

The genome of *Burkholderia cenocepacia* J2315, an epidemic pathogen of cystic fibrosis patients

Holden, M. T., Seth-Smith, H. M., Crossman, L. C., Sebahia, M., Bentley, S. D., Cerdeño-Tárraga, A. M., ... & Parkhill, J. (2009). *Journal of Bacteriology*, 191(1), 261-277.

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Outline

1. J2315 is a clinically relevant and “successful” strain of *B. cenocepacia* that is a significant and unique CF pathogen.
2. The genome of J2315 consists of 3 chromosomes and 1 plasmid.
 - a. Differences are apparent in the chromosomes between J2315 and related strains.
3. Unique genes in J2315 characterize it as a highly transmissible pathogen.
4. Analysis of pseudogenes indicates a mutation timeline.
5. Burkholderia Genome DB is a user-friendly utility for the exploration of *Burkholderia* genomes.

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***B. cenocepacia* strain J2315 is a pathogen found among CF patients**

- *B. cenocepacia* is known to cause serious lung infections in CF patients.
 - Exists as a part of the *B. cepacia* complex (BCC).
- J2315 belongs to the ET12 lineage of highly transmissible *B. cenocepacia* strains that lead to higher mortality rates.
- J2315, like other ET12 strains, has a cable pilus which enhances its role as a host-associated pathogen.
- The J2315 strain associated with higher incidences of clinical deterioration and is highly resistant.

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The *B. cenocepacia* genome consists of 3 circular chromosomes and 1 plasmid

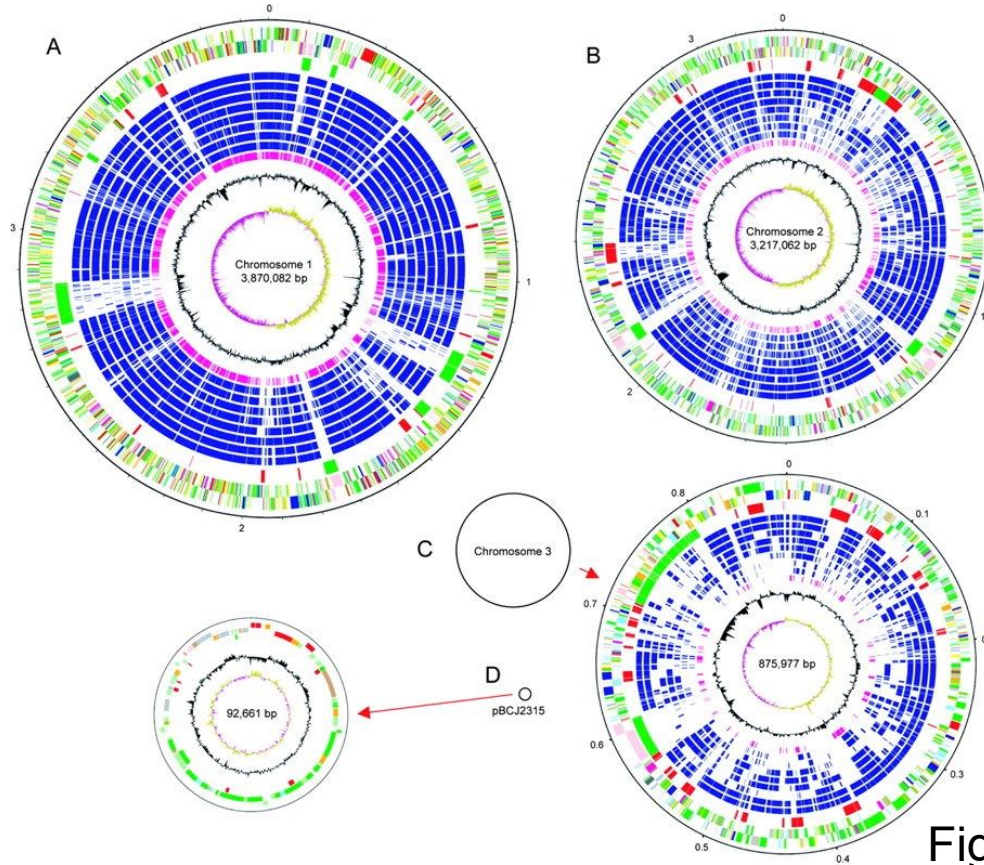


Fig. 1. (Holden et. al 2009)

J2315 contains 7,261 distinct genes

Property ^a	Chromosome 1	Chromosome 2	Chromosome 3	Plasmid	Total
Size (bp)	3,870,082	3,217,062	875,977	92,661	8,055,782
G+C content (%)	66.7	67.9	67.9	62.6	66.9
No. of CDSs	3,537	2,849	776	99	7,261
Coding (%)*	86.1	86.4	86.0	78.6	85.9
Avg gene length (bp)*	958	985	986	763	970
rRNA	4 (16S-23S-5S)	1 (16S-23S-5S)	1 (16S-23S-5S)	0	6 (16S-23S-5S)
tRNA	66	6	2	0	74
Miscellaneous RNA	15	3	2	1	21
Pseudogenes and partial genes	56	41	23	6	126
IS elements	51	16	11	1	79

Table. 1. (Holden et. al 2009)

Chromosome 1 has different functional classes than Chromosome 2 and 3

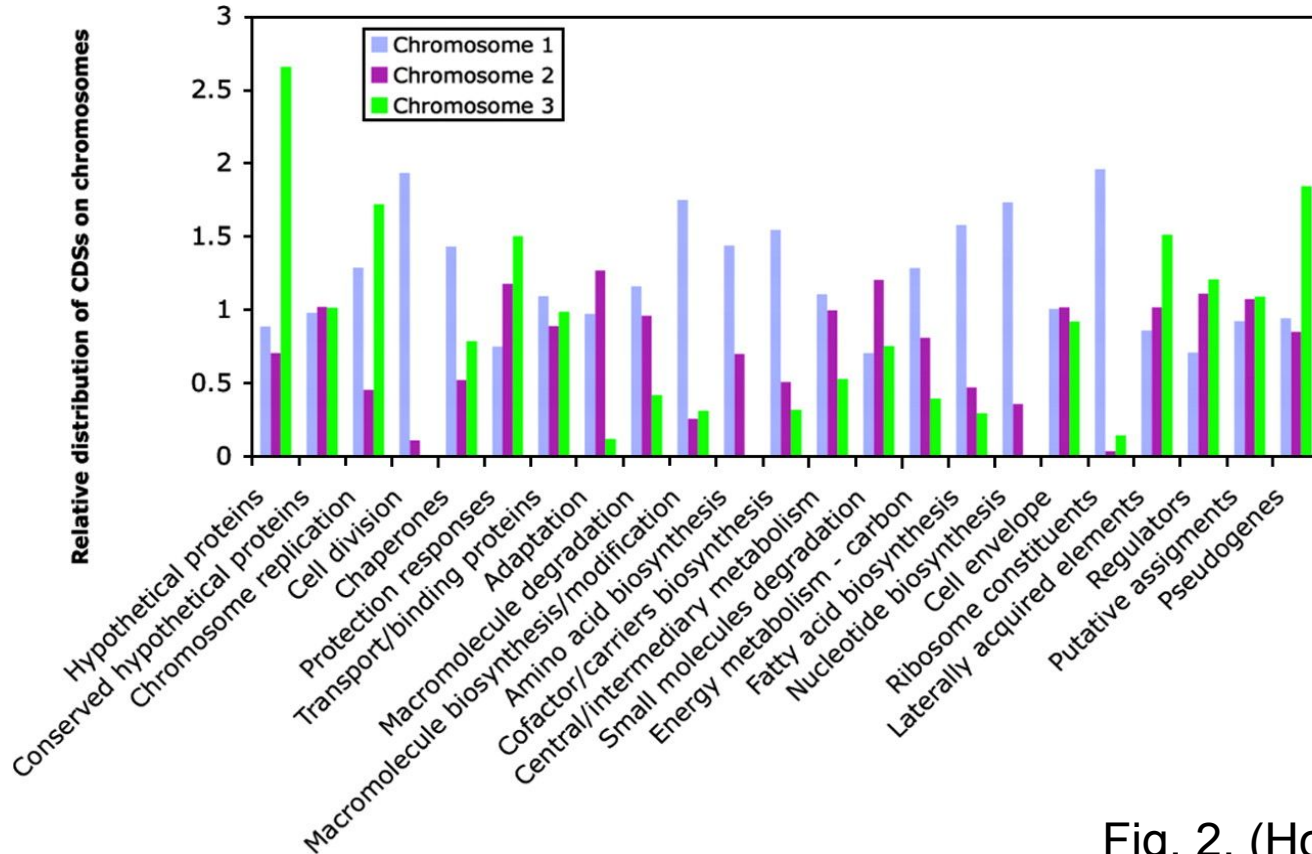


Fig. 2. (Holden et. al 2009)

J2315 has ancestral genes found among 8 other strains and species

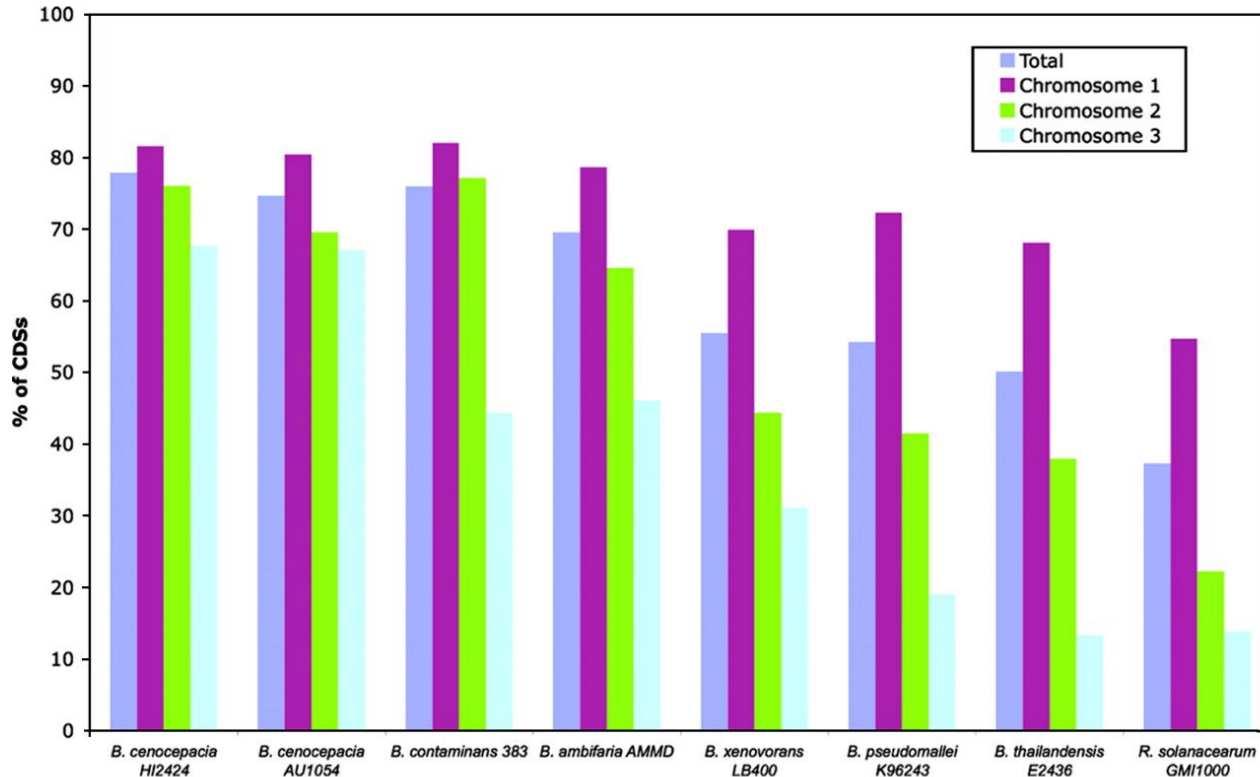


Fig. 3. (Holden et. al 2009)

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TABLE 3. Potential virulence functions encoded in the genome of *B. cenocepacia* strain J2315

Function	Notes and examples	CDSs ^a
Exoproteins	Zinc metalloproteases ZmpA and ZmpB Phospholipases C	BCAS0409 and BCAM2307 BCAL0443; BCAL1046; BCAM0408*; BCAM1969; BCAM2429; BCAM2720
Secretion	Type I secretion (T1S) Type II secretion (T2S) Type III secretion (T3S) Type IV secretion (T4S) Type V secretion (T5S) Type VI secretion (T6S)	BCAM2140 to BCAM2142; BCAM1317 to BCAM1320 BCAM3447 and BCAL3515 to BCAL3527 BCAM2045 to BCAM2057 BCAM0324 to BCAM0340; pBCA020 to pBCA059 BCAL3353; BCAM0183; BCAM2169; BCAS0321 BCAL0337 to BCAL0351
LPS and capsule	LPS biosynthesis clusters: core, O-antigen and lipid A modification Cepacian polysaccharide synthesis and export cluster Other potential surface polysaccharides biosynthetic clusters	BCAL2402 to BCAL2408; BCAL3110 to BCAL3125; BCAL1929 to BCAL1935 BCAM0854 to BCAM0865 BCAL3217* to BCAL3246*; BCAM0203 to BCAM0214; BCAM1003 to BCAM1011; BCAM1224 to BCAM1228; BCAM1330* to BCAM1340*; BCAM2032* to BCAM2035*; BCAS0294 to BCAS0297
Adhesins	22-kDa adhesion protein AdhA BuHA family proteins	BCAM2143* BCAM0219*; BCAM0223*, BCAM0224*; BCAM1115*; BCAM2418; BCAS0236; BCAS0335; pBCA011*
Fimbriae and pili	Cable pilus Chaperone-usher type fimbriae Flp-type pili Type IVa pilus	BCAM2756* to BCAM2762* BCAL1677 to BCAL1680; BCAL1826 to BCAL1828; BCAL2634a* to BCAL2637* BCAL1520 to BCAL1537; BCAS0298 to BCAS0312 BCAL0959, BCAL3445 to BCAL3447, BCAL0276 to BCAL0278
Quorum sensing	<i>N</i> -Acylhomoserine lactone regulons CepIR and CciIR <i>N</i> -Acylhomoserine lactone dependent regulator	BCAM1870 and BCAM1868; BCAM0239a* and BCAM0240*
Siderophores	Ornibactin Salicylic acid and pyochelin	BCAM0188 BCAL1688 to BCAL1702 BCAM2224 to BCAM2235
Intracellular stress	Natural resistance-associated macrophage proteins Superoxide detoxification: superoxide dismutases, peroxidase/catalase, catalases, thiol peroxidase, alkyl hydroperoxidase	BCAM0836, BCAM1764, BCAM2060, BCAS0630 and BCAS0634* BCAL2643 and BCAL2757; BCAL3299 and BCAM2107*; BCAS0635 and BCAM0931; BCAL3424; BCAM1216 and BCAM1217
Motility	Nitric oxide detoxification, flavohaemoglobin Five gene clusters on chromosome 1 encode the components of a single flagellar system Two additional flagellar components on chromosome 2 and chromosome 3	BCAL3285 BCAL0113 to BCAL0114; BCAL0140 to BCAL0144; BCAL0520 to BCAL0527; BCAL0561 to BCAL0577; BCAL3501 to BCAL3507 BCAM0987; BCAS0104

^a An asterisk (*) indicates a gene or genes associated with that function that is absent from both *B. cenocepacia* AU1054 and HI2424 genomes.

**Several virulence
functions are
encoded in the
J2315 genome**

Table. 3. (Holden et. al 2009)

TABLE 2. Genomic islands of *B. cenocepacia* strain J2315^a

Chromosome and island	Size (kb)	Coordinates	Integration site	No. of integrases	%GC	D	K	Functional note(s)
Chromosome 1								
BcenGI1	25.0	100361...125265	tRNA Arg	1	-(68.5)	-	-	Prophage, contains a group II intron; similar to ϕ K96243 from <i>B. pseudomallei</i> K96243
BcenGI2	16.4	188011...204429	tRNA Ala	1	+(55.7)	-	+	ICE element similar to GI11 in <i>B. pseudomallei</i> K96243
BcenGI3	13.1	449978...463082			+(56.5)	+	+	Miscellaneous island, possible remnant, contains type I restriction modification system (BCAL0414, BCAL0418, and BCAL0420)
BcenGI4	4.2	1032360...1036537	tRNA Met	1	+(42.8)	-	+	Miscellaneous island, contains three CDSs of possible plasmid origin; similar island in <i>B. vietnamiensis</i> G4
BcenGI5	92.8	1222566...1315385		1	+(60.3)	-	+	Miscellaneous island, contains miscellaneous metabolism, including glycosyltransferase (BCAL1147), polysaccharide deacetylase (BCAL1148), putative O-antigen acetylase (BCAL1191), possible hydroxybenzoate degradation components (BCAL1151 to BCAL1162), fusaric acid resistance-family transporter (BCAL1176 to BCAL1178), and glycerate kinase (BCAL1181)
BcenGI6	34.2	1402882...1437088	tRNA Arg	1	+(58.8)	-	+	Miscellaneous island
BcenGI7	37.7	1728919...1766584	BCAL1558		+(62.9)	-	+	Prophage, Mu-like
BcenGI8	121.9	2738065...2859923	BCAL2601	1	+(61.4)	-	+	Miscellaneous island, contains miscellaneous metabolism including D-lactate dehydrogenase (BCAL2487) and putative O-antigen acetylase (BCAL2519), glutathione S-transferase (BCAL2539), 3-isopropylmalate dehydratase (BCAL2542 and BCAL2543), MFS transporter (BCAL2525 and BCAL2545), ABC transporter (BCAL2573 to BCAL2576), and nitrilase (BCAL2585)
BcenGI9	16.3	3241588...3257909	tmRNA	1	+(62.8)	-	-	Miscellaneous island, phage origins, possible phage remnant
BcenGI10	6.3	3368693...3375006	tRNA Gly	1	+(59.4)	-	+	Miscellaneous island, inserted into divergent region
Chromosome 2								
BcenGI11	44.1	290291...334378			+(62.0)	-	+	Cenocepacia island, contains arsenic resistance (BCAM0233 to BCAM0235), antibiotic resistance (BCAM0237A), ion and sulfate family transporter (BCAM0238 and BCAM0281), and stress response CDSs (BCAM0276 and BCAM0278)
BcenGI12	46.8	1140183...1186975	tRNA SeC	1	+(63.2)	-	-	Prophage
BcenGI13	46.2	2091701...2137922	BCAM1874	1	+(54.3)	-	+	Prophage
Chromosome 3								
BcenGI14	36.7	573207...609954		1	+(62.8)	-	-	Prophage BcepMu

J2315 has accessory functions found in genomic islands that enhance virulence

- BcenGI11 island present, which promotes pathogenic character in other ET12 strains

Several gene products in J2315 result in antibiotic resistance

TABLE 4. Potential drug resistance determinants in the genome of *B. cenocepacia* strain J2315

Gene product	CDSs ^a	Resistance	Reference
Chromosome 1			
RND family efflux transporter	BCAL1079 to BCAL1081	Unknown	94
Fusaric acid resistance family transporter	BCAL1176* to BCAL1178*	Unknown	139
Fosmidomycin resistance protein	BCAL1451	Fosmidomycin	41
Fusaric acid resistance family transporter	BCAL1453 to BCAL1456	Unknown	139
MFS efflux transporter	BCAL1510 to BCAL1512	Unknown	73
RND family efflux transporter	BCAL1674 to BCAL1676	Aminoglycosides	2, 90
RND family efflux transporter protein	BCAL1778	Unknown	
RND family efflux transporter	BCAL1811 to BCAL1813	Unknown	
MATE family multidrug resistance protein	BCAL1907	Unknown	
RND family efflux transporter	BCAL2134 to BCAL2136	Unknown	
RND family efflux transporter	BCAL2820 to BCAL2822	Unknown	77
MATE family multidrug resistance protein	BCAL2907	Polymyxin B	38
Dihydrofolate reductase	BCAL2915	Trimethoprim	18
Tetracycline resistance protein, class C (pseudogene)	BCAL3259	Tetracycline	3
MFS efflux transporter	BCAL3511 and BCAL3514	Unknown, lacks HylD family component	73

Table. 4. (Holden et. al 2009)

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J2315 has many pseudogenes usually required for pathogenicity of *B. cenocepacia*

TABLE 5. Pseudogenes in the genome of *B. cenocepacia* J2315

Chromosome and gene product	CDSs	Mutation type
Chromosome 1		
Gly/Ala/Ser-rich lipoprotein	BCAL0138	Nonsense (amber)
Type I modification component of restriction-modification system	BCAL0414	Disruption, IS element
Putative transferase	BCAL0648	Frameshift
Putative PTS system, EIIA 2 component	BCAL0810	Nonsense (amber)
UvrABC system protein C 2	BCAL1014	Disruption, IS element
Putative transposase	BCAL1028	Nonsense (amber) and frameshift
IcIR family regulatory protein	BCAL1082	Nonsense (ochre)
Conserved hypothetical protein	BCAL1124a	Disruption, IS element
Conserved hypothetical protein	BCAL1132	Disruption, IS element
Conserved hypothetical protein	BCAL1169	Disruption, IS element
Conserved hypothetical protein	BCAL1302	Disruption, IS element
Putative SNF2-related helicase	BCAL1308	Disruptions, IS elements
Putative oxidoreductase	BCAL1558	Disruption, prophage
TetR family regulatory protein	BCAL1672	Frameshift
TonB-dependent receptor	BCAL1783	Nonsense (amber)
Putative DNA-binding protein	BCAL2066	Frameshift
Hypothetical protein	BCAL2219	Disruption, IS element
Conserved hypothetical protein	BCAL2279	Disruption, IS element
Putative ATP-dependent DNA helicase	BCAL2480	Disruption, IS element
Putative transposase	BCAL2496	Disruption, IS element
Putative methionine aminopeptidase	BCAL2533	Disruption, IS element
Conserved hypothetical protein	BCAL2574	Nonsense (amber)
Putative transposase-related protein	BCAL2581	Frameshift
Conserved hypothetical protein	BCAL2591	Disruption, IS element
ABC transporter ATP-binding protein	BCAL2601	Frameshift and deletion
UvrABC system protein C1	BCAL2854	Disruption, IS element
Glycosyltransferase	BCAL3125	Disruption, IS element
Putative capsule polysaccharide biosynthesis/export protein	BCAL3223	Disruption, IS element
Putative transposase	BCAL3248	Disruption, IS element
Putative transposase	BCAL3249	Disruption, IS element
Tetracycline resistance protein, class C	BCAL3259	Frameshift
Glutamate/aspartate ABC transporter ATP-binding protein GltL	BCAL3354	Frameshift
General secretory pathway protein L	BCAL3517	Frameshift

Table. 5. (Holden et. al 2009) *only chromosome 1 data is pictured

Pseudogene appearance indicates a mutation timeline between strains

TABLE 6. Distribution of virulence factor pseudogenes in *B. cenocepacia* IIIA strains^a

Strain	MLST	Distribution of virulence factor pseudogenes for (strain, factor):				
		BCAL3125§, O antigen	BCAL3223§, uncharacterized EPS	BCAL3517†, T2SS	BCAM0856†, cepacian capsule	BCAM2228†, pyochelin siderophore
J2315*	ST28	ISBcen20 interrupted†	IS407 interrupted†	110-bp deletion	11-bp deletion	Frameshift
BCC0077*	ST28	Uninterrupted	Uninterrupted	In frame	11-bp deletion	Frameshift
BCC0179*	ST28	Uninterrupted	Uninterrupted	In frame	11-bp deletion	Frameshift
BCC0162*	ST28	Uninterrupted	Uninterrupted	In frame	11-bp deletion	Frameshift
BCC0313*	ST28	Uninterrupted	Uninterrupted	In frame	11-bp deletion	Frameshift
BCC0016*	ST29	As J2315†	Uninterrupted	In frame	11-bp deletion	Frameshift
K56-2*	ST30	Uninterrupted	ISBcen13 interrupted†	In frame	11-bp deletion	Frameshift
BCC1261	ST201	No product	Uninterrupted	In frame	In frame	In frame
BCC0222	ST234	No product	Uninterrupted	In frame	In frame	In frame

Table. 6. (Holden et. al 2009)

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Burkholderia Genome DB is a publicly available and simple to use database



Burkholderia
Genome DB



Current Strain (Clear/Search All)

Burkholderia cenocepacia J2315

Gene/Product/Cross-reference Return

Exact matches



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The Burkholderia Genome Database collaborates with an international panel of expert *Burkholderia* researchers to provide high quality updates to genomes annotation and make cutting edge genome analysis data available



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Start typing and select from the list

OR choose a species (optional)

Start typing and select from the list

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Search Annotations

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Draft Genomes	274
Manually-curated annotation updates	1966
Curated GO terms	324

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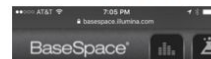
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Surface



Fix

Search options and search results are clear and understandable

168 results were returned

1 2 3 4 5 6 7 8 9 Next

★ = Reference strain (Ordered by **reference strains** first, then by **strain name, ascending**)

Strain	Assembly Status	Replicon	Locus Tag	Feature Type	Coordinates	Gene Length	Gene Name	Product Description	Clipboard
★ Burkholderia cenocepacia J2315	Complete Genome	chromosome 1	BCAL1094	CDS	1190783..1192150 (-)	1368		putative amino acid transport system, membrane protein	<input type="button" value="Add"/>
★ Burkholderia cenocepacia J2315	Complete Genome	chromosome 1	BCAL2282	CDS	2533174..2535189 (-)	2016		putative transport related membrane protein	<input type="button" value="Add"/>
★ Burkholderia cenocepacia J2315	Complete Genome	chromosome 1	BCAL3514	CDS	3851642..3853213 (+)	1572		outer membrane efflux protein	<input type="button" value="Add"/>
★ Burkholderia cenocepacia J2315	Complete Genome	chromosome 2	BCAM1707	CDS	1903701..1904567 (+)	867		putative membrane-associated amino terminal protease	<input type="button" value="Add"/>
★ Burkholderia cenocepacia J2315	Complete Genome	chromosome 3	BCAS0232	CDS	252314..253402 (+)	1089		inner membrane ABC transporter permease protein Yjff	<input type="button" value="Add"/>
★ Burkholderia cenocepacia J2315	Complete Genome	chromosome 3	BCAS0504	CDS	573366..574499 (+)	1134	BcepMu53	putative phage transmembrane acetyltransferase	<input type="button" value="Add"/>
★ Burkholderia cenocepacia J2315	Complete Genome	chromosome 1	BCAL1154	CDS	1255534..1256628 (-)	1095		putative outer membrane porin	<input type="button" value="Add"/>
★ Burkholderia cenocepacia J2315	Complete Genome	chromosome 1	BCAL2482	CDS	2746484..2747656 (-)	1173		putative outer membrane protein	<input type="button" value="Add"/>
★ Burkholderia cenocepacia J2315	Complete Genome	chromosome 2	BCAM0170	CDS	195407..196609 (-)	1203	benE	benzoate membrane transport protein	<input type="button" value="Add"/>
★ Burkholderia cenocepacia J2315	Complete Genome	chromosome 2	BCAM1921	CDS	2133744..2134778 (-)	1035		putative phage membrane protein	<input type="button" value="Add"/>
★ Burkholderia cenocepacia J2315	Complete Genome	chromosome 2	BCAM2141	CDS	2379255..2381474 (-)	2220		ABC transporter ATP-binding membrane protein	<input type="button" value="Add"/>
★ Burkholderia cenocepacia J2315	Complete Genome	chromosome 3	BCAS0538	CDS	599534..600316 (-)	783	BcepMu18	putative phage membrane protein	<input type="button" value="Add"/>
★ Burkholderia cenocepacia J2315	Complete Genome	chromosome 1	BCAL0022	CDS	23905..25689 (+)	1785		putative branched-chain amino acid ABC transporter ATP-binding membrane protein	<input type="button" value="Add"/>

Burkholderia cenocepacia J2315

Strain Overview

Organism Name	Burkholderia cenocepacia J2315
Species	Burkholderia cenocepacia
Strain	J2315
Subspecific Genetic Lineage	
Description/Title	DNA sample from a human male participant in the dbGaP study "Framingham SHARe Peri-Aortic Fat"
Scaffolds	
Contigs	
Contig N50	
Assembly Level	Complete Genome
Percent GC	
Annotated Genes	7298
References	
Partial Genes	

Annotated Features

Feature	Count
gene	7384
CDS	7114
tRNA	74
pseudo	22
misc_RNA	21
rRNA	18

Subcellular Localization

Localization	Count
Cytoplasmic	3134
Unknown	2194
Cytoplasmic Membrane	1519
Periplasmic	234
Unknown (This protein may have multiple localization sites)	210

Cross-References

NCBI BioSample Accession	SAMEA1705928
NCBI Biosample ID	25440
NCBI Taxonomy ID	9606
GOLD Accession	
NCBI Bioprojects	PRJNA339 PRJNA57953
NCBI Sequencing Assay	
NCBI Assembly	GCF_000009485.1

Related Data

Additional Genome Project Info	More on PRJNA339 More on PRJNA57953
Sequencing Information	
Genome Assembly Information	Details

Replicons

Name	Length	GC	
Burkholderia cenocepacia J2315 chromosome 1, complete genome.	3870082 bp	66.7%	Replicon details
Burkholderia cenocepacia J2315 chromosome 2, complete genome.	3217062 bp	67.3%	Replicon details
Burkholderia cenocepacia J2315 chromosome 3, complete genome.	875977 bp	66.9%	Replicon details
Burkholderia cenocepacia J2315 pBCJ2315 plasmid, complete genome.	92661 bp	62.8%	Replicon details

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Pages are well organized and the data are easily downloadable

- The data are sourced from NCBI resources and cross-references are given.

- All data updates are logged and major updates occur on a yearly schedule.

Many variations of the regular expression pattern exist

- Commonly encountered patterns included BCAL#####, BCAM#####, BCAS#####, and pBCA###.
- Each set of four letters corresponded to a certain replicon.
- It was also found that some patterns included an **A** at the end.
- All chromosomes contained genes with patterns that included a lowercase **r** before the number set.
- Related tRNA genes had letters at the end of the pattern.

Acknowledgements

Dr. John D. Dionisio

Dr. Kam D. Dahlquist

References

Holden, M. T., Seth-Smith, H. M., Crossman, L. C., Sebaihia, M., Bentley, S.

D., Cerdeño-Tárraga, A. M., ... & Parkhill, J. (2009). The genome of *Burkholderia cenocepacia* J2315, an epidemic pathogen of cystic fibrosis patients. *Journal of bacteriology*, 191(1), 261-277.

Winsor GL, Khaira B, Van Rossum T, Lo R, Whiteside MD, Brinkman FS. (2008). The *Burkholderia* Genome Database: facilitating flexible queries and comparative analyses. *Bioinformatics* 2008 Dec 1;24(23):2803-4. (PMID: 18842600)

Questions?

