



DNA SEQUENCE CONTROLS EXPRESSION OF GENE INVOLVED IN CANCER

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BACKGROUND INFORMATION

- Bcl-2 produces a protein that inhibits apoptosis
- Expression of Bcl-2 gene is regulated both transcriptionally and post-transcriptionally
- AU-rich element (ARE) recruits a number of proteins that destabilize Bcl-2 mRNA
- A 30 nucleotide region termed CA-repeated Region (CAR) identified by Jeong-Hwa Lee and coworkers contributes to constitutive decay of Bcl-2 mRNA in steady states



AIM

- To identify elements that regulate Bcl-2 mRNA stability with the use of bioinformatics



FINDING BIBLIOGRAPHIC INFORMATION AND FULL TEXT ARTICLES



U.S. National Library of Medicine
National Institutes of Health

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Jeong-Hwa Lee Bcl-2 Journal of biological chemistry

Search Clear

[Display Settings:](#) Abstract

[J Biol Chem](#). 2004 Oct 8;279(41):42758-64. Epub 2004 Aug 3.



CA repeats in the 3'-untranslated region of bcl-2 mRNA mediate constitutive decay of bcl-2 mRNA.

[Lee JH](#), [Jeon MH](#), [Seo YJ](#), [Lee YJ](#), [Ko JH](#), [Tsujimoto Y](#), [Lee JH](#).

Department of Biochemistry, The Catholic University of Korea, Seoul 137-701, Korea.

Abstract

An AU-rich element (ARE) in the 3'-untranslated region (UTR) of bcl-2 mRNA has previously been shown to be responsible for destabilizing bcl-2 mRNA during a AUF1 binding. In the present study, we investigated the effect of the region upstream of the ARE on bcl-2 mRNA stability using serial deletion constructs of the 3'-nucleotides mostly consisting of the CA repeats, located upstream of the ARE, resulted in the stabilization of bcl-2 mRNA abundance, in the absence or presence of the CA repeats in terms of destabilizing bcl-2 mRNA was proven by the substituting the CA repeats with other alternative repeats of purine/pyrimidine, but this had no effect on bcl-2 mRNA. CA repeats alone, however, failed to confer instability to bcl-2 or gfp reporter mRNAs, indicating a requirement for additional sequences in the upstream region. Deletion and replacement of a part of the region upstream of the CA repeats revealed that the entire 131-nucleotide upstream region is an essential prerequisite for the destabilization of bcl-2 mRNA. Unlike the ARE, CA repeat-mediated degradation of bcl-2 mRNA was not accelerated upon apoptotic stimulus. Moreover, the upstream CA repeats are conserved among mammals. Collectively, CA repeats contribute to the constitutive decay of bcl-2 mRNA in the steady states, thereby maintaining apoptosis in mammalian cells.

PMID: 15294893 [PubMed - indexed for MEDLINE] [Free Article](#)

FINDING BCL-2 GENE DNA SEQUENCE

site (see Fig. 1A; all nucleotide positions were based on the sequence of accession number **M13994** in GenBank™). The PCR products were

Nucleotide
Alphabet of Life

Search:

[Display Settings:](#) GenBank

Human B-cell leukemia/lymphoma 2 (bcl-2) proto-oncogene mRNA encoding bcl-2-alpha protein, complete cds

GenBank: M13994.1
[FASTA](#) [Graphics](#)

[Go to:](#)

LOCUS HUMBCL2A 5086 bp mRNA linear PRI 31-OCT-1994
DEFINITION Human B-cell leukemia/lymphoma 2 (bcl-2) proto-oncogene mRNA encoding bcl-2-alpha protein, complete cds.
ACCESSION M13994
VERSION M13994.1 GI:179366
KEYWORDS alternative splicing; bcl-2-alpha protein; proto-oncogene.
SOURCE Homo sapiens (human)
ORGANISM [Homo sapiens](#)
Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;

```

source      1..5086
            /organism="Homo sapiens"
            /mol_type="mRNA"
            /db_xref="taxon:9606"
            /map="18q21.3"
gene        1..5086
            /gene="BCL2"
mRNA        1..5086
            /gene="BCL2"
            /product="bcl2a mRNA"
CDS         1459..2178
            /gene="BCL2"
            /note="bcl2-alpha protein"
            /codon_start=1
            /protein_id="AAA51813.1"
            /db_xref="GI:179367"
            /db_xref="GDB:G00-119-031"
            /translation="MAHAGRTGYDREIVMKYIHYKLSQRGYEWDAAGDVGAAPPGAAP
            APGIFSSQPGHTPHPAASRDPVARTSPLQTPAAPGAAAGPALSFPVFPVVHLALRQAGD
            DFSRRYRGDFAEMSSQLHLTPFTARGRFATVVEELFRDGVNWRIVAFVFFGGVMCVE
            SVNREMSPLVDNIALWMTEYLNRLHTWIQDNGGWDAFVELYGPMSMRPLDFDSWLSLK
            TLLSLALVGACITLGAYLSHK"

```

Link to protein
sequence

```

ORIGIN      710 bp upstream of SstI site.
1  ggcggcggccc ctccggcgcg cctgcccggcc cgcccggcgc gctcccggccc gccgctctcc
61  gtggccccgcg cgcgctgccc cgcccgccgc tgccagcgaa ggtgcccgggg ctccggggccc
121  tccctgcccgg cggccgctcag cgctcggagc gaactgcccg acgggagggtc cgggaggcga
181  ccgtagtcgcg gcccgccgccc aggaccagga ggaggagaaa ggggtgcccag cccggaggcgg
241  ggggtgcccgg gtgggggtgca gcggaagagg ggggtccagg gggagaactt cgtagcagtc
301  atccttttta  ggaaaagagg gaaaaataaa aaccctcccc caccacctcc ttctccccac
361  ccctgcggcgc accacacaca gcgcgggcct ctagcgcctg gcaccggcgg gccaggcggg
421  tcctgccttc  atttatccag cagcttttcg gaaaatgcat ttgctgttcg gagtttaatc
481  agaagacgat  tcctgcctcc gtccccggct ccttcacgtt cccatctccc ctgtctctct
541  cctggggagg  cgtgaagcgg tcccgtggat agagattcat gcctgtgtcc gcgctgtgtt
601  gcgcgcgat  aaattgcccga gaaggggaaa acatcacagg acttctgcga atacgggact
661  gaaaattgta  attcatctgc cgccgcccgt gccaaaaaaa aactcgagct cttgagatct
721  cgggttgga  ttctgcgga  ttgacatttc tgtgaagcag aagtctggga atcgatctgg
781  aaatcctcct  aatctttact ccctctcccc ccgactcctg attcattggg aagtttcaa

```

DNA
Sequence



BCL-2 PROTEIN SEQUENCE

NCBI Resources How To

Protein

Translations of Life

Search: Protein

[Limits](#) [Advanced search](#) [Help](#)

[Display Settings:](#) GenPept

ORIGIN

1 mahagrtgyd nreivmkyih yklsqrgyew dagdvgaapp gaapapgifs sqpghtphpa
61 asrdpvarst plqtpaapga aagpalspvp pvvhlalrqa gddfsrryrg dfaemssqlh
121 ltpftargrf atvveelfrd gvnwgrivaf fefggvmcve svnremsplv dnialwmtcy
181 lnrlhtwiq dnggwafve lygpsmrplf dfswlsikt1 lslalvgaci tlgaylshk

bcl2-alpha protein [Homo sapiens]

GenBank: AAA51813.1

[FASTA](#) [Graphics](#)

[Go to:](#)

LOCUS AAA51813 239 aa linear PRI 31-OCT-1994
DEFINITION bcl2-alpha protein [Homo sapiens].
ACCESSION AAA51813
VERSION AAA51813.1 GI:179367
DBSOURCE locus HUMBCL2A accession [M13994.1](#)
KEYWORDS .
SOURCE Homo sapiens (human)
ORGANISM [Homo sapiens](#)
Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
Mammalia; Eutheria; Euarchontoglires; Primates; Haplorrhini;
Catarrhini; Hominidae; Homo.
REFERENCE
1 (residues 1 to 239)
AUTHORS Tsujimoto, Y. and Croce, C.M.
TITLE Analysis of the structure, transcripts, and protein products of
bcl-2, the gene involved in human follicular lymphoma
JOURNAL Proc. Natl. Acad. Sci. U.S.A. 83 (14), 5214-5218 (1986)
PUBMED [3523487](#)
COMMENT Clean copy sequence for [1] kindly provided by Y.Tsujimoto,
10-FEB-1987.

IDENTIFICATION OF ARE AND CAR REGIONS

- repeats (Mobylye portal)
- fuzznuc (Emboss)



Search [\[more\]](#)

Programs

- alignment
- assembly
- database
- display
- genetics
- hmm
- nucleic
- phylogeny
- protein
- sequence
- structure

Workflows

- align-family
- hmm_build_search
- protein_distance_phylogeny

Data Bookmarks [\[overview\]](#)

Jobs [\[overview\]](#)

Tutorials

- [How to use Mobylye? A step by step tutorial](#)
- [Registration information](#)
- [Sequence formats](#)
- [Alignment formats](#)

repeats ✖

repeats 1.1

Run

Reset

Search repeats in DNA sequence

* Sequence File [?](#)

Enter your data below:

- * Match bonus (input as positive) (Alpha)
- * Mismatch penalty (input as positive) (Beta)
- * Indel penalty (input as positive) (Delta)
- * Threshold score to report an alignment (Reportmax)
- * Pattern size (Size)
- * Number of characters to match to trigger dynamic programming (Lookcount) [?](#)



fuzznuc

Search for patterns in nucleotide sequences ([read the manual](#))

Unshaded fields are optional and can safely be ignored. ([hide optional fields](#))

Input section

Select an input sequence. Use one of the following three fields:

1. To access a sequence from a database, enter the USA here:

2. To upload a sequence from your local computer, select it here:

Browse...

```
ACAGAATGATCAGACCTTTG
AATGATTCTAATTTTTAAAGCAAAATATTATTTTATGAAAAGTTTACATTG
TCAAAAGTGATGAATATGGAA
TATCCAATCCTGTGCTGCTATCCTGCCAAAATCATTTTAATGGAGTCAGT
TTGCAGTATGCTCCACGTGG
TAAGATCCTCCAAGCTGCTTTAGAAAGTAAACAATGAAAGAACGTGGACGTTT
TTAATATAAAAAGCCTGTTTTG
TCTTTTGTTGTTGTTCAAAACGGGATTCCACAGAGTATTTGAAAAATGTATA
TATATTAAGAGGTCACGGGG
```

3. To enter the sequence data manually, type here:

Search pattern

Advanced section

OUTPUT FILE [outfile](#)

```

#####
# Program: fuzznuc
# Rundate: Tue 29 Mar 2011 16:27:31
# Commandline: fuzznuc
# -auto
# -sequence /geninf/prog/www/htdocs/tools/emboss/output/187596/.sequence
# -pattern ATTTA
# -nocomplement
# -out file outfile
# -rformat2 seqtable
# Report_format: seqtable
# Report_file: outfile
#####
#-----
#
# Sequence: HUMBECLZA      from: 1      to: 5086
# HitCount: 11
#
# Pattern_name Mismatch Pattern
# pattern1      0 ATTTA
#
# Complement: No
#-----
Start      End      Strand Pattern_name Mismatch Sequence
  431      435      + pattern1      . ATTTA
 1036     1040      + pattern1      . ATTTA
#####
 2377     2381      + pattern1      . ATTTA
 2400     2404      + pattern1      . ATTTA
 2429     2433      + pattern1      . ATTTA
 2433     2437      + pattern1      . ATTTA
 2437     2441      + pattern1      . ATTTA
 2931     2935      + pattern1      . ATTTA
 3906     3910      + pattern1      . ATTTA
#-----
Start      End      Strand Pattern_name Mismatch Sequence
  431      435      + pattern1      . ATTTA
 1036     1040      + pattern1      . ATTTA
 2377     2381      + pattern1      . ATTTA
 2400     2404      + pattern1      . ATTTA
 2429     2433      + pattern1      . ATTTA
 2433     2437      + pattern1      . ATTTA
 2437     2441      + pattern1      . ATTTA
 2931     2935      + pattern1      . ATTTA
 3906     3910      + pattern1      . ATTTA
 4022     4026      + pattern1      . ATTTA

```

ARE region located
approximately
between 2377 and
2441



fuzznuc

Search for patterns in nucleotide sequences ([read the manual](#))

Unshaded fields are optional and can safely be ignored. ([hide optional fields](#))

Input section

Select an input sequence. Use one of the following three fields:

1. To access a sequence from a database, enter the USA here:

2. To upload a sequence from your local computer, select it here:

```
TTAATATAAAAGCCTGTTTTG
TCTTTTGTGTTGTTCAAACGGGATTCACAGAGTATTTGAAAAATGTATA
TATATTAAGAGGTCACGGGG
GCTAATTGCTAGCTGGCTGCCTTTTGCTGTGGGGTTTTGTTACCTGGTTT
TAATAACAGTAAATGTGCCC
AGCCTCTTGGCCCCAGAAGTGTACAGTATTGTGGCTGCACCTTGCTCTAAG
AGTAGTTGATGTTGCATTTT
CCTTATTGTTAAAAAACATGTTAGAAGCAATGAATGTATATAAAAAGC
```

3. To enter the sequence data manually, type here:

Search pattern

Advanced section



OUTPUT FILE [outfile](#)

```
#####
# Program: fuzznuc
# Rundate: Tue 29 Mar 2011 16:18:18
# Commandline: fuzznuc
#   -auto
#   -sequence /geninf/prog/www/htdocs/tools/emboss/output/775580/.sequence
#   -pattern CACACACACA
#   -nocomplement
#   -outfile outfile
#   -rformat2 seqtable
# Report_format: seqtable
# Report_file: outfile
#####
```

```
#=====
#
# Sequence: HUMBCL2A      from: 1      to: 5086
# HitCount: 4
#
# Pattern_name Mismatch Pattern
# pattern1      0 CACACACACA
#
# Complement: No
#
#=====
```

CAR region located
approximately
between 2310 and
2339

Start	End	Strand	Pattern_name	Mismatch	Sequence
2310	2319	+	pattern1	.	CACACACACA
2326	2335	+	pattern1	.	CACACACACA
2328	2337	+	pattern1	.	CACACACACA
2330	2339	+	pattern1	.	CACACACACA



COMBINING THE DATA

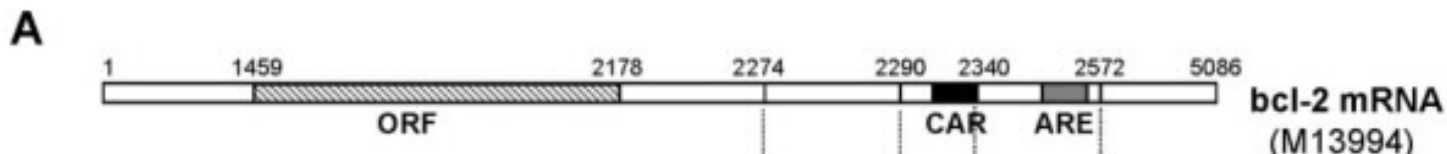
Start	End	Strand	Pattern_name	Mismatch	Sequence
431	435	+	pattern1	.	ATTTA
1036	1040	+	pattern1	.	ATTTA
2377	2381	+	pattern1	.	ATTTA
2400	2404	+	pattern1	.	ATTTA
2429	2433	+	pattern1	.	ATTTA
2433	2437	+	pattern1	.	ATTTA
2437	2441	+	pattern1	.	ATTTA
2931	2935	+	pattern1	.	ATTTA
3906	3910	+	pattern1	.	ATTTA
4022	4026	+	pattern1	.	ATTTA
4299	4303	+	pattern1	.	ATTTA

ARE region located approximately between 2377 and 2441

Start	End	Strand	Pattern_name	Mismatch	Sequence
2310	2319	+	pattern1	.	CACACACACA
2326	2335	+	pattern1	.	CACACACACA
2328	2337	+	pattern1	.	CACACACACA
2330	2339	+	pattern1	.	CACACACACA

CAR region located approximately between 2310 and 2339

From the paper,

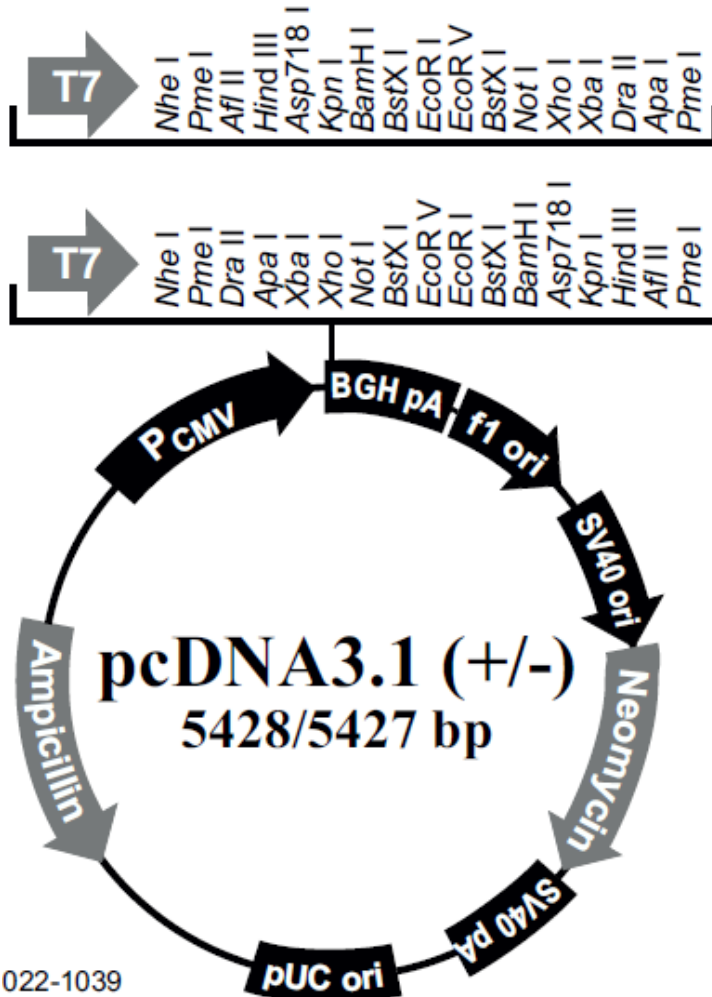


STEPS TO CLONING OF GENE

- Step 1: Choose a proper expression vector.
- Step 2: Choose the correct isoform needed.
- Step 3: Choose proper restriction sites. (Q5)
- Step 4: Design primers to amplify the cDNA.
- Step 5: Digest and insert in to the vector.



STEP 1: CHOOSE A PROPER EXPRESSION VECTOR



pcDNA is a good expression vector for protein overexpression in mammalian cells



STEP 2: CHOOSE THE CORRECT ISOFORM NEEDED.

mRNA and Protein(s)

1. [NM_000633.2](#) · [NP_000624.2](#) apoptosis regulator Bcl-2 alpha isoform **Isoform 1 --- longer**

Description	Transcript Variant: This variant (alpha) represents the longer transcript and encodes the longer isoform (alpha).
Source sequence(s)	AC021803 , AC022726 , BC027258
Consensus CDS	CCDS11981.1
UniProtKB/Swiss-Prot	P10415
Related Ensembl	ENSP00000329623 , ENST00000333681

Conserved Domains (3) [summary](#)

cd06845 Location:94 – 201 Blast Score: 401	Bcl-2_like; Apoptosis regulator proteins of the Bcl-2 family, named after B-cell lymphoma 2. This alignment model spans what have been described as Bcl-2 homology regions BH1, BH2, BH3, and BH4. Many members of this family have an additional C-terminal...
c102540 Location:7 – 30 Blast Score: 123	BH4; Bcl-2 homology region 4
TIGR00865 Location:1 – 239 Blast Score: 749	bcl-2; Apoptosis regulator

2. [NM_000657.2](#) · [NP_000648.2](#) apoptosis regulator Bcl-2 beta isoform **Isoform 2 --- shorter**

Description	Transcript Variant: This variant (beta) differs in the 3' UTR and coding region compared to variant alpha. The resulting isoform (beta) is shorter and has a distinct C-terminus compared to isoform alpha.
Source sequence(s)	AC021803 , AI401297
Consensus CDS	CCDS45882.1
UniProtKB/TrEMBL	C9JHD5
Related Ensembl	ENSP00000404214 , ENST00000444484

Conserved Domains (2) [summary](#)

cd06845 Location:94 – 197 Blast Score: 381	Bcl-2_like; Apoptosis regulator proteins of the Bcl-2 family, named after B-cell lymphoma 2. This alignment model spans what have been described as Bcl-2 homology regions BH1, BH2, BH3, and BH4. Many members of this family have an additional C-terminal...
c102540 Location:7 – 30 Blast Score: 124	BH4; Bcl-2 homology region 4

STEP 3: CHOOSE PROPER RESTRICTION SITES

Some software that can be used:

- RestrictionMapper
- <http://www.restrictionmapper.org/>
- NEB Cutter
- <http://tools.neb.com/NEBcutter2/index.php>
- Mapper
- <http://arbl.cvmbs.colostate.edu/molkit/mapper/index.html>



STEP 3: CHOOSE PROPER RESTRICTION SITES.

The screenshot shows the NEBcutter V2.0 web application running in a Microsoft Internet Explorer browser. The browser's address bar displays the URL <http://tools.neb.com/NEBcutter2/index.php>. The page features the NEBcutter V2.0 logo and navigation links for Program Guide, Help, and Comments. A descriptive paragraph explains the tool's function: finding large, non-overlapping open reading frames and restriction enzyme sites in a DNA sequence. It notes that the maximum input file size is 1 MByte and the maximum sequence length is 300 KBases. A link for "What's new in V2.0" is provided.

The main interface includes the following elements:

- Local sequence file:** A text input field with a "Browse..." button.
- GenBank number:** A text input field with a "[Browse GenBank]" button.
- or paste in your DNA sequence:** A large text area with the instruction "(plain or FASTA format)".
- Standard sequences:** Two dropdown menus, currently set to "# Plasmid vectors" and "# Viral + phage".
- Submit:** A button to process the input.
- More options:** A button to expand settings.
- Set colors:** A button to customize the output.
- The sequence is:** Radio buttons for "Linear" (selected) and "Circular".
- Enzymes to use:** A list of radio button options:
 - NEB enzymes
 - All commercially available specificities
 - All specificities
 - All + defined oligonucleotide sequences
 - Only defined oligonucleotide sequences

STEP 3: CHOOSE PROPER RESTRICTION SITES



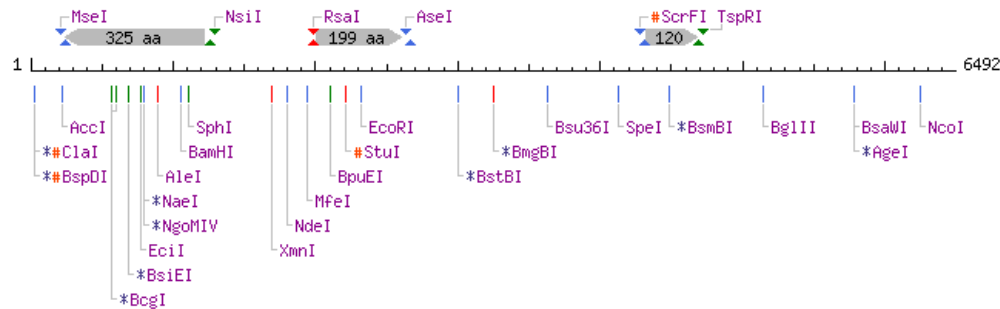
Linear Sequence: Bcl-2

[Help](#) [Comments](#)

Display: - NEB single cutter restriction enzymes
- Main non-overlapping, min. 100 aa ORFs

GC=44%, AT=56%

Cleavage code	Enzyme name code
⊠	blunt end cut
⊡	5' extension
⊣	3' extension
⊢	cuts 1 strand
	Available from NEB
	Has other supplier
	Not commercially available
	*: cleavage affected by CpG meth.
	#: cleavage affected by other meth.
	(enz.name): ambiguous site



- Main options
- New DNA
- Custom digest
- View sequence
- ORF summary
- Save project
- Print

Availability
All commercial
All

Display
2 cutters
3 cutters

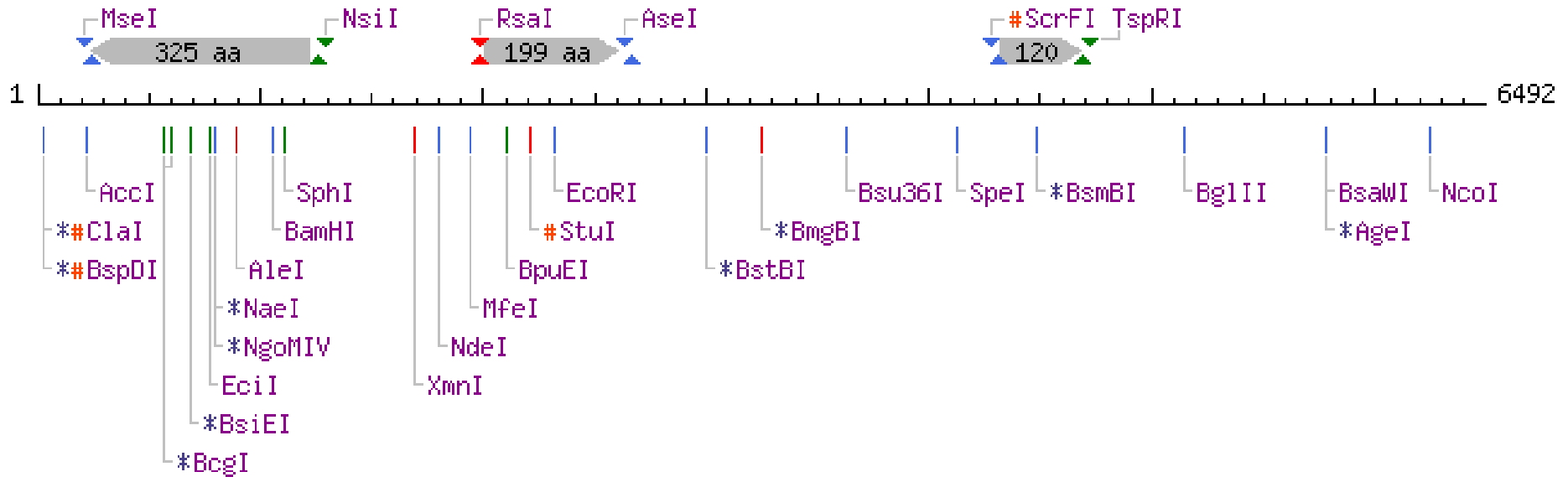
Zoom
Zoom in
More...

- List
- 0 cutters
- 1 cutters
- All sites
- Save all sites
- Flanking enzymes

Minimum ORF length to display: 100 a.a.

NEB Cutter

STEP 3: CHOOSE PROPER RESTRICTION SITES



No **HindIII** and **XhoI** cutting sites were found in human Bcl-2 cDNA sequence

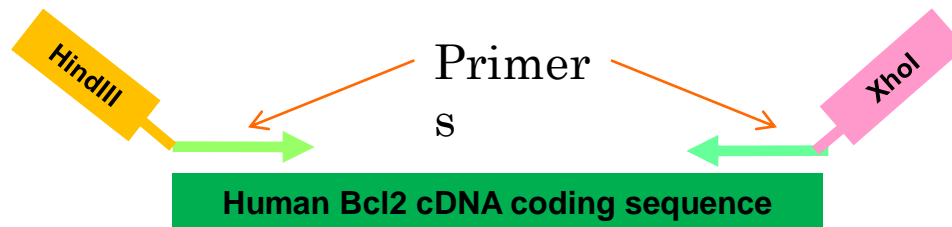


For design of the cloning PCR primers



STEP 4: DESIGN PRIMERS TO AMPLIFY THE cDNA

- There are quite a number of free primer design tools for download online.
- E.g. PerlPrimer, GeneRunner, etc.
- Add the restriction site to the 5' end of the forward and reverse primer designed by the tool for primer synthesis.



STEP 4: DESIGN PRIMERS TO AMPLIFY THE cDNA

PerlPrimer v1.1.16 - gi-72198188-ref-NM_0006332-Homo_sapiens_B-cell_CLL/lymphoma_2_BCL2_nuclear_gene_encoding_mi...

File Tools Help

Standard PCR Bisulphite PCR Real-time PCR Sequencing Primers

Primer Tm: 57 - 63 °C Difference 3 °C

Primer Length: 20 - 24 bases

Amplified range: 5' 493 - 493 3' 1212 - 1212

Amplicon size: 719 - 719 bases

Set from ORF: -10 +10

Options: Exclude %GC GC clamp

Add 5' F seq: [] Frame:

Add 5' R seq: [] Frame:

Sequence:

```
gctcgtc caatcaagaaaattctgagactattaataaataagactgtagtgtgatactgagtaaatccatgcacctaaacctttggaaaatctgcgct
gggccctccagatagctcatttcatttaagttttccctccaaggtagaatttgcaagagtgcagctggattgcatttctttggggaagcttctctttgg
tggttttggttattataccttcttaagttttcaaccaaggtttgctttgtttgtgagttactggggttattttgttttaataaaaaataagtgtaaat
aagtgtttttgtattgaaaagctttgttatcaagattttcatactttaccttccatggctcttttaagattgatacttttaagaggtggctgatattc
tgcaaacactgtacacataaaaaaacggttaaggatactttacatggttaaggtaaagtaagctccagttggccaccattagctataatggcactttgtt
tgtgttttggaaaaagtcacattgccattaaactttcctgtctgtctagtttaattgtggaagaaaaataaagtacagttgtgagatactg
```

Results:

Forward Primer	Pos	Len	Tm	Reverse Primer	Pos	Len	Tm	Amp	Ext. dimer dG	Full dimer dG
----------------	-----	-----	----	----------------	-----	-----	----	-----	---------------	---------------

5' [] 3'

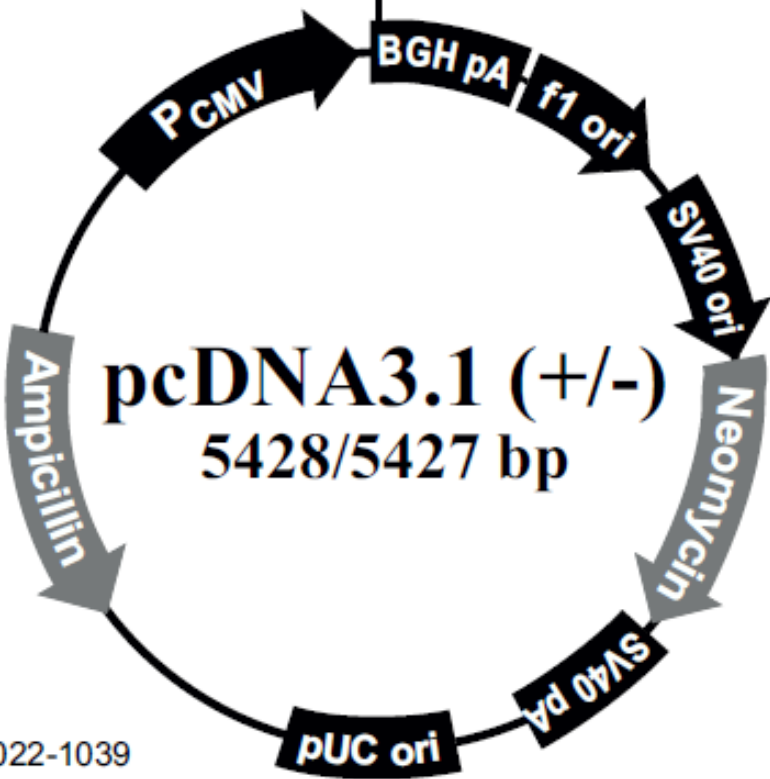
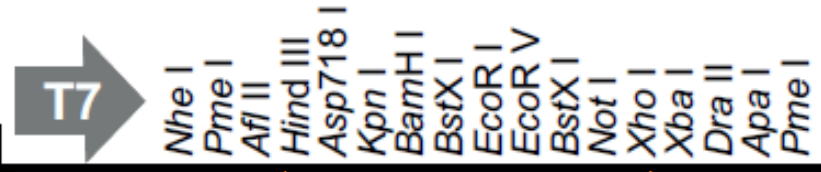
Find primers Find inwards Find outwards Cancel Copy selected

Finished ... found 0 primer pairs



STEP 5: DIGEST AND INSERT INTO THE VECTOR

Multiple Cloning Sites



HOW TO IDENTIFY THE FUNCTIONAL DOMAIN(S) OF BCL-2 PROTEIN?



Database of protein domains, families and functional sites

[Home](#) [ScanProsite](#) [ProRule](#) [Documents](#) [Downloads](#) [Links](#) [Funding](#)

PROSITE consists of [documentation entries](#) describing protein domains, families and functional sites as well as associated [patterns](#) and [profiles](#) to identify them [[More details](#) / [References](#) / [Disclaimer](#) / [Commercial users](#)].
PROSITE is complemented by [ProRule](#), a collection of rules based on profiles and patterns, which increases the discriminatory power of profiles and patterns by providing additional information about functionally and/or structurally critical amino acids [[More details](#)].

Release 20.71, of 08-Mar-2011 (1607 documentation entries, 1308 patterns, 920 profiles and 915 ProRule)

PROSITE access

add wildcard '*'

Browse:

- by documentation entry
- by ProRule description
- by taxonomic scope
- by number of positive hit

PROSITE tools

Scan a sequence against PROSITE patterns and profiles - quick scan

(Output includes graphical view and feature detection)



Enter your sequence or a UniProtKB (Swiss-Prot or TrEMBL) ID or AC [[help](#)]:

exclude patterns with a high probability of occurrence

- [ScanProsite](#) - advanced scan
- [PRATT](#) - allows to interactively generate conserved patterns from a series of unaligned proteins.
- [MyDomains - Image Creator](#) ^{beta} - allows to generate custom domain figures.



P10415
(BCL2_HUMAN) (239 aa)

RecName: Full=Apoptosis regulator Bcl-2; . *Homo sapiens* (Human)

PS50063 **BH4_2** Apoptosis regulator, Bcl-2 family BH4 motif profile : [Hits on PDB 3D structures](#): [1G5M-A, 1GJH-A, 1YSW-A, 2021-A, 2022-A, 202F-A, 2W3L-A, 2W3L-B, 2XA0-A, 2XA0-B]

11 - 30: score = 14.508

NREIVMKYIHYKLSQRGYEW

PS50062 **BCL2_FAMILY** BCL2-like apoptosis inhibitors family profile : [Hits on PDB 3D structures](#): [1G5M-A, 1GJH-A, 1YSW-A, 2021-A, 2022-A, 202F-A, 2W3L-A, 2W3L-B, 2XA0-A, 2XA0-B]

97 - 197: score = 34.696

LRQAGDDFSRRYRRDFAEMSSQLHLTPFTARGRFATVVEELFRDG-VNWGRIVAFFEFGG
VMCVESVNREMSPLVDNIALWMTTEYLNRHLHTWIQDNGGWDA

Search for Conserved Domains within a protein sequence

Now! Use **Batch CD-search** to submit multiple query proteins at once!

enter protein Query as Accession, Gi, or Sequence in FASTA format

sp10415

Submit Reset

OPTIONS

Search against database: CDD -- 38740 PSSMs

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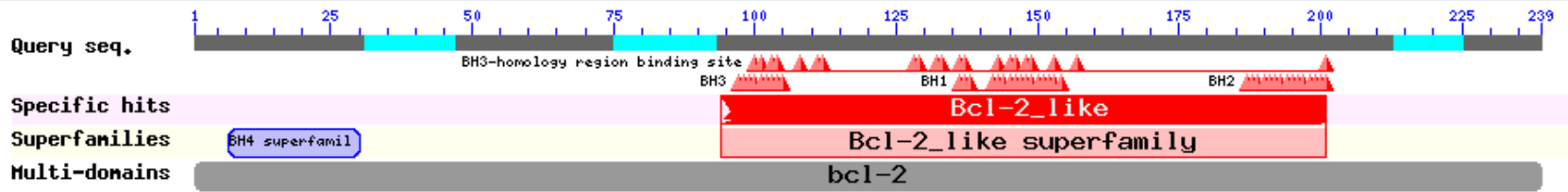
References:

- Marchler-Bauer A et al. (2011), "CDD: a Conserved Domain Database for the functional annotation of proteins.", *Nucleic Acids Res.*39(D)225-9.
- Marchler-Bauer A et al. (2009), "CDD: specific functional annotation with the Conserved Domain Database.", *Nucleic Acids Res.*37(D)205-10.
- Marchler-Bauer A, Bryant SH (2004), "CD-Search: protein domain annotations on the fly.", *Nucleic Acids Res.*32(W)327-331.

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List of domain hits

Description	PssmId	Multi-dom	E-value
Bcl-2_like [cd06845], Apoptosis regulator proteins of the Bcl-2 family, named after B-cell lymphoma 2. This ...	132900	yes	1.13e-39
BH4 superfamily [cd02540], Bcl-2 homology region 4;	154971	no	2.08e-07
bcl-2 [TIGR00865], Apoptosis regulator; in artificial membranes at acidic pH, proapoptotic Bcl-2 family proteins (including Bax ...	162075	yes	3.70e-80

List of domain hits

	Description	PssmId	Multi-dom	E-value
[-]	Bcl-2_like[cd06845], Apoptosis regulator proteins of the Bcl-2 family, named after B-cell lymphoma 2. This ...	132900	yes	1.13e-39
	<p>Apoptosis regulator proteins of the Bcl-2 family, named after B-cell lymphoma 2. This alignment model spans what have been described as Bcl-2 homology regions BH1, BH2, BH3, and BH4. Many members of this family have an additional C-terminal transmembrane segment. Some homologous proteins, which are not included in this model, may miss either the BH4 (Bax, Bak) or the BH2 (Bcl-X(S)) region, and some appear to only share the BH3 region (Bik, Bim, Bad, Bid, Egl-1). This family is involved in the regulation of the outer mitochondrial membrane's permeability and in promoting or preventing the release of apoptogenic factors, which in turn may trigger apoptosis by activating caspases. Bcl-2 and the closely related Bcl-X(L) are anti-apoptotic key regulators of programmed cell death. They are assumed to function via heterodimeric protein-protein interactions, binding pro-apoptotic proteins such as Bad (BCL2-antagonist of cell death), Bid, and Bim, by specifically interacting with their BH3 regions. Interfering with this heterodimeric interaction via small-molecule inhibitors may prove effective in targeting various cancers. This family also includes the Caenorhabditis elegans Bcl-2 homolog CED-9, which binds to CED-4, the C. Elegans homolog of mammalian Apaf-1. Apaf-1, however, does not seem to be inhibited by Bcl-2 directly.</p>			
	<p style="text-align: center;">Cd Length: 144 Bit Score: 158.26 E-value: 1.13e-39</p> <pre> 10 20 30 40 50 60 70 80 *.....*.....*.....*.....*.....*.....*.....*.....*..... gi 231632 94 HLTLRQAGDDFSRRYRRDFAE MSSQLHLTPFTARGRFATVVEELFRD-GVNWGRIVAF FEPGGVMCVESVNREMSPLVDN 172 Cdd:cd06845 36 AETLRRVGDLEEEKHRRLFENMCRQLNISPDNAYEVFQEVARELFEDgGINWGRIVALFAFGGRLAVKCV EQGLPELVRS 115 90 100 *.....*.....*..... gi 231632 173 IALWMTEYLNRLHHTWIQDNGGWDAFVEL 201 Cdd:cd06845 116 IAEWTSDFLEENLADWIQENGGWDGFVEF 144 </pre>			
[-]	BH4 super family[cd02540], Bcl-2 homology region 4;	154971	no	2.08e-07
	<p>Bcl-2 homology region 4;</p> <p>The actual alignment was detected with superfamily member pfam02180:</p> <p style="text-align: center;">Cd Length: 27 Bit Score: 51.02 E-value: 2.08e-07</p> <pre> 10 20 *.....*.....*..... gi 231632 7 TGYDNREIVMKYIHYKLSQRGYEW 30 Cdd:pfam02180 1 MSYDNRELVDVFTYKLSQRGYVW 24 </pre>			

- Two domains predicted: Bcl2_like and BH4
- Both have high scores (Bcl2-like>BH4)
- Slightly different predicted lengths of domains by two softwares



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1: HomoloGene:96314. Gene conserved in Magnoliophyta

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ATBAG1	ATBAG1 (ARABIDOPSIS THALIANA BCL-2-...	<i>Arabidopsis thaliana</i>
ATBAG3	ATBAG3 (ARABIDOPSIS THALIANA BCL-2-...	<i>Arabidopsis thaliana</i>
ATBAG2	ATBAG2 (ARABIDOPSIS THALIANA BCL-2-...	<i>Arabidopsis thaliana</i>
Os06g0126500	hypothetical protein	<i>Oryza sativa</i>
Os08g0546100	hypothetical protein	<i>Oryza sativa</i>
Os09g0524800	hypothetical protein	<i>Oryza sativa</i>

2: HomoloGene:9632. Gene conserved in Coelomata

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BOK	BCL2-related ovarian killer	<i>Homo sapiens</i>
BOK	BCL2-related ovarian killer	<i>Bos taurus</i>
Bok	BCL2-related ovarian killer protein	<i>Mus musculus</i>
Bok	BCL2-related ovarian killer	<i>Rattus norvegicus</i>
BOK	BCL2-related ovarian killer	<i>Gallus gallus</i>
boka	BCL2-related ovarian killer a	<i>Danio rerio</i>
debcl	death executioner Bcl-2 homologue	<i>Drosophila melanogaster</i>
AqaP AGAP011552	AGAP011552-PA	<i>Anopheles gambiae</i>

3: HomoloGene:527. Gene conserved in Amniota

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BCL2	B-cell CLL/lymphoma 2	<i>Homo sapiens</i>
BCL2	B-cell CLL/lymphoma 2	<i>Pan troglodytes</i>
BCL2	B-cell CLL/lymphoma 2	<i>Canis lupus familiaris</i>
BCL2	B-cell CLL/lymphoma 2	<i>Bos taurus</i>
Bcl2	B-cell leukemia/lymphoma 2	<i>Mus musculus</i>
Bcl2	B-cell CLL/lymphoma 2	<i>Rattus norvegicus</i>
BCL2	B-cell CLL/lymphoma 2	<i>Gallus gallus</i>

4: HomoloGene:116458. Gene conserved in Magnoliophyta

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Gene

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