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Craig Stephens

Santa Clara University, cstephens@scu.edu

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Microbial Genomics: Tropical Treasure?

Dispatch

Craig Stephens

A Brazilian consortium has unveiled the genomic DNA sequence of the purple-pigmented bacterium *Chromobacterium violaceum*, a dominant component of the tropical soil microbiota. The sequence provides insight into the abundant potential of this organism for biotechnological and pharmaceutical applications.

Exploring global biodiversity is a major focus of contemporary biological research, and documenting the extraordinary richness of tropical habitats is a priority. Although microbial diversity is seldom considered in this regard, it could turn out to be of great value to developing nations. New work from the Brazilian National Genome Project Consortium [1] examines the genome of a fascinating bacterium, *Chromobacterium violaceum*, a major component of tropical soil microbiota. Analysis of the *C. violaceum* genome provides important clues about its physiological adaptation to tropical soils and aquatic habitats, its capacities as an opportunistic pathogen, and its potential biotechnological and pharmaceutical applications.

The Brazilian National Genome Project Consortium, BRGene, is a model for genomics research in the developing world [2]. BRGene evolved as an umbrella organization building on the success of the Organization for Nucleotide Sequencing and Analysis, ONSA, a collaborative genomics research network based in the state of Sao Paulo. (The acronym 'ONSA' alludes to the Portuguese word for jaguar, 'onça', a playful allusion to The Institute for Genomic Research, 'TIGR', a major force in genomics research in the US.) ONSA and BRGene are 'virtual institutes' composed of numerous laboratories at Brazilian universities and research centers, each contributing sequence data to coordinated projects. This distributed strategy avoids concentrating investment in large sequencing centers; rather, it develops expertise and spreads critical equipment and funding among existing institutions, enhancing their capabilities and engendering communication and cooperation.

Brazilian genomics efforts have focused on projects with national relevance [2]. Expertise in bacterial genomics was developed early on with successful efforts to analyze the genomes of three agronomically significant pathogens: *Xylella fastidiosa*, the cause of Pierce's disease in grapes and variegated chlorosis in citrus crops [3], and *Xanthomonas campestris* and *Xanthomonas citri*, which cause canker in citrus trees [4]. Brazilian projects are not limited to microbes, of course; other efforts include analysis of sugar cane, coffee, and cancer-related genes in humans [5].

The *Chromobacterium violaceum* genome project is perhaps one of the more speculative Brazilian genome efforts. The organism is not harmful to plants, and is only a rare, opportunistic (but potentially lethal) pathogen of animals and humans. It is, however, a major component of the tropical soil microbiota [6], and highly abundant in the Rio Negro [1]. The most striking feature of *C. violaceum* is its profuse production of a purple pigment called violacein, derived from tryptophan [7] (Figure 1). Like many soil microbes, *C. violaceum* excretes 'secondary metabolites' — including violacein — as weapons against competitors and/or predators [6,8].

Secondary metabolites have an honored place in microbiology, starting with Fleming's observation of the effects of penicillin on *Staphylococci*. Since then, microbiologists have identified a treasure trove of excreted compounds, including an enormously valuable range of antibiotics and medicinal compounds. With so much microbial diversity awaiting exploration, we obviously have not exhausted nature's stock. Violacein may be poised for a spot in the pantheon of high-value microbial products. It has bacteriocidal activity against *Mycobacterium tuberculosis*, and pronounced anti-protozoal activity against organisms such as *Trypanosoma cruzi* (the cause of Chagas disease) and *Leishmania* species (agents of leishmaniasis) [9]. Possible antiviral and anti-cancer activities are being investigated as well [10].

The *C. violaceum* genome is nearly 5 megabases, encoding just over 4400 genes. Overall, the genome is most similar to that of *Ralstonia solanacearum*, a soil-borne phytopathogen. Surprisingly, nearly 10% of the *C. violaceum* genes are most closely related to those of *Pseudomonas aeruginosa*, another common soil microbe and a highly virulent opportunistic pathogen, but one which is considerably more distantly related to *C. violaceum* on the basis of ribosomal RNA sequence criteria. The similar habitats occupied by these microbes

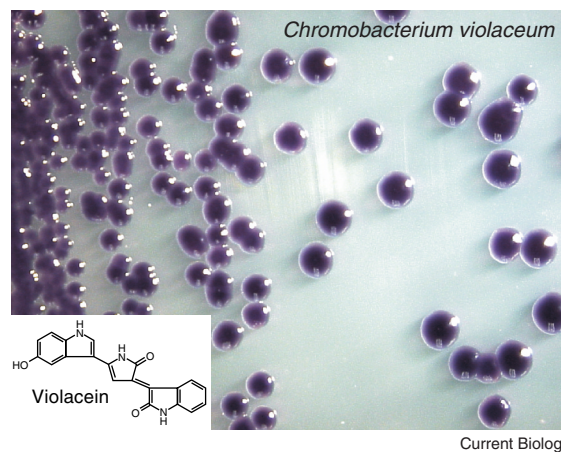


Figure 1. *Chromobacterium violaceum* colonies showing purple pigmentation due to violacein production.

The inset shows the chemical structure of violacein [6]. (Photo courtesy Daryn Baker, Santa Clara University.)

has undoubtedly steered their genomic content in comparable directions; to what extent lateral gene transfer between *C. violaceum* and pseudomonads in the crowded soil microcosm accounts for the similarity between these species has not been fully examined.

Like the genomes of *R. solanacearum* and *P. aeruginosa*, that of *C. violaceum* encodes a specialized, 'Type III' protein secretion system; but unlike those more accomplished pathogens, *C. violaceum* seems to be missing the arsenal of secreted 'effector' proteins employed to compromise host cells during infection [11]. Their absence might explain the rather poor ability of *C. violaceum* to infect humans, and its apparent harmlessness to plants. On the other hand, the *C. violaceum* genome does encode a number of gene products that potentially allow it to damage mammalian hosts, including several hemolysin-like proteins.

As might be expected for a free-living soil microbe, the *C. violaceum* genome evinces a robust and flexible physiology, capable of acquiring diverse nutrients through dozens of transport systems, and utilizing a variety of substrates and electron acceptors for aerobic or anaerobic growth. The ability of this organism to interpret and respond to complex and dynamic habitats depends on an enormous array of sensors and signaling pathways. Prominent among these is the chemotaxis system that guides flagellum-based movement toward nutrients and away from noxious compounds. Indeed, 41 distinct membrane-bound sensors for guiding chemotaxis — methyl-accepting chemotaxis proteins — are encoded in the *C. violaceum* genome, the largest number observed in a single prokaryotic genome to date. Environmentally responsive motility would thus seem to be a major adaptive feature for this microbe.

Violacein production is controlled by 'quorum sensing', a regulatory mechanism that restricts activity to conditions of high cell density. Quorum sensing evolved to control processes that are presumably beneficial when a particular organism is highly concentrated, such as bioluminescence by symbiotic bacteria inhabiting light organs of fish or squid. Quorum-sensing bacteria constitutively produce a diffusible signal molecule, an *N*-acylhomoserine lactone (AHL) [12]. When enough cells are crowded together, AHL concentrations build up to a threshold level that activates a cognate transcription factor, which then turns on expression of target genes.

In *C. violaceum*, many other gene products, in addition to the enzymes for violacein production, may be under quorum-sensing control, including enzymes for cyanide production, production of the antibiotic phenazine, and secreted hydrolytic enzymes for extracellular polymer degradation. Because violacein is so easily detected by its purple color, and quantified, violacein production by *C. violaceum* has been developed as a simple bioassay for AHL production by other bacteria [13]. Whether the potential to respond to 'foreign' AHLs is biologically significant to *C. violaceum* in natural habitats is an intriguing question for the future.

Aside from the potential medical utility of violacein, *C. violaceum* could have other practical applications. For example, the ability of this organism to synthesize polyhydroxyalkanoate polymers suggests it could be useful

in production of biodegradable plastics, a field of much current interest [14,15]. The *C. violaceum* genome sequence also revealed an acid dehalogenase, opening a door to potential applications in bioremediation, such as detoxification of chlorinated compounds that contaminate soils at industrial sites [16]. On perhaps a less environmentally friendly note, Campbell *et al.* [17] have shown that cyanide produced by *C. violaceum* cultures can be used to enhance gold recovery from ore. They proposed that on-site generation of cyanide by *C. violaceum* at remote gold mining facilities could be a practical strategy for enhancing gold production. The newly revealed genome sequence offers tantalizing clues to capabilities of this organism that are simply begging for experimental investigation. The completed *C. violaceum* genome sequence should also facilitate its genetic manipulation to further enhance valuable traits. If these efforts pan out, Brazilian scientists might truly strike gold with this microbe.

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