JOURNAL OF COMPLEMENTARY MEDICINE RESEARCH
Journal of Complementary Medicine Research, ISSN: 2146-8397 Vol. 13, No. 2, 2022 (pp. 50-52)
SHORT COMMUNICATION
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Whole- Genomic sequence of multidrug resistance Burkholderia cepacia associated with acute suppurative thyroiditis

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ABSTRACT

Burkholderia cepacia is a beta proteobacterium multidrug-resistant Gram-negative pathogen. At least nine different species cause infections in people with chronic granulomatous disease and cystic fibrosis (CF). In this report, we focused on Bcc that caused thyroiditis in people. Isolates were collected from patients with thyroiditis for complete genome sequencing. The sequencing results were 352 contigs, an estimated genome length of 23,628,288 bp, and an average G+C content of 59.99%.

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How to cite this article: Gerlach K (2022). Whole- Genomic sequence of multidrug resistance Burkholderia cepacia associated with acute suppurative thyroiditis. Journal of Complementary Medicine Research, Vol. 13, No. 2, 2022 (pp. 50-52).

INTRODUCTION

Interestingly, the thyroid gland is basically resistant to infections due to its location inside a sheath, high iodine concentration, hydrogen peroxide production, and high blood and lymphoid circulation; therefore, acute suppurative thyroiditis rarely occurs. The most common agents of thyroiditis are Staphylococcus and Streptococcus infections. Here we presented for the first time acute suppurative thyroiditis caused by Burkholderia cepacia, which consider as a rare infectious agent in adults. Burkholderia cepacia complex (Bcc) bacteria are rare but notorious opportunistic pathogens in cystic fibrosis (CF) patients. They are associated with higher rates of morbidity and mortality and lower post-lung transplant survival.[1-4] Bcc infections in CF are characterized by highly variable clinical outcomes but commonly result in a progressive decline of lung function. In extreme cases, Bcc infection can result in "cepacia syndrome", necrotizing pneumonia, and septicaemias that affects the patient's terminal prognosis.[5] Bcc infections are difficult to eradicate because the infecting strains have an innate resistance to multiple antibiotics.[3,4,6]

In this work, nine clinical isolates were isolated from samples of patients diagnosed with thyroiditis and were collected at the Al-Ramadi teaching hospital. Isolates were identified as Burkholderia epacian using Vitek. The overnight cultures were in tryptone soy broth (TSB), Burkholderia epacian were pelleted, re-suspended in 2xTSB with 25% (v/v) glycerol, and stored at -80 ℃. Then, bacterial isolates were inoculated on tryptone soy agar (TSA) and incubated at 37 ℃ overnight. Burkholderia cepacian genome sequence was assembled using the PacBio single-molecule real-time (SMRT) analysis software v2.3.0 into two high-quality contigs. There were 352 contigs, an estimated genome length of 23,628,288 bp, and an average G+C content of 59.99%. The N50 length, defined as the shortest sequence length at 50% of the genome, is 259,389 bp. The L50 count, defined as the smallest number of contigs whose length produces N50, is 29. Summary of this genome sequencing and assembly have appeared in Table 1.

The Burkholderia cepacia pdf genome was annotated using the RAST tool kit (RASTtk)[7] and assigned a unique genome identifier of 292.360. This genome is in the super kingdom Bacteria and was annotated using genetic code 11. The taxonomy of this genome is:

Cellular organisms > Bacteria > Proteobacteria > Betaproteobacteria > Burkholderiales > Burkholderiaceae > Burkholderia > Burkholderia cepacia complex > Burkholderia cepacia. This genome has 23,853 protein

KEYWORDS:
COVID-19-rehab,
COVID-19-treatment,
Exercise,
Eurythmy Therapy,
Self-help-exercise.

ARTICLE HISTORY:
Received Jan 14, 2022
Accepted Mar 16, 2022
Published Mar 04, 2022

DOI:
10.5455/jcmr.2022.13.02.09

coding sequences (CDS), 244 transfer RNA (tRNA) genes, and 13 ribosomal RNA (rRNA) genes. The annotated features are summarized in Table 2.

Also, the annotation included 6,474 hypothetical proteins and 17,379 proteins with functional assignments (Table 3). The proteins with functional assignments included 4,996 proteins with Enzyme Commission (EC) numbers,[8] 4,221 with Gene Ontology (GO) assignments,[9] and 3,712 proteins that were mapped to KEGG pathways.[10] PATRIC annotation includes two types of protein families,[11] and this genome has 11,985 proteins that belong to the genus-specific protein families (PLFams) for, and 22,468 proteins that belong to the cross-genus protein families (PGFams).

Table 1. Assembly Details

Contigs	352
GC Content	59.99
Plasmids	0
Contig L50	29
Genome Length	23,628,288 bp
Contig N50	259,389
Chromosomes	0
Job ID	assembly_136135
Job Started	June 1st 2021, 12:01:07am
Job Completed	June 1st 2021, 8:12:59am
Total Time	8h11m52s
Selected Recipe	auto

Table 2. Annotated Genome Features

CDS	23,853
tRNA	244
rRNA	13
Partial CDS	0
Miscellaneous RNA	0
Repeat Regions	0
Job ID	annotation_136135
Job Started	June 1st 2021, 8:12:59am
Job Completed	June 1st 2021, 8:34:14am
Total Time	21 minutes and 15 seconds

Many of the genes annotated have homology to known transporters,[12] virulence factors,[13][14] drug targets.[15][16] and antibiotic resistance genes.[17] The number of genes and the specific source database where homology was found is provided in Table 4.

The Genome Annotation Service in PATRIC uses k-mer-based AMR genes detection method, which utilizes PATRIC's curated collection of representative AMR gene sequence variants[18] and assigns to each AMR gene functional annotation, broad mechanism of antibiotic resistance, drug class, and, in some cases, specific antibiotic it confers resistance too. Please note that the presence of AMR-related genes (even full length) in a given genome does not directly imply an antibiotic-resistant phenotype. It is essential to consider specific AMR mechanisms, especially the absence/presence of SNP mutations conveying resistance. A summary of the AMR genes annotated in this genome and the corresponding AMR mechanism is provided in Table 5.

Table 3. Protein Features

Hypothetical proteins	6,474
Proteins with functional assignments	17,379
Proteins with EC number assignments	4,996
Proteins with GO assignments	4,221
Proteins with Pathway assignments	3,712
Proteins with PATRIC genus-specific family (PLfam) assignments	11,985
Proteins with PATRIC cross-genus family (PGfam) assignments	22,468

Table 4. Specialty Genes

	Source	Genes
	Victors	7
Antibiotic Resistance	CARD	126
Antibiotic Resistance	NDARO	33
Antibiotic Resistance	PATRIC	286
Drug Target	DrugBank	413
Drug Target	TTD	68
Transporter	TCDB	768
Virulence Factor	PATRIC_VF	115
Virulence Factor	VFDB	296
Virulence Factor	Victors	271

Table 5. Antimicrobial Resistance Genes

AMR Mechanism	Genes
Antibiotic activation enzyme	KatG
Antibiotic inactivation enzyme	AAC(3)-II,III,IV,VI,VIII,IX,X, APH(3')-I, APH(3')-II/APH(3')-XV, CatA1/CatA4 family, CatB family, CTX-M family, EreA family, Lnu(F)/Lnu(G), Mph(E)/Mph(G) family, OXA-1 family, OXA-10 family, OXA-50 family, PDC family
Antibiotic target in susceptible species	Alr, Ddl, dxr, EF-G, EF-Tu, folA, Dfr, folP, gyrA, gyrB, inhA, fabI, Iso-tRNA, kasA, MurA, rho, rpoB, rpoC, S10p, S12p
Antibiotic target protection protein	BcrC, Msr(E)
Antibiotic target replacement protein	FabG, fabV, HtdX
Efflux pump conferring antibiotic resistance	AcrAB-TolC, AcrAD-TolC, AcrEF-TolC , AcrZ, EmrAB-OMF, EmrAB-TolC, EmrD, FloR family, MacA, MacB, MdfA/Cmr, MdtABC-OMF, MdtABC-TolC, MdtL, MdtM, MexAB-OprM, MexCD-OprJ, MexCD-OprJ system, MexEF-OprN, MexEF-OprN system, MexHI-OpmD, MexHI-OpmD system, MexJK-OprM/OpmH, MexPQ-OpmE, MexPQ-OpmE system, MexVW-OprM, MexXY-OMP, QacE, SugE, Tet(A), Tet(G), Tet(J), TolC/OpmH, TriABC-OpmH
Gene conferring resistance via absence	gidB
Protein altering cell wall charge conferring antibiotic resistance	GdpD, PgsA
Protein modulating permeability to antibiotic	OccD1/OprD, OccD2/OpdC, OccD3/OpdP, OccD4/OpdT, OccD5/OpdI, OccD6/OprQ, OccD7/OpdB, OccD8/OpdJ, OccK1/OpdK, OccK10/OpdN, OccK11/OpdR, OccK2/OpdF, OccK3/OpdO, OccK4/OpdL, OccK5/OpdH, OccK6/OpdQ, OccK7/OpdD, OccK8/OprE, OccK9/OpdG, OprB, OprB family, OprD family, OprF
Regulator modulating expression of antibiotic resistance genes	AcrAB-TolC, EmrAB-TolC, H-NS, OxyR

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