

Sequence Polymorphisms of Major German Cockroach Allergens Bla g 1, Bla g 2, Bla g 4, and Bla g 5

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Key Words

Allergen · Bla g 1 · Bla g 2 · Bla g 4 · Bla g 5 · Cockroach

Abstract

Background: The allergenicity of allergens could be influenced by amino acid substitutions in B- or T-cell epitope regions. The German cockroach is known to produce potent allergens inducing strong IgE-mediated allergic reactions. This study was performed to investigate sequence variations in major allergens of the German cockroach. **Methods:** Reverse transcriptase PCR was used to amplify the cDNA sequences encoding major allergens of the German cockroach (Bla g 1, Bla g 2, Bla g 4, and Bla g 5). **Results:** The deduced amino acid sequences revealed 38 Bla g 1 variants with 1–7 amino acid substitutions (98.6–99.8% identity), 28 Bla g 2 variants with 1–3 substitutions (99.1–99.7%), 27 Bla g 4 variants with 0–32 substitutions (82.4–100%), and 8 Bla g 5 variants with 1–2 substitutions (99.0–99.5%), respectively. Bla g 1 and Bla g 2 showed sporadic amino acid substitutions despite the divergence in their sequences. Bla g 4 exhibited frequent variations, with clusters of substitutions in residues 29–38, 52–80, and 132–155. Sequence variations in Bla g 4 imply the presence of multiple isoforms and isoallergens, which may in turn have various effects on the IgE-binding capacity and T-cell responsiveness. Only 8 variants were

found in Bla g 5, with infrequent amino acid changes of one or two residues. **Conclusions:** Analyses of T-cell and IgE-binding epitope regions would clarify the effect of sequence polymorphisms on allergenicity, which in turn will aid in the design of allergen formulations for diagnosis and immunotherapy for cockroach allergies.

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Introduction

Household cockroaches are one of most important sources of indoor allergens. Six allergens from the German cockroach have been cloned and allergenically characterized. Bla g 1, thought to be involved in the digestion or metabolism of ingested foods, has a unique structural feature of tandem amino acid repeats of approximately 100 amino acids [1]. Bla g 2 is a zinc-binding protein and enzymatically inactive, even though it shares sequence homology with aspartic proteinases [2]. Bla g 2 is one of the most potent allergens, capable of eliciting IgE responses at 10- to 100-fold lower levels than that of house dust mite and cat allergens [3]. Bla g 4 is produced in the male reproductive system and transferred to the female within the spermatophore during copulation [4, 5]. Bla g 5 is a putative glutathione-S-transferase which may

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Table 1. Oligonucleotides used for the amplification of each allergen

Allergen	Primer	Sequence
Bla g 1	Blag102F	5'-GCCATAGAATTTCCTCAATAAC-3'
	Blag102R	5'-GAAACTTTCTTAGATATGGAAC-3'
Bla g 2	Bg2F2	5'-GGATCCTATGATGATTGGCCTAAAGCT-3'
	Bg2R2	5'-CTCGAGCTTAGACGCTTTCTACT-3'
Bla g 4	Bg4F	5'-GCAGTTTGGCACTATGTGC-3'
	Bg4R	5'-CTTAGTGACATGTGGAGTG-3'
Bla g 5	Bg5F	5'-CTTATAAACTGACATACTGT-3'
	Bg5R	5'-CTTACAGATCTGTAGGAGG-3'

be involved in the detoxification of harmful chemicals [6]. Bla g 6 is troponin C which binds to the calcium ion and regulates muscle contraction [7]. Interestingly, it was reported that conformational changes in troponin C by calcium binding could influence the IgE-binding reactivity [8]. Bla g 7 is a tropomyosin which mediates muscle contraction [9]. IgE-binding frequencies of each allergen have been reported to be 30–50% for Bla g 1, 54–71% for Bla g 2, 40–60% for Bla g 4, 70% for Bla g 5, and 17% for Bla g 7 [10].

The relative importance of these cockroach allergens was determined by the IgE antibody response against recombinant cockroach allergens in 118 serum samples from cockroach-sensitized subjects [11]. The prevalence of IgE antibody was highest for recombinant Bla g 2 (54.4%) and recombinant Bla g 5 (37.4%). However, 36% of the sera did not show reactivity to the five recombinant allergens (Bla g 1, Bla g 2, Bla g 4, Bla g 5, and Per a 7). Per a 7, the American cockroach tropomyosin, was used instead of Bla g 7 because it has a 98.6% amino acid sequence identity to Bla g 7, and the two are highly cross-reactive. This result strongly suggested that there must be other cockroach allergens which have not yet been identified. Furthermore, only one isoform of each allergen was used in the study by Satinover et al. [11].

Many important allergens have sequence polymorphisms, as exemplified by mite group 2 allergens [12–14] and birch pollen allergen Bet v 1 [15]. The amino acid sequence variations encoded by these polymorphisms could influence IgE-binding reactivity, T-cell response, and cytokine induction [15–17]. However, polymorphisms of cockroach allergens have not been extensively examined, except for Bla g 7 [18], even though some cockroach allergens have been found to have several isoforms [10]. The objective of this study was to describe the amino acid sequence polymorphisms of the major German cockroach allergens, Bla g 1, Bla g 2, Bla g 4, and Bla g 5.

Materials and Methods

Cockroaches

Colonies of the German cockroach, *Blattella germanica*, have been maintained in the Department of Parasitology, Yonsei University College of Medicine, Seoul, Korea, since 1999. The population used in this study originated from a pregnant female which was captured from a house in Yongsan (Seoul) using a modified trap (a small glass jar of about 1 liter) with a wide mouth, containing a food lure. Vaseline was used to keep the insects collected inside. A total of 40 nymphs were obtained from an ootheca. Their diet consisted of mouse food.

Amplification of Bla g 1.02, Bla g 2, Bla g 4, and Bla g 5 cDNA

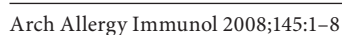
Total RNA was isolated using the TRIzol reagent (Invitrogen, Carlsbad, Calif., USA) from 6–10 adult female cockroaches for the amplification of cDNAs encoding Bla g 1.02, Bla g 2, and Bla g 5, and from 6 adult male cockroaches for the amplification of cDNAs coding for Bla g 4. First-strand cDNA was synthesized and RT-PCR was performed to amplify the cDNA clones. After an initial step at 95°C for 5 min, 35 cycles at 94°C for 30 s, 50°C for 30 s and 72°C for 1 min (2 min for Bla g 1.02 amplification) were performed. The last extension was carried out for 9 min. Three to eight independent PCR reactions were performed using three RNA preparations. The oligonucleotides used in the PCR reactions are listed in table 1. Restriction enzyme cleavage sites (*Bam*H I for the forward primer and *Xho* I for the reverse primer, underlined) were incorporated for subcloning. LA Taq DNA polymerase (TAKARA, Tokyo, Japan) was used for the amplification of Bla g 1.02. The PCR products were inserted into a pGEM T Easy vector (Promega, Madison, Wisc., USA) and sequenced in both directions at Solgent (Daejeon, Korea). DNA sequences were analyzed and aligned using the BioEdit program (www.mbio.ncsu.edu/BioEdit). All DNA sequences were translated into their amino acid sequences and compared with previously reported antigens.

Results

Bla g 1.02 Variations

A total of 63 partial Bla g 1.02 cDNA clones were sequenced and analyzed (fig. 1). We found 38 variants with one to seven amino acid substitutions at 52 different posi-

Blag 1, 2, 4, and 5 Sequence Polymorphism



128863 MIGLKLVTLFAVATITHAELQRVPLVKLVHVFINTQYAGITKIGNQFLTVFDTSNWWASQECVGGACVCPNLQKYEKLKPKYISDGNVQVKFFDTGSAVGRGIEDSLTISNLT 120

Sequence logo for the 128863 motif. The x-axis represents amino acid positions (130-240) and the y-axis represents the motif sequence (1-45). The logo shows the conservation of amino acids at each position, with 'S' at position 201, 'N' at 223, 'F' at 134, 'T' at 168, 'L' at 171, 'V' at 174, 'R' at 134, 'M' at 211, and 'T' at 238.

250 260 270 280 290 300 310 320 330 340 350
 SKAIVGPKAYVNPINEATGCVVEKTTTRICKLDCSKIPSLPDVTFVINGRNFNISQYYIQQGNLCYSGFGPCGHSDHFFIGDFFVDHYSEPNWENKMGFGRSVSY
A.....S.....
S.....T.....
D.....
E.....S.....
T.....S.....
V.....G.....

tions (98.6–99.8% identities), compared to the previously reported Bla g 1.02 (accession No. AF072220). Notably, all clones had an amino acid change at position 209 from glycine to alanine. Four other positions exhibited frequent amino acid substitutions: 116 (Asp to Asn), 175 (Phe to Thr or Leu), 282 (Lys to Arg), and 372 (Thr to Met), indicating that they are the polymorphic residues. Two clones which have sequence variations at the first seven and last seven amino acids seem to contain PCR artifact because they are determined by primer sequences.

A variant with a single amino acid change at position 209 occurred in 24 of 63 clones examined (38.1%), and was found to be the predominant form. This sequence was submitted to the GenBank database under accession No. EF202179.

Bla g 2 Variations

Twenty-eight different cDNA clones encoding different amino acid sequences were identified (fig. 2). Amino acid substitutions were found in 30 positions in the 71 clones analyzed. All but one clone contained the Gly residue instead of Val at position 143. Only one clone had Arg at this position. Three clones had a Phe to Ser amino acid change at position 347. The Ile residue at position 171 was changed to Val twice and to Thr once. Other amino acid changes were sporadic.

The substitution of the Gly residue at position 143 compared to the previously reported Bla g 2 (U28863) was seen in 43 of 71 clones (60.6%), making it a major Bla g 2 variant; this sequence was deposited in the GenBank under accession No. EF203068.

Bla g 4 Variations

Sequences from 51 cDNA clones from 6 adult male cockroaches were translated into 27 different amino acid sequences (fig. 3). An outstanding feature of Bla g 4 variants or isoallergens is the insertion or deletion of one amino acid at positions 77, 93, or 137. Four clones had no amino acid at position 77, as did two clones at position 137. Three clones had one additional amino acid Asp at position 93. In addition to this feature, many amino acids were found to be polymorphic. Frequent amino acid substitutions were found at 36 positions: 8, 13, 29, 30, 32, 34, 36, 52, 54, 56, 57, 58, 59, 62, 64, 69, 71, 73, 74, 75, 77, 92,

93, 95, 111, 132, 134, 135, 136, 138, 142, 143, 148, 149, 154, and 155. Amino acid substitutions also occurred at positions 38, 47, 60, 65, 66, 70, 79, 80, 160, and 166 at least three times. The positions where frequent amino acid substitutions occurred could be grouped into three regions: residues 29–38, 52–80, and 132–155. The amino acid substitution at position 182 (from Cys to Trp) may be the result of a primer error. They showed 82.4–100% identity with the previously reported Bla g 4 (U40767). The predominant form was comprised of 14 of 51 clones analyzed (27.8%), which was deposited in the GenBank under accession No. EF202172.

Bla g 5 Variations

An amino acid substitution of Lys for Asn at position 38 was seen in all 57 clones examined, as compared with the previously reported partial Bla g 5 sequence (accession No. U92412; fig. 4). Sporadic amino acid changes at seven other positions were identified, with eight different variants. The variant with a single amino acid substitution at Lys was the predominant form found in 50 of 57 clones (87.7%). The partial sequence of a predominant variant identified in the study was deposited in the GenBank under accession No. EF202178.

Discussion

Several dust mite allergens exist as variant proteins due to polymorphisms in their genes [19]. However, data on sequence polymorphisms of major cockroach allergens are limited. The information on two Bla g 1 isoallergens with three variants (Bla g 1.0101, AF072219; Bla g 1.0102, L47595, and Bla g 1.0201, AF072220) and three Bla g 6 isoallergens (Bla g 6.0101, DQ279092; Bla g 6.0201, DQ279093, and Bla g 6.0301, DQ279094) are available from the official website of the allergen nomenclature subcommittee (<http://www.allergen.org>). Only one isoform has been reported to date for each of Bla g 2 (U28863), Bla g 4 (U40767), and Bla g 5 (U092412). This study on the sequence polymorphisms in major German cockroach allergens revealed many sequence variations, especially in Bla g 4, which showed extensive variation in many regions. It cannot be excluded that at least some of the sequences are the results of PCR artifacts [20]. Nevertheless, the probability that the sequences obtained by RT-PCR are expressed in vivo is much higher than the probability that sequences arise from genomic screening (pseudogenes). The presence of several genes encoding for different forms may account for the sequence diversi-

Fig. 2. Amino acid sequence variations of Bla g 2. The frequency and sequence identity of each variant are shown in parentheses.

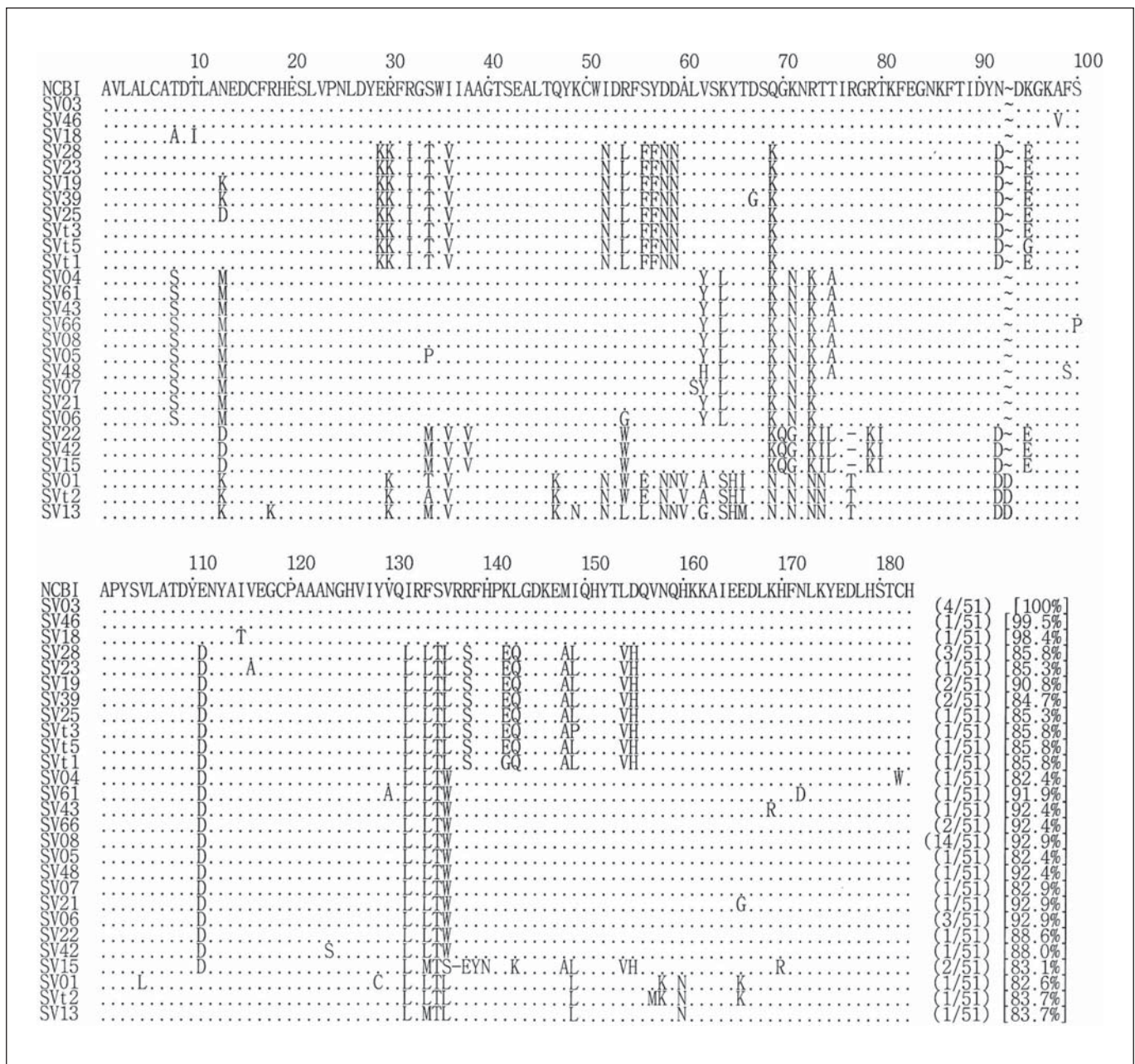


Fig. 3. Alignment of Bla g 4 variants. The inserted and deleted amino acids are denoted by ~ and - marks. The frequency and sequence identity of each variant are shown in parentheses.

fication. Another possible explanation for this sequence diversity is alternative splicing and RNA editing [21, 22]. A signal peptide cleavage site between residues 12 (Ala) and 13 (Asn) was predicted in the original Bla g 4 sequence (U40767), and residue 13 seems to be polymorphic. Alternative splicing of Bla g 4 may account for the polymorphism of residue 13 and it may also affect aller-

genicity. Some of the lipocalin proteins such as odorant-binding proteins are known to be alternatively spliced and differentially expressed [23, 24]. Pre-mRNA editing by the substitution of an inosine for an adenosine is a widespread phenomenon in animal tissues [25]. Alternative splicing and RNA editing may alter ligand-binding properties of Bla g 4, thereby influencing longevity or tar-

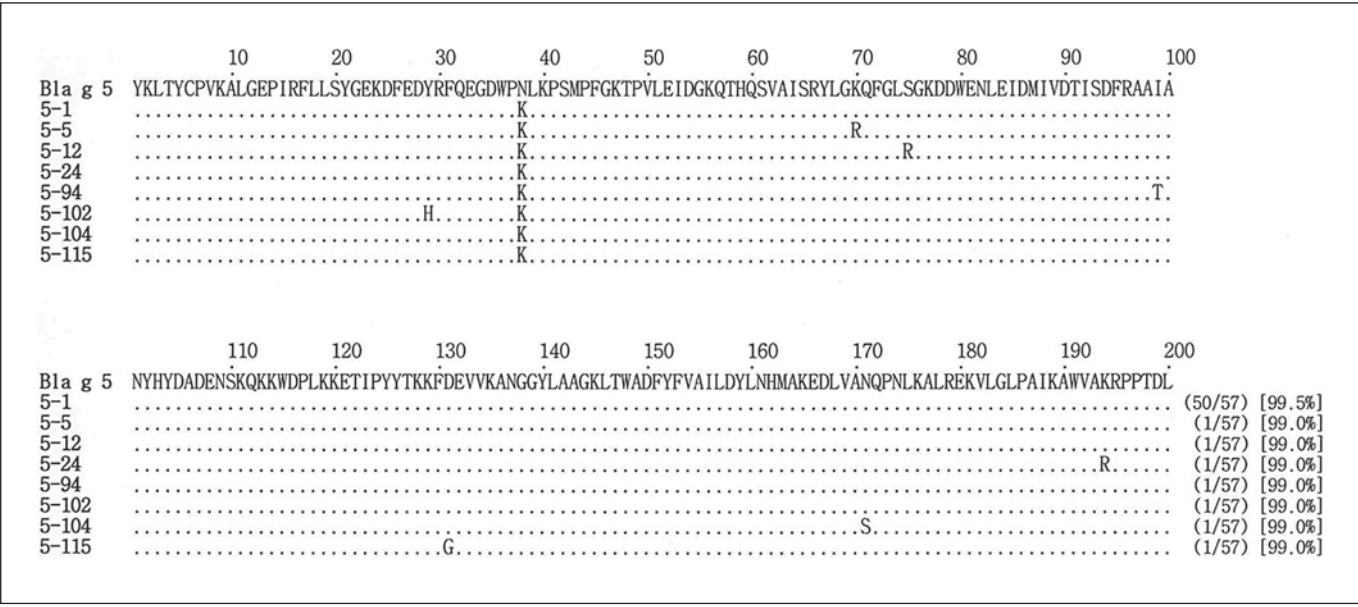


Fig. 4. Amino acid sequence variations of Bla g 5. The frequency and sequence identity of each variant are shown in parentheses.

geting the spermatophore in the female reproductive system. A study using only a single isoform of Bla g 4 might underestimate its allergenicity. However, the mechanism by which Bla g 4 sensitizes allergic individuals requires further investigation, as Bla g 4 is known to be produced in male reproductive organs and transferred to females during copulation [5].

All the Bla g 1 clones identified in this study have an amino acid substitution at position 209 from Gly to Ala regarding the previously reported sequence AF072220 (Bla g 1.0201). All the investigated clones of Bla g 2 and Bla g 5 showed amino acid changes at position 143 from Val to Gly in Bla g 2 (U28863) and at position 38 from Asn to Lys in Bla g 5 (U92412), respectively. These variations may contribute to the regional differences and effect on the sensitization and diagnosis of allergic subjects.

The allergenic consequences of these sequence variations on IgE binding and T-cell responses have yet to be determined. Sequence variations in allergens also influence their reactivity to the monoclonal antibodies produced from mice. Commercially available cockroach allergen extracts are known to vary in their quality and quantity of major allergens [26], and the standardization of allergen extracts relies not only on the extraction procedure and storage, but also on monoclonal antibodies utilized [27]. Different batches of allergen ex-

tract could potentially have different isoforms, consequently influencing the characterization of allergen extracts using monoclonal antibodies. Sometimes, even a single amino acid substitution on the surface of allergens could confer different IgE or IgG recognition patterns [28].

Different isoforms and variants could be identified from different geographical regions. Therefore, the variant which could best represent the allergen in a given environment needs to be identified for the best diagnosis and allergen-specific immunotherapy to induce active immunity to the allergen, reduce symptoms, and minimize medication usage [29].

The information obtained by the analyses of B- and T-cell epitopes will improve our understanding of the allergenicity of allergens and provide a fundamental basis for developing new agents for cockroach allergen diagnostics and immunotherapy [30, 31].

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Bla g 1

AF0702220

AIEFLNNIHDLLGIPHIPVTARKHHRRGVGITGLIDDIIAILPVDDLYALFQEKLETSPEFKALYDAIRSPEFQSIVGTL
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 EFETIVVTVDLSLPEFKNFLNFLTQTNGLNAIEFLNNIHDLLGIPHIPVTGRKHLRRGVGITGLIDDIIAILPVDDLYALFQ
 EKLETSPEFKALYDAIRSPEFQSIVETLKAMPEYQSLIQKLKDKGVDVDHIEELIHQIFNIVRDTRGLPEDLQDFLALIP
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 ELIKKLFGLSH

Bla g 1.0201

1

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 EKLETSPEFKALYDAIRSPEFQSIVETLKAMPEYQSLIQKLKDKGVDVDHIEELIHQIFNIVRDTRGLPEDLQDFLALIP
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 ELIKKLFGLSH

Bla g 1.0202 - EF202179

20

AIEFLNNIHDLLGIPHIPVTARKHHRRGVGITGLIDDIIAILPVDDLYALFQEKLETSPEFKALYDAIRSPEFQSIVGTL
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 ELIKKLFGLSH

1-9

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 ELIKKLFGLSH

5

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23

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 EFETIVVTVDLSLPEFKNFLNFLTQTNGLNAIEFLNNIHDLLGIPHIPVIARKHLRRGVGITGLIDDIIAILPVDDLYALFQ
 EKLETSPEFKALYDAIRSPEFQSIVETLKAMPEYQSLIQKLKDKGVDVDHIEELIHQIFNIVRDTRGLPEDLQDFLALIP
 IDQILAIAADYLANDAEVQA AVEYLKSDDEFETIVVTVDLSLPEFKNFLNFLTQTNGLNAIEFINNIHDLLGIPHIPATGRKH
 VRRGVGINGLIDDVIAILPVDELYALFQEKLESSPEFKALYDAIRSPEFQSIVQTLKAMPEYQDLIQRKDKGVDVDHFI
 ELIKKLFGLSH

17

AIEFLNNIHDLLGIPHIPVTARKHHRRGVGITGLIDDIIAILPVDDLYALFQEKLETSPEFKALYDAIRSPEFQSIVGTL
 EAMPEYQNLIQKLEDKGVDVDHIEELIHQIFNIVRDTRGLPEDLQDFLALIPDQVLAIAADYLANDAEVKA AVEYLKSD
 EFETIVVTVDLSLPEFKNFLNFLTQTNGLNAIEFLNNIHDLLGIPHIPVTARKHLRRGVGITGLIDDIIAILPVDDLYALFQ
 EKLETSPEFKALYDAIRSPEFQSIVETLKAMPEYQSLIQKLKDKGVDVDHIEELIHQIFNIVRDTRGLPEDLQDFLALIP
 IDQILAIAADYLANDAEVQA AVEYLKSDDEFETIVVTVDLSLPEFKNFLNFLTQTNGLNAIEFINNIHDLLGIPHIPATGRKH
 VRRGVGINGLIDDVIAILPVDELYALFQEKLESSPEFKALYDAIRSPEFQSIVQTLKAMPEYQDLIQRKDKGVDVDHFI
 ELIKKLFGLSH

10

AIEFLNNIHDLLGIPHIPVTARKHHRRGVGITGLIDDIIAILPVDDLYALFQEKLETSPEFKALYDAIRSPEFQSIVGTL
 EAMPEYQNLIQKLKDKGVDVDHIEELIHQIFNIVRDTRGLPEDLQDFLALIPDQVLAIAADYLANDAEVKA AVEYLKSD

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EFETIVVTVDSLPEFKNFLNFLTQTNGLNAIEFLNNIHDLLGIPHIPVTARKHLRRGVGITGLIDDIIAILPVDDLYALFQ
EKLETSPFEFKALYDAIHSPEFQSI VETLKAMPEYQSLIQKLKDKGVDVDHIIELI HQIFNIVRDRGLPEDLQDFLALIP
IDQILAI AADYLANDAEVQA AVEYLK SDEFETIVVTVDSLPEFKNFLNFLTQTNGLNAIEFINNIHDLLGIPHIPATGRKH
VRRGVINGLIIDDVIAILPVDEL YALFQEKLESSPEFKALYDAIRSP EFQSI VQTLKAMPEYQDLIQLRKDKGVDVDHFI
ELIKKLFGLSH

AIEFLNNIHDLGLGIPHIPVTARKHHRRGVGITGLIDDIIAILPVDDLYALFQEKLETSPEFKALYDAIRSPEFQSIVGTL
 EAMPEYQNLIQRLKDKGVDVDHIIELIHQIFNIVRDRGLPEDLQDFLALIPTDQVLAIAADYLANDAEVKAAVEYLKSD
 EFETIVVTVDLSPEFKNFLNFLTNGLNIAIEFLNNIHDLGLGIPHIPVTARKHLRRGVGITGLIDDIIAILPVDDLYALFQ
 EKLETSPEFKALYDAIRSPEFQSIVETLKAMPEYQSLIQKLKDKGVDVDHIIELIHQIFNIVRDRGLPEDLQDFLALIP
 IDQLAIAADYLANDAEVQAAVEYLKSDDEFETIVVTVDLSPEFKNFLNFLTNGLNIAIEFINNIHDLGLGIPHIPATGRKH
 VRRGVGINGLDIDDVIAILPVDELALFQEKLSSPEFKALYDAIRSPEFQSIVQTLKAMPEYQDLIQRLKDKGVDVDHFI
 ELIKKLFGLSH

AIEFLNNIHDLGLIPHIPVTARKHHRRGVGITGLIDDIIAILPVDDLALFQEKLETSPEFKALYDAIRSPEFQSIVGTL
 EAMPEYQNLIQKLKDKGVDVDHIIELIHQIFNIVRDRGLPEDLQDFLALIPTDQVLAAADYLANDAEVKAAVEYLKSD
 EFETIVVTVDLSPEFKNFLNFLTNGLNIAIEFLNNIHDLGLIPHIPVTARKHLRRGVGITGLIDDIIAILPVDDLALFQ
 EKLETSPEFKALYDATRSPEFQSIVETLKAMPEYQSLIQKLKDKGVDVDHIIELIHQIFNIVRDRGLPEDLQDFLALIP
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 ELIKKFLGLSH

AIEFLNNIHDLGLIPHIPVTARKHHRRGVGITGLIDDIIAILPVDDLALFQEKLETSPEFKALYDAIRSPEFQSIVGTL
 EAMPEYQNLIQKLKDKGVDVDHIIELIHQIFNIVRDRGLPEDLQDFLALIPTDQVLAAADYLANDAEVKAAVEYLKSD
 EFETIVVTVDLSPEFKNFLNFLTNGNLNAIEFLNNIHDLGLIPHIPVTARKHLRRGVGITGLIDDIIAILPVDGLYALFQ
 EKLETSPEFKALYDAIRSPEFQSIVETLKAMPEYQSLIQKLKDKGVDVDHIIELIHQIFNIVRDRGLPEDLQDFLALIP
 IDQLAIAADYLANDAEVQAAVEYLKSDDEFETIVVTVDLSPEFKNFLNFLTNGNLNAIEFINNIHDLGLIPHIPATGRKH
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 ELIKKFLGLSH

AIEFLNNIHDLLGIPHIPVTARKHHRRGVGITGLIDDI IAILPVDDLYALFQEKLETSPEFKALYDAIRSPEFQTIVGTL
 EAMPEYQNLIQKLKDKGVDVDHIIELIHQIFNIVRDRTRL PEDLQDFLALIP TDQVLAI AADYLANDAEVKA AVEYLKSD
 EFETIVVTVDSLPEFKNFLNFLTNGLN AIEFLNNIHDLLGIPHIPVTARKHLRRGVGITGLIDDI IAILPVDDLYALFQ
 EKLETSPEFKALYDAIRSPEFQSIVETLKAMPEYQSLIQKLKDKGVDVDHIIELIHQIFNIVRDRTRL PEDLQDFLALIP
 IDQILAI AADYLANDAEVQA AVEYLKSD EFETIVVTVDSLPEFKNFLNFLTNGLN AIEFINNIHDLLGIPHIPATGRKH
 VRRGVINGLIDDVIAILPVDEL YALFQEKL ESSPEFKALYDAIRSPEFQSIVQTLKAMPEYQDLIQR LKDKGVDVDHFI
 ELTKKLEGLSH

AIEFLNNIHDLGLIPHIPVTARKHHRRGVGITGLIDDIIAILPVDDLALFQEKLETSPEFKALYDAIRSPEFQSIVGTL
 EAMPEYQNLIQKLKDKGVDVDHIIELIHQIFNIVRDRGLPEDLQDFLALIPTDQVLAAADYLANDAEVKAAVEYLKSD
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 EKLETSPEFKALYDAIRSPEFQSIVETLKAMPEYQGLIQKLKDKGVDVDHIIELIHQIFNIVRDRGLPEDLQDFLALIP
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 ELIKKLGLSLH

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 EKLETSPEFKALYDAIRSPEFQSIVETLKAMPEYQSLIQKLKDKGVDVDHIIELIHQIFNIVRDRGLPEDLQDFLALIP
 IDQLIAAADYLANDAEVQAAVEYLKSD EFETIVVTVDLSPEFKNFLNFLTNGLN AIEFINNIHDLLGIPHIPATGRKH
 VRRGVINGLIDDVIAILPVDEL YALFQEELESSPEFKALYDAIRSPEFQSIVQTLKAMPEYQDLIQLRKDKGVDVDHFI
 ELIKKLFGLSH

AIEFLNNIHDLLGIPHIPVTARKHHRRGVGITGLIDDIIAILPVDDLYALFQEKLETSPEFKALYDAIRSPEFQSIVGTL
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 EFETIVVTVDLSPEFKNFLNFLQTNGLNAIEFLNNIHDLLGIPHIPVTARKHLRRGVGITGLIDDIIAILPVDDLYALFQ
 EKLETSPEFKALYDAIRSPEFQSIVETLKAMPEYQSLIQKLKDKGVDVDHIIELIHQIFNIVRDRTRLPEDLQDFLALIP
 IDQILAAADYLANDAEVQAAVEYLKSDDEFETIVVTVDLSPEFKNFLNFLQTNGLNAIEFINNIHDLLGIPHIPATGRKH
 VRRGVINGLIDDVIAILPVDELIALFQEKLSSPEFKALYDAIRSPEFQSIVQTLKAMPEYQDLIQRLEDKGVDVDHFI
 ELTKKLEGLSH

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2-31

AIEFLNNIHDLGLIPHIPVTARKHHRRGVGITGLIDDIIAILPVDDLIALFQEKLETSPEFKALYDAIRSPEFQSIVGTL
 EAMPEYQNLIQKLKDKGVDVDHIIELIHQIFNIVRDRGLPEDLQDFLALIPTDQVLAAADYLANDAEVKAAVEYLKSD
 EFETIVVTVDSLPEFKNFLNFLTNGLNIAIEFLNNIHDLGLIPHIPVTARKHLRRGVGITGLIDDIIAILPVDDLIALFQ
 EKLETSPEFKALYDAIRSPEFQSIVETLKAMPEYQSLIQKLKDKGVDVDHIIELIHQIFNIVRDRGLPEDLQDFLALIP
 IDQLIAAADYLANDAEVQAAVEYLKSDDEFETIVVTVDSLPEFKNFLNFLTNGLNIAIEFINNIHDLGLIPHIPATGRKH
 VRRGVGINGLDIDAIAILPVDELIALFQEKLSSPEFKALYDAIRSPEFQSIVQTLKAMPEYQDLIQLKDKGVDVDHFI
 ELIKKFLGLSH

2-33

AIEFLNNIHDLGLGIPHIPVTARKHHRRGVGITGLIDDI IAILPVDDL YALFQEKLETSPEFKALYDAIRSPEFQSIVGTL
 EAMPEYQNL IQLKDKGVDVDHIIELIHQIFNIVRDRGLPEDLRDQFLAL IPTDQVLAI AADYLANDAEVKA AVEYLKSD
 EFETIVVTVDSLPEFKNFLN FLQTNGLN AIEFLNNIHDLGLGIPHIPVTARKHLRRGVGITGLIDDI IAILPVDDL YALFQ
 EKLETSPEFKALYDAIRSPEFQSIVETLKAMPEYQSL IQLKDKGVDVDHIIELIHQIFNIVRDRGLPEDLRDQFLAL IP
 IDQLAI AADYLANDAEVQA AVEYLKSD EFETIVVTVDSLPEFKNFLN FLQTNGLN AIEFINNIHDLGLGIPHIPATGRKH
 VRRGVGINGLDIDVIAILPVDEL YALFQEKL ESSPEFKALYDAIRSPEFQSIVQTLKAMPEYQDLIQR LDKGVDVDHFI
 ELIKKLFGLSH

2-56

AIEFLNNIHDLGLIPHIPVTARKHHRRGVGITGLIDDIIAILPVDDLALFQEKLETSPEFKALYDAIRSPEFQSIVGTL
 EAMPEYQNLIQKLKDKGVDVDHIIELIHQIFNIVRDRGLPEDLQDFLALIPTDQVLAAADYLANDAEVKAAVEYLKSD
 EFETIVVTVDLSPEFKNFLNFLTNGLNAIEFLNNIHDLGLIPHIPVTARKHLRRGVGITGLIDDIIAILPVDDLALFQ
 EKLETSPEFKALYDAIRSPEFQSIVETLKAMPEYQSLIQKLKDKGVDVDHIIELIHQIFNIVRDRGLPEDLQDFLALIP
 IDQLAIAADYLANDAEVQAAVEYLKSDDEFETIVVTVDLSPEFKNFLNFLTNGLNAIEFINNIHDLGLIPHIPATGRKH
 VRRGVGINGLIDDVIAILPVDELALFQEKLESSPEFKALYDAIRSPEFQSIVQTLKAMPEYQDLIQLKDKGVDVDHFI
 ELIKKFLGLPH

2-68

AIEFLNNIHDLGLIPHIPVTARKHHRRGVGITGLIDDIIAILPVDDLALFQEKLETSPEFKALYDAIRSPEFQSIVGTL
 EAMPEYQNLIQKLKDKGVDVDHIIELIHQIFNIVRDRGLPEDLQDFLALIPTDQVLAAADYLANDAEVKAAVEYLKSD
 EFETIVVTVDLSPEFKNFLNFLTNGLNIAIEFLNNIHDLGLIPHIPVTARKHLRRGVGITGLIDDIIAILPVDDLALFQ
 EKLETSPEFKALYDAIRSPEFQSIVETLKAMPEYQSLIQKLKDKGVDVDHIIELIHQIFNIVRDRGLPEDLQDFLALIP
 IDQILAAADYLANDAEVQAAVEYLKSDDEFETIVVTVDLSPEFKNFLNFLTNGLNIAIEFINNIHDLGLIPHIPATGRKH
 VRRGVINGLIDGVIAILPVDELALFQEKLESSPEFKALYDAIRSPEFQSIVQTLKAMPEYQDLIQLRKDKGVDVDHFI
 ELTKKGLFGLSH

2-69

AIEFLNNIHDLGLIPHIPVTARKHHRRGVGITGLIDDIIAILPVDDLALFQEKLETSPEFKALYDAIRSPEFQSIVGTL
 EAMPEYQNLIQKLKDKGVDADHIIELIHQIFNIVRDRGLPEDLQDFLALIPTDQVLAAADYLANDAEVKAAVEYLKSD
 EFETIVVTVDLSPEFKNFLNFLTNGLNIAIEFLNNIHDLGLIPHIPVTARKHLRRGVGITGLIDDIIAILPVDDLALFQ
 EKLETSPEFKALYDAIRSPEFQSIVETLKAMPEYQSLIQKLKDKGVDVDHIIELIHQIFNIVRDRGLPEDLQDFLALIP
 IDQILAAADYLANDAEVQAAVEYLKSDDEFETIVVTVDLSPEFKNFLNFLTNGLNIAIEFINNIHDLGLIPHIPATGRKH
 VRRGVINGLIDDVIAILPVDELALFQEKLESSPEFKALYDAIRSPEFQSIVQTLKAMPEYQDLIQLRKDKGVDVDHFI
 ELTKGLFGLSH

2-73

AIEFLNNIHDLLGIPHIPVTARKHHRRGVGITGLIDDI IAILPVDDLYALFQEKLETSPEFKALYDAIRSPEFQSIVGTL
 EAMPEYQNLIQKLKDKGVDVDHIIELIHQIFNIVRDRGLPEDLQDFLALIPTDQVLAAADYLANDAEVKA AVEYLKSD
 EFETIVVTVDLSPEFKNFLNFLTNGLN AIEFLNNIHDLLGIPHIPVTARKHLRRGVGITELIDDI IAILPVDDLYALFQ
 EKLETSPEFKALYDAIRSPEFQSIVETLKAMPEYQSLIQKLKDKGVDVDHIIELIHQIFNIVRDRGLPEDLQDFLALIP
 IDQILAAADYLANDAEVQA AVEYLKSD EFETIVVTVDLSPEFKNFLNFLTNGLN AIEFINNIHDLLGIPHIPATGRKH
 VRRGVINGLIDDVIAILPVDEL YALFQEKL ESSPEFKALYDAIRSPEFQSIVQTLKAMPEYQDLIQLRKDKGVDVDHFI
 ELTKKGLFGLSH

2-76

AIEFLNNIHDLGLIPHIPVTARKHHRRGVGITGLIDDIIAILPVDDLALFQEKLETSPEFKALYDAIRSPEFQSIVGTL
 EAMPEYQNLIQKLKDKGVDVDHIIELIHQIFNIVRDRGLPEDLQDFLALIPTDQVLAAADYLANDAEVKAAVEYLKSD
 EFETIVVTVDLSPEFKNFLNFLTNGLNIAIEFLNNIHDLGLIPHIPVTARKHLRRGVGITGLIDDIIAILPVDDLALFQ
 EKLETSPEFKALYDAIRSPEFQSIVETLKAMPEYQSLIQKLKDKGVDVDHIIELIHQIFNIVRDRGLPEDLQDFLALIP
 IDQILAAADYLANDAEVQAAVEYLKSDDEFETIVVTVDLSPEFKNFLNFLTNGLNIAIEFINNIHDLGLIPHIPATGRKH
 VRRGVINGLIDDVIAILPVDELALFQEKLESSPEFKALYDAIRSPEFQSIVQTLKAMPEYQDLIQLKDKGVDVDHFI
 ELIKKLFGLSH

2-79

AIEFLNNIHDLGLIPHIPVTARKHHRGVTGLIDDI IAILPVDDLYALFQEKLETSPEFKALYDAIRSPEFQSIVGTL
 EAMPEYQNLIQKLKDKGVDVDHIIELIHQIFNIVRDRGLPEDLQDFLALIPTDQVLAIAADYLANDAEVKA AVEYLKSD
 EFETIVVTVDSLPEFKNFLNFLQTNGLNAIEFLNNIHDLGLIPHIPVTARKHLRRGVGITGLIDDI IAILPVDDLYALFQ

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EKLETSPEFKALYDAIRSPEFQSIIVETLKAMPEYQSLIQKLKDKGVDVDHIEELIHQIFNIVRDTRGLPEDLQDFLALIP
IDQILAIAADYLANDAEVQAAYEYLKSDEFETIVVTVDLSPEFKNFLNFLTQTNGLNAIEFINNIHDLLGIPHIPATGRKH
VRRGVGINGLIDDVIAILPVDELYALFQEKLESSPEFKALYDAIRSPEFQSIIVQTLKAMPEYQDLIQRKDKGVDVDHFI
ELIKKLFGLSH

22

AIEFLNNIHDLLGIPHIPVTARKHHRRGVGITGLIDDIIAILPVDDLYALFQEKLETSPEFKALYDAIRSPEFQSIIVGTL
EAMPEYQNLIQKLKDKGVDVDHIEELIHQIFNIVRDTRGLPEDLQDFLALIPDQVLAIAADYLANDAEVKAAYEYLKSD
EFETIVVTVDLSPEFKNFLNFLTQTNGLNAIEFLNNIHDLLGIPHIPVTARKHLRRGVGITGLIDDIIAILPVDDLYALFQ
EKLETSPEFKALYDAIRSPEFQSIIVETLKAMPEYQSLIQKLKDKGVDVDHIEELIHQIFNIVRDTRGLPEDLQDFLALIP
IDQILAIAADYLANDAEVQAAYEYLKSDEFETIVVTVDLSPEFKNFLNFLTQTNGLNAIEFINNIHDLLGIPHIPATGRKH
VRRGVGINGLIDDVIAIPVDELYALFQEKLESSPEFKALYDAIRSPEFQSIIVQTLKAMPEYQDLIQRKDKGVDVDHFI
ELIKKLFGLSH

1-31

AIEFLNNIHDLLGIPHIPVTARKHHRRGVGITGLIDDITAILPVDDLYALFQEKLETSPEFKALYDAIRSPEFQSIIVGTL
EAMPEYQNLIQKLKDKGVDVDHIEELIHQIFNIVRDTRGLPEDLQDFLALIPDQVLAIAADYLANDAEVKAAYEYLKSD
EFETIVVTVDLSPEFKNFLNFLTQTNGLNAIEFLNNIHDLLGIPHIPVTARKHLRRGVGITGLIDDIIAILPVDDLYALFQ
EKLETSPEFKALYDAIRSPEFQSIIVETLKAMPEYQSLIQKLKDKGVDVDHIEELIHQIFNIVRDTRGLPEDLQDFLALIP
IDQILAIAADYLANDAEVQAAYEYLKSDEFETIVVTVDLSPEFKNFLNFLTQTNGLNAIEFINNIHDLLGIPHIPATGRKH
VRRGVGINGLIDDVIAILPVDELYALFQEKLESSPEFKALYDAIRSPEFQSIIVQTLKAMPEYQDLIQRKDKGVDVDHFI
ELIKKLFGLSH

1-97

AIEFLNNIHDLLGIPHIPVTARKHHRRGVGITGLIDDIIAILPVDDLYALFQEKLETSPEFKALYDAIRSPEFQSIIVGTL
EAMPEYQNLIQKLKDKGVDVDHIEELIHQIFNIVRDTRGLPEDLQDFLALIPDQVLAIAADYLANDAEVKAAYEYLKSD
EFETIVVTVDLSPEFKNFLNFLTQTNGLNAIEFLNNIHDLLGIPHIPVTARKHLRRGVGITGLIDDIIAILPVDDLYALFQ
EKLETSPPFKALYDAIRSPEFQSIIVETLKAMPEYQSLIQKLKDKGVDVDHIEELIHQIFNIVRDTRGLPEDLQDFLALIP
IDQILAIAADYLANDAEVQAAYEYLKSDEFETIVVTVDLSPEFKNFLNFLTQTNGLNAIEFINNIHDLLGIPHIPATGRKH
VRRGVGINGLIDDVIAILPVDELYALFQEKLESSPEFKALYDAIRSPEFQSIIVQTLKAMPEYQDLIQRKDKGVDVDHFI
ELIKKLFGLSH

2-12

AIEFLNNIHDLLGIPHIPVTARKHHRRGVGITGLIDDIIAILPVDDLYALFQEKLETSPEFKALYDAIRSPEFQSIIVGTL
EAMPEYQNLIQKLKDKGVDVDHIEELIHQIFNIVRDTRGLPEDLQDFLALIPDQVLAIAADYPANDADEVKAAYEYLKSD
EFETIVVTVDLSPEFKNFLNFLTQTNGLNAIEFLNNIHDLLGIPHIPVTARKHLRRGVGITGLIDDIIAILPVDDLYALFQ
EKLETSPEFKALYDAIRSPEFQSIIVETLKAMPEYQSLIQKLKDKGVDVDHIEELIHQIFNIVRDTRGLPEDLQDFLALIP
IDQILAIAADYLANDAEVQAAYEYLKSDEFETIVVTVDLSPEFKNFLNFLTQTNGLNAIEFINNIHDLLGIPHIPATGRKH
VRRGVGINGLIDDVIAILPVDELYALFQEKLESSPEFKALYDAIRSPEFQSIIVQTLKAMPEYQDLIQRKDKGVDVDHFI
ELIKKLFGLSH

2-15

AIEFLNNIHDLLGIPHIPVTARKHHRRGVGITGLIDDIIAILPVDDLYALFQEKLETSPEFKALYDAIRSPEFQSIIVGTL
EAMPEYQNLIQKLKDKGVDVDHIEELIHQIFNIVRDTRGLPEDLQDFLALIPDQVLAIAADYLANDAEVKAAYEYLKSD
EFETIVVTVDLSPELKNFLNFLTQTNGLNAIEFLNNIHDLLGIPHIPVTARKHLRRGVGITGLIDDIIAILPVDDLYALFQ
EKLETGPEFKALYDAIRSPEFQSIIVETLKAMPEYQSLIQKLKDKGVDVDHIEELIHQIFNIVRDTRGLPEDLQDFLALIP
IDQILAIAADYLANDAEVQAAYEYLKSDEFETIVVTVDLSPEFKNFLNFLTQTNGLNAIEFINNIHDLLGIPHIPATGRKH
VRRGVGINGLIDDVIAILPVDELYALFQEKLESSPEFKALYDAIRSPEFQSIIVQTLKAMPEYQDLIQRKDKGVDVDHFI
ELIKKLFGLSH

2-61

AIEFLNNIHDLLGIPHIPVTARKHHRRGVGITGLIDDIIAILPVDDLYALFQEKLETSPEFKALYDAIRSPEFQSIIVGTL
EAMPEYQNLIQKLKDKGVDVDHIEELIHQIFNIVRDTRGLPEDLQDFLALIPDQVLAIAADYRANDAEVKAAYEYLKSD
EFETIVVTVDLSPEFKNFLNFLTQTNGLNAIEFLNNIHDLLGIPHIPVTARKHLRRGVGITGLIDDIIAILPVDDLYALFQ
EKLETSPEFKALYDAIRSPEFQSIIVETLKAMPEYQSLIQKLKDKGVDVDHIEELIHQIFNIVRDTRGLPEDLQDFLALIP
IDQILAIAADYLANDAEVQAAYEYLKSDEFETIVVTVDLSPEFKNFLNFLTQTNGLNAIEFINNIHDLLGIPHIPATGRKH
VRRGVGINGLIDNVIAILPVDELYALFQEKLESSPEFKALYDAIRSPEFQSIIVQTLKAMPEYQDLIQRKDKGVDVDHFI
ELIKKLFGLSH

2-62

AIEFLNNIHDLLGIPHIPVTARKHLRRGVGITGLIDDIIAILPVDDLYALFQEKLETSPEFKALYDAIRSPEFQSIIVGTL
EAMPEYQNLIQKLKDKGVDVDHIEELIHQIFNIVRDTRGLPEDLQDFLALIPDQVLAIAADYLANDAEVKAAYEYLKSD
EFETIVVTVDLSPEFKNFLNFLTQTNGLNAIEFLNNIHDLLGIPHIPVTARKHLRRGVGITGLIDDIIAILPVDDLYALFQ
EKLETSPEFKALYDAIRSPEFQSIIVETLKAMPEYQSLIQKLKDKGVDVDHIEELIHQIFNIVRDTRGLPEDLQDFLALIP
IDQILAIAADYLANDAEVQAAYEYLKSDEFETIVVTVDLSPEFKNFLNFLTQTNGLNAIEFINNIHDLLGIPHIPATGRKH
VRRGVGINGLIDDVIAILPVDELYALFQEKLESSPEFKALYDAIRSPEFQSIIVQTLKAMPEYQDLIQRKDKGVDVDHFI
ELIKKLFGLSH

4

AIEFLNNIHDLLGIPHIPVTARKHHRRGVGITGLIDDIIAILPVDDLYALFQEKLETSPEFKALYDAIRSPEFQSIVGTL
EAMPEYQNLIQKLKDKGVDVDHIEELIHQIFNIVRDTRGLPEDLQDFLALIPDQVLAIAADYLANDAEVKA AVEYLKSD
EFETIVVTVDLSPEFKNFLNFLTNGLN AIEFLNNIHVLLGIPHIPVTARKHLRRGVGITGLIDDIIAILPVDDLYALFQ
EKLETSPEFKALYDAIRSPEFQSIVETLKAMPEYQSLIQKLKDKGVDVDHIEELIHQIFNIVRDTRGLPEDLQDFLALIP
IDQILAIAADYLANDAEVQA AVEYLKSD EFETIVVTVDLSPEFKNFLNFLTQMNGLN AIEFINNIHDLLGIPHIPATGRKH
VRRGVGINGLIDDVIAILPVDELYALFQEKLESSPEFKALYDAIRSPEFQSIVQTLKAMPEYQDLIQRLKDKGVDVDHFI
ELIKKLFGLSH

11

AIEFLNNIHDLLGIPHIPVTARKHHRRGVGITGLIDDIIAILPVDDLYALFQEKLGTSPEFKALYDAIRSPEFQSIVGTL
EAMPEYQNLIQKLKDKGVDVDHIEELIHQIFNIVRDTRGLPEDLQDFLALIPDQVLAIAADYLANDAEVKA AVEYLKSD
EFETIVVTVDLSPEFKNFLNFLTNGLN AIEFLNNIHDLLGIPHIPVTARKHLRRGVGITGLIDDIIAILPVDDLYALFQ
EKLETSPEFKALYDAIRSPEFQSIVETLKAMPEYQSLIQKLKDKGVDVDHIEELIHQIFNIVRDTRGLPEDLQDFLALIP
IDQILAIAADYLANDAEVQA AVEYLKSD EFETIVVTVDLSPEFKNFLNFLTQMNGLN AIEFINNIHDLLGIPHIPATGRKH
VRRGVGINGLIDDVIAILPVDELYALFQEKLESSPEFKALYDAIRSPEFQSIVQTLKAMPEYQDLIQRLKDKGVDVDHFI
ELIKKLFGLSH

2-32

AIEFLNNIHDLLGIPHIPVTARKHHRRGVGITGLIDDIIAILPVDDLYALFQEKLETSPEFKALYDAIRSPEFQSIVGTL
EAMPEYQNLIQKLKDKGVDVDHIEELIHQIFNIVRNTRGLPEDLQDFLALIPDQVLAIAADYLANDAEVKA AVEYLKSD
EFETIVVTVDLSPETKNFLNFLTNGLN AIEFLNNIHDLLGIPHIPVTARKHLRRGVGITGLIDDIIAILPVDDLYALFQ
EKLETSPEFKALYDAIRSPEFQSIVETLKAMPEYQSLIQKLKDKGVDVDHIEELIHQIFNIVRDTRGLPEDLQDFLALIP
IDQILAIAADYLANDAEVQA AVEYLKSD EFETIVVTVDLSPEFKNFLNFLTQMNGLN AIEFINNIHDLLGIPHIPATGRKH
VRRGVGINGLIDDVIAILPVDELYALFQEKLESSPEFKALYDAIRSPEFQSIVQTLKAMPEYQDLIQRLKDKGVDVDHFI
ELIKKLFGLSH

2-74

AIEFLNNIHDLLGIPHIPVTARKHHRRGVGITGLIDDIIAILPVDDLYALFQEKLETSPEFKALYDAIRSPEFQSIVGTL
EAMPEYQNLIQKLKDKGVDVDHIEELIHQIFNIVRNTRGLPEDLQDFLALIPDQVLAIAADYLANDAEVKA AVEYLKSD
EFETIVVTVDLSPETKNFLNFLTNGLN AIEFLNNIHDLLGIPHIPVTARKHLRRGVGITGLIDDIIAILPVDDLYALFQ
EKLETSPEFKALYDAIRSPEFQSIVETLKAMPEYQSLIQKLKDKGVDVDHIEELIHQIFNIVRDTRGLPEDLQDFLALIP
IDQILAIAADYLANDAEVQA AVEYLKSD EFETIVVTVDLSPEFKNFLNFLTQMNGLN AIEFINNIHDLLGIPHIPATGRKH
VRRGVGINGLIDDVIAILPVDELYALFQEKLESSPEFKALYDAIRSPEFQSIVQTLKAMPEYQDLIQRLKDKGVDVDHFI
ELIKKLFGLSH

13

AIEFLNNIHDLLGIPHIPVTARKHHRRGVGITGLIDDIIAILPVDDLYALFQEKLETSPEFKALYDAIRSPEFQSIVGTL
EAMPEYQNLIQKLKDKGVDVDHIEELIHQIFNIVRNTRGLPEDLQDFLALIPDQVLAIAADYLANDAEVKA AVEYLKSD
EFETIVVTVDLSPETKNFLNFLTNGLN AIEFLNNIHDLLGIPHIPVTARKHLRRGVGITGLIDDIIAILPVDDLYALFQ
EKLETSPEFKALYDAIRSPEFQSIVETLKAMPEYQSLIQKLKDKGVDVDHIEELIHQIFNIVRDTRGLPEDLQDFLALIP
IDQILAIAADYLANDAEVQA AVEYLKSD EFETIVVTVDLSPEFKNFLNFLTQMNGLN AIESINNIHDLLGIPHIPATGRKH
VRRGVGINGLIDDVIAILPVDELYALFQEKLESSPEFKALYDAIRSPEFQSIVQTLKAMPEYQDLIQRLKDKGVDVDHFI
ELIKKLFGLSH

14

AIEFLNNIHDLLGIPHIPVTARKHHRRGVGITGLIDDIIAILPVDDLYALFQGKLETSPEFKALYDAIRSPEFQSIVGTL
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IDQILAIAADYLANDAEVQA AVEYLKSD EFETIVVTVDLSPEFKNFLNFLTQMNGLN AIEFINNIHDLLGIPHIPATGRKH
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ELIKKLFGLSH

3

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EKLETSPEFKALYDAIRSPEFQSIVETLKAMPEYQSLIQKLKDKGVDVDHIEELIHQIFNIVRDTRGLPEDLQDFLALIP
IDQILAIAADH LANDTEVQA AVEYLKSD EFETIVVTVDLSPEFKNFLNFLTQMNGLN AIEFINNIHDLLGIPHIPATGRKH
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ELIKKLFGLSH

2-71

AIEFLNNIHDLLGIPHIPVTARKHHRRGVGITGLIDDIIAILPVDDLYALFQEKLETSPEFKALYDAIRSPEFQSSVGTL
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EKLETSPEFKALYDAIRSPEFQSIVETLKAMPEYQSLIQKLKDKGVDVDHIEELIHQIFNIVRDTRGLPEDLQDFLALIP

Sequences Bla g 1.2.4.5 20070817Jeong KY.txt

IDQILAIADYLANDAEVQAAYEYLKSDDEFETIVVTVDLSPEFKNFLNFLQMGNLNAIEFINNIHDLLGIPHIPATGRKH
VRRGVINGLIDDVIAILPVDELYALFQEKLESSPEFKALYDAIRSPEFQSIVQTLKAMPEYQDLIQRKDKGVDVDHFI
ELIKKLFGLSH

2-40

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EKLETSPFEKALYDAIRSPEFQSIVETLKAPEYQSLIQKLKDKGVDVDHIEELIHQIFNIVRDTRGLPEDLQDFLALIP
IDQILAIADYLANDAEVQAAYEYLKSDDEFETIVVTVDLSPEFKNFLNFLQMGNLNAIEFINNIHDLLGIPHIPATGRKH
VRRGVINGLIDDVIAILPVDELYALFQEKLESSPEFKALYDAIRSPEFQSIVQTLKAMPEYQDLIQRKDKGVDVDHFI
ELIKKLFGLSH

Bla g 2

U28863

MIGLKLVTVLFAVATITHAAELQRVPLYKLVHVFINTQYAGITKIGNQNFLTTFDSTSCNVVVASQECVGGACVCPNLQK
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SKAIIVGPKAYVNPINEAIGCVVEKTTTTRICKLDCSKIPSLPDVTFVINGRNFNISSQYYIQNGNLCSYSGFQPCGHSD
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Bla g 2.0101

1-43

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LENFVEENLIAPVFSIHARFQDGEHFGEIIFGGSDWKYVDGEFTYVPLVGDDSWKFRLDGVKIGDTTVAPAGTQAIIDT
SKAIIVGPKAYVNPINEAIGCVVEKTTTTRICKLDCSKIPSLPDVTFVINGRNFNISSQYYIQNGNLCSYSGFQPCGHSD
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Bla g 2.0201

44-45

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46

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47

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48

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LENFVEENLIAPVFSIHARFQDGEHFGEIIFGGSDWKYVDGESTYVPLVGDDSWKFRLDGVKIGDTTVAPAGTQAIIDT
SKAIIVGPKAYVNPINEAIGCVVEKTTTTRICKLDCSKIPSLPDVTFVINGRNFNISSQYYIQNGNLCSYSGFQPCGHSD
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49

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LENFVEENLIAPVFSIHARFQDGEHFGEIIFGGSDWKYVDGEFTYVPLVGDDSWKFRLDGVKIGDTTVAPAGTQAIIDT
SKAIIVGPKAYVNPINEAIGCVVEKTTTTRICKLDCSKIPSLPDVTFVINGRNFNISSQYYIQNGNLCSYSGFQPCGHSD
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50

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LENFVEENLIAPVFSIHARFQDGEHFGEIIFGGSDWKYVDGEFTYVPLVGDDSWKFRLDGVKIGDTTVAPAGTQAIIDT

Sequences Bla g 1.2.4.5 20070817Jeong KY.txt

SKAIIVGPKAYVNPINEAIGCVVEKTTTTRICKLDCKSLPDVTFVINGRNFNISSQYYIQNGNLCSYSGFQPCGHSD
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51

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SKAIIVGPKAYVNPINEAIGCVVEKTTTTRICKLDCKSLPDVTFVINGRNFNISSQYYIQNGNLCSYSGFQPCGHSD
HFFIGDFFVDHYYSEFNWENKTMGFGRSVESV

52

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53

MIGLKLVTVLFAVATITHAAELQRVPLYKLVHVFINTQYAGITKIGNQNFLTTFDSTSCNWWWASQECVGGACVCPNLQK
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LENFVEENLIAPVFSIHARFQDGEHFGEIIFGGSDWKYVDGEFTYVPLVGDDSWKFRLDGVKIGDTTVAPAGTQAIIDT
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54

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LENFVEENLIAPVFSIHARFQDGEHFGEIIFGGSDWKYVDGEFTYVPLVGDDSWKFRLDGVKIGDTTVAPAGTQAIIDT
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55

MIGLKLVTVLFAVATITHAAELQRVPLYKLVHVFINTQYAGITKIGNQNFLTTFDSTSCNWWWASQECVGGACVCPNLQK
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LENFVEENLIAPVFSIHARFQDGEHFGEIIFGGSDWKYVDGEFTYVPLVGDDSWKFRLDGVKIGDTTVAPAGTQAIIDT
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56

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SKAIIVGPKAYVNPINEAIGCVVEKTTTTRICKLDCKSLPDVTFVINGRNFNISSQYYIQNGNLCSYSGFQPCGHSD
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57

MIGLKLVTVLFAVATITHAAELQRVPLCKLVHVFINTQYAGITKIGNQNFLTTFDSTSCNWWWASQECVGGACVCPNLQK
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LENFVEENLIAPVLSIHARFQDGEHFGEIIFGGSDWKYVDGEFTYVPLVGDDSWKFRLDGVKIGDTTVAPAGTQAIIDT
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58

MIGLKLVTVLFAVATITHAAELQRVPLYKLVHVFINTQYAGITKIGNLNFLTTFDSTSCNWWWASQECVGGACVCPNLQK
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LENFVEENLIAPVFSIHARFQDGEHFGEIIFGGSDWKYVDGEFTYVPLVGDDSWKFRLDGVKIGDTTVAPAGTQAIIDT
SKAIIVGPKAYVNPINEAIGCVVEKTTTTRICKLDCKSLPDVTFVINGRNFNISSQYYIQNGNLCSYSGFQPCGHSD
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59

MIGLKLVTVLFAVATITHAAELQRVPLYKLVHVFINTQYAGITKIGNQNFLTTFDSTSCNWWWASQECVGGACVCPNLQK
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LENFVEENLIAPVFSIHARFQDGEHFGEIIFGGSDWKYVDGEFTYVPLVGDDSWKFRLDGVKIGDTTVAPAGTQAIIDT
SKAIIVGPKAYVNPINEAIGCVVEKTTTTRICKLDCKSLPDVTFVINGRNFNISSQYYIQNGNLCSYSGFQPCGHSD
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60

MIGLKLVTVLFAVATITHAAELQRVPLYKLVHVFINTQYAGITKIGNQNFLTTFDSTSCNWWWASQECVGGACVCPNLQK

Sequences Bla g 1.2.4.5 20070817Jeong KY.txt

YEKLPKYISDGNVQVKFFDTGSAVGRGIEDSLTISNLTTSQQDIVLADELSQEVCLISADGVVGLAAGPCPNALKGKTV
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SKAIIVGPKAYVNPINEAIGCVVEKTTTTRICKLDCSKIPSLPDVTFVINGRNFNTSSQYYIQNGNLCYSGFQPCGHSD
HFFIGDFFVDHYYSEFNWENKTMGFGRSVESV

61

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62

MIGLKLVTVLFAVATITHAAELQRVPLYKLVHVFINTQYAGITKIGSQNFLTVFDSTSCNWWWASQECVGGACVCPNLQK
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63

MIGLKLVTVLFAVATITHAAELQRVPLYKLVHVFINTQYAGITKIGNQNFLTVFDSTSCNWWWASQECVGGACVCPNLQK
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64

MIGLKLVTVLFAVATITHAAELQRVPLYKLVHVFINTQYAGITKIGNQNFLTVFDSTSCNWWWASQECVGGACVCPNLQK
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65

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66

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LENFVEENLIAPVFSIHARFQDGEHFGEIIFGGSDWKYVDGEFTYVPLMGDDSWKFRLDGVKIGDTTVAPAGTQAIIDT
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67

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SKAIIVGPKAYVNPINEAIGCVVEKTTTTRICKLDCSKIPSLPDVTFVINGRNFNISSQYYIQNGNLCYSGFQPCGHSD
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68

MIGLKLVTVLFAVATITHAAELQRVPLYKLVHVFINTQYAGITKIGNQNFLTVFDSTSCNWWWASQECVGGACVCPNLQK
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69

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Sequences Bla g 1.2.4.5 20070817Jeong KY.txt

70

MIGLKLVTVLFAVATITHAAELQRVPLYKLVHVFINTQYAGITKIGNQNFLTTFDSTSCNVVVASQECVGGACVCPNLQK
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LENFVEENLIAPVFSIHARFQDGEHFGEIIFGGSDWKYVDGEFTYVPLVGDDSWKFRLDGVKIGDTTVAPAGTQAIIDT
SKAIIVGPKAYVNPINEAIGCVVEKTTTTRICKLDCSKIPSLPDVTFVINGRNFNISSQYYIQNGNLCSYSGFQPCGHSD
HFFIGDFFVDHYYSEFNWENKTMGFGRSVESV

71

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Bla g 4

NCBI

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NCBI U40767

SV03

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uguale a NCBI U40767

SV46

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SV18

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SV28

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SV23

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SV19

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SV39

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SV25

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SVt3

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SVt5

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Sequences Bla g 1.2.4.5 20070817Jeong KY.txt

KAIEEDLKHFNLKYEDLHSTCH

SVt1

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SV04

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SV61

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SV43

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KAIEEDLRHFNLKYEDLHSTCH

SV66

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SV08

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SV05

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SV48

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SV07

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SV21

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SV06

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SV22

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SV42

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SV15

Sequences B1a g 1.2.4.5 20070817Jeong KY.txt

AVLALCATDTLAEDECFRHESLVPNLDERFRGMWVIVAGTSEALTQYKCWIDWFSYDDALVSKYTDSKQGNKILIGKIK
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SV01

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Svt2

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SV13

AVLALCATDTLAKEDCFKHESLVPNLDEYKFRGMWVIAAGTSEALTQYNCWNDLFLYNNVLGSSHMDSNGNNNTITGRT
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B1a g 5

YKLTYPVKALGEPPIRFLLSYGEKDFEDYRFQEGDWPVKLPSPMPFGKTPVLEIDGKQTHQSVAISRYLGKQFGLSGKDDW
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5-1

YKLTYPVKALGEPPIRFLLSYGEKDFEDYRFQEGDWPVKLPSPMPFGKTPVLEIDGKQTHQSVAISRYLGKQFGLSGKDDW
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B1a g 5.0201

5-5

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5-12

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5-24

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5-94

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5-102

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5-104

YKLTYPVKALGEPPIRFLLSYGEKDFEDYRFQEGDWPVKLPSPMPFGKTPVLEIDGKQTHQSVAISRYLGKQFGLSGKDDW
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5-115

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NHMAKEDLVANQPNLKALREKVLGLPAIKAWVAKRPPTDL