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BIVM (basic, immunoglobulin-like variable motif-containing) gene, transcriptional products, and uses thereof

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Litman et al.

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(45) **Date of Patent: May 2, 2006**

(54) **BIVM (BASIC, IMMUNOGLOBULIN-LIKE VARIABLE MOTIF-CONTAINING) GENE, TRANSCRIPTIONAL PRODUCTS, AND USES THEREOF**

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(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

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(65) **Prior Publication Data**

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Related U.S. Application Data

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(51) **Int. Cl.**
C07H 21/02 (2006.01)
C07H 21/04 (2006.01)

(52) **U.S. Cl.** **536/23.1**; 536/24.3; 536/24.33; 424/265.1

(58) **Field of Classification Search** 536/23.1, 536/24.3, 24.33; 424/265.1; 435/4
See application file for complete search history.

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(57) **ABSTRACT**

The subject invention provides polynucleotide sequences, designated BIVM, and transcriptional/translational products obtained from the polynucleotide sequences of the invention. The subject invention also provides polynucleotide and polypeptide sequences provided by SEQ ID NOs:1–28. Also provided are methods of detecting the presence of BIVM nucleic acids or polypeptides in samples suspected of containing BIVM genes, BIVM transcriptional products, or BIVM translational products. These methods are also useful for the detection of BIVM orthologs. Other embodiments provide polypeptide and/or nucleic acid vaccines for the induction of an immune response to in an individual. Kits for detecting the presence of BIVM genes, orthologs thereof, BIVM polypeptides, or BIVM transcriptional products are also provided.

15 Claims, 15 Drawing Sheets

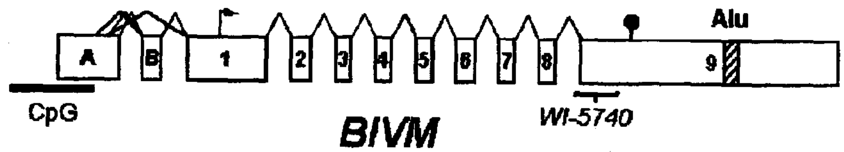

FIG. 1A

```
    AGTAACGCCTTCTCCAAGTGGATGGCGGGGTGGACACGCGTCCCGGCGCCCCGGGCTCCC   60
    TGGGATATGTAGTTCGCGACAGGACGAGCGGAAATACTGCCAGGATTTTACCACCTCTCG   120
    CCCATTTATTTACTTCTCGGTCACCGCTTTCGGGGACAGATAAACACCACAGATGCCCA   180
    TCAAAGGGGCGCACGGGTCTGGAGGCGCAGCTCAGGTTTTTGCGTTGGTCACCCTGCCCT   240
    CCGCACGTGGAGAGGGCAGGCATAAAGCACCTTGAAAGGAAGGTGCTGTCAATGCTATCC   300
    GACGACCTGTCGCCGGGCACCGCAGCATCCTCGCTCGCTCCGATGGGACGAGGGACGCCG   360
    GCCCCAGGGTAACAGGAGGCGCCTCGCCGGCCGCGCGCTGGATGCTGTGATCCAGGTCCG   420
    GAGCCGGGTTCCGCCGCGGCCGCAGCGACCCGACCCCACCCGACAGGCCAGAGGAATCAG   480
    TTTAGACTTGAAATTCAGTTTTTCCTGAAACTGATCAGAAGTTAGTGACACCTTGATTGG   540
    ATCCGTTTTTCTGTCAGGAGCTCATTTTGCAGCTCTCAAGCTTTTATAGCATGCTGTAAA   600
    CAATTGTCAAAGTTGTTTATCAAGAAACAGATAGAGTTGCAACTTGTTTCTAGTAATAGA   660
    AACTTTTACACTGCATTCAATGCCTAACGTTGCAGAAACAGAAAGGTCAAATGATTCTGG   720
1                          M  P  N  V  A  E  T  E  R  S  N  D  S  G
    AAATGGTGAGCACAAATCTGAGAGAAAGTCACCTGAAGAGAATCTACAAGGTGCTGTAAA   780
15   N  G  E  H  K  S  E  R  K  S  P  E  E  N  L  Q  G  A  V  K
    ATCTTTCTGCACAAGTGCCTCAGGAGCACCCTTGGGTCCCAAAGGAGATGGTCATTATCC   840
35   S  F  C  T  S  A  S  G  A  P  L  G  P  K  G  D  G  H  Y  P
    ATGGAGTTGTCCAGTGACTCATACACGGGAAAAAATTTATGCCATCTGTTCGGACTATGC   900
55   W  S  C  P  V  T  H  T  R  E  K  I  Y  A  I  C  S  D  Y  A
    CTTTCTCAACCAGGCGACCTCAATCTATAAAACTCCAAATCCATCCCGCTCTCCTTGCCT   960
75   F  L  N  Q  A  T  S  I  Y  K  T  P  N  P  S  R  S  P  C  L
    CCCTGATAGTACCTCTTTATCTGCTGGAAATAATTCATCAAGATACATTGGTATCCCGAC   1020
95   P  D  S  T  S  L  S  A  G  N  N  S  S  R  Y  I  G  I  P  T
    TAGTACATCGGAAATTATCTACAATGAAGAAAATAGCTTGGAAAACTTATCCAACAGCCT   1080
115  S  T  S  E  I  I  Y  N  E  E  N  S  L  E  N  L  S  N  S  L
    GGGCAAGCTACCTCTCGCATGGGAAATTGATAAATCTGAATTTGATGGGGTGACCACAAA   1140
135  G  K  L  P  L  A  W  E  I  D  K  S  E  F  D  G  V  T  T  N
    TTCGAAACACAAATCAGGCAATGCAAAGAAACAAGTTTCCAAGAGAAAAACTTCAGATAA   1200
155  S  K  H  K  S  G  N  A  K  K  Q  V  S  K  R  K  T  S  D  K
    AAAGGGAAGATATCAGAAGGAATGTCCTCAGCATTCTCCTCTTGAAGATATTAAACAGCG   1260
175  K  G  R  Y  Q  K  E  C  P  Q  H  S  P  L  E  D  I  K  Q  R
    GAAAGTATTAGACCTCAGACGATGGTACTGCATAAGCCGACCACAGTATAAGACTTCTTG   1320
195  K  V  L  D  L  R  R  W  Y  C  I  S  R  P  Q  Y  K  T  S  C
    TGGCATCTCTTCATTAATTTCTTGTTGGAATTTCTTATACAGCACAATGGGAGCTGGAAA   1380
215  G  I  S  S  L  I  S  C  W  N  F  L  Y  S  T  M  G  A  G  N
    CCTTCCACCTATTACCCAAGAAGAAGCTTTACATATTCTGGGCTTTCAACCTCCATTTGA   1440
235  L  P  P  I  T  Q  E  E  A  L  H  I  L  G  F  Q  P  P  F  E
    AGATATTAGGTTTGGTCCTTTCACGGGGAATACAACACTTATGAGGTGGTTTAGACAAAT   1500
255  D  I  R  F  G  P  F  T  G  N  T  T  L  M  R  W  F  R  Q  I
    TAATGACCACTTCCATGTAAAAGGATGCTCTTATGTTCTATATAAGCCTCATGGGAAGAA   1560
275  N  D  H  F  H  V  K  G  C  S  Y  V  L  Y  K  P  H  G  K  N
    TAAAACAGCAGGAGAAACTGCTTCAGGGGCCCTGTCAAAGTTAACCCGTGGATTGAAAGA   1620
295  K  T  A  G  E  T  A  S  G  A  L  S  K  L  T  R  G  L  K  D
    TGAATCGCTGGCTTATATCTATCATTGCCAAAATCATTATTTTTGTCCAATTGGCTTCGA   1680
315  E  S  L  A  Y  I  Y  H  C  Q  N  H  Y  F  C  P  I  G  F  E
    AGCAACCCCTGTTAAAGCTAATAAAGCATTCAGCAGGGGACCTCTCTCACCACAGGAAGT   1740
335  A  T  P  V  K  A  N  K  A  F  S  R  G  P  L  S  P  Q  E  V
    TGAATATTGGATCTTAATTGGAGAATCAAGTAGAAAACATCCTGCCATTCACTGTAAAAA   1800
```

FIG. 1B

```
335 A  T  P  V  K  A  N  K  A  F  S  R  G  P  L  S  P  Q  E  V
    TGAATATTGGATCTTAATTGGAGAATCAAGTAGAAAACATCCTGCCATTCACTGTAAAAA  1800
355 E  Y  W  I  L  I  G  E  S  S  R  K  H  P  A  I  H  C  K  K
    ATGGGCAGATATTGTTACTGATCTAAACACTCAAAATCCAGAATACCTGGATATCCGGCA  1860
375 W  A  D  I  V  T  D  L  N  T  Q  N  P  E  Y  L  D  I  R  H
    CTTAGAGAGGGGACTGCAGTATAGAAAAACAAAGAAGGTTGGGGAAATTTGCATTGCAT  1920
395 L  E  R  G  L  Q  Y  R  K  T  K  K  V  G  G  N  L  H  C  I
    CATAGCATTCCAGAGACTTAACTGGCAAAGATTTGGCCTTTGGAACTTTCCATTTGGAAC  1980
415 I  A  F  Q  R  L  N  W  Q  R  F  G  L  W  N  F  P  F  G  T
    CATTAGACAAGAATCACAACCTCCAACACATGCCCAGGGAATTGCCAAATCTGAGAGTGA  2040
435 I  R  Q  E  S  Q  P  P  T  H  A  Q  G  I  A  K  S  E  S  E
    AGACAATATTTCCAAGAAGCAGCATGGGCGTCTGGGCCGGTCTTTCAGTGCTAGTTTCCA  2100
455 D  N  I  S  K  K  Q  H  G  R  L  G  R  S  F  S  A  S  F  H
    TCAGGACTCGGCATGGAAAAAGATGTCTAGTATCCATGAGAGAAGGAACAGTGGTTACCA  2160
475 Q  D  S  A  W  K  K  M  S  S  I  H  E  R  R  N  S  G  Y  Q
    GGGTTACAGTGATTACGATGGGAATGATTGACTATGCTTGCTACTGAACAGCTGGCATTA  2220
495 G  Y  S  D  Y  D  G  N  D
    TATATGAAACTGCTATATACAGGACTGTATAAAGACAGTAGAAGATTTAGTAAGCCTAC  2280
    ATTAAATAGGAGCAGATCTTGTGGTATAAAAAATAACCTTGTAGTTCTCCAGATACTAAG  2340
    CTTGTATATGATTATGGTGGGTGATTTCAGATATATAAGCAGATAAGCACAGATTATTGT  2400
    CCTTTCAAGTTAAGAGTATATAATCTGGACAGAAAATTTCACAAAATTCAATAAAATTAC  2460
    AACTGTTGTCTAAATAAGTGAAACACAAATTCACTTAATAGCATCAAGATTTGAAATACT  2520
    TAAGCATGAAGTGACTTTTATAATGACTCGATCCCTAGACATTTGTTACAGATAGTTTTA  2580
    TGCCTAAGACCAAGATGTAAAGTACCATCTGCCCTTAAAAAAAATTGGGGCTGTCAATTT  2640
    CTAGTTTTCACTCATGGTTAACACGCATTTAAAATTATTTCATGAGTCTAGTAGTTCTTT  2700
    GATTTATAGCAGGATCTTGCTTGCCTCATTTGTTTCCTGGTTATGTTCTTAGGATTCTGA  2760
    CTAAGAGGCAAAAGAGAAAAGACTCAAGAAACTGATCCTGgagatcgagaccatcctggc  2820
    taacatggtgaaaccccgtctctactaaacatacaaaaaattagccgggtgtagtggtgg  2880
    gcacctgtagtcctagctactcgagaggctgaggcaggagaatggcgtgaacccgggagg  2940
    tggagcttgcagtgagcggagatcgcgccactgcactccagcctgggcgacagggcaaga  3000
    ctctgtctcAAAAAAAAAAAAAAAAAAAAAAGACGGATCCTTTTTTTTGGTGCAAATGGGT  3060
    GACTTAGTGCATTGATTCAGATTTTTAAAATTTCTTGATGTGGTTTGTAATAATCAAATA  3120
    TTGACAAGAACCTTAGGTCTCGAAAGACTTTTATAAGTCTAGATGACGTTTGCCTTAGGG  3180
    GTAAAGTAAAAGAACAATTGGCACCTTAAGTTTCTATACCCAAGGTTATCTGTGAAATGA  3240
    GATCTCCTGATATTTGATTGCTTTCTCAGTATGGAGTCATATGTTGATAACAGTACTGAA  3300
    GATGCATAAGAAATGCCCAAGTCACTCAGAGGACAACTACCCATATTCCAGACTCTGAGC  3360
    TGTTTCCTTTTTAAAAATCATATAGACAATTAGCTGTTTGAAGTGAGTATTAAATATTTC  3420
    AGAAGTGTGAATTTCATGTATTTGAGCTCCTCTAGTTGCTGTTGGTTTTTCTTCTGCTGC  3480
    CAACCTGTGACTCACAAATGACTAGGATCTCTTGTTCTTTAATTTTAGGGTCTTGTTCCA  3540
    GGACTCAAATCAGTAACTTGGTGATTACAAGGTGCTGAATGTGTTGGTAACCATATCGCA  3600
    ATACACCTCAAGGAAAAGGTTCAGATTTTTATTTTTAAAATATTTTCATTTTTTTCTTGA  3660
    ATTTTATATCCGTTTGTTCACTCGTACATGCCTAGCCTACAGAAGGGGATATATATTATG  3720
    AAATGGTCATTTTTCTGAAGAGAATATTTTGCTTGAAATGCAAAGGACTGAAAGAGATTT  3780
    GTAGGTTGTTGATTTTGTTACTTCATACTGGAACTTTTAAAAAGATTTCATCAAATAAAG  3840
    TTTTGTTTTCTACTTTT                                             3857
```

FIG. 1C

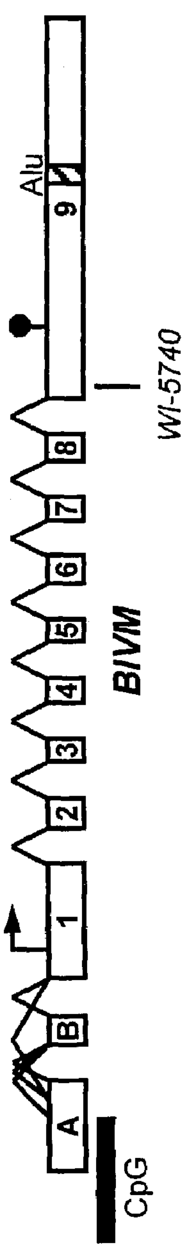

FIG. 2

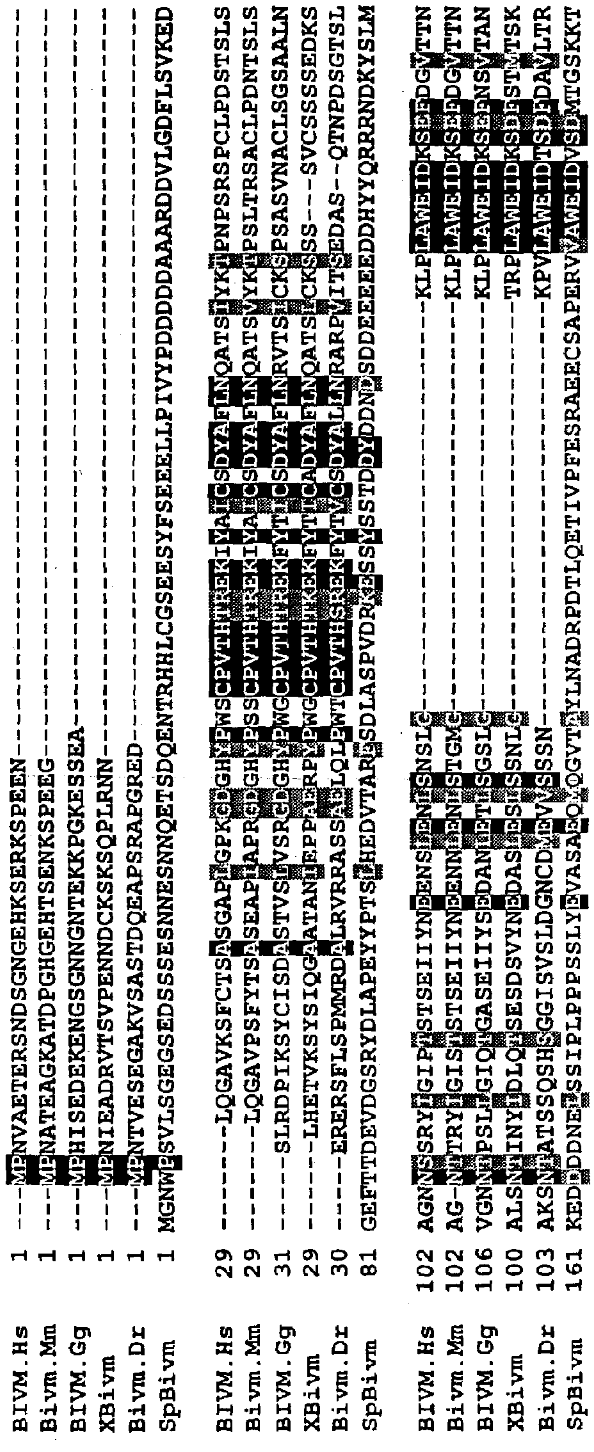

FIG. 3A

FIG. 3B

```
                                                                    M1
BIVM.Hs  155 SKHKSGNAKKQVSKRKTSDKKGRYQKECPQHS--PLEDIKQRKVLDLRRWYCISRPQYKTSCGISSLISCWNFLYSTMGA
Bivm.Mm  154 LIHKSGNVKKQFSKKKTSDKKGRHQRECLHYS--PLDDVKQRKVLDLRRWYCISRPQYKTSCGISSLISCWNFLYSIMGA
BIVM.Gg  159 HKNKAGNMKKQVAKKKSSDKKSKQYKECPQLS--ALEDVKERKVLDLRRWYCISRPQYKTSCGISSLVSCWNFLYSTLGA
XBivm    153 LKR-SG--VKKQTPKKKPDRKAKPLRDCPQHL--ILDDVKQRKVLDLRRWYCISRPQYKTSCGISSLVSCWNFLYSTLGA
Bivm.Dr  155 KARTSNLKKFNTKKMKSSDRPSRNLQDVPPQA--SLDEIKQRKVLDLRRWYCISRPQYKTSCGISSLVSCWNFLYSTLGA
SpBivm   241 KKRPPN-KLSKAKSRKSSSKGSMDSAYIPPTVSTTPELLAQRKCLDQKRWFCVSRPQYSKSCGLSSLVSCWNYLFSTLGG

                                    M2
BIVM.Hs  233 GNLPPITQEEALHILGFQPPFEDIRFGPFTGNTTLMRWFRQINDHFHVKGCSYVVLYKPHGKNKTAGETASGALSKLTRGL
Bivm.Mm  232 GNLPPITQEEALHILGFQPPFEDIRFGPFTGNTTLMRWFRQINDHFHVKGCSYVVLYKPHGKNKTAGETAPGALSKLTRGL
BIVM.Gg  237 GSLPPITQEEALHILGFQPPFEEIRFGPFTGNTTLMRWFRQINDHFHIKGCSYVVLYKPHGKNKTAGETAVGALAKLTRGL
XBivm    228 GSLPPITQEEALHILGFQPPFEEIRFGPFTGNTTLMRWFRQINDHFHVKGCSYVVLYKPHGKNKTAGETAVGALSKLTQGL
Bivm.Dr  233 GSLPPISQEEALHILGFQPPFEDIKFGPFTGNATLMRWFRQINDNFRVRGCSYILYKPHGKHKTAGETAEGALMKLTQGL
SpBivm   320 GTMPPITQEQALNVLGFQPPFGEIRFGPFTGNATLMRWFKQLNDHYRVRGRAYFQYKPHGRSRTVGRTSAQGLHLLRQGL

             M3b  M3a
BIVM.Hs  313 KDESLAYIYHCQNHYFCPIGFEATPVKANKAFSRGPLSPQEVEYWILIGESSRKHPAIHCKKWADIVTDLNTQNPEYLDI
Bivm.Mm  312 KDESLAYIYHCQNHYFCPIGFEATPVKANKAFSRGPLSSQEVEYWILIGESSRKHPAIHCKRWADIVTDLNTQNPEFLDI
BIVM.Gg  317 KDESMAYIYHCQNHYFCPIGFEATPVKASKAYR-GRVLQQEVEYWILIGEPSRKHPTIHCKRWTDIVTDLNTQNPEYLDI
XBivm    308 KEDSTAYVYHCQNHYFCPIGFEATPVKASKAYR-GQLFPHEVEYWILIGEPSRKHPTIHCKKWADIVTDLNTQNPEYFDI
Bivm.Dr  313 KDESMAYIYHCQNHYFCPVGYEATPLKAAKAYR-GPLPLNEMEHWILIGEPSRKHPAIHCKKWADIVTDLNTQNPEYLDI
SpBivm   400 KDPNMAFIYHCHNHYFCPIGYEDVPLKAVDAYR-DPLNLDEVETWILIGDPSRKQPGIHCFKWEDISTDLNCQNPDYLNI

BIVM.Hs  393 RHLERGLQYRKTKKVGGNLHCIIAFQRLNWQRFGLWNFPFGTIRQESQPPTHAQGIA--KSESEDNISKKQHGRLGRSFS
Bivm.Mm  392 RHLERGLQFRKIKKVGGNLHCIIAFQRLSWQRFGPWNFPFGTITQESQHPTHVPGIA--KSESEDNISKKQHGRLGRSFS
BIVM.Gg  396 RHLERGLQHRKTKKVGGNLHCIIAFQRLNWQRFGPWNIPFGSVRQDKQSQTQGQGIA--KSESEDNISKKQHGRLGRSFS
XBivm    387 RHTERGLQYRKTKKVGGNLHCLLAFQRLSWQRFGPWPLQLGTLRPEPQPPVQGRRIP--KSESEDNVSKKQHGRLGRSFS
Bivm.Dr  392 RHIERGIQYRKTKKVGGNLHCIMAFQRVNWQKLGPWALNLENLRHDLHHQAPEHRG---QASTEDSSEERTVKRLGRSLS
SpBivm   479 RKLRLGVQQRRTKRTGGNLHCIMAFCRSAGFLTRPTKSKKEGAMKDTSSNSKSRKSGSVRMSGRKVGESKSEGMVGRPAP

BIVM.Hs  471 AS---------------------------------FHQDSAWKKMSSIHERRNSGYQGYSDYDGND
Bivm.Mm  470 AS---------------------------------FHQDSAWKNMSSIHERRNSGYHSFRDYNGND
BIVM.Gg  474 AG---------------------------------FHQLSTWK-KSSLRERRNSGYQSYNDYDGDD
XBivm    465 AG---------------------------------FQQELAWKRMCNIRERRGSGSPESDTD
Bivm.Dr  469 TG---------------------------------NKPENAWKRLSNTAEYRHRGSPDSDLDEDITD
SpBivm   559 GGSVPCLQTGKADSSDIIEHFAFETVSCDHSSEGRSCRSEVVKKTKSESQVGRRRAKASVVKQEDKEIRVKSSEA.....
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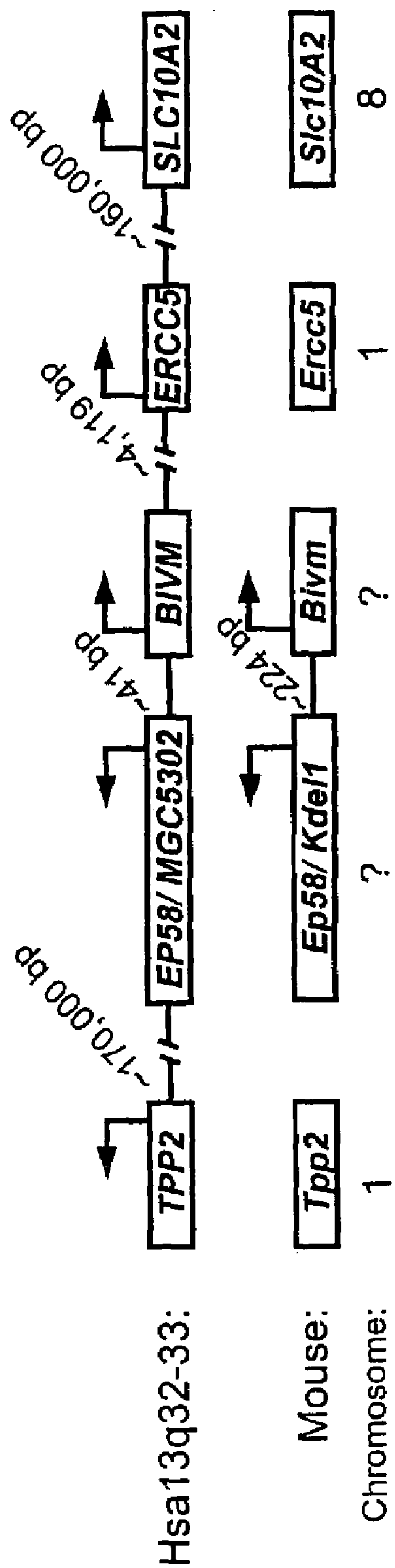

Hsa13q32-33:
TPP2
~170,000 bp
EP58/ MGC5302
~41 bp
BIVM
~4,119 bp
ERCC5
~160,000 bp
SLC10A2
Mouse:
Tpp2
Ep58/ Kdel1
~224 bp
Bivm
Ercc5
Slc10A2
Chromosome:
1
?
?
1
8

FIG. 4

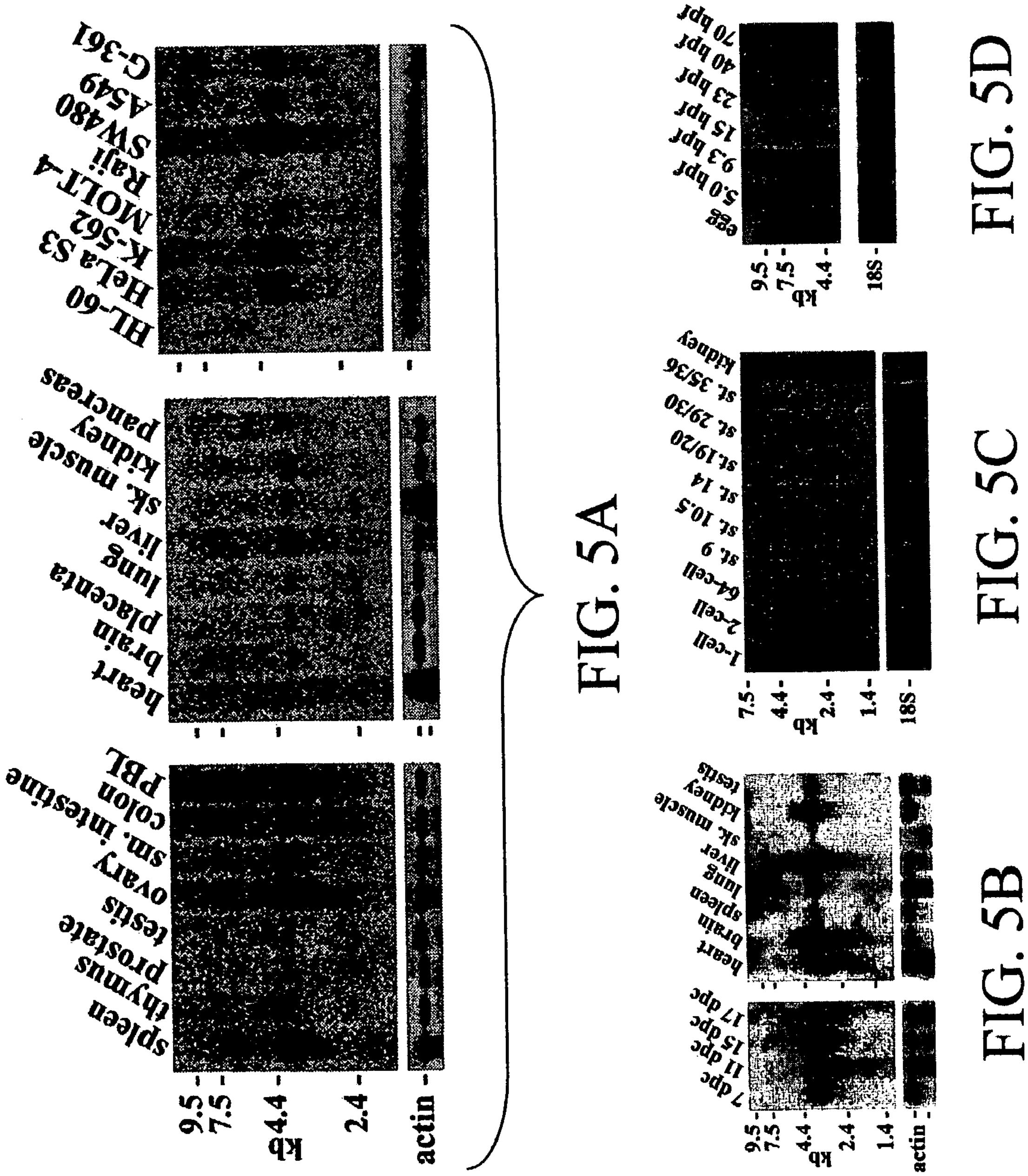


FIG. 5A

FIG. 5B

FIG. 5C

FIG. 5D

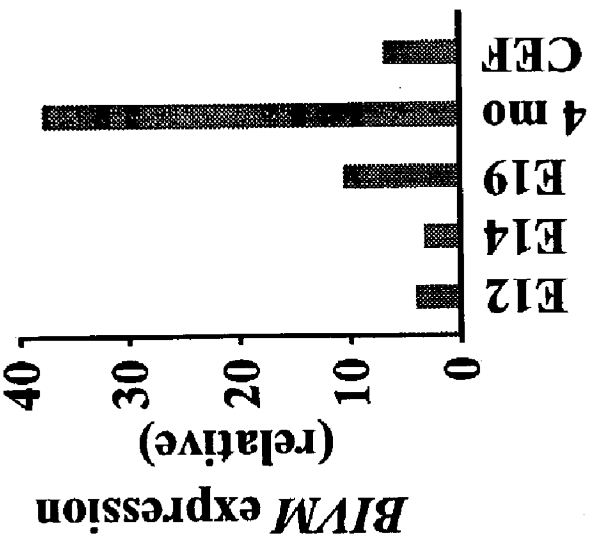

BIVM expression (relative)
40
30
20
10
0
E12
E14
E19
4 mo
CEF

FIG. 5F

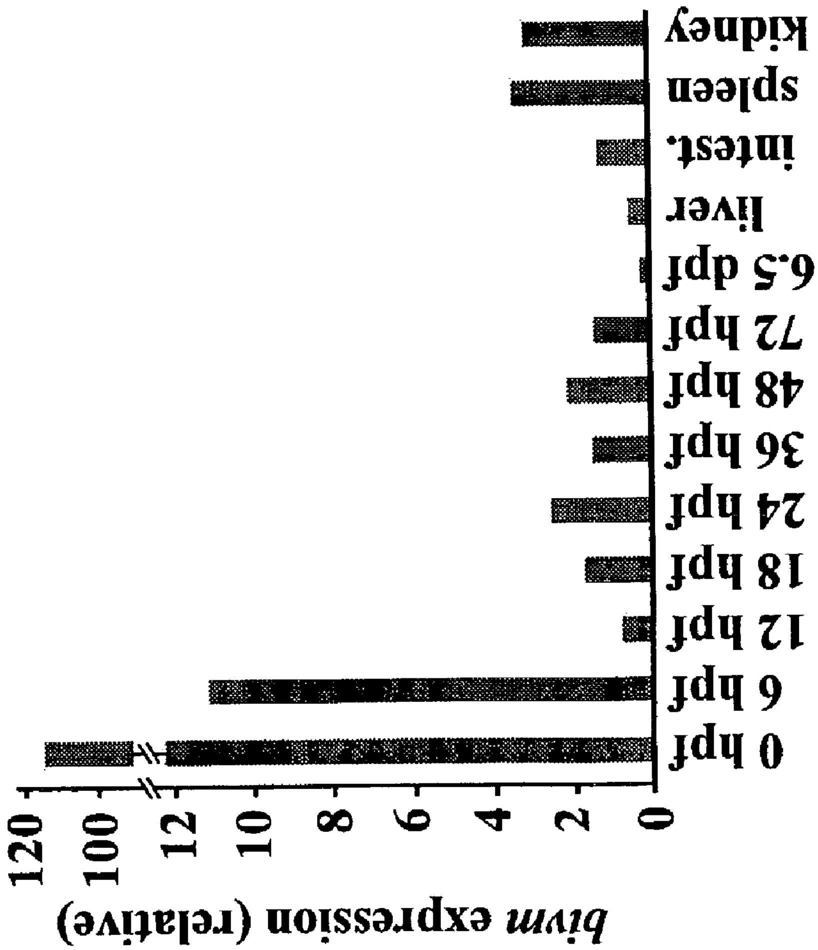

bivm expression (relative)
120
100
12
10
8
6
4
2
0
0 hpf
6 hpf
12 hpf
18 hpf
24 hpf
36 hpf
48 hpf
72 hpf
6.5 dpf
liver
intest.
spleen
kidney

FIG. 5E

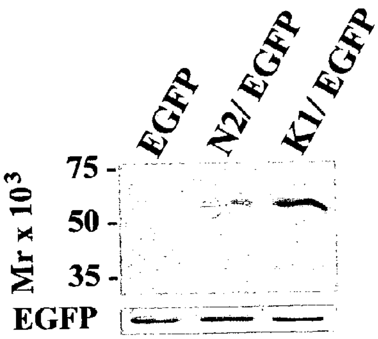


FIG. 6A

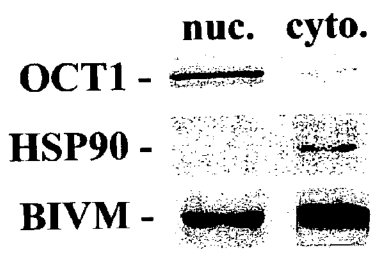


FIG. 6B

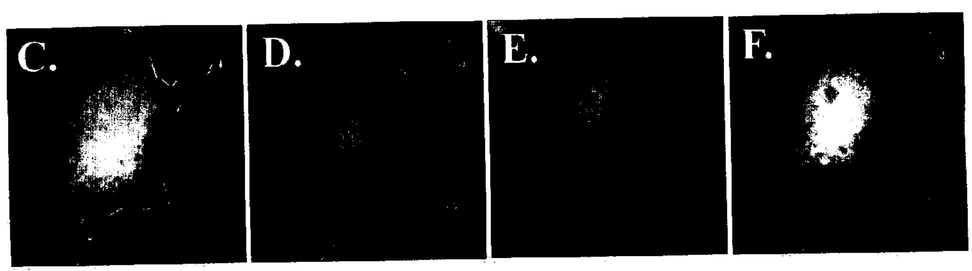


FIG. 6C FIG. 6D FIG. 6E FIG. 6F

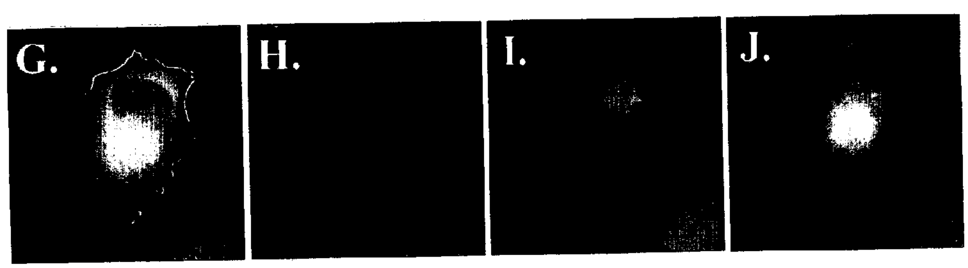


FIG. 6G FIG. 6H FIG. 6I FIG. 6J

```
    GCACATCTTGCAGGTCAAAACGAACACCCCCTCCTTCGATATCCTCTCAGACCCTACACT 60
    CTCAATTGTGTTACAGACCGGGCATGGGAAGAACTTGCTACGGCCGGCTTTCTTAGGGGG 120
    CGCCGCCCTTGTCCTCTTCTTCTTTCCCATCCTCCTGTCCTCTTTTTGTGACTGTTTGTG 180
    ACTAGACGCCGTTTCTAACAAAATTGCCAAGCATGTATGCAAAATTAAAATGGAAAGATA 240
1                                                    M  E  R  Y
    CCCCAGACAACGGTTAGACGACGGCAGGTGGCAGTGCGTGGCAGCGCAGTACAGATACTC 300
5    P  R  Q  R  L  D  D  G  R  W  Q  C  V  A  A  Q  Y  R  Y  S
    CTGCGCCATCTCATGCCTTGTGAGCATATTCAATCATCTCTTCAACAGAGACATGACCCT 360
25   C  A  I  S  C  L  V  S  I  F  N  H  L  F  N  R  D  M  T  L
    GGACGAGTGTATTGCTATTCTCTTTCCAGACCTGAAAGAAGACCCACGACACTATGATTT 420
45   D  E  C  I  A  I  L  F  P  D  L  K  E  D  P  R  H  Y  D  F
    TGGACCTCAGGCTTCTAACAGTGCTGTTCAAAGCTGGTTCAAGACCCTCTGCATGCACTA 480
65   G  P  Q  A  S  N  S  A  V  Q  S  W  F  K  T  L  C  M  H  Y
    TGGCCTTTCTGGCACCTCTTGCACGATATACAAGGAGCAGGGCAGAACGAGAACTGCGTG 540
85   G  L  S  G  T  S  C  T  I  Y  K  E  Q  G  R  T  R  T  A  C
    TAGCAAGCAAGAGGCACTTAAGAATATCATCACTGCTTTGAATACGCCAAGATGTGCGTT 600
105  S  K  Q  E  A  L  K  N  I  I  T  A  L  N  T  P  R  C  A  L
    ACTGTATCACTGCTTGAACCATTACTGCATAATCGTAGGCTATATAATAAGTCCATCTAC 660
125  L  Y  H  C  L  N  H  Y  C  I  I  V  G  Y  I  I  S  P  S  T
    GCCTAATAGACCAAGTAATCATTGCGTCTTCAGCGGGGATGATGGATGCACCCTCAAGCT 720
145  P  N  R  P  S  N  H  C  V  F  S  G  D  D  G  C  T  L  K  L
    CCTGTGTGCAGACGGCACAGAAGCCGAGGACGTGGACGATAGTAATATTTGGTTAATAGT 780
165  L  C  A  D  G  T  E  A  E  D  V  D  D  S  N  I  W  L  I  V
    GGCAGACTGTGGGAAAGGAACTGCTCCCCTTAGGTCACTGACCTGGGAATTTGTACATAA 840
185  A  D  C  G  K  G  T  A  P  L  R  S  L  T  W  E  F  V  H  K
    AGATATATCTACCCGACCTCCGTATGCATATAACGCTAGGTGCCCTGAGAGAGGACTGCT 900
205  D  I  S  T  R  P  P  Y  A  Y  N  A  R  C  P  E  R  G  L  L
    AAGGAAAACAGAATCAAAGGGATATATACCAGTTGAGATAGACTCAGTGCTTGTTAACAG 960
225  R  K  T  E  S  K  G  Y  I  P  V  E  I  D  S  V  L  V  N  S
    CACGGGAGTATCCACCTGTGTTAGATCTGGTGGCGTCATCAAGGGATCGTCGCACTGCAT 1020
245  T  G  V  S  T  C  V  R  S  G  G  V  I  K  G  S  S  H  C  I
    CATTGGATTTGTTAGTGACTAGAGCCCCGTTTATTACTCCCGGACGAAAGTATAACTATT 1080
265  I  G  F  V  S  D  *
    AACACCACAAGCACAACGATAGCTCCAGTAGAGCAGAGCCGAAGCACTTGAGGCAGCGAG 1140
    GCCTCCAAATACCCACATAGAACGTCACAGATGATAGCTGTCCATGTCGCAATTGACAAG 1200
    GTTAACGGGAAGGTTGAAACAGGCGAGGGCGTCCATCTGGTACGTTGTACTTTGGTTGTT 1260
    GAATATTGAACTGTTGTAAGTGTTGATTTGCTGGGTATATCTATTGCTTATGTACCGAAA 1320
    AAGGGCATTGCAAACGTCATATATTGCATCTATCTGATGAACACAGACCCCAGTTTTTTG 1380
    AAGATTTGCAAGTCTTCTTTGTGGTGGGGCATTCATATATGAATAAGAGCAGACTTCTCC 1440
    GCAGGCAAAGGACATGGACTGAATGGCATGCTCGTAACCAGTTAGGTCCAGTGCTTTGGT 1500
    TCGTGCATAGTATTTAAAGACCTTCTGAAGAAGGATGGTTTGAAATAGGGTCGTCCTGTC 1560
    CACACAGTCCAGGCAGTTTATCCGCGGATAGCACTTCTGAACAAAGTCAGGAAGAGCAAC 1620
    TCCGACATCACCGCTAGGAACTAGAACTGTGCTTGTGGCTATGTCATCTGCTAACTGGTG 1680
    ATACTCTGTGTTGCTGTGTCTACGTATGTTGTAGTTCATCAACTTAACGTTGAGGGAGTT 1740
    CTTGCGGCGAGAATCAGCAGTTTTTCTCATAGACTCGGTAAAGAACGCCGTCAGAGCCGC 1800
    TCATCGGCGGTCTCAAGGCTTTTCTTTTCACTGGCAGCAATGGAGTCATCCAAAAGATCG 1860
    ACTTCATTTTTGAGGAGGTTGACGATAAGTATCTCTGCGTCTGCAGTCACTAAGTTACCC 1920
    AATAGAAGGCTTATATGCCTTTGCAAGAGACTACTAAACTGAGCGAGGCCCTGCTCTTCA 1980
    TGAGCCCCATCTGGGAAGCGTATGGCAGGAGTGAACTTGTAAGTAAAAAAAAAAAAAAAA 2040
```

FIG. 7A

```
BIVM    189 EDIKQRKVLDLRRWYCISRPQYKTSCGISSLIISCWNFLYSTMGAGNLPPH
BIVML     1 MERYPRQRLDDGRWQCVAA-QYRYSCAISCLVSIENHLFNRDMT-----L

                                           M2
BIVM    239 TQEEALHILGFQPPFEDIRFGPFTGNITLMRWFRQINDHFHVKGCSYVLY
BIVML    45 DECIAILFPDLKEDPRHYDFGPQASNSAVQSWFKTLCMHYGLSGTSCTIY

                                            M3b
BIVM    289 KPHGKNKTAGETASGALSKITRGLKDESLAYIYHCQNHYFCPIGFEATPV
BIVML    94 KEQGRTRTACSKQE-ALKNIITALNTPRCALLYHCLNHYCIIVGYIISPS

BIVM    339 KANKAFSRGPLSPQEVEYWILIGESSRKHPAIHCKKWADIVTDLNTQNPE
BIVML   119 TPN-------------------------RPSNHCVFSGDDGCTLKLLCAD

BIVM    389 YLDIRHLERGLQYRKTKKVCGNLHCIIAFQRLNWQRFGLWNFPFGTIRQE
BIVML   166 GTEAEDVDDSNIWLIVADCC---KGTAPLRSLTWEFVHKDISTRPPYAYN

BIVM    439 SQPPTHAQGIAKSESEDNISKKQHGRLGRSFSASFHQDSAWKKMSSIHER
BIVML   212 ARCP-ERGLFRKTESKGYIPVEIDSVLVNSTGVSTCVRSCGVIKGSSHC-

BIVM    489 RNSGYQGYSDYDGND
BIVML   264 -IIG--FVSD
```

FIG. 7B

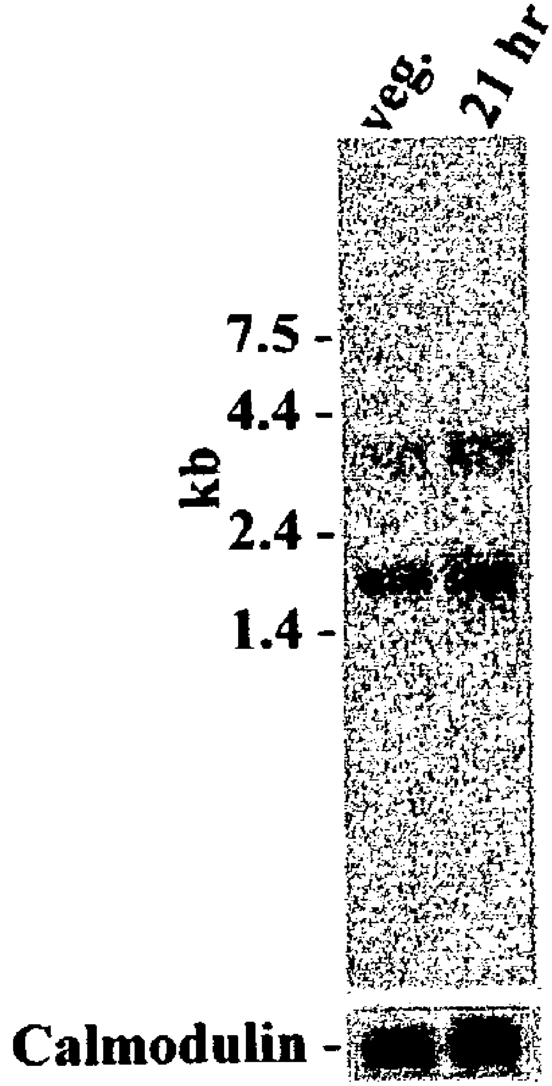
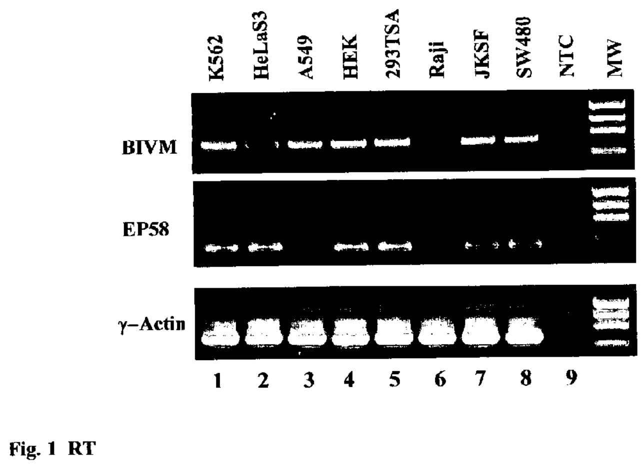
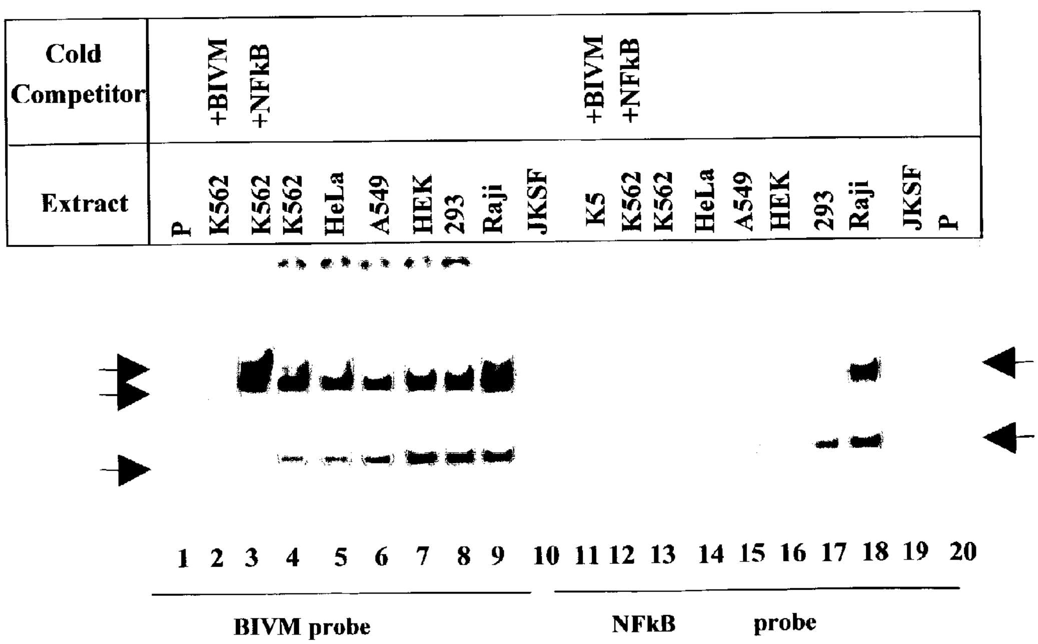


FIG. 7C



K562
HeLaS3
A549
HEK
293TSA
Raji
JKSF
SW480
NTC
MW
BIVM
EP58
γ-Actin
1 2 3 4 5 6 7 8 9
Fig. 1 RT

FIG. 8



Cold Competitor
+BIVM
+NFkB
+BIVM
+NFkB
Extract
P
K562
K562
K562
HeLa
A549
HEK
293
Raji
JKSF
K5
K562
K562
HeLa
A549
HEK
293
Raji
JKSF
P
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20
BIVM probe
NFkB probe

FIG. 10

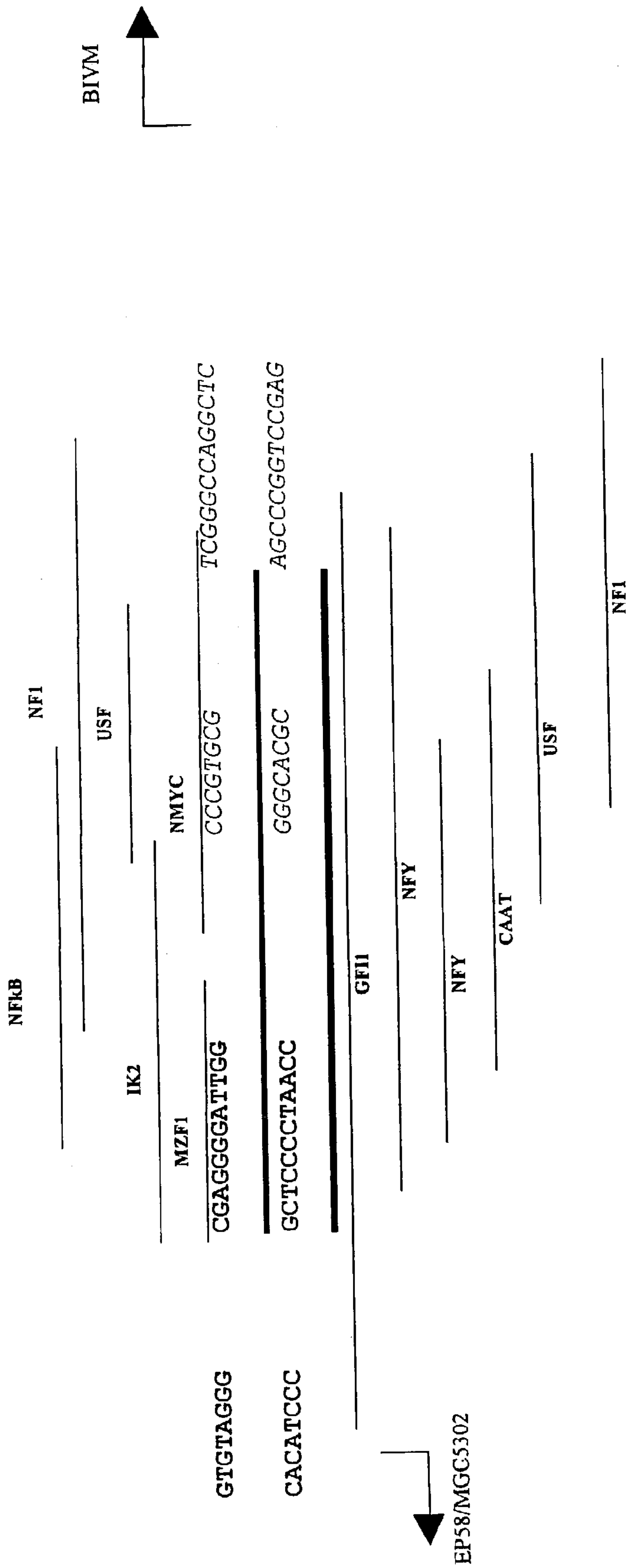

BIVM
NFkB
NF1
USF
IK2
MZF1
NMYC
GTGTAGGG
CGAGGGGATTGG
CCCGTGCG
TCGGGCCAGGCTC
CACATCCC
GCTCCCCTAACC
GGGCACGC
AGCCCCGGTCCGAG
GFI1
NFY
NFY
CAAT
USF
NF1
EP58/MGC5302

FIG. 9

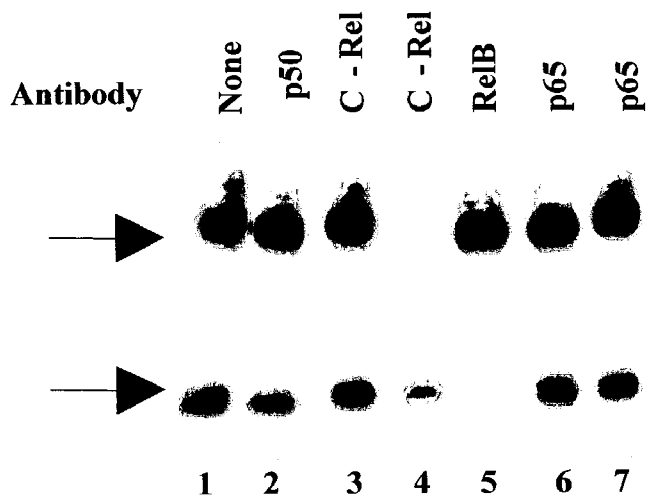

Antibody
None
p50
C -Rel
C -Rel
RelB
p65
p65
1
2
3
4
5
6
7

FIG. 11

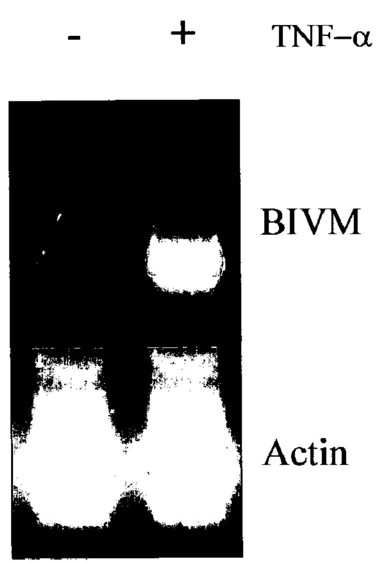

-
+
TNF-α
BIVM
Actin

FIG. 12

FIG. 13A

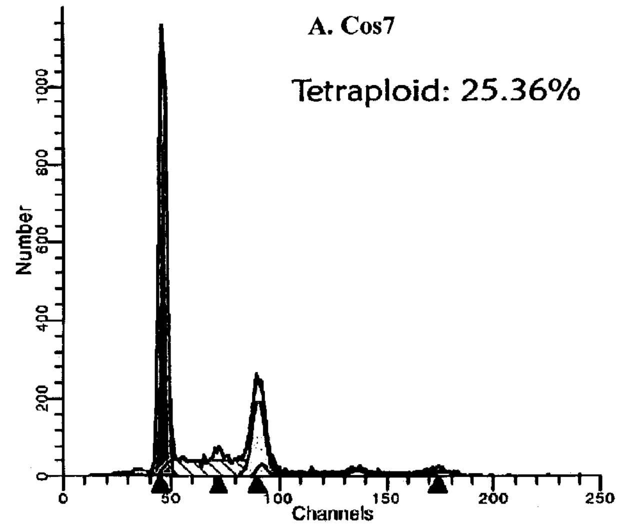


FIG. 13B

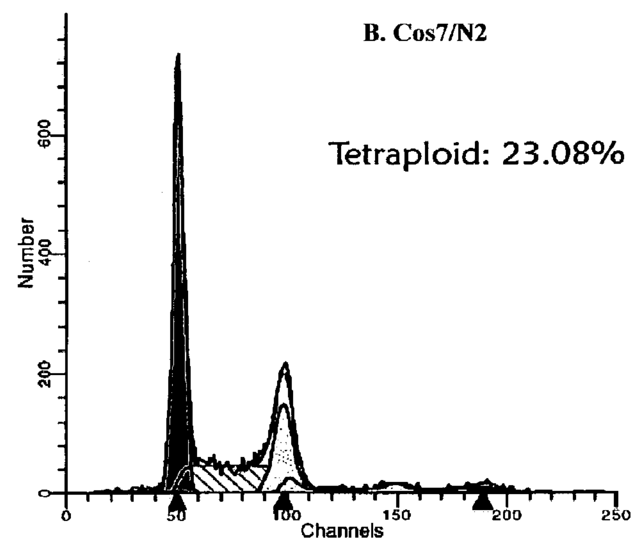
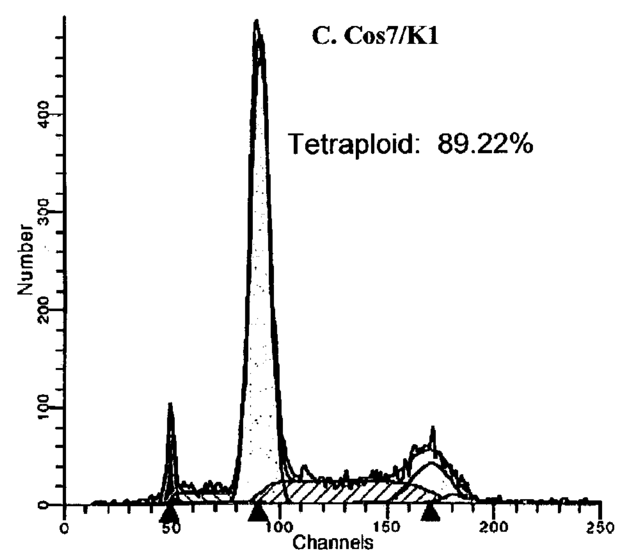


FIG. 13C



BIVM (BASIC, IMMUNOGLOBULIN-LIKE VARIABLE MOTIF-CONTAINING) GENE, TRANSCRIPTIONAL PRODUCTS, AND USES THEREOF

CROSS REFERENCE TO RELATED APPLICATION

The application claims priority to U.S. Provisional Application Ser. No. 60/373,146, filed Apr. 16, 2002, which is hereby incorporated by reference in its entirety, including all figures, nucleic acid sequences, amino acid sequences, and tables.

The subject invention was made with government support under a research project supported by the National Institutes of Health Grant No. AI23338. The government may have certain rights in this invention.

BACKGROUND OF INVENTION

Considerable uncertainty remains with regards to the total number of human genes. Initial interpretations of genomic sequences resulted in estimates that placed the numbers of genes in man in the range of 30,000 to 40,000 (Lander, E. S., et al. [2001] "Initial Sequencing and Analysis of the Human Genome," *Nature,* 409:860–921; Ventner, J. C., et al. [2001] "The Sequence of the Human Genome," *Science,* 291:1304–51). Subsequent re-examination of the sequence data suggests the number of genes in the human genome is likely to be between 65,000 and 75,000 (Wright, F. A., et al. [2001] "A Draft Annotation and Overview of the Human Genome," *Genome Biology* 2:1.1–1.39). Predictions of 35,000 to 120,000 genes have been projected on the basis of EST sequences (Ewing, B., et al. [2000] "Analysis of Expressed Sequence Tags Indicates 35,000 Human Genes," *Nature Genet.* 25:232–234; Liang, F., et al. [2000], "Gene Index Analysis of the Human Genome Estimates Approximately 120,000 Genes," *Nature Genet.* 25:239–240). New genes continue to be recognized through inspection of genomic sequences as well as through a variety of different biochemical, immunological and other directed approaches.

The immunoglobulin superfamily (IgSF) represents a particularly large and extensively diversified family of genes (Barclay, A. N., et al. [1997] *The Leucocyte Antigen Facts-Book*, Academic Press, San Diego). Each IgSF member encodes at least one Ig that consists of ~100 amino acid residues that are arranged in two β sheets, which are comprised of anti-parallel β strands that are linked by an intrachain disulfide. Although the majority of genes in the IgSF function in the immune response, other IgSF genes are involved with cell-adhesion or growth factor recognition. IgSF domains are the most abundant domain type found in leukocyte membrane proteins.

In the course of an electronic EST database search for novel human genes encoding Ig domains, we identified an anonymous EST (IMAGE 785450; GenBank AA449273) (Hawke, N. A., et al. [1999] "Expanding Our Understanding of Immunoglobulin, T-cell Antigen Receptor, and Novel Immune-Type Receptor Genes: a Subset of the Immunoglobulin Gene Superfamily," *Immunogenetics* 50:124–133) and cloned the corresponding full-length cDNA. The predicted structure of the protein encoded by this gene, which is termed BIVM (basic, immunoglobulin-like variable motif-containing), includes short peptide motifs characteristic of an Ig variable (V) region, one of the subtypes of Ig domains. However, it lacks significant sequence identity to any group of proteins heretofore described.

We have determined the sequence of BIVM cDNA in species representative of critical points in phylogeny, examined the intracellular distribution of a recombinant form of BIVM, characterized its expression patterns in various tissues at different times in development, and defined other features of the gene that further emphasize its unique character. In addition, we have identified a BIVM-like gene in the protozoan parasite, *Giardia lamblia.*

BRIEF SUMMARY

The subject invention provides polynucleotide sequences, designated BIVM, and transcriptional/translational products obtained from the polynucleotide sequences of the invention (SEQ ID Nos:1–28). The subject invention also provides methods of detecting the presence of BIVM nucleic acids, transcriptional products, or polypeptides in samples suspected of containing BIVM genes. These methods are also useful for the detection of BIVM orthologs. Other embodiments provide polypeptide and/or nucleic acid vaccines for the induction of an immune response. Kits for detecting the presence of BIVM genes, orthologs thereof, BIVM polypeptides, or BIVM transcriptional products obtained from the polynucleotide sequences are also provided.

BRIEF DESCRIPTION OF THE TABLES AND DRAWINGS

The file of this patent contains at least one drawing executed in color. Copies of this patent with color drawings will be provided by the Patent and Trademark Office upon request and payment of the necessary fee.

Table I. Exon-intron organization of human BIVM. Three alternative splice donors in the 5' untranslated region are designated A_1, A_2, and A_3. Nucleotide positions are relative to FIG. **1**, intron length and splice donor/acceptor sequences are shown. Coding sequence is in upper case.

FIG. **1**. Human BIVM The nucleotide sequence (SEQ ID NO: 1) and predicted amino acid translation product (SEQ ID NO: 2) of a human BIVM transcript. Translational start and stop codons are in reverse text. RNA splice junctions are underlined (see Table I). Nucleotides at 5' ends, defined by analyses of RACE products, are boxed. Nucleotide numbering is on the right; amino acid numbering is on the left. The M1 (GX_6C), M2 (WFRQ), M3a and M3b (YFC and YHC) motifs are shaded. The Alu sequence in the 3' untranslated region is in lower case.

FIG. **2**. Predicted genomic organization of human BIVM. BIVM consists of nine coding exons (exons 1–9) and two 5' untranslated region exons (A and B). Alternative splice donor sites are present within exon A (see Table I); transcripts have been identified that include exon A, but not exon B. The CpG island is denoted by a solid bar, the Alu sequence is denoted by a hatched bar, and the location of the sequence-tagged site (STS) marker, WI-5740, is indicated (see also FIG. **1**A).

FIG. **3**. BIVM is well conserved among deuterostomes. ClustalW alignment of the human BIVM peptide sequence (BIVM.Hs; (SEQ ID NO: 2)) with orthologous sequences from mouse (BIVM.Mm (SEQ ID NO: 27)), chicken (BIVM.Gg: (SEQ ID NO: 8)) *Xenopus* (XBIVM; (SEQ ID NO: 5)), zebrafish (BIVM.Dr: (SEQ ID NO: 11)), and sea urchin (SpBIVM: (SEQ ID NO: 13)). The sea urchin sequence lacks a stop codon and therefore is predicted to encode a longer polypeptide (indicated by . . .). The M1, M2, M3a and M3b motifs are indicated. The highly conserved domain within BIVM is indicated with arrowheads.

Identical residues are shown in reverse text (black), similarities are shaded (gray). Gaps introduced to maintain/maximize alignment are indicated with (–).

FIG. **4**. Syntenic relationship between the human BIVM region and the mouse genome. The relative locations of human BIVM and flanking genes on chromosome 13q32–33; known corresponding chromosomal map positions are indicated for mouse. Transcription direction is indicated with arrows. Approximate distances between genes (if known) are indicated.

FIG. **5**. Expression of BIVM. RNA blots of BIVM expression from (A) human tissues and cell lines, (B) mouse embryos and somatic tissues, (C) *Xenopus* embryos and kidney, and (D) sea urchin embryos. Approximately 2 μg of polyA+ RNA/track was analyzed in human and mouse; ~10 μg of total RNA/track was analyzed in *Xenopus* and sea urchin. Actin is used as a loading control with human and mouse blots; 18S ribosomal RNA is used as a loading control with *Xenopus* and sea urchin blots. Real time PCR analysis of BIVM expression in (E), developing zebrafish embryos and adult tissues, and in (F) chicken bursa at various stages of embryonic development. The quantity of BIVM (designated on the left) is relative and normalized (see Methods). Note that the level of zebrafish BIVM expression in the 0 hpf embryo is approximately 10 times the level detected at 6 hpf. Time points in the analysis of bursa are days of embryonic life (e.g. E12) and chicken embryonic fibroblasts (CEFs) were included as a control. Days post coitus=dpc, stage=st., hour post fertilization=hpf, days post fertilization=dpf and intestine=intest.

FIG. **6**. BIVM localizes to the nucleus and the cytoplasm. (A) Western analysis of whole cell lysates from pIRES2-EGFP (EGFP), pBIVM-N2/EGFP (N2/EGFP) and pBIVM-K1/EGFP (K1/EGFP) transfected Cos-7 cells. Recombinant BIVM is detected with an anti-V5 antibody. EGFP is shown as a transfection and loading control. Note that only a single protein corresponding to the 5' ATG is generated from the endogenous transcript (pBIVM-N2); protein synthesis is increased by modification of the translational start site (pBIVMK1). Size standards are indicated. (B) Western analysis of nuclear and cytoplasmic fractions from pBIVM-K1/EGFP transfected Cos-7 cells. OCT-1 (Pombo, A., et al. [1998] "Regional and Temporal Specialization in the Nucleus: A Transcriptionally-Active Nuclear Domain Rich in PTF, Oct1 and PIKA Antigens Associated with Specific Chromosomes Early in the Cell Cycle," *EMBO J.* 1768) and HSP90 (Perdew, G. H., et al. [1991] "Evidence that the 90-kDa Heatshock Protein (HSP90) Exists in Cytosol in Heteromeric Complexes Containing HSP70 and Three Other Proteins with Mr 63,000, 56,000, and 50,000," *J Biol Chem* 6708) are nuclear and cytoplasmic markers, respectively. (C–J) Immunocytochemical localization of BIVM. Cos7 cells transiently transfected with pBIVM-K1 were analyzed by conventional fluorescent microscopy. Recombinant BIVM (green), actin s(red), nuclei (blue), and overlayered images are shown. Note that levels of nuclear BIVM vary (compare C to G).

FIG. **7**. *Giardia* BVIM-like sequence. (A) The nucleotide sequence (SEQ ID NO: 14) and predicted amino acid translation product (SEQ ID NO: 15) of a *Giardia lamblia* BIVM-like (BIVML) transcript. Translational start and stop codons are in reverse text. Numbering is as in FIG. **1**. Grey shading indicates conserved motifs. A sequence resembling predicted giardial initiator regions is boxed. A classic giardial polyadenylation signal sequence is underlined. (B) Alignment of the predicted BIVML protein (SEQ ID NO: 15) with the C-terminal region of human BIVM (SEQ ID NO: 2). Labeling is as in FIG. **3**. (C) RNA blot (10 μg/track) probed for BIVML in vegetative-stage (veg) and 21 hr encysting *Giardia. Calmodulin* is shown as loading control.

FIG. **8**. RT-PCR analysis of extracts from BIVM expressing and non-expressing human cell lines indicated that EP58/MGC5302 was expressed in all cell lines that express BIVM but not in a BIVM non-expressing cell line.

FIG. **9**. Potential binding sites contained in the 41 bp region separating the BIVM and EP58/MGC5302 genes revealed sites for cell type specific factors such as the myeloid zinc finger-1 (MZF-1), the hematopoietic-expressed Ikaros-2 (IK2) factor, and the ubiquitously expressed transcription factors NF1, USF, NFκB, and NMYC.

FIG. **10**. Detection of bands representing NFκB-specific binding constitutively present in nuclear extracts.

FIG. **11**. Binding of the 41 bp intergenic region by NFκB complexes containing c-Rel and RelB factors, which are constitutively present in the nuclear extracts from the BIVM expressing K562 cell line.

FIG. **12**. TNF-α activated NFκB increases the expression of BIVM in the BIVM-expressing HeLa cell line (DNS). A cell line devoid of basal BIVM expression, the Raji Burkitt's lymphoma line, is induced to express BIVM by TNF-α.

FIG. **13**. Flow cytometer analyses of cells stained with propidium iodide.

BRIEF DESCRIPTION OF THE SEQUENCES

SEQ ID NO: 1—human BIVM cDNA

SEQ ID NO: 2—human BIVM amino acid sequence

SEQ ID NO: 3—human BIVM gemonic sequence with upstream partial sequence of MGC5302 gene and downstream partial sequence of ERCC5 gene

SEQ ID NO: 4—*Xenopus* BIVM open reading frame

SEQ ID NO: 5—*Xenopus* BIVM amino acid sequence

SEQ ID NO: 6—Chicken BIVM open reading frame

SEQ ID NO: 7—Alternatively spliced chicken BIVM open reading frame

SEQ ID NO: 8—Chicken BIVM amino acid sequence

SEQ ID NO: 9—Alternatively splice chicken BIVM amino acid sequence

SEQ ID NO: 10—Zebrafish BIVM open reading frame

SEQ ID NO: 11—Zebrafish BIVM amino acid sequence

SEQ ID NO: 12—Sea urchin BIVM partial coding sequence

SEQ ID NO: 13—Sea urchin BIVM partial amino acid sequence

SEQ ID NO: 14—*Giardia* BIVM-like open reading frame

SEQ ID NO: 15—*Giardia* BIVM-like amino acid sequence

SEQ ID NO: 16—Lancelet BIVM partial coding sequence

SEQ ID NO: 17—Lancelet BIVM partial amino acid sequence

SEQ ID NO: 18—Mouse BIVM exon A nucleotide sequence

SEQ ID NO: 19—Mouse BIVM exon B nucleotide sequence

SEQ ID NO: 20—Mouse BIVM exon C nucleotide sequence

SEQ ID NO: 21—Mouse BIVM exon 1 nucleotide sequence

SEQ ID NO: 22—Alternative mouse BIVM 5' end clone (6359)

SEQ ID NO: 23—Alternative mouse BIVM 5' end clone (6358)

SEQ ID NO: 24—Alternative mouse BIVM 5' end clone (6356)

SEQ ID NO: 25—Alternative mouse BIVM 5' end clone (cDNA)

SEQ ID NO: 26—Mouse BIVM cDNA with clone 6359 5' end

SEQ ID NO: 27—Mouse BIVM amino acid sequence

SEQ ID NO: 28—Mouse BIVM genomic sequence with upstream partial sequence of KDEL gene

SEQ ID NO: 29—Human BIVM exon A^1 splice donor sequence

SEQ ID NO: 30—Human BIVM exon A^2 splice donor sequence

SEQ ID NO: 31—Human BIVM exon A^3 splice donor sequence

SEQ ID NO: 32—Human BIVM exon B splice acceptor sequence

SEQ ID NO: 33—Human BIVM exon B splice donor sequence

SEQ ID NO: 34—Human BIVM exon 1 splice acceptor sequence

SEQ ID NO: 35—Human BIVM exon 1 splice donor sequence

SEQ ID NO: 36—Human BIVM exon 2 splice acceptor sequence

SEQ ID NO: 37—Human BIVM exon 2 splice donor sequence

SEQ ID NO: 38—Human BIVM exon 3 splice acceptor sequence

SEQ ID NO: 39—Human BIVM exon 3 splice donor sequence

SEQ ID NO: 40—Human BIVM exon 4 splice acceptor sequence

SEQ ID NO: 41—Human BIVM exon 4 splice donor sequence

SEQ ID NO: 42—Human BIVM exon 5 splice acceptor sequence

SEQ ID NO: 43—Human BIVM exon 5 splice donor sequence

SEQ ID NO: 44—Human BIVM exon 6 splice acceptor sequence

SEQ ID NO: 45—Human BIVM exon 6 splice donor sequence

SEQ ID NO: 46—Human BIVM exon 7 splice acceptor sequence

SEQ ID NO: 47—Human BIVM exon 7 splice donor sequence

SEQ ID NO: 48—Human BIVM exon 8 splice acceptor sequence

SEQ ID NO: 49—Human BIVM exon 8 splice donor sequence

SEQ ID NO: 50—Human BIVM exon 9 splice acceptor sequence

SEQ ID NO: 51—HSMAP5 primer

SEQ ID NO: 52—HSMAP6 primer

SEQ ID NO: 53—xfbivmMAPF1 primer

SEQ ID NO: 54—xfbivmMAPR1 primer

SEQ ID NO: 55—M1 amino acid motif

SEQ ID NO: 56—M2 amino acid motif

SEQ ID NO: 57—M3a amino acid motif

SEQ ID NO: 58—M3b amino acid motif

SEQ ID NO: 59—BIVM N-terminus region of homology

SEQ ID NO: 60—BIVM C-terminus region of homology

SEQ ID NO: 61—BIVM amino acid motif 1

SEQ ID NO: 62—BIVM amino acid motif 2

SEQ ID NO: 63—BIVM amino acid motif 3

SEQ ID NO: 64—BIVM amino acid motif 4

DETAILED DESCRIPTION OF THE INVENTION

The subject invention provides isolated and/or purified nucleotide sequences comprising: a) a polynucleotide sequence, or fragment thereof, or a polynucleotide encoding an amino acid sequence, or fragment of said amino acid sequence, of a sequence selected from the group consisting of SEQ ID NOs: 1–64 (or the complements of said polynucleotide sequences or fragments thereof); b) a polynucleotide sequence, or fragment thereof, comprising a sequence having at least about 20% to 99.99% identity to a polynucleotide selected from the group consisting of SEQ ID NOs: 1–28; c) a polynucleotide sequence encoding a polypeptide comprising a sequence selected from the group consisting of SEQ ID NOs: 2, 5, 7, 8, 9, 11, 13, 15, 17, or 27; d) splice variants of SEQ ID NOs: 1–3 or 6–9; or e) a polynucleotide sequence encoding a polypeptide fragment of SEQ ID NOs: 2, 5, 7, 8, 9, 11, 13, 15, 17, or 27, wherein said fragment has substantially the same biological or serologic activity as the native (or intact) polypeptide.

Nucleotide, polynucleotide, or nucleic acid sequence(s) are understood to mean, according to the present invention, either a double-stranded DNA, a single-stranded DNA, or products of transcription of the said DNAs (e.g., RNA molecules). It should also be understood that the present invention does not relate to the genomic nucleotide sequences encoding BIVM in their natural/native environment or natural/native state. The nucleic acid, polynucleotide, or nucleotide sequences of the invention have been isolated, purified (or partially purified), by separation methods including, but not limited to, ion-exchange chromatography, molecular size exclusion chromatography, affinity chromatography, or by genetic engineering methods such as amplification, cloning, or subcloning.

Optionally, the polynucleotide sequences of the instant invention can also contain one or more polynucleotides encoding heterologous polypeptide sequences (e.g., tags that facilitate purification of the polypeptides of the invention (see, for example, U.S. Pat. No. 6,342,362, hereby incorporated by reference in its entirety; Altendorf et al. [1999-WWW, 2000] "Structure and Function of the F_0 Complex of the ATP Synthase from *Escherichia Coli,*" *J. of Experimental* Biology 203:19–28, The Co. of Biologists, Ltd., G.B.; Baneyx [1999] "Recombinant Protein Expression in *Escherichia coli*," Biotechnology 10:411–21, Elsevier Science Ltd.; Eihauer et al. [2001] "The FLAG™ Peptide, a Versatile Fusion Tag for the Purification of Recombinant Proteins," *J. Biochem Biophys Methods* 49:455–65; Jones et al. [1995] *J. Chromatography* 707:3–22; Jones et al. [1995] "Current Trends in Molecular Recognition and Bioseparation," *J. of Chromatography A.* 707:3–22, Elsevier Science B. V.; Margolin [2000] "Green Fluorescent Protein as a Reporter for Macromolecular Localization in Bacterial Cells," *Methods* 20:62–72, Academic Press; Puig et al. [2001] "The Tandem Affinity Purification (TAP) Method: A General Procedure of Protein Complex Purification," *Methods* 24:218–29, Academic Press; Sassenfeld [1990] "Engineering Proteins for Purification," TibTech 8:88–93; Sheibani [1999] "Prokaryotic Gene Fusion Expression Systems and Their Use in Structural and Functional Studies of Proteins," *Prep. Biochem. & Biotechnol.* 29(1):77–90, Marcel Dekker, Inc.; Skerra et al. [1999] "Applications of a Peptide Ligand for Streptavidin: the Strep-tag", *Biomolecular Engineering* 16:79–86, Elsevier Science, B. V.; Smith [1998] "Cookbook for Eukaryotic Protein Expression: Yeast, Insect, and Plant Expression Systems," The Scientist

12(22):20; Smyth et al. [2000] "Eukaryotic Expression and Purification of Recombinant Extracellular Matrix Proteins Carrying the Strep II Tag", *Methods in Molecular Biology* 139:49–57; Unger [1997] "Show Me the Money: Prokaryotic Expression Vectors and Purification Systems," *The Scientist* 11(17):20, each of which is hereby incorporated by reference in their entireties), or commercially available tags from vendors such as such as STRATAGENE (La Jolla, Calif.), NOVAGEN (Madison, Wis.), QIAGEN, Inc., (Valencia, Calif.), or In Vitrogen (San Diego, Calif.).

TABLE 1

Splice variants of BIVM(SEQ ID NOs:29–50)

Seq ID No.	Exon	Splice Donor	Splice Acceptor	Position	Intron (bp)
29	A^1	CGGCCCCAGGgtaac	—	1-415	—
30	A^2	TGTGATCCAGGgtccg	—	1-365	—
31	A^3	CAGGCCAGAGgtacc	—	1-473	—
33/32	B	TTTCTGTCAGgtgat	ttccctaaagGAATC	474-557	5785
35/34	1	CACAAATCAGgtaag	ttcctcttagGAGCT	558-1157	1754
37/36	2	TCAGACGATGgtgat	tgtattctagGCAAT	1158-1284	8682
39/38	3	GAGCTGGAAAgtaag	gtgttctcagGTACT	1285-1380	4481
41/40	4	CACTTATGAGgtatg	tcttttgtagCCTTC	1381-1485	609
43/42	5	GGAGAAACTGgtagg	ttactttcagGTGGT	1486-1580	216
45/44	6	AAGCATTCAGgtaag	tttttaatagCTTCA	1581-1713	9405
49/48	7	AACAAAGAAGgtaag	ttaactatagATGGG	1714-1800	2768
50	8	—	ttcttctcagGTTGG	1801-1897	4089
50	9	—	ttcttctcagGTTGG	1898-3029	832

Other aspects of the invention provide vectors containing one or more of the polynucleotides of the invention. The vectors can be vaccine, replication, or amplification vectors. In some embodiments of this aspect of the invention, the polynucleotides are operably associated with regulatory elements capable of causing the expression of the polynucleotide sequences. Such vectors include, among others, chromosomal, episomal and virus-derived vectors, e.g., vectors derived from bacterial plasmids, from bacteriophage, from transposons, from yeast episomes, from insertion elements, from yeast chromosomal elements, from viruses such as baculoviruses, papova viruses, such as SV40, vaccinia viruses, adenoviruses, fowl pox viruses, pseudorabies viruses and retroviruses, and vectors derived from combinations of the aforementioned vector sources, such as those derived from plasmid and bacteriophage genetic elements (e.g., cosmids and phagemids).

As indicated above, vectors of this invention can also comprise elements necessary to provide for the expression and/or the secretion of a polypeptide encoded by the nucleotide sequences of the invention in a given host cell. The vector can contain one or more elements selected from the group consisting of a promoter, signals for initiation of translation, signals for termination of translation, and appropriate regions for regulation of transcription. In certain embodiments, the vectors can be stably maintained in the host cell and can, optionally, contain signal sequences directing the secretion of translated protein. Other embodiments provide vectors that are not stable in transformed host cells. Vectors can integrate into the host genome or be autonomously-replicating vectors.

In a specific embodiment, a vector comprises a promoter operably linked to a protein or peptide-encoding nucleic acid sequence, one or more origins of replication, and, optionally, one or more selectable markers (e.g., an antibiotic resistance gene). Non-limiting exemplary vectors for the expression of the polypeptides of the invention include pBr-type vectors, pET-type plasmid vectors (Promega), pBAD plasmid vectors (Invitrogen) or those provided in the examples below. Furthermore, vectors according to the invention are useful for transforming host cells for the cloning or expression of the nucleotide sequences of the invention.

Promoters which may be used to control expression include, but are not limited to, the CMV promoter, the SV40 early promoter region (Bernoist and Chambon [1981] *Nature* 290:304–310), the promoter contained in the 3' long terminal repeat of Rous sarcoma virus (Yamamoto, et al. [1980] *Cell* 22:787–797), the herpes thymidine kinase promoter (Wagner et al. [1981] *Proc. Natl. Acad. Sci. USA* 78:1441–1445), the regulatory sequences of the metallothionein gene (Brinster et al. [1982] *Nature* 296:39–42); prokaryotic vectors containing promoters such as the β-lactamase promoter (Villa-Kamaroff, et al. [1978] *Proc. Natl. Acad. Sci. USA* 75:3727–3731), or the tac promoter (DeBoer, et al. [1983] *Proc. Natl. Acad. Sci. USA* 80:21–25); see also, "Useful Proteins from Recombinant Bacteria" in *Scientific American*, 1980, 242:74–94; plant expression vectors comprising the nopaline synthetase promoter region (Herrera-Estrella et al. [1983] *Nature* 303:209–213) or the cauliflower mosaic virus 35S RNA promoter (Gardner, et al. [1981] *Nucl. Acids Res.* 9:2871), and the promoter of the photosynthetic enzyme ribulose biphosphate carboxylase (Herrera-Estrella et al. [1984] *Nature* 310:115–120); promoter elements from yeast or fungi such as the Gal 4

promoter, the ADC (alcohol dehydrogenase) promoter, PGK (phosphoglycerol kinase) promoter, and/or the alkaline phosphatase promoter.

The subject invention also provides for "homologous" or "modified" nucleotide sequences. Modified nucleic acid sequences will be understood to mean any nucleotide sequence obtained by mutagenesis according to techniques well known to persons skilled in the art, and exhibiting modifications in relation to the normal sequences. For example, mutations in the regulatory and/or promoter sequences for the expression of a polypeptide that result in a modification of the level of expression of a polypeptide according to the invention provide for a "modified nucleotide sequence". Likewise, substitutions, deletions, or additions of nucleic acid to the polynucleotides of the invention provide for "homologous" or "modified" nucleotide sequences. In various embodiments, "homologous" or "modified" nucleic acid sequences have substantially the same biological or serological activity as the native (naturally occurring) BIVM polypeptides. A "homologous" or "modified" nucleotide sequence will also be understood to mean a splice variant of the polynucleotides of the instant invention (see Table I) or any nucleotide sequence encoding a "modified polypeptide" as defined below.

A homologous nucleotide sequence, for the purposes of the present invention, encompasses a nucleotide sequence having a percentage identity with the bases of the nucleotide sequences of between at least (or at least about) 20.00% to 99.99% or higher. The aforementioned range of percent identity is to be taken as including, and providing written description and support for, any fractional percentage, in intervals of 0.01%, between 20.00% and 99.99% or higher. These percentages are purely statistical and differences between two nucleic acid sequences can be distributed randomly and over the entire sequence length.

In various embodiments, homologous sequences exhibiting a percentage identity with the bases of the nucleotide sequences of the present invention can have 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99 percent identity with the polynucleotide sequences of the instant invention.

Both protein and nucleic acid sequence homologies may be evaluated using any of the variety of sequence comparison algorithms and programs known in the art. Such algorithms and programs include, but are by no means limited to, TBLASTN, BLASTP, FASTA, TFASTA, and CLUSTALW (Pearson and Lipman [1988] *Proc. Natl. Acad. Sci. USA* 85(8):2444–2448; Altschul et al. [1990] *J. Mol. Biol.* 215 (3):403–410; Thompson et *Nucleic Acids Res.* 22(2):4673–4680; Higgins et al. [1996] *Methods Enzymol.* 266:383–402; Altschul et al. [1990] *J. Mol. Biol.* 215(3): 403–410; Altschul et al. [1993] *Nature Genetics* 3:266–272).

The subject invention also provides nucleotide sequences complementary to any of the polynucleotide sequences disclosed herein. Thus, the invention is understood to include any DNA whose nucleotides are complementary to those of the sequence of the invention, and whose orientation is reversed (e.g., an antisense sequence).

The present invention further provides fragments of the polynucleotide sequences provided herein. Representative fragments of the polynucleotide sequences according to the invention will be understood to mean any nucleotide fragment having at least 8 or 9 successive nucleotides, preferably at least 12 successive nucleotides, and still more preferably at least 15 or at least 20 successive nucleotides of the sequence from which it is derived. In other embodiments, fragments contain from one nucleotide less than the full length polynucleotide sequence to fragments comprising up to, and including 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 105, 110, 115, 120, 125, 130, 135, 140, 145, 150, 155, 160, 165, 170, 175, 180, 185, 190, 195, 200, 205, 210, 215, 220, 225, 230, 235, 240, 245, 250, or 255 consecutive nucleotides of a particular sequence disclosed herein. Yet other embodiments provide fragments (or detection probes) comprising nucleotides 1446 to 1697 or 1447 to 1698 of FIG. **1** (SEQ ID NO:1). It is to be understood that such fragments refer only to portions of the disclosed polynucleotide sequences that are not listed in a publicly available database or prior art references.

Among these representative fragments, those capable of hybridizing under stringent conditions with a nucleotide sequence according to the invention are preferred. Conditions of high or intermediate stringency are provided infra and are chosen to allow for hybridization between two complementary DNA fragments. Hybridization conditions for a polynucleotide of about 300 bases in size will be adapted by persons skilled in the art for larger- or smaller-sized oligonucleotides, according to methods well known in the art (see, for example, Sambrook et al. [1989]).

The subject invention also provides detection probes (e.g., fragments of the disclosed polynucleotide sequences) for hybridization with a target sequence or an amplicon generated from the target sequence. Such a detection probe will advantageously have as sequence a sequence of at least 9, 12, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, or 100 nucleotides. Alternatively, detection probes can comprise 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 105, 110, 115, 120, 125, 130, 135, 140, 145, 150, 155, 160, 165, 170, 175, 180, 185, 190, 195, 200, 205, 210, 215, 220, 225, 230, 235, 240, 245, 250, or 255 consecutive nucleotides of the disclosed nucleic acids. The detection probes can also be used as labeled probe or primer in the subject invention. Labeled probes or primers are labeled with a radioactive compound or with another type of label. Alternatively, non-labeled nucleotide sequences may be used directly as probes or primers; however, the sequences are generally labeled with a radioactive element (^{32}P, ^{35}S, ^{3}H, ^{125}I) or with a molecule such as biotin, acetylaminofluorene, digoxigenin, 5-bromo-deoxyuridine, or fluorescein to provide probes that can be used in numerous applications.

The nucleotide sequences according to the invention may also be used in analytical systems, such as DNA chips. DNA chips and their uses are well known in the art and (see for example, U.S. Pat. Nos. 5,561,071; 5,753,439; 6,214,545; Schena et al. [1996] *BioEssays* 18:427–431; Bianchi et al. [1997] *Clin. Diagn. Virol.* 8:199–208; each of which is hereby incorporated by reference in their entireties) and/or are provided by commercial vendors such as Affymetrix, Inc. (Santa Clara, Calif.).

Various degrees of stringency of hybridization can be employed. The more severe the conditions, the greater the complementarity that is required for duplex formation. Severity of conditions can be controlled by temperature, probe concentration, probe length, ionic strength, time, and the like. Preferably, hybridization is conducted under moderate to high stringency conditions by techniques well

known in the art, as described, for example, in Keller, G. H., M. M. Manak [1987] *DNA Probes*, Stockton Press, New York, N.Y., pp. 169–170.

By way of example, hybridization of immobilized DNA on Southern blots with ^{32}P-labeled gene-specific probes can be performed by standard methods (Maniatis et al. [1982] *Molecular Cloning: A Laboratory Manual*, Cold Spring Harbor Laboratory, New York). In general, hybridization and subsequent washes can be carried out under moderate to high stringency conditions that allow for detection of target sequences with homology to the exemplified polynucleotide sequence. For double-stranded DNA gene probes, hybridization can be carried out overnight at 20–25° C. below the melting temperature (Tm) of the DNA hybrid in 6×SSPE, 5× Denhardt's solution, 0.1% SDS, 0.1 mg/ml denatured DNA. The melting temperature is described by the following formula (Beltz et al. [1983] *Methods of Enzymology*, R. Wu, L. Grossman and K. Moldave [eds.] Academic Press, New York 100:266–285).

T_m=81.5° C.+16.6 Log[Na+]+0.41(% G+C)−0.61(% formamide)−600/length of duplex in base pairs.

Washes are typically carried out as follows:

(1) twice at room temperature for 15 minutes in 1×SSPE, 0.1% SDS (low stringency wash);

(2) once at T_m−20° C. for 15 minutes in 0.2×SSPE, 0.1% SDS (moderate stringency wash).

For oligonucleotide probes, hybridization can be carried out overnight at 10–20° C. below the melting temperature (T_m) of the hybrid in 6×SSPE, 5× Denhardt's solution, 0.1% SDS, 0.1 mg/ml denatured DNA. T_m for oligonucleotide probes can be determined by the following formula:

T_m (° C.)=2(number T/A base pairs)+4(number G/C base pairs) (Suggs et al. [1981] *ICN-UCLA Symp. Dev. Biol. Using Purified Genes*, D. D. Brown [ed.], Academic Press, New York, 23:683–693).

Washes can be carried out as follows:

(1) twice at room temperature for 15 minutes 1×SSPE, 0.1% SDS (low stringency wash;

2) once at the hybridization temperature for 15 minutes in 1×SSPE, 0.1% SDS (moderate stringency wash).

In general, salt and/or temperature can be altered to change stringency. With a labeled DNA fragment >70 or so bases in length, the following conditions can be used:

Low: 1 or 2×SSPE, room temperature
Low: 1 or 2×SSPE, 42° C.
Moderate: 0.2× or 1×SSPE, 65° C.
High: 0.1×SSPE, 65° C.

By way of another non-limiting example, procedures using conditions of high stringency can also be performed as follows: Pre-hybridization of filters containing DNA is carried out for 8 h to overnight at 65° C. in buffer composed of 6×SSC, 50 mM Tris-HCl (pH 7.5), 1 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.02% BSA, and 500 μg/ml denatured salmon sperm DNA. Filters are hybridized for 48 h at 65° C., the preferred hybridization temperature, in pre-hybridization mixture containing 100 μg/ml denatured salmon sperm DNA and 5–20×10^6 cpm of ^{32}P-labeled probe. Alternatively, the hybridization step can be performed at 65° C. in the presence of SSC buffer, 1×SSC corresponding to 0.15M NaCl and 0.05 M Na citrate. Subsequently, filter washes can be done at 37° C. for 1 h in a solution containing 2×SSC, 0.01% PVP, 0.01% Ficoll, and 0.01% BSA, followed by a wash in 0.1×SSC at 50° C. for 45 min. Alternatively, filter washes can be performed in a solution containing 2×SSC and 0.1% SDS, or 0.5×SSC and 0.1% SDS, or 0.1×SSC and 0.1% SDS at 68° C. for 15 minute intervals. Following the wash steps, the hybridized probes are detectable by autoradiography. Other conditions of high stringency which may be used are well known in the art (see, for example, Sambrook et al. [1989] *Molecular Cloning, A Laboratory Manual, Second Edition*, Cold Spring Harbor Press, N.Y., pp. 9.47–9.57; and Ausubel et al. [1989] *Current Protocols in Molecular Biology*, Green Publishing Associates and Wiley Interscience, N.Y., each incorporated herein in its entirety).

A further non-limiting example of procedures using conditions of intermediate stringency are as follows: Filters containing DNA are pre-hybridized, and then hybridized at a temperature of 60° C. in the presence of a 5×SSC buffer and labeled probe. Subsequently, filters washes are performed in a solution containing 2×SSC at 50° C. and the hybridized probes are detectable by autoradiography. Other conditions of intermediate stringency which may be used are well known in the art (see, for example, Sambrook et al. [1989] *Molecular Cloning, A Laboratory Manual, Second Edition*, Cold Spring Harbor Press, N.Y., pp. 9.47–9.57; and Ausubel et al. [1989] *Current Protocols in Molecular Biology*, Green Publishing Associates and Wiley Interscience, N.Y., each of which is incorporated herein in its entirety).

Duplex formation and stability depend on substantial complementarity between the two strands of a hybrid and, as noted above, a certain degree of mismatch can be tolerated. Therefore, the probe sequences of the subject invention include mutations (both single and multiple), deletions, insertions of the described sequences, and combinations thereof, wherein said mutations, insertions and deletions permit formation of stable hybrids with the target polynucleotide of interest. Mutations, insertions and deletions can be produced in a given polynucleotide sequence in many ways, and these methods are known to an ordinarily skilled artisan. Other methods may become known in the future.

It is also well known in the art that restriction enzymes can be used to obtain functional fragments of the subject DNA sequences. For example, Bal31 exonuclease can be conveniently used for time-controlled limited digestion of DNA (commonly referred to as "erase-a-base" procedures). See, for example, Maniatis et al. [1982] *Molecular Cloning: A Laboratory Manual*, Cold Spring Harbor Laboratory, New York; Wei et al. [1983] *J. Biol. Chem.* 258:13006–13512. The nucleic acid sequences of the subject invention can also be used as molecular weight markers in nucleic acid analysis procedures.

The invention also provides host cells transformed by a polynucleotide according to the invention and the production of BIVM (or BIVM ortholog) polypeptides by the transformed host cells. In some embodiments, transformed cells comprise an expression vector containing BIVM, or BIVM ortholog, polynucleotide sequences. Other embodiments provide for host cells transformed with nucleic acids. Yet other embodiments provide transformed cells comprising an expression vector containing fragments of BIVM, or BIVM ortholog, polynucleotide sequences. Transformed host cells according to the invention are cultured under conditions allowing the replication and/or the expression of the nucleotide sequences of the invention. Expressed polypeptides are recovered from culture media and purified, for further use, according to methods known in the art.

The host cell may be chosen from eukaryotic or prokaryotic systems, for example bacterial cells (Gram negative or Gram positive), yeast cells, animal cells, plant cells, and/or insect cells using baculovirus vectors. In some embodiments, the host cell for expression of the polypeptides include, and are not limited to, those taught in U.S. Pat. Nos. 6,319,691; 6,277,375; 5,643,570; 5,565,335; Unger [1997] *The Scientist* 11(17):20; or Smith [1998] *The Scientist*

12(22):20, each of which is incorporated by reference in its entirety, including all references cited within each respective patent or reference. Other exemplary, and non-limiting, host cells include *Staphylococcus* spp., *Enterococcus* spp., *E. coli*, and *Bacillus subtilis*; fungal cells, such as *Streptomyces* spp., *Aspergillus* spp., *S. cerevisiae, Schizosaccharomyces pombe, Pichia pastoris, Hansela polymorpha, Kluveromyces lactis*, and *Yarrowia lipolytica*; insect cells such as *Drosophila* S2 and *Spodoptera* Sf9 cells; animal cells such as CHO, COS, HeLa, C127, 3T3, BHK, 293 and Bowes melanoma cells; and plant cells. A great variety of expression systems can be used to produce the polypeptides of the invention and polynucleotides can be modified according to methods known in the art to provide optimal codon usage for expression in a particular expression system.

Furthermore, a host cell strain may be chosen that modulates the expression of the inserted sequences, modifies the gene product, and/or processes the gene product in the specific fashion. Expression from certain promoters can be elevated in the presence of certain inducers; thus, expression of the genetically engineered polypeptide may be controlled. Furthermore, different host cells have characteristic and specific mechanisms for the translational and post-translational processing and modification (e.g., glycosylation, phosphorylation) of proteins. Appropriate cell lines or host systems can be chosen to ensure the desired modification and processing of the foreign protein expressed. For example, expression in a bacterial system can be used to produce an unglycosylated core protein product whereas expression in yeast will produce a glycosylated product. Expression in mammalian cells can be used to provide "native" glycosylation of a heterologous protein. Furthermore, different vector/host expression systems may effect processing reactions to different extents.

Nucleic acids and/or vectors can be introduced into host cells by well-known methods, such as, calcium phosphate transfection, DEAE-dextran mediated transfection, transfection, microinjection, cationic lipid-mediated transfection, electroporation, transduction, scrape loading, ballistic introduction and infection (see, for example, Sambrook et al. [1989] *Molecular Cloning: A Laboratory Manual,* 2^{nd} Ed., Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y.).

The subject invention also provides for the expression of a polypeptide, derivative, or a variant (e.g., a splice variant) encoded by a polynucleotide sequence disclosed herein. Alternatively, the invention provides for the expression of a polypeptide fragment obtained from a polypeptide, derivative, or a variant encoded by a polynucleotide fragment derived from the polynucleotide sequences disclosed herein. In either embodiment, the disclosed sequences can be regulated by a second nucleic acid sequence so that the polypeptide or fragment is expressed in a host transformed with a recombinant DNA molecule according to the subject invention. For example, expression of a protein or peptide may be controlled by any promoter/enhancer element known in the art.

The subject invention also provides nucleic acid based methods for the identification of the presence of the BIVM gene, or orthologs thereof, in a sample. These methods can utilize the nucleic acids of the subject invention and are well known to those skilled in the art (see, for example, Sambrook et al. [1989] or Abbaszadega [2001] "Advanced Detection of Viruses and Protozoan Parasites in Water," *Reviews in Biology and Biotechnology,* 1(2):21–26). Among the techniques useful in such methods are enzymatic gene amplification (or PCR), Southern blots, Northern blots, or other techniques utilizing nucleic acid hybridization for the identification of polynucleotide sequences in a sample. Thus, the subject invention can provide nucleic acid based methodologies for the identification of *G. lamblia* in environmental or biological samples and provides sensitive assays for the diagnosis of *G. lamblia* infections. Alternatively, the nucleic acids can be used to screen individuals for cancers, tumors, or malignancies associated with dysregulation of the BIVM gene or its transcriptional products.

The subject invention also provides polypeptides encoded by nucleotide sequences of the invention. The subject invention also provides fragments of at least 5 amino acids of a polypeptide encoded by the polynucleotides of the instant invention. In some embodiments, the polypeptide fragments are reactive with antibodies found in the serum of an individual infected with *G. lamblia.*

In the context of the instant invention, the terms polypeptide, peptide and protein are used interchangeably. Likewise, the terms variant and homologous are also used interchangeably. It should be understood that the invention does not relate to the polypeptides in natural form or native environment. Peptides and polypeptides according to the invention have been isolated or obtained by purification from natural sources (or their native environment), chemically synthesized, or obtained from host cells prepared by genetic manipulation (e.g., the polypeptides, or fragments thereof, are recombinantly produced by host cells). Polypeptides according to the instant invention may also contain non-natural amino acids, as will be described below.

"Variant" or "homologous" polypeptides will be understood to designate the polypeptides containing, in relation to the native polypeptide, modifications such as deletion, addition, or substitution of at least one amino acid, truncation, extension, or the addition of chimeric heterologous polypeptides. Optionally, "variant" or "homologous" polypeptides can contain a mutation or post-translational modifications. Among the "variant" or "homologous" polypeptides, those whose amino acid sequence exhibits 20.00% to 99.99% (inclusive) identity to the native polypeptide sequence are preferred. The aforementioned range of percent identity is to be taken as including, and providing written description and support for, any fractional percentage, in intervals of 0.01%, between 50.00% and, up to, including 99.99%. These percentages are purely statistical and differences between two polypeptide sequences can be distributed randomly and over the entire sequence length.

"Variant" or "homologous" polypeptide sequences exhibiting a percentage identity with the polypeptides of the present invention can, alternatively, have 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 91, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99 percent identity with the polypeptide sequences of the instant invention. The expression equivalent amino acid is intended here to designate any amino acid capable of being substituted for one of the amino acids in the basic structure without, however, essentially modifying the biological activities of the corresponding peptides and as provided below.

By way of example, amino acid substitutions can be carried out without resulting in a substantial modification of the biological activity of the corresponding modified polypeptides; for example, the replacement of leucine with valine or isoleucine; aspartic acid with glutamic acid; glutamine with asparagine; arginine with lysine; and the

reverse substitutions can be performed without substantial modification of the biological activity of the polypeptides.

In other embodiments, homologous polypeptides according to the subject invention also include various splice variants identified within the BIVM coding sequence (see Table I).

The subject invention also provides biologically active fragments of a polypeptide according to the invention and includes those peptides capable of eliciting an immune response. In one embodiment, an immune response directed against *G. lamblia* is provided. The immune response can provide components (either antibodies or components of the cellular immune response (e.g., B-cells, helper, cytotoxic, and/or suppressor T-cells)) reactive with the biologically active fragment of a polypeptide, the intact, full length, unmodified polypeptide disclosed herein, or both the biologically active fragment of a polypeptide and the intact, full length, unmodified polypeptides disclosed herein. Biologically active fragments according to the invention comprise from five (5) amino acids to one amino acid less than the full length of any polypeptide sequence provided herein. Alternatively, fragments comprising 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 35, 40,45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 105, 110, 115, 120, 125, 130, 135, 140, 145, 150, 155, 160, 165, 170, 175, 180, 185, 190, 195, 200, 205, 210, 215, 220, 225, 230, 235, 240, 245, 250, or 255 consecutive amino acids of a disclosed polypeptide sequence are provided herein.

Fragments, as described herein, can be obtained by cleaving the polypeptides of the invention with a proteolytic enzyme (such as trypsin, chymotrypsin, or collagenase) or with a chemical reagent, such as cyanogen bromide (CNBr). Alternatively, polypeptide fragments can be generated in a highly acidic environment, for example at pH 2.5. Such polypeptide fragments may be equally well prepared by chemical synthesis or using hosts transformed with an expression vector containing nucleic acids encoding polypeptide fragments according to the invention. The transformed host cells contain a nucleic acid and are cultured according to well-known methods; thus, the invention allows for the expression of these fragments, under the control of appropriate elements for regulation and/or expression of the polypeptide fragments.

Modified polypeptides according to the invention are understood to designate a polypeptide obtained by variation in the splicing of transcriptional products of the BIVM gene, genetic recombination, or by chemical synthesis as described below. Modified polypeptides contain at least one modification in relation to the normal polypeptide sequence. These modifications can include the addition, substitution, deletion of amino acids contained within the polypeptides of the invention.

In order to extend the life of the polypeptides of the invention, it may be advantageous to use non-natural amino acids, for example in the D form, or alternatively amino acid analogs, such as sulfur-containing forms of amino acids. Alternative means for increasing the life of polypeptides can also be used in the practice of the instant invention. For example, polypeptides of the invention, and fragments thereof, can be recombinantly modified to include elements that increase the plasma, or serum half-life of the polypeptides of the invention. These elements include, and are not limited to, antibody constant regions (see for example, U.S. Pat. No. 5,565,335, hereby incorporated by reference in its entirety, including all references cited therein), or other elements such as those disclosed in U.S. Pat. Nos. 6,319,691; 6,277,375; or 5,643,570, each of which is incorporated by reference in its entirety, including all references cited within each respective patent. Alternatively, the polynucleotides and genes of the instant invention can be recombinantly fused to elements that are useful in the preparation of immunogenic constructs for the purposes of vaccine formulation or elements useful for the isolation of the polypeptides of the invention.

The polypeptides, fragments, and immunogenic fragments of the invention may further contain linkers that facilitate the attachment of the fragments to a carrier molecule for the stimulation of an immune response or diagnostic purposes. The linkers can also be used to attach fragments according to the invention to solid support matrices for use in affinity purification protocols. In this aspect of the invention, the linkers specifically exclude, and are not to be considered anticipated, where the fragment is a subsequence of another peptide, polypeptide, or protein as identified in a search of protein sequence databases as indicated in the preceding paragraph. In other words, the non-identical portions of the other peptide, polypeptide, of protein is not considered to be a "linker" in this aspect of the invention. Non-limiting examples of "linkers" suitable for the practice of the invention include chemical linkers (such as those sold by Pierce, Rockford, Ill.), peptides which allow for the connection of the immunogenic fragment to a carrier molecule (see, for example, linkers disclosed in U.S. Pat. Nos. 6,121,424; 5,843,464; 5,750,352; and 5,990,275, hereby incorporated by reference in their entirety). In various embodiments, the linkers can be up to 50 amino acids in length, up to 40 amino acids in length, up to 30 amino acids in length, up to 20 amino acids in length, up to 10 amino acids in length, or up to 5 amino acids in length.

In other specific embodiments, the polypeptides, peptides, derivatives, or analogs thereof may be expressed as a fusion, or chimeric protein product (comprising the protein, fragment, analog, or derivative joined via a peptide bond to a heterologous protein sequence (e.g., a different protein)). Such a chimeric product can be made by ligating the appropriate nucleic acid sequences encoding the desired amino acid sequences to each other by methods known in the art, in the proper coding frame, and expressing the chimeric product by methods commonly known in the art (see, for example, U.S. Pat. No. 6,342,362, hereby incorporated by reference in its entirety; Altendorf et al. [1999-WWW, 2000] "Structure and Function of the F_o Complex of the ATP Synthase from *Escherichia Coli," J. of Experimental Biology* 203:19–28, The Co. of Biologists, Ltd., G.B.; Baneyx [1999] "Recombinant Protein Expression in *Escherichia coli," Biotechnology* 10:411–21, Elsevier Science Ltd.; Eihauer et al. [2001] "The FLAG™ Peptide, a Versatile Fusion Tag for the Purification of Recombinant Proteins," *J. Biochem Biophys Methods* 49:455–65; Jones et al. [1995] *J. Chromatography* 707:3–22; Jones et al. [1995] "Current Trends in Molecular Recognition and Bioseparation," *J. Chromatography A.* 707:3–22, Elsevier Science B. V.; Margolin [2000] "Green Fluorescent Protein as a Reporter for Macromolecular Localization in Bacterial Cells," *Methods* 20:62–72, Academic Press; Puig et al. [2001] "The Tandem Affinity Purification (TAP) Method: A General Procedure of Protein Complex Purification," *Methods* 24:218–29, Academic Press; Sassenfeld [1990] "Engineering Proteins for Purification," *TibTech* 8:88–93; Sheibani [1999] "Prokaryotic Gene Fusion Expression Systems and Their Use in Structural and Functional Studies of Proteins," *Prep. Biochem. & Biotechnol.* 29(1):77–90, Marcel Dekker, Inc.; Skerra et al. [1999] "Applications of a Peptide Ligand for Streptavidin: The Strep-tag", *Biomolecular Engineering*

16:79–86, Elsevier Science, B. V.; Smith [1998] "Cookbook for Eukaryotic Protein Expression: Yeast, Insect, and Plant Expression Systems," The Scientist 12(22):20; Smyth et al. [2000] "Eukaryotic Expression and Purification of Recombinant Extracellular Matrix Proteins Carrying the Strep II Tag", *Methods in Molecular Biology,* 139:49–57; Unger [1997] "Show Me the Money: Prokaryotic Expression Vectors and Purification Systems," *The Scientist* 11(17):20, each of which is hereby incorporated by reference in their entireties). Alternatively, such a chimeric product may be made by protein synthetic techniques, e.g., by use of a peptide synthesizer.

Another embodiment of the subject invention provides for the use of polypeptides encoded by the polynucleotides of the subject invention for the induction of an immune response or protective immunity in a subject to which the polypeptides are administered. In this aspect of the invention, compositions containing polypeptide are administered to a subject in amounts sufficient to induce an immune response, and/or induce protective immunity. The composition administered to the subject may, optionally, contain an adjuvant and may be delivered to the subject in any manner known in the art for the delivery of immunogen to a subject. Compositions may be formulated in any carriers, including for example, carriers described in E. W. *Martin's Remington's Pharmaceutical Science*, Mack Publishing Company, Easton, Pa.

The expression of the BIVM gene or BIVM gene product (e.g., DNA, RNA, or polypeptide) is dysregulated in a variety of cancers, tumors, and/or malignancies. Non-limiting examples of such cancers, tumors, and/or malignancies include prostate cancer, breast cancer, melanoma, chronic myelogenous leukemia, cervical cancer, adenocarcinomas, lymphoblastic leukemia, colorectal cancer, and lung carcinoma. Accordingly, the present invention provides a method for screening, or aiding in the diagnosis of, an individual suspected of having a malignancy or cancer. The subject invention provides methods comprising the steps of determining the amount of BIVM in a biological sample obtained from said individual and comparing the measured amount of BIVM to the amount of BIVM found in the normal population. The presence of a significantly increased amount of BIVM is associated with an indication of a malignancy or cancer. BIVM gene product can be detected by well-known methodologies including, and not limited to, Western blots, enzyme linked immunoassays (ELISAs), radioimmunoassays (RIAs), Northern blots, Southern blots, PCR-based assays, or other assays for the quantification of gene product known to the skilled artisan. This information, in conjunction with other information available to the skilled practitioner, assists in making a diagnosis.

The terms "comprising", "consisting of" and "consisting essentially of" are defined according to their standard meaning and may be substituted for one another throughout the instant application in order to attach the specific meaning associated with each term.

Following examples illustrate procedures for practicing the invention. These examples should not be construed as limiting. All percentages are by weight and all solvent mixture proportions are by volume unless otherwise noted.

EXAMPLE 1

Identification of BIVM

Human BIVM was identified originally as an EST (IMAGE #785450; GenBank AA449273) that encodes the two short motifs WFRQ (motif 2 [M2]) and YFC (motif 3a [M3a]), which correspond to framework region 2 (FR2) and FR3 of an Ig V domain, respectively (Barclay, A. N., et al. [1997] *The Leucocyte Antigen FactsBook*, Academic Press, San Diego). The W in M2 and C in M3a correspond to W^{41} and C^{104} of the IMGT numbering system. Complete sequencing of this EST, overlapping ESTs (IMAGE #2184889, GenBank AI538125; IMAGE 136117, GenBank R33273; IMAGE 1060823, GenBank AA568610; and IMAGE 785450, GenBank AA449273) and RACE strategies were used to resolve the complete mRNA sequence.

Human BIVM mRNA is 3857 nucleotides and encodes a 503 amino acid protein (FIG. **1**). No proteins with significant identities (E<0.01) to BIVM have been identified using BLAST analyses. Searches of current motif databases (BLOCKS, PRINTS, Conserved Domain Database, Domain Architecture Retrieval Tool, Simple Modular Architecture Research Tool) also failed to identify any additional significant motifs within the BIVM protein.

In addition to the shared M2 and M3a motifs, a second V domain FR3 motif, YHC (M3b), is located several residues amino terminal of M3a. Furthermore, a putative FR1 motif (M1), encoding the conserved V domain residues G^{16} and C^{23} (IMGT amino acid numbering), was identified by visual inspection of BIVM peptide sequences (FIG. **1**).

The 42 amino acids between M1 and M2 in BIVM are inconsistent with the sequence relationship in a V region in which the corresponding motifs would be separated by no more than 12 residues. This increased distance between C^{23} and C^{104} of M1 and M3a (or M3b), which normally form a disulfide bridge and stabilize the Ig domain architecture, strongly suggests that BIVM is not a member of the IgSF. Since these peptide motifs are extremely short, it could be argued that their presence in BIVM may be a random occurrence. However, it should be emphasized that in the original search of the EST database, only 17 sequences were identified that encode W(Y/F)R(Q/H) and YFC that are correctly spaced and maintain an open reading frame. Of these 17 sequences, 16 were TCR cDNAs (encoding WYRQ) and one was BIVM (encoding WFRQ) (Hawke, N. A., et al. [1999] "Expanding Our Understanding of Immunoglobulin, T-cell Antigen Receptor, and Novel Immune-Type Receptor Genes: a Subset of the Immunoglobulin Gene Superfamily," *Immunogenetics* 50:124–133).

EXAMPLE 2

Genomic Organization of BIVM

GeneBridge 4 radiation hybrid panel mapping (Gyapay, G., et al. [1996] "A Radiation Hybrid Map of the Human Genome," *Hum Mol Genet* 5:339–346) localized BIVM on chromosome 13q32–33 (data not shown). Examination of the publicly available Human Genome Project database revealed the exon-intron structure of BIVM. A 5' truncated BIVM sequence (hypothetical protein FLJ20159) was initially placed on the publicly available human genome map at 13q14–q21. The 5' untranslated region of BIVM consists of two separate exons (designated exons A and B), followed by the coding region consisting of nine exons; the exon/intron boundaries are indicated in Table I.

Inspection of genomic sequence localizes BIVM between ERCC5 and "hypothetical protein" MGC5302, a human ortholog of the gene encoding the mouse protein Kdel1/EP58 (Kimata, Y., et al. [2000] "Identification of a Novel Mammalian Endoplasmicreticulum-Resident KDEL Protein Using an EST Database Motif Search," *Gene* 261:321–327).

A CpG island is located in the 5' untranslated region of BIVM; the 3' untranslated region contains an Alu sequence (FIGS. **1** and **2**). The Alu polyA sequence in the 3' untranslated region leads to the spurious production of 3' truncated cDNAs including many that are represented as ESTs.

Multiple 5' untranslated region splice variants were observed in analysis of 5' RACE products. Specifically, exon A has at least 3 splice donor sequences and exon B, which has a poor splice acceptor sequence, can be absent from the mature transcript (FIGS. **1** and **2**; Table I). In addition, it is likely that multiple transcriptional start sites are present (FIG. **1**).

EXAMPLE 3

BIVM is Highly Conserved within Deuterostome Species

BIVM orthologs were identified in: mouse, chicken, *Xenopus* and zebrafish in order to address its potential phylogenetic conservation, as well as to define conserved motifs potentially relevant to function. In addition, a partial sequence for a BIVM ortholog was identified in sea urchin. The identity of the human BIVM protein to these orthologs ranges from 35–87% overall and is consistent with the phylogenetic relationships of the species considered (FIG. **3**; see below). The C-terminal region of BIVM shares the highest degree of interspecific sequence identity. The N-terminus of this peptide domain is RK(V/C)LD and the C-terminus is GGNLHC. This region includes all of the V domain motifs, and is 220 amino acids in human (indicated by arrowheads in FIG. **3**).

The corresponding domains in mouse, chicken, *Xenopus*, zebrafish and sea urchin are 97%, 91%, 91%, 87% and 64% identical to the human domain, respectively. In addition, BIVM ESTs have been identified from an ascidian, sea squirt (*Halocynthia roretzi*) (e.g., GenBank AV385966), and a BIVM cDNA fragment has been isolated from a protochordate (cephalochordate), lancelet (*Branchiostoma floridae*), using an RT-PCR strategy (Yoder and Litman, GenBank AF411393). Their sequences within this domain are highly conserved.

EXAMPLE 4

Close Physical Linkage of BIVM and EP58/MGC5302

Human BIVM maps between EP58/MGC5302 and ERCC5 on 13q. The human EP58 EST (that extends most 5'), places the transcriptional start sites of EP58 and BIVM only 41 bp apart. We identified a mouse BIVM genomic clone (from a ë FixII library), which also encodes the 5' end of Ep58/Kdel1 (FIG. **4**). The mapping position of Ep58/Kdel1 and BIVM in mouse has not yet been determined. The tight physical linkage of the EP58 to BIVM (41 bp in human and 224 bp in mouse) is consistent with a shared regulatory control system that functions in opposite directions (FIG. **4**). Notably, both Ep58 and BIVM appear to be ubiquitously expressed (FIG. **5**) (Kimata, Y., et al. [2000] "Identification of a Novel Mammalian Endoplasmicreticulum-Resident KDEL Protein Using an EST Database Motif Search," *Gene* 261:321–327). Finally, zebrafish BIVM has been mapped to linkage group 6 (LG6); however, its linkage relationship to kdel1 is unknown.

EXAMPLE 5

Expression of Human BIVM

The human BIVM transcript is ~3.8 kb and appears to be expressed ubiquitously; the highest relative levels of expression are in spleen, ovary, small intestine, colon, peripheral leukocytes and liver (FIG. **5**A). Additional RNA dot blot analyses indicate expression of BIVM in human testes, ovary, aorta, appendix, trachea, pituitary gland, bladder, uterus, spinal cord, salivary gland, stomach, mammary gland and bone marrow as well as in several fetal tissues (data not shown). Notably, BIVM expression was not detected in fetal spleen, adult thymus and certain cancer cell lines (e.g., promyelocytic leukemia, HL-60, and Burkitt's lymphoma Raji) while significant expression was evident in other lines (e.g., HeLa, S3, and colorectal adenocarcinoma, SW480).

EXAMPLE 6

Expression of BIVM in Other Species

The predominant mouse BIVM transcript also is 3.8 kb (FIG. **5**B), of which ~3.3 kb have been sequenced. Comparisons of 5' mouse BIVM RACE products indicate that the 5' untranslated region undergoes alternative RNA splicing, which, like in the human gene, does not affect the coding sequences. The highest levels of expression of mouse BIVM are in heart, brain, liver and kidney (FIG. **5**B).

A major difference between the expression of human and mouse BIVM is observed in the spleen, in which expression is high in the human but appears to be minimal in the mouse. In the developing mouse embryo, BIVM expression is detected at a uniform level after gastrulation (FIG. **5**B). An ~2.1 kb XBIVM cDNA was identified in *Xenopus* that is consistent with the length of the predominant transcript observed in RNA blotting (FIG. **5**C). The broad, diffuse nature of the principal hybridizing band could reflect sequence heterogeneity. The nature of the larger transcript (~4.4 kb) is unknown. Northern blot analysis of sea urchin RNA detects two SpBIVM transcripts of ~7.4 and 8 kb (FIG. **5**D), which are notably longer than the human and mouse forms. The additional sequence in these transcripts might be a result of additional 5' or 3' untranslated regions and/or could reflect polyadenylation effects. Extended 3' untranslated regions are encountered frequently with sea urchin mRNA.

Real-time PCR was used to analyze BIVM expression levels throughout development in zebrafish (FIG. **5**E). As observed in *Xenopus* and sea urchin, there is a large maternal store of BIVM transcript in the 1-cell embryo (0 hpf in zebrafish) which appears to be quickly lost after the initial cellular division(s). In zebrafish, the level of BIVM expression drops by ~90% within the first 6 hours of life (midgastrula stage) and is comparatively undetectable by 12 hpf (post-gastrula stage). Although comparable stages of development were not examined in mouse (see above), it is likely that this early embryonic regulation of BIVM expression will be conserved.

We noted BIVM expression in chicken bursa, which serves as the primary site of B lymphocyte differentiation. BIVM expression in chicken bursa decreases slightly between embryonic day 12 and day 14, increases significantly at day 19, and is the highest in the 4 month old chicken bursa, in which levels are 6-fold greater than observed in embryonic fibroblasts (CEFs; FIG. **5**F). Expression of BIVM in other tissues in chicken has not been characterized.

EXAMPLE 7

BIVM Encodes a Nuclear/Cytoplasmic Protein

The relatively high predicted pI of BIVM (9.1) suggests that it may bind other proteins and/or DNA (or other nucleic acids). The levels of BIVM produced from the native pBIVM-N2 construct and modified pBIVM-K1 construct (see Methods) were compared in whole cells lysates from transiently transfected Cos7 cells. BIVM levels are higher in cells transfected with the modified pBIVM-K1 (FIG. **6**A), which was used in all subsequent transfection experiments. It should be noted that the size of this recombinant protein (with C-terminal epitope tags) is ~61 KDa, whereas the native protein (without post-translational modifications) is predicted to be ~57 kDa. The observation that a single protein is generated from this transcript argues that translation does not begin at a more 3' ATG as suggested by the "hypothetical protein" FLJ20159 GenBank entries (which are predicted to encode a ~27 kDa protein). Western analysis using antibodies that recognize the V5 peptide sequence indicate that the epitope-tagged BIVM is present both in cytoplasmic and nuclear fractions (FIG. **6**B). These results were confirmed by direct immunohistochemical localization of BIVM in the cytoplasm and nucleus (FIG. **6**C-J). Variation in the relative amounts of BIVM in the nucleus was observed in individual cells. Thus, it is possible that the BIVM protein enters and exits the nucleus in a regulated or cell-cycle-dependent manner.

EXAMPLE 8

Giardia may have Acquired a BIVM Ortholog by Horizontal Gene Transfer

A tBLASTn search identified a BIVM-like gene (named BIVML) in the genome of the primitive protozoan parasite, *Giardia lamblia* (McArthur, A. G., et al. [2000] "The *Giardia* Genome Project Database," *FEMS Microbiol Lett* 189:271–273). The 2045 nucleotide BIVML cDNA is predicted to encode a 270 amino acid protein (predicted MW ~30 kDa; Pi=7.56) with no predicted signal peptide, membrane spanning regions or nuclear localization signal- thus, it is likely to be cytosolic. BIVML contains 17 cysteine residues (6.2%) throughout the protein (FIG. **7**A). Known giardial proteins that are secreted to the trophozite surface or the cyst wall are also highly cysteine rich. This sequence is 22–25% identical and 46–49% similar to the carboxyl-terminal region of all deuterostome BIVM peptides described here, correlates directly with the conserved domain described above, and includes the M2 and M3b motifs (FIG. **7**B). Northern analysis detects an ~2.0 kb BIVML transcript as well as a larger transcript of unknown identity in both vegetatively growing and encysting cells (FIG. **7**C).

BIVML is unusual in having long untranslated regions consistent with the size of the transcript. The 5' and 3' untranslated regions were determined by RACE and are 229 nucleotides and 983 nucleotides, respectively (FIG. **7**A). most transcripts of giardial chromosomal genes characterized to date have very short (<20 nucleotides) untranslated regions, although exceptions are being noted.

The identification of a BIVM ortholog in such an early branching eukaryote was unexpected since tBLASTn searches of the currently available *S. cerevisiae* and *Drosophila* as well as *S. pombe* and *C. elegans* genome databases failed to identify any sequences exhibiting significant identity to BIVM. Furthermore, it has not been possible to identify BIVM-like sequences in the complete genomes of *Campylobacter jejuni* (Parkhill, J., et al. [2000] "Complete DNA Sequence of a Serogroup A Strain of *Neisseria Meningitidis* Z2491," *Nature* 404:502–506), *Mycobacterium leprae* (Cole, S. T., et al. [2001] "Massive Gene Decay in the Leprosy Bacillus," Nature 409:1007–11), *Mycobacterium tuberculosis* (Cole, S. T., et al. [1998] "Deciphering the Biology of *Mycobacterium* Tuberculosis from the Complete Genome Sequence," *Nature* 393:537–544), or *Neisseria menigitidis* (Parkhill, J., et al. [2000] "The Genome Sequence of the Food-Borne Pathogen *Campylobacter Jejuni* Reveals Hypervariable Sequences," *Nature* 403:665–668). In DNA hybridization studies, a *Giardia* BIVML probe failed to cross-hybridize to *Trichomonas foetus, Trichomonas vaginalis* or *Entamoeba histolytica* genomic DNA (data not shown).

The identification of a BIVM-like gene in the *Giardia* genome, but not in other similar proteostome genomes, taken together with the fact that *Giardia* is parasitic, suggests that BIVML may have been acquired via horizontal gene transfer from a higher eukaryotic host.

EXAMPLE 9

Physical Linkage of Human and Mouse BIVM to the EP58/MGC5302-EP58/Kdel1 Gene

The transcriptional start site of the human EP58/MGC5302 sequence (GenBank XM_015844) is only 41 bp from that of BIVM; BIVM and EP58 genes are in a head-to-head orientation, in opposite transcriptional orientation. The mouse EP58/Kdel1 and BIVM genes share the same physical orientation separated by 224 bp. This exceedingly tight physical linkage and close spacing of BIVM and EP58 suggests that common regulatory elements located in or near the intergenic region potentially control the expression of both genes. RT-PCR analysis of extracts from BIVM expressing and non-expressing human cell lines indicated that EP58/MGC5302 was expressed in all cell lines that express BIVM but not in the BIVM non-expressing cell line, Raji (FIG. **8**). Based on these results, it is possible that these genes are co-regulated and that the transacting factors associated with the 41 bp intergenic region linking these genes control their expression.

EXAMPLE 10

DNA Binding Activity on the BIVM-EP58/MGC5302 41 bp Intergenic Region

A MatInspector V2.2 search for potential binding sites contained in the 41 bp region separating the BIVM and EP58/MGC5302 genes revealed sites for cell type specific factors such as the myeloid zinc finger-1 (MZF-1), the hematopoietic-expressed Ikaros-2 (IK2) factor, and the ubiquitously expressed transcription factors NF1, USF, NFκB, and NMYC (FIG. **9**). Nearly identical sites also were predicted for the mouse 224 bp Bivm-Kdel1 intergenic region. MZF-1 and IK2 are expressed in the K562 human erythroleukemia cell line and IK2 is expressed in the Raji Burkitt's lymphoma cell line. Based on this information, electrophoretic mobility shift assays (EMSAs) were performed to compare protein binding to the 41 bp region in nuclear extracts from BIVM expressing and non-expressing cells (FIG. **10**).

MZF-1 and IK2-specific binding would be expected to produce unique bands in the K562 and Raji nuclear extracts that are not observed in nuclear extracts from non-lymphoid

cell lines. In addition, an NFκB consensus sequence was used as probe and competitor (Santa Cruz Biotechnology) to detect bands representing NFκB-specific binding that may be constitutively present in the nuclear extracts (FIG. **10**). Significant DNA binding activity was observed with the 41 bp BIVM-specific probe in all extracts assayed, producing 1 minor band and two major bands (FIG. **10**; Lanes **4**–**10**), one of which was competed by the addition of cold NFκB-specific probe, indicating that NFκB complexes may be present (FIG. **10**; Lane **3**). One major band was detected with the NFκB consensus probe in the nuclear extracts from BIVM expressing lines (FIG. **10**; Lanes **13**–**17**) that was competed by the BIVM-specific probe (FIG. **10**; Lane **11**). An additional complex also was observed bound to the NFκB-specific probe in the extracts from a BIVM non-expressing line (FIG. **10**; Lane **18**). Together these results show that the 41 bp BIVM-EP58/MGC5302 intergenic region supports DNA binding activity and that the bound complexes include factors that also bind the NFκB consensus probe. Similar DNA binding activity was observed in the BIVM non-expressing Raji cell line as in the BIVM expressing cells and may result from constitutive nuclear NFκB factors and suggests either that additional flanking regions function in BIVM gene regulation or that protein co-factors or other mechanisms, such as methylation-dependent promoter silencing, could play a role in BIVM expression. The presence of a CpG island 5' of the BIVM gene, together with the lack of both BIVM and EP58/MGC5302 expression in the Raji cell lines, supports the latter hypothesis.

EXAMPLE 11

Regulation of BIVM Expression by TNF-α or Other Inducing Agents

As described above, the 41 bp intergenic region contains putative sites for ubiquitous transacting factors and an NFκB site that appears to be bound by NFκB complexes containing c-Rel and RelB factors, which are constitutively present in the nuclear extracts from the BIVM expressing K562 cell line (FIG. **11**). NFκB comprises a large family of transcription factors, most of which are sequestered in the cytoplasm through inhibitor binding. Activation of the cell by various agents, such as the proinflammatory cytokine TNF-α, leads to phosphorylation-induced degradation of the inhibitor and nuclear translocation of additional NFκB transacting factors. Although constitutive factors may drive basal BIVM expression, TNF-α activated NFκB increases the expression of BIVM in the BIVM-expressing HeLa cell line (DNS). Furthermore, a cell line devoid of basal BIVM expression, the Raji Burkitt's lymphoma line, is induced to express BIVM by TNF-α (FIG. **12**). The specific TNF-α activated factors associated with the BIVM promoter can be defined using antibody shift assays.

EXAMPLE 12

Characteristics of Recombinant BIVM Protein

The BIVM encoded protein has a high proportion of lysine and arginine residues and a predicted isoelectric point (pI) of 9.1. The net positive charge under physiological conditions suggests that BIVM may interact with other proteins and/or DNA. Western blot analysis and cytoimmunofluorescence studies utilizing transfected, epitope-tagged BIVM expression constructs revealed that BIVM is present in both cytoplasmic and nuclear fractions. Variation in the relative amounts of nuclear recombinant BIVM was observed in individual cells and may reflect regulated or cell cycle-dependent BIVM nuclear import/export. The Cos7 cells that have been transformed stably with BIVM exhibit a decreased cell doubling time compared to untransformed Cos7 cells, suggesting the potential role for BIVM in cell cycle regulation. Furthermore, preliminary studies of Cos7 BIVM stable transformants stained with a nuclear stain (DAPI) reveal a high proportion of cells containing multiple nuclei compared to untransformed cells. Flow cytometer analyses of these cells stained with propidium iodide indicate that ~90% of the cells contain tetraploid or greater DNA content, consistent with the presence of multiple nuclei (FIG. **13**; Panel **3**). This phenomenon was not observed in a G418-resistant, BIVM-revertant cell line, which has lost expression of recombinant BIVM and exhibits both a nuclear morphology and a diploid DNA content similar to that of the untransformed parental line (FIG. **13**; Panels **1** & **2**).

EXAMPLE 13

Identification of BIVM Protein Binding Partners

The high proportion of lysine and arginine residues and the net charge of the protein (pI 9. 1) suggest that BIVM may interact with proteins and/or DNA (or other nucleosides). Specifically, protein-protein interactions are being assayed using the BacterioMatch two hybrid system (Stratagene). This system provides a rapid, selective approach to identify BIVM-specific protein interactions in vivo. Mouse Bivm has been utilized initially as we can take advantage of mouse cDNA libraries that are commercially available for this system (Stratagene) and because the results obtained can be used to complement concurrent BIVM knock out mice studies now underway in our laboratory. Although it is possible that BIVM may function differently in human and mouse, the 87% sequence conservation between human and mouse BIVM protein, strong synteny in BIVM flanking genes, and the tight physical linkage observed between the BIVM and EP58 genes, is consistent with functional equivalence.

EXAMPLE 14

Materials and Methods

EXAMPLE 14A

General Methods

RNA was isolated with RNAzol B (Teltest, Friendswood, Tex.) or Trizol (Gibco BRL, Rockville, Md.). Mouse genomic DNA (ë FixII) and liver cDNA (ë ZAPII) libraries were screened using standard procedures (Strong, S. J., et al. [1999] "A Novel Multigene Family Encodes Diversified Variable Regions," *Proc Natl Acad Sci USA* 96:15080–15085). DNA sequencing and the analysis of DNA sequences were carried out as described previously (Rast, J. P. et al. [1994] "T Cell Receptor Gene Homologs are Present in the Most Primitive Jawed Vertebrates," *Proc. Natl. Acad. Sci. USA* 91:9248–9252). Alignments were constructed using ClustalW 1.8. Identity relationships were examined using BLAST and ALIGN software. Rapid amplification of cDNA ends (RACE) utilized a standard protocol (Mertineit, C., et al. [1998] "Sex-Specific Exons Control DNA Methyltransferase in Mammalian Germ Cells," *Development* 125:889–897) or the GeneRacer kit (Invitrogen,

Carlsbad, Calif.). The RNA sources for RACE were: human HeLa cells, mouse liver, chicken bursa, *Xenopus laevis* liver, zebrafish (*Danio rerio*) liver, 15 hpf sea urchin (*Strongylocentotus purpuratus*) embryos, and vegetative-stage *Giardia lamblia*.

EXAMPLE 14B

Genomic Mapping

Human BIVM was mapped using HSMAP5 (CCATGCCTCTCTACTACTCACTCCCAACAC) and HSMAP6 (GGTAAGAAGAACACCATTGTGTTTGAAGGC) intronic primers (which correspond to sequence between exon 8 and 9) and the GeneBridge 4 radiation hybrid (RH) panel (Gyapay, G., et al. [1996] "A Radiation Hybrid Map of the Human Genome," *Hum Mol Genet* 5:339–346) (Research Genetics, Huntsville, Ala.). Zebrafish BIVM (see below) was mapped using the zfBIVMMAPF1 (CAATGCCTAACACTGTGGAAAGTGAAGGCG) and zfBIVMMAPR1 (GATAACTGTCGAGCTCGGTTGAGCAGGGC) primers and the T51 RH panel (Glusman, G., et al. [1996] "Sequence Analysis in the Olfactory Receptor Gene Cluster on Human Chromosome 17: Recombinatorial Events Affecting Receptor Diversity," *Genomics* 37:147–160) (Research Genetics). Additional gene mapping data were derived from the Human-Mouse Homology Map and the Mouse Genome Informatics Database (Blake, J. A., et al. and Mouse Genome Database Group [2001] "The Mouse Genome Database(MGD): Integration Nexus for the Laboratory Mouse," *Nucleic Acids Res* 29:91–94).

EXAMPLE 14C

Identification of BIVM Orthologs

Mouse BIVM Partial sequence of the mouse BIVM gene was obtained by screening a mouse genomic library with a human BIVM cDNA probe. A mouse BIVM cDNA was recovered by screening a liver cDNA library with a probe corresponding to mouse exon 6.

Chicken BIVM tBLASTn searches using the human BIVM sequence identified a chicken (*Gallus gallus*) bursal EST (GenBank AJ399198) encoding an avian ortholog (BIVM). RACE strategies identified a complete open reading frame cDNA. A single RNA-splicing variant, which encodes an additional 23 amino acids, also has been sequenced (GenBank AF411388; data not shown).

Xenopus XBIVM Partial *Xenopus laevis* XBIVM sequence was identified as an oocyte EST (GenBank BF047666) using tBLASTn searches with the human BIVM sequence. RACE strategies resolved a complete open reading frame cDNA.

Zebrafish BIVM Touchdown PCR (Don, R. H., et al. [1991] "'Touchdown' PCR to Circumvent Spurious Priming During Gene Amplification," *Nucleic Acids Res* 19:4008) and nested degenerate primers, designed with CODE-HOP software (Rose, T. M., et al. [1998] "Consensus-Degenerate Hybrid Oligonucleotide Primers for Amplification of Distantly Related Sequences," *Nucleic Acids Res* 26:1628–35), were used to amplify BIVM cDNA fragments from zebrafish liver. Primers for the primary PCR were designed to amplify the coding sequence between the amino acid motifs GNTTLMWRF and YFCPIGFEA; primers for the nested PCR were designed to amplify the sequence between motifs WFRQINDHF and YRHQNHYFCP. PCR products of the expected size were gel purified, cloned and sequenced. Full-length clones were derived by RACE.

Sea urchin SpBIVM A fragment of the sea urchin SpBIVM cDNA was recovered from 20 hpf embryo cDNA using nested PCR as described for zebrafish. RACE strategies identified a 1,899 nucleotide coding region that corresponds to the complete open reading frame of BIVM from other species; as of yet it has not been possible to identify a stop codon.

Giardia lamblia BIVM-like The *Giardia lamblia* BIVML sequence was initially identified with a tBLASTn search of the High Throughput Genomic (HTGS) database with the human BIVM sequence. BIVML is encoded in four overlapping genomic clones (clone KJ1556, GenBank #AC049185; clone MJ4898, GenBank AC083097; clone EJ2770, GenBank #AC038625; and clone K10613, GenBank #AC046875). RACE was used to identify the complete, 2,045 nucleotide cDNA.

EXAMPLE 14D

Transient Transfections

The coding region of human BIVM was cloned into pcDNA3.1/V5-His TOPO (Invitrogen) in order to generate pBIVM-N2, which encodes a BIVM-V5 fusion protein (the V5 epitope is at the C terminus). A similar construct, pBIVM-K1, was generated in which the translational start sequence was modified in order to increase protein synthesis, as described in Kozak, M. [1996], "Interpreting cDNA Sequences: Some Insights from Studies on Translation," *Mamm. Genome* 7:563–574. Both of these constructs were then subcloned into pIRES2-EGFP (Clontech, Palo Alto, Calif.) to create pBIVM-N2/EGFP and pBIVM-K1/EGFP, which produced recombinant BIVM and EGFP from the same plasmid. Cos7 cells (~60% confluent) were transiently transfected with expression constructs using the GENEJAMMER™ transfection reagent according to manufacturer's instructions (Stratagene, La Jolla, Calif.).

EXAMPLE 14E

Western Blots

Whole cell lysates were prepared from transfected cells in the presence of 1× Protease Inhibitor Cocktail Set III (Calbiochem, San Diego, Calif.) essentially as recommended by Santa Cruz Biotechnology. Nuclear and cytoplasmic extracts were prepared from transfected cells essentially as described in Yu, C. L., et al. [1995] "Enhanced DNA-Binding Activity of a Stat3-Related Protein in Cells Transformed by the Src Onco Protein," *Science* 269:81–83. Protein concentrations were determined using Protein Assay Reagent (Bio-Rad, Hercules, Calif.). Whole cell, nuclear, and cytoplasmic extracts were separated by SDS-polyacrylamide gel electrophoresis (10% polyacrylamide), transferred to Immobilon P filters (Millipore, Bedford, Mass.) and blocked prior to incubation with mouse anti-V5 monoclonal antibody (Invitrogen), anti-OCT1 polyclonal antibody (Santa Cruz) or anti-HSP90 monoclonal antibody (StressGen Biotechnologies Corp, Victoria, BC, Canada). Following incubation with alkaline phosphatase-conjugated secondary antibodies, reactive proteins were detected using Western Blue Stabilizer Substrate (Promega, Madison, Wis.).

EXAMPLE 14F

Immunohistochemistry

Transfected Cos7 cells were fixed for 15 minutes with 3% paraformaldehyde, permeabilized in 1% Triton-X 100, incubated with primary antibodies, washed and incubated with

secondary antibodies and 2 μg/ml Hoechst 33258. Primary antibodies included a mouse anti-V5 monoclonal antibody and an anti-actin polyclonal antibody (ICN Pharmaceuticals, Inc., Costa Mesa, Calif.) that were detected with a Cy2-conjugated, anti-mouse antibody (Jackson Immuno Research Laboratories, West Grove, Pa.) and a Cy3-conjugated, anti-rabbit antibody (Sigma, St. Louis, Mo.), respectively.

EXAMPLE 14G

RNA Blots

Multiple Tissue Northern (MTN™) blots (human and mouse) were obtained from Clontech. In addition, 10 μg of *Xenopus*, sea urchin and *Giardia lamblia* total RNA were subjected to electrophoresis through 1.2% agarose, 2.2 M formaldehyde gels and transfer to nylon membranes (Zetaprobe™-GT; BioRad). RNA blots were hybridized with radiolabeled probes in Expresshyb ™ (Clontech). The *Giardia* RNA blot was hybridized with single strand-specific probes as described in Knodler, L. A., et al. [1999] "Developmental Gene Regulation in *Giardia Lamblia*: First Evidence for an Encystation-Specific Promoter and Differential 5' mRNA Processing," *Mol Microbiol* 2:327–340. Blots were stripped and reprobed with actin, 18S rRNA or *Calmodulin* probes.

EXAMPLE 14H

Quantitative PCR

Real time PCR analysis detected BIVM expression from chicken bursa and zebrafish embryos and tissues using a GeneAmp 5700 Sequence Detection System (PE Biosystems, Foster City, Calif.) with SYBR Green detection. Each PCR series was done in triplicate. The relative expression levels were determined for each transcript from plasmid standards that were included in each experiment and normalized to the expression of SI17 rRNA (chicken bursa) or S26 rRNA (zebrafish) levels.

All patents, patent applications, provisional applications, and publications referred to or cited herein are incorporated by reference in their entirety, including all figures and tables, to the extent they are not inconsistent with the explicit teachings of this specification.

It should be understood that the examples and embodiments described herein are for illustrative purposes only and that various modifications or changes in light thereof will be suggested to persons skilled in the art and are to be included within the spirit and purview of this application.

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tctgctcctt gtggcaggtt ctcttaatct gagtggcaca ccagggtaat atgtatttaa  92940
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agtcagttga ctcccttcag gacctaatat aatgttctcc tcaaggcatc acattaaaaa  93840
ttttcaggag catcttcata aatctttgca gaattggatt aatgggtaat atggttttta  93900
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taaacagtat tgcattaata tatatggaaa tttatgtaat tctaccactg ttttaagaaa 93960
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tataattact aaagtgagaa taatttatta acacatttta aacattttac aagtaacatg 94080
aataattatc ttccagataa gactaataaa ttttctacat gttgaataaa aataactctt 94140
gaatatacca gtctacttca gatgtcttca aaactcagat ttgaacgtca agtttgaatg 94200
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ggctccttga cccaaggcct tcatttagac tcttgtcatt tttcatctag actgttccaa 94320
taatcttcta attagcttgt aaggtcacca gttcttcagc tcctgctgtc agatgtagtt 94380
cttaaatatc aaatctgatc atgtcaattc ctgttctaat aatctttatt agctcctcct 94440
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acctgtttta tagcatttat caaggtattg acatttgttc agttgtctgc cccttccgtg 96420

atctcagtag caaacttgta gtacaactaa tttaggttct ttatttttcc acttgcatcc 96480

tgagcaacct caataaaagg tgcattttct ttcttttgta aacacaaagt gtagcattgt 96540

ttggtctact tgattagagt tacaacctct gtacattctt gaaactaaga agaccagcag 96600

acagagaata tctgtagaat cttctcagga attggtttca acataagggt ccaagacctt 96660

ggcattgctg aggttttcag aattctatct tttaagttaa gcctgtgact atttactaat 96720

ctgaaaatat ctttaacttc tttttttaa tctgtaggca tttctaagaa gcacatgaca 96780

ttcagctttg aatagaagat tcatttgaat gacagtttct ttcatttagt agaggggatt 96840

ttactttaaa ttttgctgac aggttttcgt gacagccctc aaatggaagc ttgaattc 96898

<210> SEQ ID NO 4
<211> LENGTH: 2129
<212> TYPE: DNA
<213> ORGANISM: Xenopus sp.
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (74)..(74)
<223> OTHER INFORMATION: n = a, c, g, or t.
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (292)..(294)
<223> OTHER INFORMATION: Translation initiation codon (ATG)
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (1771)..(1773)
<223> OTHER INFORMATION: Translation termination codon (TGA)
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (1810)..(1884)
<223> OTHER INFORMATION: Repeat
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (1888)..(1962)
<223> OTHER INFORMATION: Repeat

<400> SEQUENCE: 4

gaagaagagg agaatggtag gacggagcca gcagctttat gacaaaatag gttgaaaatt 60

gttgattgag gcanccgctg tgggatgtgc aaagattgta agctgttgtg agtggcagag 120

atctctggcc ccatttggat ccccgtacct atgtttgtta cgtaattgtt ttactggcga 180

acaaggtctc agttaaagga tgaagctcat tcggtgagac ttttattgac caaaacatag 240

tcaatatttt tgttgtgatt tgcaccgaac tgcattgttc atcttcattc aatgcctaac 300

atagaagcgg acagagttac aagcgttccc gaaaataacg actgcaaatc caagagtcag 360

cctctgagga ataatctcca tgaaactgta aaatcctaca gtatacaagg tgctgccaca 420

gcaaatatcg agcctcctgc agaaagacct tatccctggg gatgtcctgt gacacacaca 480

aaggaaaagt tctataccat ctgcgcagac tacgcctttt tgaatcaagc aacatctctt 540

tgcaaatcgt ctagttctgt ctgcagctca agctcagagg acaaatctgc tctgagcaat 600

acaataaatt acattgatct tcagaccagc gaatcagatt ctgtatacaa cgaggatgca 660

agcttggagt ctttatctag caatcttggt acacgtccgc ttgcctggga aattgataaa 720

tcagacttca gcacaatgac ttccaagtta aaaagatcag gtgtaaaaaa acaaacacct 780

aagaagaaac ctgacaggaa ggcaaaacca ttaagggact gtcctcaaca cttaatcctg 840

gatgatgtta aacagcggaa agttctagac ctcagacgat ggtattgtat cagtcgaccc 900

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cagtacaaga cctcgtgtgg catttcttct ctggtatcat gctggaactt tctttacagt    960

actctgggag caggaagcct cccaccaatt actcaagagg aagctttaca tattttgggc   1020

tttcaaccac cctttgaaga gattaggttt ggtcctttta ctgggaacac aactttgatg   1080

agatggttca gacaaatcaa tgatcatttc catgtaaaag gatgctccta tgttctgtat   1140

aagccgcatg gcaagaacaa gacagcagga gaaactgctg ttggggcact atcaaagtta   1200

acacaagggt taaaagaaga ctcaacagcc tacgtctatc attgtcagaa tcattatttt   1260

tgcccaattg gttttgaggc aacccctgtg aaggcatcca aagcatacag gggccaactt   1320

ttcccgcatg aagtggagta ctggatttta attggtgagc caagcagaaa acaccctaca   1380

attcactgca aaaagtgggc agatattgtt actgacttaa atactcaaaa tccagaatat   1440

tttgatatta gacacactga aagaggcctt cagtacagga aacaaaaaa ggttggagga   1500

aaccttcact gccttctggc atttcagaga ctcagctggc aaagatttgg tccatggccc   1560

ttacagcttg gaaccccttag gccagaaccc cagccacccg tacaaggaag aagaatccct   1620

aaatctgaaa gtgaggataa tgtctccaag aaacagcatg ggcgtctggg gaggtcattt   1680

agtgctggat ttcagcaaga gcttgcatgg aaaagaatgt gtaatatacg tgaacgcagg   1740

ggcagtggct cacctgaaag tgatacggac tgagaaggaa atgattaaat tatacaaagt   1800

cagtgttact tgtagttttg ggttcatggc actacgatta aactaaacat tagtcatata   1860

atgctggaca tggttggcag acattatttg tagttttggg ttcatggcac taccattaag   1920

ctaaacatta gtcatataat gctggacatg gttggtagac atctatagtg ctctcccatt   1980

aatcataaaa cctttgcaaa ctttttacaa tcatttatga acttattgct caaatgccat   2040

tcctgatcta cagtatactg ggtattgtat actgccatgt caggagtatt ttcattaatt   2100

aataaaattg gagtttaaaa tcaaaaaaa                                     2129
```

<210> SEQ ID NO 5
<211> LENGTH: 493
<212> TYPE: PRT
<213> ORGANISM: Xenopus sp.

<400> SEQUENCE: 5

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Met Pro Asn Ile Glu Ala Asp Arg Val Thr Ser Val Pro Glu Asn Asn
1               5                   10                  15

Asp Cys Lys Ser Lys Ser Gln Pro Leu Arg Asn Asn Leu His Glu Thr
            20                  25                  30

Val Lys Ser Tyr Ser Ile Gln Gly Ala Ala Thr Ala Asn Ile Glu Pro
        35                  40                  45

Pro Ala Glu Arg Pro Tyr Pro Trp Gly Cys Pro Val Thr His Thr Lys
    50                  55                  60

Glu Lys Phe Tyr Thr Ile Cys Ala Asp Tyr Ala Phe Leu Asn Gln Ala
65                  70                  75                  80

Thr Ser Leu Cys Lys Ser Ser Ser Ser Val Cys Ser Ser Ser Ser Glu
                85                  90                  95

Asp Lys Ser Ala Leu Ser Asn Thr Ile Asn Tyr Ile Asp Leu Gln Thr
            100                 105                 110

Ser Glu Ser Asp Ser Val Tyr Asn Glu Asp Ala Ser Leu Glu Ser Leu
        115                 120                 125

Ser Ser Asn Leu Gly Thr Arg Pro Leu Ala Trp Glu Ile Asp Lys Ser
    130                 135                 140

Asp Phe Ser Thr Met Thr Ser Lys Leu Lys Arg Ser Gly Val Lys Lys
145                 150                 155                 160
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Gln Thr Pro Lys Lys Lys Pro Asp Arg Lys Ala Lys Pro Leu Arg Asp
                165                 170                 175

Cys Pro Gln His Leu Ile Leu Asp Asp Val Lys Gln Arg Lys Val Leu
            180                 185                 190

Asp Leu Arg Arg Trp Tyr Cys Ile Ser Arg Pro Gln Tyr Lys Thr Ser
        195                 200                 205

Cys Gly Ile Ser Ser Leu Val Ser Cys Trp Asn Phe Leu Tyr Ser Thr
    210                 215                 220

Leu Gly Ala Gly Ser Leu Pro Pro Ile Thr Gln Glu Glu Ala Leu His
225                 230                 235                 240

Ile Leu Gly Phe Gln Pro Pro Phe Glu Glu Ile Arg Phe Gly Pro Phe
                245                 250                 255

Thr Gly Asn Thr Thr Leu Met Arg Trp Phe Arg Gln Ile Asn Asp His
            260                 265                 270

Phe His Val Lys Gly Cys Ser Tyr Val Leu Tyr Lys Pro His Gly Lys
        275                 280                 285

Asn Lys Thr Ala Gly Glu Thr Ala Val Gly Ala Leu Ser Lys Leu Thr
    290                 295                 300

Gln Gly Leu Lys Glu Asp Ser Thr Ala Tyr Val Tyr His Cys Gln Asn
305                 310                 315                 320

His Tyr Phe Cys Pro Ile Gly Phe Glu Ala Thr Pro Val Lys Ala Ser
                325                 330                 335

Lys Ala Tyr Arg Gly Gln Leu Phe Pro His Glu Val Glu Tyr Trp Ile
            340                 345                 350

Leu Ile Gly Glu Pro Ser Arg Lys His Pro Thr Ile His Cys Lys Lys
        355                 360                 365

Trp Ala Asp Ile Val Thr Asp Leu Asn Thr Gln Asn Pro Glu Tyr Phe
    370                 375                 380

Asp Ile Arg His Thr Glu Arg Gly Leu Gln Tyr Arg Lys Thr Lys Lys
385                 390                 395                 400

Val Gly Gly Asn Leu His Cys Leu Leu Ala Phe Gln Arg Leu Ser Trp
                405                 410                 415

Gln Arg Phe Gly Pro Trp Pro Leu Gln Leu Gly Thr Leu Arg Pro Glu
            420                 425                 430

Pro Gln Pro Pro Val Gln Gly Arg Arg Ile Pro Lys Ser Glu Ser Glu
        435                 440                 445

Asp Asn Val Ser Lys Lys Gln His Gly Arg Leu Gly Arg Ser Phe Ser
    450                 455                 460

Ala Gly Phe Gln Gln Glu Leu Ala Trp Lys Arg Met Cys Asn Ile Arg
465                 470                 475                 480

Glu Arg Arg Gly Ser Gly Ser Pro Glu Ser Asp Thr Asp
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<210> SEQ ID NO 6
<211> LENGTH: 2841
<212> TYPE: DNA
<213> ORGANISM: Gallus sp.
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (235)..(237)
<223> OTHER INFORMATION: Translation initiation codon (ATG)
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (1750)..(1752)
<223> OTHER INFORMATION: Translation termination codon (TAG)

<400> SEQUENCE: 6

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cccctgcgtc gcgcactgcg tctgtttccg gcgcgggcac attccccgct ccgccgcggg    120
cccgcgcagg tacctcacct tgcagtaaca atggaggcag cgatgcaaac tatgtggtaa    180
ttaaaaataa gcaaaaccat tcctcgcagt acaagacgct tccaatatta ttcaatgcct    240
cacatctcag aagatgaaaa ggagaatggt tctggaaaca atggaaacac tgaaaagaaa    300
cctgggaaag aatcctcaga agcttctctt cgtgatccta taaagtcgta ctgcatctca    360
gatgcctcca ctgtgtcttt ggtgtccagg ggagatggac attacccatg ggatgtcct     420
gtgactcaca cacgagagaa attttatacc atttgctcag actatgcttt tttaaacaga    480
gtaacatcta tttgtaaaag cccaagtgct tcagttaacg cctgcctgtc aggcagtgct    540
gccttaaacg ttggaaataa cacacctagc ttactgggca ttcaaactgg tgcttcggag    600
ataatctaca gtgaagatgc taacttggaa accttgtctg gcagccttgg aaagcttcca    660
ctggcatggg aaattgacaa atcagaattc aacagcgtga ctgcgaatca taaaaacaaa    720
gcaggcaaca tgaagaaaca agtggcaaag aaaaagtcct cagacaaaaa aagcaaacag    780
tacaaggagt gtcctcagct gtctgctctt gaagatgtga aggagaggaa agtgttggac    840
ctccgaagat ggtactgtat tagccgacct cagtacaaga cttcttgtgg aatttcttca    900
ttagtgtctt gctggaattt cttatatagt acgctgggag ctggcagttt accacctatt    960
actcaagaag aagctttgca tatattgggt tttcaacccc catttgagga gatcaggttt   1020
ggtcccttca ctggaaatac gactttaatg agatggttta ggcaaataaa tgatcacttc   1080
catatcaagg gttgctcata tgttctgtat aaacctcatg gaaagaacaa gacagctgga   1140
gaaactgctg tgggggccct tgcaaagcta acacgtggac tgaaagatga atcaatggcc   1200
tacatctacc attgccaaaa ccattatttt tgcccaattg gatttgaagc aactccagta   1260
aaagctagta aagcgtatag aggtcgtgtt ttgcagcaag aagtagaata ctggatctta   1320
attggagagc cgagcagaaa acatccaacg atacactgta aaggtggac agatattgtc    1380
actgacctaa acacccaaaa tccagagtac ctagatattc ggcacctaga gagaggactg   1440
cagcatcgga aaacaaagaa ggttggagga aatcttcatt gcatcatcgc ctttcagaga   1500
cttaactggc aaagatttgg tccttggaat attccatttg gaagtgtcag acaggataaa   1560
caatcccaaa cacaaggaca aggtattgcc aaatctgaga gtgaagacaa tatctctaaa   1620
aaacaacatg gacgactggg tcgatctttc agtgctggtt tccatcaaga atctacatgg   1680
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ggagatgatt agaattaact ttaggtaata gagtttatat atcaaagtta gttttaatca   1800
acacagaata ggggtttatt agtcctagga tacatgtgaa tagaaaatat ggcataagat   1860
acagctttgt aatccttaaa tcaattatga attatatggt tgcagtggat aaaagagcag   1920
attgaaatta gccaatgtaa taaacagatt tcattgaaaa tacttgatat tcagaagcat   1980
gaaaatgtat tatatgactt tataaaaagg gttatactgc atatggtgta aggataaaag   2040
taaacatttg ccttcctttt tagcactcca ttttgttaag gctgctgata tccagtgaga   2100
agaaagaaat tgaataggtt agaaaacctt gtcagattaa caaaattgaa tgtatattct   2160
caatctagtt gtcagtagaa ttctgtgagt cagataatcc tgttttgtag gtagatccca   2220
gttatttttc ccatagctag atacctgttt taaactgaga agaattgctg gtggcaagga   2280
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ctgtgagctc tggtgagcag tgactgcata acacaggctt gtgaaaatca tttttataaa   2400

gctgcattta acctgagccc aatgaactgg ctgaacagtg tgttctgctg gcaattcttt   2460

tccttgttca gtctcaaaac tcctgttgtt tttgtgctgc tctcttgatt ttgtatgaag   2520

gtgatgcaag tgccgacaac tgctggcagc ccttatgata tacctctatg ccagcaaaca   2580

atccaagtct tttcaggtgt ccatgtgcag tttttttttt ttcctttctg gtttattcag   2640

ttgtttgccc aaatgcatct cgacagttgt aactttgtgt gcgaatgtcc acacctgctc   2700

aaggattttt tttttttac ataaaacaat ttgtcatgta atgcagggtt tttgtaggtt    2760

gatgctgttg ttaaccaaaa atggagggag acttttggac tttcgttcat tcaataaaat   2820

ttgttttatt taaaaaaaaa a                                             2841
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<210> SEQ ID NO 7
<211> LENGTH: 3038
<212> TYPE: DNA
<213> ORGANISM: Gallus sp.
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (235)..(237)
<223> OTHER INFORMATION: Translation initiation codon (ATG)
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (1281)..(1352)
<223> OTHER INFORMATION: Sequence of alternative splicing
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (1822)..(1824)
<223> OTHER INFORMATION: Translation termination codon (TAG)
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (1982)..(2106)
<223> OTHER INFORMATION: Sequence of alternative splicing

<400> SEQUENCE: 7

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ggacactgac atggactgaa ggagtagaaa gcaggtgagc gctcgtcgtg gcttctcccc     60

cccctgcgtc gcgcactgcg tctgtttccg gcgcgggcac attccccgct ccgccgcggg    120

cccgcgcagg tacctcacct tgcagtaaca atggaggcag cgatgcaaac tatgtggtaa    180

ttaaaaataa gcaaaaccat tcctcgcagt acaagacgct tccaatatta ttcaatgcct    240

cacatctcag aagatgaaaa ggagaatggt tctggaaaca atggaaacac tgaaaagaaa    300

cctgggaaag aatcctcaga agcttctctt cgtgatccta taaagtcgta ctgcatctca    360

gatgcctcca ctgtgtcttt ggtgtccagg ggagatggac attacccatg ggatgtcct     420

gtgactcaca cacgagagaa attttatacc atttgctcag actatgcttt tttaaacaga    480

gtaacatcta tttgtaaaag cccaagtgct tcagttaacg cctgcctgtc aggcagtgct    540

gccttaaacg ttggaaataa cacacctagc ttactgggca ttcaaactgg tgcttcggag    600

ataatctaca gtgaagatgc taacttggaa accttgtctg gcagccttgg aaagcttcca    660

ctggcatggg aaattgacaa atcagaattc aacagcgtga ctgcgaatca taaaaacaaa    720

gcaggcaaca tgaagaaaca agtggcaaag aaaaagtcct cagacaaaaa aagcaaacag    780

tacaaggagt gtcctcagct gtctgctctt gaagatgtga aggagaggaa agtgttggac    840

ctccgaagat ggtactgtat tagccgacct cagtacaaga cttcttgtgg aatttcttca    900

ttagtgtctt gctggaattt cttatatagt acgctgggag ctggcagttt accacctatt    960

actcaagaag aagctttgca tatattgggt tttcaacccc catttgagga gatcaggttt   1020

ggtcccttca ctggaaatac gactttaatg agatggttta ggcaaataaa tgatcacttc   1080

catatcaagg gttgctcata tgttctgtat aaacctcatg gaaagaacaa gacagctgga   1140
```

gaaactgctg tgggggccct tgcaaagcta acacgtggac tgaaagatga atcaatggcc 1200

tacatctacc attgccaaaa ccattatttt tgcccaattg gatttgaagc aactccagta 1260

aaagctagta aagcgtatag gttgctggat ttggactcgg gagacctggg ttcggttccc 1320

agttcaaccg cagacttcca ttgtgatttt agaggtcgtg ttttgcagca agaagtagaa 1380

tactggatct taattggaga gccgagcaga aaacatccaa cgatacactg taaaaggtgg 1440

acagatattg tcactgacct aaacacccaa aatccagagt acctagatat tcggcaccta 1500

gagagaggac tgcagcatcg gaaaacaaag aaggttggag gaaatcttca ttgcatcatc 1560

gcctttcaga gacttaactg gcaaagattt ggtccttgga atattccatt tggaagtgtc 1620

agacaggata aacaatccca aacacaagga caaggtattg ccaaatctga gagtgaagac 1680

aatatctcta aaaaacaaca tggacgactg ggtcgatctt tcagtgctgg tttccatcaa 1740

gaatctacat ggaaaaagtc tagtcttcgt gagaggagga acagcgggta tcagagctat 1800

aatgattatg atggagatga ttagaattaa ctttaggtaa tagagtttat atatcaaagt 1860

tagttttaat caacacagaa taggggttta ttagtcctag gatacatgtg aatagaaaat 1920

atggcataag atacagcttt gtaatcctta aatcaattat gaattatatg gttgcagtgg 1980

atgacatctg atacatgaac tgacagataa gcacagatta ttgtactttt gtaatcaaaa 2040

gcagatatga cagctaaatc aatcacttat tttgaagtta ctatactata tcctgatctg 2100

tgagaataaa agagcagatt gaaattagcc aatgtaataa acagatttca ttgaaaatac 2160

ttgatattca gaagcatgaa aatgtattat atgactttat aaaaagggtt atactgcata 2220

tggtgtaagg ataaaagtaa acatttgcct tcctttttag cactccattt tgttaaggct 2280

gctgatatcc agtgagaaga aagaaattga ataggttaga aaaccttgtc agattaacaa 2340

aattgaatgt atattctcaa tctagttgtc agtagaattc tgtgagtcag ataatcctgt 2400

tttgtaggta gatcccagtt atttttccca tagctagata cctgttttaa actgagaaga 2460

attgctggtg gcaaggaagg tttgaagatg gacatttact gcttttgctc tgtggatatg 2520

gtagcagatt ttctatcctg tgagctctgg tgagcagtga ctgcataaca caggcttgtg 2580

aaaatcattt ttataaagct gcatttaacc tgagcccaat gaactggctg aacagtgtgt 2640

tctgctggca attcttttcc ttgttcagtc tcaaaactcc tgttgttttt gtgctgctct 2700

cttgattttg tatgaaggtg atgcaagtgc cgacaactgc tggcagccct tatgatatac 2760

ctctatgcca gcaaacaatc caagtctttt caggtgtcca tgtgcagttt tttttttttc 2820

ctttctggtt tattcagttg tttgcccaaa tgcatctcga cagttgtaac tttgtgtgcg 2880

aatgtccaca cctgctcaag gatttttttt tttttacata aaacaatttg tcatgtaatg 2940

cagggttttt gtaggttgat gctgttgtta accaaaaatg gagggagact tttggacttt 3000

cgttcattca ataaaatttg ttttatttaa aaaaaaaa 3038

<210> SEQ ID NO 8
<211> LENGTH: 505
<212> TYPE: PRT
<213> ORGANISM: Gallus sp.

<400> SEQUENCE: 8

Met Pro His Ile Ser Glu Asp Glu Lys Glu Asn Gly Ser Gly Asn Asn
1   5   10   15

Gly Asn Thr Glu Lys Lys Pro Gly Lys Glu Ser Ser Glu Ala Ser Leu
            20   25   30

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Arg Asp Pro Ile Lys Ser Tyr Cys Ile Ser Asp Ala Ser Thr Val Ser
        35                  40                  45

Leu Val Ser Arg Gly Asp Gly His Tyr Pro Trp Gly Cys Pro Val Thr
    50                  55                  60

His Thr Arg Glu Lys Phe Tyr Thr Ile Cys Ser Asp Tyr Ala Phe Leu
65                  70                  75                  80

Asn Arg Val Thr Ser Ile Cys Lys Ser Pro Ser Ala Ser Val Asn Ala
                85                  90                  95

Cys Leu Ser Gly Ser Ala Ala Leu Asn Val Gly Asn Asn Thr Pro Ser
            100                 105                 110

Leu Leu Gly Ile Gln Thr Gly Ala Ser Glu Ile Ile Tyr Ser Glu Asp
        115                 120                 125

Ala Asn Leu Glu Thr Leu Ser Gly Ser Leu Gly Lys Leu Pro Leu Ala
    130                 135                 140

Trp Glu Ile Asp Lys Ser Glu Phe Asn Ser Val Thr Ala Asn His Lys
145                 150                 155                 160

Asn Lys Ala Gly Asn Met Lys Lys Gln Val Ala Lys Lys Lys Ser Ser
                165                 170                 175

Asp Lys Lys Ser Lys Gln Tyr Lys Glu Cys Pro Gln Leu Ser Ala Leu
            180                 185                 190

Glu Asp Val Lys Glu Arg Lys Val Leu Asp Leu Arg Arg Trp Tyr Cys
        195                 200                 205

Ile Ser Arg Pro Gln Tyr Lys Thr Ser Cys Gly Ile Ser Ser Leu Val
    210                 215                 220

Ser Cys Trp Asn Phe Leu Tyr Ser Thr Leu Gly Ala Gly Ser Leu Pro
225                 230                 235                 240

Pro Ile Thr Gln Glu Glu Ala Leu His Ile Leu Gly Phe Gln Pro Pro
                245                 250                 255

Phe Glu Glu Ile Arg Phe Gly Pro Phe Thr Gly Asn Thr Thr Leu Met
            260                 265                 270

Arg Trp Phe Arg Gln Ile Asn Asp His Phe His Ile Lys Gly Cys Ser
        275                 280                 285

Tyr Val Leu Tyr Lys Pro His Gly Lys Asn Lys Thr Ala Gly Glu Thr
    290                 295                 300

Ala Val Gly Ala Leu Ala Lys Leu Thr Arg Gly Leu Lys Asp Glu Ser
305                 310                 315                 320

Met Ala Tyr Ile Tyr His Cys Gln Asn His Tyr Phe Cys Pro Ile Gly
                325                 330                 335

Phe Glu Ala Thr Pro Val Lys Ala Ser Lys Ala Tyr Arg Gly Arg Val
            340                 345                 350

Leu Gln Gln Glu Val Glu Tyr Trp Ile Leu Ile Gly Glu Pro Ser Arg
        355                 360                 365

Lys His Pro Thr Ile His Cys Lys Arg Trp Thr Asp Ile Val Thr Asp
    370                 375                 380

Leu Asn Thr Gln Asn Pro Glu Tyr Leu Asp Ile Arg His Leu Glu Arg
385                 390                 395                 400

Gly Leu Gln His Arg Lys Thr Lys Lys Val Gly Gly Asn Leu His Cys
                405                 410                 415

Ile Ile Ala Phe Gln Arg Leu Asn Trp Gln Arg Phe Gly Pro Trp Asn
            420                 425                 430

Ile Pro Phe Gly Ser Val Arg Gln Asp Lys Gln Ser Gln Thr Gln Gly
        435                 440                 445

Gln Gly Ile Ala Lys Ser Glu Ser Glu Asp Asn Ile Ser Lys Lys Gln
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    450                 455                 460

His Gly Arg Leu Gly Arg Ser Phe Ser Ala Gly Phe His Gln Glu Ser
465                 470                 475                 480

Thr Trp Lys Lys Ser Ser Leu Arg Glu Arg Arg Asn Ser Gly Tyr Gln
                485                 490                 495

Ser Tyr Asn Asp Tyr Asp Gly Asp Asp
            500                 505


<210> SEQ ID NO 9
<211> LENGTH: 529
<212> TYPE: PRT
<213> ORGANISM: Gallus sp.

<400> SEQUENCE: 9

Met Pro His Ile Ser Glu Asp Glu Lys Glu Asn Gly Ser Gly Asn Asn
1               5                   10                  15

Gly Asn Thr Glu Lys Lys Pro Gly Lys Glu Ser Ser Glu Ala Ser Leu
            20                  25                  30

Arg Asp Pro Ile Lys Ser Tyr Cys Ile Ser Asp Ala Ser Thr Val Ser
        35                  40                  45

Leu Val Ser Arg Gly Asp Gly His Tyr Pro Trp Gly Cys Pro Val Thr
    50                  55                  60

His Thr Arg Glu Lys Phe Tyr Thr Ile Cys Ser Asp Tyr Ala Phe Leu
65                  70                  75                  80

Asn Arg Val Thr Ser Ile Cys Lys Ser Pro Ser Ala Ser Val Asn Ala
                85                  90                  95

Cys Leu Ser Gly Ser Ala Ala Leu Asn Val Gly Asn Asn Thr Pro Ser
            100                 105                 110

Leu Leu Gly Ile Gln Thr Gly Ala Ser Glu Ile Ile Tyr Ser Glu Asp
        115                 120                 125

Ala Asn Leu Glu Thr Leu Ser Gly Ser Leu Gly Lys Leu Pro Leu Ala
    130                 135                 140

Trp Glu Ile Asp Lys Ser Glu Phe Asn Ser Val Thr Ala Asn His Lys
145                 150                 155                 160

Asn Lys Ala Gly Asn Met Lys Lys Gln Val Ala Lys Lys Lys Ser Ser
                165                 170                 175

Asp Lys Lys Ser Lys Gln Tyr Lys Glu Cys Pro Gln Leu Ser Ala Leu
            180                 185                 190

Glu Asp Val Lys Glu Arg Lys Val Leu Asp Leu Arg Arg Trp Tyr Cys
        195                 200                 205

Ile Ser Arg Pro Gln Tyr Lys Thr Ser Cys Gly Ile Ser Ser Leu Val
    210                 215                 220

Ser Cys Trp Asn Phe Leu Tyr Ser Thr Leu Gly Ala Gly Ser Leu Pro
225                 230                 235                 240

Pro Ile Thr Gln Glu Glu Ala Leu His Ile Leu Gly Phe Gln Pro Pro
                245                 250                 255

Phe Glu Glu Ile Arg Phe Gly Pro Phe Thr Gly Asn Thr Thr Leu Met
            260                 265                 270

Arg Trp Phe Arg Gln Ile Asn Asp His Phe His Ile Lys Gly Cys Ser
        275                 280                 285

Tyr Val Leu Tyr Lys Pro His Gly Lys Asn Lys Thr Ala Gly Glu Thr
    290                 295                 300

Ala Val Gly Ala Leu Ala Lys Leu Thr Arg Gly Leu Lys Asp Glu Ser
305                 310                 315                 320
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Met Ala Tyr Ile Tyr His Cys Gln Asn His Tyr Phe Cys Pro Ile Gly
                325                 330                 335

Phe Glu Ala Thr Pro Val Lys Ala Ser Lys Ala Tyr Arg Leu Leu Asp
            340                 345                 350

Leu Asp Ser Gly Asp Leu Gly Ser Val Pro Ser Ser Thr Ala Asp Phe
        355                 360                 365

His Cys Asp Phe Arg Gly Arg Val Leu Gln Gln Glu Val Glu Tyr Trp
    370                 375                 380

Ile Leu Ile Gly Glu Pro Ser Arg Lys His Pro Thr Ile His Cys Lys
385                 390                 395                 400

Arg Trp Thr Asp Ile Val Thr Asp Leu Asn Thr Gln Asn Pro Glu Tyr
                405                 410                 415

Leu Asp Ile Arg His Leu Glu Arg Gly Leu Gln His Arg Lys Thr Lys
            420                 425                 430

Lys Val Gly Gly Asn Leu His Cys Ile Ile Ala Phe Gln Arg Leu Asn
        435                 440                 445

Trp Gln Arg Phe Gly Pro Trp Asn Ile Pro Phe Gly Ser Val Arg Gln
    450                 455                 460

Asp Lys Gln Ser Gln Thr Gln Gly Gln Gly Ile Ala Lys Ser Glu Ser
465                 470                 475                 480

Glu Asp Asn Ile Ser Lys Lys Gln His Gly Arg Leu Gly Arg Ser Phe
                485                 490                 495

Ser Ala Gly Phe His Gln Glu Ser Thr Trp Lys Lys Ser Ser Leu Arg
            500                 505                 510

Glu Arg Arg Asn Ser Gly Tyr Gln Ser Tyr Asn Asp Tyr Asp Gly Asp
        515                 520                 525

Asp
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<210> SEQ ID NO 10
<211> LENGTH: 1946
<212> TYPE: DNA
<213> ORGANISM: Danio rerio
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (165)..(167)
<223> OTHER INFORMATION: Translation initiation codon (ATG)
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (1671)..(1673)
<223> OTHER INFORMATION: Translation termination codon (TAA)

<400> SEQUENCE: 10

cgttgaaaca gctaggcagt cagagaggtc gcgcagcgca ttttatataa aatattcttg     60

ctgaacttgc gagtcggtgg attattttgg gactgagtca tcatatctgc ggtacacctg    120

acctgttggt tattctctta accatcatcc cagttctcca ttcaatgcct aacactgtgg    180

aaagtgaagg cgccaaggta tccgctagta cagatcagga ggccccatca cgggccccgg    240

gacgagagga tgaacgtgag cgcagcttcc tgagccccat gatgcgagat gctctgcggg    300

tacgacgggc ctccagcgca gagctccagc ttccatggac gtgccctgta acccactcca    360

gggagaagtt ctacaccgtc tgctcggact atgccctgct caaccgagct cgaccagtta    420

tcacatccga agatgcatca cagaccaatc ctgacagcgg gacatcatta gccaagagca    480

acacagcaac atcttctcag agtcactcag gggaataag cgtatcttta gatgggaact     540

gtgatatgga ggttgtgtcc tccagcaaca agcctgtgct ggcctgggag attgacacct    600

cagatttcga tgccgtttta acccggaaag ccagaacaag taatttgaag aaattcaaca    660
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ctaagaaaat gaaatcatct gacaggccaa gcagaaacct gcaagatgtc ccgccacaag    720

cctctctaga tgaaatcaaa cagagaaaag tgctggacct ccgtagatgg tactgcatca    780

gccgaccaca gtataaaaca tcatgtggaa tctcttcact tgtttcttgc tggaactttc    840

tctacagtac tctcggagca ggcagtctcc cacctatttc tcaagaagaa gctctgcata    900

tacttggatt tcagcctccg tttgaagata tcaaatttgg accatttact ggcaatgcca    960

ctttaatgag atggttcaga caaatcaatg ataattttcg tgttcggggt tgctcatata   1020

ttctgtacaa gcctcatggg aagcacaaga cagcaggaga gacagccgag gggcgctca   1080

tgaagcttac acagggtctt aaagacgaat ccatggccta catttatcac tgtcagaatc   1140

actacttctg tcctgtgggc tatgaagcta ctccactgaa agcagccaaa gcatacaggg   1200

gaccactgcc tcttaatgag atggagcact ggattctcat tggtgaacca agccggaaac   1260

atcctgcaat ccactgtaaa aaatgggcag acatcgtgac ggacctaaat actcagaacc   1320

cagaatactt agacattcgc catattgaga gaggcataca gtatcgcaaa accaagaagg   1380

ttggaggcaa tctgcattgc atcatggcct tccagagagt gaactggcaa aaattgggac   1440

catgggcgct gaatctggaa aacctgaggc atgatctcca tcatcaggct ccagaacaca   1500

gaggccaagc ttcaacagag gacagttctg aggagcgaac ggtgaaacgc ctgggtaggt   1560

ctctcagcac ggggaacaag cctgaaaatg cctggaagcg tttgtccaac acagccgagt   1620

acaggcacag aggctctcca gacagtgacc tggatgaaga catcactgac taaatatgaa   1680

gggccaggtg ggtttcgaca cttttattca agattattaa ccttccaggt tattagctat   1740

agttaaaggt tacaatccgg tatgaggttg tgatgtaaga gttagtgctc agactggtaa   1800

acttaaaaat ggaagtttga cgccaataag aatatgggaa agagctcttg tggaggacat   1860

ctgtgtaata ctgacagcaa tgtgaattaa gttacactgg ctttggtgat gtgccgataa   1920

ataaaggttt aaaatactaa aaaaaa                                        1946
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<210> SEQ ID NO 11
<211> LENGTH: 502
<212> TYPE: PRT
<213> ORGANISM: Danio rerio

<400> SEQUENCE: 11

Met Pro Asn Thr Val Glu Ser Glu Gly Ala Lys Val Ser Ala Ser Thr
1               5                   10                  15

Asp Gln Glu Ala Pro Ser Arg Ala Pro Gly Arg Glu Asp Glu Arg Glu
            20                  25                  30

Arg Ser Phe Leu Ser Pro Met Met Arg Asp Ala Leu Arg Val Arg Arg
        35                  40                  45

Ala Ser Ser Ala Glu Leu Gln Leu Pro Trp Thr Cys Pro Val Thr His
    50                  55                  60

Ser Arg Glu Lys Phe Tyr Thr Val Cys Ser Asp Tyr Ala Leu Leu Asn
65                  70                  75                  80

Arg Ala Arg Pro Val Ile Thr Ser Glu Asp Ala Ser Gln Thr Asn Pro
                85                  90                  95

Asp Ser Gly Thr Ser Leu Ala Lys Ser Asn Thr Ala Thr Ser Ser Gln
            100                 105                 110

Ser His Ser Gly Gly Ile Ser Val Ser Leu Asp Gly Asn Cys Asp Met
        115                 120                 125

Glu Val Val Ser Ser Ser Asn Lys Pro Val Leu Ala Trp Glu Ile Asp
    130                 135                 140
```

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Thr Ser Asp Phe Asp Ala Val Leu Thr Arg Lys Ala Arg Thr Ser Asn
145                 150                 155                 160

Leu Lys Lys Phe Asn Thr Lys Lys Met Lys Ser Ser Asp Arg Pro Ser
                165                 170                 175

Arg Asn Leu Gln Asp Val Pro Pro Gln Ala Ser Leu Asp Glu Ile Lys
            180                 185                 190

Gln Arg Lys Val Leu Asp Leu Arg Arg Trp Tyr Cys Ile Ser Arg Pro
        195                 200                 205

Gln Tyr Lys Thr Ser Cys Gly Ile Ser Ser Leu Val Ser Cys Trp Asn
    210                 215                 220

Phe Leu Tyr Ser Thr Leu Gly Ala Gly Ser Leu Pro Pro Ile Ser Gln
225                 230                 235                 240

Glu Glu Ala Leu His Ile Leu Gly Phe Gln Pro Pro Phe Glu Asp Ile
                245                 250                 255

Lys Phe Gly Pro Phe Thr Gly Asn Ala Thr Leu Met Arg Trp Phe Arg
            260                 265                 270

Gln Ile Asn Asp Asn Phe Arg Val Arg Gly Cys Ser Tyr Ile Leu Tyr
        275                 280                 285

Lys Pro His Gly Lys His Lys Thr Ala Gly Glu Thr Ala Glu Gly Ala
    290                 295                 300

Leu Met Lys Leu Thr Gln Gly Leu Lys Asp Glu Ser Met Ala Tyr Ile
305                 310                 315                 320

Tyr His Cys Gln Asn His Tyr Phe Cys Pro Val Gly Tyr Glu Ala Thr
                325                 330                 335

Pro Leu Lys Ala Ala Lys Ala Tyr Arg Gly Pro Leu Pro Leu Asn Glu
            340                 345                 350

Met Glu His Trp Ile Leu Ile Gly Glu Pro Ser Arg Lys His Pro Ala
        355                 360                 365

Ile His Cys Lys Lys Trp Ala Asp Ile Val Thr Asp Leu Asn Thr Gln
    370                 375                 380

Asn Pro Glu Tyr Leu Asp Ile Arg His Ile Glu Arg Gly Ile Gln Tyr
385                 390                 395                 400

Arg Lys Thr Lys Lys Val Gly Gly Asn Leu His Cys Ile Met Ala Phe
                405                 410                 415

Gln Arg Val Asn Trp Gln Lys Leu Gly Pro Trp Ala Leu Asn Leu Glu
            420                 425                 430

Asn Leu Arg His Asp Leu His His Gln Ala Pro Glu His Arg Gly Gln
        435                 440                 445

Ala Ser Thr Glu Asp Ser Ser Glu Glu Arg Thr Val Lys Arg Leu Gly
    450                 455                 460

Arg Ser Leu Ser Thr Gly Asn Lys Pro Glu Asn Ala Trp Lys Arg Leu
465                 470                 475                 480

Ser Asn Thr Ala Glu Tyr Arg His Arg Gly Ser Pro Asp Ser Asp Leu
                485                 490                 495

Asp Glu Asp Ile Thr Asp
            500
```

<210> SEQ ID NO 12
<211> LENGTH: 2062
<212> TYPE: DNA
<213> ORGANISM: Strongylocentrotus purpuratus
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (164)..(166)
<223> OTHER INFORMATION: translation initiation codon (ATG)

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<400> SEQUENCE: 12

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gcagtttgtg tgtgattctc aatctcattg tgcgcattat aggcctatag ctttcgggaa      60
aacagacaga ttagtgcttt gcaaaccttg catacattga ggcaaccaga aagttgggct     120
caactttcag ataacctttg acctttcctg ggcctgaggt ataatgggta actggccttc     180
agttctctct ggtgagggaa gtgaggacag cagcagcgag agcaacaacg aaagcaacaa     240
ccaggaaacc agtgatcagg aaaacacaag acatcatctc tgtggctcag aggagagcta     300
cttctccgag gaggaactcc ttcccattgt ctaccctgat gatgatgatg atgctgctgc     360
tcgtgatgac gtgttgggag acttcttgtc cgttaaagaa gatggagagt ttacaactga     420
cgaggttgat gggtctcgat atgacctagc acccgagtat taccccacct ctcttcatga     480
agacgtcact gcgagattct cagatcttgc ctcacctgta gatcgcaaag aaagcagcta     540
cagcagcact gacgactatg atgacaatga cagtgatgat gaggaggagg aggaggatga     600
ccactattac caaagaagga ggaatgataa atattcccta atgaaggaag acgatgatga     660
taatgagctc tccagcattc cactgccacc tccctcatca ctgtatgaag ttgcatcagc     720
tgagcagatg caaggggtca cagcttacct gaatgctgac cgacctgaca cactccaaga     780
aaccatcgtc ccttttgaga gtcgtgcaga agagtgcagt gcccctgaga gggtggttgc     840
atgggagata gacgtcagcg acatgacggg atccaagaag actaagaaga gaccacccaa     900
taaactttca aaggcaaaat caaggaaaag ttcatcgaaa ggtagcatgg atagtgccta     960
tatcccgcca actgtatcaa caacacctga gctcctagca cagagaaagt gcttggacca    1020
aaagagatgg ttttgtgtga gtagacccca gtacagcaag tcatgtggcc tatcgtcctt    1080
ggtttcttgc tggaactacc tgttcagtac cctaggaggg ggcaccatgc cccccatcac    1140
ccaggagcaa gcccttaacg tcctggggtt ccaaccaccc ttcggtgaga tccgttttgg    1200
gcctttcaca gggaatgcca ccctcatgag gtggttcaag cagctgaatg atcactacag    1260
agtgagagga agggcatact tccagtacaa accccatggc aggagtagaa cagtgggaag    1320
aacatctgcc caaggtttac atctgttacg acaagggttg aaggatccta acatggcttt    1380
catataccac tgccataacc actacttctg ccccattgga tacgaagatg tgcctctgaa    1440
ggctgtagat gcatacaggg atcctttaaa ccttgatgag gtagagacat ggatactgat    1500
cggtgatcct agtagaaagc aaccaggaat ccactgtttc aaatgggaag acatcagcac    1560
agatctgaac tgccagaacc ctgactatct caacatccgc aagctacggc ttggagtgca    1620
gcagaggagg acaaagagaa ccggtggcaa cttgcactgc atcatggcct tctgtcgcag    1680
tgcaggcttt ctcaccagac caaccaagag caagaaagag ggtgcaatga aggacacttc    1740
tagtaacagc aagagtagga agtctggctc cgttcggatg tcaggacgta aggttggcga    1800
gagtaagagt gaggggatgg tggggcgtcc agctccagga gggagtgtgc catgtctgca    1860
gactggcaaa gcggacagta gcgatatcat cgagcacttt gcttttgaga ctgtgagttg    1920
cgaccatagc agtgagggcc gaagctgtag atcagaagtt gttaaaaaga ctaaaagtga    1980
atctcaggtt ggcagacgaa gggcaaaggc atctgttgta aagcaggagg ataaggagat    2040
cagagtgaag agttctgagg ca                                             2062
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<210> SEQ ID NO 13
<211> LENGTH: 633
<212> TYPE: PRT
<213> ORGANISM: Strongylocentrotus purpuratus

<400> SEQUENCE: 13

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Met Gly Asn Trp Pro Ser Val Leu Ser Gly Glu Gly Ser Glu Asp Ser
1               5                   10                  15

Ser Ser Glu Ser Asn Asn Glu Ser Asn Asn Gln Glu Thr Ser Asp Gln
            20                  25                  30

Glu Asn Thr Arg His His Leu Cys Gly Ser Glu Glu Ser Tyr Phe Ser
        35                  40                  45

Glu Glu Glu Leu Leu Pro Ile Val Tyr Pro Asp Asp Asp Asp Asp Ala
    50                  55                  60

Ala Ala Arg Asp Asp Val Leu Gly Asp Phe Leu Ser Val Lys Glu Asp
65                  70                  75                  80

Gly Glu Phe Thr Thr Asp Glu Val Asp Gly Ser Arg Tyr Asp Leu Ala
                85                  90                  95

Pro Glu Tyr Tyr Pro Thr Ser Leu His Glu Asp Val Thr Ala Arg Phe
            100                 105                 110

Ser Asp Leu Ala Ser Pro Val Asp Arg Lys Glu Ser Ser Tyr Ser Ser
        115                 120                 125

Thr Asp Asp Tyr Asp Asp Asn Asp Ser Asp Asp Glu Glu Glu Glu Glu
    130                 135                 140

Asp Asp His Tyr Tyr Gln Arg Arg Arg Asn Asp Lys Tyr Ser Leu Met
145                 150                 155                 160

Lys Glu Asp Asp Asp Asp Asn Glu Leu Ser Ser Ile Pro Leu Pro Pro
                165                 170                 175

Pro Ser Ser Leu Tyr Glu Val Ala Ser Ala Glu Gln Met Gln Gly Val
            180                 185                 190

Thr Ala Tyr Leu Asn Ala Asp Arg Pro Asp Thr Leu Gln Glu Thr Ile
        195                 200                 205

Val Pro Phe Glu Ser Arg Ala Glu Glu Cys Ser Ala Pro Glu Arg Val
    210                 215                 220

Val Ala Trp Glu Ile Asp Val Ser Asp Met Thr Gly Ser Lys Lys Thr
225                 230                 235                 240

Lys Lys Arg Pro Pro Asn Lys Leu Ser Lys Ala Lys Ser Arg Lys Ser
                245                 250                 255

Ser Ser Lys Gly Ser Met Asp Ser Ala Tyr Ile Pro Pro Thr Val Ser
            260                 265                 270

Thr Thr Pro Glu Leu Leu Ala Gln Arg Lys Cys Leu Asp Gln Lys Arg
        275                 280                 285

Trp Phe Cys Val Ser Arg Pro Gln Tyr Ser Lys Ser Cys Gly Leu Ser
    290                 295                 300

Ser Leu Val Ser Cys Trp Asn Tyr Leu Phe Ser Thr Leu Gly Gly Gly
305                 310                 315                 320

Thr Met Pro Pro Ile Thr Gln Glu Gln Ala Leu Asn Val Leu Gly Phe
                325                 330                 335

Gln Pro Pro Phe Gly Glu Ile Arg Phe Gly Pro Phe Thr Gly Asn Ala
            340                 345                 350

Thr Leu Met Arg Trp Phe Lys Gln Leu Asn Asp His Tyr Arg Val Arg
        355                 360                 365

Gly Arg Ala Tyr Phe Gln Tyr Lys Pro His Gly Arg Ser Arg Thr Val
    370                 375                 380

Gly Arg Thr Ser Ala Gln Gly Leu His Leu Leu Arg Gln Gly Leu Lys
385                 390                 395                 400

Asp Pro Asn Met Ala Phe Ile Tyr His Cys His Asn His Tyr Phe Cys
                405                 410                 415
```

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```
Pro Ile Gly Tyr Glu Asp Val Pro Leu Lys Ala Val Asp Ala Tyr Arg
            420                 425                 430

Asp Pro Leu Asn Leu Asp Glu Val Glu Thr Trp Ile Leu Ile Gly Asp
        435                 440                 445

Pro Ser Arg Lys Gln Pro Gly Ile His Cys Phe Lys Trp Glu Asp Ile
    450                 455                 460

Ser Thr Asp Leu Asn Cys Gln Asn Pro Asp Tyr Leu Asn Ile Arg Lys
465                 470                 475                 480

Leu Arg Leu Gly Val Gln Gln Arg Arg Thr Lys Arg Thr Gly Gly Asn
                485                 490                 495

Leu His Cys Ile Met Ala Phe Cys Arg Ser Ala Gly Phe Leu Thr Arg
            500                 505                 510

Pro Thr Lys Ser Lys Lys Glu Gly Ala Met Lys Asp Thr Ser Ser Asn
        515                 520                 525

Ser Lys Ser Arg Lys Ser Gly Ser Val Arg Met Ser Gly Arg Lys Val
    530                 535                 540

Gly Glu Ser Lys Ser Glu Gly Met Val Gly Arg Pro Ala Pro Gly Gly
545                 550                 555                 560

Ser Val Pro Cys Leu Gln Thr Gly Lys Ala Asp Ser Ser Asp Ile Ile
                565                 570                 575

Glu His Phe Ala Phe Glu Thr Val Ser Cys Asp His Ser Ser Glu Gly
            580                 585                 590

Arg Ser Cys Arg Ser Glu Val Val Lys Lys Thr Lys Ser Glu Ser Gln
        595                 600                 605

Val Gly Arg Arg Arg Ala Lys Ala Ser Val Val Lys Gln Glu Asp Lys
    610                 615                 620

Glu Ile Arg Val Lys Ser Ser Glu Ala
625                 630

<210> SEQ ID NO 14
<211> LENGTH: 2031
<212> TYPE: DNA
<213> ORGANISM: Giardia lamblia
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (230)..(232)
<223> OTHER INFORMATION: Translation initiation codon (ATG)
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (1040)..(1042)
<223> OTHER INFORMATION: Translation termination codon (TAG)

<400> SEQUENCE: 14

gcacatcttg caggtcaaaa cgaacacccc ctccttcgat atcctctcag accctacact      60

ctcaattgtg ttacagaccg ggcatgggaa gaacttgcta cggccggctt tcttaggggg     120

cgccgccctt gtcctcttct tctttcccat cctcctgtcc tctttttgtg actgtttgtg     180

actagacgcc gtttctaaca aaattgccaa gcatgtatgc aaaattaaaa tggaaagata     240

ccccagacaa cggttagacg acggcaggtg gcagtgcgtg gcagcgcagt acagatactc     300

ctgcgccatc tcatgccttg tgagcatatt caatcatctc ttcaacagag acatgaccct     360

ggacgagtgt attgctattc tctttccaga cctgaaagaa gacccacgac actatgattt     420

tggacctcag gcttctaaca gtgctgttca aagctggttc aagaccctct gcatgcacta     480

tggcctttct ggcacctctt gcacgatata caaggagcag ggcagaacga gaactgcgtg     540

tagcaagcaa gaggcactta agaatatcat cactgctttg aatacgccaa gatgtgcgtt     600

actgtatcac tgcttgaacc attactgcat aatcgtaggc tatataataa gtccatctac     660
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gcctaataga ccaagtaatc attgcgtctt cagcggggat gatggatgca ccctcaagct    720

cctgtgtgca gacggcacag aagccgagga cgtggacgat agtaatattt ggttaatagt    780

ggcagactgt gggaaaggaa ctgctcccct taggtcactg acctgggaat ttgtacataa    840

agatatatct acccgacctc cgtatgcata taacgctagg tgccctgaga gaggactgct    900

aaggaaaaca gaatcaaagg gatatatacc agttgagata gactcagtgc ttgttaacag    960

cacgggagta tccacctgtg ttagatctgg tggcgtcatc aagggatcgt cgcactgcat   1020

cattggattt gttagtgact agagccccgt ttattactcc cggacgaaag tataactatt   1080

aacaccacaa gcacaacgat agctccagta gagcagagcc gaagcacttg aggcagcgag   1140

gcctccaaat acccacatag aacgtcacag atgatagctg tccatgtcgc aattgacaag   1200

gttaacggga aggttgaaac aggcgagggc gtccatctgg tacgttgtac tttggttgtt   1260

gaatattgaa ctgttgtaag tgttgatttg ctgggtatat ctattgctta tgtaccgaaa   1320

aagggcattg caaacgtcat atattgcatc tatctgatga acacagaccc cagttttttg   1380

aagatttgca agtcttcttt gtggtggggc attcatatat gaataagagc agacttctcc   1440

gcaggcaaag gacatggact gaatggcatg ctcgtaacca gttaggtcca gtgctttggt   1500

tcgtgcatag tatttaaaga ccttctgaag aaggatggtt tgaaataggg tcgtcctgtc   1560

cacacagtcc aggcagttta tccgcggata gcacttctga acaaagtcag gaagagcaac   1620

tccgacatca ccgctaggaa ctagaactgt gcttgtggct atgtcatctg ctaactggtg   1680

atactctgtg ttgctgtgtc tacgtatgtt gtagttcatc aacttaacgt tgagggagtt   1740

cttgcggcga gaatcagcag tttttctcat agactcggta aagaacgccg tcagagccgc   1800

tcatcggcgg tctcaaggct tttcttttca ctggcagcaa tggagtcatc caaaagatcg   1860

acttcatttt tgaggaggtt gacgataagt atctctgcgt ctgcagtcac taagttaccc   1920

aatagaaggc ttatatgcct ttgcaagaga ctactaaact gagcgaggcc ctgctcttca   1980

tgagccccat ctgggaagcg tatggcagga gtgaacttgt aagtaaaaaa a             2031
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<210> SEQ ID NO 15
<211> LENGTH: 270
<212> TYPE: PRT
<213> ORGANISM: Giardia lamblia

<400> SEQUENCE: 15

Met Glu Arg Tyr Pro Arg Gln Arg Leu Asp Asp Gly Arg Trp Gln Cys
1               5                   10                  15

Val Ala Ala Gln Tyr Arg Tyr Ser Cys Ala Ile Ser Cys Leu Val Ser
            20                  25                  30

Ile Phe Asn His Leu Phe Asn Arg Asp Met Thr Leu Asp Glu Cys Ile
        35                  40                  45

Ala Ile Leu Phe Pro Asp Leu Lys Glu Asp Pro Arg His Tyr Asp Phe
    50                  55                  60

Gly Pro Gln Ala Ser Asn Ser Ala Val Gln Ser Trp Phe Lys Thr Leu
65                  70                  75                  80

Cys Met His Tyr Gly Leu Ser Gly Thr Ser Cys Thr Ile Tyr Lys Glu
                85                  90                  95

Gln Gly Arg Thr Arg Thr Ala Cys Ser Lys Gln Glu Ala Leu Lys Asn
            100                 105                 110

Ile Ile Thr Ala Leu Asn Thr Pro Arg Cys Ala Leu Leu Tyr His Cys
        115                 120                 125
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Leu Asn His Tyr Cys Ile Ile Val Gly Tyr Ile Ile Ser Pro Ser Thr
    130                 135                 140

Pro Asn Arg Pro Ser Asn His Cys Val Phe Ser Gly Asp Asp Gly Cys
145                 150                 155                 160

Thr Leu Lys Leu Leu Cys Ala Asp Gly Thr Glu Ala Glu Asp Val Asp
                165                 170                 175

Asp Ser Asn Ile Trp Leu Ile Val Ala Asp Cys Gly Lys Gly Thr Ala
            180                 185                 190

Pro Leu Arg Ser Leu Thr Trp Glu Phe Val His Lys Asp Ile Ser Thr
        195                 200                 205

Arg Pro Pro Tyr Ala Tyr Asn Ala Arg Cys Pro Glu Arg Gly Leu Leu
    210                 215                 220

Arg Lys Thr Glu Ser Lys Gly Tyr Ile Pro Val Glu Ile Asp Ser Val
225                 230                 235                 240

Leu Val Asn Ser Thr Gly Val Ser Thr Cys Val Arg Ser Gly Gly Val
                245                 250                 255

Ile Lys Gly Ser Ser His Cys Ile Ile Gly Phe Val Ser Asp
            260                 265                 270


<210> SEQ ID NO 16
<211> LENGTH: 196
<212> TYPE: DNA
<213> ORGANISM: Branchiostoma floridae

<400> SEQUENCE: 16

tgatttgtgg ttccggcaga tcaatgatca tttccatgta aaaggatgct cctatgttct     60

gtataagccg catggcaaga acaagacagc aggagaaact gctgttgggg cactatcaga    120

gttaacacaa gggttaaaag aagacccaac agcctacgtc tatcattgcc agaaccacta    180

cttctgcccc aatccc                                                    196


<210> SEQ ID NO 17
<211> LENGTH: 65
<212> TYPE: PRT
<213> ORGANISM: Branchiostoma floridae

<400> SEQUENCE: 17

Asp Leu Trp Phe Arg Gln Ile Asn Asp His Phe His Val Lys Gly Cys
1               5                   10                  15

Ser Tyr Val Leu Tyr Lys Pro His Gly Lys Asn Lys Thr Ala Gly Glu
            20                  25                  30

Thr Ala Val Gly Ala Leu Ser Glu Leu Thr Gln Gly Leu Lys Glu Asp
        35                  40                  45

Pro Thr Ala Tyr Val Tyr His Cys Gln Asn His Tyr Phe Cys Pro Asn
    50                  55                  60

Pro
65


<210> SEQ ID NO 18
<211> LENGTH: 382
<212> TYPE: DNA
<213> ORGANISM: Mus musculus
<220> FEATURE:
<221> NAME/KEY: 5'UTR
<222> LOCATION: (1)..(382)
<223> OTHER INFORMATION: Exon A - untranslated

<400> SEQUENCE: 18

ccccaactac tttcgtccct tccctccgtc cctcactctc cctcctcctt tctccccccc     60
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taccttcctt tctacttctt ttttcaactt tggagcacgg ctttctggca accttaaata 120

ctacagttgc gcaactagca tgtctggagt cacagcaaag atttcccaac ttatattttg 180

ttcaaggtat ccaccgcaaa tggcaggtat atagtaaacg ctgaaaggga ggctaggtgt 240

tatcaatgat acccagtcac tcggtgctat tcttgtgcgc tcaatgggac gaaagattct 300

gggccttggg taggagactt ggagatgcaa gatctggtgt tgccttccag caccagagtt 360

ccgggaccca acaggaacag ag 382

<210> SEQ ID NO 19
<211> LENGTH: 42
<212> TYPE: DNA
<213> ORGANISM: Mus musculus
<220> FEATURE:
<221> NAME/KEY: 5'UTR
<222> LOCATION: (1)..(42)
<223> OTHER INFORMATION: Exon B - untranslated

<400> SEQUENCE: 19

ccctggaagg atctgggtcg agctgagtct ctgaggagag at 42

<210> SEQ ID NO 20
<211> LENGTH: 311
<212> TYPE: DNA
<213> ORGANISM: Mus musculus
<220> FEATURE:
<221> NAME/KEY: 5'UTR
<222> LOCATION: (1)..(311)
<223> OTHER INFORMATION: Exon C - untranslated

<400> SEQUENCE: 20

ttttcttccg gctgggagtg agggagcagg ccgggaggag gttacaaggc tttagatctg 60

gtcttggcca gtggggacta gggacgcctg gcactgggtt ggccaccgca ggacagtagt 120

gggaacccgg cacagtagcg ctgcagcagt tgcacttgca acatccctgc tctcccggtt 180

ctcctccacc tgcacctttg tcaccttcag gtgcttcgga gcctcaaaga gggggcagtg 240

ggaagtctcc tggctcctca gagtctgaac tccagagggc atcatgtgct gcatgaatct 300

catactcaca g 311

<210> SEQ ID NO 21
<211> LENGTH: 601
<212> TYPE: DNA
<213> ORGANISM: Mus musculus
<220> FEATURE:
<221> NAME/KEY: 5'UTR
<222> LOCATION: (1)..(125)
<223> OTHER INFORMATION: Exon 1 - untranslated
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (126)..(128)
<223> OTHER INFORMATION: Translation initiation codon (ATG)

<400> SEQUENCE: 21

gatcccattt gtcagctctc aagccttttt agaatcctgt gaacatttgc caaagttgct 60

tttttttttt ttaaagagag ggttgcggct tcttcctagg aacagagaca tctgcatttg 120

ctctcatgcc taacgccact gaagctggaa aagccactga tcctggacat ggtgagcaca 180

catctgagaa caagtcacca gaagagggtc tacaaggtgc tgtaccatct ttctacacaa 240

gtgcctcaga agcacccata gcgcccagag gagatgggca ttatccatcg agttgtccag 300

tgactcacac tcgagagaaa atttatgcga tctgctcaga ttatgccttc ctcaaccagg 360

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caacatcagt ctacaaaact cctagcctaa cccgctctgc ttgcctccct gataacacct 420

ctctttctgc tggaaatact acaagatata ttggaatttc aactagtaca tcagaaataa 480

tctataatga aggaaaataa cttggaaaac ttgtccactg gcatgggcaa gctacctctt 540

gcatgggaga ttgataaatc tgaatttgat ggggtgacta caaatttgat acataagtca 600

g 601

<210> SEQ ID NO 22
<211> LENGTH: 912
<212> TYPE: DNA
<213> ORGANISM: Mus musculus
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (1)..(912)
<223> OTHER INFORMATION: Alternative BIVM 5' end clone (6359)
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (1)..(210)
<223> OTHER INFORMATION: Alternatively spliced exon A
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (211)..(311)
<223> OTHER INFORMATION: Alternatively spliced exon C
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (312)..(912)
<223> OTHER INFORMATION: Exon 1
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (437)..(439)
<223> OTHER INFORMATION: Translation initiation codon

<400> SEQUENCE: 22

atattttgtt caaggtatcc accgcaaatg gcaggtatat agtaaacgct gaaagggagg 60

ctaggtgtta tcaatgatac ccagtcactc ggtgctattc ttgtgcgctc aatgggacga 120

aagattctgg gccttgggta ggagacttgg agatgcaaga tctggtgttg ccttccagca 180

ccagagttcc gggacccaac aggaacagag gtgcttcgga gcctcaaaga gggggcagtg 240

ggaagtctcc tggctcctca gagtctgaac tccagagggc atcatgtgct gcatgaatct 300

catactcaca ggatcccatt tgtcagctct caagcctttt tagaatcctg tgaacatttg 360

ccaaagttgc ttttttttt tttaaagaga gggttgcggc ttcttcctag gaacagagac 420

atctgcattt gctctcatgc ctaacgccac tgaagctgga aaagccactg atcctggaca 480

tggtgagcac acatctgaga acaagtcacc agaagagggt ctacaaggtg ctgtaccatc 540

tttctacaca agtgcctcag aagcacccat agcgcccaga ggagatgggc attatccatc 600

gagttgtcca gtgactcaca ctcgagagaa aatttatgcg atctgctcag attatgcctt 660

cctcaaccag gcaacatcag tctacaaaac tcctagccta acccgctctg cttgcctccc 720

tgataacacc tctctttctg ctggaaatac tacaagatat attggaattt caactagtac 780

atcagaaata atctataatg aaggaaaata acttggaaaa cttgtccact ggcatgggca 840

agctacctct tgcatgggag attgataaat ctgaatttga tggggtgact acaaatttga 900

tacataagtc ag 912

<210> SEQ ID NO 23
<211> LENGTH: 912
<212> TYPE: DNA
<213> ORGANISM: Mus musculus
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (1)..(912)
<223> OTHER INFORMATION: Alternative BIVM 5' end clone (6358)

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<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (1)..(311)
<223> OTHER INFORMATION: Exon C
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (312)..(912)
<223> OTHER INFORMATION: Exon 1
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (437)..(439)
<223> OTHER INFORMATION: Translation initiation codon

<400> SEQUENCE: 23

ttttcttccg gctgggagtg agggagcagg ccgggaggag gttacaaggc tttagatctg     60

gtcttggcca gtggggacta gggacgcctg gcactgggtt ggccaccgca ggacagtagt    120

gggaacccgg cacagtagcg ctgcagcagt tgcacttgca acatccctgc tctcccggtt    180

ctcctccacc tgcacctttg tcaccttcag gtgcttcgga gcctcaaaga gggggcagtg    240

ggaagtctcc tggctcctca gagtctgaac tccagagggc atcatgtgct gcatgaatct    300

catactcaca ggatcccatt tgtcagctct caagcctttt tagaatcctg tgaacatttg    360

ccaaagttgc tttttttttt tttaaagaga gggttgcggc ttcttcctag gaacagagac    420

atctgcattt gctctcatgc ctaacgccac tgaagctgga aaagccactg atcctggaca    480

tggtgagcac acatctgaga acaagtcacc agaagagggt ctacaaggtg ctgtaccatc    540

tttctacaca agtgcctcag aagcacccat agcgcccaga ggagatgggc attatccatc    600

gagttgtcca gtgactcaca ctcgagagaa aatttatgcg atctgctcag attatgcctt    660

cctcaaccag gcaacatcag tctacaaaac tcctagccta acccgctctg cttgcctccc    720

tgataacacc tctctttctg ctggaaatac tacaagatat attggaattt caactagtac    780

atcagaaata atctataatg aaggaaaata acttggaaaa cttgtccact ggcatgggca    840

agctacctct tgcatgggag attgataaat ctgaatttga tggggtgact acaaatttga    900

tacataagtc ag                                                          912


<210> SEQ ID NO 24
<211> LENGTH: 888
<212> TYPE: DNA
<213> ORGANISM: Mus musculus
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (1)..(888)
<223> OTHER INFORMATION: Alternative BIVM 5' end clone (6356)
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (1)..(186)
<223> OTHER INFORMATION: Alternatively spliced exon A
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (187)..(287)
<223> OTHER INFORMATION: Alternatively spliced exon C
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (288)..(888)
<223> OTHER INFORMATION: Exon 1
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (413)..(415)
<223> OTHER INFORMATION: Translation initiation codon (ATG)

<400> SEQUENCE: 24

ccccaactac tttcgtccct tccctccgtc cctcactctc cctcctcctt tctccccccc     60

taccttcctt tctacttctt ttttcaactt tggagcacgg ctttctggca accttaaata    120
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ctacagttgc gcaactagca tgtctggagt cacagcaaag atttcccaac ttatattttg    180

ttcaaggtgc ttcggagcct caaagagggg gcagtgggaa gtctcctggc tcctcagagt    240

ctgaactcca gagggcatca tgtgctgcat gaatctcata ctcacaggat cccatttgtc    300

agctctcaag ccttttttaga atcctgtgaa catttgccaa agttgctttt ttttttttta    360

aagagagggt tgcggcttct tcctaggaac agagacatct gcatttgctc tcatgcctaa    420

cgccactgaa gctggaaaag ccactgatcc tggacatggt gagcacacat ctgagaacaa    480

gtcaccagaa gagggtctac aaggtgctgt accatctttc tacacaagtg cctcagaagc    540

acccatagcg cccagaggag atgggcatta tccatcgagt tgtccagtga ctcacactcg    600

agagaaaatt tatgcgatct gctcagatta tgccttcctc aaccaggcaa catcagtcta    660

caaaactcct agcctaaccc gctctgcttg cctccctgat aacacctctc tttctgctgg    720

aaatactaca agatatattg gaatttcaac tagtacatca gaaataatct ataatgaagg    780

aaaataactt ggaaaacttg tccactggca tgggcaagct acctcttgca tgggagattg    840

ataaatctga atttgatggg gtgactacaa atttgataca taagtcag                 888
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<210> SEQ ID NO 25
<211> LENGTH: 668
<212> TYPE: DNA
<213> ORGANISM: Mus musculus
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (1)..(668)
<223> OTHER INFORMATION: Alternative BIVM 5' end clone (cDNA)
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (1)..(42)
<223> OTHER INFORMATION: Exon B
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (43)..(143)
<223> OTHER INFORMATION: Alternatively spliced Exon C
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (144)..(668)
<223> OTHER INFORMATION: Alternatively spliced Exon 1
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (193)..(193)
<223> OTHER INFORMATION: Translation initiation codon (ATG)

<400> SEQUENCE: 25

ccctggaagg atctgggtcg agctgagtct ctgaggagag atgtgcttcg gagcctcaaa     60

gagggggcag tgggaagtct cctggctcct cagagtctga actccagagg gcatcatgtg    120

ctgcatgaat ctcatactca cagagagggt tgcggcttct tcctaggaac agagacatct    180

gcatttgctc tcatgcctaa cgccactgaa gctggaaaag ccactgatcc tggacatggt    240

gagcacacat ctgagaacaa gtcaccagaa gagggtctac aaggtgctgt accatctttc    300

tacacaagtg cctcagaagc acccatagcg cccagaggag atgggcatta tccatcgagt    360

tgtccagtga ctcacactcg agagaaaatt tatgcgatct gctcagatta tgccttcctc    420

aaccaggcaa catcagtcta caaaactcct agcctaaccc gctctgcttg cctccctgat    480

aacacctctc tttctgctgg aaatactaca agatatattg gaatttcaac tagtacatca    540

gaaataatct ataatgaagg aaaataactt ggaaaacttg tccactggca tgggcaagct    600

acctcttgca tgggagattg ataaatctga atttgatggg gtgactacaa atttgataca    660

taagtcag                                                             668
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<210> SEQ ID NO 26
<211> LENGTH: 3312
<212> TYPE: DNA
<213> ORGANISM: Mus musculus
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (1)..(209)
<223> OTHER INFORMATION: Exon A
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (210)..(309)
<223> OTHER INFORMATION: Exon C
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (310)..(911)
<223> OTHER INFORMATION: Exon 1
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (437)..(439)
<223> OTHER INFORMATION: Translation initiation codon
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (912)..(1038)
<223> OTHER INFORMATION: Exon 2
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (1039)..(1134)
<223> OTHER INFORMATION: Exon 3
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (1135)..(1239)
<223> OTHER INFORMATION: Exon 4
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (1240)..(1334)
<223> OTHER INFORMATION: Exon 5
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (1335)..(1467)
<223> OTHER INFORMATION: Exon 6
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (1468)..(1554)
<223> OTHER INFORMATION: Exon 7
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (1555)..(1651)
<223> OTHER INFORMATION: Exon 8
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (1652)..(3312)
<223> OTHER INFORMATION: Exon 9
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (1943)..(1945)
<223> OTHER INFORMATION: Translation termination codon (TGA)

<400> SEQUENCE: 26

atattttgtt caaggtatcc accgcaaatg gcaggtatat agtaaacgct gaaagggagg 60

ctaggtgtta tcaatgatac ccagtcactc ggtgctattc ttgtgcgctc aatgggacga 120

aagattctgg gccttgggta ggagacttga ggatgcagat ctggtgttgc cttccagcac 180

cagagttccg ggacccaaca ggaacagagg tgcttcggag cctcaaagag ggcagtggg 240

aagtctcctg gctcctcaga gtctgaactc cagagggcat catgtgctgc atgaatctca 300

tactcacagg atcccatttg tcagctctca agccttttta gaatcctgtg aacatttgcc 360

aaagttgctt tttttttttt tttaaagaga gggttgcggc ttcttcctag gaacagagac 420

atctgcattt gctctcatgc ctaacgccac tgaagctgga aaagccactg atcctggaca 480

tggtgagcac acatctgaga acaagtcacc agaagagggt ctacaaggtg ctgtaccatc 540

tttctataca agtgcctcag aagcacccat agcgcccaga ggagatgggc attatccatc 600

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gagttgtcca gtgactcaca ctcgagagaa aatttatgcg atctgctcag attatgcctt    660
cctcaaccag gcaacatcag tctacaaaac tcctagccta acccgctctg cttgcctccc    720
tgataacacc tctctttctg ctggaaatac tacaagatat attggaattt caactagtac    780
atcagaaata atctataatg aagaaaataa cttggaaaac ttgtccactg gcatgggcaa    840
gctacctctt gcatgggaga ttgataaatc tgaatttgat ggggtgacta caaatttgat    900
acataagtca ggcaatgtaa agaaacaatt ttccaagaag aaaacgtcgg ataaaaaagg    960
gcggcatcag agggagtgtc tccactattc tcctcttgat gatgttaaac aacgcaaagt   1020
gttagacctt aggcgatggt actgcataag ccgaccacag tacaagactt catgtggtat   1080
ctcctcattg atttcttgtt ggaatttctt atacagcata atgggagctg ggaatctccc   1140
acctattacc caagaagagg cattacatat tttgggcttc caaccccat ttgaagatat   1200
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acaagaatca caacatccca cacatgtccc gggaattgcc aaatctgaga gtgaggacaa   1800
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tcatttttct cttgaatttc atatccatct atccactcat atatgtttag cctacagaat   3180

tacaaactag tcctgtttct gaagaggttc tttagcttga aatgtaaagg actgaaagat   3240

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<210> SEQ ID NO 27
<211> LENGTH: 502
<212> TYPE: PRT
<213> ORGANISM: Mus musculus

<400> SEQUENCE: 27

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Glu His Thr Ser Glu Asn Lys Ser Pro Glu Glu Gly Leu Gln Gly Ala
            20                  25                  30

Val Pro Ser Phe Tyr Thr Ser Ala Ser Glu Ala Pro Ile Ala Pro Arg
        35                  40                  45

Gly Asp Gly His Tyr Pro Ser Ser Cys Pro Val Thr His Thr Arg Glu
    50                  55                  60

Lys Ile Tyr Ala Ile Cys Ser Asp Tyr Ala Phe Leu Asn Gln Ala Thr
65                  70                  75                  80

Ser Val Tyr Lys Thr Pro Ser Leu Thr Arg Ser Ala Cys Leu Pro Asp
                85                  90                  95

Asn Thr Ser Leu Ser Ala Gly Asn Thr Thr Arg Tyr Ile Gly Ile Ser
            100                 105                 110

Thr Ser Thr Ser Glu Ile Ile Tyr Asn Glu Glu Asn Asn Leu Glu Asn
        115                 120                 125

Leu Ser Thr Gly Met Gly Lys Leu Pro Leu Ala Trp Glu Ile Asp Lys
    130                 135                 140

Ser Glu Phe Asp Gly Val Thr Thr Asn Leu Ile His Lys Ser Gly Asn
145                 150                 155                 160

Val Lys Lys Gln Phe Ser Lys Lys Lys Thr Ser Asp Lys Lys Gly Arg
                165                 170                 175

His Gln Arg Glu Cys Leu His Tyr Ser Pro Leu Asp Asp Val Lys Gln
            180                 185                 190

Arg Lys Val Leu Asp Leu Arg Arg Trp Tyr Cys Ile Ser Arg Pro Gln
        195                 200                 205

Tyr Lys Thr Ser Cys Gly Ile Ser Ser Leu Ile Ser Cys Trp Asn Phe
    210                 215                 220

Leu Tyr Ser Ile Met Gly Ala Gly Asn Leu Pro Pro Ile Thr Gln Glu
225                 230                 235                 240

Glu Ala Leu His Ile Leu Gly Phe Gln Pro Pro Phe Glu Asp Ile Arg
                245                 250                 255

Phe Gly Pro Phe Thr Gly Asn Thr Thr Leu Met Arg Trp Phe Arg Gln
            260                 265                 270

Ile Asn Asp His Phe His Val Lys Gly Cys Ser Tyr Val Leu Tyr Lys
        275                 280                 285

Pro His Gly Lys Asn Lys Thr Ala Gly Glu Thr Ala Pro Gly Ala Leu
    290                 295                 300

Ser Lys Leu Thr Arg Gly Leu Lys Asp Glu Ser Leu Ala Tyr Ile Tyr
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305                 310                 315                 320

His Cys Gln Asn His Tyr Phe Cys Pro Ile Gly Phe Glu Ala Thr Pro
                325                 330                 335

Val Lys Ala Asn Lys Ala Phe Ser Arg Gly Pro Leu Ser Ser Gln Glu
            340                 345                 350

Val Glu Tyr Trp Ile Leu Ile Gly Glu Ser Ser Arg Lys His Pro Ala
        355                 360                 365

Ile His Cys Lys Arg Trp Ala Asp Ile Val Thr Asp Leu Asn Thr Gln
    370                 375                 380

Asn Pro Glu Phe Leu Asp Ile Arg His Leu Glu Arg Gly Leu Gln Phe
385                 390                 395                 400

Arg Lys Ile Lys Lys Val Gly Gly Asn Leu His Cys Ile Ile Ala Phe
                405                 410                 415

Gln Arg Leu Ser Trp Gln Arg Phe Gly Phe Trp Asn Phe Pro Phe Gly
            420                 425                 430

Thr Ile Thr Gln Glu Ser Gln His Pro Thr His Val Pro Gly Ile Ala
        435                 440                 445

Lys Ser Glu Ser Glu Asp Asn Ile Ser Lys Lys Gln His Gly Arg Leu
    450                 455                 460

Gly Arg Ser Phe Ser Ala Ser Phe His Gln Asp Ser Ala Trp Lys Asn
465                 470                 475                 480

Met Ser Ser Ile His Glu Arg Arg Asn Ser Gly Tyr His Ser Phe Arg
                485                 490                 495

Asp Tyr Asn Gly Asn Asp
            500


<210> SEQ ID NO 28
<211> LENGTH: 34562
<212> TYPE: DNA
<213> ORGANISM: Mus musculus
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (349)..(554)
<223> OTHER INFORMATION: KDEL exon
<220> FEATURE:
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<222> LOCATION: (1630)..(2075)
<223> OTHER INFORMATION: KDEL exon
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<222> LOCATION: (2300)..(2681)
<223> OTHER INFORMATION: Exon A
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<221> NAME/KEY: misc_feature
<222> LOCATION: (2794)..(2835)
<223> OTHER INFORMATION: Exon B
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (3269)..(3579)
<223> OTHER INFORMATION: Exon C
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (9571)..(10171)
<223> OTHER INFORMATION: Exon 1
<220> FEATURE:
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<222> LOCATION: (9696)..(9698)
<223> OTHER INFORMATION: Translation initiation codon (ATG)
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (10945)..(11071)
<223> OTHER INFORMATION: Exon 2
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (12030)..(12125)
<223> OTHER INFORMATION: Exon 3
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<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (12562)..(12666)
<223> OTHER INFORMATION: Exon 4
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (12885)..(12979)
<223> OTHER INFORMATION: Exon 5
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (16786)..(16962)
<223> OTHER INFORMATION: n = a, c, g, or t; length of "nnnnnnnnnn" nucleotides is undetermined.
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (20099)..(20231)
<223> OTHER INFORMATION: Exon 6
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (21686)..(21772)
<223> OTHER INFORMATION: Exon 7
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (24881)..(24977)
<223> OTHER INFORMATION: Exon 8
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (25952)..(27613)
<223> OTHER INFORMATION: Exon 9
<220> FEATURE:
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<222> LOCATION: (26243)..(26245)
<223> OTHER INFORMATION: Translation termination codon (TGA)

<400> SEQUENCE: 28

ccagacttgg tcctttgcaa gtgcttttca ctgccgagcc atctctctag cttttttttt 60

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aacttttcta gtaatgtttc ttggtcttta gtgaattata atccccatgt aaataatcaa 180

tatctctctt ttgccaagtt gcctaattta gttttcaatt agaaaaacat ctagtttttt 240

tttccattta gtgaaaaaag tatgctaagt ttttgataga attcttattg atggaatgac 300

atgccttttt gtatacaaat cctaccataa atttttgttt caaaatacct cttaaaacat 360

aaggagactc ggcaacatgt tgcccatggt gtttaacctc tatcttcaga tttctgtagc 420

tggcatacat tctgtatctt actatgaagg aaccgtcctt tcgatctaaa acctggacac 480

caactctcgt gaactgctca tcgggtgctg agattttaac ctggaacacc ttttcacctg 540

gagaagatgt aaacctgtta tggaaaacaa tgagagatga gggttatttt taagatcaaa 600

tgcacgctac ttattctctt taatgtgtaa aggttggacc ttctgcttta tcctgatttt 660

aagatattgt tgttcgatta ctctcttagg cttttaggac cagaaccaat atgatagaac 720

aaagataaaa aagaaaacaa taataacata aaataatttc attagatagt tgccaggaga 780

taacacttaa gactagcaat ctatttagca taccaaatag agcactatca gtgtactatt 840

attaattcat aaccaacaca gctggcaatt tgtcatttgt aacatgttta cttcaaggga 900

tgaccttatt tgaaaaattg ttcttaatgg cttaaaatac aatccagtac tgtggggcta 960

gggagatagc tgaatggttt agagcattta ccattatgta aaagacttag ttcagttcct 1020

agtatccatt gtccttaagg ctcacaacta tctgcagttt cagctcaagg agattcaagg 1080

ccctcttctg gcttcctcca gcacttgggt gtgagtatac accctaccca catcatgtaa 1140

ttaaaatatt actactaata aaagtctaac aaatatacca gtactctaaa ttatgtttag 1200

ttatgggggа aatcaaaata actggtcatc atgttagtaa cacaagtgtt ttggactgaa 1260

tattcctgca ttttgaatgc atttagtttc tagtgtttag ttttcccatt taaaaataac 1320

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cacaacccga gcggtggcat gtccaggaga aggatgccac acgttctgct gaacctggtt   2040
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gcctgcgctg tgaccagtct tagtaaagtc ttctgctagt ggatgagtgg gtcagagtgg   2220
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<223> OTHER INFORMATION: BIVM Exon A2 splice donor sequence

<400> SEQUENCE: 30

tgtgatccag gtccg                                                      15


<210> SEQ ID NO 31
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (1)..(15)
<223> OTHER INFORMATION: BIVM Exon A3 splice donor sequence

<400> SEQUENCE: 31

caggccagag gtacc                                                      15


<210> SEQ ID NO 32
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (1)..(15)
<223> OTHER INFORMATION: BIVM Exon B splice acceptor sequence

<400> SEQUENCE: 32

ttccctaaag gaatc                                                      15


<210> SEQ ID NO 33
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (1)..(15)
<223> OTHER INFORMATION: BIVM Exon B splice donor sequence

<400> SEQUENCE: 33

tttctgtcag gtgat                                                      15


<210> SEQ ID NO 34
<211> LENGTH: 15
<212> TYPE: DNA
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<213> ORGANISM: Homo sapiens
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (1)..(15)
<223> OTHER INFORMATION: BIVM Exon 1 splice acceptor sequence

<400> SEQUENCE: 34

ttcctcttag gagct 15

<210> SEQ ID NO 35
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (1)..(15)
<223> OTHER INFORMATION: BIVM Exon 1 splice donor sequence

<400> SEQUENCE: 35

cacaaatcag gtaag 15

<210> SEQ ID NO 36
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (1)..(15)
<223> OTHER INFORMATION: BIVM Exon 2 splice acceptor sequence

<400> SEQUENCE: 36

tgtattctag gcaat 15

<210> SEQ ID NO 37
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (1)..(15)
<223> OTHER INFORMATION: BIVM Exon 2 splice donor sequence

<400> SEQUENCE: 37

tcagacgatg gtgat 15

<210> SEQ ID NO 38
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (1)..(15)
<223> OTHER INFORMATION: BIVM Exon 3 splice acceptor sequence

<400> SEQUENCE: 38

gtgttctcag gtact 15

<210> SEQ ID NO 39
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (1)..(15)
<223> OTHER INFORMATION: BIVM Exon 3 splice donor sequence

<400> SEQUENCE: 39

gagctggaaa gtaag 15

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<210> SEQ ID NO 40
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (1)..(15)
<223> OTHER INFORMATION: BIVM Exon 4 splice acceptor sequence

<400> SEQUENCE: 40

tcttttgtag ccttc 15

<210> SEQ ID NO 41
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (1)..(15)
<223> OTHER INFORMATION: BIVM Exon 4 splice donor sequence

<400> SEQUENCE: 41

cacttatgag gtatg 15

<210> SEQ ID NO 42
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (1)..(15)
<223> OTHER INFORMATION: BIVM Exon 5 splice acceptor sequence

<400> SEQUENCE: 42

ttactttcag gtggt 15

<210> SEQ ID NO 43
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (1)..(15)
<223> OTHER INFORMATION: BIVM Exon 5 splice donor sequence

<400> SEQUENCE: 43

ggagaaactg gtagg 15

<210> SEQ ID NO 44
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (1)..(15)
<223> OTHER INFORMATION: BIVM Exon 6 splice acceptor sequence

<400> SEQUENCE: 44

tttttaatag cttca 15

<210> SEQ ID NO 45
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (1)..(15)

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<223> OTHER INFORMATION: BIVM Exon 6 splice donor sequence

<400> SEQUENCE: 45

aagcattcag gtaag 15

<210> SEQ ID NO 46
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (1)..(15)
<223> OTHER INFORMATION: BIVM Exon 7 splice acceptor sequence

<400> SEQUENCE: 46

ttatatttag caggg 15

<210> SEQ ID NO 47
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (1)..(15)
<223> OTHER INFORMATION: BIVM Exon 7 splice donor sequence

<400> SEQUENCE: 47

actgtaaaaa gtatg 15

<210> SEQ ID NO 48
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (1)..(15)
<223> OTHER INFORMATION: BIVM Exon 8 splice acceptor sequence

<400> SEQUENCE: 48

ttaactatag atggg 15

<210> SEQ ID NO 49
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (1)..(15)
<223> OTHER INFORMATION: BIVM Exon 8 splice donor sequence

<400> SEQUENCE: 49

aacaaagaag gtaag 15

<210> SEQ ID NO 50
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (1)..(15)
<223> OTHER INFORMATION: BIVM Exon 9 splice acceptor sequence

<400> SEQUENCE: 50

ttcttctcag gttgg 15

<210> SEQ ID NO 51
<211> LENGTH: 30

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<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: HSMAP5 primer

<400> SEQUENCE: 51

ccatgcctct ctactactca ctcccaacac 30

<210> SEQ ID NO 52
<211> LENGTH: 30
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: HSMAP6 primer

<400> SEQUENCE: 52

ggtaagaaga acaccattgt gtttgaaggc 30

<210> SEQ ID NO 53
<211> LENGTH: 30
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: zfbivmMAPF1 primer

<400> SEQUENCE: 53

caatgcctaa cactgtggaa agtgaaggcg 30

<210> SEQ ID NO 54
<211> LENGTH: 29
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: zfbivmMAPR1 primer

<400> SEQUENCE: 54

gataactgtc gagctcggtt gagcagggc 29

<210> SEQ ID NO 55
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: M1 amino acid motif
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (2)..(7)
<223> OTHER INFORMATION: Xaa = any amino acid

<400> SEQUENCE: 55

Gly Xaa Xaa Xaa Xaa Xaa Xaa Cys
1 5

<210> SEQ ID NO 56
<211> LENGTH: 4
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: M2 amino acid motif
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (2)..(2)
<223> OTHER INFORMATION: Xaa = Tyr or Phe
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (4)..(4)
<223> OTHER INFORMATION: Xaa = Gln or His

<400> SEQUENCE: 56

Trp Xaa Arg Xaa
1

<210> SEQ ID NO 57
<211> LENGTH: 3
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: M3a amino acid motif

<400> SEQUENCE: 57

Tyr Phe Cys
1

<210> SEQ ID NO 58
<211> LENGTH: 3
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: M3b amino acid motif

<400> SEQUENCE: 58

Tyr His Cys
1

<210> SEQ ID NO 59
<211> LENGTH: 5
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: BIVM N-terminus region of homology
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (3)..(3)
<223> OTHER INFORMATION: Xaa = Val or Cys

<400> SEQUENCE: 59

Arg Lys Xaa Leu Asp
1 5

<210> SEQ ID NO 60
<211> LENGTH: 6
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: BIVM C-terminus region of homology

<400> SEQUENCE: 60

Gly Gly Asn Leu His Cys
1 5

<210> SEQ ID NO 61
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: BIVM amino acid motif 1

<400> SEQUENCE: 61

Gly Asn Thr Thr Leu Met Trp Arg Phe
1 5

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<210> SEQ ID NO 62
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: BIVM amino acid motif 2

<400> SEQUENCE: 62

Tyr Phe Cys Pro Ile Gly Phe Glu Ala
1               5


<210> SEQ ID NO 63
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: BIVM amino acid motif 3

<400> SEQUENCE: 63

Trp Phe Arg Gln Ile Asn Asp His Phe
1               5


<210> SEQ ID NO 64
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: BIVM amino acid motif 4

<400> SEQUENCE: 64

Tyr Arg His Gln Asn His Tyr Phe Cys Pro
1               5                   10
```

We claim:

1. An isolated or recombinant polynucleotide:

a) comprising SEQ ID NO: 1;

b) comprising a polynucleotide sequence complementary to a polynucleotide sequence comprising SEQ ID NO: 1;

c) comprising a fragment of SEQ ID NO: 1 that spans i) nucleotides 1446 to 1697, or ii) nucleotides 1446 to 1698;

d) comprising a polynucleotide encoding a polypeptide comprising the amino acid sequence of SEQ ID NO: 2;

e) comprising a vector comprising a polynucleotide sequence as set forth in **1**a), **1**b), **1**c), or **1**d);

f) comprising a promoter operably linked to a polynucleotide sequence as set forth **1**a), **1**b), **1**c), or **1**d);

g) comprising a polynucleotide as set forth in **1**a), **1**b), **1**c), or **1**d) and a detectable label; or

h) comprising a polynucleotide as set forth in **1**a) **1**b), **1**c), or **1**d) and a heterologous polynucleotide sequence encoding a heterologous polypeptide sequence.

2. A composition comprising culture media and a transformed host cell comprising a polynucleotide sequence according to claim **1**.

3. The composition according to claim **2**, wherein said host cell is selected from the group consisting of Gram negative bacterial cells, Gram positive bacterial cells, yeast cells, animal cells, plant cells, and insect cells.

4. A method of detecting the presence of the BIVM gene comprising:

a) contacting a sample suspected of containing the BIVM gene with a polynucleotide according to claim **1** under conditions that allow for the formation of a hybrid comprising the BIVM gene and a polynucleotide according to claim **1**; and

b) detecting the formation of said hybrid, wherein the formation of a hybrid is indicative of the presence or differential expression of the BIVM gene in said sample and the absence of the formation of a hybrid is indicative of a sample lacking said BIVM gene.

5. The method according to claim **4**, wherein said sample is a biological or environmental sample.

6. The method according to claim **4**, wherein said method is selected from the group consisting of Southern blots, Northern blots, enzymatic gene amplification and methods utilizing DNA chips.

7. The isolated or recombinant polynucleotide according to claim **1**, wherein said polynucleotide comprises the polynucleotide sequence of SEQ ID NO; 1.

8. The isolated or recombinant polynucleotide according to claim **1**, wherein said polynucleotide comprises a polynucleotide sequence complementary to the polynucleotide sequence of SEQ ID NO: 1.

9. The isolated or recombinant polynucleotide according to claim **1**, wherein said polynucleotide comprises a frag-

ment of SEQ ID NO: 1 that spans i) nucleotides 1446 to 1697, or ii) nucleotides 1446 to 1698.

10. The isolated or recombinant polynucleotide according to claim **1**, wherein said polynucleotide encodes a polypeptide comprising the amino acid sequence of SEQ ID NO:2.

11. The isolated or recombinant polynucleotide according to claim **1**, wherein said polynucleotide comprises a vector comprising a polynucleotide sequence as set forth in claim **1***a*), **1***b*), **1***c*), or **1***d*).

12. The isolated or recombinant polynucleotide according to claim **1**, wherein said polynucleotide comprises a promoter operably linked to a polynucleotide sequence as set forth in claim **1***a*), **1***b*), **1***c*), or **1***d*).

13. The isolated or recombinant polynucleotide according to claim **1**, wherein said polynucleotide as set forth in claim **1***a*), **1***b*), **1***c*), or **1***d*) further comprises a detectable label.

14. The isolated or recombinant polynucleotide according to claim **1**, wherein said polynucleotide as set forth in **1***a*),

1*b*), **1***c*), or **1***d*) further comprises a heterologous polynucleotide sequence encoding a heterologous polypeptide sequence.

15. The polynucleotide according to claim **10**, wherein said polynucleotide comprises nucleotides 680 through 2188 of SEQ ID NO1.

* * * * *

UNITED STATES PATENT AND TRADEMARK OFFICE

CERTIFICATE OF CORRECTION

PATENT NO. : 7,038,030 B2
APPLICATION NO. : 10/417476
DATED : May 2, 2006
INVENTOR(S) : Gary W. Litman et al.

It is certified that error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

<u>Column 9,</u>
Line 53, "Thompson et *Nucleic*" should read --Thompson *et al.* [1994] *nucleic*--.

<u>Column 21,</u>
Line 42, "signal- thus" should read --signal; thus--.

<u>Column 28,</u>
Line 12, "SI17 rRNA" should read --S17 rRNA--.

<u>Column 217,</u>
Line 6, "SEQ ID NO1" should read --SEQ ID NO:1--.

Signed and Sealed this

Eighth Day of August, 2006

JON W. DUDAS
Director of the United States Patent and Trademark Office