Reference Sequence (RefSeq) Database Non-redundant genomic, RNA and protein sequence records, from microbes to human https://www.ncbi.nlm.nih.gov/refseq National Center for Biotechnology Information • National Library of Medicine • National Institutes of Health • Department of Health and Human Services

Scope

The Reference Sequence (RefSeq) database is a collection of standard sequences intended to represent genomic sequences, transcripts, and translated products that occur naturally in an organism (<u>www.ncbi.nlm.nih.gov/refseq/</u>). The taxonomic range of the collection spans much of the planet's diversity and includes eukaryotes, bacteria, archaea, and viruses. Each sequence record is based on public sequence data submitted to the International Nucleotide Sequence Database Collaboration (INSDC), but in contrast to the public sequence archives, the RefSeq collection is largely non-redundant. Other attributes that distinguish RefSeq from INSDC records are listed below.



Automatic processing of public sequence records, collaboration with authoritative scientists or groups outside NCBI, and curation by biological experts at NCBI are at the center of the RefSeq processing pipelines. The product is a collection that is richly annotated with structural and functional features, actively maintained, and flexible enough to provide se-

guence standards to meet the needs of different research communities. For example, RefSegGene records support clinical laboratory testing for human disease, curated vertebrate transcript records support genome annotation pipelines and browsers, and ribosomal RNA records are provided as type standards for bacterial and archaeal genomes. The RefSeg collection is also a key element unifying several of the molecular resources provided by NCBI.

Taxonomic Node	Release 97 Count	Attribute	INSDC*	RefSeq		
Archaea	1323	Accession includes underscore ('_')	No	Yes		
Bacteria	60021	INSDC member	Yes	No		
Fungi	12561	Source of sequence	Submitter	INSDC		
Invertebrate	3817	Source of annotation	Submitter	Multiple		
Mitochondrion	10048	Owner of sequence record	Submitter	NCBI		
Plant	4343	Redundancy	High	Low No		
Plasmid	4476	Archive of experimental data	Yes			
Plastid	4506	· · · ·		-		
Protozoa	565	Review of experimental data	No	Yes		
Vertebrate_mammalian	1170	Curation by NCBI	No	Yes		
Vertebrate_other	4278	Regular update schedule	No	Yes		
Virus	9305	* The INSDC includes NCBI (USA), ENA (Europe), and DDBJ (

RefSeq also started to anno-

tated experimentally verified functional elements onto genomic records, with NG_ initialed accession. More information on this effort is at: www.ncbi.nlm.nih.gov/refseq/functionalelements/

Access

RefSeq records are available by

- Searching in the nucleotide or protein databases (www.ncbi.nlm.nih.gov/nuccore and www.ncbi.nlm.nih.gov/protein)
- BLASTing against selected databases (<u>blast.ncbi.nlm.nih.gov</u>), and
- Downloading through FTP (<u>ftp.ncbi.nlm.nih.gov/refseq/</u> and <u>ftp.ncbi.nlm.nih.gov/genomes/refseq/</u>)

RefSeq records are also available through hyperlinks displayed from many NCBI resources, including Gene, Genome, BioProject, dbSNP, ClinVar, Protein Clusters, and more. RefSeq filters in the Entrez Nucleotide or Protein databases allows the quick retrieval of relevant RefSeq records from the query result. This filter (refseq[filter]) is also available to the Entrez Programming Utilities (EUtils, <u>www.ncbi.nlm.nih.gov/books/NBK25501/</u>) for programmatic access. RefSeq records are found in the general nucleotide (NT) and non-redundant protein (NR) BLAST databases. RefSeq-only databases are also available from the Database pull-down list:

- Reference RNA sequences (refseq_rna)
- Reference proteins (refseq_protein)
- Reference genomic sequences (refseq_genomic)
- NCBI genomes (chromosome) includes only the chromosome level records
- 16S ribosomal RNA sequences (Bacteria and Archaea)

In addition, RefSeq sub-project and organism oriented BLAST databases are available from organism-specific BLAST pages, e.g., Human genome, Microbes, as well as the RefSeqGene project page. The complete RefSeq collection, subsets defined by taxonomic node (e.g., plants) or type of molecule, or key model organisms can be downloaded by FTP (<u>ftp.ncbi.nlm.nih.gov/refseq/release/</u> and <u>ftp.ncbi.nlm.nih.gov/genomes/refseq/</u>).

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Record Display

The Nucleotide database displays Reference Sequences in GenBank format by default (**A**). You can access the FASTA and graphical displays using links (**B**) at the top of the page. Use links in the collapsible sections to the right (**C**) to access relevant records from other sources, such as PubMed and Gene (**D**). Refer to the COMMENT section (**E**) for information about the INSDC source data used to derive this record. For some records, this section may also include a review status, a summary of the gene function in the summary paragraph, as well as structured reports of transcript evidence, gene and sequence attributes of biological interest, and more. Refer to the table (**F**) for summary of biological attributes that may be included in the COMMENT section. For more details, see <u>www.pubmed.gov/26553804</u>.

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FlyBase	Database of Drosophila C	Gene & Genomics				,				
RGD	Rat Genome Database					ins detailed annotation of exons,				
EcoGene	EcoGene Database		(misc_feature) of	the gene,	coding	iscellaneous features sequences (CDS) and protein				
TAIR	The Arabidopsis Informat	ion Resource	products. Many fe	eatures inc	clude c	ross-references to related records				
SGD	Saccharomyces Genome		in other database up link names and			where. The table (left, H) sums				
BeeBase	hymenoptera genome da	tabase			-s uley					

Links to RefSeq Entries from Other Resources

RefSeq records are integral parts of many other NCBI resources. For example, the Gene full report page (**A**) reports the RefSeq curation status (**B**). Click the in-page navigation link "NCBI Reference Sequences (RefSeq)" (**C**) to bring the section in focus and see a detailed summary of individual RefSeq entries for the Gene record. Display the record in "Gene Table" format (**D**) to get details on the exon/intron structure, their genomic coordinates, and links to FASTA sequence.

	Full Report - A	Send to: +	Hide sidebar >>
	KCNC1 potassi	um voltage-gated channel subfamily C member 1 [Homo sapiens (human)]	
Format	www.ncbi.nlm	.nih.gov/gene/3746	Table of contents
Full Report	Summary		Summary
Full Report (text)	Official Symbol	KCNC1 provided by HGNC	Genomic context
Gene Table		potassium voltage-gated channel subfamily C member 1 provided by HGNC	Genomic regions, transcripts, and products
Gene Table (text)	Primary source	HGNC:HGNC:6233	Expression
 GeneRIF Summary 	See related	Ensembl:ENSG00000129159 MIM:176258; Vega:OTTHUMG00000166359	Bibliography
Summary (text)	Gene type RefSeg status		Phenotypes
Tabular	Organism	Homo sapiens	Variation
Tabular (text)	Lineage	Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi; Mammalia; Eutheria; Euarchontoglires;	Pathways from BioSystems
O ASN.1	Also known as	Primates; Haplorrhini; Catarrhini; Hominidae; Homo KV4; EPM7; NGK2; KV3.1	Interactions
O XML	Summary	This gene encodes a member of a family of integral membrane proteins that mediate the voltage-dependent	General gene information
		potassium ion permeability of excitable membranes. Alternative splicing is thought to result in two transcript	Markers, Clone Names, Homology, Gene Ontology
		variants encoding isoforms that differ at their C-termini. These isoforms have had conflicting names in the	General protein information
		literature: the longer isoform has been called both "b" and "alpha", while the shorter isoform has been called both "a" and "beta" (PMIDs 1432046, 12091563). [provided by RefSeq. Oct 2014]	NCBI Reference Sequences (RefSeq)
	Expression	Biased expression in brain (RPKM 5.1) and testis (RPKM 0.7) See more	Related sequences
	Orthologs	mouse all	Additional links

RefSeq mRNA records are an integral part of the genome annotation process. The "Genomic regions, transcripts, and products" section of the report presents this graphically using the embedded Sequence Viewer (SV) display (E), with

the alternatively spliced transcripts shown at the top (**F**). Tracks below the transcripts provide additional supporting evidence from RNA-seq data (**G**).

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Complete RefSeq proteomes from a

selected subset of organisms representing key taxonomic groups, are also input into HomoloGene, which identifies homologd through a comprehensive set of calculations. In addition, the NCBI eukaryotic genome annotation pipeline automatically analyzes the RefSeq proteins it processes to identify homologous genes. Both sets of homologs are available under the "Homology" heading (H) of the "General gene information" section of the Gene full report page.

General gene information		Homologs from comprehensive analysis of complete RefSeq						
Markers	proteomes from selected organisms l	HomolGene.						
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Homologs of the KCNC1 gene: The KCNC1 gene is conserved in chimpanzee, Rhesus monkey, dog, cow, mouse, rat, chicken, zebrafish,								
mosquito, and C.elegans.								
Orthologs from Annotation Pipelin	: 246 organisms have orthologs with human gene KCN	NC1						
Orthologs								
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Gene Ontology Provided by GO		annotation pipeline.						

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Searching RefSeg Using BLAST

The NCBI BLAST web service (blast.ncbi.nlm.nih.gov) provides a way to search the public databases maintained at NCBI using sequences as the query. You can search against RefSeq entries using search pages listed under the "Basic BLAST" section by selecting

seq_genomes, refseq_ge seq protein. To search ag genome assemblies of a sp use the organism-specific E listed in the "BLAST Genon the BLAST homepage. To genomic data available for listed, type the name in the select from the suggested l "Search". This will retrieve search page with that datas database.

To search against RefSeq for bacteria and archaea, u Microbes link (C) from the E homepage, which points to crobial Genome BLAST pa (shown in part). In this page default database is set to a representative subset (D) selected by the research community and/or by NCBI computation. Use the Organism input box (E) to limit the search to specific taxa by typing and selecting from the suggested list. Check the "All Genomes" radio button (F) to see other microbial genomes available for selection. Hold ctrl key and click to select multiple datasets.

Additional Information

Documentation

The RefSeg homepage (www.ncbi.nlm.nih.gov/refseg) eral description of the project and many technical details. Other documents available include:

The NCBI Handbook RefSeg Chapter at www.ncbi.nlm.nih.gov/books/ NBK21091

Or, upload file

Choose Search

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Optional

- The RefSeq FAQ at www.ncbi.nlm.nih.gov/books/NBK50680 •
- Release notes at ftp.ncbi.nlm.nih.gov/refseq/release/release-notes
- Pruitt KD. et. al. 2014. RefSeg: an update on mammalian reference sequences. Nucleic Acids Res. 42 (Database issue):D756-63 (www.ncbi.nlm.nih.gov/pubmed/24259432).

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RefSeq: an update on prokaryotic genome annotation and curation. Haft DH, et al. Nucleic Acids Res. 2018 Jan • 4:46(D1):D851-D860 (www.ncbi.nlm.nih.gov/pubmed/29112715)

Alternative ways for data access

The RefSeg sequence data are released on a regular schedule. Data files from the release are available from the RefSeq FTP site (ftp.ncbi.nlm.nih.gov/refseq) and the genomes ftp site (ftp.ncbi.nlm.nih.gov/genomes/refseq). The Aspera download site (www.ncbi.nlm.nih.gov/public) provides a faster alternative, which requires Aspera browser plugin (downloads.asperasoft.com/connect2/). In addition, EUtils can be used to access the RefSeq dataset from the Nucleotide and Protein databases programmatically. The EDirect package provides command line access to RefSeq data and allows flexible workflow and data parsing (www.ncbi.nlm.nih.gov/books/NBK179288/).

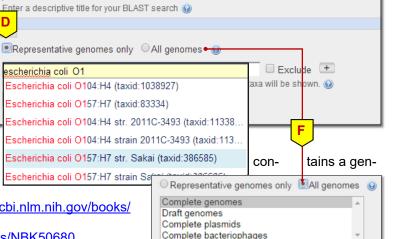
Feedback and technical assistance

- For RefSeq record update requests, contact www.ncbi.nlm.nih.gov/RefSeq/update.cgi
- For questions and feedback on NCBI resources in general, contact info@ncbi.nlm.nih.gov
- For guestions and problems encountered during BLAST searches, contact blast-help@ncbi.nlm.nih.gov



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