PROF_PAT 1.3: Updated database of patterns used to detect local similarities

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ABSTRACT
Motivation.
When analysing novel protein sequences, it is now essential to extend search strategies to include a range of 'secondary' databases. Pattern databases have become vital tools for identifying distant relationships in sequences, and hence for predicting protein function and structure. The main drawback of such methods is the relatively small representation of proteins in trial samples at the time of their construction. Therefore a negative result of an amino acid sequence comparison with such a databank forces a researcher to search for similarities in the original protein banks. We developed a database of patterns constructed for groups of related proteins with maximum representation of amino acid sequences of SWISS-PROT in the groups.
Results.
Software tools and a new method have been designed to construct patterns of protein families. By using such method, a new version of databank of protein family patterns, PROF_PAT 1.3, is produced. This bank is based on SWISS-PROT (rl.38) and TrEMBL (rl.11), and contains patterns of more than 13,000 groups of related proteins in a format similar to that of the PROSITE. Motifs of patterns, which had the minimum level of probability to be found in random sequences, were selected. Flexible fast search program accompanies the bank. The researcher can specify a similarity matrix (the type PAM, BLOSUM and other). Variable levels of similarity can be set (permitting search strategies ranging from exact matches to increasing levels of "fuzziness").
Availability.
The Internet address for comparing sequences with the bank is: http://wwwmgs.bionet.nsc.ru/mgs/programs/prof_pat/. The local version of the bank and search programs (approximately 50 Mb) is available via ftp: ftp://ftp.bionet.nsc.ru/pub/biology/vector/prof_pat/, and ftp://ftp.ebi.ac.uk/pub/databases/prof_pat/. Another appropriate way for its external use is to mail amino acid sequences to bachin@vector.nsc.ru for comparison with PROF_PAT 1.3.
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INTRODUCTION

Up to now, the main method of suggesting possible functions of the newly deciphered amino acid sequences has been to search them for similarity with sequences available in protein banks such as PIR (Barker et al., 1999), SWISS-PROT (Bairoch and Apweiler, 1999) and others. As these banks grow larger, such comparisons become more promising but at the same time more time-consuming. In addition, in the case of distant proteins the search for global similarity of complete sequences may fail to show a positive result, because the conservative blocks responsible for their special functions may prove to be relatively short and scattered all over the sequence. This may be why a number of works appeared in the last few years, aimed at the selection of sites in groups of related proteins. These sites are representative of a protein family as a whole, and both identify new proteins and refine structural and functional properties of those already known. Such databases as PROSITE (Hofmann, et al., 1999), BLOCKS (Henikoff and Henikoff, 1991, Henikoff, et al., 1999), PRINTS (Attwood et al., 1999) are among the most well known and accessible via Internet. There is also a number of other similar databases i.e. PFAM (Bateman, et al., 1999), SBASE (Murvai, et al., 1999), IDENTIFY (Nevill-Manning, et al. 1998).

The advantages of such databases, representing protein families, arise from comparing an amino acid sequence with a relatively small pattern as a representative of a protein family, and not with a set of long sequences of this family. Furthermore, comparison algorithms could be simplified because there is no need of sequence alignment, which also speeds up the process. The level of noise (random similarity) is lower, because comparison is usually made with patterns that are already characterised and represent conservative intervals of positions. This appears most clearly when a family is represented by a few relatively short pattern motifs.

However the common shortcoming found for the most part in secondary databases, is the fact that they contain a limited number of patterns (profiles, motifs, alignments or other representations of protein families). In general, PROSITE contains well-defined manually constructed patterns. BLOCKS and PRINTS in the beginning were in some extent expansions of PROSITE with subsequent developments. In turn, IDENTIFY is based on BLOCKS and PRINTS.

We have devoted our efforts to develop a technique and construct patterns for the greatest possible number of proteins belonging to the SWISS-PROT+TrEMBL (Bachinsky et al., 1996, 1997). We are convinced that if a secondary bank is not really representative, it would not be widely used. It is because of negative results in the comparison of a sequence with this bank that the user is forced to consult other banks or make direct comparisons of the sequence with large banks of sequences.

SYSTEMS AND METHODS

Programs for using patterns were written in Microsoft Visual C++ 5.0. for IBM compatible computers running Windows 95 or Windows NT. Amino acid sequences were taken from release 38 of the bank SWISS-PROT and release 11 of TrEMBL (1999). The selection of related proteins was made using modified FASTA 2.0. algorithm (Pearson, 1994). Multiple alignments of the amino acid sequences were performed by means of CLUSTALV program (Higgins, et al., 1992) and the default set of parameters.

ALGORITHMS

The selection and concurrent alignment of related protein groups. All full-length sequences of prototype banks that were over 30 amino acids in length were combined in one file. In order to select groups of related proteins, a special program was written based on FASTA 2.0 (Pearson, 1994). The first sequence of the file was compared with all other sequences. The sequences were regarded as similar if $score/\ln(l_1)/\ln(l_2)*\ln100*\ln100 > 80$. The sequences similar in the sense of FASTA form a primary set of related proteins. Then the next sequence not included in a group of related proteins was compared with all other proteins, and so on.

It is known that in the case of distant protein homology many algorithms of multiple alignment lead to doubtful results strongly dependent on parameters such as, insertion penalties, similarity matrix, etc. To provide quality alignment, the pairwise similarity level was prescribed 30% or more, for it is known that at smaller similarity global alignment often makes no sense (Vogt, et al., 1995; Patthy, 1987). Pairwise similarity of the proteins belonging to a set was assessed by the program CLUSTALV (Higgins et al., 1992). Then, if not all pairs of proteins had 30% similarity, the set was divided into subsets so that all pairwise similarities were at least 30%. Thus, more than 13,000 subsets or groups were obtained, containing more than 100 000 sequences.

Proteins of every subset were aligned together. The files containing aligned sequences were supplemented with two fields: DE (description(s) of proteins forming the group), and KW (key words; mainly the union of values of field KW for proteins falling into the set). Patterns were constructed based on such aligned families.

The construction of patterns of protein families. We will regard the combination of motifs that represent relatively conservative intervals of positions of aligned proteins of the family as a pattern of a family of related proteins.

Let there be an interval of positions of an aligned family of related proteins of length *n*. A_i denotes a subset of amino acids of 20 standard ones, located in a position *i* of the interval. An amino acid sequence of length *n* will be considered to belong to the given interval (motif), if for every position $a_i \in A_i$, where a_i is the amino acid located in position *i* of the sequence. To every position *i* of a group of aligned proteins the value $P_i = \sum_{a_l \in A_i} p_l$ that is the frequency of occurrence in proteins one of amino acids from A_i located in this position may be ascribed. Here p_l is the frequency of occurrence in proteins of amino acid a_l, located in this position. Q_j - the product of the values P_i for positions falling into interval of positions *j* and may, accordingly, be the characteristic of this interval. The value Q_j constitutes an assessment of probability that a random amino acid sequence of length *n* will belong to interval *j*. The smaller Q_j is, the smaller is the probability that, in a protein (a random sequence) not related to the given group, a fragment belonging to the interval can be found. Thus the smaller Q_j is, the greater is its ability to differentiate fragments of proteins of the trial sample from fragments of other proteins, i.e. its specificity.

Some positions may be marked as ‘passive’ or ‘non-meaningful’ (in comparison with patterns of PROSITE). They do not influence the definition of value Q_j, and comparison of these positions is not implemented in pattern analysis (any amino acids are acceptable). In our case all positions that had more than 4 amino acids and/or the total frequency of amino acid occurrence more than 0.2, were regarded as passive. Having analysed the structure of the bank PROSITE, we found out that about 80% of the bank’s patterns fall into the following boundaries: up to 10 ‘active’ positions and a total length of no more than 20 positions. We also used these limits when choosing pattern motifs.

Having set some critical value of the *Q’*, for a series of chosen proteins one can get a set of motifs R(Q’, l_1, l_2), the borders of which are limited to l_1, l_2. Characteristics of motif *j* are the value Q_j that determines its specificity, and length *n*.

To ensure an effective realisation of comparison algorithm between sequences and patterns, we demand that every motif should contain an ungapped section of no less than four active positions.

The motifs of patterns are represented by ambiguous words of the type:
K-[D,E] - F - [I,V] - C - X - [A, S, T] - X - [M, N, D]. Thus, an initial pattern of a protein family is an ordered combination of non-overlapping motifs of the type r:A_1-A_2-A_3-...-A_n. Here *r* is position number of an aligned group of proteins (the trial sample), where the motif begins, A_i is a set of amino acids, located in $r+i-1$ position of the trial sample. For a passive position $A_i = X$: any amino acid is acceptable. The number of motifs does not exceed 5 per 100 positions.

Each pattern is compared with all sequences of the initial file. If not less than 60% of motifs of a pattern reveal similarity with a sequence that is not included in other families, an attempt to include this sequence into the trial sample is made. If any motif is non-specific (i.e. it matches many sequences, but other motifs of the pattern do not match them) the motif is excluded from the pattern.

COMPARISON OF AMINO ACID SEQUENCES WITH PATTERNS

The searches for exact matching between fragments and pattern motifs of amino acid sequences. The main algorithm for comparing an amino acid sequence with the pattern database uses the modification of finite automaton of Aho-Corasic (Aho and Corasic, 1975), constructed based on a set of samples, which are to be searched for in the input text. The automaton is presented as an oriented tree-like graph, where nodes are states of the automaton and arcs are admissible transitions from some states to the others, marked with symbols from the alphabet *S* of the amino acid designation. The automaton works in cycles. In every cycle one more symbol of a text is read, which determines the transition of the automaton from the current state into a new one. The behaviour of the automaton is characterised by three functions: function of transitions *G(s,a)*; rejections’ function *F(s)* and output function *O(s)*. The values of these functions are calculated once when constructing the automaton based on a given set of samples. In Figure 1. the functions of the automaton constructed on the set of samples R={r_1, r_2, r_3, r_4, r_5} = {HE, SHE, HIS, HER, HERS} are illustrated.

The function of transitions $s'=G(s,a)$ determines into what state *s’* the automaton passes from a current state *s*, if the input symbol is *'a'*. When there is no admissible transition, a situation called ‘rejection’ arises which indicates that the comparison has failed.

The values of the rejections’ function *F(s)* are calculated in the situations, when *G(s,a)* = ‘rejection’. In this case a backward move does not occur through the text to the beginning of another fragment of the sequence (exit to the initial state of the automaton). A new sample is being examined from the break site of the previous one. It provides linear dependence of the search time on the length of the query sequence. *F(s)* indicates into what state the automaton passes from a current state *s*, if the next symbol of the text does not coincide with a label of any of the arcs, which go out from *s*. The transitions ‘upon rejections’ are the ones that guarantee the returnless manner of text scanning.

The output function *O(s)* indicates the list of motifs, represented by a sample (as a sequence of arc labels on the way from initial state ‘0’ into ‘s’), a successful search for which is realised as the automaton passes into state *s*.

When constructing the automaton, in every motif four neighbouring positions are chosen (the core of a motif), having minimum value of the product P_i and containing no passive positions. Then this core is converted into exactly determined words of length 4 that act as samples in constructing automaton. If coincidence of a current fragment of an input sequence and one of the automaton samples is observed, comparison is performed (up to the first non coincidence) of all the other motif positions from the list of the output function, and the corresponding fragments of the sequence (the stage of extending the core). According to the results of this stage, the final decision is made on whether there is similarity or not.

The search for distant similarity. To reveal a distant similarity, the algorithm of comparison is modified. The user specifies the matrix of similarity of amino acid residues [e.g., using the one from families PAM (Dayhoff, 1978), BLOSUM, etc.] and *D* - the level of similarity within the limits of motif. For all states of the automaton, the function of rejection is set to zero. Besides, a sequence as a whole does not input to the automaton, but specially processed words. Preparing words, additional to the initial fragment and the search process are as follows:

A. For every fragment of the input sequence of length 4 the value S_o is calculated - the sum of values of diagonal elements of the matrix of similarity for amino acids of the fragment. Then the value $S_o = S_{04} + 6*S_m$ is calculated, where $S_m = \sum_{1}^{20} p_l * t_i$ is average value of diagonal elements s_{ii} of the scoring matrix, p_l is the frequency of occurrence in proteins of amino acid i. The coefficient 6 is chosen because of the length 10 is the most usual for motifs.

B. Supplementary 'similar' words are constructed. For each possible word of length 4, the sum of elements of the similarity matrix $S = \sum_{i=1}^{4} s_{kl}^{(i)}$ is calculated. Here *k* and *l* are indices of amino acids of the initial fragment and the supplementary word in corresponding positions *i*, $s_{kl}^{(i)}$ is an element of the similarity matrix. If *S* does not differ from the sum of diagonal elements for the corresponding amino acids of the fragment by a value greater than $(100-D)*S_o/100$, where D (%) is the point of similarity, specified by the user, the word is accepted.

C. All these words are passed to the entry of the automaton consecutively. In the case of coincidence with the sample, the following values are calculated: S_0^1 the sum of diagonal values of the similarity matrix for amino acids of the fragment, corresponding to active positions of the motif, and $S^1 = \sum_{1}^{4} \max(s_{kl}^{(i)})$ similarity of the motif to the fragment. Here *k* is index of amino acid, located in the position of the fragment, $\max(s_{kl}^{(i)})$ is the maximum value of similarity for amino acid *k* of the fragment and amino acids *l*, located in position *i* of the motif. If $S^1 > S_0^1 *D/100$, then the decision is made about the existence of the prescribed degree of similarity.

The comparison of patterns with the parent banks. To examine the recognising ability of the patterns and exclude certain motifs, which are non-specific for a given family, all patterns were compared with all the proteins of the SWISS-PROT+TrEMBL. In the routine comparison between patterns and the banks, only exact similarities of two or more motifs per a pattern were registered, i.e. the cases when fragments of amino acid sequences belong to the motifs. The comparisons made the inclusion of hundreds of sequences into trial samples possible.

The similarity is regarded as 'positive' one, if at least one of the two following conditions is met.

1. Query sequence belongs to the trial sample.
2. 2. All words of one of the DE fields of the pattern (the names of the proteins forming the family) are present in the field DE (protein name) of the sequence.

The last condition needs some clarification. Proteins are considered to be related to the trial sample proteins, if they have the same name that the trial sample has, possibly supplemented with words HYPOTHETICAL, PROBABLE, POSSIBLE, PRECURSOR, CHAIN, etc., descriptions of localisation of sequences (MITOCHONDRION, CHLOROPLAST, PLASMID), its composition in the case of polyproteins, a note concerning the type of the chain, etc.

The similarity is considered 'conditionally positive' (UNKNOWN), if at least one of the DE or KW words of the pattern coincides with one of the words determined in fields DE and/or KW of the sequence. Thus, proteins are defined as conditionally related if they possess some common function (e.g., hydrolases, dehydrogenases, oxidoreductases, etc.) or some specific features of their structure (for instance, transmembrane segments). All other cases of similarity are regarded as false positive. As a result of comparison with the bank, a pattern bank entry is created, similar in its structure to entries of PROSITE. The example of such entry is given in Figure 2. Descriptions of the fields are given in Table 1.

DISCUSSION

In the first version of PROF_PAT, patterns were selected in accordance with the principle of small variability of several physicochemical properties of amino acids (Bachinsky, et al., 1997). However, the use of this bank in actual practice revealed its shortcomings. Its large size and the time-consuming procedure of comparison compelled us to modify its construction principles to a certain extant.

In version 1.3. presented here, the total number of motifs in more than 13,000 patterns is over 200,000 with specificities varying from one expected false positive prediction in 10^8 tests and higher. The total combined length of patterns is about 2 million positions.

To find a distant similarity, a very fast flexible comparison procedure is employed, using the modified algorithm of Aho-Corasic (Aho and Corasic, 1975), various matrices of similarity/distance for amino acid residues, the predetermined grade of similarity between a fragment of an amino acid sequence and a pattern motif.

The results of comparison of patterns with all sequences of release 38 of the SWISS-PROT and release 11 of TrEMBL are given in Table 2. Patterns identify nearly 130 000 of amino acid sequences as having shown 'positive' or 'conditionally-positive' similarity. In the latter case, the similar sequences, not included into the trial samples, are usually identified.

Almost all sequences of the trial samples are recognised by all motifs of the corresponding patterns. Certain violations of this rule are due only to the presence of non-standard symbols in the particular sequences of the trial samples that have fallen into the intervals of positions represented by pattern motifs.

A number of cases of false-positive similarity may be divided into two classes. Sometimes it is a really chance similarity. However, sometimes two or more pattern motifs show similarity to the fragments of a certain sequence; the order of the fragments' locations often correspond to that of the motifs' locations, which increases even more the certainty that the similarity is not random. In most cases, false-positive similarity is revealed with sequences described only as products of some genes, and this information is not included into descriptions of patterns (see some examples in Table 3.).

All patterns were searched in proteins of more recent version of SWISS-PROT that were absent in parent version (file new_seq.dat on the EBI server, 21, September 1999). This comparison was made with the purpose of testing PROF_PAT for sensitivity and to work through the technology of the bank update. The first 500 complete long sequences (i.e. 30 or more amino acid residues in length) that do not contain words 'PUTATIVE' or 'HYPOTHETICAL' were selected for testing. Comparison was carried out at level of similarity 80 %. Matrix 250PAM was used. 73 sequences were not identified (no significant matchings). Two sequences were identified by patterns that have DE fields different from DE fields of the sequences. There were 425 sequences identified as 'positive'. Of these 500 sequences 285 contain links to PROSITE patterns, and 245 sequences contain links to PFAM. From 1480 new sequences of TrEMBL described as ORFs, 419 were undoubtedly identified. It should be mentioned that some of these matchings refer the sequences to patterns or protein groups described as ORFs or HYPOTHETICAL PROTEINS also. IDENTIFY assigns biological functions to 25-30% of all proteins encoded by the Saccharomyces cerevisiae genome and by several bacterial genomes (Nevill-Manning, et al. 1998). Thus, the results of comparisons for these two banks are alike.

Some other comparisons of the PROF_PAT and other secondary banks are presented in Table 4. They show that PROF_PAT exceeds the most popular banks PROSITE, PRINTS, and BLOCKS under such index as number of patterns and motifs. The more pattern motifs show similarity to the sites of a query sequence, the higher would be the likelihood that the amino acid sequence is related to proteins of the trial sample (Henikoff and Henikoff, 1991), especially if the order of the motifs coincides with that of the sample proteins. We can not make direct bulk comparisons of PROF_PAT with other banks because other banks (with the exception of PRINTS) do not provide search of many sequences in one connection.

Thus, we have constructed a bank of patterns for protein families, representing about two-thirds of the full-length protein sequences of the bank SWISS-PROT release 38 and TrEMBL release 11. The fast flexible search program for close and distant similarity provides comparisons of amino acid sequences of interest with the bank of patterns in the interactive mode. The PROF_PAT technology update has been developed and tested, so the new versions of PROF_PAT will be created following each new versions of SWISS-PROT+TrEMBL.

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FIGURE LEGENDS

Fig. 1. Illustrations of the functions of the Aho-Corasic automaton constructed on the set of samples R={r_1, r_2, r_3, r_4, r_5} = {HE, SHE, HIS, HER, HERS}. a) Graph representation of transition function *G(s,a).* b) Rejections' function *F(s).* c) Output function *O(s).* d) Transition of Automaton from state to state if the input text is "ushers"

Fig. 2. An example of the pattern bank entry.

Table 1.

Descriptions of fields of PROF_PAT 1.3. entries

Identificator of a field	Value of the field
ID	Unique identificator of a pattern (entry)
DT	Date of creation/edition
DE	Description of the pattern, usually - descriptions (DE) of sequences of the trial sample
KW	Key words
PR	The set of ACs of sequences of the trial sample
RE	Release of parent bank
AC	Identifier and margins of the motif of the pattern
PA	Motif of the pattern
FR	Occurrence frequency of matching of the motif to random fragment of amino acid sequence
DR	The set of ACs of amino acid sequences of parent bank that match the motif: T - true, ? – unknown, F - false positive
NR	The statistics of matches of the motif to amino acid sequences of the parent bank: X(У), where X is the total number of matches, У - the number of sequences where matches have been revealed
*/	The end of the motif
//	The end of the pattern

Table 2.

Results of comparisons of sequences of parent banks with patterns of PROF_PAT 1.3.

Number of sequences with positive matches	127,634
Number of sequences with conditionally-positive matches	2,317
Number of sequences with false-positive matches	1238
Number of sequences of trial samples that do not match one or more motifs of the patterns	2177
Number of sequences of trial samples that do not match any motif of the patterns	0

Table 3.

Some cases of false-positive similarity have been revealed, when patterns of PROF_PAT 1.1. bank were searched for SWISS-PROT+TrEMBL bank

Descriptions of protein families (patterns)	Entry names of related sequences	Number of similar motifs/ number. of motifs in the pattern	Descriptions of sequences	Comments
SERINE THREONINE KINASE	Q26345	5/15	FU (FUM1)=SEGMENT POLARITY GENE FUSED {28-BP DELETION}.	The sequence matches motifs of the N-end of the pattern
FLORAL HOMEOTIC PROTEIN AGL AGAMOUS PROTEIN MADS BOX PROTEIN DAL2 PROTEIN	Q41876	5/9	ZAG1.	
COLLAGEN	Q20927	4/7	F57B7.3.	
RNA-DIRECTED RNA POLYMERASE (EC 2.7.7.48) READTHROUGH PROTEIN REPLICASE REPLICATION-ASSOCIATED PROTEIN	Q84126 Q88598	20/66 20/66	52KDA UNKNOWN IN FUNCTION PROTEIN 54 KDA PROTEIN	The sequences match motifs of the C-end of the pattern
ZINC-FINGER PROTEIN	Q60980	6/19	BKLF.	
PHOSPHOLIPASE	Q63693	**29/30**	PHO**D**PHOLIPASE C DELTA4.	An error in protein DE
ATP SYNTHASE A CHAIN (EC 3.6.1.34) (PROTEIN 6) ATPASE ATP SYNTHASE SUBUNIT 6	Q35294	4/12	URF-RMC	The sequence matches motifs of the N-end of the pattern
PROTEIN B15	VC16_VACCC	4/8	PROTEIN C16/B22.	
CANAVALIN BETA-CONGLYCININ	Q39816	11/23	7S STORAGE PROTEIN ALPHA SUBUNIT.	The sequence matches motifs of the C-end of the pattern
TRANSPOSASE MARINER PROTEIN	YKC6_CAEEL	5/10	HYPOTHETICAL 29.3 KD PROTEIN B0280.6 IN CHROMOSOME III.	The sequence matches motifs of the C-end of the pattern
MASC PROTEIN	Q50586	4/15	HYPOTHETICAL 63.1 KD PROTEIN.	
MUCIN	Q22902	**9/11**	COSMID C16D9.	The sequence matches motifs of the N-end of the pattern
NUCLEOLAR PROTEIN NUCLEOPHOSMIN-RETINOIC ACID RECEPTOR ALPHA FUSION PROTEIN	Q14115	7/14	P80 PROTEIN.	The sequence matches motifs of the N-end of the pattern
PROTEIN KINASE	Q24096 Q24590	4/18 4/18	LATS. TUMOR SUPPRESSOR.	

Table 3. (continued)

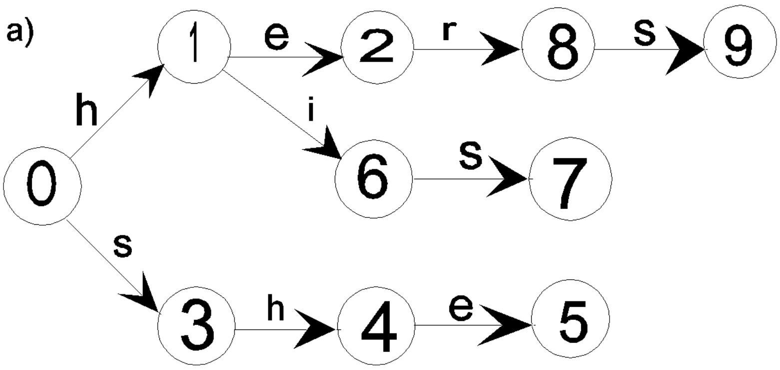
RNA-DIRECTED RNA POLYMERASE (EC 2.7.7.48) REPLICASE	Q65014 Q83423 Q83426	8/29 5/29 5/29	PROTEIN OF 33 KDA. PROTEIN 29. 29K PROTEIN.	The sequences match motifs of the N-end of the pattern
SPLICING FACTOR RNA BINDING PROTEIN 1	Q62093	**4/5**	PR264/SC35.	The sequence matches motifs of the N-end of the pattern
SUPPRESSOR OF FORKED PROTEIN CLEAVAGE STIMULATION FACTOR	Q24539	13/34	39 KD PROTEIN.	The sequence matches motifs of the N-end of the pattern
TRANSCRIPTION FACTOR	Q18694	3/9	C47G2.2.	
TRANSPOSASE TNIA	Q47380	9/26	INVASIN	The sequence doesn't match the INVASIN pattern. The membership to this class of proteins is doubtful
TRANSALDOLASE (EC 2.2.1.2)	Q49705 Q49698	6/18 6/18	B1496_F2_65. B1496_F1_27.	The sequences match motifs of the N-end (Q49705) and C-end (Q49698) of the pattern
TRANSPOSASE	ADPR_LACLA	5/12	ATP-DEPENDENT PROTEASE (EC 3.4.21.-).	The sequence doesn't match the patterns of ATP-dependent proteases
PROBABLE TRANSPOSASE FOR INSERTION SEQUENCE ELEMENT IS701	Q55975 Q55976	5/11 5/11	HYPOTHETICAL 16.4 KD PROTEIN HYPOTHETICAL 13.5 KD PROTEIN.	The sequences match motifs of the N-end (Q55975) and C-end Q55976) of the pattern
RECEPTOR-LIKE TYROSINE-PROTEIN KINASE (EC 2.7.1.112)	Q23677	12/15	ZK938.5.	The sequence matches motifs of the C-end of the pattern
CAPSID PROTEIN	COA3_AAV2	13/32	PROBABLE COAT PROTEIN 3.	
PROTEIN VP2	Q84387	4/23	HYPOTHETICAL 7.9 KD PROTEIN.	It is a C-fragment of VP2 protein
ANAEROBIC RIBONUCLEOSIDE-TRIPHOSPHATE REDUCTASE (EC 1.17.4.2)	Q38428	19/28	ORF (55.11).	The virus genome contains a C-fragment of bacterial protein
DIHYDROPYRIMIDINASE	Q21773	8/20	R06C7.3	
REVERSE TRANSCRIPTASE	Q63305	15/57	LONG INTERSPERSED REPETITIVE DNA CONTAINING 7 ORF'S.	It is a C-fragment of transcriptase
DEHYDROGENASE DIOXYGENASE	Q52459	**9/9**	THE FIRST START CODON IN THE ORF IS FOUND AT POSITION 2466.	Besides of the sequence matches all motifs of the pattern, it hasn't 30%similarity with all proteins of the trial sample

Table 4.

Some characteristics of secondary banks in comparison with PROF_PAT.

The name of the bank its release/parent banks	Number of patterns (entries)	Number of motifs	The source of data
PROF_PAT 1.3. August 1999 / SWISS-PROT 38 + TrEMBL 11	>13,000	>200,000	http://wwwmgs.bionet.nsc.ru /programs/prof_pat
PROSITE 15, July 1998	1,031	1,366	http://www.expasy.ch/prosite/
PFAM 4.0, May 1999 / SWISS-PROT 37 + TrEMBL 9	1,465		http://www.sanger.ac.uk/Pfam
PRINTS 22.0, March 1999	1,100	6,510	http://www.biochem.ucl.ac.uk /bsm/dbbrowser
BLOCKS 11.0, July 1998	994	4,034	http://www.blocks.fhcrc.org/
SBASE 6.0	1,037	2,459	http://base.icgeb.trieste.it/sbase
PIMA	22,416		Ladunga I., *et al.* (1997)
IDENTIFY, 1998 /PRINTS+BLOCKS	7,000	50,000	http://motif.stanford.edu/identify

a)



b)

s	1	2	3	4	5	6	7	8	9
F(s)	0	0	0	1	2	0	3	0	3

c)

s	Q(s)
2	{he}
5	{she, he}
7	{his}
8	{her}
9	{hers}

d) T= u s h e r s

s 0 0 3 4 5
2 8 9

```
ID   00004;
DT   Thu Aug  5 14:35:08 1999
DE   4-HYDROXYPHENYLPYRUVATE DIOXYGENASE (EC 1.13.11.27) (4HPPD)
KW   OXIDOREDUCTASE; DIOXYGENASE; IRON; ACETYLATION.
PR   P32754, P49429, Q02110, Q22633, Q27203, Q00415,
PR   O42764, Q53586;
RE   SWISS-PROTEIN(rl.37)+TREMBL(rl.8)
AC   00004_1 (47-56)
PA   [FW]-[AVWY]-V-G-N-A-K-Q-[AV]-A
FR   frequency = 4.02065e-12
DR   P32754, T; P49429, T; Q02110, T; Q22633, T; Q27203, T;
DR   Q00415, T; O42764, T; Q53586, T;
NR   /TOTAL=8(8); /POSITIVE=8(8); /UNKNOWN=0(0); /FALSE_POS=0(0);
NR   /FALSE_NEG=0;
*/

...

AC   00004_12 (391-400)
PA   D-R-P-T-[LV]-F-[FILY]-E-[IV]-I
FR   frequency = 4.6197e-12
DR   P32754, T; P49429, T; Q02110, T; Q22633, T; Q27203, T;
DR   O23920, T; Q00415, T; O42764, T; Q53586, T; Q18347, ?;
NR   /TOTAL=10(10); /POSITIVE=9(9); /UNKNOWN=1(1); /FALSE_POS=0(0);
NR   /FALSE_NEG=0;
*/
//
```