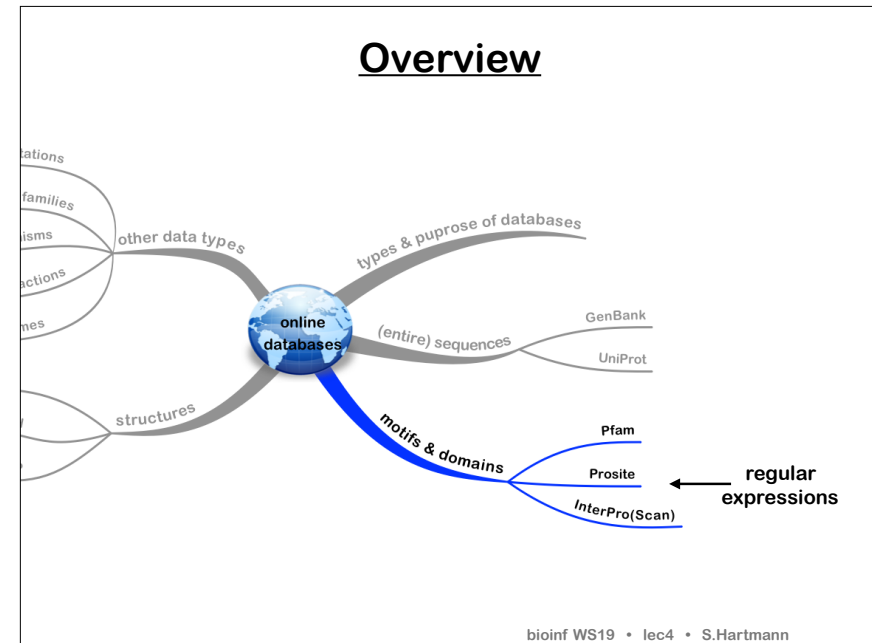


Online resources (II), regular expressions Nov 08, 2019



Protein domains & architectures

protein domains

- functional and evolutionary units of proteins
- have specific and conserved functions
- function independently or with other domains
- together determine the protein's function
- most eukaryotic proteins contain ≥ 2 domains

architecture

- ordered domain arrangement in a given protein



Motif and domain databases

sequence

cDNA, gDNA, protein



MYALKRELWCVLLLCGAICTSPSQETHRRRLRGVRSYRVTCRDEKTMQIYQQHQSRLRPLLRGNRVEHCWCNDGQTQ
CHSVFVKSCSEPRCFNGGTCLQAIYFSDFCVQCPVGFIGRQCEIDARATCYEDQGITRYGTWSTTESGAECVNWNTS
GLASMPYNGRRPDVAVKLGNGHNYCRNPDKDSKPWCYIFKAKEYSPDFCSTPACTKEKEECYTGKGLDYRGTRSLTM
SGAFCLPWNLSLVMGKIYTAWNNAQTLGLGKHNYCRNPDGDTQPCWCHLKHKLWHEYCDLPQCVCGLRQYKEPQ
FRIRGGLYADITSHFWQAAIFVKNRRSPGERFLCGGILISSCWVLSAAHCFQERFPPIHVRVVLGRYRLVPGEEQ
AFEVEKYIVHKEFDDDDTYDNDIALQLKSDSLTCAQESDAVRTVCLPEANLQLPDWTECELSGYGKHEASSPFYSER
LKEAHVRLYPSSRCTSKHLFNKTTITNNMLCAGDTRSGGDNANLHDAQCGDSSGGPLVCMKGNHMTLVGVISWGLGCGQ
KDVPGVYTKVTNYLNIWIRDNTRF

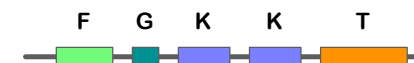
function



convert zymogen plasminogen to plasmin

motifs/domains

- 1 fibronectin
- 1 growth factor
- 2 Kringle
- 1 trypsin



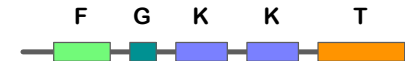
Motif and domain databases

- purposes:
 - group sequences that contain conserved patterns into “families”
 - annotate patterns and their families
 - scan new sequences against stored patterns
- identification/assignment of patterns:
 - Hidden Markov models (e.g., Pfam) (statistical models of conserved sequences)
 - regular expressions (e.g., Prosite) (syntax to describe patterns)
 - and more

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Pfam

- entries are based on functional domains



- available information:
 - domain combinations containing a given domain
 - sequences in which the domain occurs
 - species in which the domain has been found
 - 3D structures, if available
 - ...

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A Pfam entry

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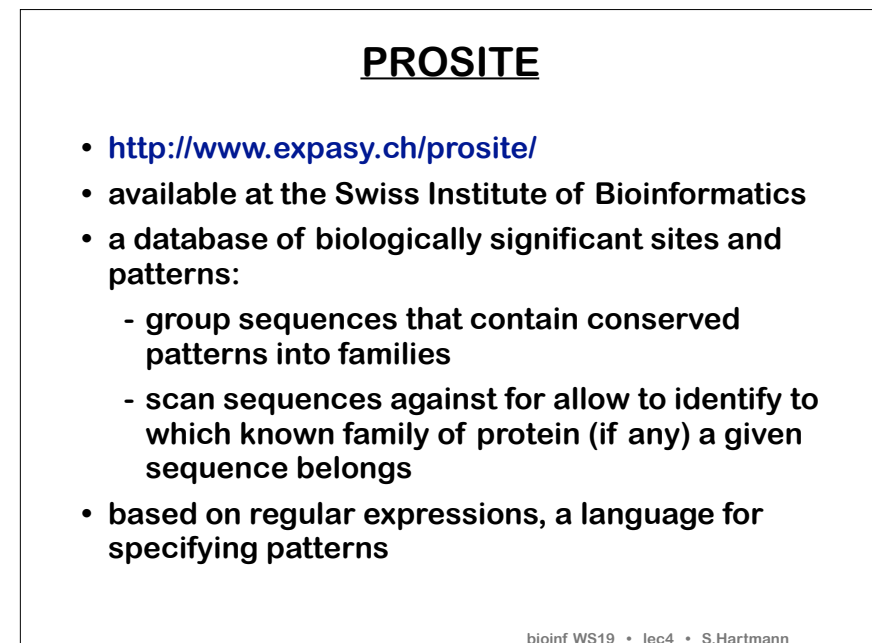
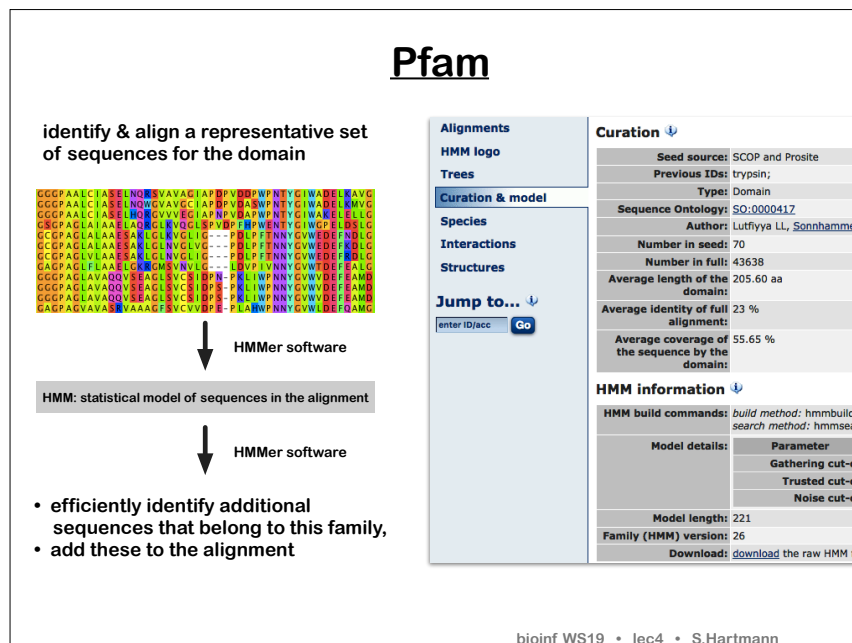
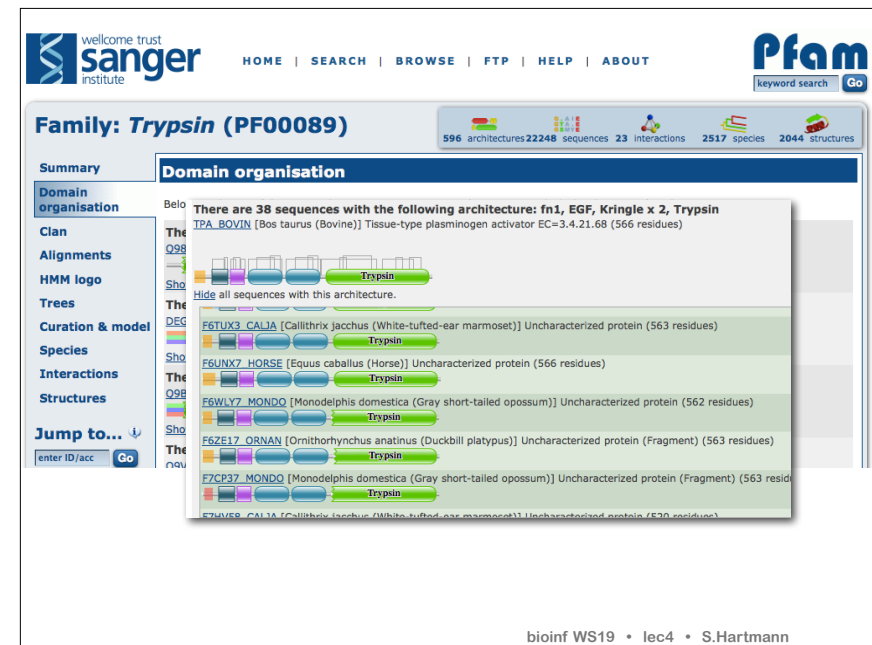
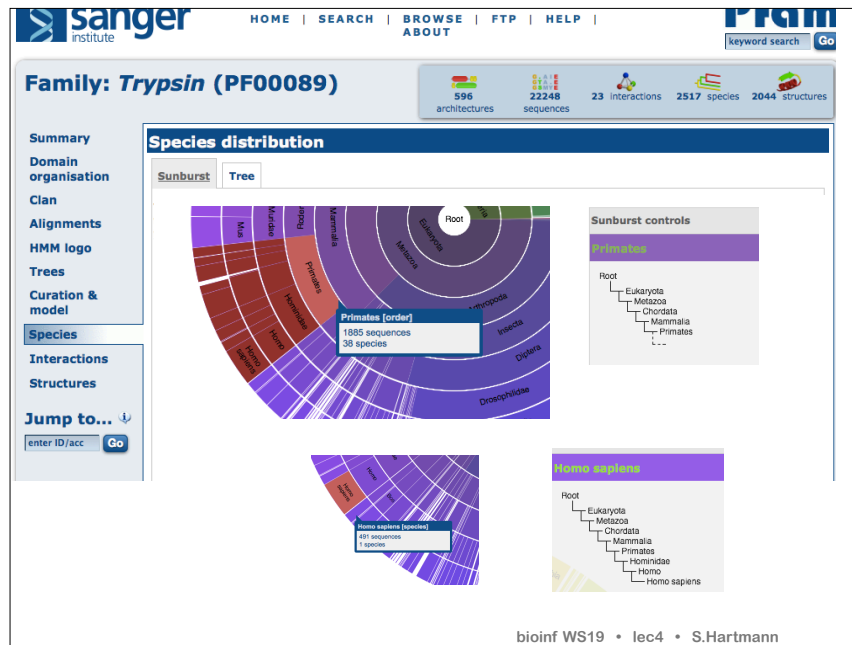
taxonomic levels:

- superkingdom
- kingdom
- phylum
- class
- order
- family
- genus
- species

Colour assignments

- Archea
- Bacteria
- Eukaryota
- Other sequences
- Viruses
- Unclassified
- Unclassified sequence
- Viroids

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Database of protein domains, families and functional sites

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

Release 20.131 of 27-Oct-2016 contains 1773 documentation entries, 1309 patterns, 1172 profiles and 1193 ProRule.

Search

Search

Browse

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

Quick Scan mode of ScanProsite

Quickly find matches of your protein sequences to PROSITE signatures (max. 10 sequences) [?] [?] [?]

Enter UniProtKB accessions or identifiers or PDB identifiers or sequences in FASTA format

Scan Clear

☐ Exclude motifs with a high probability of occurrence from the scan

For more scanning options go to [ScanProsite](#)

Other tools

- **PRATT** - allows to interactively generate conserved patterns from a series of unaligned proteins.
- **MyDomains - Image Creator** - allows to generate custom domain figures.



Entry: **PS00028**

General information about the entry

Entry name [info]	ZINC_FINGER_C2H2_1
Accession [info]	PS00028
Entry type [info]	PATTERN
Date [info]	APR-1990 (CREATED); JUN-1994 (DATA UPDATE); SEP-2016 (INFO UPDATE).
PROSITE Doc. [info]	PDOC00028

Name and characterization of the entry

Description [info]	Zinc finger C2H2 type domain signature.
Pattern [info]	C-x(2,4)-C-x(3)-[LIVNFYWC]-x(8)-H-x(3,5)-H.

Numerical results [info]

Numerical results for UniProtKB/Swiss-Prot release 2016_10 which contains 552'884 sequence entries.

Total number of hits	13'329 in 2'300 different sequences
Number of true positive hits	12'992 in 2'049 different sequences
Number of 'unknown' hits	26 in 12 different sequences
Number of false positive hits	311 in 239 different sequences
Number of false negative sequences	96
Number of 'partial' sequences	1
Precision (true positives / (true positives + false positives))	97.66 %
Recall (true positives / (true positives + false negatives))	99.27 %

Comments [info]

Taxonomic range [info]	Archaea, Eukaryotes, Eukaryotic viruses
Maximum number of repetitions [info]	35
Site [info]	zinc at position 1



[Home](#) [ScanProsite](#) [ProRule](#) [Documents](#)

ScanProsite Results Viewer

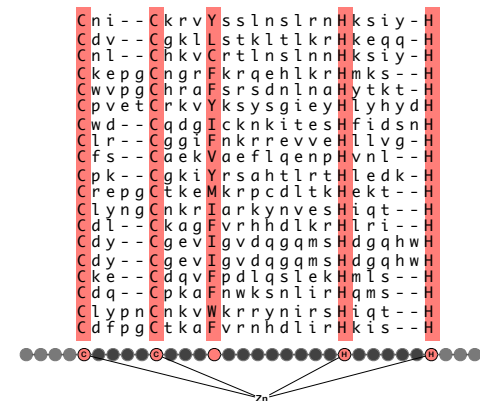
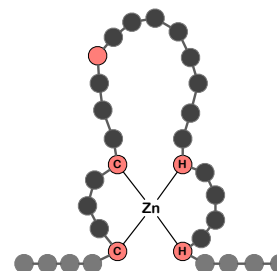
USERSEQ1 (660 aa)

MAHALVTFRDVDTIDFSQKEWELDTTQKLYRDVMLENNYNNLVSLGYSGSKPDVITLLEQGKEPCV
AARDVTGRQYPGLLSRHKTKKLSSEKDIHDISLSKGSKIEKSKTLHLKGSIFRNEWQSKSEFEQQQ
GLKERSISQKKIIFPKMSTDRKKHPSFTLNQRIHNSEKSCDSNLVQHGKIDSVDKHDCEGSGTFNN
VYQLTLHQKIHTGKSKCEKCGKVFSSHQTLHQRFHTGKFPYECQECGKTFILYPQLNRHQKI
HTGKKPYMKCKDKSFFSRLELTQHKKRIHTGKKSYECKECGKVFQVFPYFKEHERIHTGKKPYECK
ECGKAFSVCGQLTRHQKIHTGVKPYECKECGKTFRLSFYLTEHRRTHAGKKPYECKECGKSFNVGR
QLNRHKAHTGKIPFACKVCEKAFPSYGDRLVHSRIHTGKPYECKECGKAFMLRSVLTEHQRLHT
GVKPYECKECGKTFRVRSQISLHKKIHTDVKPYKVCRCGKTFRFGYLTQHRIHTGKPYECKEC
GKAFIRRGNLKEHLKIHSGLKPYDCKEKGKSFRRGQFTEHQKIHTGVKPYECKECGKAFSRSDVL
RIHQRIHTGKPYECKCGKAFRLNSHLTEHQRIHTGKPYECKVCRKAFRQYSHLYQHOKTHNVI

Hits by **PS00028** **ZINC_FINGER_C2H2_1** Zinc finger C2H2 type domain signature

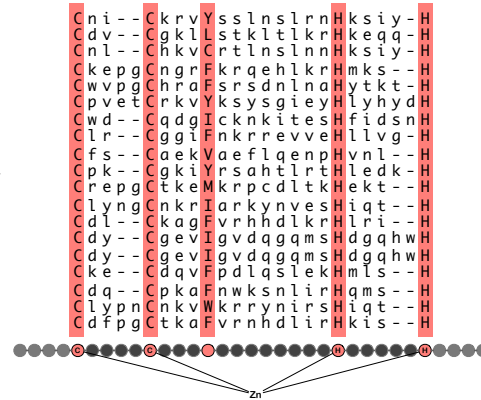
215 - 237: CkcekCgkvFshsyqltLHqrf..H

C2H2 zinc finger DNA binding protein



C2H2 zinc finger DNA binding protein

C followed by
any 2 to 4 letters followed by
C followed by
any 3 letters followed by
C followed by
one of L,I,V,M,F,Y,W,C followed by
any 8 letters followed by
H followed by
any 3 to 5 letters followed by
H



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A Prosite regular expression

Name and characterization of the entry

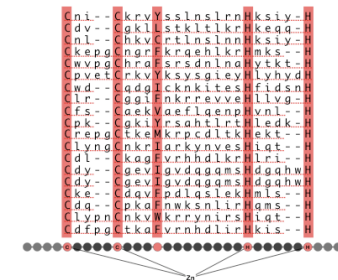
Description [info]

Zinc finger C2H2 type domain signature.

Pattern [info]

C-x(2,4)-C-x(3)-[LIVMFYWC]-x(8)-H-x(3,5)-H.

C-x(2,4)-C-x(3)-[LIVMFYWC]-x(8)-H-x(3,5)-H



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Regular expressions

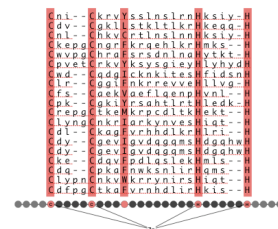
a powerful language for specifying patterns
used in different contexts and in different “dialects”

- linux terminals
- text editors
- protein motif databases (e.g., Prosite)
- ...

patterns

- exact and inexact patterns

```
seq1 ATGACTGCAATTTTAGAG
seq2 ATGAATGTTTTATCATGT
seq3 ATGGTAAACATTCGTTTA
seq4 ATGCTTAATATATTTAAT
seq5 ATGCTTACTCTCAAACTT
seq6 ATGGTAACCATTAAGCC
seq7 ATGAAATTTAACCAGAT
seq8 ATGAATCCACTGGTTTCT
***
```



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Regular expressions

a powerful language for specifying patterns
used in different contexts and in different “dialects”


- linux terminals
- text editors
- protein motif databases (e.g., Prosite)
- ...


patterns

- exact and inexact patterns
- in biological sequences: proteins, DNA
- in everyday life

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Linux regular expressions, using grep

```
grep Mus species.txt  Mus musculus
```

```
grep Sus species.txt  Sus scrofa
```

regular expressions (regex)

Linux regular expressions

characters

- exact matches: **ATG A Mus Sus 2 37**

metacharacters

- characters with special meaning: **[] . ? * + { } \ () | ^ \$**

metasymbols

- sequences of characters with special meaning
\t \n \w

Linux regular expressions, using grep

```
grep [MS]us species.txt
```

```
grep -E 'MT{2,}NG' proteins.fasta
```

regular expressions (regex)

grep parameters

- E allows “extended” regex syntax
- o -i -c ...

quotes to protect special characters

Translation: Prosite to grep/linux

Trefoil motif:

plays a role in the renewal and pathology of mucous epithelia

[KRH]-x(2)-C-x-[FYPSTV]-x(3,4)-[ST]-x(3)-C-x(4)-C-C-[FYWH]

Prosite regex	grep regex
One of the amino acids K, R, or H	[KRH]
any two amino acids	.{2}
a C	C
any one amino acid	.{1}
one of F, Y, P, S, T, or V	[FYPSTV]
any three or four amino acids	.{3,4}
either S or T	[ST]
any three amino acids	.{3}
a C	C
any four amino acids	.{4}
two Cs	C{2}
any one of the amino acids F, Y, W, H	[FYWH]

Translation: Prosite to grep/linux

C-x(2,4)-C-x(3)-[LIVMFYWC]-x(8)-H-x(3,5)-H

Some disadvantages of regex

- too rigid to pick up divergent sequences
- short patterns will find false positives

False positive hits (sequences which do not belong to the set under consideration):

11014_ASPM2 (P0C9K3), ABC3G_LAGLA (Q694B8), AEGA_ECOLI (P37127),
 APO3_ARATH (Q9F850), ARGD_DACHD (Q9K8V5), AT517_HUMAN (Q8T556),
 AT119_HUMAN (Q9T559), AT519_MOUSE (P59509), BICAP_DIDMA (Q4G289),
 BRAT_DROME (Q9MQ29), CACD2_XENTR (Q5DF48), CBIX_BACHE (Q8T690),
 CBIX_STYR3 (Q55451), CPAH_MOUSE (P06909), CPB3_CAERE (Q683D4),

False negative hits (sequences which belong to the set under consideration, but which have not been picked up by the pattern or profile):

APTX_CIOIN (P61802), APTX_DANRE (P61799), APTX_DROME (Q8M5G8),
 APTX_KENLA (Q77287), APTX_XENTR (P61801), BH140_ARATH (Q9M041),
 DPF3_DANRE (A9F4C0), ELBOR_DROME (Q9V258), F170A_HUMAN (A1A519),
 F170A_MACFA (Q661M5), F170A_MOUSE (Q661M6), HAKAT_CHICK (Q58H54),
 HAKAT_HUMAN (Q75803), HAKAT_MACFA (Q48718), HAKAT_MOUSE (Q87122),

- cannot include information about relative frequencies

CKCEKCGKVFHSYQLTLHQRF--H
 CIA--CGVNMEIIPVKHIHPAGIKH
 CIM--CGINMEIVPLAHTHPSGKTH
 CLV--CGVSEMEVIPHALQHHSGKKH
 CLV--CGVSMDLVPLRYIHPSGGKH
 CLM--CAVSMELVPLRYIHPSGKKH
 CLI--CGMVMDLVPLAYVHSAGEKH

C-x(2,4)-C-x(3)-[LIVMFYWC]-x(8)-H-x(3,5)-H

Motif and domain databases

Database	URL
PROSITE	http://www.expasy.org/prosite/
PRINTS	http://bioinf.man.ac.uk/dbbrowser/PRINTS/
Pfam	http://www.sanger.ac.uk/Software/Pfam/
ProDom	http://prodes.toulouse.inra.fr/prodom/current/html/home.php
BLOCKS	http://www.blocks.fhcrc.org/
SMART	http://smart.embl-heidelberg.de/
TIGRfam	http://www.tigr.org/TIGRFAMs/index.shtml
SUPERFAMILY	http://supfam.mrc-lmb.cam.ac.uk/SUPERFAMILY/
SBASE	http://www3.icgeb.trieste.it/~sbasesrv/main.html
CDD	http://www.ncbi.nlm.nih.gov/Structure/cdd/cdd.shtml
...	...
...	...

InterPro

- an integrated documentation resource for protein families, domains and sites.
- it combines a number of databases that use different approaches to classify domains
 - PROSITE (regular expressions and profiles)
 - Gene3D, PANTHER, PIRSF, Pfam, SMART, SUPERFAMILY and TIGRFAMs (hidden Markov models (HMMs))
 - PRINTS (groups of aligned, un-weighted motifs)
 - ProDom (PSI-BLAST approach)
- entries are
 - linked to entries in UniProt (and other databases)

InterPro

InterPro
Protein sequence analysis & classification

Search InterPro...
Examples: IPR020405, kinase, P51587, PF02932, GO:0007165

Home Search Release notes Download About InterPro Help Contact

Overview

- Proteins matched (56160)
- Domain architectures (1625)
- Pathways & interactions
- Species
- Structures
- Literature (9)
- Cross-references (4)

Domain
Serine proteases, trypsin domain (IPR001254)

Short name: *Trypsin_dom*

Domain relationships

- Peptidase S1, PA clan (IPR009003)
 - Serine proteases, trypsin domain (IPR001254)
 - Peptidase S1A, nudel (IPR015420)

Description

This entry represents the active-site-containing domain found in the trypsin family members. The catalytic activity of the serine proteases from the trypsin family is provided by a charge relay system involving an aspartic acid residue hydrogen-bonded to a histidine, which itself is hydrogen-bonded to a serine. The sequences in the vicinity of the active site serine and histidine residues are well conserved in this family of proteases [PMID: 3136396]. A partial list of proteases known to belong to the trypsin family is shown below.

Contributing signatures

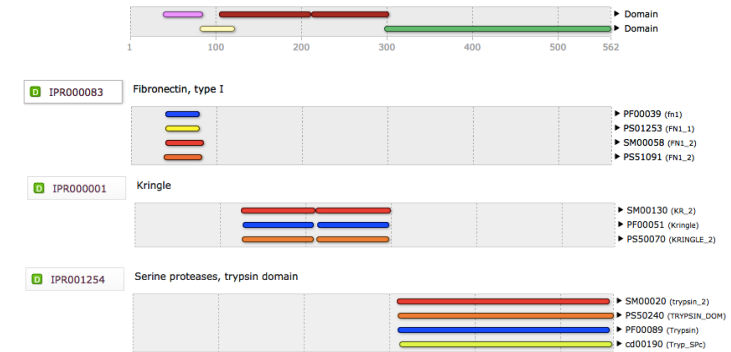
Signatures from InterPro member databases are used to construct an entry.

- PROSITE profiles**
 - P550240 (TRYPSIN_DOM)
- CD0**
 - cd00190 (Tryp_SpC)
- SMART**
 - SM00020 (Tryp_SpC)
- Pfam**
 - PF00089 (Trypsin)

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InterproScan

Domains and repeats



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Today's exercise

1. regular expressions

- patterns in protein sequences
 - thionins
 - zinc fingers
 - patterns in DNA sequences
 - OPTIONAL: restriction enzyme recognition sites
- proteins.fasta**
- dna.fasta**

2. domain databases: Pfam

NOTE: open these two files in the terminal or with text-only editors!

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Terms and concepts

- domain databases
 - organization
 - purpose
 - examples
- regular expressions
 - definition, application
 - relationship to protein domains
 - syntax Prosite vs. linux terminal
 - grep (-o, -E)
 - metacharacters [] . ? * + { } \

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