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The rhomboids: a near ubiquitous family of intramembrane serine proteases evolved via multiple horizontal gene transfers

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The rhomboids: a near ubiquitous family of intramembrane serine proteases evolved via multiple horizontal gene transfers

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Abstract

Background. The rhomboid family consists of polytopic membrane proteins, which show a level of evolutionary conservation that is unique among membrane proteins. The rhomboids are present in nearly all sequenced genomes of archaea, bacteria and eukaryotes, with the exception of several species with small genomes. On the basis of experimental studies with the developmental regulator Rhomboid from *Drosophila* and the AarA protein from the bacterium *Providencia stuartii*, the rhomboids are thought to be intramembrane serine proteases whose signaling function is conserved in eukaryotes and prokaryotes.

Results. Phylogenetic tree analysis suggests that, despite the broad distribution in all three kingdoms of life, the rhomboid family was not present in the last universal common ancestor of the extant life forms, but instead evolved in bacteria and has been acquired by archaea and eukaryotes via several independent horizontal gene transfer events. In eukaryotes, two distinct, ancient horizontal acquisitions apparently gave rise to the two major subfamilies typified by Rhomboid and PARL (presenilin-associated Rhomboid-

like protein), respectively. The subsequent evolution of the rhomboid family in eukaryotes proceeded via multiple duplications and functional diversification through the addition of extra transmembrane helices and other domains in different orientations relative to the conserved core that harbors the protease activity.

Conclusions. Although the near universal presence of the rhomboid family in bacteria, archaea and eukaryotes appears to suggest that this protein is part of the heritage of the last universal common ancestor, phylogenetic tree analysis indicates bacterial origin with subsequent dissemination via horizontal gene transfer. This emphasizes the importance of explicit phylogenetic analysis for the reconstruction of ancestral life forms. A hypothetical scenario of origin of intracellular membrane proteases from membrane transporters is proposed.

Background

Polytopic transmembrane proteins are, in general, not particularly strongly conserved during evolution. Inspection of the database of Clusters of Orthologous Groups of proteins (COGs) [1] revealed only one family of such proteins that is represented in most of the sequenced bacterial, archaeal and eukaryotic genomes. The prototype of this family is the Rhomboid (RHO) protein from *Drosophila melanogaster*, a developmental regulator involved in epidermal growth factor (EGF)-dependent signaling pathways [2-4]. Not only were homologs of Rhomboid detected in prokaryotes and eukaryotes, but the pattern of sequence conservation in this family appeared uncharacteristic of non-enzymatic membrane proteins, such as transporters [5, 6]. Specifically, several polar amino acid residues are conserved in nearly all members of the Rhomboid family, suggesting the possibility of an enzymatic activity. Since three of these conserved residues were histidines, it has been hypothesized that rhomboid family proteins could function as metal-dependent membrane proteases [5, 6]. Recently, however, it has been shown that RHO cleaves a transmembrane helix (TMH) in the membrane-bound precursor of the TGF α -like growth factor Spitz, enabling the released Spitz to activate the EGF receptor, and that a conserved serine and a conserved histidine in RHO are essential for this cleavage [7, 8]. Thus, it appears that Rhomboid family proteins are a distinct group of intramembrane serine proteases. Altogether, the genome of *Drosophila* encodes 7 RHO paralogs (now designated RHO1-7, with the original Rhomboid becoming RHO-1), at least three of which are involved in distinct EGF-dependent pathways, apparently through proteolytic activation of diverse ligands of the EGF receptor [9, 10].

The newly discovered intramembrane proteolytic activity of RHO places the rhomboid family within the framework of regulated intramembrane proteolysis (RIP), a new paradigm of signal transduction, which appears to be prominent in all forms of life [11, 12]. Under RIP, signaling proteins undergo site-specific proteolysis within TMH, resulting in the release of active fragments, which are the actual effectors in signal transduction cascades. Until recently, the only characterized cases of RIP in eukaryotes involved presenilin, an aspartyl protease, which cleaves a transmembrane helix in type I membrane proteins, such as amyloid precursor protein (APP), Notch, and Ire1 [13], and S2P, a metalloprotease, which cleaves a TMH in a type 2 transmembrane protein, the sterol-dependent transcription factor SREBP [11]. Notably, S2P has highly conserved bacterial homologs, and the protease domain of presenilin also might be homologous to bacterial and archaeal type IV prepilin peptidases, although, in this case, the sequence similarity is very low [14, 15].

In the case of the rhomboid family, the existence of homologs of RHO in most prokaryotes is particularly remarkable because animal RHO proteins are involved in signaling pathways that are not found outside metazoa, which seems to make functional conservation in prokaryotes a remote possibility. The only prokaryotic protein of the rhomboid family that has been characterized experimentally in considerable detail is AarA from the bacterium *Providencia stuartii* [16, 17]. This protein is involved in the export of a quorum-sensing peptide, a function that, in physiological terms, resembles that of RHO, although the signaling molecules, other than RHO and AarA, are obviously unrelated [18]. In a striking recent development, two independent research groups have shown that several bacterial rhomboid family proteins, including AarA, were capable of cleaving the EGFR receptor ligands (Spitz, Keren and Gurken) that are normally cleaved

by RHO paralogs [19, 20]. The cleavage depended on the conserved serine and histidine residues paralogs [19] and, moreover, transgenic flies that expressed AarA developed a phenotype indistinguishable from that induced by overexpression of RHO, whereas RHO could substitute for AarA in *Providencia stuartii* [20]. These unexpected findings demonstrated the conservation of a RIP mechanism producing extracellular signals in eukaryotes and prokaryotes.

The near ubiquity of rhomboid family proteins among bacteria, archaea and eukaryotes, along with the remarkable functional conservation, suggest that a signaling mechanism mediated by rhomboids might have functioned already in the last common ancestor of all extant life forms, with subsequent loss in several lineages. To address this possibility, we performed a detailed phylogenetic analysis of the rhomboid family.

Results and Discussion

Sequence and structural features and phyletic distribution and of the rhomboid family

Although the sequence similarity between eukaryotic and prokaryotic rhomboid family proteins is relatively low (at the level of 15-10% identity in the conserved region), the entire superfamily could be retrieved from the protein sequence databases within three iterations of the PSI-BLAST program with a high statistical significance and without any false positives. The conserved core of the rhomboid family consists of six conserved TMH (Fig. 1). The predicted catalytic serine is located in TMH5, whereas the predicted catalytic histidine is in TMH7; TMH3 contains two additional histidines and an asparagine, which are conserved in the great majority of the rhomboid family proteins (Fig. 1). The roles of these conserved residues are not known, but, given the remarkable

evolutionary conservation, it seems likely that they also contribute to catalysis; indeed, it has been shown that the conserved asparagine is required for the cleavage of Spitz by RHO.

When examining the multiple alignment of the Rhomboid superfamily proteins, we noticed that several eukaryotic members appear to be inactivated proteases as indicated by the loss of the predicted catalytic serine or histidine (Fig. 1 and data not shown); these inactivated forms could be regulators of active rhomboid proteases. Several other proteins lack one or more of the conserved residues in TMH3; it remains unclear whether or not these are active proteases.

Bacterial and archaeal members of the Rhomboid superfamily contain 6 TMH, whereas the eukaryotic members typically have an additional, 7th TMH, which may be attached to the core either from the N-terminus or from the C-terminus as discussed below.

The phyletic distribution pattern of the rhomboid family shows that this intramembrane protease is extremely common in all three kingdoms of life, but is not necessarily essential for cell function. Rhomboids are missing in the microsporidium *Encephalitozoon cuniculi*, a eukaryotic intracellular parasite with a highly degraded genome, the archaea *Methanothermobacter thermoautotrophicus* and *Thermoplasma volcanium*, and several bacterial species, primarily parasites with small genomes but also species with moderate-size genomes, such as *Xylella fastidiosum* (see COG0705 at <http://www.ncbi.nlm.nih.gov/COG/>). On two occasions, a representative of the rhomboid family is present in only one of a pair of relatively close genomes (present in *T. acidophilum* but missing in *T. volcanium*; present in the spirochete *Treponema pallidum*

but missing in the related bacterium *Borrelia burgdorferi*), which suggests relatively recent, repeated losses of this gene. Most of the prokaryotic species encode a single gene coding for a rhomboid family protein, although some have two-three paralogs (see COG0705 at <http://www.ncbi.nlm.nih.gov/COG/>); in contrast, eukaryotes show expansion of the rhomboid family, with 7 members in *Drosophila*, and as many as 13 in *Arabidopsis*.

Phylogeny and evolutionary history of the rhomboid family

The multiple alignment of the 6-TMH core of the rhomboid family (Fig. 1) was employed to construct a phylogenetic tree using the least-square algorithm with subsequent optimization using the maximum likelihood method (see Materials and Methods). Only the conserved regions including the TMH and short adjacent stretches shown in Figure 1 were used as the input for tree building, whereas the poorly conserved intervening regions were omitted to avoid the noise from potentially misaligned residues. The resulting phylogenetic tree of the rhomboid family presents a complex and unexpected picture (Fig. 2). Neither the eukaryotic nor the archaeal subsets of the family appear to form monophyletic clades. Instead, the eukaryotic rhomboids are split between two major subfamilies, which are positioned in the midst of different prokaryotic branches (Fig. 2). The first subfamily, which includes 6 of the 7 *Drosophila* rhomboids, clusters with a distinct prokaryotic assemblage, which consists primarily of Gram-positive bacteria as well as a subset of archaeal rhomboids; this clade is strongly supported by bootstrap analysis (Fig. 2). The proteins in this group of eukaryotic rhomboids, which we designated the RHO-subfamily, typically have an extra TMH

added C-terminally of the 6-TMH core; some of these proteins also contain EF-hand Ca-binding domains N-terminally of the core (Fig. 2).

The second eukaryotic subfamily, which we designated the PARL-subfamily, after presenilin-associated rhomboid-like protein (PARL), the human ortholog of *Drosophila* Rhomboid 7 [6], resides within a large, heterogeneous prokaryotic cluster (Fig. 2). Within this subfamily, PARL and its orthologs from other animals and fungi, have a distinct domain architecture, with an extra TMH added to the N-terminus of the core, whereas the rest have only the core (a C-terminal TMH and a ubiquitin-associated domain are appended in one *Arabidopsis* protein; Fig. 2). Thus, the existence of two distinct subfamilies of eukaryotic rhomboids is supported by features of domain architectures that appear to comprise shared derived characters. Within these two major eukaryotic subfamilies, evolution apparently proceeded via both ancient and more recent duplications. Several lineage-specific expansions of paralogs [21] are noticeable, in insects, mammals and plants (Fig. 2).

Archaeal rhomboids are scattered over the phylogenetic tree, with two major clusters and three more isolated proteins joining different bacterial branches (Fig. 2). There is no indication of an affinity between any of the archaeal and eukaryotic rhomboids. Although many of the bacterial rhomboids form phylogenetically coherent clusters corresponding to the established bacterial lineages, there are also several clusters that have odd composition, such as grouping of proteobacterial and Gram-positive species; some of these clusters are well supported by bootstrap (see clusters 1-4 in Fig. 2).

The phylogenetic tree of the rhomboid family tree shown in Figure 2 clearly follows neither the “standard model” scenario [22, 23], with the major split between the archaeo-eukaryotic and bacterial lineages nor the “mitochondrial” scenario, which postulates acquisition of a gene by eukaryotes from the pro-mitochondrial endosymbiont. Neither can this tree be explained by postulating a small number of lineage-specific gene losses. The parsimonious interpretation of the rhomboid family seems to be that the evolutionary history of this family had been replete with horizontal gene transfer (HGT) and lineage-specific gene loss events. In particular, in spite of the presence of rhomboids in the majority of modern life forms from all three primary kingdoms, phylogenetic analysis suggests that this family had not been inherited from LUCA. Instead, the tree topology seems to indicate that this family emerged in some bacterial lineage and afterwards had been widely disseminated via HGT, and then lost in some lineages. Both archaea and eukaryotes seems to have acquired rhomboids on several independent occasions. In particular, at least two HGT events seem to have contributed to the origin of eukaryotic rhomboids, one of them yielding the RHO-subfamily and the other one the PARL-subfamily, with a possible additional HGT in plants (Fig. 2). Given the broad phyletic representation of both subfamilies of eukaryotic rhomboids, both the RHO-subfamily and the PARL-subfamily must have been acquired via HGT at an early stage of eukaryotic evolution, definitely before the divergence of the major crown-group lineages. This early epoch in eukaryotic evolution is thought to have been dominated by HGT from multiple bacterial symbionts [24, 25].

Two alternatives to this multiple-HGT scenario may be considered. One of them would postulate that LUCA already had multiple, paralogous rhomboids, which evolved

via a series of ancient gene duplications, and the odd topology of the phylogenetic tree is due primarily to differential loss of these ancient paralogs. Although this cannot be ruled formally, this hypothesis implies the existence of extremely elaborate signaling system in LUCA, which is hardly compatible with the existing general notions regarding this primitive life form. The second possibility is that the topology of the tree in Figure 2 is simply random. However, the strong bootstrap support for many nodes and the presence of several phylogenetically coherent clusters (above all, the RHO and PARL subfamilies in eukaryotes, but also some of the archaeal and bacterial clusters) seem to argue against this explanation.

The multiple-HGT interpretation of the evolutionary history of the rhomboid family is, at least at first glance, distinctly counter-intuitive, given that this family is nearly ubiquitous among the extant life forms. Indeed, when attempts are made to construct parsimonious evolutionary scenarios on the basis of phyletic patterns [25, 26], there is no chance that such a widespread family is not assigned to LUCA. It should be realized, however, that these approaches are inherently probabilistic and extensive HGT can fool them. For the rhomboid family, this mode of evolution seems to be particularly plausible (Fig. 3). It seems likely that the ultimate ancestor of the rhomboid family evolved from a non-enzymatic integral membrane protein, probably a transporter that might have been involved in an early, primitive form of export of signaling peptides in bacteria. The protease active center might have evolved in such a transporter by chance emergence of the suitable catalytic amino acid within two or three of the TMH (Fig. 3). This would enable the transition from simple transport to the RIP mode of controlled export of signaling molecules. Emergence of RIP could have conferred a major selective

advantage on the respective bacteria and might have resulted in an evolutionary sweep whereby the gene carrying this trait had been repeatedly fixed, rather than eliminated, after HGT. In terms of the evolution of sequence itself, the requirements for the conservation of the protease activity apparently “locked” the rhomboid family in the regime of relatively slow evolution, which ensures the significant sequence similarity among all family members (Fig. 1). The scenario of origin from non-catalytic transporters might potentially apply to other integral membrane enzymes, including intramembrane proteases involved in RIP, such as presenilins and their homologs [14, 15] and the archaeo-eukaryotic signal peptide peptidase [27].

Conclusions

The rhomboid family may be the most widespread and conserved group of integral membrane proteins. In and by itself, this would suggest that this family is part of the gene repertoire of LUCA. However, phylogenetic analysis strongly suggests a different scenario, one of emergence in a bacterial lineage with subsequent multiple independent HGT events and gene losses. In particular, eukaryotes probably acquired their two major rhomboid subfamilies, RHO and PARL, as the result of two independent, early HGT events. These events introducing RIP as a means of intercellular communication might have been pivotal in the evolution of eukaryotic multicellularity along the lines discussed previously with regard to the apparent bacterial origin of key components of eukaryotic programmed cell death machinery [28]. Subsequent evolution of rhomboids in eukaryotes proceeded via lineage-specific expansion of paralogs [21], followed by diversification through the addition of an extra TMH in different positions

relative to the catalytic core, some limited domain accretion (Fig. 2), and sequence divergence.

Phylogenetic analysis of the rhomboid family described here carries a general message for studies aimed at the reconstruction of ancestral life forms, particularly LUCA. Although most of the (nearly) ubiquitous protein families probably do derive from LUCA, explicit phylogenetic analysis is required to ascertain this in each individual case.

Material and Methods

The non-redundant (NR) protein sequence database at the National Center for Biotechnology Information (NIH, Bethesda) was searched iteratively using the PSI-BLAST program with multiple starting queries [29]. PSI-BLAST was normally run with expectation (E) value of 0.01 as the cut-off for inclusion of sequences into the position-specific scoring matrix. Multiple alignments of protein sequences were constructed using the ClustalW program [30] and manually adjusted on the basis of the examination of PSI-BLAST search outputs and the superposition of the predicted transmembrane helices. Transmembrane helices were predicted using the programs TMpred[31] and TMAP[32].

Phylogenetic trees were built using the least-square method [33] implemented in the FITCH program of the PHYLIP package [34], with subsequent local rearrangement using the PROTML program of the MOLPHY package to obtain the maximum likelihood tree [35]. The reliability of the tree topology was assessed using the RELB bootstrap method of MOLPHY, with 10000 replications [36].

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Figure legends

Figure 1. **Multiple alignment of the conserved core of the rhomboid family proteins.**

The alignment includes the majority of the detected rhomboid family proteins; some closely related sequences were omitted. Only the six conserved (predicted) transmembrane helices and short surrounding regions are shown. The boundaries of the predicted TMH are indicated by shading and overline and the TMH are numbered 1-6. The number of amino acid residues in the omitted terminal and internal regions are indicated. The consensus shows amino acid residues present in at least 90% of the aligned sequences; h stands for hydrophobic residues (A,C,I,L,V,M,F,Y,W) and s for small residues (G,A,S,D,N,V). The proposed catalytic serine (TMH4) and histidine (TMH6) as well as conserved residues in TMH3 with possible ancillary roles in catalysis are highlighted with color. The proteins are identified with the gene identification (GI) number from the non-redundant database and an abbreviated species name. Bacterial species are color-coded green, eukaryotic species blue and archaeal species orange.

Species name abbreviations: Aerpe, *Aeropyrum pernix*, Agrtu, *Agrobacterium tumefaciens*, Anoga, *Anopheles gambiae*, Arath, *Arabidopsis thaliana*; Arcfu, *Archaeoglobus fulgidus*, Bacsu, *Bacillus subtilis*, Brume, *Brucella melitensis*, Caeel, *Caenorhabditis elegans*, Caucr, *Caulobacter crescentus*, Chlte, *Chlorobium tepidum*, Cloac, *Clostridium acetobutylicum*, Corgl, *Corynebacterium glutamicum*, Deira, *Deinococcus radiodurans*, Dicdi, *Dictyostelium discoideum*, Drome, *Drosophila melanogaster*, Escco, *Escherichia coli*, Haein, *Haemophilus influenzae*, Halsp, *Halobacterium sp.*, Homsa, *Homo sapiens*, Lacla, *Lactococcus lactis*, Lisin, *Listeria*

innocua, Metja, *Methanococcus jannaschii*, Metka, *Methanopyrus kandleri*, Metma, *Methanosarcina mazei*, Meslo, *Mesorhisobium loti*, Mycle, *Mycobacterium leprae*, Myctu, *Mycobacterium tuberculosis*, Neucr, *Neurospora crassa*, Nosp, *Nostoc sp.*, Prost, *Providencia stuartii*, Pyrab, *Pyrococcus abyssi*, Pyrae, *Pyrobaculum aerophilum*, Ralso, *Ralstonia solanaraceum*, Sacce, *Saccharomyces cerevisiae*, Schpo, *Schizosaccharomyces pombe*, Sinme, *Sinorhisobium meliloti*, Strco, *Streptomyces coelicolor*, Strpn, *Streptococcus pneumoniae*, Sulso, *Sulfolobus solfataricus*, Sulto, *Sulfolobus tokodaii*, Synsp, *Synechocystis sp.*, Theac, *Thermoplasma acidophilum*, Thema, *Thermotoga maritima*, Thete, *Thermus thermophilus*, Vibch, *Vibrio cholerae*, Xanca, *Xanthomonas campestris*, Xylfa, *Xylella fastidiosa*.

Figure 2. Phylogenetic tree of the rhomboid family.

The sequences and their regions used for the construction of the tree are exactly those shown in Fig. 1. The color coding and abbreviations are as in Fig. 1. The two major eukaryotic subfamilies are denoted as RHO and PARL (see text) and four clusters containing unexpected, from a phylogenetic viewpoint, sets of species are denoted 1-4. Although the tree is shown in a rooted form for convenience, this is an unrooted tree; in particular, the placement of the “root” in the midst of the PARL subfamily is arbitrary. Internal nodes with at least 70% RELL bootstrap supported are denoted by circles. Domain architectures are connected to the respective proteins by brackets or by lines. The domain key is shown in the bottom of the figure.

Figure 3

A hypothetical scenario for the origin and dissemination of the rhomboid family proteases.

The figure schematically shows the proposed three stages of evolution of the rhomboid family:

I – the progenitor of the rhomboid family functions as a transporter for a regulatory peptide in some bacterial lineage

II – the catalytic site of the intramembrane protease evolves allowing the switch to RIP as the mechanism of the regulatory peptide release

III – the emergence of RIP is followed by a burst of HGT

R, regulatory peptide; the transmembrane helices of rhomboid are designated as in Fig. 1, their topology in the membrane is based on that proposed in Ref. 7; the catalytic histidine and serine are shown and connected by a dotted line to indicate the proposed charge-relay system of the protease; possible ancillary catalytic residues are not shown.

	TMH1	TMH2	TMH3
6325010 Sacce	17 LTTGLVVFLLTAIYLLSFFIFA	14 LQMSRLSLYLPHLHLSLPHLLFNVLAIWAPLNLFEET	4 YTGVLNLSALFAGPAGIYCLLGLKLLY
19075999 Schpo	10 ILKLPITWQIIPYIAILVYA	21 RQLEIITTYVTLHLSMLHIVNFVSLPAMSQFEKK	5 CILVTVIPYTLFPGIMHLLIVYHFFL
21593075 Arath	25 LTSSVVVVCGVIYILCLLGT	17 FQVYRFYTAIIFHGSLLHVLFNMMALVPMGSELERI	6 LYLTVLLATTNAVLHLLIASLAGYN
19570079 Dicdi	39 ATKVTSIICSILFALSIVAP	19 LDNRLLIILSNFAHLSIYHIVNMTITFDLAK-LERL	1 FGTLKYFYLLLFSGITNLIICLFY
18676811 Arath	28 PPTVTLATLSPHLDHVVLPNPK	15 KDWQRLLIHLHSHADDVHLYFNMMASMLWKGINLERR	0 LGSRRWFAYITLAFSGVSLTGVYLLQ
18401578 Arath	33 PPVTASLLAANTLVYLRPAF	21 KDLKRLFLSAFYHVNEPHLVNMMSLWKGIKLETS	0 MGSSEFASMVFTLIGMSQGVTLLLA
11498616 Arcfu	133 ANNTVLICTILFFISIVAP	17 AMPVQLITSMFLHVEFVHFFVMMFVLLFFGTLELRR	0 LGDRKYLEIFFVSGLAGNVGYIAYS
63215836 Sacce	143 KNLVYALLGINVAVFGLWQL	18 TSKISIIIGSAFSSHQEFVHLMGNMMLALWSFGTSLAM	0 LGASNFFSLVYMNMSIAGSLFSLWYP
11066250 Homsa	166 QRTVTGIIAANLVFCLWRV	18 VLCSPMLLSTFSHPSLHMAANMYVLSWSSSIIVNI	0 LGQEQFMAVYLSAGVINSFVSYLKG
17647867 Drome	145 DKMFAPILLCNLAVAFAMWRV	18 VVCWPMPLSTFSHYSAMHLFANMYVMHSFANAAAVS	0 LGKEQFLAVYLSAGVPSLMSVLYK
18394631 Arath	133 RDVVLGLVLIANAGVFMWRV	19 GRHLTLITSAFSHIDIGHIVSNMIGLYFFGTSIARN	0 FGPQFLKLYLAGALGGSVFLIHH
19112976 Schpo	117 IMVAVIVCLVNGVVFVHWDL	30 GRWWTLVVSIIFSQNLALHLLVNCVAIYSFSLIVYK	0 FGVVKALSIVYLAGVFGNYVALQRM
21295914 Anoga	163 ERIFAPICALNVIVYGLWRI	18 AVCWPMPLSTFSHYSLFIHANMYVLSHFSHAAVAT	0 LGREQFLGVYLSAGVIASFVSHVFK
22327066 Arath	81 ANGIWFILINLIGIYLDHF	15 PAWYQFVTAIFCHANWNHLSNLFLLYIFGKLVLEE	0 EGNFGLWLSYVLTGVCANVSWLVL
7509358 Caeel	392 PWFYTIWITTIQIFVCLLSLL	257 NQFYRLFTSLFVHAGVIHLALSLLFQYVVMKDLENL	0 IASKRMALYFASGIGGNLASAIFV
13375799 Homsa	165 PYFTYWLFFVHVHIIPLLVC	230 DQFYRLWLSLFLHAGVVHCLVSVVVFQMTILRDLEKL	0 AGWHRITAIIFILSGITGNLASAIFV
17647863 Drome	1246 PFTYIWLWVIVVIVLILSII	236 DQYRLTLTSLCMLHAGVHLLAIFLIFQHLFLADLERL	0 IGTVTRTAIVYILMSGIVLTAIFL
15240744 Arath	55 SWLVPMFVVANVAVFVAMF	57 KEGWRLLTCIWLHAGVHLGLANMLSLVFIGIRLEQQ	0 FGFVRIIGVYLLSGIGGSVLSLFI
16944591 Neucr	161 PFFVYVFTTQIAVFAELV	56 NQWWRFITPMLHAGVIHIGFNMLLQMTIGKEMERS	0 IGSIRFFIVYVSAGIFGFVMMGNFA
8923409 Homsa	61 PVFIISISLAELAVFIYAV	26 EEARWRFISYMLVHAGVHIGFNMLCMLQVGLPLEMV	0 HKGLRVGLVYLAGVLSAGVLSVFK
17647865 Drome	72 PWFILLMSFVQISLHWIASE	13 VEYWRLLTYMLLHSDYWHLSLNICFQCFIGICLEVE	0 QGHWRVAVVYVGGVAGSLANAWLQ
17647869 Drome	102 PWFILVISIIEIAIFAYDRA	26 LQVWRFFSYMFLHANVHFLGFNIVIQLFFGIPLEVM	0 HGTARIGVIYAGVAGSLGTSVVD
17864410 Drome	98 PFFIILATLLEVLVFLWVGA	15 LQVWRFLSYALLHSAWHLGLYVNVLTQLLFGVPLELV	0 HGSLRTGVYIMAGVLAGSLGTSVVD
21264326 Homsa	163 PWFMITVTLLEVAFFLYNGV	26 AQVWRYLTYIFMHAGIEHLGLNVVQLLVGVPLEMV	0 HGATRIGLVYVAGVAGSLAVSVAD
17933592 Drome	179 PLTMVLFISIIEIMFLVDVI	31 YEGWRVFSVMFVHVGIMHLMNLIQIFLGLIALELV	0 HHWRVGLVYLAGVLAGSMGTSVVD
17977674 Drome	168 PFFIILVTLLEVLVFLWVGA	24 HEIWRFLTYMVLHAGVHIGFNMLVAVQVGLPLEMV	0 HGSTRICACVYFSGVLAGSLGTSVVD
17553192 Caeel	174 PIFMLLITIQIGVIFFFVYE	33 GEAWRFFSYMFLHAGLHLLGNVLIQLLVGLPLEVA	0 HKIWRIGPIYLLAVTSGSLQYAI
21297308 Anoga	157 PLFVILVTVFVGLGFFVYHSL	24 QEVWRFLTYMVLHAGVHIGFNMLIQLLVGLPLEMV	0 HGSTRIGCVYLAGVLAGSLGTSVVD
3219925 Schpo	77 RSLVLSIIGINVGVPALWRA	20 INMPSMIVSAFSGHAGVHIGFNMLVAVYFAPAVDV	0 FGNNOQVAFYISLISLGNVSLHLLH
15218144 Arath	48 TWLVSVFVLLQVLFVAVTMG	52 HEIWRILTSIPWLSGGLPHLFINLGLSIFVGIYMEQQ	0 FGPLRIAVIYFSLGIMGSLFAVLFV
15222545 Arath	153 RRWTVLLAINVIMYIAQIA	18 QQLWRLATASVLANPMLMNCYSLNSIGPTAESL	0 GGPKRFLAVLTSVAVKILRVLV
15231701 Arath	14 ATSCVTLTCSVIVLIVIKKS	15 GHYWRMITSALSHISVHLVFNMSALWSLGV-VEQL	8 YLHYTLVLLVSVSGVLIIGIYHLLI
18312405 Pyrae	15 PFTVKALVFINVAVFIYELL	16 SEPVRWVTHMFLHGGGLHIVGNMIIYLVWFGDNVEDH	0 YGHFRFLALYLMWGLAAAFVHYWAV
15789622 Halsp	94 AFLFLGVMVTFVIQYGIAP	22 EYVWTVTSVFAGGGFSHIVLNSIVLYFFGPIVEDR	0 IGSKKFVALFLGAGLAGLQVAGS
20093492 Metka	1 MSLTMLMFLNLVAVLVSVG	21 VHPCLTIVYFLHANLHLLFLMGLLTFGVQLERV	0 LSTSEFLVYLLSGLMGLAQAL
21226784 Metma	24 ASPSMIAIFLCIVSFFLEMV	19 TRPWTLTYIFLHAGLGHLLFNMIIVLYFFGTALERK	0 VGNKQLLGGFFAGLISAIYGFYFLS
14520881 Pyrab	28 TFSLMIITAVFIYEVIVGF	16 GQWRLLTAIFLHMGVHFLANAFVFLYGLTLEGI	0 VGTKRFLIVFFASALAGNVLFTL
14601690 Aerpe	19 PIVNMSIITANFAFIVGLT	29 ERLTYVTFSMFLHGSWAHILGNMIIYLYIFGDNIESI	0 LGRARYIILYISGSLGAVVPHIASI
15669882 Metja	1 -MINLIVIGICIAMFISV	16 NMPVQVITSIIFMHAGIIFHLLVNMVLFVIFGTYLENI	0 VGSKKYLIIFLPSGIIGNLAIYAG
15790000 Halsp	96 GVPWGTLLVAGIVAGFYTLV	18 APYLGVLTSIPHANLGHVDTGNLIGTLALAPVAEYA	7 RGTAAFGRSWRTVYVAGVVFPA
15897391 Sulso	35 TFFLMLFVTLGFMVGLLATF	18 GYSELFTSIFITNSFVDFIFNFISLYVYIYIFGSR	0 AGKHEY-GIFILAGILGNLLTVIFY
15920355 Sulto	28 TVVLTILITIGIYIIGQILSL	18 GFYVWVITSIIFVTPNFDWAFNTIAMFYIYWLKGE	0 AGKLEY-IIFLFIAGLISLISLYLY
16081803 Theac	2 FLFALFVFLLLGLVLISSYPGA	7 RTPWGLFTSIFIDYDGSNGVEYFLIFAILLSAANTSH	6 KRVAVALLSAGVSIANLLDLAL
15598282 Pseae	85 SPMTAAVLLTFFVAAVAYTL	33 GQWRFLTPMLIHFQWGLHLANAMWFELGRRIEFR	0 QGRPMLLGLTLLFGLVSNVQYAVS
17549219 Raliso	1 -MISSILLANVIVVAELF	24 FSPWQLTYAFHLASVPHLVNMFPMFGRDVERA	0 LGRVRTGVLYLSAGVLSAAPTQAMV
17549744 Raliso	205 PHLTHALIALNVLAWLATLV	6 GEWRLLSATFLHAGVHLHAGVHLLVFNMIIGLYAAGVTVERI	0 YGPVAYLLIYLAGLGLSALSFA
17987022 Brume	17 VIALIGLCVAVVYQNYILS	27 AVIFTFISYSFMSHGSFAHIAVNMIIWLAAGFSGPLAGR	0 IGAVRMILFVWVTSVAVGLTHYALH
19553712 Corgl	45 VRTGLTIAIGYVVVIAVHL	23 SALWGITPSMLLHGSFHLIGNTPVGFIFSLIGMS	3 VFWEVTIAGLIGGLGTWIFGGIT
20806909 Thete	14 PVITLSLIIINSLIFFTLSS	32 SNLYVITFMYLHGNTPHLISINMMIWLWFGDNVEDR	0 MGHIRFLIFVYLLSAGVLAGVFLVFN
21220616 Strco	39 LCCLLFLISPAAGLNPVYGT	27 GSALTPTALFVHGSWVHLLGNMFLYVFGAMTEER	0 MGRLOFALFYLCGGYALVGYAGAN
21222264 Strco	84 HLVTKILIGINAVFVIAQQA	28 GEWYRLVTMFTHEEIVHIGFNMTSLWFLGGPLEAA	0 LGRARYLALYVLSGALSVLALY
21224370 Strco	135 ANLVVFLTPFGMGASGDG	54 SPELSVLTAMFLHGSVHLLGNMFLWIFGNNVEDR	0 MGHVPPFLFYGVCGYAATYFALLD
21229496 Xanca	13 PRWAVPLLFAAVLWALWSI	33 GSVLRLFTALFLHADWSHLLGNLFLVLLFGLPAERI	0 LGPWRLLLLLFLGGAASNLAAIFAI
21230863 Xanca	1 -MITLILTAITGIVSWMAFN	18 QKYDRLLTYGFIHADLGHVFNMTLFFFGRIEDV	0 MTRLTGTSVLYPLFYLAGLIVSLP
21233650 Xanca	140 SRVLRAFNLSLAELLLVAV	19 DGLIGLITAPYFLHAGVHLHAGVHLLVFNMIIGLYAAGVTVERI	3 ATAMALPMLVTLGGLGAWLLGDDPS
21675030 Chlte	17 PPAIKAIITINIVFLFQNS	24 FHLWQPIYTLFLHGSFAHIFNMFALWFMGVEIENY	0 WGRTRNFVSFYFCIGGALINLLAT
1168254 Prost	21 IALTTLVILLANVAVFYQIV	25 GDWWRYPISMLLHNSGTHLAFNCLALFVIGICERA	0 YGKFKLLAIYIISGIGALFSAWQ
13470470 Meslo	16 VLAIVIGICAAVFLQQYVNL	26 FLFRPPTIYAFMHGGFAHIAIMNVWLAAGFSPLANR	0 LGLRFLFAVYFVAVTGLSAGVFLVFN
13473011 Meslo	17 QVVTIGLIVVNALVVCATAL	33 PESLSYLYTSFLHADIFHLGGNMLFLWVFGDNVEDA	0 LGHIRYLIYFYLCAIAGAAFQGLVA
15606530 Aquae	14 PIVNLSIIVACSLIWLWYEW	31 KQPYTLTTHMFLHGSWGHIGNMVFLWVFGDNVEDK	0 LGKFRYIIFYILCGLGAALTQPTFIS
15607252 Myctu	37 PUVTITLISLNAFLVPMQVT	17 GQTYRLTYSAFLLHGSVHLLGNMFLWVFGDNVEDM	0 LGLRFLGALYVLSAGVLAGVFLVFN
15608477 Myctu	37 VVGGTITLTFVALLYLVELI	18 DGLWGVIFAPLLHANWHHLMANTIPLVLGLFMTLA	3 RFWWATAIWIWLLGGLGTWILGNVGS
15639966 Trep	13 TNVTLSLVLANGAVFVITSL	18 RMYQVIFTYQFVHSGVHLLFNMLGLVFFGQTIKKE	0 MGSSEMLLFYVLLVGLTSCGAGACAA
15640131 Vibch	97 GVFTLFIIMALCIIFTLQTF	19 WQIWRVSHALLHGSVHLLFNMLWVFGDNVEDR	0 LGSVRLIKLFLVYCAIAGALFHGFA
15641983 Vibch	32 LGTITPHDVLNLLXLLAISL	23 GQWRRLTGNFAHNFNAHWANLALWISFVFKPT	0 ARQLLIPLLIISLAVGVMILASDMQ
15643350 Thema	3 KRAVYFILLNFNAFVMMTF	29 GDWFRILTALFVHGGILHILFNSYALYFGLIVEDI	0 YGTEKFLVGYFFTGIVGNLATHVFI
15643845 Thema	14 PYVTIALILINVVVVFYELM	30 FSLLPFITMFLHGGFVHLLGNMFLWIFGDNTEDE	0 MGHVGYTLFVLSAGVLAGVFLVFN
15672152 Lacla	15 AFYILSITILLVNLWQFPTY	25 SQMWRFLTALFIHIGWAHVLLNVATLFFIGRQIENV	0 FGWLRFTLTYLLSGIFGNAMVLLT
15803931 Escco	94 GPVTWVMMIACVVVFIAMQI	19 FEFWRYPFTHALMFLHSLMHLFNLLWWWLGGAVEKR	0 LGSGLIVITLISALLSGYVQQRFS
15806990 Deira	50 VKAAAGVTAGLIALLWGOEV	20 FEFVHVFPTAPFLHAGFPHLIANTVPLAVLAFMTAVR	3 RFLVATFLIALVLLGAGLWLLGRSFS
15827590 Mycle	36 MVGGVTITLTFMALLYLVELI	18 DVLWGISFAPVLANWQHLVANTIPLVLGLFIALA	3 RFIWVTAMVWIFGGSATWILGNMGS
15837251 Xylfa	10 PVTTKGLLTNVVVFLFQMM	27 FMPWQLLTYGFLHGGFVHLLGNMFLWVFGDNVEDM	0 WGEKRFLTYVLCVAGAGVQCQLLS
15837656 Xylfa	19 WLNAVPLFFFAVLIIFLWFSI	33 GSALRLFTALFLHADWHLHAGVHLLGNLFLVLLIFGLPAERI	0 LGSWRLLLLFLGALANLAAVLTII
15838777 Xylfa	4 LMITLILIAMNAVSWLSFN	18 RQYDRILTGYFVHANISHLLFNMTLFFGSMIEAV	0 MGELTGSLLTYPLFYLAGLVLISL
15889057 Agrtu	32 LVGILAAALAIYVVPAYLLS	27 EWLTVPTVYSFHLGGIEHILFNGLWMAFGAPVLR	0 IGTVRFVLLWCISAASAFGHAAALN
15891346 Agrtu	36 QVVTITLISLNAFLVPMQVT	24 PDLTIVTYAFLLHGSVHLLGNMFLWVFGDNVEDA	0 LGHFRFLIFVYLLCAIAGALFHGFA
15894241 Cloac	141 MRVTVILVIVNFIVVIGISAW	26 GQYRLTICMFLHAGIIFHIGANMYSLSYMGYMLENI	0 YGKLRXTAIYFISGITASFFSYIFS
15903945 Strpn	12 VTSFLLVTLVFLMLLMTA	25 EQVWRLLSAIFVHIGWEHFIVNMLSLYLLGQVEEII	0 FGSKQFFLYLLSGMAGLVAHFVFS
15966395 Sinme	17 QVVTITLVIDFVANLAI	34 PDEFITVYSFHLHGSVHLLGNMFLWVFGDNVEDA	0 LGHFRFLIFVYLLCAIAGALFHGFA
16077528 Bacsu	15 YPVVTFILALQAVLWFLS	21 GEWWRLLTPILLHAGFHLFNMSMIFLPAALERM	0 LGKARFLLYVYAGSGIIGNITVYTE
16079543 Bacsu	177 PFTTYLFIALQILMFLSLEI	23 GEWWRLLTPIVHLHIGIAHLLNLTALWSVGTAVERM	0 YGSGRFLLYLISAGITVCSIASVFS
16126863 Caucr	12 NAPWPAALVAAAVIIPHLLL	20 GRWTGAVTMLFHLHGSVHLLGNMFLWVFGDNVEDR	0 LGLNVRRGGGIFCLFYLVCGVIAGVG
16272560 Haein	9 GKITLILTALCVLIYLAQQL	19 SEVWRVYISHVTLHLSNHLFNLSWFFIFGGMERT	0 FGSVKLLMLYVVASAITGVVQNVVS
16332120 Synsp	13 LQSQFSIIVLSLAFVWLEI	20 EGLRVLISHTAPFLHAGFHLIANSVFFVFLAWLVMQ	3 DFWIVTITIMVWVAGLWVLIAPNT
16800442 Lisin	182 PIVTYFSIGLIVAAFLWVTF	23 GEWWRVIFSPFLHSGLHLASNAVMLYIVGAWAERI	0 YGKWRYLITLILLGGICGNIASPALN
17231423 Nosspp	14 PYFTYGLGMNVLVFLPHEVS	25 GEWPTLTSQFLHGGVHLLGNMFLWVFGDNVEDR	0 LGHFYKYLIFVYLLCAIAGALFHGFA
17232329 Nosspp	14 PYVTVGLIAANLAFVLEAN	3 PEWATLITSQFLHGGVHLLGNMFLWVFGDNVEDR	0 LGHARYLLIFVYLLCAIAGALFHGFA
consensus/90%h.....hhh..h...hh...h.H.sh.HhhhN.h..h.hs..ht..hhh...shhs.hh..h..

	TMH4	TMH5	TMH6
6325010	Sacce	4 VAGASGWCPTLFAYSYFVKSQI	2 SSFWG FFGLCVGYAIGYKESWF
19075999	Schpo	6 IAGLSGWAFIFASCVHSFPQR	2 ASFIG ASGAVMGYCTPFMLGSI
21593075	Arath	12 AIGFSGILFSMIVETSLSGVT	2 VSLLG LCGILSGFSYSYGLFNF
19570079	Dicdi	8 HLGFSGVLFPALYIENSNSGRD	2 SSFIG FSGIVVGLFIKGYLDI
18676811	Homsa	16 AVGFSGVLFPALKVLNHYCPGG	2 TSFAG LAGLVLGLMYTQGLPK
18401578	Arath	17 AVGFSGVLFPAMKVVLSQAEDY	2 ASFLG LGGILAGIYYLKLKGSY
11498616	Arcfu	8 ALGASAAIFGVMGCLAI IAP EI	10 VANIA LAGLAVGLYKRLGRR
6321538	Sacce	4 FGGLSGVLGGLGHWCNIFQYLA	10 IANGA VGGLLVGCLSGLLGGL
11066250	Homsa	25 TLGASGAI AALMGVLTLLNPG	8 VAQLA LAGLIGLGYAKLRE
17647867	Drome	5 VVGASAAIFGGLLCLTMLRPMS	6 VAHAG LVGMIVGGVLLALYRPS
18394631	Arath	10 SLGASGALFGVLGCFSYLFPFA	8 FDYAA LGGSMGVLYGWYISKA
19112976	Schpo	8 SLGASGAIMTVLAAVCTKIPEG	8 FDHAA LGGALFGIYVVTYGH
21295914	Anoga	8 SLGASGAIMTLLAYVCTQYPTD	8 FDHAA LGGAMGFIFWATYGAQ
22327066	Arath	22 GLGASGAVNAIMLLDIFLHPRA	6 ISGSA LGGAAVAA-IAWARIRK
7509358	Caeel	60 LLGASGAVYATAAIFACLFPYT	11 VAFDA VSGTFFGVVSSFLLLPA
13375799	Homsa	8 SLGASGAIMGILAYVCSQYPTD	8 FDHAA LGGALFGFVWCHFGSON
17647863	Drome	5 SVGASGAVFGLFAISVLVKMSW	12 VNHIA LSGALVGVVLLVWLSKF
15240744	Arath	4 AVGFSQAQCGILAAVIVCCDN	0 -VDNWA LFGTIFGLLTTIIFPY
16944591	Neucr	4 EVGPAGSQFGLLACLVELFQS	0 -IDNIA IFGFLSGLLLAFAFLPY
8923409	Homsa	4 VVGPSASLGGVVVALTALVWM	1 LNFLGGLLAGVIGCGLLTMSLVPF
17647865	Drome	4 SVGASGALFGLLGSMSELFTN	0 -VDNFA VGGFVTGFLGFIILLAR
17647869	Drome	5 TTGASGALFGI IALLLDLlys	0 -LDNFA IGGFLAGLALGICVLOS
17864410	Drome	4 LVGASGGVYALMGVYPMNVN	9 VSFAA IAGGFAGMSIGYTVFSC
21264326	Homsa	4 LMGASAGVYAMLGSHVPHVLN	9 TSLEA IGGVAGILCGFIVYRR
17933592	Drome	4 LVGASGGVYALLAAHLANITLN	12 VSYIA LTGALAGLTIGFLVKN
17977674	Drome	4 LVGASGGVYALLAAHLANVLLN	12 VSYIA MTGALAGISVGLLRLRQ
17553192	Caeel	4 VVGSGGVYALVSAHLANIVMN	11 PSFVA LGGVAVGITLGVVLRN
21297308	Anoga	4 LAGASGGVYALTAHIATIIMN	7 IGYVA LSGAVAGLLVIGVLRN
3219925	Schpo	4 LVGASGGVYALLAAHLANVLLN	25 VSYVA LAGAIAGLTIGLLVKS
15218144	Arath	4 LVGASAGVYALIFAHVANVILN	8 VSHLA IAGAVTGLFFGYVVLVN
15222545	Arath	9 IVGASGGVYALLAYAVLFPFR	5 IAHFA LGGMAGSGVLLWRW-LR
15231701	Arath	5 VVGASGAVFGVAGALVAVIROY	3 VDNAA LGGIGGCLLACTLIPAR
18312405	Pyrae	6 LVGASGAI SGMMGAAARYGFRR	9 IAWEA IGGFIAGFFGIPMLDRP
15789622	Halsp	20 AVGASGAI SGVLAGYVMVLYPHA	9 VAYFA IGGFIAGALTALIYRRR
20093492	Metka	1 HIGASGLIYGWLGYLIVRGFIN	5 VSWQG LFGALGGIGAGAFIASD
21226784	Metma	6 VVGASGAIAGIMGAYFVLPFSA	11 IAWWA IGGFISGVLLNRFFLRD
14520881	Pyrab	6 LVGASGAI SAIVLGAFLFPFRA	6 VAYLA LVGFLGFAFAVWRFR
14601690	Aerpe	5 TLGASGAI PGLFGATAALVR--	3 ISWQA VGGLVAGAVIGYAMLHA
15669882	Metja	6 LIGASGAIAGVLAGYLVLYPRA	8 VAYVA VVGFVVGMLIAWPLRRG
15790000	Halsp	10 MVGASGAIYGVFAALVLEPNL	4 IAHTA LSGFLVGLYMGYRIKRM
15897391	Sulso	6 IIGASGAVSALIGTYLALFPFA	6 VAWSA IAGVVFIVYGLYVRAA
15920355	Sulto	12 SLGASGAVSALVFAFVLLKWP	4 INHSA LAGAAFVGMFMLEPFR
16081803	Theac	1 HLGASGVTHGLMFLVFLVGLLR	5 VSWQG LAGAVAGLIAALLRLR
15598282	Pseae	4 LVGASGGVYALLAAHLANVMLN	11 VSYVA LTGALAGLTIGLLVKN
17549219	Ralso	6 TIGASGAI PGLVLAFAFMFPDR	9 IAYFA LGGMLFGYIYIVIRRNE
17549744	Ralso	19 VVGASGAI MGIAAASVYILIKV	2 VDNAA IGGAIIGALISIAIYILV
17987022	Brume	11 SLGASGAIYIAAATSYYFPNA	15 IDHAA LGGGIFGWLYAKYGYST
19553712	Corgl	6 LVGASGAI SGVMGAAARFGFRT	9 IAWEA IGGFVAGFFGLRWFDRR
20806909	Thete	6 LIGASGAIAGVVYAYLILYPRV	5 ISWAC IGGI IAGAVLVLRSSR
21220616	Strco	5 SGGASGGLFGIVGALLSTIEGVL	2 VNIFA FGGLVTLGLVLYFYGIW
21222264	Strco	22 AVGASGAI SGVLAGYALLIPFS	9 IAFWA VGGFLTGVVALPLVDD
21224370	Strco	4 SSSGAAFFGLIGAMLSALAKN	0 -IDNFA IGGFISGFLGFLVLFK
21229496	Xanca	10 SVGASGAI FGLVGSVAVFIIRH	1 IDNWG IGGLLGTTAMTWLLGPQ
21230863	Xanca	12 AVGYS CVVPGWMTILSVKQPS	2 ASFLG LSGILVGYAISWGLIG
21233650	Xanca	9 MVGASGAI SGVLAGYMKMFPFA	9 VAWYA IGGFITGYLLVDFYFRK
21675030	Chlte	5 TAGASGAVFGLFGATFMVAR--	3 ISWQG VGGLVTGALVAATYVYA
1168254	Prost	6 HIGASGLIFGWLAFLVFGFLV	8 VSWQG LSGAVAGVVAAYLLSAP
13470470	Meslo	9 LIGASGSIFAILGLIFPAAGFRK	4 VSHLT LLLGVLFANGYIRIRFGI
13473011	Meslo	3 FGGLSGVVYALAGYLVILQORA	5 IANTA LAGLISGVVLAWFDSQR
15606530	Aquae	1 YVGLSGTLHGLFAYALNEALN	9 VATEA LAGLVGGLLAAAGHCLF
15607252	Myctu	4 SVGASGAI FGLIGLIFPAAGFRK	7 INNAA LGGFLSGMLLGYTSPF
15608477	Myctu	6 MVGASGAVSGVMGAYFVLPFYS	4 IAWWA IGGFVYGMINGYILMR
15639966	Trepa	8 SVGASGAI PGMALAI LAPHL	6 IAHTI LAGLITGLIFGKLLYR
15640131	Vibch	4 SAGAS TSIFGLFAAVVLAFFT	4 VSIWA IGGAIIGLALLSAIFAPK
15641983	Vibch	14 AVGFSG VVFAFAGFALLKYPLA	13 VAVQG LFGFLGALAAVAVLVH
15643350	Thema	3 FGGLSGVVYALMGYVWVLRGERD	6 MANGA IAGLAVGLAMAFVDSL
15643845	Thema	1 HLGAS ELVFGYLA LLLGCVGWGE	5 ISWEA LFGF IGGLVAAALLHRK
15672152	Lacla	6 HIGVSGLIFGWLAFLVFGFLV	8 VSWQG LCGAISGVVVAAYLLSAP
15803931	Escco	8 VLGASGGVYVGLL MAYGMLFPNE	5 VAHFT LGGMLFGWLLIRYWRGQ
15806990	Deira	6 IIGASGAVSALIGSVMKLPFPA	6 VAWSA LAGFVSGVVYVGSVRAT
15827590	Mycle	12 SLGASGAVSALVFAAVLLQPWA	4 INHSA LSGAAFVGMFMLEPFR
15837251	Xylfa	6 LIGASGVVSALMGAAACRFAPV	10 IAWDA VFGFLGFLFSLFDRP
15837656	Xylfa	6 LIGASGAVSVMVAAYFLLHPRV	5 VSWQA VGGILAGAIMVIFMRRP
15838777	Xylfa	4 SVGASGAI FGLLGAAVVFGFKL	3 IDIFA FGGFLGGVVSVILGRT
15889057	Agрту	5 SSGASGGIFGLLSYYTYDFLK	2 VNVVA IGGILGGIMYAVVYLI
15891346	Agрту	4 AAGAS TSLVGLFAIIVLRYAT	3 ISLAG IGGAVGAFIYAVVPR
15894241	Cloac	5 SAGASGGIFGLFAYYVTVDYLK	2 VDIWA TGGTLTGILLSLFFKI
15903945	Strpn	6 LIGASGAI SGVVAAYFLLHPKV	5 VSWQA VGGIVAGLVVLLVLRP
15966395	Sinme	5 HVGASGAI PGLFGVYLFVMLFR	3 INMMA LFGICGFLSFLCVQK
16077528	Bacsu	3 SAGASGAI FGLGALLVVALSN	3 IDNSG IGGIIGGFAAAALGLP
16079543	Bacsu	5 SYGQSGVVYALMGSAASMLLD	5 IDSFV AMAFGSSAIFIIISY
16126863	Caucr	11 VVGASGAIAGLMGAAARTMDSA	10 VAWEA LIGFVAVVLLIGPFARW
16272560	Haain	3 FFGLSGVVYAVLGYVPIRDKLN	7 MGNAA ISGLIVGLINGFIDSKL
16332120	Synsp	1 TVGAS ILIFGLFGLFRGWFO	5 VSWQG LFGF IGGAI AAWLARE
16800442	Lisin	3 SVGAS TAVFAVMGALLYLVLK	3 IDIAG IGGLVGFLLAGALSPL
17231423	Nossp	6 SLGASGAI SGVLAGYLVIRFQA	14 VAYWA IGGFVFGIILAPLGLF
17232329	Nossp	6 SLGASGAI SGVLAGYLVIRFPNA	14 IAYWA AGGFIFGALLGPIGLF
consensus/90%		.hGhSssh.uhhh.....	hs..sHh.Ghh.Ghhh.....



