.89	1.4E-03
CLV04_0944	RNA polymerase sigma-28 (SigD/FliA/WhiG) subunit	COG1191	K	1.80	5.5E-04	2.62	7.5E-05
CLV04_0949	flagellar hook-associated protein 2	COG1345	N	2.35	3.6E-07	3.37	6.5E-08
CLV04_0957	flagellar motor switch protein FliN/FliY	COG1886	N	1.24	1.4E-03	1.69	2.8E-04
CLV04_1181	undecaprenyl-diphosphatase	COG3038	C	0.83	1.4E-03	0.79	3.1E-03
CLV04_1182	cytochrome b561		S	0.84	5.3E-04	0.65	5.1E-03
CLV04_1368	diguanylate cyclase/phosphodiesterase		T	1.37	2.5E-05	1.00	5.6E-04
CLV04_1441	patatin-like phospholipase			1.02	4.4E-05	0.57	5.9E-03
CLV04_1552	methionine synthase (B12-independent)	COG0620	E	1.12	6.4E-04	0.81	8.8E-03
CLV04_1696	POT family proton-dependent oligopeptide transporter	COG3104	E	1.60	4.9E-06	0.64	9.5E-03
CLV04_1836	flagellar hook-length control protein FliK		S	0.54	3.3E-03	0.50	8.8E-03
CLV04_1947	Mu transposase-like protein		L	0.55	7.6E-03	0.63	5.7E-03
CLV04_2053	heptosyltransferase-3	COG0859	M	0.66	3.8E-03	0.69	4.5E-03
CLV04_2068	amino acid ABC transporter substrate-binding protein (PAAT family)	COG0834	E	0.60	7.4E-03	0.66	6.6E-03
CLV04_2137	poly(3-hydroxybutyrate) depolymerase		S	1.23	4.2E-04	1.09	1.7E-03
CLV04_2165	amino acid ABC transporter substrate-binding protein (PAAT family)		E	0.83	6.9E-04	0.71	3.5E-03
CLV04_2168	DeoR family transcriptional regulator	COG1349	K	1.32	2.7E-03	1.48	2.0E-03
CLV04_2195	IS4 family transposase	COG3039	L	0.81	9.0E-03	0.96	5.2E-03
CLV04_2467	Mor transcription activator family protein		S	1.93	1.8E-05	1.52	2.2E-04
CLV04_2468	peptidoglycan L-alanyl-D-glutamate endopeptidase CwlK		M	1.46	9.7E-05	1.48	1.6E-04

CLV04_2469	hypothetical protein			1.45	8.0E-03	1.68	5.9E-03
CLV04_2470	hypothetical protein			1.14	2.5E-03	1.18	3.3E-03
CLV04_2473	phage gp37-like protein		S	2.10	2.4E-04	1.92	8.0E-04
CLV04_2479	phage baseplate assembly protein V	COG4384	S	1.18	4.5E-03	1.12	9.3E-03
CLV04_3199	long-chain acyl-CoA synthetase	COG1022	I	0.86	9.4E-04	0.80	2.4E-03
CLV04_3591	SprA family protein		S	1.42	3.1E-05	1.06	5.9E-04
CLV04_3679	spermidine export protein MdtI	COG2076	P	0.69	4.9E-03	0.95	9.3E-04
CLV04_3894	phosphotransacetylase	COG0280, COG0857	C	1.59	2.5E-04	1.11	5.0E-03
CLV04_4047	hypothetical protein	COG3014	S	1.73	4.1E-05	1.50	2.4E-04
CLV04_4083	flagellar basal-body rod modification protein FlgD	COG1843	N	1.32	2.3E-04	2.07	1.1E-05
CLV04_4084	flagellar hook protein FlgE	COG1749	N	1.96	1.1E-05	2.50	2.6E-06
CLV04_4085	flagellar basal-body rod protein FlgF	COG4787	N	2.47	5.8E-07	2.56	1.0E-06
CLV04_4086	flagellar basal-body rod protein FlgG	COG4786	N	1.89	1.1E-05	2.67	1.4E-06
CLV04_4087	flagellar L-ring protein precursor FlgH	COG2063	N	2.30	5.0E-06	2.96	1.4E-06
CLV04_4089	flagellar protein FlgJ			1.85	1.4E-04	2.19	7.4E-05
CLV04_4090	flagellar hook-associated protein 1 FlgK	COG1256	N	1.05	2.3E-03	2.90	1.4E-06
CLV04_4091	flagellar hook-associated protein 3 FlgL	COG1344	N	0.85	8.7E-03	3.00	1.3E-06
CLV04_4092	hypothetical protein			1.75	1.1E-05	2.94	3.5E-07
CLV04_4268	S-PFT family hemolysin	COG3210	U	0.84	2.9E-04	0.75	1.2E-03
CLV04_4281	hypothetical protein			1.18	1.9E-04	0.79	6.0E-03
CLV04_4420	diguanylate cyclase (GGDEF)-like protein		T	1.18	4.8E-05	0.72	3.6E-03
Genes upregulated by translation inhibition							
CLV04_0034	ring-1,2-phenylacetyl-CoA epoxidase subunit PaaA	COG3396	Q	-1.67	3.5E-05	-1.73	4.4E-05
CLV04_0035	uncharacterized protein (TIGR00369 family)		Q	-1.20	1.1E-03	-1.69	8.5E-05
CLV04_0049	GST-like protein	COG0625	O	-0.52	2.0E-03	-0.52	3.4E-03
CLV04_0117	putative PurR-regulated permease PerM	COG0628	S	-0.67	6.9E-03	-0.91	1.3E-03
CLV04_0128	FKBP-type peptidyl-prolyl cis-trans isomerase FkpA	COG0545	O	-2.08	4.9E-08	-0.79	8.6E-04
CLV04_0149	hypothetical protein			-2.99	3.1E-07	-2.24	1.1E-05
CLV04_0157	6,7-dimethyl-8-ribityllumazine synthase	COG0054	H	-0.88	3.2E-04	-0.81	1.1E-03
CLV04_0158	NusB antitermination factor	COG0781	K	-2.88	1.2E-08	-1.79	3.6E-06
CLV04_0176	hypothetical protein			-1.18	1.6E-03	-2.13	1.2E-05
CLV04_0190	uncharacterized protein DUF1843		S	-0.85	9.1E-03	-2.96	2.3E-07
CLV04_0191	uncharacterized protein DUF1843			-1.56	1.7E-03	-2.98	6.5E-06
CLV04_0197	type III secretion system major needle protein (YscF/MxiH/PrgI family)		U	-1.98	4.2E-06	-2.79	3.5E-07
CLV04_0200	DNA-binding winged helix-turn-helix (wHTH) protein	COG0457	K	-0.63	5.9E-03	-0.70	5.1E-03
CLV04_0208	invasion protein B family protein		U	-1.38	3.9E-05	-1.52	2.8E-05
CLV04_0211	surface presentation of antigens protein		S	-0.86	2.4E-03	-1.59	2.2E-05
CLV04_0212	type III secretion system apparatus protein YscQ/HrcQ	COG1886	U	-0.93	8.5E-04	-1.62	1.1E-05
CLV04_0213	type III secretion protein R	COG4790	U	-1.21	1.6E-04	-1.59	2.1E-05
CLV04_0214	type III secretion protein S	COG4794	U	-1.55	2.5E-05	-1.36	1.6E-04
CLV04_0215	type III secretion protein T	COG4791	U	-1.61	2.6E-04	-1.38	1.6E-03
CLV04_0216	type III secretion protein U	COG1377	N	-1.65	1.5E-04	-1.16	4.9E-03
CLV04_0217	type III secretion system low calcium response chaperone LcrH/SycD	COG0457	S	-1.85	1.4E-06	-1.27	1.0E-04
CLV04_0218	type III secretion system translocon protein (YopB/IpaB/SipB family)		D	-0.46	9.3E-03	-1.00	4.3E-05
CLV04_0226	AraC family two component transcriptional regulator		T	-2.47	1.6E-05	-2.50	2.7E-05
CLV04_0234	hypothetical protein			-1.35	1.8E-04	-1.10	1.7E-03
CLV04_0261	hypothetical protein			-1.72	1.9E-06	-1.28	7.0E-05
CLV04_0270	D-fructose 1,6-bisphosphatase	COG0158	G	-0.68	3.7E-03	-0.82	1.5E-03
CLV04_0320	ATP-dependent Clp protease ATP-binding subunit ClpX	COG1219	O	-1.39	7.8E-06	-0.81	1.6E-03
CLV04_0321	ATP-dependent Clp protease proteolytic subunit ClpP	COG0740	O	-1.18	6.6E-06	-0.85	2.6E-04
CLV04_0322	trigger factor	COG0544	O	-1.19	1.9E-04	-1.02	1.1E-03

CLV04_0352	1-deoxy-D-xylulose 5-phosphate reductoisomerase	COG0743	I	-0.57	9.0E-03	-0.62	9.0E-03
CLV04_0424	type VI secretion system secreted protein VgrG	COG4253	S	-1.35	6.4E-06	-0.98	2.5E-04
CLV04_0437	hypothetical protein			-0.67	6.4E-03	-1.05	3.5E-04
CLV04_0462	hypothetical protein			-4.44	1.9E-08	-4.48	5.9E-08
CLV04_0480	indole-3-glycerol phosphate synthase	COG0134	E	-1.40	2.5E-06	-0.92	2.6E-04
CLV04_0561	hypothetical protein			-2.08	3.4E-05	-1.15	6.9E-03
CLV04_0594	molecular chaperone Hsp33	COG1281	O	-1.67	3.5E-07	-1.01	9.6E-05
CLV04_0616	AraC-like protein		S	-2.23	9.5E-06	-2.71	2.5E-06
CLV04_0617	hypothetical protein	COG0442	J	-1.42	3.9E-03	-1.71	1.5E-03
CLV04_0618	GTP cyclohydrolase II	COG0807	H	-1.54	2.2E-05	-2.07	2.0E-06
CLV04_0620	phenylacetate-CoA ligase	COG0463, COG1541	Q	-1.21	4.8E-04	-1.81	2.0E-05
CLV04_0622	4-hydroxy-2-oxoheptanedioate aldolase	COG3836	G	-2.45	5.3E-07	-2.95	1.9E-07
CLV04_0623	uncharacterized protein (DUF697 family)		S	-3.04	8.0E-07	-3.46	4.8E-07
CLV04_0624	hypothetical protein			-1.55	4.4E-05	-1.71	3.4E-05
CLV04_0626	putative ATP-binding cassette transporter	COG4615	V	-1.64	1.5E-06	-1.77	1.4E-06
CLV04_0627	regulator of protease activity HflC (stomatin/prohibitin superfamily)	COG0330	O	-1.72	5.8E-06	-1.78	9.0E-06
CLV04_0628	condensation domain-containing protein	COG0318, COG1020	Q	-1.67	9.0E-06	-1.48	5.8E-05
CLV04_0629	hypothetical protein			-2.29	9.1E-04	-1.93	5.7E-03
CLV04_0651	ubiquinone/menaquinone biosynthesis C-methylase UbiE	COG0500	Q	-2.71	2.8E-07	-3.11	1.8E-07
CLV04_0653	amino acid adenylation domain-containing protein	COG3321	Q	-5.11	2.6E-08	-5.86	4.5E-08
CLV04_0654	amino acid adenylation domain-containing protein	COG0318, COG1020	Q	-4.44	1.8E-07	-5.45	7.3E-08
CLV04_0662	hypothetical protein			-1.21	3.6E-03	-1.60	7.3E-04
CLV04_0685	uncharacterized protein YndB with AHSA1/START domain	COG3832	S	-1.24	9.5E-05	-1.05	7.7E-04
CLV04_0702	amino acid adenylation domain-containing protein	COG0318	Q	-3.44	2.4E-07	-1.69	6.7E-04
CLV04_0703	hypothetical protein	COG1960	I	-3.03	3.3E-07	-1.50	5.4E-04
CLV04_0710	hypothetical protein			-0.75	9.8E-03	-0.89	5.2E-03
CLV04_0741	thioredoxin-like protein		O	-1.37	3.9E-05	-1.44	4.6E-05
CLV04_0746	acetyl-CoA carboxylase carboxyltransferase subunit alpha	COG0777	I	-1.34	1.1E-06	-0.83	2.1E-04
CLV04_0748	tryptophan synthase beta chain	COG0133	E	-0.76	2.3E-04	-0.61	2.2E-03
CLV04_0820	hypothetical protein	COG3631	S	-1.35	1.1E-03	-1.85	1.2E-04
CLV04_0844	beta-glucosidase (glycosyl hydrolase family 9)		S	-0.62	3.4E-03	-0.71	2.0E-03
CLV04_0845	putative NBD/HSP70 family sugar kinase	COG1940	K	-1.41	6.9E-05	-0.92	4.5E-03
CLV04_0879	intracellular septation protein	COG2917	D	-1.05	2.3E-04	-0.72	6.5E-03
CLV04_0882	peptidyl-prolyl cis-trans isomerase C	COG0760	O	-1.24	1.1E-05	-0.66	3.7E-03
CLV04_0884	peptidyl-prolyl cis-trans isomerase C	COG0760	O	-1.09	1.1E-04	-1.07	2.4E-04
CLV04_0886	peptidase S41-like protein		S	-2.06	7.7E-06	-1.41	5.6E-04
CLV04_0917	hypothetical protein	COG4378	S	-1.16	9.7E-03	-2.19	9.8E-05
CLV04_0990	D-alpha,beta-D-heptose 7-phosphate 1-kinase	COG2870	H	-0.81	3.9E-05	-0.52	2.7E-03
CLV04_0991	UDP-glucose dehydrogenase	COG1004	M	-0.77	2.4E-04	-0.56	4.7E-03
CLV04_0996	SSU ribosomal protein S1P	COG0539	J	-0.97	8.2E-03	-1.16	4.0E-03
CLV04_1023	flavin reductase (DIM6/NTAB) family NADH-FMN oxidoreductase RutF	COG1853	S	-1.32	4.2E-06	-1.00	1.3E-04
CLV04_1028	hypothetical protein			-1.73	9.6E-06	-2.65	3.4E-07
CLV04_1071	thiol:disulfide interchange protein DsbC	COG1651	O	-2.26	5.6E-08	-0.70	3.6E-03
CLV04_1128	peptidylprolyl isomerase/peptidyl-prolyl cis-trans isomerase A (cyclophilin A)/peptidyl-prolyl cis-tı	COG0652	O	-1.94	1.8E-07	-0.70	4.6E-03
CLV04_1153	thiol:disulfide interchange protein DsbB	COG1495	O	-1.67	1.8E-07	-0.91	1.4E-04
CLV04_1195	DNA-binding CsgD family transcriptional regulator		S	-2.54	1.5E-05	-1.24	8.3E-03
CLV04_1196	transaldolase	COG0176	G	-2.04	9.3E-06	-1.84	5.1E-05
CLV04_1197	FHS family L-fucose permease-like MFS transporter	COG0738	G	-1.67	4.2E-05	-1.97	1.7E-05
CLV04_1207	putative cold-shock DNA-binding protein	COG1278	K	-4.93	4.4E-06	-2.32	6.6E-03
CLV04_1208	ribosomal protein S18 acetylase RimI-like enzyme	COG0454	K	-2.06	4.0E-05	-2.25	3.1E-05
CLV04_1209	O-acetylserine/cysteine efflux transporter	COG0697	E, G	-3.03	7.3E-07	-3.32	6.5E-07

CLV04_1210	ornithine--oxo-acid transaminase/hypothetical protein	COG4992	E	-1.56	2.7E-04	-2.65	2.3E-06
CLV04_1211	hypothetical protein			-2.24	1.3E-06	-3.03	1.6E-07
CLV04_1212	heme oxygenase-like protein			-2.58	1.4E-07	-3.18	5.9E-08
CLV04_1213	TENA/THI-4/PQQC family protein		S	-3.07	4.4E-08	-3.41	5.9E-08
CLV04_1223	polyisoprenoid-binding protein YceI	COG2353	S	-3.96	5.8E-11	-0.81	9.2E-04
CLV04_1256	regulator of protease activity HflC (stomatin/prohibitin superfamily)	COG0330	O	-1.12	2.9E-04	-0.90	2.9E-03
CLV04_1264	hypothetical protein			-1.47	3.5E-05	-0.96	2.6E-03
CLV04_1289	biopolymer transport protein ExbB	COG0811	U	-1.03	1.8E-06	-0.50	2.3E-03
CLV04_1296	Fe-S cluster biosynthesis and repair protein YggX	COG2924	P	-1.92	1.2E-07	-0.65	3.8E-03
CLV04_1299	FAD-dependent sensor of blue light		S	-1.23	3.6E-05	-0.70	6.6E-03
CLV04_1311	ubiquinone biosynthesis monooxygenase Coq7	COG2941	H	-1.07	2.8E-04	-0.84	3.5E-03
CLV04_1324	hypothetical protein	COG0339	E	-2.02	2.0E-07	-1.56	5.9E-06
CLV04_1325	DNA-binding MarR family transcriptional regulator		K	-2.62	8.8E-07	-1.31	1.2E-03
CLV04_1334	enamine deaminase RidA (YjgF/YER057c/UK114 family)	COG0251	J	-1.40	2.8E-05	-1.20	2.1E-04
CLV04_1338	stearoyl-CoA desaturase (delta-9 desaturase)	COG1398	I	-0.93	8.7E-06	-0.55	1.5E-03
CLV04_1353	3-oxoacyl-[acyl-carrier-protein] synthase II	COG0304	I	-1.73	8.8E-07	-0.90	7.0E-04
CLV04_1355	3-oxoacyl-[acyl-carrier-protein] reductase		I	-1.45	7.2E-07	-0.78	5.2E-04
CLV04_1356	[acyl-carrier-protein] S-malonyltransferase	COG0331	I	-1.15	8.7E-07	-0.69	2.1E-04
CLV04_1434	chitin binding protein	COG3397, COG3979	G	-1.03	6.0E-03	-1.10	6.0E-03
CLV04_1488	GTP-binding protein HflX	COG2262	S	-0.85	5.4E-05	-0.50	6.0E-03
CLV04_1498	nucleoside diphosphate kinase	COG0105	F	-1.43	1.8E-07	-0.93	2.4E-05
CLV04_1518	cysteine synthase	COG0031	E	-0.92	6.6E-05	-0.58	4.6E-03
CLV04_1523	4-hydroxy-3-methylbut-2-enyl diphosphate reductase	COG0761	I	-1.41	2.4E-07	-0.47	7.4E-03
CLV04_1585	LSU ribosomal protein L9P	COG0359	J	-3.85	3.9E-09	-1.34	2.0E-04
CLV04_1586	SSU ribosomal protein S18P	COG0238	J	-3.65	2.3E-08	-1.01	5.5E-03
CLV04_1588	SSU ribosomal protein S6P	COG0360	J	-2.41	1.5E-07	-0.89	2.1E-03
CLV04_1619	LSU ribosomal protein L19P	COG0335	J	-2.08	4.5E-07	-1.36	5.6E-05
CLV04_1620	tRNA (guanine37-N(1)-) methyltransferase	COG0336	J	-1.26	6.2E-05	-0.78	4.8E-03
CLV04_1622	SSU ribosomal protein S16P	COG0228	J	-1.45	1.7E-06	-0.70	2.0E-03
CLV04_1640	iron-sulfur cluster insertion protein	COG0316	C	-2.08	1.9E-08	-0.84	2.1E-04
CLV04_1642	SSU ribosomal protein S9P	COG0103	J	-3.43	1.5E-09	-1.50	1.1E-05
CLV04_1643	LSU ribosomal protein L13P	COG0102	J	-2.25	3.6E-07	-1.10	5.1E-04
CLV04_1734	hypothetical protein	COG1610	S	-2.18	4.1E-07	-1.19	3.3E-04
CLV04_1754	CDP-4-dehydro-6-deoxyglucose reductase	COG0543	C	-1.85	2.3E-07	-0.79	1.3E-03
CLV04_1771	uncharacterized protein DUF4149			-3.06	2.0E-09	-1.22	6.7E-05
CLV04_1772	transcription elongation factor GreA	COG0782	K	-2.74	3.0E-08	-1.25	1.4E-04
CLV04_1777	type II secretion system protein M (GspM)	COG3149	U	-0.97	4.1E-04	-0.92	1.2E-03
CLV04_1782	general secretion pathway protein H	COG2165	U	-1.15	1.7E-04	-0.80	5.1E-03
CLV04_1783	type II secretion system protein G (GspG)	COG2165	U	-1.25	9.0E-05	-1.00	1.1E-03
CLV04_1787	type II secretion system protein D (GspD)	COG1450	U	-0.79	2.4E-04	-0.76	5.4E-04
CLV04_1788	type II secretion system (T2SS) protein C			-0.94	7.0E-05	-0.54	9.2E-03
CLV04_1802	putative porin		M	-1.74	1.1E-05	-2.37	1.2E-06
CLV04_1803	competence protein ComEA	COG1555	L	-1.98	1.2E-06	-2.09	1.5E-06
CLV04_1823	uncharacterized protein (TIGR00255 family)	COG1561	S	-0.93	3.2E-05	-0.52	5.4E-03
CLV04_1869	DNA-binding MarR family transcriptional regulator		K	-2.90	8.6E-05	-3.21	6.3E-05
CLV04_1870	TonB family protein	COG0810	M	-2.16	5.7E-03	-3.03	6.2E-04
CLV04_1908	ferritin-like protein			-0.62	5.8E-03	-0.96	3.5E-04
CLV04_1960	flavin reductase (DIM6/NTAB) family NADH-FMN oxidoreductase RutF	COG1853	S	-1.25	8.5E-06	-0.76	1.3E-03
CLV04_1989	carbonic anhydrase/acetyltransferase-like protein (isoleucine patch superfamily)	COG0663	S	-1.36	4.4E-05	-0.81	5.5E-03
CLV04_2010	LSU ribosomal protein L27P	COG0211	J	-2.69	4.9E-08	-0.82	4.2E-03
CLV04_2032	beta-hydroxylase	COG3555	O	-0.93	5.4E-05	-1.17	1.2E-05

CLV04_2064	hypothetical protein	COG3470	P	-1.10	5.9E-03	-1.24	4.4E-03
CLV04_2065	Cupredoxin-like domain-containing protein		S	-1.46	1.5E-04	-1.05	3.7E-03
CLV04_2066	high-affinity iron transporter	COG0672	P	-1.32	2.3E-04	-1.08	1.9E-03
CLV04_2080	type IV pilus assembly protein PilX			-2.09	1.9E-04	-2.08	3.6E-04
CLV04_2081	hypothetical protein			-3.23	4.1E-06	-3.26	8.2E-06
CLV04_2082	hypothetical protein		U	-2.65	4.1E-04	-2.83	4.0E-04
CLV04_2083	pilin/secretion family protein with methylation motif	COG4970	U	-4.07	1.8E-07	-3.71	1.1E-06
CLV04_2093	arsenate reductase	COG1393	P	-0.88	4.2E-04	-0.71	3.7E-03
CLV04_2111	undecaprenyl-phosphate 4-deoxy-4-formamido-L-arabinose transferase	COG0463	M	-0.47	5.6E-03	-0.47	9.1E-03
CLV04_2151	TetR family transcriptional regulator		K	-0.70	6.5E-03	-1.34	5.6E-05
CLV04_2175	ATP synthase F1 subcomplex delta subunit	COG0712	C	-1.52	6.8E-06	-0.79	3.3E-03
CLV04_2177	F-type H+-transporting ATPase subunit c	COG0636	C	-1.33	8.5E-06	-0.62	8.1E-03
CLV04_2189	osmotically-inducible protein OsmY	COG2823	S	-1.96	2.7E-09	-0.45	3.8E-03
CLV04_2213	ATP-binding cassette subfamily B protein/ATP-binding cassette subfamily C protein/ATP-binding c	COG1132	V	-1.12	6.7E-04	-1.10	1.3E-03
CLV04_2214	ATP-binding cassette subfamily B protein/ATP-binding cassette subfamily C protein/ATP-binding c	COG1132	V	-0.94	4.7E-03	-1.21	1.2E-03
CLV04_2248	hypothetical protein		T	-2.24	1.0E-05	-1.23	3.9E-03
CLV04_2313	putative hydrolase of the HAD superfamily	COG1011	S	-1.48	5.8E-06	-1.04	3.4E-04
CLV04_2315	hypothetical protein	COG3646	K	-1.40	6.1E-06	-1.16	7.9E-05
CLV04_2336	LPS-assembly lipoprotein	COG2980	M	-1.45	3.1E-07	-0.95	4.3E-05
CLV04_2356	BirA family biotin operon repressor/biotin-[acetyl-CoA-carboxylase] ligase	COG0340, COG1654	H	-0.84	2.4E-03	-0.95	1.6E-03
CLV04_2357	rfaE bifunctional protein nucleotidyltransferase chain/domain	COG2870	M	-1.39	4.9E-05	-0.89	4.0E-03
CLV04_2408	UDP-N-acetylglucosamine 1-carboxyvinyltransferase	COG0766	M	-2.12	5.8E-08	-1.12	6.7E-05
CLV04_2422	putative MFS family arabinose efflux permease		P	-1.51	2.9E-05	-1.36	1.4E-04
CLV04_2432	demethylmenaquinone methyltransferase/2-methoxy-6-polyprenyl-1,4-benzoquinol methylase	COG0500	H	-0.99	4.6E-03	-2.47	1.9E-06
CLV04_2458	myo-inositol-1(or 4)-monophosphatase	COG0483	G	-0.66	2.8E-03	-0.64	5.9E-03
CLV04_2498	formiminoglutamase	COG0010	E	-1.72	1.9E-03	-3.58	7.1E-06
CLV04_2499	imidazolonepropionase	COG1228	E	-1.86	8.5E-04	-3.37	9.0E-06
CLV04_2565	muramoyltetrapeptide carboxypeptidase LdcA involved in peptidoglycan recycling	COG1619	V	-0.85	1.2E-03	-0.68	9.5E-03
CLV04_2566	N-acetylglutamate synthase-like GNAT family acetyltransferase		S	-1.46	8.5E-06	-0.84	2.2E-03
CLV04_2579	hypothetical protein	COG3150	S	-1.16	2.8E-03	-1.20	3.5E-03
CLV04_2580	hypothetical protein			-1.20	2.0E-04	-1.01	1.4E-03
CLV04_2597	glutathione S-transferase	COG0625	O	-2.45	5.8E-08	-1.70	4.9E-06
CLV04_2598	putative O-methyltransferase YrrM	COG4122	Q	-0.89	2.1E-03	-1.16	4.4E-04
CLV04_2599	LysR substrate binding domain-containing protein		K	-1.06	1.2E-03	-0.95	4.1E-03
CLV04_2636	pyridoxamine 5'-phosphate oxidase	COG0259	H	-1.68	3.3E-07	-0.93	2.3E-04
CLV04_2661	sulfite dehydrogenase (cytochrome) subunit SorA apoprotein	COG2041	S	-1.41	5.4E-05	-1.09	8.9E-04
CLV04_2664	5-(carboxyamino)imidazole ribonucleotide mutase	COG0041	F	-2.01	4.0E-06	-0.98	4.9E-03
CLV04_2666	TPR repeat protein			-0.94	1.5E-03	-0.87	4.4E-03
CLV04_2682	YggT family protein	COG0762	S	-1.85	1.5E-06	-0.74	8.5E-03
CLV04_2739	glyoxylase-like metal-dependent hydrolase (beta-lactamase superfamily II)	COG0491	S	-1.30	6.7E-07	-0.60	1.6E-03
CLV04_2756	glycosyltransferase involved in cell wall biosynthesis	COG0463	M	-1.17	2.7E-03	-1.34	1.5E-03
CLV04_2757	glycosyltransferase involved in cell wall biosynthesis		M	-1.87	1.5E-04	-1.56	1.1E-03
CLV04_2758	transketolase	COG3958	G	-1.18	7.4E-03	-1.48	2.5E-03
CLV04_2759	transketolase subunit A	COG3959	G	-1.49	2.0E-03	-1.58	2.0E-03
CLV04_2761	hypothetical protein			-1.30	6.5E-03	-1.42	6.0E-03
CLV04_2763	membrane fusion protein	COG0845	U	-1.46	7.8E-05	-1.40	2.0E-04
CLV04_2764	colicin V processing peptidase	COG2274	V	-1.16	9.3E-05	-1.21	1.2E-04
CLV04_2768	nucleoside-diphosphate-sugar epimerase	COG0451	G, M	-1.41	4.0E-06	-0.75	2.4E-03
CLV04_2817	LSU ribosomal protein L34P	COG0230	J	-1.44	3.1E-03	-1.51	3.5E-03
CLV04_2820	protein translocase subunit yidC	COG0706	U	-0.68	1.4E-03	-0.74	1.2E-03
CLV04_2836	rare lipoprotein A	COG0797	M	-1.18	4.9E-06	-1.60	5.8E-07

CLV04_2837	tRNA (cytidine/uridine-2'-O-)-methyltransferase	COG0219	J	-1.49	4.8E-07	-0.60	3.0E-03
CLV04_2864	rod shape-determining protein MreB	COG1077	D	-1.01	3.9E-05	-0.63	3.3E-03
CLV04_2867	aspartyl/glutamyl-tRNA(Asn/Gln) amidotransferase subunit B	COG0064	J	-0.80	2.0E-04	-0.58	4.0E-03
CLV04_2896	uncharacterized protein DUF3224		S	-1.51	7.5E-06	-0.92	1.2E-03
CLV04_2915	dipeptidyl-peptidase 7		S	-1.28	8.3E-05	-0.97	1.5E-03
CLV04_2936	ectoine hydroxylase-related dioxygenase (phytanoyl-CoA dioxygenase family)	COG5285	Q	-1.43	4.1E-04	-1.80	9.6E-05
CLV04_2941	protein translocase subunit secA	COG0653	U	-0.59	3.6E-03	-1.01	9.5E-05
CLV04_2945	glutamate--cysteine ligase		H	-1.14	1.8E-04	-1.66	1.2E-05
CLV04_2948	glutathione synthase	COG0189	H	-0.86	1.9E-04	-0.74	1.1E-03
CLV04_2949	diacylglycerol kinase	COG0818	M	-1.27	3.1E-05	-0.89	1.3E-03
CLV04_2962	DNA-binding NtrC family response regulator	COG2204	T	-0.65	4.2E-04	-0.62	1.0E-03
CLV04_2983	exodeoxyribonuclease-3	COG0708	L	-0.51	4.4E-03	-0.49	8.8E-03
CLV04_2991	nicotinamidase-related amidase	COG1335	Q	-1.69	1.0E-03	-1.42	5.9E-03
CLV04_2992	D-3-phosphoglycerate dehydrogenase	COG0111	E	-1.12	1.1E-03	-1.14	1.5E-03
CLV04_3017	type IV pilus assembly protein PilA	COG4969	U	-0.64	2.4E-03	-0.82	5.9E-04
CLV04_3018	type IV pilus assembly protein PilA	COG4969	U	-0.59	8.6E-04	-0.77	1.6E-04
CLV04_3030	translation elongation factor 1A (EF-1A/EF-Tu)	COG0050	J	-1.24	1.8E-04	-0.96	2.3E-03
CLV04_3032	protein translocase subunit secE/sec61 gamma	COG0690	U	-2.26	6.8E-08	-1.31	4.1E-05
CLV04_3033	transcription antitermination protein nusG	COG0250	K	-1.76	3.5E-05	-1.20	1.5E-03
CLV04_3034	LSU ribosomal protein L11P	COG0080	J	-1.78	4.5E-07	-1.35	1.5E-05
CLV04_3035	LSU ribosomal protein L1P	COG0081	J	-1.60	1.5E-06	-1.33	2.0E-05
CLV04_3037	LSU ribosomal protein L10P	COG0244	J	-2.98	6.7E-09	-1.25	6.0E-05
CLV04_3038	LSU ribosomal protein L12P	COG0222	J	-3.14	9.8E-08	-1.14	1.7E-03
CLV04_3046	LSU ribosomal protein L3P	COG0087	J	-1.82	1.4E-06	-0.95	9.4E-04
CLV04_3047	LSU ribosomal protein L4P	COG0088	J	-2.28	4.7E-07	-1.12	6.4E-04
CLV04_3048	LSU ribosomal protein L23P	COG0089	J	-2.82	7.0E-06	-1.33	6.2E-03
CLV04_3049	LSU ribosomal protein L2P	COG0090	J	-2.49	3.1E-07	-1.41	1.4E-04
CLV04_3050	SSU ribosomal protein S19P	COG0185	J	-2.47	5.6E-08	-1.47	1.7E-05
CLV04_3051	LSU ribosomal protein L22P	COG0091	J	-2.46	9.9E-08	-1.42	4.1E-05
CLV04_3052	SSU ribosomal protein S3P	COG0092	J	-2.23	5.5E-07	-1.26	2.4E-04
CLV04_3053	LSU ribosomal protein L16P	COG0197	J	-2.20	1.8E-07	-1.19	1.2E-04
CLV04_3055	SSU ribosomal protein S17P	COG0186	J	-3.10	1.3E-07	-0.96	7.2E-03
CLV04_3056	LSU ribosomal protein L14P	COG0093	J	-2.85	6.5E-08	-1.59	4.9E-05
CLV04_3057	LSU ribosomal protein L24P	COG0198	J	-3.84	1.5E-06	-2.02	1.2E-03
CLV04_3058	LSU ribosomal protein L5P	COG0094	J	-3.22	3.4E-07	-1.95	8.4E-05
CLV04_3059	SSU ribosomal protein S14P	COG0199	J	-3.12	7.8E-08	-2.02	1.3E-05
CLV04_3060	SSU ribosomal protein S8P	COG0096	J	-3.18	3.6E-08	-2.20	2.7E-06
CLV04_3061	LSU ribosomal protein L6P	COG0097	J	-3.28	9.9E-08	-1.89	4.1E-05
CLV04_3062	LSU ribosomal protein L18P	COG0256	J	-3.34	3.8E-08	-1.90	2.1E-05
CLV04_3063	SSU ribosomal protein S5P	COG0098	J	-3.68	5.0E-08	-1.95	4.4E-05
CLV04_3064	LSU ribosomal protein L30P	COG1841	J	-3.28	1.9E-07	-1.79	2.3E-04
CLV04_3065	LSU ribosomal protein L15P	COG0200	J	-2.99	1.7E-09	-1.61	2.2E-06
CLV04_3066	protein translocase subunit secY/sec61 alpha	COG0201	U	-3.27	9.4E-10	-1.59	2.6E-06
CLV04_3069	SSU ribosomal protein S13P	COG0099	J	-2.49	9.9E-08	-1.10	4.1E-04
CLV04_3070	SSU ribosomal protein S11P	COG0100	J	-2.67	2.2E-06	-1.05	9.0E-03
CLV04_3071	SSU ribosomal protein S4P	COG0522	J	-2.25	1.3E-07	-1.07	2.8E-04
CLV04_3072	DNA-directed RNA polymerase subunit alpha	COG0202	K	-3.08	7.8E-09	-1.46	2.2E-05
CLV04_3073	LSU ribosomal protein L17P	COG0203	J	-3.02	4.3E-10	-1.67	4.6E-07
CLV04_3094	putative acyl-CoA dehydrogenase	COG1960	I	-1.56	1.2E-03	-1.30	7.3E-03
CLV04_3095	ornithine cyclodeaminase	COG2423	E	-2.56	5.8E-06	-2.16	5.6E-05
CLV04_3097	ParB-like nuclease family protein	COG1475	K	-3.34	8.8E-07	-2.08	1.9E-04

CLV04_3098	adenylyl-sulfate kinase	COG0529	P	-2.32	1.1E-04	-1.62	3.4E-03
CLV04_3100	putative NAD(P)/FAD-binding protein YdhS	COG4529	S	-2.10	4.5E-05	-1.57	9.9E-04
CLV04_3101	amino acid adenylation domain-containing protein		Q	-1.55	1.2E-04	-1.29	1.0E-03
CLV04_3102	sulfotransferase family protein			-1.64	1.1E-05	-1.23	2.9E-04
CLV04_3104	methyltransferase family protein		S	-1.70	1.3E-05	-1.26	3.4E-04
CLV04_3105	hypothetical protein			-1.44	1.1E-03	-1.20	6.2E-03
CLV04_3160	LysR family transcriptional regulator		K	-1.80	1.4E-07	-0.53	9.2E-03
CLV04_3178	ATP-binding cassette subfamily B multidrug efflux pump	COG1132	V	-2.01	1.2E-04	-4.94	6.5E-08
CLV04_3185	GDSL-like lipase/acylhydrolase family protein	COG2755	E	-0.91	8.8E-03	-1.08	4.3E-03
CLV04_3195	hypothetical protein	COG0012	J	-1.51	2.9E-06	-0.76	2.6E-03
CLV04_3197	amino acid ABC transporter substrate-binding protein (PAAT family)	COG0834	E	-1.04	5.3E-03	-1.37	1.2E-03
CLV04_3266	type VI secretion system protein ImpK	COG3455	S	-1.45	4.9E-06	-0.65	8.5E-03
CLV04_3270	type VI secretion system protein ImpL	COG3523	S	-0.66	2.9E-04	-0.86	4.9E-05
CLV04_3271	type VI secretion system protein ImpM	COG3913	S	-1.53	7.3E-06	-1.43	2.8E-05
CLV04_3272	type VI secretion system protein ImpB	COG3516	S	-2.05	1.7E-05	-1.26	2.1E-03
CLV04_3273	type VI secretion system protein ImpC	COG3517	S	-0.68	1.6E-04	-1.06	4.9E-06
CLV04_3274	type VI secretion system secreted protein Hcp	COG3157	S	-1.48	1.5E-05	-0.98	1.0E-03
CLV04_3276	type VI secretion system secreted protein VgrG	COG4253	S	-0.98	1.0E-04	-1.01	1.4E-04
CLV04_3280	type VI secretion system protein ImpH	COG3520	S	-0.61	4.0E-03	-0.62	5.6E-03
CLV04_3281	hypothetical protein			-1.11	3.4E-04	-0.76	8.9E-03
CLV04_3283	hypothetical protein			-0.77	1.1E-03	-0.77	1.7E-03
CLV04_3285	type VI secretion system protein ImpA	COG3515	S	-0.72	2.7E-04	-0.66	9.9E-04
CLV04_3349	uncharacterized protein DUF4124			-2.69	1.1E-06	-1.62	3.4E-04
CLV04_3351	uncharacterized protein (DUF2147 family)	COG4731	S	-1.52	3.1E-07	-0.56	4.3E-03
CLV04_3361	NADH dehydrogenase subunit A	COG0838	C	-1.51	2.2E-05	-0.77	9.0E-03
CLV04_3363	NADH dehydrogenase subunit C	COG0852	C	-1.08	2.3E-05	-0.64	3.1E-03
CLV04_3364	NADH dehydrogenase subunit D	COG0649	C	-0.56	4.8E-03	-0.59	5.2E-03
CLV04_3365	NADH dehydrogenase subunit E	COG1905	C	-1.29	1.9E-06	-0.82	2.5E-04
CLV04_3366	NADH dehydrogenase subunit F	COG1894	C	-0.81	6.9E-04	-0.90	5.5E-04
CLV04_3367	NADH dehydrogenase subunit G	COG1034	C	-0.67	2.3E-03	-0.83	7.2E-04
CLV04_3368	NADH dehydrogenase subunit H	COG1005	C	-1.24	2.8E-05	-1.07	1.9E-04
CLV04_3369	NADH dehydrogenase subunit I	COG1143	C	-1.60	2.5E-06	-1.10	1.7E-04
CLV04_3370	NADH dehydrogenase subunit J	COG0839	C	-1.85	3.5E-07	-1.39	1.2E-05
CLV04_3371	NADH dehydrogenase subunit K	COG0713	C	-1.24	3.8E-05	-1.00	5.0E-04
CLV04_3372	NADH dehydrogenase subunit L	COG1009	C	-0.85	2.8E-04	-1.05	7.8E-05
CLV04_3374	NADH dehydrogenase subunit N	COG1007	C	-0.98	1.1E-03	-1.50	5.4E-05
CLV04_3375	uncharacterized protein DUF2818		S	-0.95	3.2E-03	-1.37	2.6E-04
CLV04_3376	ribonuclease I	COG3719	J	-1.54	1.8E-04	-1.03	7.2E-03
CLV04_3394	Tir chaperone family protein CesT			-1.69	7.2E-05	-1.03	7.0E-03
CLV04_3406	biotin carboxylase /acetyl-CoA carboxylase carboxyltransferase subunit alpha	COG0439	I	-0.68	4.8E-04	-0.59	2.2E-03
CLV04_3407	biotin carboxyl carrier protein	COG0511	I	-1.88	1.4E-07	-0.76	1.2E-03
CLV04_3472	cytochrome c5	COG3245	C	-1.13	6.2E-03	-1.51	1.2E-03
CLV04_3473	FAD-linked oxidoreductase	COG0277	C	-1.00	9.7E-03	-1.46	1.1E-03
CLV04_3525	co-chaperone protein HscB	COG1076	O	-1.13	3.3E-03	-1.17	4.1E-03
CLV04_3527	FeS assembly scaffold apoprotein IscU /modular FeS cluster scaffolding protein NifU	COG0822	C	-1.82	1.5E-05	-0.96	6.3E-03
CLV04_3529	BadM/Rrf2 family transcriptional regulator	COG1959	K	-0.97	7.1E-03	-1.33	1.2E-03
CLV04_3540	thioredoxin	COG0526	O	-2.18	7.0E-07	-1.11	1.0E-03
CLV04_3541	glutathione peroxidase	COG0386	O	-1.55	9.1E-06	-1.72	6.8E-06
CLV04_3651	hypothetical protein	COG3022	S	-0.96	5.1E-05	-0.68	1.9E-03
CLV04_3714	ProQ/FINO family protein		S	-1.99	1.2E-07	-1.19	4.5E-05
CLV04_3717	nicotinamidase-related amidase	COG1335	Q	-1.11	9.6E-04	-1.13	1.4E-03

CLV04_3722	organic hydroperoxide reductase OsmC/OhrA	COG1764	O	-1.43	9.0E-07	-0.72	1.2E-03
CLV04_3723	protein disulfide-isomerase	COG0526	O	-1.49	4.5E-07	-1.25	6.6E-06
CLV04_3736	protein translocase subunit secF	COG0341	U	-2.11	3.8E-07	-1.12	3.3E-04
CLV04_3737	preprotein translocase subunit SecD	COG0342	U	-0.83	6.7E-04	-0.86	9.2E-04
CLV04_3738	protein translocase subunit yajC	COG1862	U	-2.84	3.8E-08	-1.07	8.2E-04
CLV04_3741	Ser-tRNA(Thr) hydrolase /threonyl-tRNA synthetase	COG0441	J	-0.74	2.1E-04	-0.49	7.6E-03
CLV04_3743	LSU ribosomal protein L35P	COG0291	J	-2.62	2.0E-06	-1.09	7.0E-03
CLV04_3744	LSU ribosomal protein L20P	COG0292	J	-3.21	3.6E-08	-1.08	1.4E-03
CLV04_3745	phenylalanyl-tRNA synthetase alpha subunit	COG0016	J	-1.25	1.1E-05	-1.25	2.1E-05
CLV04_3746	phenylalanyl-tRNA synthetase beta subunit	COG0072, COG0073	J	-1.15	1.2E-06	-1.33	6.9E-07
CLV04_3775	CRISPR-associated Cas3 family helicase	COG1203	L	-1.65	1.5E-06	-1.08	1.9E-04
CLV04_3777	CRISPR-associated Cse2 family protein		L	-2.24	5.1E-06	-1.99	3.6E-05
CLV04_3779	CRISPR-associated Cas5e family protein		L	-1.77	1.7E-05	-1.62	7.7E-05
CLV04_3780	CRISPR-associated Cse3 family protein		L	-2.34	4.5E-07	-1.71	2.8E-05
CLV04_3797	LytTR family two component transcriptional regulator	COG3279	T	-1.09	4.4E-05	-0.64	5.6E-03
CLV04_3798	hypothetical protein	COG2972	T	-1.51	1.3E-07	-1.08	8.3E-06
CLV04_3837	translation initiation factor 2 (bIF-2)	COG0532	J	-1.05	5.5E-05	-0.77	1.3E-03
CLV04_3842	polyribonucleotide nucleotidyltransferase	COG1185	J	-0.54	9.0E-03	-0.75	1.5E-03
CLV04_3866	arginine succinyltransferase	COG3138	E	-0.69	3.1E-03	-0.87	9.8E-04
CLV04_3883	ATP-dependent helicase HrpA	COG1643	L	-0.89	5.6E-04	-1.43	1.5E-05
CLV04_3890	signal transduction histidine kinase		T	-1.38	9.4E-05	-1.04	1.9E-03
CLV04_3891	histidine kinase	COG4585	T	-0.76	5.2E-03	-0.87	3.5E-03
CLV04_3911	short chain enoyl-CoA hydratase	COG1024	I	-1.33	2.0E-06	-0.62	4.1E-03
CLV04_3936	adenosylcobyric acid synthase (glutamine-hydrolysing)	COG1492	H	-0.73	2.2E-03	-0.93	5.0E-04
CLV04_3961	K+-transporting ATPase ATPase B chain	COG2216	P	-1.23	1.8E-05	-0.84	9.2E-04
CLV04_3962	K+-transporting ATPase ATPase A chain	COG2060	P	-0.75	2.0E-03	-0.73	3.8E-03
CLV04_3968	N-acetylglutamate synthase-like GNAT family acetyltransferase		S	-2.41	2.2E-04	-2.45	3.2E-04
CLV04_3979	methyltransferase family protein		S	-3.25	1.8E-09	-2.13	3.6E-07
CLV04_4010	deoxyadenosine/deoxycytidine kinase	COG1428	F	-1.82	1.1E-06	-0.72	8.4E-03
CLV04_4039	D-alpha,beta-D-heptose 1,7-bisphosphate phosphatase	COG0241	E	-1.34	2.4E-06	-0.81	5.2E-04
CLV04_4066	hypothetical protein			-1.63	2.6E-05	-0.94	4.9E-03
CLV04_4067	hypothetical protein			-0.97	1.0E-03	-0.93	2.2E-03
CLV04_4094	asparagine synthase (glutamine-hydrolysing)	COG0367	E	-1.58	3.3E-05	-1.64	4.3E-05
CLV04_4129	fucose-binding lectin II (PA-IIL)		S	-2.22	7.7E-06	-2.20	1.7E-05
CLV04_4131	cysteinyl-tRNA synthetase	COG0215	J	-1.14	3.5E-05	-0.70	3.5E-03
CLV04_4132	LSU ribosomal protein L31P	COG0254	J	-3.40	1.7E-09	-2.25	2.4E-07
CLV04_4154	pseudolysin/vibriolysin	COG3227	E	-2.97	1.0E-07	-3.49	6.5E-08
CLV04_4157	RimJ/RimL family protein N-acetyltransferase		S	-1.73	4.3E-05	-1.37	7.3E-04
CLV04_4182	chemotaxis protein MotB	COG1360	N	-0.46	7.0E-03	-0.75	3.4E-04
CLV04_4186	ribosomal large subunit pseudouridine synthase C	COG0564	J	-0.76	4.2E-03	-0.85	2.9E-03
CLV04_4190	hypothetical protein	COG1099	S	-0.84	1.5E-03	-1.79	2.0E-06
CLV04_4195	ferritin-like protein			-1.18	5.5E-05	-1.94	7.2E-07
CLV04_4196	hypothetical protein			-0.86	2.9E-03	-1.94	3.6E-06
CLV04_4208	ribosomal protein S18 acetylase RimI-like enzyme		S	-1.24	1.9E-04	-1.20	4.4E-04
CLV04_4242	single-strand binding protein	COG0629	L	-2.71	3.2E-09	-0.75	1.1E-03
CLV04_4246	catechol 2,3-dioxygenase-like lactoylglutathione lyase family enzyme			-2.16	2.9E-08	-0.61	6.0E-03
CLV04_4324	RND family efflux transporter MFP subunit		S	-1.24	3.3E-06	-0.80	4.1E-04
CLV04_4325	HAE1 family hydrophobic/amphiphilic exporter-1	COG0841	V	-0.40	8.9E-03	-0.65	5.2E-04
CLV04_4365	uncharacterized Zn-binding protein involved in type VI secretion	COG4104	S	-4.30	4.4E-07	-3.04	4.0E-05
CLV04_4366	hypothetical protein			-4.23	3.5E-09	-2.58	1.9E-06
CLV04_4388	hypothetical protein			-2.94	1.2E-06	-2.19	4.1E-05

CLV04_4422	threonine dehydrogenase-like Zn-dependent dehydrogenase	COG1063	C	-1.50	7.5E-06	-1.83	2.1E-06
CLV04_4435	signal peptidase I	COG0681	U	-1.66	7.3E-07	-0.87	6.4E-04
CLV04_4452	ribosome biogenesis GTPase	COG1162	S	-5.41	8.4E-11	-5.67	4.9E-10
CLV04_4453	uncharacterized membrane protein YoaT (DUF817 family)	COG3739	S	-3.65	1.2E-10	-3.64	8.1E-10
CLV04_4473	histidyl-tRNA synthetase	COG0124	J	-3.50	1.8E-09	-1.05	9.2E-04
Genes upregulated by translation inhibition moduladed by air system							
CLV04_0472	dipeptidase D	COG2195	E	-0.57	1.8E-03	-0.52	5.8E-03
CLV04_0474	putative Zn-dependent protease	COG0312	S	-1.12	3.6E-04	-0.89	3.4E-03
CLV04_0655	non-ribosomal peptide synthase protein (TIGR01720 family)/amino acid adenylation domain-cont	COG1020	Q	-4.27	8.6E-08	-5.03	5.9E-08
CLV04_0656	polyketide-type polyunsaturated fatty acid synthase PfaA	COG3321	Q	-3.70	1.3E-06	-4.36	6.5E-07
CLV04_0657	PfaB family protein	COG0764	Q	-3.10	3.7E-06	-4.06	6.5E-07
CLV04_0658	PfaD family protein	COG2070	S	-2.87	1.3E-05	-3.87	1.5E-06
CLV04_0659	medium-chain acyl-[acyl-carrier-protein] hydrolase	COG3208	Q	-3.38	6.3E-06	-3.36	1.4E-05
CLV04_0660	4'-phosphopantetheinyl transferase	COG2091	H	-2.64	1.3E-04	-3.10	5.6E-05
CLV04_0661	polysaccharide pyruvyl transferase WcaK-like protein			-1.64	1.0E-04	-2.15	1.6E-05
CLV04_1214	hypothetical protein			-1.07	9.6E-04	-1.00	2.6E-03
CLV04_1215	violacein biosynthesis enzyme VioE			-3.07	5.0E-07	-3.68	2.2E-07
CLV04_1216	anthraniloyl-CoA monooxygenase	COG0654	C, H	-3.79	7.9E-09	-3.84	4.5E-08
CLV04_1217	kynurenine 3-monooxygenase	COG0654	H	-4.28	7.1E-08	-4.29	1.8E-07
CLV04_1218	iminophenyl-pyruvate dimer synthase VioB			-4.14	3.1E-07	-4.01	9.1E-07
CLV04_1219	monoamine oxidase		S	-6.10	3.6E-10	-4.85	4.5E-08
CLV04_2088	hypothetical protein			-0.93	5.0E-03	-1.08	2.9E-03
CLV04_2204	adenosine deaminase		F	-0.92	2.1E-04	-1.22	2.9E-05
CLV04_2269	hypothetical protein	COG1896	S	-2.75	1.6E-07	-2.26	2.6E-06
CLV04_2291	phosphoribosylamine--glycine ligase	COG0151	F	-0.73	3.1E-03	-0.68	8.2E-03
CLV04_2493	hypothetical protein			-1.80	5.4E-06	-1.76	1.4E-05
CLV04_2537	carbohydrate ABC transporter substrate-binding protein (CUT1 family)		G	-0.96	9.0E-03	-1.58	3.5E-04
CLV04_2637	pseudolysin	COG3227	E	-1.51	1.6E-03	-2.90	9.0E-06
CLV04_2753	hypothetical protein			-1.68	1.1E-05	-0.96	2.2E-03
CLV04_2839	biotin synthase	COG0502	H	-2.87	4.9E-09	-2.08	3.4E-07
CLV04_2850	aromatic amino acid:proton symporter (AAT family)	COG1113	E	-0.97	3.9E-04	-0.84	2.1E-03
CLV04_3096	cysteine synthase A	COG0031	E	-2.74	1.5E-06	-2.19	2.7E-05
CLV04_3159	cviR	COG2771	K	-0.62	1.2E-03	-0.81	2.4E-04
CLV04_3520	fatty acid desaturase	COG3239	I	-0.77	2.5E-03	-1.96	7.0E-07
CLV04_3521	diaminopimelate decarboxylase	COG0019	E	-0.94	9.5E-04	-1.71	9.1E-06
CLV04_3776	CRISPR-associated Cse1 family protein		L	-1.99	4.5E-07	-1.78	3.3E-06
CLV04_3778	CRISPR-associated Cse4 family protein		L	-1.56	5.7E-06	-1.54	1.4E-05
CLV04_4098	phenazine biosynthesis protein phzE	COG0512	E, H	-2.48	2.4E-06	-1.22	2.3E-03

Table supplement 2. Differential gene expression values of the genes identified in the genetic screen.

		WT No Antibiotic VS Spectinomycin		WT No Antibiotic VS Tetracycline		*airR* No Antibiotic VS Spectinomycin		*airR* No Antibiotic VS Tetracycline	
Gene ID	Predicted Function	Log_2(Fold change)	P Value	Log_2(Fold change)	P Value	Log_2(Fold change)	P Value	Log_2(Fold change)	P Value
Conserved response									
CLV04_2302	Oxidoreductase molybdopterin binding domain protein	-0.57	5.3E-02	-0.32	3.3E-01	-0.75	1.8E-02	-0.64	5.9E-02
CLV04_2301	Sensor histidine kinase	-0.14	5.0E-01	-0.01	9.8E-01	-0.29	1.7E-01	-0.27	2.6E-01
CLV04_3834	Long chain fatty-acid CoA ligase	0.02	8.9E-01	**-0.47**	**2.9E-03**	0.23	7.6E-02	**-0.41**	**7.9E-03**
CLV04_1656	Phosphoenolpyruvate synthase	0.48	2.5E-02	-0.05	8.6E-01	0.34	1.0E-01	-0.03	9.0E-01
Variable response									
CLV04_2730	SAM-dependent methyltransferase	0.22	1.9E-01	0.17	3.9E-01	**-0.47**	**9.3E-03**	-0.17	3.6E-01
CLV04_2412	Transcriptional repressor *cdeR*	0.55	1.5E-02	-0.04	8.9E-01	**-0.56**	**1.1E-02**	0.25	2.9E-01
CLV04_1292	Phosphoglyceromutase	**0.41**	**8.5E-03**	0.08	6.2E-01	0.14	3.3E-01	0.02	8.9E-01
CLV04_2695	Phosphoglycerate kinase	-0.30	2.2E-01	0.35	1.9E-01	-0.13	6.1E-01	0.25	3.5E-01
CLV04_1869	MarR family transcriptional regulator	**-2.90**	**8.6E-05**	**-3.21**	**6.3E-05**	**-2.95**	**6.3E-05**	**-2.51**	**6.2E-04**
CLV04_3464	GntR family transcriptional regulator	0.47	2.71E-02	0.44	5.4E-02	-0.19	3.2E-01	0.07	7.6E-01
CLV04_3178	Multidrug ABC transporter ATP-binding protein	**-2.01**	**1.2E-04**	**-4.94**	**6.5E-08**	**-3.10**	**1.6E-06**	**-4.75**	**1.7E-07**
CLV04_1011	Enoyl-CoA hydratase	**2.93**	**8.6E-08**	**2.53**	**6.5E-07**	**2.86**	**7.1E-08**	**2.21**	**2.3E-06**

Table supplement 3. Genes differentially expressed between *C. violaceum* ATCC31532 WT and airR mutant in the absence of antibiotics.

				No Antibiotic WT VS *airR*	
Gene ID	Predicted Function	COGs ID	COG Category	Log_2(Fold change)	P Value
CLV04_0653	amino acid adenylation domain-containing protein	COG3321	Q	1.84	1.1E-02
CLV04_0654	amino acid adenylation domain-containing protein	COG0318, COG1020	Q	2.21	1.0E-02
CLV04_0655	non-ribosomal peptide synthase protein (TIGR01720 family)/amino acid adenylation domain-c	COG1020	Q	2.33	4.0E-03
CLV04_0656	polyketide-type polyunsaturated fatty acid synthase PfaA	COG3321	Q	2.68	3.9E-03
CLV04_0657	PfaB family protein	COG0764	Q	2.88	1.8E-03
CLV04_0658	PfaD family protein	COG2070	S	2.83	5.1E-03
CLV04_0661	polysaccharide pyruvyl transferase WcaK-like protein			2.08	1.8E-03
CLV04_2297	nicotinamidase-related amidase	COG1335	Q	-1.38	9.8E-03
CLV04_2298	MarR family transcriptional regulator	COG1846	K	-1.45	1.2E-03
CLV04_2785	TetR family transcriptional regulator		K	1.23	4.3E-03
CLV04_4095	cytochrome c		S	2.20	9.8E-03
CLV04_4096	p-hydroxybenzoate 3-monooxygenase	COG0654	Q	2.79	1.2E-03
CLV04_4097	GMP synthase (glutamine-hydrolysing)	COG0518	F	2.36	2.2E-03
CLV04_4099	glutathione S-transferase	COG0625	O	1.28	4.8E-02
CLV04_4100	glutamate racemase	COG0796	M	1.23	2.6E-02

Table supplement 4. Primers used in this study.

Name	Sequence
KanTopo_MluIFor	CACCACGCGTACAGCAAGCGAACCGGAATTG
KanTopo_MluIRev	ACACGCGTCTCATGAGCGGATACATATTTGAATG
GenPATseq1	CTTGGATGCCCGAGGCATAG
GenPATseq2	CTGTACAAAAAAACAGTCATAACAAGCCATG
AR1A	GGCCACGCGTCGACTAGTACNNNNNNNNNNGTAAT
AR1B	GGCCACGCGTCGACTAGTACNNNNNNNNNNGATGC
AR2	GGCCACGCGTCGACTAGTAC
MuCv0535/6_Afor	CACCACATGTGCTGCCGCTTTACCGTTGAC
MuCv0535/6_Arev	CGCGAATTGGCTTGAAACCGATCAGCATGCCATTTCGCCTCCCGCCGA
MuCv0535/6_Bfor	TCGGCGGGAGGCGAAATGGCATGCTGATCGGTTTCAAGCCAATTCGCG
MuCv0535/6_Brev	TAACATGTCGGCAACCAAGCCATGTCATG
pACYC184Cm_For	TAGCATGCGTTTTTATCAGGCTCTGGGAGGC
pACYC184Cm_Rev	CACCGCATGCGATAGAAACAGAAGCCACTGGAGC
pJN105Mob_For	TAGGCGCGCCTGTGGTCAAGCTCGTGGGC
pJN105Mob_Rev	CACCGGCGCGCCCAATTCGTTCAAGCCGAGATCGGC
CV1055_For	CACCTCTAGAAGGAGGGTTTTGCCATGCCTTG
CV1055_Rev	CGAGCTCTTAGAGCACGCGGGTAAGCAG
CviI_For	CACCTCTAGAAGGAGGCTTGAGTGAAAAAGTTCTAC
CviI_Rev	CGAGCTCTCAATGCGAATAATCGTACTCACGCC
CviR_For	CACCTCTAGACAAGGAAGACTCGCTCATGGTGATCTC
CviR_Rev	CGAGCTCTCATTCGTTCGCTACGGTCGAGG
CV0536_For	CACCTCTAGACATCGTGGTGCGTTGATGAGAATTCC
CV0536_Rev	CCGAGCTCTCAGACCAGCTCAACCGGC
CV0535/6_For	CACCTCTAGAGAATCGGCGGGAGGCGAAATGA
CviR_For	CACCTCTAGACAAGGAAGACTCGCTCATGGTGATCTC
CviR_Rev	CGAGCTCTCATTCGTTCGCTACGGTCGAGG
RTCvvioSFor	GCCTTGCATCACCCGCAG
RTCvvioSRev	TGATCCTGGCCGGCCAATTG
RTCvcviRFor	CATGGCCGGTCACATCGAGAC
RTCvcviRRev	CAGTCGCTGGGGTAGCTGAC
RTdnaGFor	TCGCTGGAGCAACTGATGCAAATG
RTdnaGRev	TGGTAGTTGGCGGTGATCGC

Table supplement 5. Chromobacterium spp. genomes used for phylogenetic reconstruction.

Name	Strain Name	GenBank Assembly accession
Chromobacterium vaccinii 21-1	211	CP017707.1
Chromobacterium violaceum 16-454	16454	MUKS00000000.1
Chromobacterium violaceum 16-419A	16419A	MUKQ00000000.1
Chromobacterium violaceum 16-419B	16419B	MUKR00000000.1
Chromobacterium violaceum ATCC12472	ATCC12472	AE016825.1
Chromobacterium violaceum ATCC31532	ATCC315322	PKBZ00000000.1
Chromobacterium sp. ATCC 53434	ATCC53434	CP025429.1
Chromobacterium sp. C-61	C61	CAEE00000000.1
Chromobacterium aquaticum CC-SEYA-1	CCSEYA1	MQZY00000000.1
Chromobacterium violaceum strain CV1192	CV1192	CP024028.1
Chromobacterium violaceum strain CV1197	CV1197	CP024029.1
Chromobacterium haemolyticum DSM 19808	DSM19808	JONK00000000.1
Chromobacterium amazonense DSM26508	DSM26508	MKCR00000000.1
Chromobacterium subtsugae F49	F49	JWJN00000000.1
Chromobacterium sp. F49	F492	LQNP00000000.1
Chromobacterium violaceum GHPS1	GHPS1	NHOO00000000.1
Chromobacterium violaceum GN5	GN5	JWPW00000000.1
Chromobacterium haemolyticum H3973	H3973	MUKT00000000.1
Chromobacterium haemolyticum H4137	H4137	MUKU00000000.1
Chromobacterium haemolyticum H5244	H5244	MUKV00000000.1
Chromobacterium violaceum H5524	H5524	MUKW00000000.1
Chromobacterium violaceum H5525	H5525	MUKX00000000.1
Chromobacterium sphagni IIBBL 14B-1	IIBBL14B1	MKCT00000000.1
Chromobacterium sphagni IIBBL 37-2	IIBBL372	MKCS00000000.1
Chromobacterium violaceum L_1B5_1	L1B51	JYGI00000000.1
Chromobacterium sp. LK1	LK1	LDUI00000000.1
Chromobacterium sp. LK11	LK11	LDUR00000000.1
Chromobacterium violaceum LK15	LK15	LDUT00000000.1
Chromobacterium violaceum LK17	LK17	LDUU00000000.1
Chromobacterium violaceum LK30	LK30	LDUX00000000.1
Chromobacterium violaceum LK6	LK6	LDUM00000000.1
Chromobacterium pseudoviolaceum LMG 3953	LMG3953	MQZX00000000.1
Chromobacterium subtsugae MWU12-2387	MWU122387	MQZZ00000000.1
Chromobacterium sp. MWU13-2610	MWU132610	PPTF00000000.1
Chromobacterium sp. MWU14-2602	MWU142602	PQWB00000000.1
Chromobacterium vaccinii MWU205	MWU205	JZJL00000000.1
Chromobacterium subtsugae MWU2387	MWU2387	LCWR00000000.1
Chromobacterium subtsugae MWU2576	MWU2576	LCWQ00000000.1
Chromobacterium subtsugae MWU2920	MWU2920	LCWP00000000.1
Chromobacterium vaccinii MWU328	MWU328	JZJJ00000000.1
Chromobacterium subtsugae MWU3535	MWU3525	LCWO00000000.1
Chromobacterium piscinae ND17	ND17	JTGE00000000.1
Chromobacterium subtsugae PRAA4-1	PRAA41	JYKA00000000.1
Chromobacterium haemolyticum T124	T124	JRFR00000000.1

Table supplement 6. Genes expressed differentially in response to streptomycin and tetracycline that are modulated by airR.

				WT No Antibiotic VS Spectinomycin		WT No Antibiotic VS Tetracycline		*airR* No Antibiotic VS Spectinomycin		*airR* No Antibiotic VS Tetracycline		Tetracycline WT VS *airR*		Spectinomycin WT VS *airR*	
Gene ID	Predicted Function	COGs ID	COG Category	Log_2(Fold change)	P Value	Log_2(Fold change)	P Value	Log_2(Fold change)	P Value	Log_2(Fold change)	P Value	Log_2(Fold change)	P Value	Log_2(Fold change)	P Value
Genes downregulated at translation inhibition moduladed by *air* system															
CLV04_0005	hypothetical protein			1.78	1.3E-04	1.86	1.7E-04	-2.00	5.3E-06	-0.60	7.6E-02	-2.17	5.6E-04	-3.49	3.4E-07
CLV04_0010	EAL domain-containing protein (putative c-di-GMP-specific phosphodiesterase class I)	COG2200	T	0.85	1.1E-03	0.67	8.3E-03	-0.36	7.7E-02	0.13	6.1E-01	-0.61	7.7E-02	-1.27	1.3E-04
CLV04_0012	type 4 prepilin peptidase 1	COG1989	O	1.35	1.2E-04	1.70	3.5E-05	-0.25	3.3E-01	0.43	1.4E-01	-0.74	1.2E-01	-1.08	2.0E-03
CLV04_0013	hypothetical protein			1.47	1.2E-04	1.10	1.7E-03	-2.21	4.4E-07	-0.98	2.6E-03	-1.64	5.9E-04	-3.24	7.9E-08
CLV04_0062	alcohol dehydrogenase	COG1454	C	2.63	2.1E-03	2.32	7.8E-03	1.03	1.6E-01	2.18	1.2E-02	-0.36	9.3E-01	-1.82	2.3E-02
CLV04_0330	L-lysine exporter family protein LysE/ArgO	COG1279	E	1.43	6.9E-05	1.48	1.0E-04	-0.46	5.7E-02	0.61	3.1E-02	-0.87	4.3E-02	-1.90	1.8E-05
CLV04_0508	hypothetical protein			2.01	1.1E-05	1.36	4.1E-04	0.62	3.5E-02	0.80	1.7E-02	-0.13	9.6E-01	-0.96	9.8E-03
CLV04_0571	single-strand binding protein	COG0629	L	2.56	2.7E-05	1.80	5.8E-04	0.11	7.8E-01	0.83	4.6E-02	-0.89	2.5E-01	-2.38	2.2E-04
CLV04_0794	hypothetical protein	COG0438	M	1.06	4.2E-03	1.15	4.0E-03	0.27	3.9E-01	0.69	5.5E-02	-0.41	6.8E-01	-0.74	3.7E-02
CLV04_0827	succinylglutamate desuccinylase	COG2988	E	1.01	4.1E-04	0.72	6.7E-03	0.17	4.4E-01	0.38	1.2E-01	-0.17	8.7E-01	-0.66	1.2E-02
CLV04_0942	chemotaxis protein MotB	COG1360	N	0.92	6.8E-04	0.89	1.4E-03	-0.15	4.9E-01	0.46	5.9E-02	-0.27	6.9E-01	-0.91	1.7E-03
CLV04_0944	RNA polymerase sigma-28 (SigD/FliA/WhiG) subunit	COG1191	K	1.80	5.5E-04	2.62	7.5E-05	0.26	5.1E-01	1.19	1.1E-02	-1.45	5.4E-02	-1.56	3.3E-03
CLV04_0949	flagellar hook-associated protein 2	COG1345	N	2.35	3.6E-07	3.37	6.5E-08	1.31	5.9E-05	2.09	3.5E-06	-1.65	5.9E-04	-1.40	2.2E-04
CLV04_0957	flagellar motor switch protein FliN/FliY	COG1886	N	1.24	1.4E-03	1.69	2.8E-04	-0.76	9.4E-03	0.57	8.8E-02	-1.40	1.0E-02	-2.29	1.9E-05
CLV04_1181	undecaprenyl-diphosphatase	COG3038	C	0.83	1.4E-03	0.79	3.1E-03	0.13	5.7E-01	0.36	1.5E-01	0.05	9.8E-01	-0.22	3.2E-01
CLV04_1182	cytochrome b561		S	0.84	5.3E-04	0.65	5.1E-03	0.16	4.1E-01	0.11	6.5E-01	-0.13	8.9E-01	-0.26	2.0E-01
CLV04_1368	diguanylate cyclase/phosphodiesterase		T	1.37	2.5E-05	1.00	5.6E-04	0.35	9.9E-02	0.55	2.4E-02	-0.34	5.3E-01	-0.91	2.0E-03
CLV04_1441	patatin-like phospholipase			1.02	4.4E-05	0.57	5.9E-03	0.13	4.7E-01	0.35	7.7E-02	0.03	9.8E-01	-0.63	4.3E-03
CLV04_1552	methionine synthase (B12-independent)	COG0620	E	1.12	6.4E-04	0.81	8.8E-03	0.11	6.9E-01	0.07	8.4E-01	-0.22	8.3E-01	-0.49	8.8E-02
CLV04_1696	POT family proton-dependent oligopeptide transporter	COG3104	E	1.60	4.9E-06	0.64	9.5E-03	0.54	1.4E-02	0.05	8.5E-01	-0.51	1.5E-01	-0.98	1.3E-03
CLV04_1836	flagellar hook-length control protein FliK		S	0.54	3.3E-03	0.50	8.8E-03	-0.15	3.6E-01	0.08	6.6E-01	-0.17	7.3E-01	-0.45	1.4E-02
CLV04_1947	Mu transposase-like protein		L	0.55	7.6E-03	0.63	5.7E-03	0.31	1.1E-01	0.19	3.9E-01	-0.11	9.2E-01	0.09	6.6E-01
CLV04_2053	heptosyltransferase-3	COG0859	M	0.66	3.8E-03	0.69	4.5E-03	-0.04	8.7E-01	0.40	7.0E-02	-0.18	8.1E-01	-0.58	1.1E-02
CLV04_2068	amino acid ABC transporter substrate-binding protein (PAAT family)	COG0834	E	0.60	7.4E-03	0.66	6.6E-03	-0.11	6.2E-01	0.26	2.6E-01	-0.04	9.8E-01	-0.35	1.0E-01
CLV04_2137	poly(3-hydroxybutyrate) depolymerase		S	1.23	4.2E-04	1.09	1.7E-03	0.69	1.5E-02	0.23	4.4E-01	-0.86	5.1E-02	-0.55	6.9E-02
CLV04_2165	amino acid ABC transporter substrate-binding protein (PAAT family)		E	0.83	6.9E-04	0.71	3.5E-03	-0.18	3.5E-01	0.48	3.2E-02	-0.11	9.2E-01	-0.89	1.1E-03
CLV04_2168	DeoR family transcriptional regulator	COG1349	K	1.32	2.7E-03	1.48	2.0E-03	0.47	2.0E-01	0.69	9.0E-02	-0.75	3.6E-01	-0.81	5.1E-02
CLV04_2195	IS4 family transposase	COG3039	L	0.81	9.0E-03	0.96	5.2E-03	0.29	3.0E-01	0.26	4.1E-01	-0.53	3.9E-01	-0.35	2.4E-01
CLV04_2467	Mor transcription activator family protein		S	1.93	1.8E-05	1.52	2.2E-04	0.43	1.3E-01	0.61	5.8E-02	-0.59	3.5E-01	-1.18	3.0E-03
CLV04_2468	peptidoglycan L-alanyl-D-glutamate endopeptidase CwlK		M	1.46	9.7E-05	1.48	1.6E-04	0.06	8.5E-01	0.56	5.8E-02	-0.75	1.1E-01	-1.24	1.1E-03
CLV04_2469	hypothetical protein			1.45	8.0E-03	1.68	5.9E-03	-0.12	8.1E-01	0.40	4.6E-01	-1.10	2.6E-01	-1.40	1.3E-02
CLV04_2470	hypothetical protein			1.14	2.5E-03	1.18	3.3E-03	-0.05	8.9E-01	0.65	6.5E-02	-0.47	6.0E-01	-1.14	4.3E-03
CLV04_2473	phage gp37-like protein		S	2.10	2.4E-04	1.92	8.0E-04	0.23	5.8E-01	0.78	7.9E-02	-1.21	1.0E-01	-1.94	1.3E-03
CLV04_2479	phage baseplate assembly protein V	COG4384	S	1.18	4.5E-03	1.12	9.3E-03	0.67	5.2E-02	1.01	1.3E-02	-0.47	6.7E-01	-0.86	3.2E-02
CLV04_3199	long-chain acyl-CoA synthetase	COG1022	I	0.86	9.4E-04	0.80	2.4E-03	0.10	6.3E-01	0.20	3.9E-01	-0.54	1.5E-01	-0.68	7.1E-03
CLV04_3591	SprA family protein		S	1.42	3.1E-05	1.06	5.9E-04	0.33	1.5E-01	0.43	9.3E-02	-0.29	6.8E-01	-0.76	8.5E-03
CLV04_3679	spermidine export protein MdtI	COG2076	P	0.69	4.9E-03	0.95	9.3E-04	0.10	6.6E-01	0.46	5.9E-02	-0.35	5.3E-01	-0.45	5.1E-02
CLV04_3894	phosphotransacetylase	COG0280, COG0857	C	1.59	2.5E-04	1.11	5.0E-03	0.35	2.6E-01	0.76	3.5E-02	-0.53	5.0E-01	-1.41	1.6E-03
CLV04_4047	hypothetical protein	COG3014	S	1.73	4.1E-05	1.50	2.4E-04	0.76	7.4E-03	1.03	2.0E-03	-1.23	9.0E-03	-1.74	1.8E-04
CLV04_4083	flagellar basal-body rod modification protein FlgD	COG1843	N	1.32	2.3E-04	2.07	1.1E-05	0.21	4.2E-01	1.01	2.4E-03	-1.34	5.2E-03	-1.39	4.6E-04
CLV04_4084	flagellar hook protein FlgE	COG1749	N	1.96	1.1E-05	2.50	2.6E-06	0.96	2.6E-03	1.38	4.2E-04	-1.43	3.9E-03	-1.29	1.2E-03
CLV04_4085	flagellar basal-body rod protein FlgF	COG4787	N	2.47	5.8E-07	2.56	1.0E-06	0.88	1.7E-03	1.36	1.9E-04	-1.40	3.4E-03	-1.79	8.7E-05
CLV04_4086	flagellar basal-body rod protein FlgG	COG4786	N	1.89	1.1E-05	2.67	1.4E-06	0.28	3.0E-01	1.32	3.9E-04	-1.57	2.2E-03	-1.84	7.1E-05
CLV04_4087	flagellar L-ring protein precursor FlgH	COG2063	N	2.30	5.0E-06	2.96	1.4E-06	0.54	6.3E-02	1.46	4.2E-04	-1.60	5.2E-03	-1.86	1.9E-04
CLV04_4089	flagellar protein FlgJ			1.85	1.4E-04	2.19	7.4E-05	0.40	2.0E-01	1.00	1.1E-02	-1.47	1.7E-02	-1.72	8.5E-04
CLV04_4090	flagellar hook-associated protein 1 FlgK	COG1256	N	1.05	2.3E-03	2.90	1.4E-06	0.41	1.6E-01	1.52	2.6E-04	-1.79	1.5E-03	-1.04	4.0E-03
CLV04_4091	flagellar hook-associated protein 3 FlgL	COG1344	N	0.85	8.7E-03	3.00	1.3E-06	-0.43	1.4E-01	1.52	2.9E-04	-1.79	1.8E-03	-1.60	2.7E-04
CLV04_4092	hypothetical protein			1.75	1.1E-05	2.94	3.5E-07	0.47	6.1E-02	1.65	4.2E-05	-1.51	2.2E-03	-1.50	1.9E-04
CLV04_4268	S-PFT family hemolysin	COG3210	U	0.84	2.9E-04	0.75	1.2E-03	0.07	7.1E-01	0.42	4.0E-02	-0.22	6.9E-01	-0.65	3.8E-03
CLV04_4281	hypothetical protein			1.18	1.9E-04	0.79	6.0E-03	0.09	7.3E-01	0.07	8.1E-01	-0.59	1.6E-01	-0.97	2.2E-03
CLV04_4420	diguanylate cyclase (GGDEF)-like protein		T	1.18	4.8E-05	0.72	3.6E-03	0.21	2.9E-01	0.24	2.8E-01	-0.40	3.3E-01	-0.89	1.5E-03
Genes upregulated by translation inhibition moduladed by air system															
CLV04_0472	dipeptidase D	COG2195	E	-0.57	1.8E-03	-0.52	5.8E-03	-0.13	4.0E-01	-0.31	7.3E-02	0.03	9.8E-01	0.27	9.5E-02
CLV04_0474	putative Zn-dependent protease	COG0312	S	-1.12	3.6E-04	-0.89	3.4E-03	-0.42	9.5E-02	-0.40	1.5E-01	0.46	3.6E-01	0.67	1.5E-02
CLV04_0655	non-ribosomal peptide synthase protein (TIGR01720 family)/amino acid adenylation d	COG1020	Q	-4.27	8.6E-08	-5.03	5.9E-08	-5.42	1.6E-08	-5.11	1.7E-07	2.25	8.9E-04	1.19	1.0E-02
CLV04_0656	polyketide-type polyunsaturated fatty acid synthase PfaA	COG3321	Q	-3.70	1.3E-06	-4.36	6.5E-07	-4.88	1.3E-07	-4.65	7.6E-07	2.39	1.9E-03	1.49	6.1E-03
CLV04_0657	PfaB family protein	COG0764	Q	-3.10	3.7E-06	-4.06	6.5E-07	-4.49	1.8E-07	-4.49	6.9E-07	2.46	7.3E-04	1.49	4.3E-03
CLV04_0658	PfaD family protein	COG2070	S	-2.87	1.3E-05	-3.87	1.5E-06	-4.30	1.0E-06	-4.14	6.1E-06	2.55	6.4E-04	1.39	6.5E-03
CLV04_0659	medium-chain acyl-[acyl-carrier-protein] hydrolase	COG3208	Q	-3.38	6.3E-06	-3.36	1.4E-05	-4.20	2.3E-06	-3.38	6.6E-05	1.99	5.8E-03	1.20	1.1E-02
CLV04_0660	4'-phosphopantetheinyl transferase	COG2091	H	-2.64	1.3E-04	-3.10	5.6E-05	-3.06	1.2E-04	-2.81	6.4E-04	2.08	6.3E-03	1.37	1.0E-02
CLV04_0661	polysaccharide pyruvyl transferase WcaK-like protein			-1.64	1.0E-04	-2.15	1.6E-05	-1.83	4.9E-05	-2.30	2.0E-05	1.93	5.9E-04	1.89	1.3E-04
CLV04_1214	hypothetical protein			-1.07	9.6E-04	-1.00	2.6E-03	0.35	2.3E-01	-0.69	2.8E-02	0.43	4.7E-01	1.55	2.2E-04
CLV04_1215	violacein biosynthesis enzyme VioE			-3.07	5.0E-07	-3.68	2.2E-07	-1.36	2.0E-03	-2.29	5.4E-05	1.91	5.0E-04	2.23	3.7E-05
CLV04_1216	anthraniloyl-CoA monooxygenase	COG0654	C, H	-3.79	7.9E-09	-3.84	4.5E-08	-1.99	6.3E-06	-2.42	3.7E-06	1.89	1.8E-04	2.27	2.3E-06
CLV04_1217	kynurenine 3-monooxygenase	COG0654	H	-4.28	7.1E-08	-4.29	1.8E-07	-2.44	2.6E-05	-2.71	3.2E-05	2.20	4.0E-04	2.46	2.3E-05
CLV04_1218	iminophenyl-pyruvate dimer synthase VioB			-4.14	3.1E-07	-4.01	9.1E-07	-2.95	1.1E-05	-2.81	6.2E-05	1.90	2.5E-03	1.89	4.9E-04
CLV04_1219	monoamine oxidase		S	-6.10	3.6E-10	-4.85	4.5E-08	-4.07	5.6E-08	-3.73	6.1E-07	1.88	3.2E-04	2.79	4.9E-07
CLV04_2088	hypothetical protein			-0.93	5.0E-03	-1.08	2.9E-03	-0.68	2.7E-02	-0.60	6.7E-02	0.55	3.6E-01	0.32	2.7E-01
CLV04_2204	adenosine deaminase		F	-0.92	2.1E-04	-1.22	2.9E-05	-0.38	5.5E-02	-0.64	6.4E-03	0.68	1.1E-02	0.63	5.3E-03
CLV04_2269	hypothetical protein	COG1896	S	-2.75	1.6E-07	-2.26	2.6E-06	-2.13	3.3E-06	-1.12	3.1E-03	1.60	5.9E-04	1.07	1.1E-03
CLV04_2291	phosphoribosylamine--glycine ligase	COG0151	F	-0.73	3.1E-03	-0.68	8.2E-03	-0.48	3.0E-02	-0.27	2.6E-01	0.21	7.7E-01	0.06	8.0E-01
CLV04_2493	hypothetical protein			-1.80	5.4E-06	-1.76	1.4E-05	-0.90	2.9E-03	-0.55	7.3E-02	1.31	1.7E-03	1.00	1.7E-03
CLV04_2537	carbohydrate ABC transporter substrate-binding protein (CUT1 family)		G	-0.96	9.0E-03	-1.58	3.5E-04	-0.35	3.1E-01	-0.92	1.6E-02	0.46	5.4E-01	0.42	2.0E-01
CLV04_2637	pseudolysin	COG3227	E	-1.51	1.6E-03	-2.90	9.0E-06	-1.16	1.6E-02	-2.21	2.7E-04	1.64	5.3E-03	1.30	6.1E-03
CLV04_2753	hypothetical protein			-1.68	1.1E-05	-0.96	2.2E-03	-0.22	3.9E-01	-0.48	9.1E-02	1.10	6.2E-03	2.07	6.7E-06
CLV04_2839	biotin synthase	COG0502	H	-2.87	4.9E-09	-2.08	3.4E-07	-1.84	4.7E-07	-1.13	1.8E-04	1.06	8.4E-04	1.15	7.0E-05

CLV04_2850	aromatic amino acid:proton symporter (AAT family)	COG1113	E	-0.97	3.9E-04	-0.84	2.1E-03	0.14	5.6E-01	-0.39	1.2E-01	0.46	2.5E-01	1.12	4.1E-04
CLV04_3096	cysteine synthase A	COG0031	E	-2.74	1.5E-06	-2.19	2.7E-05	-1.73	1.5E-04	-1.49	1.2E-03	1.17	1.1E-02	1.49	8.4E-04
CLV04_3159	cviR	COG2771	K	-0.62	1.2E-03	-0.81	2.4E-04	-0.22	1.7E-01	-0.37	3.9E-02	0.36	2.1E-01	0.32	5.6E-02
CLV04_3520	fatty acid desaturase	COG3239	I	-0.77	2.5E-03	-1.96	7.0E-07	0.19	4.4E-01	-1.20	1.8E-04	1.18	5.9E-04	1.37	1.2E-04
CLV04_3521	diaminopimelate decarboxylase	COG0019	E	-0.94	9.5E-04	-1.71	9.1E-06	0.74	7.9E-03	-1.31	1.5E-04	1.02	5.5E-03	2.30	1.4E-06
CLV04_3776	CRISPR-associated Cse1 family protein		L	-1.99	4.5E-07	-1.78	3.3E-06	-1.17	1.2E-04	-1.33	1.1E-04	0.81	1.0E-02	1.19	1.8E-04
CLV04_3778	CRISPR-associated Cse4 family protein		L	-1.56	5.7E-06	-1.54	1.4E-05	-0.33	1.6E-01	-0.80	4.6E-03	0.92	6.1E-03	1.41	7.1E-05
CLV04_4098	phenazine biosynthesis protein phzE	COG0512	E, H	-2.48	2.4E-06	-1.22	2.3E-03	-0.42	2.4E-01	-0.75	5.8E-02	1.55	3.5E-03	3.14	1.1E-06