



UniProt Knowledgebase

Swiss-Prot Protein Knowledgebase

TrEMBL Protein Database

User Manual

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Contact details

You can send us [general questions and suggestions](#), [updates or corrections to UniProt](#), [submit new protein sequence data](#), or [e-mail us](#) directly.

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Until 2002, the EBI/SIB Swiss-Prot + TrEMBL databases and the PIR Protein Sequence Database (PIR-PSD) coexisted as protein databases with differing protein sequence coverage and annotation priorities. In 2002, EBI, SIB, and PIR (at the Georgetown University Medical Center and National Biomedical Research Foundation) joined forces as the UniProt consortium. The primary mission of the consortium is to support biological research by maintaining a high quality database that serves as a stable, comprehensive, fully classified, richly and accurately annotated protein sequence knowledgebase, with extensive cross-references and querying interfaces freely accessible to the scientific community.

The UniProt Knowledgebase (UniProtKB) provides the central database of protein sequences with accurate, consistent, rich sequence and functional annotation.

The UniProt Knowledgebase consists of two sections: Swiss-Prot - a section containing manually-annotated records with information extracted from literature and curator-evaluated computational analysis, and TrEMBL - a section with computationally analyzed records that await full manual annotation.

1.1. The Swiss-Prot Protein Knowledgebase[Table of contents](#)

Swiss-Prot is an annotated protein sequence database. It was established in 1986 and maintained collaboratively, since 1987, by the group of Amos Bairoch first at the Department of Medical Biochemistry of the University of Geneva and now at the SIB Swiss Institute of Bioinformatics and the EMBL Data Library (now the EMBL Outstation - The European Bioinformatics Institute (EBI)). The Swiss-Prot Protein Knowledgebase consists of sequence entries. Sequence entries are composed of different line types, each with their own format. For standardization purposes the format of Swiss-Prot follows as closely as possible that of the EMBL Nucleotide Sequence Database.

Swiss-Prot distinguishes itself from protein sequence databases by four distinct criteria:

a) Annotation

In Swiss-Prot, as in many sequence databases, two classes of data can be distinguished: the core data and the annotation.

For each sequence entry the core data consists of:

- The sequence data;
- The citation information (bibliographical references);
- The taxonomic data (description of the biological source of the protein).

The annotation consists of the description of the following items:

- Function(s) of the protein;
- Posttranslational modification(s) such as carbohydrates, phosphorylation, acetylation and GPI-anchor;
- Domains and sites, for example, calcium-binding regions, ATP-binding sites, zinc fingers, homeoboxes, SH2 and SH3 domains and kringle;
- Secondary structure, e.g. alpha helix, beta sheet;
- Quaternary structure, i.g. homodimer, heterotrimer, etc.;
- Similarities to other proteins;
- Disease(s) associated with any number of deficiencies in the protein;
- Sequence conflicts, variants, etc.

We try to include as much annotation information as possible in Swiss-Prot. To obtain this information we use, in addition to the publications that report new sequence data, review articles to periodically update the annotations of families or groups of proteins. We also make use of external experts, who have been recruited to send us their comments and updates concerning specific groups of proteins.

We believe that having systematic recourse both to publications other than those reporting the core data and to subject referees represents a unique and beneficial feature of Swiss-Prot.

In Swiss-Prot, annotation is mainly found in the comment lines (CC), in the feature table (FT) and in the keyword lines (KW). Most comments are classified by 'topics'; this approach permits the easy retrieval of specific categories of data from the database.

b) Minimal redundancy

Many sequence databases contain, for a given protein sequence, separate entries which correspond to different literature reports. In Swiss-Prot we try as much as possible to merge all these data so as to minimize the redundancy of the database. If conflicts exist between various sequencing reports, they are indicated in the feature table of the corresponding entry.

c) Integration with other databases

It is important to provide the users of biomolecular databases with a degree of integration between the three types of sequence-related databases (nucleic acid sequences, protein sequences and protein tertiary structures) as well as with specialized data collections. Swiss-Prot is currently cross-referenced to more than 100 different databases. Cross-references are provided in the form of pointers to information related to Swiss-Prot entries and found in data collections other than Swiss-Prot. This extensive network of cross-references allows Swiss-Prot to play a major role as a focal point of biomolecular database interconnectivity.

d) Documentation

Swiss-Prot is distributed with a large number of index files and specialized documentation files. Some of these files have been available for a long time (this user manual, the release notes, the various indices for authors, citations, keywords, etc.), but many have been created recently and we are continuously adding new files. ['Documentation files' section](#) contains an up-to-date descriptive list of all distributed document files.

1.2. The computer-annotated supplement TrEMBL

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TrEMBL is the computer-annotated section of the UniProt Knowledgebase. It contains translations of all coding regions in the DDBJ/EMBL/GenBank nucleotide databases, and protein sequences extracted from the literature or submitted to UniProtKB, which are not yet integrated into Swiss-Prot. TrEMBL allows these sequences to be made publicly available quickly without diluting the high quality annotation found in Swiss-Prot.

The information in a TrEMBL entry is initially derived directly from the underlying DDBJ/EMBL/GenBank nucleotide entry and the quality of data is directly dependent on the information provided by the submitter of the nucleotide entry. This information may be enhanced later by automatic annotation procedures (see below) but if not, it remains as provided by the submitter until the entry is manually annotated and added to Swiss-Prot.

After creation of a TrEMBL entry, a number of steps are taken to improve the data quality for users:

a) Automatic annotation

Records waiting in TrEMBL for full manual annotation are enhanced by automatic annotation. Information is transferred from well-characterised entries in Swiss-Prot to unannotated entries in TrEMBL which belong to groups defined by InterPro, a database of protein families, domains and functional sites. This process brings the standard of annotation in TrEMBL closer to that found in Swiss-Prot through the addition of accurate, high-quality information to TrEMBL entries, thus improving the quality of data available to the user.

b) Redundancy removal

Sequences from the same organism which are full-length and which have 100% identity are merged into a single entry to reduce redundancy.

2. Conventions used in the database

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The following sections describe the general conventions used in the knowledgebase to achieve uniformity of presentation. Experienced users of the EMBL Database can skip these sections and directly refer to [this document](#), which lists the minor differences in format between the two data collections.

2.1. General structure of the database

The UniProt Knowledgebase is composed of sequence entries. Each entry corresponds to a single contiguous sequence as contributed to the bank or reported in the literature. In some cases, entries have been assembled from several papers that report overlapping sequence regions. Conversely, a single paper can provide data for several entries, e.g. when related sequences from different organisms are reported.

References to positions within a sequence are made using sequential numbering, beginning with 1 at the N-terminal end of the sequence.

The sequence data correspond to the precursor form of a protein before posttranslational modifications and processing.

2.2. Status

To distinguish the fully annotated entries in the Swiss-Prot section of the UniProt Knowledgebase from the computer-annotated entries in the TrEMBL section, the 'status' of each entry is indicated in the first (ID) line of each entry. The two defined classes are:

Reviewed	Entries that have been manually reviewed and annotated by UniProtKB curators (Swiss-Prot section of the UniProt Knowledgebase).
Unreviewed	Computer-annotated entries that have not been reviewed by UniProtKB curators (TrEMBL section of the UniProt Knowledgebase).

2.3. Structure of a sequence entry

The entries in the UniProt Knowledgebase are structured so as to be usable by human readers as well as by computer programs. The explanations, descriptions, classifications and other comments are in ordinary English. Wherever possible, symbols familiar to biochemists, protein chemists and molecular biologists are used.

Each sequence entry is composed of lines. Different types of lines, each with their own format, are used to record the various data that make up the entry. A sample sequence entry is shown below.

```
ID   GRAA_HUMAN           Reviewed;           262 AA.
AC   P12544; A4PHN1; Q6IB36;
DT   01-OCT-1989, integrated into UniProtKB/Swiss-Prot.
DT   11-JAN-2011, sequence version 2.
DT   11-DEC-2019, entry version 199.
DE   RecName: Full=Granzyme A;
DE       EC=3.4.21.78;
DE   AltName: Full=CTL tryptase;
DE   AltName: Full=Cytotoxic T-lymphocyte proteinase 1;
DE   AltName: Full=Fragmentin-1;
DE   AltName: Full=Granzyme-1;
DE   AltName: Full=Hanukkah factor;
DE   Short=H factor;
```

DE Short=HF;
DE Flags: Precursor;
GN Name=GZMA; Synonyms=CTLA3, HFSP;
OS Homo sapiens (Human).
OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi; Mammalia;
OC Eutheria; Euarchontoglires; Primates; Haplorrhini; Catarrhini; Hominidae;
OC Homo.
OX NCBI_TaxID=9606;
RN [1]
RP NUCLEOTIDE SEQUENCE [MRNA] (ISOFORM ALPHA), AND VARIANT THR-121.
RC TISSUE=T-cell;
RX PubMed=3257574; DOI=10.1073/pnas.85.4.1184;
RA Gershenfeld H.K., Hershberger R.J., Shows T.B., Weissman I.L.;
RT "Cloning and chromosomal assignment of a human cDNA encoding a T cell- and
RT natural killer cell-specific trypsin-like serine protease.";
RL Proc. Natl. Acad. Sci. U.S.A. 85:1184-1188(1988).
RN [2]
RP NUCLEOTIDE SEQUENCE [LARGE SCALE MRNA] (ISOFORM ALPHA), AND VARIANT
RP THR-121.
RA Ebert L., Schick M., Neubert P., Schatten R., Henze S., Korn B.;
RT "Cloning of human full open reading frames in Gateway(TM) system entry
RT vector (pDONR201).";
RL Submitted (JUN-2004) to the EMBL/GenBank/DDBJ databases.
RN [3]
RP NUCLEOTIDE SEQUENCE [LARGE SCALE GENOMIC DNA].
RX PubMed=15372022; DOI=10.1038/nature02919;
RA Schmutz J., Martin J., Terry A., Couronne O., Grimwood J., Lowry S.,
RA Gordon L.A., Scott D., Xie G., Huang W., Hellsten U., Tran-Gyamfi M.,
RA She X., Prabhakar S., Aerts A., Altherr M., Bajorek E., Black S.,
RA Branscomb E., Caoile C., Challacombe J.F., Chan Y.M., Denys M.,
RA Detter J.C., Escobar J., Flowers D., Fotopulos D., Glavina T., Gomez M.,
RA Gonzales E., Goodstein D., Grigoriev I., Groza M., Hammon N., Hawkins T.,
RA Haydu L., Israni S., Jett J., Kadner K., Kimball H., Kobayashi A.,
RA Lopez F., Lou Y., Martinez D., Medina C., Morgan J., Nandkeshwar R.,
RA Noonan J.P., Pitluck S., Pollard M., Predki P., Priest J., Ramirez L.,
RA Retterer J., Rodriguez A., Rogers S., Salamov A., Salazar A., Thayer N.,
RA Tice H., Tsai M., Ustaszewska A., Vo N., Wheeler J., Wu K., Yang J.,
RA Dickson M., Cheng J.-F., Eichler E.E., Olsen A., Pennacchio L.A.,
RA Rokhsar D.S., Richardson P., Lucas S.M., Myers R.M., Rubin E.M.;
RT "The DNA sequence and comparative analysis of human chromosome 5.";
RL Nature 431:268-274(2004).
RN [4]
RP NUCLEOTIDE SEQUENCE [LARGE SCALE MRNA] (ISOFORM ALPHA), AND VARIANT
RP THR-121.
RC TISSUE=Blood;
RX PubMed=15489334; DOI=10.1101/gr.2596504;
RG The MGC Project Team;
RT "The status, quality, and expansion of the NIH full-length cDNA project:
RT the Mammalian Gene Collection (MGC).";
RL Genome Res. 14:2121-2127(2004).
RN [5]
RP NUCLEOTIDE SEQUENCE [GENOMIC DNA] OF 1-72, NUCLEOTIDE SEQUENCE [MRNA] OF
RP 1-34 (ISOFORM BETA), ALTERNATIVE PROMOTER USAGE, AND INDUCTION.
RX PubMed=17180578; DOI=10.1007/s10038-006-0099-9;
RA Ruike Y., Katsuma S., Hirasawa A., Tsujimoto G.;
RT "Glucocorticoid-induced alternative promoter usage for a novel 5' variant
RT of granzyme A.";
RL J. Hum. Genet. 52:172-178(2007).
RN [6]
RP NUCLEOTIDE SEQUENCE [GENOMIC DNA] OF 1-23.
RA Goralski T.J., Krensky A.M.;
RT "The upstream region of the human granzyme A locus contains both positive
RT and negative transcriptional regulatory elements.";
RL Submitted (NOV-1995) to the EMBL/GenBank/DDBJ databases.
RN [7]
RP PROTEIN SEQUENCE OF 29-53.
RX PubMed=3047119;
RA Poe M., Bennett C.D., Biddison W.E., Blake J.T., Norton G.P., Rodkey J.A.,
RA Sigal N.H., Turner R.V., Wu J.K., Zweerink H.J.;
RT "Human cytotoxic lymphocyte tryptase. Its purification from granules and
RT the characterization of inhibitor and substrate specificity.";
RL J. Biol. Chem. 263:13215-13222(1988).
RN [8]
RP PROTEIN SEQUENCE OF 29-40, AND CHARACTERIZATION.
RX PubMed=3262682;
RA Hameed A., Lowrey D.M., Lichtenheld M., Podack E.R.;
RT "Characterization of three serine esterases isolated from human IL-2
RT activated killer cells.";
RL J. Immunol. 141:3142-3147(1988).
RN [9]
RP PROTEIN SEQUENCE OF 29-39, AND CHARACTERIZATION.
RX PubMed=3263427;
RA Kraehenbuhl O., Rey C., Jenne D.E., Lanzavecchia A., Groscurth P.,
RA Carrel S., Tschopp J.;
RT "Characterization of granzymes A and B isolated from granules of cloned
RT human cytotoxic T lymphocytes.";
RL J. Immunol. 141:3471-3477(1988).
RN [10]

RP FUNCTION AS SET PROTEASE.
RX PubMed=11555662; DOI=10.1074/jbc.m108137200;
RA Beresford P.J., Zhang D., Oh D.Y., Fan Z., Greer E.L., Russo M.L., Jaju M.,
RA Lieberman J.;
RT "Granzyme A activates an endoplasmic reticulum-associated caspase-
RT independent nuclease to induce single-stranded DNA nicks.";
RL J. Biol. Chem. 276:43285-43293(2001).
RN [11]
RP FUNCTION AS SET PROTEASE.
RX PubMed=12628186; DOI=10.1016/s0092-8674(03)00150-8;
RA Fan Z., Beresford P.J., Oh D.Y., Zhang D., Lieberman J.;
RT "Tumor suppressor NM23-H1 is a granzyme A-activated DNase during CTL-
RT mediated apoptosis, and the nucleosome assembly protein SET is its
RT inhibitor.";
RL Cell 112:659-672(2003).
RN [12]
RP FUNCTION, AND INTERACTION WITH APEX1.
RX PubMed=12524539; DOI=10.1038/ni885;
RA Fan Z., Beresford P.J., Zhang D., Xu Z., Novina C.D., Yoshida A.,
RA Pommier Y., Lieberman J.;
RT "Cleaving the oxidative repair protein Ape1 enhances cell death mediated by
RT granzyme A.";
RL Nat. Immunol. 4:145-153(2003).
RN [13]
RP FUNCTION AS SET PROTEASE.
RX PubMed=16818237; DOI=10.1016/j.molcel.2006.06.005;
RA Chowdhury D., Beresford P.J., Zhu P., Zhang D., Sung J.S., Demple B.,
RA Perrino F.W., Lieberman J.;
RT "The exonuclease TREX1 is in the SET complex and acts in concert with NM23-
RT H1 to degrade DNA during granzyme A-mediated cell death.";
RL Mol. Cell 23:133-142(2006).
RN [14]
RP GLYCOSYLATION [LARGE SCALE ANALYSIS] AT ASN-170.
RC TISSUE=Liver;
RX PubMed=19159218; DOI=10.1021/pr8008012;
RA Chen R., Jiang X., Sun D., Han G., Wang F., Ye M., Wang L., Zou H.;
RT "Glycoproteomics analysis of human liver tissue by combination of multiple
RT enzyme digestion and hydrazide chemistry.";
RL J. Proteome Res. 8:651-661(2009).
RN [15]
RP 3D-STRUCTURE MODELING OF 29-262.
RX PubMed=3237717; DOI=10.1002/prot.340040306;
RA Murphy M.E.P., Moulton J., Bleackley R.C., Gershenfeld H., Weissman I.L.,
RA James M.N.G.;
RT "Comparative molecular model building of two serine proteinases from
RT cytotoxic T lymphocytes.";
RL Proteins 4:190-204(1988).
RN [16]
RP X-RAY CRYSTALLOGRAPHY (2.4 ANGSTROMS) OF 29-262 IN COMPLEX WITH A
RP TRIPEPTIDE CMK INHIBITOR.
RX PubMed=12819769; DOI=10.1038/nsb944;
RA Bell J.K., Goetz D.H., Mahrus S., Harris J.L., Fletterick R.J., Craik C.S.;
RT "The oligomeric structure of human granzyme A is a determinant of its
RT extended substrate specificity.";
RL Nat. Struct. Biol. 10:527-534(2003).
RN [17]
RP X-RAY CRYSTALLOGRAPHY (2.5 ANGSTROMS) OF 29-262 IN COMPLEX WITH SUBSTRATE.
RX PubMed=12819770; DOI=10.1038/nsb945;
RA Hink-Schauer C., Estebanez-Perpina E., Kurschus F.C., Bode W., Jenne D.E.;
RT "Crystal structure of the apoptosis-inducing human granzyme A dimer.";
RL Nat. Struct. Biol. 10:535-540(2003).
CC -!- FUNCTION: Abundant protease in the cytosolic granules of cytotoxic T-
CC cells and NK-cells which activates caspase-independent cell death with
CC morphological features of apoptosis when delivered into the target cell
CC through the immunological synapse. It cleaves after Lys or Arg. Cleaves
CC APEX1 after 'Lys-31' and destroys its oxidative repair activity.
CC Cleaves the nucleosome assembly protein SET after 'Lys-189', which
CC disrupts its nucleosome assembly activity and allows the SET complex to
CC translocate into the nucleus to nick and degrade the DNA.
CC {ECO:0000269|PubMed:11555662, ECO:0000269|PubMed:12524539,
CC ECO:0000269|PubMed:12628186, ECO:0000269|PubMed:16818237}.
CC -!- CATALYTIC ACTIVITY:
CC Reaction=Hydrolysis of proteins, including fibronectin, type IV
CC collagen and nucleolin. Preferential cleavage: -Arg-|-Xaa-, -Lys-|-
CC Xaa- >> -Phe-|-Xaa- in small molecule substrates.; EC=3.4.21.78;
CC -!- SUBUNIT: Homodimer; disulfide-linked. Interacts with APEX1.
CC {ECO:0000269|PubMed:12524539, ECO:0000269|PubMed:12819769,
CC ECO:0000269|PubMed:12819770}.
CC -!- SUBCELLULAR LOCATION: [Isoform alpha]: Secreted. Cytoplasmic granule.
CC -!- ALTERNATIVE PRODUCTS:
CC Event=Alternative promoter usage; Named isoforms=2;
CC Name=alpha;
CC IsoId=P12544-1; Sequence=Displayed;
CC Name=beta;
CC IsoId=P12544-2; Sequence=VSP_038571, VSP_038572;
CC -!- INDUCTION: Dexamethasone (DEX) induces expression of isoform beta and
CC represses expression of isoform alpha. The alteration in expression is
CC mediated by binding of glucocorticoid receptor to independent promoters

CC adjacent to the alternative first exons of isoform alpha and isoform
CC beta. {ECO:0000269|PubMed:17180578}.

CC -!- SIMILARITY: Belongs to the peptidase S1 family. Granzyme subfamily.
CC {ECO:0000255|PROSITE-ProRule:PRU00274}.

CC -!- CAUTION: Exons 1a and 1b of the sequence reported in PubMed:17180578
CC are of human origin, however exon 2 shows strong similarity to the rat
CC sequence. {ECO:0000305}.

CC -!- WEB RESOURCE: Name=Atlas of Genetics and Cytogenetics in Oncology and
CC Haematology;
CC URL="http://atlasgeneticsoncology.org/Genes/GZMAID51130ch5q11.html";

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DR EMBL; M18737; AAAS2647.1; -; mRNA.
DR EMBL; CR456968; CAG33249.1; -; mRNA.
DR EMBL; AC091977; -; NOT_ANNOTATED_CDS; Genomic_DNA.
DR EMBL; BC015739; AAH15739.1; -; mRNA.
DR EMBL; AB284134; BAF56159.1; -; mRNA.
DR EMBL; U40006; AAD00009.1; -; Genomic_DNA.
DR CCDS; CCDS3965.1; -. [P12544-1]
DR PIR; A31372; A31372.
DR RefSeq; NP_006135.1; NM_006144.3. [P12544-1]
DR PDB; 1HF1; Model; -; A=29-262.
DR PDB; 1OP8; X-ray; 2.50 A; A/B/C/D/E/F=29-262.
DR PDB; 1ORF; X-ray; 2.40 A; A=29-262.
DR PDBsum; 1HF1; -.
DR PDBsum; 1OP8; -.
DR PDBsum; 1ORF; -.
DR SMR; P12544; -.
DR BioGRID; 109256; 17.
DR IntAct; P12544; 4.
DR STRING; 9606.ENSP00000274306; -.
DR ChEMBL; ChEMBL4307; -.
DR MEROPS; S01.135; -.
DR iPTMnet; P12544; -.
DR PhosphoSitePlus; P12544; -.
DR BioMuta; GZMA; -.
DR DMDM; 317373360; -.
DR jPOST; P12544; -.
DR MassIVE; P12544; -.
DR MaxQB; P12544; -.
DR PaxDb; P12544; -.
DR PeptideAtlas; P12544; -.
DR PRIDE; P12544; -.
DR ProteomicsDB; 52858; -. [P12544-1]
DR ProteomicsDB; 52859; -. [P12544-2]
DR DNASU; 3001; -.
DR Ensembl; ENST00000274306; ENSP00000274306; ENSG00000145649. [P12544-1]
DR GeneID; 3001; -.
DR KEGG; hsa:3001; -.
DR UCSC; uc003jpm.4; human. [P12544-1]
DR CTD; 3001; -.
DR DisGeNET; 3001; -.
DR EuPathDB; HostDB:ENSG00000145649.7; -.
DR GeneCards; GZMA; -.
DR HGNC; HGNC:4708; GZMA.
DR HPA; HPA054134; -.
DR MIM; 140050; gene.
DR neXtProt; NX_P12544; -.
DR OpenTargets; ENSG00000145649; -.
DR PharmGKB; PA29086; -.
DR eggNOG; KOG3627; Eukaryota.
DR eggNOG; COG5640; LUCA.
DR GeneTree; ENSGT00940000159928; -.
DR HOGENOM; CLU_006842_1_0_1; -.
DR InParanoid; P12544; -.
DR OMA; YPCYDPA; -.
DR OrthoDB; 1105435at2759; -.
DR PhylomeDB; P12544; -.
DR TreeFam; TF333630; -.
DR BRENDA; 3.4.21.78; 2681.
DR SIGNOR; P12544; -.
DR EvolutionaryTrace; P12544; -.
DR GeneWiki; GZMA; -.
DR GenomeRNAi; 3001; -.
DR Pharos; P12544; Tbio.
DR PRO; PR:P12544; -.
DR Proteomes; UP000005640; Chromosome 5.
DR RNAct; P12544; protein.
DR Bgee; ENSG00000145649; Expressed in 150 organ(s), highest expression level in leukocyte.
DR Genevisible; P12544; HS.
DR GO; GO:0005576; C:extracellular region; IEA:UniProtKB-SubCell.
DR GO; GO:0001772; C:immunological synapse; TAS:UniProtKB.
DR GO; GO:0005634; C:nucleus; TAS:UniProtKB.
DR GO; GO:0042803; F:protein homodimerization activity; IDA:UniProtKB.
DR GO; GO:0004252; F:serine-type endopeptidase activity; IDA:UniProtKB.
DR GO; GO:0006915; P:apoptotic process; TAS:UniProtKB.

DR GO; GO:0019835; P:cytolysis; IEA:UniProtKB-KW.
 DR GO; GO:0006955; P:immune response; TAS:UniProtKB.
 DR GO; GO:0043392; P:negative regulation of DNA binding; IDA:UniProtKB.
 DR GO; GO:0032078; P:negative regulation of endodeoxyribonuclease activity; IDA:UniProtKB.
 DR GO; GO:0051354; P:negative regulation of oxidoreductase activity; IDA:UniProtKB.
 DR GO; GO:0043065; P:positive regulation of apoptotic process; IDA:UniProtKB.
 DR GO; GO:0051603; P:proteolysis involved in cellular protein catabolic process; IDA:UniProtKB.
 DR GO; GO:0009617; P:response to bacterium; IEA:Ensembl.
 DR CDD; cd00190; Tryp_SPC; 1.
 DR InterPro; IPR009003; Peptidase_S1_PA.
 DR InterPro; IPR001314; Peptidase_S1A.
 DR InterPro; IPR001254; Trypsin_dom.
 DR InterPro; IPR018114; TRYP SIN_HIS.
 DR InterPro; IPR033116; TRYP SIN_SER.
 DR Pfam; PF00089; Trypsin; 1.
 DR PRINTS; PR00722; CHYMOTRYPSIN.
 DR SMART; SM00020; Tryp_SPC; 1.
 DR SUPFAM; SSF50494; SSF50494; 1.
 DR PROSITE; PS50240; TRYP SIN_DOM; 1.
 DR PROSITE; PS00134; TRYP SIN_HIS; 1.
 DR PROSITE; PS00135; TRYP SIN_SER; 1.
 PE 1: Evidence at protein level;
 KW 3D-structure; Alternative promoter usage; Apoptosis; Cytolysis;
 KW Direct protein sequencing; Disulfide bond; Glycoprotein; Hydrolase;
 KW Polymorphism; Protease; Reference proteome; Secreted; Serine protease;
 KW Signal; Zymogen.
 FT SIGNAL 1..26
 FT /note="In isoform alpha"
 FT PROPEP 27..28
 FT /note="Activation peptide (in isoform alpha)"
 FT /evidence="ECO:0000269|PubMed:3047119,
 FT ECO:0000269|PubMed:3262682, ECO:0000269|PubMed:3263427"
 FT /id="PRO_0000027393"
 FT CHAIN 29..262
 FT /note="Granzyme A"
 FT /id="PRO_0000027394"
 FT DOMAIN 29..259
 FT /note="Peptidase S1"
 FT /evidence="ECO:0000255|PROSITE-ProRule:PRU00274"
 FT ACT_SITE 69
 FT /note="Charge relay system"
 FT ACT_SITE 114
 FT /note="Charge relay system"
 FT ACT_SITE 212
 FT /note="Charge relay system"
 FT CARBOHYD 170
 FT /note="N-linked (GlcNAc...) asparagine"
 FT /evidence="ECO:0000269|PubMed:19159218"
 FT DISULFID 54..70
 FT DISULFID 148..218
 FT DISULFID 179..197
 FT DISULFID 208..234
 FT VAR_SEQ 1..17
 FT /note="Missing (in isoform beta)"
 FT /evidence="ECO:0000303|PubMed:17180578"
 FT /id="VSP_038571"
 FT VAR_SEQ 18..23
 FT /note="LLLIPE -> MTKGLR (in isoform beta)"
 FT /evidence="ECO:0000303|PubMed:17180578"
 FT /id="VSP_038572"
 FT VARIANT 121
 FT /note="M -> T (in dbSNP:rs3104233)"
 FT /evidence="ECO:0000269|PubMed:15489334,
 FT ECO:0000269|PubMed:3257574, ECO:0000269|Ref.2"
 FT /id="VAR_024291"
 FT CONFLICT 33..34
 FT /note="NE -> DT (in Ref. 5; no nucleotide entry)"
 FT /evidence="ECO:0000305"
 FT CONFLICT 36
 FT /note="T -> V (in Ref. 5; no nucleotide entry)"
 FT /evidence="ECO:0000305"
 FT CONFLICT 47
 FT /note="S -> K (in Ref. 5; no nucleotide entry)"
 FT /evidence="ECO:0000305"
 FT CONFLICT 49..52
 FT /note="DRKT -> KPDS (in Ref. 5; no nucleotide entry)"
 FT /evidence="ECO:0000305"
 FT CONFLICT 62
 FT /note="D -> N (in Ref. 5; no nucleotide entry)"
 FT /evidence="ECO:0000305"
 FT CONFLICT 71..72
 FT /note="NL -> IP (in Ref. 5; no nucleotide entry)"
 FT /evidence="ECO:0000305"
 FT STRAND 43..47
 FT /evidence="ECO:0000244|PDB:1ORF"
 FT STRAND 49..51
 FT /evidence="ECO:0000244|PDB:1ORF"
 FT STRAND 53..60

```

FT          /evidence="ECO:0000244|PDB:1ORF"
FT  STRAND  63..66
FT          /evidence="ECO:0000244|PDB:1ORF"
FT  STRAND  77..81
FT          /evidence="ECO:0000244|PDB:1ORF"
FT  STRAND  83..87
FT          /evidence="ECO:0000244|PDB:1ORF"
FT  STRAND  93..95
FT          /evidence="ECO:0000244|PDB:1ORF"
FT  STRAND  97..102
FT          /evidence="ECO:0000244|PDB:1ORF"
FT  TURN    108..110
FT          /evidence="ECO:0000244|PDB:1ORF"
FT  STRAND  116..122
FT          /evidence="ECO:0000244|PDB:1ORF"
FT  STRAND  127..130
FT          /evidence="ECO:0000244|PDB:1ORF"
FT  STRAND  147..154
FT          /evidence="ECO:0000244|PDB:1ORF"
FT  STRAND  156..160
FT          /evidence="ECO:0000244|PDB:1ORF"
FT  STRAND  167..174
FT          /evidence="ECO:0000244|PDB:1ORF"
FT  HELIX   176..179
FT          /evidence="ECO:0000244|PDB:1ORF"
FT  TURN    182..189
FT          /evidence="ECO:0000244|PDB:1ORF"
FT  STRAND  195..199
FT          /evidence="ECO:0000244|PDB:1ORF"
FT  STRAND  215..218
FT          /evidence="ECO:0000244|PDB:1ORF"
FT  STRAND  221..228
FT          /evidence="ECO:0000244|PDB:1ORF"
FT  STRAND  241..245
FT          /evidence="ECO:0000244|PDB:1ORF"
FT  HELIX   248..258
FT          /evidence="ECO:0000244|PDB:1ORF"
SQ  SEQUENCE 262 AA; 28999 MW; FD773628BA6F301B CRC64;
    MRNSYRFLAS SLSVVVSLLL IPEDVCEKII GGNEVTPHSR PYMVLSSLDR KTICAGALIA
    KDWVLTAAHC NLNKRSQLIL GAHSITREEP TKQIMLVKKE FPYPCYDPAT REGDLKLLQL
    MEKAKINKYV TILHLPKKGD DVKPGTMCQV AGWGRTHNSA SWSDTLREVN ITIIDRKVCN
    DRNHYNFNPV IGMNVMVAGS LRGRDSCNG DSGSPLLCEG VFRGVTSGFL ENKCGDPRGP
    GVIYLLSKKH LNWIIMTIK AV

```

//

Entries from the TrEMBL section follow the same format. For format differences see the description of the distinct line types.

Each line begins with a two-character line code, which indicates the type of data contained in the line. The current line types and line codes and the order in which they appear in an entry, are shown in the table below.

Line code	Content	Occurrence in an entry
ID	Identification	Once; starts the entry
AC	Accession number(s)	Once or more
DT	Date	Three times
DE	Description	Once or more
GN	Gene name(s)	Optional
OS	Organism species	Once or more
OG	Organelle	Optional
OC	Organism classification	Once or more
OX	Taxonomy cross-reference	Once
OH	Organism host	Optional
RN	Reference number	Once or more
RP	Reference position	Once or more
RC	Reference comment(s)	Optional
RX	Reference cross-reference(s)	Optional
RG	Reference group	Once or more (Optional if RA line)
RA	Reference authors	Once or more (Optional if RG line)
RT	Reference title	Optional
RL	Reference location	Once or more
CC	Comments or notes	Optional
DR	Database cross-references	Optional
PE	Protein existence	Once
KW	Keywords	Optional
FT	Feature table data	Once or more in Swiss-Prot, optional in TrEMBL

SQ	Sequence header	Once
(blanks)	Sequence data	Once or more
//	Termination line	Once; ends the entry

As shown in the above table, some line types are found in all entries, others are optional. Some line types occur many times in a single entry. Each entry must begin with an identification line (ID) and end with a terminator line (//).

A detailed description of each line type is given in the next section of this document. It must be noted that, with the exception of GN, all line types exist in the EMBL Database. A description of the format differences between the UniProt Knowledgebase and EMBL databases is given in [this document](#).

The two-character line-type code that begins each line is always followed by three blanks, so that the actual information begins with the sixth character. In general, information is not extended beyond character position 75, there are however a few exceptions where lines may be longer (e.g. OH lines, CC lines that contain the 'WEB RESOURCE' topic (see section [3.22](#)), etc.).

2.4. Evidence attributions

The evidence for annotations are available in UniProtKB entries. An individual evidence description consists of a mandatory evidence type, represented by a code from the [Evidence Codes Ontology \(ECO\)](#) and, where applicable, the source of the data which is usually another database record that is represented by the database name and record identifier, but in the case of publications that are not in PubMed we indicate instead the corresponding UniProtKB reference number.

Examples:

a) An evidence type without source

```
{ECO:000305}
{ECO:000250}
{ECO:000255}
```

b) An evidence type with source

```
{ECO:000269|PubMed:10433554}
{ECO:000303|Ref.6}
{ECO:000305|PubMed:16683188}
{ECO:000250|UniProtKB:Q8WUF5}
{ECO:000312|EMBL:BAG16761.1}
{ECO:000313|EMBL:BAG16761.1}
{ECO:000255|HAMAP-Rule:MF_00205}
{ECO:000256|HAMAP-Rule:MF_00205}
{ECO:000244|PDB:1K83}
{ECO:000213|PDB:1K83}
```

c) Several evidences

```
{ECO:000269|PubMed:10433554, ECO:000303|Ref.6}
```

3. The different line types

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3.1. The ID line

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The ID (IDentification) line is always the first line of an entry. The general form of the ID line is:

```
ID EntryName Status; SequenceLength.
```

3.1.1. Entry name

The first item on the ID line is the entry name of the sequence. This name is a useful means of identifying a sequence, but it is not a stable identifier as is the accession number (see [3.2](#)).

a) Swiss-Prot entry names

The Swiss-Prot entry name consists of up to 11 uppercase alphanumeric characters. Swiss-Prot uses a general purpose naming convention that can be symbolized as **X**_{**Y**}, where:

- **X** is a mnemonic code of at most 5 alphanumeric characters representing the protein name. Examples: B2MG is for Beta-2-microglobulin, HBA is for Hemoglobin alpha chain and INS is for Insulin, CAD17 for Cadherin-17;
- The '_' sign serves as a separator;
- **Y** is a mnemonic species identification code of at most 5 alphanumeric characters representing the biological source of the protein. This code is generally made of the first three letters of the genus and the first two letters of the species.

Examples:

PSEPU is for *Pseudomonas putida* and NAJNI is for *Naja nivea*.

However, for species most commonly encountered in the database, self-explanatory codes are used. There are 16 of those codes: BOVIN for Bovine, CHICK for Chicken, ECOLI for *Escherichia coli*, HORSE for Horse, HUMAN for Human, MAIZE for Maize (*Zea mays*), MOUSE for Mouse, PEA for Garden pea (*Pisum sativum*), PIG for Pig, RABIT for Rabbit, RAT for Rat, SHEEP for Sheep, SOYBN for Soybean (*Glycine max*), TOBAC for Common tobacco (*Nicotina tabacum*), WHEAT for Wheat (*Triticum aestivum*), and YEAST for Baker's yeast (*Saccharomyces cerevisiae*).

As it was not possible to apply the above rules to viruses, they were given arbitrary, but generally easy-to-remember identification codes.

Examples of complete protein sequence entry names are: RL1_ECOLI for ribosomal protein L1 from *Escherichia coli*, AFTIN_HUMAN for Aftiphilin from *human*, SODC_DROME for Superoxide dismutase [Cu-Zn] from *Drosophila melanogaster*.

The names of all the presently-defined species identification codes are listed in the document file [speclist.txt](#).

b) TrEMBL entry names

The TrEMBL entry name consists of up to **16** uppercase alphanumeric characters. TrEMBL uses a general purpose naming convention similar to that of Swiss-Prot, where:

- **X** is identical to the **accession number** of the entry
- The '_' sign serves as a separator;
- **Y** is a mnemonic species identification code.

As it is not possible in a reasonable timeframe to manually assign organism codes to all species represented in TrEMBL, "virtual" codes have been defined that regroup organisms at a certain taxonomic level. Such codes are prefixed by the number "9" and generally correspond to a "pool" of organisms, which can be 'wide' as a kingdom. Here are some examples of such codes:

```
9BACT B      2: N=Bacteria
9CNID E    6073: N=Cnidaria
9FUNG E    4751: N=Fungi
9REOV V   10880: N=Reoviridae
9TETR E    32523: N=Tetrapoda
9VIRI E    33090: N=Viridiplantae
```

These type of "virtual" codes are also listed in the document file [speclist.txt](#).

Examples of complete TrEMBL entry names are O95417_HUMAN, Q9VVG0_DROME, P71025_BACSU or Q9SR52_ARATH.

3.1.2. Status

The second item on the ID line indicates the status of the entry (see section [2.2](#)).

3.1.3. Length of the molecule

The third and last item of the ID line is the length of the molecule, which is the total number of amino acids in the sequence. This number includes the positions reported to be present but which have not been determined (coded as 'X'). The length is followed by the letter code 'AA' (Amino Acids).

3.1.4. Examples of identification lines

Two examples of Swiss-Prot ID lines are shown below:

```
ID  CYC_BOVIN      Reviewed;      104 AA.
ID  GIA2_GIALA     Reviewed;      296 AA.
```

Example of a TrEMBL ID line:

```
ID  Q5JU06_HUMAN   Unreviewed;    268 AA.
```

3.2. The AC line

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The AC (ACcession number) line lists the accession number(s) associated with an entry. The format of the AC line is:

```
AC  AC_number_1; [ AC_number_2; ] ... [ AC_number_N; ]
```

An example of an accession number line is shown below:

```
AC  P00321;
```

Semicolons separate the accession numbers and a semicolon terminates the list. If necessary, more than one AC line can be used. Example:

```
AC  Q16653; O00713; O00714; O00715; Q13054; Q13055; Q14855; Q92891;
AC  Q92892; Q92893; Q92894; Q92895; Q93053; Q96KU9; Q96KV0; Q96KV1;
AC  Q99605;
```

The purpose of accession numbers is to provide a stable way of identifying entries from release to release. It is sometimes necessary for reasons of consistency to change the names of the entries, for example, to ensure that related entries have similar names. However, an accession number is always conserved, and therefore allows unambiguous citation of entries.

Researchers who wish to cite entries in their publications should **always cite the first accession number**. This is commonly referred to as the 'primary accession number'. 'Secondary accession numbers' are sorted alphanumerically.

We strongly advise those users who have programs performing mappings of Swiss-Prot to another data resource to use Swiss-Prot accession numbers to identify an entry.

Entries will have more than one accession number if they have been merged or split. For example, when two entries are merged into one, the accession numbers from both entries are stored in the AC line(s).

If an existing entry is split into two or more entries (a rare occurrence), the original accession numbers are retained in all the derived entries and a new primary accession number is added to all the entries.

An accession number is dropped only when the data to which it was assigned have been completely removed from the database. Accession numbers deleted from Swiss-Prot are listed in the document file [delac_sp.txt](#) and those deleted from TrEMBL are listed in [delac_tr.txt](#).

UniProtKB accession numbers consist of 6 or 10 alphanumeric characters in the format:

1	2	3	4	5	6	7	8	9	10
[A-N,R-Z]	[0-9]	[A-Z]	[A-Z, 0-9]	[A-Z, 0-9]	[0-9]				
[O,P,Q]	[0-9]	[A-Z, 0-9]	[A-Z, 0-9]	[A-Z, 0-9]	[0-9]				
[A-N,R-Z]	[0-9]	[A-Z]	[A-Z, 0-9]	[A-Z, 0-9]	[0-9]	[A-Z]	[A-Z,0-9]	[A-Z,0-9]	[0-9]

The three patterns can be combined into the following regular expression:

```
[OPQ][0-9][A-Z0-9]{3}[0-9]||[A-NR-Z][0-9]([A-Z][A-Z0-9]{2}[0-9]){1,2}
```

Here are some examples of valid accession numbers: P12345, Q1AAA9, O456A1, P4A123 and A0A022YWF9.

3.3. The DT line

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The DT (DaTe) lines show the date of creation and last modification of the database entry.

The format of the DT line in Swiss-Prot is:

```
DT DD-MMM-YYYY, integrated into UniProtKB/database_name.
DT DD-MMM-YYYY, sequence version x.
DT DD-MMM-YYYY, entry version x.
```

Where 'DD' is the day, 'MMM' the month and 'YYYY' the year, respectively. The dates shown in DT lines correspond to the date of the release at which an entry was integrated or updated. There are always three DT lines in each entry, each of them is associated with a specific comment:

- The first DT line indicates when the entry first appeared in the database. The associated comment, 'integrated into UniProtKB/database_name', indicates in which section of UniProtKB, Swiss-Prot or TrEMBL, the entry can be found;
- The second DT line indicates when the sequence data was last modified. The associated comment, 'sequence version', indicates the sequence version number. The sequence version number of an entry is incremented by one when the amino acid sequence shown in the sequence record is modified;
- The third DT line indicates when data other than the sequence was last modified. The associated comment, 'entry version', indicates the entry version number. The entry version number is incremented by one whenever any data in the flat file representation of the entry is modified.

Example of a block of Swiss-Prot DT lines:

```
DT 01-OCT-1996, integrated into UniProtKB/Swiss-Prot.
DT 01-OCT-1996, sequence version 1.
DT 07-FEB-2006, entry version 49.
```

Example of a block of TrEMBL DT lines:

```
DT 01-FEB-1999, integrated into UniProtKB/TrEMBL.
DT 15-OCT-2000, sequence version 2.
DT 15-DEC-2004, entry version 5.
```

Whenever the sequence of an entry is updated there is always also an annotation update. The date in the third DT line is thus always at least as recent as the one in the second DT line.

Note that sequence and entry versions are not reset when an entry moves from Swiss-Prot to TrEMBL. The date of integration into Swiss-Prot can be more recent than the last sequence update.

```
DT 25-OCT-2005, integrated into UniProtKB/Swiss-Prot.
DT 01-NOV-1996, sequence version 1.
DT 07-FEB-2006, entry version 35.
```

A comprehensive archive of UniProtKB/Swiss-Prot and UniProtKB/TrEMBL entry versions is available: the [UniProtKB Sequence/Annotation Version Database \(UniSave\)](#) is a repository of UniProtKB/Swiss-Prot and UniProtKB/TrEMBL entry versions. Unlike the UniProt Knowledgebase, which contains only the latest Swiss-Prot and TrEMBL entry and sequence versions, the UniProtKB Sequence/Annotation Version Database provides access to all versions of these entries. This allows to track sequence changes, to find out when a given annotation appeared in an entry and how it evolved.

3.4. The DE line

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The DE (DEscription) lines contain general descriptive information about the sequence stored. This information is generally sufficient to identify the protein precisely.

a) The DE line in Swiss-Prot

The description always starts with the recommended name (RecName) of the protein. Alternative names (AltName) are indicated thereafter.

The DE line contains 3 categories, as well as several subcategories, of protein names:

Category Field	Subcategory Field	Cardinality	Description
RecName:		1 in UniProtKB/Swiss-Prot 0-1 in UniProtKB/TrEMBL	The name recommended by the UniProt consortium.
	Full=	1	The full name.
	Short=	0-n	An abbreviation of the full name or an acronym.
	EC=	0-n	An Enzyme Commission number.
AltName:		0-n	A synonym of the recommended name.
	Full=	0-1	The full name.
	Short=	0-n	An abbreviation of the full name or an acronym.
	EC=	0-n	An Enzyme Commission number.
AltName:	Allergen=	0-1	See allergen.txt .
AltName:	Biotech=	0-1	A name used in a biotechnological context.
AltName:	CD_antigen=	0-n	See cdlist.txt .
AltName:	INN=	0-n	The international nonproprietary name: A generic name for a pharmaceutical substance or active pharmaceutical ingredient that is globally recognized and is a public property.
SubName:		0 in UniProtKB/Swiss-Prot 0-n in UniProtKB/TrEMBL	A name provided by the submitter of the underlying nucleotide sequence.
	Full=	1	The full name.
	EC=	0-n	An Enzyme Commission number.

Each name is shown on a separate line; lines may therefore exceed 80 characters.

Protein naming guidelines are described in the [International protein nomenclature guidelines](#).

```

DE   RecName: Full=Annexin A5;
DE           Short=Annexin-5;
DE   AltName: Full=Annexin V;
DE   AltName: Full=Lipocortin V;
DE   AltName: Full=Endonexin II;
DE   AltName: Full=Calphobindin I;
DE   AltName: Full=CBP-I;
DE   AltName: Full=Placental anticoagulant protein I;
DE           Short=PAP-I;
DE   AltName: Full=PP4;
DE   AltName: Full=Thromboplastin inhibitor;
DE   AltName: Full=Vascular anticoagulant-alpha;
DE           Short=VAC-alpha;
DE   AltName: Full=Anchorin CII;

DE   RecName: Full=Granulocyte colony-stimulating factor;
DE           Short=G-CSF;
DE   AltName: Full=Pluripoietin;
DE   AltName: Full=Filgrastim;
DE   AltName: Full=Lenograstim;
DE   Flags: Precursor;

```

A block of DE lines may further contain multiple **Includes:** and/or **Contains:** sections and a separate field **Flags:** to indicate whether the protein sequence is a precursor or a fragment:

Field	Cardinality	Value
Includes:	0-n	A block of protein names as described in the table above.
Contains:	0-n	A block of protein names as described in the table above.

Flags:	0-1	Precursor and/or Fragment or Fragments
---------------	-----	--

If a protein is known to be cleaved into multiple functional components, the description starts with the name of the precursor protein, followed by 'Contains:' section(s). Each individual component is described in a separate 'Contains:' section. Alternative names (AltName) are allowed for each individual component. Example:

```
DE  RecName: Full=Corticotropin-lipotropin;
DE  AltName: Full=Pro-opiomelanocortin;
DE      Short=POMC;
DE  Contains:
DE    RecName: Full=NPP;
DE  Contains:
DE    RecName: Full=Melanotropin gamma;
DE    AltName: Full=Gamma-MSH;
DE  Contains:
DE    RecName: Full=Potential peptide;
DE  Contains:
DE    RecName: Full=Corticotropin;
DE    AltName: Full=Adrenocorticotrophic hormone;
DE      Short=ACTH;
DE  Contains:
DE    RecName: Full=Melanotropin alpha;
DE    AltName: Full=Alpha-MSH;
DE  Contains:
DE    RecName: Full=Corticotropin-like intermediary peptide;
DE      Short=CLIP;
DE  Contains:
DE    RecName: Full=Lipotropin beta;
DE    AltName: Full=Beta-LPH;
DE  Contains:
DE    RecName: Full=Lipotropin gamma;
DE    AltName: Full=Gamma-LPH;
DE  Contains:
DE    RecName: Full=Melanotropin beta;
DE    AltName: Full=Beta-MSH;
DE  Contains:
DE    RecName: Full=Beta-endorphin;
DE  Contains:
DE    RecName: Full=Met-enkephalin;
DE  Flags: Precursor;
```

If a protein is known to include multiple functional domains each of which is described by a different name, the description starts with the name of the overall protein, followed by 'Includes:' section(s). All the domains are listed in a separate 'Includes:' section. Alternative names (AltName) are allowed for each individual domain. Example:

```
DE  RecName: Full=CAD protein;
DE  Includes:
DE    RecName: Full=Glutamine-dependent carbamoyl-phosphate synthase;
DE      EC=6.3.5.5;
DE  Includes:
DE    RecName: Full=Aspartate carbamoyltransferase;
DE      EC=2.1.3.2;
DE  Includes:
DE    RecName: Full=Dihydroorotase;
DE      EC=3.5.2.3;
```

In rare cases, the functional domains of an enzyme are cleaved, but the catalytic activity can only be observed, when the individual chains reorganize in a complex. Such proteins are described in the DE line by a combination of both 'Includes:' and 'Contains:', in the order given in the following example:

```
DE  RecName: Full=Arginine biosynthesis bifunctional protein argJ;
DE  Includes:
DE    RecName: Full=Glutamate N-acetyltransferase;
DE      EC=2.3.1.35;
DE    AltName: Full=Ornithine acetyltransferase;
DE      Short=OATase;
DE    AltName: Full=Ornithine transacetylase;
DE  Includes:
DE    RecName: Full=Amino-acid acetyltransferase;
DE      EC=2.3.1.1;
DE    AltName: Full=N-acetylglutamate synthase;
DE      Short=AGS;
DE  Contains:
DE    RecName: Full=Arginine biosynthesis bifunctional protein argJ alpha chain;
DE  Contains:
DE    RecName: Full=Arginine biosynthesis bifunctional protein argJ beta chain;
```

When the mature form of a protein is derived by processing of a precursor, we indicate this fact using the Flag 'Precursor'; in such cases the sequence displayed does not correspond to the mature form of the protein.

```
DE  RecName: Full=Chondroitin proteoglycan 3;
DE  Flags: Precursor;
```

If the complete sequence is not determined, we indicate it in the 'Flags' section with 'Fragment' or 'Fragments'. Example:

```

DE   RecName: Full=Dihydrodipicolinate reductase;
DE       Short=DHPR;
DE       EC=1.3.1.26;
DE   Flags: Fragment;

```

b) The DE line in TrEMBL

The format of the DE line in TrEMBL follows closely the format used in Swiss-Prot. However, as TrEMBL is not manually annotated, the description is derived directly from the underlying nucleotide entry and its accuracy relies on the information provided by the submitter of the nucleotide entry. It is why TrEMBL entries usually have submitted name (SubName) instead of a recommended name (RecName). The description may later be improved by automatic annotation procedures (see section [Automatic annotation](#)) but if not, it remains as provided by the submitter until the entry is manually annotated and added to Swiss-Prot.

3.5. The GN line

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The GN (Gene Name) line indicates the name(s) of the gene(s) that code for the stored protein sequence. The GN line contains three types of information:

1. **Gene names** (a.k.a. gene symbols). The name(s) used to represent a gene. As there can be more than one name assigned to a gene, we make a distinction between the one which we believe should be used as the official gene name and the other names which are listed as "Synonyms".
2. **Ordered locus names** (a.k.a. OLN, ORF numbers, CDS numbers or Gene numbers). A name used to represent an ORF in a completely sequenced genome or chromosome. It is generally based on a prefix representing the organism and a number which usually represents the sequential ordering of genes on the chromosome. Depending on the genome sequencing center, numbers are only attributed to protein-coding genes, or also to pseudogenes, or also to tRNAs and other features. If two predicted genes have been merged to form a new gene, both gene identifiers are indicated, separated by a slash (see last example). Examples: HI0934, Rv3245c, At5g34500, YER456W, YAR042W/YAR044W.
3. **ORF names** (a.k.a. sequencing names or contig names or temporary ORFNames). A name temporarily attributed by a sequencing project to an open reading frame. This name is generally based on a cosmid numbering system. Examples: MtCY277.28c, SYGP-ORF50, SpBC2F12.04, C06E1.1, CG10954.

The format of the GN line is:

```

GN   Name=<name>; Synonyms=<name1>[, <name2>...]; OrderedLocusNames=<name1>[, <name2>...];
GN   ORFNames=<name1>[, <name2>...];

```

None of the above four tokens are mandatory. But a "**Synonyms**" token can only be present if there is a "**Name**" token.

If there is more than one gene, GN line blocks for the different genes are separated by the following line:

```
GN   and
```

Example:

```

GN   Name=Jon99Cii; Synonyms=SER1, SER5, Ser99Da; ORFNames=CG7877;
GN   and
GN   Name=Jon99Ciii; Synonyms=SER2, SER5, Ser99Db; ORFNames=CG15519;

```

Wrapping is done preferentially at a semicolon, otherwise at a comma.

It often occurs that more than one name has been assigned to an individual locus, in which case all the synonyms will be listed alphabetically and case-insensitively. Example:

```

GN   Name=hns; Synonyms=bg1Y, cur, drdX, hnsA, msyA, osmZ, pilG, topS;
GN   OrderedLocusNames=b1237, c1701, z2013, ECs1739;

```

3.6. The OS line

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The OS (Organism Species) line specifies the organism which was the source of the stored sequence. In the rare case where all the species information will not fit on a single line, more than one OS line is used. The last OS line is terminated by a period.

The species designation consists, in most cases, of the Latin genus and species designation followed by the English name (in parentheses). For viruses, only the common English name is given.

Examples of OS lines are shown here:

```

OS   Escherichia coli.
OS   Homo sapiens (Human).
OS   Solanum melongena (Eggplant) (Aubergine).
OS   Avian leukosis virus RSA (RSV-SRA) (Rous sarcoma virus (strain
OS   Schmidt-Ruppin A)).

```

The names (official name, common name, synonym) concerning one species are cut across lines when they do not fit into a single line:

```
OS   Epizootic hemorrhagic disease virus 2 (strain Alberta) (EHDV-2).
```

The OG (OrGanelle) line indicates if the gene coding for a protein originates from mitochondria, a plastid, a nucleomorph or a plasmid.

The format of the OG line is:

```
OG Hydrogenosome.
OG Mitochondrion.
OG Nucleomorph.
OG Plasmid name.
OG Plastid.
OG Plastid; Apicoplast.
OG Plastid; Chloroplast.
OG Plastid; Organellar chromatophore.
OG Plastid; Cyanelle.
OG Plastid; Non-photosynthetic plastid.
```

Where 'name' is the name of the plasmid.

Hydrogenosomes are membrane-enclosed redox organelles found in some anaerobic unicellular eukaryotes which contain hydrogenase and produce hydrogen and ATP by glycolysis. They are thought to have evolved from mitochondria; most hydrogenosomes lack a genome, but some like (e.g. the anaerobic ciliate *Nyctotherus ovalis*) have retained a rudimentary genome.

Mitochondria are redox-active membrane-bound organelles found in the cytoplasm of most eukaryotic cells. They are the site of sthe reactions of oxidative phosphorylation, which results in the formation of ATP.

Nucleomorphs are reduced vestigial nuclei found in the plastids of cryptomonad and chlorachniophyte algae. The plastids originate from engulfed eukaryotic phototrophs.

Plastids are classified based on either their taxonomic lineage or in some cases on their photosynthetic capacity.

Apicoplasts are the plastids found in Apicomplexa parasites such as *Eimeria*, *Plasmodium* and *Toxoplasma*; they are not photosynthetic.

Chloroplasts are the plastids found in all land plants and algae with the exception of the glaucocystophyte algae (see below). Chloroplasts in green tissue are photosynthetic; in other tissues they may not be photosynthetic and then may also have secondary information relating to subcellular location (e.g. amyloplasts, chromoplasts).

Organellar chromatophores are the photosynthetic plastids found in *Paulinella chromatophora*, a photosynthetic thecate amoeba of the Cercozoa lineage. At 1 Mb this plastid is 3 times larger than the largest known plastid; it is not clear if it is derived from the same endosymbiotic event that is thought to have led to all other plastids.

Cyanelles are the plastids found in the glaucocystophyte algae. They are also photosynthetic but their plastid has a vestigial cell wall between the 2 envelope membranes.

Non-photosynthetic plastid is used when the plastid in question derives from a photosynthetic lineage but the plastid in question is missing essential genes. Some examples are *Aneura mirabilis*, *Epifagus virginiana*, *Helicosporidium* (a liverwort, higher plant and green alga respectively).

The term Plastid is used when the capacities of the organism are unclear; for example in the parasitic plants of the *Cuscuta* lineage, where sometimes young tissue is photosynthetic.

If an entry reports the sequence of a protein identical in a number of plasmids, the names of these plasmids will all be listed in the OG lines of that entry. The plasmid names are separated by commas, the last plasmid name is preceded by the word 'and'. Plasmid names are never written across two lines. Example:

```
OG Plasmid R6-5, Plasmid IncFII R100 (NR1), and
OG Plasmid IncFII R1-19 (R1 drd-19).
```

The document [plasmid.txt](#) lists all the plasmid names that are used in the database in the context of the OG line.

3.8. The OC line

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The OC (Organism Classification) lines contain the taxonomic classification of the source organism. The taxonomic classification used is that maintained at the NCBI (see <https://www.ncbi.nlm.nih.gov/Taxonomy/>) and used by the nucleotide sequence databases (EMBL/GenBank/DDBJ). The NCBI's taxonomy reflects current phylogenetic knowledge. It is a sequence-based taxonomy as much as possible and based on published authorities wherever possible. Because of the inherent ambiguity of evolutionary classification and the specific needs of database users (e.g. trying to track down the phylogenetic history of a group of organisms or to elucidate the evolution of a molecule), this taxonomy strives to accurately reflect current phylogenetic knowledge. The NCBI's taxonomy is intended to be informative and helpful; no claim is made that it is the best or the most exact.

The classification is listed top-down as nodes in a taxonomic tree in which the most general grouping is given first. The classification may be distributed over several OC lines, but nodes are not split or hyphenated between lines. Semicolons separate the individual items and the list is terminated by a period.

The format of the OC line is:

```
OC Node[; Node...].
```

For example the classification lines for a human sequence would be:

```
OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi; Mammalia;
OC Eutheria; Euarchontoglires; Primates; Haplorrhini; Catarrhini; Hominidae;
OC Homo.
```

3.9. The OX line

[Table of contents](#)

The OX (Organism taxonomy cross-reference) line is used to indicate the identifier of a specific organism in a taxonomic database. The format of the OX line is:

```
OX Taxonomy_database_Qualifier=Taxonomic code;
```

Currently the cross-references are made to the taxonomy database of NCBI, which is associated with the qualifier 'TaxID' and a taxonomic code.

Examples:

```
OX NCBI_TaxID=9606;
OX NCBI_TaxID=562;
```

3.10. The OH line

[Table of contents](#)

The OH (Organism Host) line is optional and appears only in viral entries. It indicates the host organism(s) that are susceptible to be infected by a virus.

A virus being an inert particle outside its hosts, the virion has neither metabolism, nor any replication capability, nor autonomous evolution. Identifying the host organism(s) is therefore essential, because features like virus-cell interactions and posttranslational modifications depend mostly on the host.

The format of the OH line is:

```
OH NCBI_TaxID=TaxID; HostName.
```

The *HostName* consists of the official name and, optionally, a common name and/or synonym. The length of an OH line may exceed 80 characters.

Example for Simian hepatitis A virus:

```
OH NCBI_TaxID=9481; Callithrix.
OH NCBI_TaxID=9536; Cercopithecus hamlyni (Owl-faced monkey) (Hamlyn's monkey).
OH NCBI_TaxID=9539; Macaca (macaques).
OH NCBI_TaxID=9598; Pan troglodytes (Chimpanzee).
```

3.11. The reference (RN, RP, RC, RX, RG, RA, RT, RL) lines

[Table of contents](#)

3.11.1. Introduction

These lines comprise the literature citations. The citations indicate the sources from which the data has been abstracted. The reference lines for a given citation occur in a block, and are always in the order RN, RP, RC, RX, RG, RA, RT and RL. Within each such reference block, the RN line occurs once, the RC, RX and RT lines occur zero or more times, and the RP, RG/RA and RL lines occur one or more times. If several references are given, there will be a reference block for each.

An example of a complete reference is:

```
RN [1] {ECO:0000305, ECO:0000312|EMBL:AAK28740.1}
RP NUCLEOTIDE SEQUENCE [MRNA] (ISOFORMS A AND C), FUNCTION, INTERACTION WITH
RP PKC-3, SUBCELLULAR LOCATION, TISSUE SPECIFICITY, DEVELOPMENTAL STAGE, AND
RP MUTAGENESIS OF PHE-175 AND PHE-221.
RC STRAIN=Bristol N2 {ECO:0000269|PubMed:11134024};
RX PubMed=11134024; DOI=10.1074/jbc.m008990200;
RA Zhang L., Wu S.-L., Rubin C.S.;
RT "A novel adapter protein employs a phosphotyrosine binding domain and
RT exceptionally basic N-terminal domains to capture and localize an atypical
RT protein kinase C: characterization of Caenorhabditis elegans C kinase
RT adapter 1, a protein that avidly binds protein kinase C3.";
RL J. Biol. Chem. 276:10463-10475(2001).
```

The formats of the individual lines are explained below.

3.11.2. The RN line

The RN (Reference Number) line gives a sequential number to each reference citation in an entry. This number is used to indicate the reference in comments and feature table notes. The format of the RN line is:

```
RN [n]
```

where 'n' denotes the nth reference for this entry. The reference number is always between square brackets.

3.11.3. The RP line

The RP (Reference Position) lines describe the extent of the work relevant to the entry carried out by the authors. The format of the RP line is:

RP COMMENT.

It should contain a description of the information that has been propagated in the Swiss-Prot entry.

A typical comment is "NUCLEOTIDE SEQUENCE". This item might be tagged with a qualifier, indicating the origin of the sequence data. Valid names of this qualifiers are:

- GENOMIC DNA: the individual gene has been sequenced
- GENOMIC RNA: the individual gene has been sequenced
- MRNA: the individual cDNA has been sequenced
- LARGE SCALE GENOMIC DNA: the gene has been sequenced as part of a genome project
- LARGE SCALE MRNA: the cDNA has been sequenced as part of a large-scale cDNA project

If 2 qualifiers apply, both are indicated, separated by a '/'.

The 'LARGE SCALE ANALYSIS' is another typical tag added in references that report large screen results to indicate that results have not been extensively studied.

Typical examples of RP lines are shown below:

```
RP    NUCLEOTIDE SEQUENCE [LARGE SCALE GENOMIC DNA].
RP    NUCLEOTIDE SEQUENCE [GENOMIC DNA / MRNA] (ISOFORM 1).
RP    NUCLEOTIDE SEQUENCE [GENOMIC RNA / MRNA].
RP    NUCLEOTIDE SEQUENCE [GENOMIC DNA], AND PROTEIN SEQUENCE OF 21-35.
RP    PROTEIN SEQUENCE OF 39-76; 95-118 AND 125-138, AND DISULFIDE BONDS.
RP    SEQUENCE REVISION TO 76-84 AND 129.
RP    STRUCTURE BY NMR.
RP    X-RAY CRYSTALLOGRAPHY (1.8 ANGSTROMS).
RP    CHARACTERIZATION.
RP    MUTAGENESIS OF TYR-65.
RP    REVIEW.
RP    VARIANT ALA-1368.
RP    VARIANTS HDLD1 ARG-597 AND ARG-1477, AND VARIANT HDLD2 LEU-693 DEL.
RP    NUCLEOTIDE SEQUENCE [GENOMIC DNA], PROTEIN SEQUENCE OF 2-23; 3-18; 241-257;
RP    319-340 AND 382-391, FUNCTION, CATALYTIC ACTIVITY, COFACTOR, ACTIVITY
RP    REGULATION, SUBUNIT, AND DISRUPTION PHENOTYPE.
RP    NUCLEOTIDE SEQUENCE [MRNA], PROTEIN SEQUENCE OF 154-171; 302-308; 312-328;
RP    377-384 AND 419-431, FUNCTION, SUBCELLULAR LOCATION, AND MUTAGENESIS OF
RP    ARG-331; GLY-332 AND ARG-333.
RP    PHOSPHORYLATION [LARGE SCALE ANALYSIS] AT SER-295; SER-391; SER-479;
RP    SER-491 AND SER-710, AND IDENTIFICATION BY MASS SPECTROMETRY [LARGE SCALE
RP    ANALYSIS].
```

3.11.4. The RC line

The RC (Reference Comment) lines are optional lines which are used to store comments relevant to the reference cited. The format of the RC line is:

RC TOKEN1=Text; TOKEN2=Text; ...

The currently defined tokens and their order in the RC line are:

```
STRAIN
PLASMID
TRANSPOSON
TISSUE
```

Reference comment line topics may span lines. Examples of RC lines:

```
RC    STRAIN=Sprague-Dawley; TISSUE=Liver;
RC    STRAIN=Holstein; TISSUE=Lymph node, and Mammary gland;
RC    STRAIN=301 / Serotype 2a;
```

```

RC   STRAIN=cv. SP753012-0; TISSUE=Leaf;

RC   PLASMID=R1 (R7268); TRANSPOSON=Tn3;

RC   STRAIN=AL.012, AZ.026, AZ.180, DC.005, GA.039, GA2181, IL.014, IL2.17,
RC   IN.018, KY.172, KY2.37, LA.013, MI.035, MN.001, MNB027, MS.040, NY.016,
RC   OH.036, TN.173, TN2.38, UT.002, and VA.015;

```

3.11.5. The RX line

The RX (Reference cross-reference) line is an optional line which is used to indicate the identifier assigned to a specific reference in a bibliographic database. The format of the RX line is:

```
RX   Bibliographic_db=IDENTIFIER[; Bibliographic_db=IDENTIFIER...];
```

Where the valid bibliographic database names and their associated identifiers are:

Name	Identifier
MEDLINE	Eight-digit MEDLINE Unique Identifier (UI)
PubMed	PubMed Unique Identifier (PMID)
DOI	Digital Object Identifier (DOI)
AGRICOLA	AGRICOLA Unique Identifier

Example of RX lines:

```

RX   MEDLINE=83283433; PubMed=6688356;

RX   PubMed=15626370; DOI=10.1016/j.toxicon.2004.10.011;

RX   MEDLINE=22709107; PubMed=12788972; DOI=10.1073/pnas.1130426100;

RX   AGRICOLA=IND20551642; DOI=10.1007/BF00224104;

```

3.11.6. The RG line

The Reference Group (RG) line lists the consortium name associated with a given citation. The RG line is mainly used in submission reference blocks, but can also be used in paper references, if the working group is cited as an author in the paper. RG line and [RA line](#) (Reference Author) can be present in the same reference block; at least one RG or RA line is mandatory per reference block. An example of the use of RG lines is shown below:

```
RG   The mouse genome sequencing consortium;
```

3.11.7. The RA line

The RA (Reference Author) lines list the authors of the paper (or other work) cited. The RA line is present in most references, but might be missing in references that cite a reference group (see [RG line](#)). At least one RG or RA line is mandatory per reference block.

All of the authors are included, and are listed in the order given in the paper. The names are listed surname first followed by a blank, followed by initial(s) with periods. The authors' names are separated by commas and terminated by a semicolon. Author names are not split between lines. An example of the use of RA lines is shown below:

```

RA   Galinier A., Bleicher F., Negre D., Perriere G., Duclos B., Cozzone A.J.,
RA   Cortay J.-C.;

```

As many RA lines as necessary are included in each reference.

An author's initials can be followed by an abbreviation such as 'Jr' (for Junior), 'Sr' (Senior), 'II', 'III' or 'IV' (2nd, 3rd and 4th). Example:

```
RA   Nasoff M.S., Baker H.V. II, Wolf R.E. Jr.;
```

3.11.8. The RT line

The RT (Reference Title) lines give the title of the paper (or other work) cited as exactly as possible given the limitations of the computer character set. The format of the RT line is:

```
RT   "Title.";
```

Example of a set of RT lines:

```

RT   "New insulin-like proteins with atypical disulfide bond pattern
RT   characterized in Caenorhabditis elegans by comparative sequence analysis
RT   and homology modeling.";

```

It should be noted that the format of the title is not always identical to that displayed at the top of the published work:

- Major title words are not capitalized;
- The text of a title ends with either a period '.', a question mark '?' or an exclamation mark '!';
- Double quotation marks '"' in the text of the title are replaced by single quotation marks ' ';
- Titles of articles published in a language other than English have been translated into English;

- Greek letters are written in full (alpha, beta, etc.).

3.11.9. The RL line

The RL (Reference Location) lines contain the conventional citation information for the reference. In general, the RL lines alone are sufficient to find the paper in question.

a) Journal citations

The RL line for a journal citation includes the journal abbreviation, the volume number, the page range and the year. The format for such an RL line is:

```
RL   Journal_abbrev Volume:First_page-Last_page(YYYY).
```

Journal names are abbreviated according to the conventions used by the National Library of Medicine (NLM) and are based on the existing ISO and ANSI standards. A list of the abbreviations currently in use is given in the document file [jourlist.txt](#)

An example of an RL line is:

```
RL   J. Mol. Biol. 168:321-331(1983).
```

When a reference is made to a paper which is 'in press' at the time the database is released, the page range, and possibly the volume number, are indicated as '0' (zero). An example of such an RL line is shown here:

```
RL   Int. J. Parasitol. 0:0-0(2005).
```

b) Electronic publications

The RL line for an electronic publication includes an '(er)' prefix. The format is indicated below:

```
RL   (er) Free text.
```

Examples:

```
RL   (er) Plant Gene Register PGR98-023.
```

```
RL   (er) Worm Breeder's Gazette 15(3):34(1998).
```

c) Book citations

A variation of the RL line format is used for papers found in books or other types of publication, which are then cited using the following format:

```
RL   (In) Editor_1 I., Editor_2 I., Editor_X I. (eds.);
RL   Book_name, pp.[Volume:]First_page-Last_page, Publisher, City (YYYY).
```

Examples:

```
RL   (In) Boyer P.D. (eds.);
RL   The enzymes (3rd ed.), pp.11:397-547, Academic Press, New York (1975).
```

```
RL   (In) Rich D.H., Gross E. (eds.);
RL   Proceedings of the 7th American peptide symposium, pp.69-72, Pierce
RL   Chemical Co., Rockford IL. (1981).
```

```
RL   (In) Magnusson S., Ottesen M., Foltmann B., Dano K., Neurath H. (eds.);
RL   Regulatory proteolytic enzymes and their inhibitors, pp.163-172, Pergamon
RL   Press, New York (1978).
```

d) Unpublished observations

For unpublished observations the format of the RL line is:

```
RL   Unpublished observations (MMM-YYYY).
```

Where 'MMM' is the month and 'YYYY' is the year.

We use the 'unpublished observations' RL line to cite communications by scientists to Swiss-Prot of unpublished information concerning various aspects of a sequence entry.

e) Thesis

For Ph.D. theses the format of the RL line is:

```
RL   Thesis (Year), Institution_name, Country.
```

An example of such a line is given here:

```
RL   Thesis (1977), University of Geneva, Switzerland.
```

f) Patent applications

For patent applications the format of the RL line is:

Where 'Pat num' is the international publication number of the patent, 'DD' is the day, 'MMM' is the month and 'YYYY' is the year. Example:

g) Submissions

RL Submitted (MMM-YYYY) to Database name.

the EMBL/GenBank/DDBJ databases
UniProtKB
the PDB data bank
the PIR data bank

RL Submitted (OCT-1995) to the EMBL/GenBank/DDBJ databases.

RL Submitted (APR-2004) to UniProtKB.

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The format of a comment block is:

```
CC      -!- TOPIC: First line of a comment block;
CC          second and subsequent lines of a comment block.
```

Topic	Description
ALLERGEN	Information relevant to allergenic proteins
ALTERNATIVE PRODUCTS	Description of the existence of related protein sequence(s) produced by alternative splicing of the same gene, alternative promoter usage, ribosomal frameshifting or by the use of alternative initiation codons; see 3.22.15
BIOPHYSICOCHEMICAL PROPERTIES	Description of the information relevant to biophysical and physicochemical data and information on pH dependence, temperature dependence, kinetic parameters, redox potentials, and maximal absorption; see 3.22.8
BIOTECHNOLOGY	Description of the use of a specific protein in a biotechnological process
CATALYTIC ACTIVITY	Description of the reaction(s) catalyzed by an enzyme [1]
CAUTION	Warning about possible errors and/or grounds for confusion
COFACTOR	Description of any non-protein substance required by an enzyme for its catalytic activity
DEVELOPMENTAL STAGE	Description of the developmentally-specific expression of mRNA or protein
DISEASE	Description of the disease(s) associated with a deficiency of a protein
DISRUPTION PHENOTYPE	Description of the effects caused by the disruption of the gene coding for the protein; see 3.22.27
DOMAIN	Description of the domain structure of a protein
ACTIVITY REGULATION	Description of the regulatory mechanism of an enzyme, transporter, microbial transcription factor
FUNCTION	General description of the function(s) of a protein
INDUCTION	Description of the compound(s) or condition(s) that regulate gene expression
INTERACTION	Conveys information relevant to binary protein-protein interaction 3.22.12
MASS SPECTROMETRY	Reports the exact molecular weight of a protein or part of a protein as determined by mass spectrometric methods; see 3.22.23
MISCELLANEOUS	Any comment which does not belong to any of the other defined topics
PATHWAY	Description of the metabolic pathway(s) with which a protein is associated
PHARMACEUTICAL	Description of the use of a protein as a pharmaceutical drug
POLYMORPHISM	Description of polymorphism(s)
PTM	Description of any chemical alternation of a polypeptide (proteolytic cleavage, amino acid modifications including crosslinks). This topic complements information given in the feature table or indicates polypeptide modifications for which position-specific data is not available.
RNA EDITING	Description of any type of RNA editing that leads to one or more amino acid changes

SEQUENCE CAUTION	Description of protein sequence reports that differ from the sequence that is shown in UniProtKB due to conflicts that are not described in FT CONFLICT lines, such as frameshifts, erroneous gene model predictions, etc. See 3.22.36
SIMILARITY	Description of the similarity(ies) (sequence or structural) of a protein with other proteins
SUBCELLULAR LOCATION	Description of the subcellular location of the chain/peptide/isoform. See 3.22.13
SUBUNIT	Description of the quaternary structure of a protein and any kind of interactions with other proteins or protein complexes; except for receptor-ligand interactions, which are described in the topic FUNCTION.
TISSUE SPECIFICITY	Description of the tissue-specific expression of mRNA or protein
TOXIC DOSE	Description of the lethal dose (LD), paralytic dose (PD) or effective dose of a protein
WEB RESOURCE	Description of a cross-reference to a network database/resource for a specific protein; see 3.22.38

Note:

[1] For the 'CATALYTIC ACTIVITY' topic: To allow the curation of reactions at the level of specific enzymes instead of enzyme classes, and to use standardized names for reactants, we use chemical reaction descriptions from the [Rhea database](#) whenever possible. For catalytic activities that can only be described in the form of free text, we follow the recommendations of the Nomenclature Committee of the International Union of Biochemistry and Molecular Biology (IUBMB) as published in Enzyme Nomenclature, NC-IUBMB, Academic Press, New-York, (1992).

3.12.1. Examples for each comment line topic

We show here, for each of the defined topics, two examples of their usage:

```
CC  -!- ALLERGEN: Causes an allergic reaction in human. Binds to IgE. Partially
CC  heat-labile allergen that may cause both respiratory and food-allergy
CC  symptoms in patients with the bird-egg syndrome.
CC  {ECO:0000269|PubMed:11488669}.

CC  -!- ALLERGEN: Causes an allergic reaction in human. Minor allergen of
CC  bovine dander.

CC  -!- ALTERNATIVE PRODUCTS:
CC  Event=Alternative splicing; Named isoforms=4;
CC  Comment=Additional isoforms seem to exist. Experimental confirmation
CC  may be lacking for some isoforms.;
CC  Name=1; Synonyms=AIRE-1;
CC  IsoId=043918-1; Sequence=Displayed;
CC  Name=2; Synonyms=AIRE-2;
CC  IsoId=043918-2; Sequence=VSP_004089;
CC  Name=3; Synonyms=AIRE-3;
CC  IsoId=043918-3; Sequence=VSP_004089, VSP_004090;
CC  Name=4;
CC  IsoId=043918-4; Sequence=VSP_004089, VSP_043529;

CC  -!- ALTERNATIVE PRODUCTS:
CC  Event=Alternative splicing, Alternative initiation; Named isoforms=3;
CC  Name=Alpha;
CC  IsoId=P51636-1; Sequence=Displayed;
CC  Name=Beta;
CC  IsoId=P51636-2; Sequence=VSP_018696;
CC  Name=C;
CC  IsoId=P51636-3; Sequence=VSP_038114, VSP_038115;

CC  -!- BIOPHYSICOCHEMICAL PROPERTIES:
CC  Kinetic parameters:
CC  KM=5 uM for pyridoxal phosphate {ECO:0000269|PubMed:10080917};
CC  KM=12.2 mM for D-alanine {ECO:0000269|PubMed:10080917};
CC  KM=17.9 mM for L-alanine {ECO:0000269|PubMed:10080917};
CC  pH dependence:
CC  Optimum pH is 8-10. {ECO:0000269|PubMed:10080917};
CC  Temperature dependence:
CC  Highly active at low temperatures, even at 0 degree Celsius.
CC  Thermolabile. {ECO:0000269|PubMed:10080917};

CC  -!- BIOPHYSICOCHEMICAL PROPERTIES:
CC  Kinetic parameters:
CC  KM=98 uM for ATP;
CC  KM=688 uM for pyridoxal;
CC  Vmax=1.604 mmol/min/mg enzyme;
CC  pH dependence:
CC  Optimum pH is 6.0. Active from pH 4.5 to 10.5.;

CC  -!- BIOTECHNOLOGY: The effect of PG can be neutralized by introducing an
CC  antisense PG gene by genetic manipulation. The Flav'r Sav'r tomato
CC  produced by Calgene (Monsanto) in such a manner has a longer shelf life
CC  due to delayed ripening.

CC  -!- BIOTECHNOLOGY: Used in the food industry for high temperature
CC  liquefaction of starch-containing mash and in the detergent industry
CC  to remove starch. Sold under the name Termamyl by Novozymes.
```

CC -!- CATALYTIC ACTIVITY:
CC Reaction=ATP + L-glutamate + NH4(+) = ADP + H(+) + L-glutamine +
CC phosphate; Xref=Rhea:RHEA:16169, ChEBI:CHEBI:15378,
CC ChEBI:CHEBI:28938, ChEBI:CHEBI:29985, ChEBI:CHEBI:30616,
CC ChEBI:CHEBI:43474, ChEBI:CHEBI:58359, ChEBI:CHEBI:456216; EC=6.3.1.2;

CC -!- CATALYTIC ACTIVITY:
CC Reaction=(2R)-2,3-dihydroxy-3-methylbutanoate + NADP(+) = (2S)-2-
CC acetoacetate + H(+) + NADPH; Xref=Rhea:RHEA:22068, ChEBI:CHEBI:15378,
CC ChEBI:CHEBI:49072, ChEBI:CHEBI:57783, ChEBI:CHEBI:58349,
CC ChEBI:CHEBI:58476; EC=1.1.1.86; Evidence={ECO:0000255|HAMAP-
CC Rule:MF_00435};

CC -!- CATALYTIC ACTIVITY:
CC Reaction=(2R,3R)-2,3-dihydroxy-3-methylpentanoate + NADP(+) = (S)-2-
CC ethyl-2-hydroxy-3-oxobutanoate + H(+) + NADPH; Xref=Rhea:RHEA:13493,
CC ChEBI:CHEBI:15378, ChEBI:CHEBI:49256, ChEBI:CHEBI:49258,
CC ChEBI:CHEBI:57783, ChEBI:CHEBI:58349; EC=1.1.1.86;
CC Evidence={ECO:0000255|HAMAP-Rule:MF_00435};

CC -!- CAUTION: It is uncertain whether Met-1 or Met-3 is the initiator.
CC {ECO:0000305}.

CC -!- COFACTOR:
CC Name=pyridoxal 5'-phosphate; Xref=ChEBI:CHEBI:597326;
CC Evidence={ECO:0000250|UniProtKB:P15505};

CC -!- COFACTOR:
CC Name=FAD; Xref=ChEBI:CHEBI:57692;
CC Evidence={ECO:0000255|HAMAP-Rule:MF_01202};

CC -!- WEB RESOURCE: Name=Wikipedia; Note=Amyloid beta entry;
CC URL="http://en.wikipedia.org/wiki/Amyloid_beta";

CC -!- DEVELOPMENTAL STAGE: Expressed early during conidial (dormant spores)
CC differentiation.

CC -!- DEVELOPMENTAL STAGE: Detected in embryonic skin (12.5 dpc and 14.5 dpc)
CC during the formation of hair follicles and at 15.5 dpc in the enamel
CC knot of the developing tooth. Detected in the basal layer of the
CC epidermis and hair follicles of P2 mice.

CC -!- DISEASE: Glycogen storage disease 9D (GSD9D) [MIM:300559]: A metabolic
CC disorder characterized by slowly progressive, predominantly distal
CC muscle weakness and atrophy. Clinical features include exercise
CC intolerance with early fatigability, pain, cramps and occasionally
CC myoglobinuria. {ECO:0000269|PubMed:12825073}. Note=The disease is
CC caused by mutations affecting the gene represented in this entry.

CC -!- DISEASE: Adrenoleukodystrophy (ALD) [MIM:300100]: A peroxisomal
CC metabolic disorder characterized by progressive multifocal
CC demyelination of the central nervous system and by peripheral adrenal
CC insufficiency (Addison disease). It results in mental deterioration,
CC corticospinal tract dysfunction, and cortical blindness. Different
CC clinical manifestations exist like: cerebral childhood ALD (CALD),
CC adult cerebral ALD (ACALD), adrenomyeloneuropathy (AMN) and 'Addison
CC disease only' (ADO) phenotype. {ECO:0000269|PubMed:10369742,
CC ECO:0000269|PubMed:10480364, ECO:0000269|PubMed:10551832,
CC ECO:0000269|PubMed:10737980, ECO:0000269|PubMed:10980539,
CC ECO:0000269|PubMed:11248239, ECO:0000269|PubMed:11438993,
CC ECO:0000269|PubMed:11810273, ECO:0000269|PubMed:15643618,
CC ECO:0000269|PubMed:21700483, ECO:0000269|PubMed:21889498,
CC ECO:0000269|PubMed:23651979, ECO:0000269|PubMed:26686776,
CC ECO:0000269|PubMed:7581394, ECO:0000269|PubMed:7717396,
CC ECO:0000269|PubMed:7825602, ECO:0000269|PubMed:7849723,
CC ECO:0000269|PubMed:7904210, ECO:0000269|PubMed:8040304,
CC ECO:0000269|PubMed:8566952, ECO:0000269|PubMed:8651290,
CC ECO:0000269|PubMed:9452087}. Note=The disease is caused by mutations
CC affecting the gene represented in this entry.

CC -!- DISEASE: Note=The promoter region of ABCD1 is deleted in the chromosome
CC Xq28 deletion syndrome which involves ABCD1 and the neighboring gene
CC BCAP31. {ECO:0000269|PubMed:11992258}.

CC -!- DISRUPTION PHENOTYPE: Mice display impaired B-cell development which
CC does not progress past the progenitor stage.
CC {ECO:0000269|PubMed:12097390}.

CC -!- DISRUPTION PHENOTYPE: Death before reaching adulthood, probably due to
CC lethal epilepsy. Mice display severe defects in the olfactory bulbs,
CC the hippocampus, and the cerebellum. These defects appear to result
CC from impaired cytokinesis followed by the induction of apoptosis in
CC specific neuroblast populations. {ECO:0000269|PubMed:11086988}.

CC -!- DOMAIN: The N-terminal domain (1-374) is sufficient for the exchange
CC factor activity.

CC -!- DOMAIN: The B chain is composed of two domains, each domain consists of
CC 3 homologous subdomains (alpha, beta, gamma).

CC -!- ACTIVITY REGULATION: The activity of this enzyme could be controlled by
CC adenylation under conditions of abundant glutamine.
CC {ECO:0000250|UniProtKB:Q3V5W6}.

CC -!- ACTIVITY REGULATION: Activated by Gram-negative bacterial
CC lipopolysaccharides and chymotrypsin.

CC -!- FUNCTION: Binds to actin and affects the structure of the cytoskeleton.
CC At high concentrations, profilin prevents the polymerization of actin,
CC whereas it enhances it at low concentrations. By binding to PIP2, it
CC inhibits the formation of IP3 and DG. Inhibits androgen receptor (AR)
CC and HTT aggregation and binding of G-actin is essential for its
CC inhibition of AR (By similarity). {ECO:0000250}.

CC -!- FUNCTION: Inhibitor of fungal polygalacturonase. It is an important
CC factor for plant resistance to phytopathogenic fungi. Substrate
CC preference is polygalacturonase (PG) from *A.niger* >> PG of *F.oxysporum*,
CC *A.solani* or *B.cinerea*. Not active on PG from *F.moniliforme*.
CC {ECO:0000269|PubMed:10228150, ECO:0000269|PubMed:9304859}.

CC -!- INDUCTION: By heat shock, salt stress, oxidative stress, glucose
CC limitation and oxygen limitation.

CC -!- INDUCTION: By infection, plant wounding, or elicitor treatment of cell
CC cultures.

CC -!- INTERACTION:
CC P53323; Q03705: CGI121; NbExp=9; IntAct=EBI-3809, EBI-912262;
CC P53323; P46984: GON7; NbExp=6; IntAct=EBI-3809, EBI-26178;
CC P53323; Q03835: GRX3; NbExp=3; IntAct=EBI-3809, EBI-22178;
CC P53323; P32642: GRX4; NbExp=11; IntAct=EBI-3809, EBI-22211;
CC P53323; P36132: KAE1; NbExp=21; IntAct=EBI-3809, EBI-26411;

CC -!- INTERACTION:
CC Q99259; Q6RW13: AGTRAP; NbExp=3; IntAct=EBI-743184, EBI-741181;
CC Q99259; Q6RW13-2: AGTRAP; NbExp=6; IntAct=EBI-743184, EBI-11522760;
CC Q99259; Q96DZ9: CMTM5; NbExp=4; IntAct=EBI-743184, EBI-2548702;
CC Q99259; Q96DZ9-2: CMTM5; NbExp=6; IntAct=EBI-743184, EBI-11522780;
CC Q99259; P46952: HAAO; NbExp=8; IntAct=EBI-743184, EBI-743215;
CC Q99259; Q969L2: MAL2; NbExp=6; IntAct=EBI-743184, EBI-944295;
CC Q99259; P16333: NCK1; NbExp=2; IntAct=EBI-743184, EBI-389883;
CC Q99259; Q13188: STK3; NbExp=3; IntAct=EBI-743184, EBI-992580;

CC -!- MASS SPECTROMETRY: Mass=24948; Mass_error=6; Method=MALDI;
CC Evidence={ECO:0000269|PubMed:11101899};

CC -!- MASS SPECTROMETRY: Mass=15706; Method=MALDI;
CC Evidence={ECO:0000269|PubMed:10531593};

CC -!- MASS SPECTROMETRY: [Isoform B]: Mass=13822; Method=MALDI; Note=The
CC measured range is 19-140.; Evidence={ECO:0000269|PubMed:10531593};

CC -!- MISCELLANEOUS: Binds to bacitracin.

CC -!- MISCELLANEOUS: Called DUO because the encoded protein is closely
CC related to but shorter than TRIO.

CC -!- PATHWAY: Porphyrin-containing compound metabolism; protoporphyrin-IX
CC biosynthesis; 5-aminolevulinate from L-glutamyl-tRNA(Glu): step 2/2.
CC -!- PATHWAY: Porphyrin-containing compound metabolism; chlorophyll
CC biosynthesis.

CC -!- PATHWAY: Nitrogen metabolism; (S)-allantoin degradation.
CC {ECO:0000255|HAMAP-Rule:MF_00616}.

CC -!- PHARMACEUTICAL: Available under the names Avonex (Biogen), Betaseron
CC (Berlex) and Rebif (Serono). Used in the treatment of multiple
CC sclerosis (MS). Betaseron is a slightly modified form of IFNβ1 with two
CC residue substitutions.

CC -!- PHARMACEUTICAL: Available under the name Proleukin (Chiron). Used in
CC patients with renal cell carcinoma or metastatic melanoma.

CC -!- POLYMORPHISM: The allelic form of the enzyme with Gln-192 (allozyme A)
CC hydrolyzes paraoxon with a low turnover number and the one with Arg-192
CC (allozyme B) with a high turnover number. {ECO:0000269|PubMed:7916578,
CC ECO:0000269|PubMed:8098250}.

CC -!- POLYMORPHISM: In human populations there are two major allelic forms,
CC alpha-1 (1-1) with 83 residues and alpha-2 (2-2) with 142 residues.
CC These alleles determine 3 possible genotypes, homozygous (1-1 or 2-2)
CC and heterozygous (2-1), and 3 major phenotypes HP*1F/HP*1S and HP*2FS.
CC The two main alleles of HP*1 are called HP*1F (fast) and HP*1S (slow).
CC The alleles exhibit different oligomerization properties. In healthy
CC males, but not in females, the Hp 2-2 phenotype is associated with
CC higher serum iron, decreased antimicrobial and antioxidant capability,
CC and less efficient clearance from the circulation, than Hp 1-1 and 2-1.
CC The sequence displayed in this entry corresponds to allele alpha-2 (2-

```

CC      2). {ECO:0000269|PubMed:4018023, ECO:0000269|PubMed:6330675,
CC      ECO:0000269|PubMed:6546723}.

CC      -!- PTM: N-glycosylated and probably also O-glycosylated.

CC      -!- PTM: A soluble short form may be released by proteolytic cleavage from
CC      the long membrane-anchored form. {ECO:0000250|UniProtKB:P78423}.

CC      -!- RNA EDITING: Modified_positions=393 {ECO:0000269|PubMed:10611383}, 431
CC      {ECO:0000269|PubMed:10611383}, 472 {ECO:0000269|PubMed:10611383}, 495
CC      {ECO:0000269|PubMed:10611383};

CC      -!- RNA EDITING: Modified_positions=59 {ECO:0000269|PubMed:12527781,
CC      ECO:0000269|PubMed:12711687}, 78 {ECO:0000269|PubMed:12527781,
CC      ECO:0000269|PubMed:12711687}, 94 {ECO:0000269|PubMed:12527781,
CC      ECO:0000269|PubMed:12711687}, 98 {ECO:0000269|PubMed:12527781,
CC      ECO:0000269|PubMed:12711687}, 102 {ECO:0000269|PubMed:12527781,
CC      ECO:0000269|PubMed:12711687}, 121 {ECO:0000269|PubMed:12527781,
CC      ECO:0000269|PubMed:12711687}; Note=The nonsense codon at position 59 is
CC      modified to a sense codon. The stop codon at position 121 is created by
CC      RNA editing.;

CC      -!- SEQUENCE CAUTION:
CC      Sequence=AAA24007.1; Type=Frameshift; Evidence={ECO:0000305};

CC      -!- SIMILARITY: Belongs to the annexin family. {ECO:0000255|PROSITE-
CC      ProRule:PRU01245, ECO:0000305}.

CC      -!- SUBCELLULAR LOCATION: Cell membrane; Lipid-anchor, GPI-anchor. Golgi
CC      apparatus.
CC      -!- SUBCELLULAR LOCATION: [Megakaryocyte-potentiating factor]: Secreted.
CC      -!- SUBCELLULAR LOCATION: [Isoform 3]: Secreted.

CC      -!- SUBUNIT: Homotetramer. {ECO:0000269|PubMed:11997398,
CC      ECO:0000269|PubMed:1610806, ECO:0000269|PubMed:9837940}.

CC      -!- SUBUNIT: Heterodimer; disulfide-linked heterodimer of a light chain
CC      (LC) and a heavy chain (HC). The LC has the proteolytic/pharmacological
CC      activity, while the N- and C-termini of the HC mediate channel
CC      formation and toxin binding, respectively. Interacts with host
CC      receptors synaptotagmin-1 and -2 (SYT1 and SYT2) (PubMed:15123599,
CC      PubMed:17185412, PubMed:20219474). {ECO:0000269|PubMed:15123599,
CC      ECO:0000269|PubMed:17185412, ECO:0000269|PubMed:20219474}.

CC      -!- TISSUE SPECIFICITY: Shoots, roots, and cotyledon from dehydrating
CC      seedlings.

CC      -!- TISSUE SPECIFICITY: Expressed at high levels in brain and ovary. Lower
CC      levels in small intestine. In brain regions, detected in all regions
CC      tested. Highest levels in the cerebellum and cerebral cortex.

CC      -!- TOXIC DOSE: PD(50) is 0.36 mg/kg by injection in blowfly larvae, in
CC      PubMed:12885226.
CC      -!- TOXIC DOSE: PD(50) is 0.557 mg/kg by injection in blowfly larvae, in
CC      PubMed:15824108.

CC      -!- TOXIC DOSE: [Sarafotoxin-C]: LD(50) is 0.3 mg/kg by intravenous
CC      injection into mice. {ECO:0000269|PubMed:3176048}.

CC      -!- WEB RESOURCE: Name=CD40Lbase; Note=CD40L defect database;
CC      URL="http://bioinf.uta.fi/CD40Lbase/";

```

3.12.2. Syntax of the topic 'BIOPHYSICOCHEMICAL PROPERTIES'

```

CC      -!- BIOPHYSICOCHEMICAL PROPERTIES:
CC      Absorption:
CC      Abs(max)=xx nm;
CC      Note=free_text;
CC      Kinetic parameters:
CC      KM=xx unit for substrate [(free_text)];
CC      Vmax=xx unit enzyme [free_text];
CC      Note=free_text;
CC      pH dependence:
CC      free_text;
CC      Redox potential:
CC      free_text;
CC      Temperature dependence:
CC      free_text;

```

A BIOPHYSICOCHEMICAL PROPERTIES block must contain at least one of the properties Absorption, Kinetic parameters, pH dependence, Redox potential, Temperature dependence and may have any combination of these properties (ordered as indicated above). The meaning of these subtopics is as follows:

Property	Description
Absorption	indicates the wavelength at which photoreactive proteins such as opsins and DNA photolyases show maximal

	absorption
Kinetic parameters	mentions the Michaelis-Menten constant (KM) and maximal velocity (Vmax) of enzymes
pH dependence	describes the optimum pH for enzyme activity and/or the variation of enzyme activity with pH variation
Redox potential	reports the value of the standard (midpoint) oxido-reduction potential(s) for electron transport proteins
Temperature dependence	indicates the optimum temperature for enzyme activity and/or the variation of enzyme activity with temperature variation; the thermostability/thermolability of the enzyme is also mentioned when it is known

3.12.3. The topic 'INTERACTION'

The CC line topic INTERACTION conveys information relevant to binary protein-protein interaction. It is automatically derived from the [IntAct](#) database and is updated on a monthly basis. The occurrence is one INTERACTION topic per entry, with each binary interaction being presented in a separate line. Each data line can be longer than 80 characters.

Interactions can be derived by any appropriate experimental method, but must be confirmed by a second experiment, if resulting from a single yeast- two-hybrid experiment. For large-scale experiments, interactions are considered if a high confidence is assigned from the authors.

The format of the CC line topic INTERACTION is:

```
CC  -!- INTERACTION:
CC      <Interactant>; <Interactant>;( Xeno;)? NbExp=<Experiments>; IntAct=<IntActId>, <IntActId>;
CC      <Interactant>; <Interactant>;( Xeno;)? NbExp=<Experiments>; IntAct=<IntActId>, <IntActId>;
CC      ...
```

where

- <Interactant> represents a UniProtKB protein.
- the first <Interactant> is represented by: (<Accession>|<IsoId>|<ProductId>)
- the second <Interactant> is represented by: (<Accession>|<IsoId>|<ProductId> [<Accession>])(: <Gene>)?
- <IsoId> is a UniProtKB isoform ID.
- <ProductId> is a UniProtKB product ID, i.e. a [feature identifier](#).
- <Gene> is either the gene name, ordered locus name or ORF name of the gene that encodes the UniProtKB protein.
- <Experiments> is the number of experiments in IntAct that support an interaction.
- <IntActId> is an IntAct protein ID.
- 'Xeno' is an optional flag that indicates that the interacting proteins are derived from different species. This may be due to the experimental set-up or may reflect a pathogen-host interaction.
- IntAct=IntActId, IntActId identifies the interaction in IntAct by using the two IntAct protein identifiers.

Examples:

Binary interactions with different isoforms that are described in P11309.

[P11309](#)

```
CC  -!- INTERACTION:
CC      P11309-1; Q9BZS1-1: FOXP3; NbExp=3; IntAct=EBI-1018629, EBI-9695448;
CC      P11309-2; Q9UNQ0: ABCG2; NbExp=5; IntAct=EBI-1018633, EBI-1569435;
```

Binary interaction with a product of proteolytic cleavage.

[P27958](#):

```
CC  -!- INTERACTION:
CC      PRO_0000037566; Q9NPY3: CD93; Xeno; NbExp=2; IntAct=EBI-6377335, EBI-1755002;
```

[Q9NPY3](#):

```
CC  -!- INTERACTION:
CC      Q9NPY3; PRO_0000037566 [P27958]; Xeno; NbExp=2; IntAct=EBI-1755002, EBI-6377335;
```

Examples of interaction lines are given below. The CC INTERACTION topics are not complete; only explained interaction lines are indicated.

```
CC  -!- INTERACTION:
CC      Q9NQ11; Q2M2I8: AAK1; NbExp=2; IntAct=EBI-6308763, EBI-1383433;
```

In the typical example the current protein, Q9NQ11, is interacting with Q2M2I8 which is further characterized by its gene name "AAK1". The interaction is supported by two experiments stored in IntAct. Experimental details for this interaction can be found by querying IntAct with "EBI-6308763, EBI-1383433".

```
CC  -!- INTERACTION:
CC      P27449; Q9UHP7-3: CLEC2D; NbExp=3; IntAct=EBI-721179, EBI-11749983;
```

The current protein, P27449, interacts with an isoform of Q9UHP7 defined by the IsoID Q9UHP7-3.

```
CC  -!- INTERACTION:
CC      P62799; P84233; NbExp=2; IntAct=EBI-302085, EBI-350041;
```

No gene name information for the interacting protein is available.

```
CC  -!- INTERACTION:
CC      P03612; P03612; NbExp=2; IntAct=EBI-781118, EBI-781118;
```

The protein self-associates.

```
CC  -!- INTERACTION:
CC      Q9NVC6; Q9D8C6: Med11; Xeno; NbExp=2; IntAct=EBI-394562, EBI-6260909;
```

The source organisms of the interacting proteins are different.

```
CC  -!- INTERACTION:
CC      Q9UNA1; O14613: CDC42EP2; NbExp=3; IntAct=EBI-1390913, EBI-3438291;
CC      Q9UNA1-2; O14613: CDC42EP2; NbExp=3; IntAct=EBI-16430964, EBI-3438291;
```

Different isoforms of the current protein are shown to interact with the same protein (O14613). This is reflected by different IntActIDs for the current protein.

Example entry with many interaction lines: [Q02821](#).

3.12.4. Syntax of the topic 'SUBCELLULAR LOCATION'

The document [subcell.txt](#), lists the controlled vocabularies used in the comment line (CC) topic SUBCELLULAR LOCATION, their definitions and further information such as synonyms or relevant GO terms in the following format:

Line code	Content	Occurrence in an entry
ID	Identifier (location)	Once; starts an entry
IT	Identifier (topology)	Once; starts a 'topology' entry
IO	Identifier (orientation)	Once; starts an 'orientation' entry
AC	Accession (SL-xxxx)	Once
DE	Definition	Once or more
SY	Synonyms	Optional; Once or more
SL	Content of subcell. loc. lines	Once
HI	Hierarchy ('is-a')	Optional; Once or more
HP	Hierarchy ('part-of')	Optional; Once or more
KW	Associated keyword (accession)	Optional; Once or more
GO	Gene ontology (GO) mapping	Optional; Once or more
WW	Interesting links or references	Optional; Once or more
//	Terminator	Once; ends an entry

Example:

```
ID  Cyanelle.
AC  SL-0082
DE  A cyanelle is a photosynthetic organelle of glaucocystophyte algae.
DE  Cyanelles are surrounded by a double membrane and, in between, a
DE  peptidoglycan wall. Thylakoid membrane architecture and the presence
DE  of carboxysomes are cyanobacteria-like. Historically, the term
DE  cyanelle is derived from a classification as endosymbiotic
DE  cyanobacteria, and thus is not fully correct.
SY  Muroplast; Cyanoplast.
SL  Plastid, cyanelle.
HI  Plastid.
KW  KW-0194
GO  GO:0009842; cyanelle
//
```

The format of SUBCELLULAR LOCATION is:

```
CC  -!- SUBCELLULAR LOCATION:(( Molecule:)?( Location\..+)?( Note=Free_text( Flag)?\..)?
```

Where:

- *Molecule*: Isoform, chain or peptide name
- *Location* = *Subcellular_location*(*Flag*)?(; *Topology*(*Flag*)?); *Orientation*(*Flag*)?);
 - *Subcellular_location*: SL-line of subcell.txt ID-record
 - *Topology*: SL-line of subcell.txt IT-record

- *Orientation*: SL-line of subcell.txt IO-record

Note: Perl-style multipliers indicate whether a pattern (as delimited by parentheses) is optional (?) or may occur 1 or more times (+).

Examples:

When no chain/peptide/isoform is specified, the subcellular location corresponds to that of the mature protein.

```
CC  -!- SUBCELLULAR LOCATION: Cytoplasm {ECO:0000269|PubMed:12867153}.
CC      Endoplasmic reticulum membrane {ECO:0000269|PubMed:12867153};
CC      Peripheral membrane protein {ECO:0000269|PubMed:12867153}. Golgi
CC      apparatus membrane {ECO:0000269|PubMed:12867153}; Peripheral membrane
CC      protein {ECO:0000269|PubMed:12867153}.

CC  -!- SUBCELLULAR LOCATION: Cell membrane {ECO:0000250}; Peripheral membrane
CC      protein {ECO:0000250}. Secreted {ECO:0000250}. Note=The last 22 C-
CC      terminal amino acids may participate in cell membrane attachment.
CC  -!- SUBCELLULAR LOCATION: [Isoform 2]: Cytoplasm {ECO:0000305}.

CC  -!- SUBCELLULAR LOCATION: Golgi apparatus, trans-Golgi network membrane
CC      {ECO:0000269|PubMed:17919502, ECO:0000269|PubMed:19033537,
CC      ECO:0000269|PubMed:22240481, ECO:0000269|PubMed:24706876}; Multi-pass
CC      membrane protein {ECO:0000255}. Late endosome
CC      {ECO:0000269|PubMed:11231950, ECO:0000269|PubMed:15681833}.
CC      Note=Predominantly found in the trans-Golgi network (TGN). Localized in
CC      the trans-Golgi network under low copper conditions, redistributes to
CC      cytoplasmic vesicles when cells are exposed to elevated copper levels,
CC      and then recycles back to the trans-Golgi network when copper is
CC      removed (PubMed:10942420). {ECO:0000269|PubMed:10942420,
CC      ECO:0000269|PubMed:22240481, ECO:0000269|PubMed:24706876,
CC      ECO:0000269|PubMed:9307043}.
CC  -!- SUBCELLULAR LOCATION: [Isoform 1]: Golgi apparatus membrane
CC      {ECO:0000269|PubMed:9307043}; Multi-pass membrane protein
CC      {ECO:0000269|PubMed:9307043}.
CC  -!- SUBCELLULAR LOCATION: [Isoform 2]: Cytoplasm
CC      {ECO:0000269|PubMed:9307043}.
CC  -!- SUBCELLULAR LOCATION: [WND/140 kDa]: Mitochondrion
CC      {ECO:0000269|PubMed:9600907}.
```

3.12.5. Syntax of the topic 'ALTERNATIVE PRODUCTS'

The format of the CC line topic ALTERNATIVE PRODUCTS is:

```
CC  -!- ALTERNATIVE PRODUCTS:
CC      Event=Event(, Event)*; Named isoforms=Number_of_isoforms;
(CC      Comment=Free_text;)?
(CC      Name=Isoform_name; (Synonyms=Synonym(, Synonym)*);)?
CC      IsoId=Isoform_identifier(, Isoform_identifier)*;
CC      Sequence=(Displayed|External|Not described|Feature_identifier(, Feature_identifier)*);
(CC      Note=Free_text;)?+
```

Note: Variable values are represented in italics. Perl-style multipliers indicate whether a pattern (as delimited by parentheses) is optional (?), may occur 0 or more times (*), or 1 or more times (+). Alternative values are separated by a pipe symbol (|).

Topic	Description
Event	Biological process that results in the production of the alternative forms. It lists one or a combination of the following values (Alternative promoter usage, Alternative splicing, Alternative initiation, Ribosomal frameshifting). Format: Event=controlled vocabulary; Example: Event=Alternative splicing;
Named isoforms	Number of isoforms listed in the topics 'Name' currently only for 'Event=Alternative splicing'. Format: Named isoforms=number; Example: Named isoforms=6;
Comment	Any comments concerning one or more isoforms; optional; Format: Comment=free text; Example: Comment=Experimental confirmation may be lacking for some isoforms;
Name	A common name for an isoform used in the literature or assigned by Swiss-Prot; currently only available for spliced isoforms. Format: Name=common name; Example: Name=Alpha;
Synonyms	Synonyms for an isoform as used in the literature; optional; currently only available for spliced isoforms. Format: Synonyms=Synonym_1[, Synonym_n]; Example: Synonyms=B, KL5;
IsoId	Unique identifier for an isoform, consisting of the Swiss-Prot accession number, followed by a dash and a number. Format: IsoId=acc#-isoform_number[, acc#-isoform_number]; Example: IsoId=P05067-1;
Sequence	Information on the isoform sequence; the term ' Displayed ' indicates, that the sequence is shown in the entry; a lists of feature identifiers (VSP_#) indicates that the isoform is annotated in the feature table; the FTIDs enable programs to create the sequence

	of a splice variant; if the accession number of the IsoId does not correspond to the accession number of the current entry, this topic contains the term ' External '; ' Not described ' points out that the sequence of the isoform is unknown. Format: Sequence=VSP_#[, VSP_#] Displayed External Not described; Example: Sequence=Displayed; Example: Sequence=VSP_000013, VSP_000014; Example: Sequence=External; Example: Sequence=Not described;
Note	Lists isoform-specific information; optional. It may specify the event(s), if there are several. Format: Note=Free text; Example: Note=No experimental confirmation available;

Example of the CC lines and the corresponding FT lines for an entry with alternative splicing:

```

CC  -!- ALTERNATIVE PRODUCTS:
CC      Event=Alternative promoter usage, Alternative splicing; Named isoforms=11;
CC      Name=1; Synonyms=Non-muscle isozyme;
CC      IsoId=Q15746-1; Sequence=Displayed;
CC      Name=2;
CC      IsoId=Q15746-2; Sequence=VSP_004791;
CC      Name=3A;
CC      IsoId=Q15746-3; Sequence=VSP_004794;
CC      Name=3B;
CC      IsoId=Q15746-4; Sequence=VSP_004791, VSP_004794;
CC      Name=4;
CC      IsoId=Q15746-5; Sequence=VSP_004793;
CC      Name=Del-1790;
CC      IsoId=Q15746-6; Sequence=VSP_004795;
CC      Name=5; Synonyms=Smooth-muscle isozyme;
CC      IsoId=Q15746-7; Sequence=VSP_018845;
CC      Name=6; Synonyms=Telokin;
CC      IsoId=Q15746-8; Sequence=VSP_018846;
CC      Name=7;
CC      IsoId=Q15746-9; Sequence=VSP_053791;
CC      Name=8;
CC      IsoId=Q15746-10; Sequence=VSP_018846, VSP_004795;
CC      Name=9;
CC      IsoId=Q15746-11; Sequence=VSP_018845, VSP_004795;
...
FT  VAR_SEQ      1..1760
FT                /note="Missing (in isoform 6 and isoform 8)"
FT                /evidence="ECO:0000303|PubMed:10536370,
FT                ECO:0000303|PubMed:14702039, ECO:0000303|PubMed:15489334"
FT                /id="VSP_018846"
FT  VAR_SEQ      1..1200
FT                /note="Missing (in isoform 7)"
FT                /evidence="ECO:0000303|PubMed:14702039"
FT                /id="VSP_053791"
FT  VAR_SEQ      1..922
FT                /note="Missing (in isoform 5 and isoform 9)"
FT                /evidence="ECO:0000303|PubMed:8575746, ECO:0000303|Ref.8"
FT                /id="VSP_018845"
FT  VAR_SEQ      437..506
FT                /note="VSGIPKPEVAWFLEGTTPVRRQEGSIEVYDAGSHYLCLLKARTRDSGTYSCT
FT                ASNAQGQLSCSWTLQVER -> G (in isoform 2 and isoform 3B)"
FT                /evidence="ECO:0000303|PubMed:10198165,
FT                ECO:0000303|PubMed:15507455"
FT                /id="VSP_004791"
FT  VAR_SEQ      1473..1545
FT                /note="Missing (in isoform 4)"
FT                /evidence="ECO:0000303|PubMed:10198165"
FT                /id="VSP_004793"
FT  VAR_SEQ      1655..1705
FT                /note="Missing (in isoform 3A and isoform 3B)"
FT                /evidence="ECO:0000303|PubMed:10198165"
FT                /id="VSP_004794"
FT  VAR_SEQ      1790
FT                /note="Missing (in isoform Del-1790, isoform 8 and isoform
FT                9)"
FT                /evidence="ECO:0000303|PubMed:10536370,
FT                ECO:0000303|PubMed:14702039, ECO:0000303|PubMed:15489334,
FT                ECO:0000303|PubMed:8575746"
FT                /id="VSP_004795"

CC  -!- ALTERNATIVE PRODUCTS:
CC      Event=Alternative splicing, Alternative initiation; Named isoforms=3;
CC      Comment=Isoform 1 and isoform tumor suppressor ARF arise due to the
CC      use of two alternative first exons joined to a common exon 2 at the
CC      same acceptor site but in different reading frames, resulting in two
CC      completely different isoforms.;
CC      Name=1; Synonyms=CDKN2A, p16INK4a;
CC      IsoId=O77617-1; Sequence=Displayed;
CC      Name=3;
CC      IsoId=O77617-2; Sequence=VSP_018701;
CC      Name=tumor suppressor ARF; Synonyms=p19ARF;
CC      IsoId=O77618-1; Sequence=External;
..

```

```

FT   VAR_SEQ           1..34
FT   /note="Missing (in isoform 3)"
FT   /evidence="ECO:0000305"
FT   /id="VSP_018701"

```

3.12.6. Syntax of the topic 'MASS SPECTROMETRY'

```
CC   -!- MASS SPECTROMETRY: ([ProductName]: )?Mass=mass(; Mass_error=error)?; Method=method; (; Note=free_text)?; Evidence=references;
```

Where:

- 'ProductName' is the name of an isoform or product of proteolytic cleavage;
- 'Mass=XXX' is the determined molecular weight (MW);
- 'Mass_error=XX' (optional) is the accuracy or error range of the MW measurement;
- 'Method=XX' is the ionization method;
- 'Note={Free text}'. Comment in free text format;
- 'Evidence=PubMed:/Ref.n' indicates the relevant reference'.

3.12.7. DISRUPTION PHENOTYPE

Note that we only describe effects caused the complete absence of a gene and thus a protein in vivo (null mutants caused by random or target deletions, insertions of a transposable element etc.) To avoid description of phenotypes due to partial or dominant negative mutants, missense mutations are not described in this comment, but in FT MUTAGEN instead. Defects caused by transient inactivation by methods such as RNA interference (RNAi) or blockage by antibodies are not described in this comment due to the difficulty to interpret results, except for C. elegans RNAi studies, which are widely used and done in vivo.

3.12.8. Syntax of the topic 'SEQUENCE CAUTION'

The format of the SEQUENCE CAUTION topic is:

```
CC   -!- SEQUENCE CAUTION:
      Sequence=Sequence; Type=Type; [ Note=Note;]
```

Where:

- *Sequence* is the sequence which differs from the UniProtKB sequence. It is described by one of:
 - an EMBL protein identifier (with version number)
 - an EMBL accession number.
 - a literature reference (e.g. Ref.3).
- *Type* describes the cause for the sequence difference(s) and is one of:
 - Frameshift
 - Erroneous initiation
 - Erroneous termination
 - Erroneous gene model prediction
 - Erroneous translation
 - Miscellaneous discrepancy
- *Note* is an optional free text explanation.

These lines will not be wrapped and their length may therefore exceed 80 characters.

3.12.9. Syntax of the topic 'WEB RESOURCE'

```
CC   -!- WEB RESOURCE: ([ProductName]: )?Name=ResourceName[; Note=FreeText][; URL=WWWAddress].
```

Where:

- 'ProductName' is the name of an isoform or product of proteolytic cleavage;
- 'Name' is the name of the database;
- 'Note' (optional) is a free text note;
- 'URL' is the WWW address (URL) of the database;

The length of these lines may exceed 80 characters because long URL addresses are not wrapped into multiple lines.

3.13. The DR line

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3.13.1. Definition

The DR (Database cross-Reference) lines are used as pointers to information in external data resources that is related to UniProtKB entries. The full list of all databases to which UniProtKB is cross-referenced can be found in the document [dbxref.txt](#). It also contains references describing these resources and provides links to their web sites.

For example, if the X-ray crystallographic atomic coordinates of a sequence are stored in the Protein Data Bank (PDB) there will be one DR line pointing to each of the corresponding entries in PDB. For a sequence translated from a nucleotide sequence there will be DR line(s) pointing to the relevant entry(ies) in the EMBL/GenBank/DDBJ database which correspond to the DNA or RNA sequence(s) from which it was translated.

The format of the DR line is:

DR RESOURCE_ABBREVIATION; RESOURCE_IDENTIFIER; OPTIONAL_INFORMATION_1[; OPTIONAL_INFORMATION_2][; OPTIONAL_INFORMATION_3].

The cross-references to the EMBL/GenBank/DBJ nucleotide sequence database and PROSITE are described in sections [3.25](#) and [3.25.117](#).

3.13.2. Resource abbreviation

The first field of the DR line, the 'RESOURCE_ABBREVIATION', is the abbreviated name of the referenced resource. The currently defined abbreviations are listed below.

Abbreviation	Description
EMBL	Nucleotide sequence database of EMBL/EBI (see 3.25)
ABCD	ABCD database of sequenced antibodies with their known targets
Allergome	Allergome; a platform for allergen knowledge
Antibodypedia	Antibodypedia antibody database
ArachnoServer	ArachnoServer: Spider toxin database
Araport	Araport: Arabidopsis Information Portal
Bgee	Bgee dataBase for Gene Expression Evolution
BindingDB	The Binding Database
BioCyc	Collection of Pathway/Genome Databases
BioGRID	BioGRID, The Biological General Repository for Interaction Datasets
BioGRID-ORCS	BioGRID-ORCS database of CRISPR phenotype screens
BioMuta	BioMuta curated single-nucleotide variation and disease association database
BMRB	Biological Magnetic Resonance Data
BRENDA	BRENDA Comprehensive Enzyme Information System
CarbonylDB	CarbonylDB database of protein carbonylation sites
CAZy	Carbohydrate-Active enZymes
CCDS	The Consensus CDS (CCDS) project
CDD	Conserved Domains Database
ChEMBL	A database of bioactive drug-like small molecules.
ChiTaRS	A database of human, mouse and fruit fly chimeric transcripts and RNA-sequencing data
CGD	Candida genome database
CLAE	Database of Characterized Lignocellulose-Active Enzymes
ComplexPortal	A manually curated, encyclopaedic resource of macromolecular complexes from a number of key model organisms
COMPLUYEAST-2DPAGE	2-D database at Universidad Complutense de Madrid
CollecTF	CollecTF database of bacterial transcription factor binding sites
ConoServer	ConoServer: Cone snail toxin database
CORUM	CORUM comprehensive resource of mammalian protein complexes
CPTAC	The CPTAC Assay Portal serves as a centralized public repository of "fit-for-purpose," multiplexed quantitative mass spectrometry-based proteomic targeted assays.
CPTC	CPTAC Antibody Portal
CTD	Comparative Toxicogenomics Database
DEPOD	Human DEPhosphorylation Database
dictyBase	Dictyostelium discoideum online informatics resource
DIP	Database of interacting proteins
DisGeNET	DisGeNET discovery platform integrating information on gene-disease associations
DisProt	Database of protein disorders
DMDM	Domain mapping of disease mutations
DNASU	The DNASU plasmid repository
DOSAC-COBS-2DPAGE	2D-PAGE database from the dipartimento oncologico di III Livello
DrugBank	The DrugBank database (DrugBank)
DrugCentral	DrugCentral Online Drug Compendium
EchoBASE	The integrated post-genomic database for E. coli (EchoBASE)
eggNOG	evolutionary genealogy of genes: Non-supervised Orthologous Groups
ELM	The Eukaryotic Linear Motif resource for functional sites in proteins
Ensembl	Database of automatically annotated sequences of large genomes (Ensembl database)
EnsemblBacteria	This databases is part of Ensembl Genomes, which has been created to complement the existing Ensembl site, the focus of which are vertebrate genomes.
EnsemblFungi	This databases is part of Ensembl Genomes, which has been created to complement the existing Ensembl site, the focus of which are vertebrate genomes.
EnsemblMetazoa	This databases is part of Ensembl Genomes, which has been created to complement the existing Ensembl site,

	the focus of which are vertebrate genomes.
EnsemblPlants	This databases is part of Ensembl Genomes, which has been created to complement the existing Ensembl site, the focus of which are vertebrate genomes.
EnsemblProtists	This databases is part of Ensembl Genomes, which has been created to complement the existing Ensembl site, the focus of which are vertebrate genomes.
EPD	The Encyclopedia of Proteome Dynamics is a resource that contains data from multiple, large-scale proteomics experiments aimed at characterising proteome dynamics in both human cells and model organisms.
ESTHER	The server ESTHER (ESTerases and alpha/beta-Hydrolase Enzymes and Relatives) is dedicated to the analysis of proteins or protein domains belonging to the superfamily of alpha/beta-hydrolases, exemplified by the cholinesterases.
euHCVdb	The European Hepatitis C Virus database
EuPathDB	Eukaryotic Pathogen Database Resources
EvolutionaryTrace	The Evolutionary Trace ranks amino acid residues in a protein sequence by their relative evolutionary importance.
ExpressionAtlas	Information on gene expression patterns under different biological conditions.
FlyBase	Drosophila genome database (FlyBase)
Gene3D	Database of structural assignments for genes (Gene3D)
GeneCards	GeneCards: human genes, protein and diseases
GeneDB	GeneDB pathogen genome database from Sanger Institute
GeneID	Database of genes from NCBI RefSeq genomes
GeneReviews	GeneReviews, a resource of expert-authored, peer-reviewed disease descriptions.
GeneTree	The phylogenetic gene trees that are available at https://www.ensembl.org/ and https://ensemblgenomes.org/ .
Genevisible	Genevisible is a free resource to explore public expression data for a gene of interest and find the top five tissues, cell lines, cancers or perturbations in which it has the highest expression or response.
GeneWiki	GeneWiki, an initiative that aims to create seed articles for every notable human gene.
GenomeRNAi	Database of phenotypes from RNA interference screens in Drosophila and Homo sapiens.
GlyConnect	GlyConnect integrated glycodata platform
GlyGen	Computational and Informatics Resources for Glycoscience
GO	Gene Ontology (GO) database
Gramene	Comparative mapping resource for grains (Gramene)
GuidetoPHARMACOLOGY	An expert-driven guide to pharmacological targets and the substances that act on them
HGNC	Human gene nomenclature database (HGNC)
HAMAP	Database of microbial protein families (HAMAP)
HOGENOM	Homologous genes from fully sequenced organisms database
HPA	Human Protein Atlas
IDEAL	IDEAL database of Intrinsically Disordered proteins
IMGT/GENE-DB	IMGT genome database for vertebrate immunoglobulin and T-cell receptor genes
InParanoid	InParanoid: Eukaryotic Ortholog Groups
IntAct	Protein interaction database and analysis system (IntAct)
InterPro	Integrated resource of protein families, domains and functional sites (InterPro)
IPI	International Protein Index
iPTMnet	iPTMnet integrated resource for PTMs in systems biology context
jPOST	Japan Proteome Standard Repository/Database
KEGG	Kyoto encyclopedia of genes and genomes
LegioList	Legionella pneumophila (strains Paris and Lens) genome database
Leproma	Mycobacterium leprae genome database (Leproma)
MaizeGDB	Maize Genetics/Genomics Database (MaizeGDB)
MalaCards	MalaCards human disease database
MassIVE	Mass Spectrometry Interactive Virtual Environment
MaxQB	MaxQB - The MaxQuant DataBase
MEROPS	Peptidase database (MEROPS)
MetOSite	MetOSite database of experimentally confirmed sulfoxidized methionines
MGI	Mouse Genome Informatics Database (MGI)
MIM	Mendelian Inheritance in Man Database (MIM)
MINT	Molecular INTERaction database
MoonDB	A database of extreme multifunctional and moonlighting proteins
MoonProt	A database for moonlighting proteins
neXtProt	neXtProt, the human protein knowledge platform

NIAGADS	NIAGADS Genomics Database
OGP	USC-OGP 2-DE database
OMA	Identification of Orthologs from Complete Genome Data
OpenTargets	Target Validation Platform
Orphanet	Orphanet; a database dedicated to information on rare diseases and orphan drugs
OrthoDB	Database of Orthologous Groups
PANTHER	Protein ANALysis THrough Evolutionary Relationships (PANTHER) Classification System
PathwayCommons	Pathway Commons web resource for biological pathway data
PATRIC	Pathosystems Resource Integration Center
PaxDb	A comprehensive absolute protein abundance database
PCDDb	The Protein Circular Dichroism Data Bank
PDB	3D-macromolecular structure Protein Data Bank (PDB)
PDBsum	PDB sum
PeptideAtlas	PeptideAtlas
PeroxiBase	Peroxidase superfamilies database
Pfam	Pfam protein domain database
PharmGKB	The Pharmacogenetics and Pharmacogenomics Knowledge Base
Pharos	Pharos NIH Druggable Genome Knowledgebase
PHI-base	Pathogen-Host Interaction database
PhosphoSitePlus	Phosphorylation site database
PhylomeDB	Database for complete collections of gene phylogenies
PIR	Protein sequence database of the Protein Information Resource (PIR)
PIRSF	Protein classification system of PIR (PIRSF)
PlantReactome	Curated source of core pathways and reactions in plant biology
PomBase	Schizosaccharomyces pombe database
PRIDE	PRoteomics IDentifications database
PRINTS	Protein Fingerprint database (PRINTS)
PRO	PRO provides an ontological representation of protein-related entities.
ProMEX	Protein Mass spectra EXtraction database
PROSITE	PROSITE protein domain and family database (see 3.25.117)
Proteomes	UniProt Proteomes database
ProteomicsDB	ProteomicsDB human proteome resource
PseudoCAP	Pseudomonas aeruginosa Community Annotation Project
Reactome	Curated resource of core pathways and reactions in human biology
REBASE	Restriction enzymes and methylases database (REBASE)
RefSeq	NCBI reference sequences
REPRODUCTION-2DPAGE	2D-PAGE database from the Lab of Reproductive Medicine at the Nanjing Medical University
RGD	Rat Genome Database (RGD)
RNAct	RNAct Protein–RNA interaction prediction database
SABIO-RK	Biochemical Reaction Kinetics Database
SASBDB	Small Angle Scattering Biological Data Bank
SFLD	Structure-Function Linkage Database
SGD	Saccharomyces Genome Database (SGD)
SignalLink	A signaling pathway resource with multi-layered regulatory networks
SIGNOR	A signaling network open resource (SIGNOR)
SMART	Simple Modular Architecture Research Tool (SMART)
SMR	The SWISS-MODEL Repository (SMR)
STRING	STRING: functional protein association networks
SUPFAM	Superfamily database of structural and functional annotation
SWISS-2DPAGE	2D-PAGE database from the Geneva University Hospital (SWISS-2DPAGE)
SwissLipids	SwissLipids knowledge resource for lipid biology
SwissPalm	SwissPalm database of S-palmitoylation events
TAIR	The Arabidopsis Information Resource (TAIR)
TCDB	Transport Classification Database
TIGRFAMs	TIGR protein family database (TIGRFAMs)
TopDownProteomics	TopDownProteomics is a resource from the Consortium for Top Down Proteomics that hosts top down proteomics data presenting validated proteoforms to the scientific community.

TreeFam	TreeFam database of animal gene trees
TubercuList	Mycobacterium tuberculosis H37Rv genome database (TubercuList)
UCD-2DPAGE	UCD-2DPAGE: University College Dublin 2-DE Proteome Database.
UCSC	UCSC genome browser
UniCarbKB	UniCarbKB, a new collaborative approach to glycomics.
UniLectin	UniLectin database of carbohydrate-binding proteins
UniPathway	UniPathway: a resource for the exploration and annotation of metabolic pathways
VectorBase	Bioinformatics resource for invertebrate vectors of human pathogens
VGNC	Vertebrate Gene Nomenclature Committee database
World-2DPAGE	The World-2DPAGE database
WormBase	A multi-species resource for nematode biology and genomics (WormBase)
WBParaSite	WormBase ParaSite (WBParaSite) resource for parasitic worms (helminths)
Xenbase	Xenopus laevis and tropicalis biology and genome database
ZFIN	Zebrafish Information Network genome database (ZFIN)

3.13.3. The resource identifier

The second field of the DR line, the 'RESOURCE_IDENTIFIER', is an unambiguous pointer to a record in the referenced resource.

- For Allergome, Antibodypedia, ArachnoServer, Bgee, BioCyc, BioGRID, BioGRID-ORCS, CCDS, CDD, ChEMBL, CGD, CollecTF, ComplexPortal, ConoServer, CPTAC, CTD, DIP, DisGeNET, DisProt, DMDM, DNASU, DrugBank, EchoBASE, eggNOG, EvolutionaryTrace, FlyBase, Gene3D, GeneDB, GeneID, GeneReviews, GeneTree, GeneWiki, GenomeRNAi, GlyConnect, GO, GuidetoPHARMACOLOGY, HOGONOM, HPA, IDEAL, InterPro, KEGG, MEROPS, MGI, MIM, MINT, CLAE, neXtProt, NIAGADS, OpenTargets, Orphanet, OrthoDB, PANTHER, PATRIC, Pfam, PharmGKB, PHI-base, PIR, PlantReactome, PRINTS, PRO, Proteomes, ProteomicsDB, Reactome, REBASE, RefSeq, REPRODUCTION-2DPAGE, RGD, SGD, SMART, SUPFAM, SwissLipids, TAIR, TCDB, TIGRFAMs, TreeFam, UCSC, UniPathway, VGNC, World-2DPAGE, Xenbase or ZFIN the resource identifier is the accession number (also called the Unique Identifier in some databases) of the referenced entry.
- For ABCD, BindingDB, BMRB, CarbonylDB, COMPLUYEAST-2DPAGE, CORUM, CPTC, DEPOD, DOSAC-COBS-2DPAGE, DrugCentral, ELM, EPD, ExpressionAtlas, GlyGen, InParanoid, IntAct, iPTMnet, jPOST, MassIVE, MaxQB, MetOSite, MoonDB, MoonProt, OGP, PathwayCommons, PaxDb, PCDDb, PeptideAtlas, Pharos, PhosphoSitePlus, PhylomeDB, PRIDE, ProMEX, RNAct, SABIO-RK, SASBDB, Signalink, SIGNOR, SMR, STRING, SWISS-2DPAGE, SwissPalm, TopDownProteomics, UCD-2DPAGE, UniCarbKB or UniLectin the resource identifier is the UniProtKB accession number.
- For Araport, BioMuta, dictyBase, ESTHER, GeneCards, Genevisible, IMGT/GENE-DB, MalaCards, Peroxisbase, PomBase, PseudoCAP the resource identifier is the official gene name.
- For BRENDA, the resource identifier is an EC number.
- For ChiTaRS, the resource identifier is a gene name.
- For CAZy, the resource identifier is the CAZy family number.
- For Ensembl, EnsemblBacteria, EnsemblFungi, EnsemblMetazoa, EnsemblPlants, EnsemblProtists, Gramene, VectorBase, WormBase and WBParaSite, the resource identifier is a transcript identifier.
- For EuPathDB, the primary identifier is a combination of the child database name and the accession number in this database. Both are concatenated by a '!'.
- For HGNC, the resource identifier is the unique identifier assigned by the HUGO Gene Nomenclature Committee.
- For HAMAP, the resource identifier is the unique identifier of a HAMAP signature.
- For PDB, the resource identifier is the entry name.
- For PDBsum, the resource identifier is the PDB entry name.
- For PIRSF, the resource identifier is the protein family number.
- For OMA, the primary identifier consists of an OMA group fingerprint.
- For MaizeGDB, the resource identifier is the 'Gene-product' accession ID.
- For LegioList, Leproma or TubercuList, the resource identifier is the genome Open Reading Frame (ORF) code.
- For euHCVdb, the resource identifier is an EMBL accession number.

3.13.4. The optional information 1

The third field of the DR line, the 'OPTIONAL_INFORMATION_1', is used to provide optional information.

- For RefSeq this field is the nucleotide sequence identifier.
- For CDD, InterPro, PANTHER, Pfam, PIR, PRINTS, REBASE, SFLD, SMART, SUPFAM or TIGRFAMs, this field is the entry name.
- For PDB, this field is the structure determination method, which is controlled vocabulary that currently includes: X-ray (for X-ray crystallography), NMR (for NMR spectroscopy), EM (for electron microscopy and cryo-electron diffraction), Fiber (for fiber diffraction), IR (for infrared spectroscopy), Model (for predicted models) and Neutron (for neutron diffraction).
- For dictyBase, FlyBase, CGD, HGNC, MGI, PomBase, RGD, SGD, Xenbase, VGNC or ZFIN, this field is the gene designation. If the gene designation is not available, a dash ('-') is used.
- For GO, this field is a 1-letter abbreviation for one of the 3 ontology aspects, separated from the GO term by a column. If the term is longer than 46 characters, the first 43 characters are indicated followed by 3 dots ('...'). The abbreviations for the 3 distinct aspects of the ontology are P (biological Process), F (molecular Function), and C (cellular Component).
- For HAMAP, this field contains the HAMAP entry name for a protein family.
- For Ensembl, EnsemblBacteria, EnsemblFungi, EnsemblMetazoa, EnsemblPlants, EnsemblProtists, Gramene, VectorBase, WormBase and WBParaSite, this field is a protein identifier.
- For ESTHER and PIRSF, this field is the protein family name.
- For BioGRID-ORCS, this field indicates the number of hits in CRISPR screens.

- For IntAct and BioGRID, this field indicates the number of interactors.
- For MIM, this field distinguishes between MIM "gene" and "phenotype" entries. Note that some MIM entries describe both a gene and a phenotype. In such a case, this field indicates "gene+phenotype".
- For Allergome, this field is the name of the allergen.
- For ABCD, Antibodypedia and CPTC, this field is the number of antibodies.
- For ArachnoServer and ConoServer, this field is the name of the toxin.
- For CAZy, this field is the CAZy family name.
- For Orphanet, this field is the name of the disease caused by defects in the protein.
- For ChiTaRS and UCSC, this field is the organism name.
- For BRENDA and Genevisible, this field is an organism code.
- For eggNOG, this field is the taxonomic scope.
- For GlyConnect and GlyGen, this field contains details about the glycans and glycosylation sites.
- For PeroxiBase, this field is a name given by the database curators, based on organism and peroxidase classification.
- For Reactome and PlantReactome, this field is the name of the pathway.
- For UniPathway, this field is the identifier of the reaction.
- For DrugBank, this field is a drug generic name for which the protein is a target.
- For TCDB, this field is the transport classification family name.
- For Bgee and ExpressionAtlas, this field is the expression pattern.
- For TAIR, this field is the TAIR locus name (AGI number).
- For MoonDB, this field indicates the entry type ("Curated" or "Predicted").
- For RNAct, this field indicates the molecule type (usually "protein").
- For Pharos, this field indicates the development/druggability level.
- For BindingDB, BioCyc, BMRB, CarbonylDB, CCDS, ChEMBL, COMPLUYEAST-2DPAGE, CollecTF, CORUM, CPTAC, CTD, DEPOD, DIP, DisGeNET, DisProt, DMDM, DNASU, DOSAC-COBS-2DPAGE, DrugCentral, EchoBASE, ELM, EPD, EuPathDB, EvolutionaryTrace, Gene3D, GeneCards, GeneDB, GeneID, GeneReviews, GeneTree, GeneWiki, GenomeRNAi, GuidetoPHARMACOLOGY, HOGENOM, HPA, InParanoid, iPTMnet, jPOST, KEGG, LegioList, Leproma, MaizeGDB, MalaCards, MassIVE, MaxQB, MEROPS, MetOSite, MINT, MoonProt, CLAE, nextProt, NIAGADS, OMA, OGP, OpenTargets, OrthoDB, PathwayCommons, PATRIC, PaxDb, PCDDb, PDBsum, PeptideAtlas, PharmGKB, PHI-base, PhosphoSitePlus, PhylomeDB, PRIDE, PRO, ProMEX, ProteomicsDB, PseudoCAP, REPRODUCTION-2DPAGE, SABIO-RK, SASBDB, SignalLink, SIGNOR, SMR, STRING, SWISS-2DPAGE, SwissLipids, SwissPalm, TAIR, TopDownProteomics, TreeFam, TubercuList, UCD-2DPAGE, UniCarbKB, UniLectin and World-2DPAGE, this field is not used and a dash ('-') is displayed in that field.

3.13.5. The optional information 2

A number of DR lines possess a fourth field, the 'OPTIONAL_INFORMATION_2', which is used to provide further optional information.

- For the protein domain/family or structural databases CDD, Gene3D, HAMAP, PANTHER, Pfam, PIRSF, SFLD, SMART, SUPFAM and TIGRFAMs, this field is the number of hits found in the sequence.
- For Ensembl, EnsemblBacteria, EnsemblFungi, EnsemblMetazoa, EnsemblPlants, EnsemblProtists, Gramene, VectorBase, WormBase and WBParaSite, this field is a gene identifier.
- For GO, this field is a 3-character GO evidence code. The GO evidence code is followed by the source database from which the cross-reference was obtained, separated by a colon. The definitions of the evidence codes are: IDA=inferred from direct assay, IMP=inferred from mutant phenotype, IGI=inferred from genetic interaction, IPI=inferred from physical interaction, IEP=inferred from expression pattern, TAS=traceable author statement, NAS=non-traceable author statement, IC=inferred by curator, ISS=inferred from sequence or structural similarity.
- For PDB, this field indicates the resolution of structures that were determined by X-ray crystallography or electron microscopy.

3.13.6. The optional information field 3

A number of DR lines possess a fifth field, the 'OPTIONAL_INFORMATION_3', which is used to provide further optional information.

- For PDB, this field indicates the chain(s) and the corresponding range, of which the structure has been determined. If the range is unknown, a dash is given rather than the range positions (e.g. 'A/B=-'), if the chains and the range is unknown, a dash is used.
- For WormBase, this field indicates the gene designation.

3.13.7. The optional isoform sequence identifier field

Some of the resources to which we link contain information that is specific to an isoform sequence and where this is known, we indicate the corresponding UniProtKB isoform sequence identifier in our DR lines:

- Ensembl
- Gramene
- RefSeq
- UCSC
- EnsemblBacteria
- EnsemblFungi
- EnsemblMetazoa
- EnsemblPlants
- EnsemblProtists
- CCDS
- WBParaSite
- SwissLipids
- TopDownProteomics

Examples of complete DR lines are shown here:

```
DR    EMBL; U29082; AAA68403.1; -; Genomic_DNA.
```

DR ABCD; 075084; 10 sequenced antibodies.

DR Allergome; 3541; Asc s 1.0101.

DR Antibodypedia; 740; 5394 antibodies.

DR ArachnoServer; AS000173; kappa-hexatoxin-Hv1b.

DR Araport; AT4G08920; -.

DR Bgee; ENSRNOG0000001873; Expressed in 9 organ(s), highest expression level in skeletal muscle tissue.

DR BindingDB; P06709; -.

DR BioCyc; EcoCyc:USHA-MONOMER; -.

DR BioGRID; 69392; 1.

DR BioGRID-ORCS; 55343; 19 Hits in 787 CRISPR Screens.

DR BioMuta; TF; -.

DR BMRB; A1D240; -.

DR BRENDA; 3.5.99.5; 3804.

DR CarbonylDB; Q14789; -.

DR CAZy; GH109; Glycoside Hydrolase Family 109.

DR CCDS; CCDS18166.1; -. [089019-1]

DR CDD; cd01948; EAL; 1.

DR ChEMBL; ChEMBL4259; -.

DR ChiTaRS; ATP6AP1; drosophila.

DR CGD; CAL0001939; orf19.773.

DR CollecTF; EXPREG_00000150; -.

DR COMPLUYEAST-2DPAGE; P41797; -.

DR ConoServer; 2838; ArIA precursor.

DR CORUM; P59998; -.

DR CPTAC; CPTAC-311; -.

DR CPTC; P31751; 6 antibodies.

DR CTD; 282646; -.

DR dictyBase; DDB0191351; myoB.

DR DIP; DIP:37N; -.

DR DisGeNET; 348; -.

DR DisProt; DP00239; -.

DR DMDM; 44887889; -.

DR DNASU; 1400; -.

DR DOSAC-COBS-2DPAGE; P02774; -.

DR DrugBank; APRD00096; Tegaserod.

DR DrugCentral; P35372; -.

DR EchoBASE; EB4119; -.

DR eggNOG; ENOG410IEUN; Eukaryota.

DR ELM; P12931; -.

DR Ensembl; ENST00000383775; ENSP00000373285; ENSG00000154813. [Q96FX2-2]

DR EnsemblBacteria; EBSTAT00000032812; EBSTAP00000031682; EBSTAG00000032810.

DR EnsemblFungi; YDR365W-B; YDR365W-B; YDR365W-B.

DR EnsemblMetazoa; FBtr0071603; FBpp0071529; FBgn0020306.

DR EnsemblPlants; AT1G66340.1; AT1G66340.1; AT1G66340.

DR EnsemblProtists; DDB0305146; DDB0305146; DDB_G0286833.

DR EPD; P00451; -.

DR ESTHER; bacbr-grsb; Thioesterase.

DR euHCVdb; AF271632; -.

DR EuPathDB; GiardiaDB:GL50803_13101; -.

DR EvolutionaryTrace; P06611; -.

DR ExpressionAtlas; Q10Q48; baseline.

DR FlyBase; FBgn0000055; Adh.

DR Gene3D; 2.40.128.50; -; 2.

DR GeneCards; LIPE; -.

DR GeneDB; H25N7.01:pep; -.

DR GeneID; 36674; -.

DR UniCarbKB; P00750; -.

DR GeneReviews; MAGEL2; -.

DR GeneTree; EMGT00050000006238; -.

DR Genevisible; P31946; HS.

DR GeneWiki; Dock7; -.

DR GenomeRNAi; 37724; -.

DR GlyConnect; 1545; 8 N-Linked glycans (1 site).

DR GlyGen; P13591; 6 sites, 2 N-linked glycans (1 site).

DR GO; GO:0003677; F:DNA binding; IPI:SGD.

DR Gramene; OS03T0727600-01; OS03T0727600-01; OS03G0727600.

DR GuidetoPHARMACOLOGY; 2242; -.

DR HGNC; HGNC:12849; YWHAB.

DR HAMAP; MF_00120; GatA; 1.

DR HOGENOM; CLU_142929_0_0_1; -.

DR HPA; CAB004311; -.

DR IDEAL; IID00450; -.

DR IMGT_GENE-DB; IGHM; -.

DR InParanoid; 004196; -.

DR IntAct; P14653; 1.

DR InterPro; IPR001650; Helicase_C.

DR iPTMnet; Q15796; -.

DR jPOST; P49429; -.

DR KEGG; bsu:BG10490; -.

DR Legiolist; lpp2301; -.

DR Leproma; ML0485; -.

DR MaizeGDB; 25342; -.

DR MalaCards; LIPE; -.

DR MassIVE; Q8IY92; -.

DR MaxQB; 094656; -.

DR MEROPS; M41.009; -.

DR MetOSite; P10987; -.
DR MGI; MGI:87920; Adfp.
DR MIM; 140050; gene.
DR MINT; MINT-640764; -.
DR MoonDB; P02730; Curated.
DR MoonProt; P02730; -.
DR CLAE; MAN26A_PIRSP; -.
DR neXtProt; NX_Q69383; -.
DR NIAGADS; ENSG00000203710; -.
DR OGP; P31946; -.
DR OMA; GLCHYFS; -.
DR OpenTargets; ENSG00000157764; -.
DR Orphanet; 64; Alstrom syndrome.
DR OrthoDB; EOG94QWM6; -.
DR PANTHER; PTHR12103; HAD-IG-Ncltids; 1.
DR PathwayCommons; P01042; -.
DR PATRIC; fig|511145.12.peg.1604; -.
DR PaxDb; P85829; -.
DR PCDDb; Q70Q12; -.
DR PDB; 1NB3; X-ray; 2.80 A; A/B/C/D=116-335, P/R/S/T=98-105.
DR PDBsum; 1HF1; -.
DR PeptideAtlas; P32494; -.
DR PeroxiBase; 79; AtPrx03.
DR Pfam; PF00017; SH2; 1.
DR PharmGKB; PA134908332; -.
DR Pharos; Q7Z3E2; Tdark.
DR PHI-base; PHI:5282; -.
DR PhosphoSitePlus; P01266; -.
DR PhylomeDB; A4WFL4; -.
DR PIR; A00682; KIPGA.
DR PlantReactome; R-OSA-5608118; Auxin signalling.
DR PIRSF; PIRSF006414; Ftr_formyl_trnsf; 1.
DR PomBase; SPAC1565.08; cdc48.
DR PRIDE; P10144; -.
DR PRINTS; PR00237; GPCRRHODOPSN.
DR PRO; PR:O42634; -.
DR ProMEX; P49200; -.
DR PROSITE; PS00107; PROTEIN_KINASE_ATP; 2.
DR ProteomicsDB; 62174; -.
DR PseudoCAP; PA0892; -.
DR Reactome; REACT_1675.1; mRNA Processing.
DR REBASE; 993; EcoRI.
DR RefSeq; NP_611010.4; NM_137166.4.

```

DR   REPRODUCTION-2DPAGE; IPI00022774; -.
DR   RGD; 70968; Ddah1.
DR   RNaAct; Q9Y2I1; protein.
DR   SABIO-RK; P10172; -.
DR   SASBDB; Q15326; -.
DR   SFLD; SFLDS00014; RuBisCO; 1.
DR   SGD; S000000170; AAR2.
DR   SignalLink; P41935; -.
DR   SIGNOR; P00533; -.
DR   SMART; SM00369; LRR_TYP; 2.
DR   SMR; P38479; -.
DR   STRING; P23946; -.
DR   SUPFAM; SSF48371; ARM-type_fold; 1.
DR   SWISS-2DPAGE; P10599; -.
DR   SwissLipids; SLP:000000316; -.
DR   SwissPalm; Q13530; -.
DR   TAIR; locus:2064097; AT2G38610.
DR   TCDB; 1.A.1.11.11; voltage-gated ion channel (VIC) superfamily.
DR   TIGRFAMs; TIGR00630; uvra; 1.
DR   TopDownProteomics; P10599-1; -. [P10599-1]
DR   TreeFam; TF324882; -.
DR   TubercuList; Rv0001; -.
DR   UCD-2DPAGE; P02648; -.
DR   UCSC; uc001o1c.4; human. [A5YM72-3]
DR   UniCarbKB; O02197; -.
DR   UniLectin; P84801; -.
DR   UniPathway; UPA00842; UER00808.
DR   VectorBase; AAEL004386-RA; AAEL004386-PA; AAEL004386.
DR   VGNC; VGNC:29101; FOXP1.
DR   World-2DPAGE; 0001:P77845; -.
DR   WormBase; F26C11.2; CE01560; WBGene00006744; unc-4.
DR   WBParaSite; Bm6838; Bm6838; WBGene00227099.
DR   Xenbase; XB-FEAT-481105; hdac3.
DR   ZFIN; ZDB-GENE-980526-290; hoxb1b.

```

3.14. Cross-references to the nucleotide sequence database

The specific format for cross-references to the EMBL/GenBank/DDBJ nucleotide sequence database is:

```
DR   EMBL; ACCESSION_NUMBER; PROTEIN_ID; STATUS_IDENTIFIER; MOLECULE_TYPE.
```

where 'PROTEIN_ID' stands for the 'Protein Sequence Identifier'. It is a string which is stored, in nucleotide sequence entries, in a qualifier called '/protein_id' which is tagged to every CDS in the nucleotide database. Example from EMBL:

```

FT   CDS 302..2674
FT   /protein_id="CAA03857.1"
FT   /db_xref="SWISS-PROT:P26345"
FT   /gene="recA"
FT   /product="RecA protein"

```

The Protein Sequence Identifier (Protein_ID) consists of a stable ID portion (8 characters: 3 letters followed by 5 numbers) plus a period and a version number. The version number only changes when the protein sequence coded by the CDS changes, while the stable part remains unchanged. The

Protein_ID effectively replaces what was previously known as the 'PID'.

The 'STATUS_IDENTIFIER' provides information about the relationship between the sequence in the entry and the CDS in the corresponding EMBL entry:

a) In most cases the translation of the EMBL nucleotide sequence CDS results in the same sequence as shown in the corresponding entry or the differences are mentioned in the feature (FT) lines as CONFLICT, VARIANT or VAR_SEQ and in the RP lines. The status identifier is then a dash ('-').

Example:

```
DR   EMBL; AJ297977; CAC17465.1; -; Genomic_DNA.
```

```
DR   EMBL; X56491; CAA39846.1; ALT_FRAME; mRNA.
```

b) In some cases the translation of the EMBL nucleotide sequence CDS results in a sequence different from the sequence shown in the corresponding entry. When the differences are either not mentioned in the feature (FT) lines as CONFLICT, VARIANT or VAR_SEQ (see [below](#)) and in the RP lines, or do simply not meet the criteria for such situations, the differences are indicated as follows:

1. If the difference is due to a different start of the sequence (i.e. Swiss-Prot believes that the start of the sequence is upstream or downstream of the site annotated as the start of the sequence in the EMBL database), the status identifier shows the comment 'ALT_INIT'. Example:

```
DR   EMBL; L29151; AAA99430.1; ALT_INIT; mRNA.
```

2. If the difference is due to a different termination of the sequence (i.e. Swiss-Prot believes that the termination of the sequence is upstream or downstream of the site annotated as the end of the sequence in the EMBL database), the status identifier shows the comment 'ALT_TERM'. Example:

```
DR   EMBL; L20562; AAA26884.1; ALT_TERM; Genomic_DNA.
```

3. If the difference is due to frameshifts in the EMBL sequence, the status identifier shows the comment 'ALT_FRAME'. Example:

```
DR   EMBL; X56420; CAA39814.1; ALT_FRAME; mRNA.
```

4. If the difference is not due to any of the cases mentioned above (e.g. wrong intron-exon boundaries given in the EMBL entry) or to a mixture of the cases mentioned above, the status identifier shows the comment 'ALT_SEQ'. Example:

```
DR   EMBL; M28482; AAA26378.1; ALT_SEQ; Genomic_DNA.
```

c) In some cases the nucleotide sequence of a complete CDS is divided into exons present in different EMBL entries. We point to the exon-containing EMBL entries by citing the Protein_ID as optional information field 1 and adding the comment 'JOINED' as the status identifier. These EMBL entries do not contain a CDS feature but contain exons joined to a CDS feature which is labeled with the given Protein_ID.

Example:

```
DR   EMBL; M63397; AAA51662.1; -; Genomic_DNA.
DR   EMBL; M63395; AAA51662.1; JOINED; Genomic_DNA.
DR   EMBL; M63396; AAA51662.1; JOINED; Genomic_DNA.
```

In the above example the Swiss-Prot sequence is derived from the CDS labeled with the Protein_ID AAA51662. This CDS feature can be found in the EMBL entry M63397. Exons belonging to this CDS are not only found in EMBL entry M63397, but also in the EMBL entries M63395 and M63396.

d) In some cases there is no CDS feature key annotating a protein translation in an EMBL entry and thus no Protein_ID for the CDS. Therefore it is not possible for us to point to a Protein_ID in the optional information field 1. In these cases we point to the relevant EMBL entries by including a dash ('-') in the position of the missing Protein_ID and 'NOT_ANNOTATED_CDS' into the status identifier.

Example:

```
DR   EMBL; AJ243418; -; NOT_ANNOTATED_CDS; mRNA.
```

The 'MOLECULE_TYPE' provides information about the biological source of the molecule. The molecule type is controlled vocabulary, which corresponds to that of The International Nucleotide Sequence Database Collaboration (INSD) comprised of DDBJ (Japan), the EMBL-Bank(UK) and GenBank (USA). Relevant to the UniProt Knowledgebase are the following values:

- Genomic_DNA: any genomic DNA; includes nuclear, organelle, plasmid ...
- Genomic_RNA: genomic RNA
- Transcribed_RNA: any transcribed RNA that is not mRNA; includes immature RNA (pre-RNA)
- mRNA: mRNA; includes cDNA
- Viral_cRNA: positive cRNA molecule from a single stranded genomic RNA
- Unassigned_DNA: unknown in vivo DNA
- Unassigned_RNA: unknown in vivo RNA
- Other_DNA: synthetic DNA
- Other_RNA: synthetic RNA
- -: unknown

3.14.1. Cross-references to the PROSITE database

The specific format for cross-references to the PROSITE protein domain and family database is:

DR PROSITE; ACCESSION_NUMBER; ENTRY_NAME; NUMBER_OF_MATCHES.

Where 'ACCESSION_NUMBER' stands for the accession number of the PROSITE pattern or profile entry; 'ENTRY_NAME' is the name of the entry and 'NUMBER_OF_MATCHES' is the number of matches of the pattern or profile in that particular protein sequence.

Examples of PROSITE cross-references:

DR PROSITE; PS00107; PROTEIN_KINASE_ATP; 2.

DR PROSITE; PS00028; ZINC_FINGER_C2H2_1; 4.

3.15. The PE line

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The PE (Protein existence) line gives indication on the evidences that we currently have for the existence of a protein. Because most protein sequences are derived from translation of nucleotide sequences and are mere predictions, the PE line indicates what the evidences are of the existence of a protein.

Note that the 'PE' line does not give information on the accuracy or correctness of the sequence displayed. While it gives information on the existence of a protein, it may happen that the sequence slightly differ, especially for sequences derived from gene model predictions from genomic sequences.

The format of the PE line is:

PE *Level: Evidence;*

With the following values:

- 1: Evidence at protein level
- 2: Evidence at transcript level
- 3: Inferred from homology
- 4: Predicted
- 5: Uncertain

Example:

PE 1: Evidence at protein level;

The status 'Evidence at protein level' indicates that there is clear experimental evidence (such as a characterization paper, partial to complete Edman sequencing, clear identification by mass spectrometry (MSI), X-ray or NMR structure, detection by antibodies etc.) for the existence of this protein.

The status 'Evidence at transcript level' is used to indicate that the existence of a protein has not been strictly proved but that expression data (presence of cDNAs, RT-PCR, Northern blots) indicates the existence of a transcript.

The status 'Inferred from homology' is used to indicate that the existence of a protein is probable because clear orthologs exist in closely related species.

The status 'Predicted' is used for entries without evidence at protein, transcript, or homology levels.

The status 'Uncertain' indicates that the existence of the protein is unsure.

Criteria used to assign a PE level to entries are described in the document file [pe_criteria.txt](#)

3.16. The KW line

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The KW (KeyWord) lines provide information that can be used to generate indexes of the sequence entries based on functional, structural, or other categories. The keywords chosen for each entry serve as a subject reference for the sequence. The document [keywordlist.txt](#) lists all the keywords and a definition of their usage in the database. Often several KW lines are necessary for a single entry. The list of keywords associated to one entry can be downloaded using the following URL:

https://www.uniprot.org/uniprot/?query=reviewed%3ayes+keyword%3a*&force=yes&format=tab&columns=id,keywords.

The format of the KW line is:

KW Keyword[; Keyword...].

More than one keyword may be listed on each KW line; semicolons separate the keywords, and the last keyword is followed by a period. An entry often contains several KW lines. Keywords may consist of more than one word (they may contain blanks), but are never split between lines. The keywords are stored by alphabetical order. An example of KW lines in an entry is:

KW 3D-structure; Alternative splicing; Alzheimer disease; Amyloid;
 KW Apoptosis; Cell adhesion; Coated pits; Copper;
 KW Direct protein sequencing; Disease mutation; Endocytosis;
 KW Glycoprotein; Heparin-binding; Iron; Membrane; Metal-binding;
 KW Notch signaling pathway; Phosphorylation; Polymorphism;
 KW Protease inhibitor; Proteoglycan; Serine protease inhibitor; Signal;
 KW Transmembrane; Zinc.

TrEMBL makes use of the same controlled list of keywords as is used in Swiss-Prot but, as most keywords in an entry are added during the annotation process, TrEMBL entries generally contain fewer keywords than Swiss-Prot entries. The main sources of TrEMBL keywords are:

- The underlying nucleotide entry. The nucleotide databases add keywords and any which are also found in the UniProtKB controlled list are added to the corresponding TrEMBL entry.
- The program which creates TrEMBL entries. This adds keywords based on information in the underlying nucleotide entry. For example, if a nucleotide entry contains the word "kinase" in the description, the program adds the keyword "Kinase" to the corresponding TrEMBL entry.
- Automatic annotation.

3.17. The FT line

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The FT (Feature Table) lines provide a precise but simple means for the annotation of the sequence data. The table describes regions or sites of interest in the sequence. In general the feature table lists posttranslational modifications, binding sites, enzyme active sites, local secondary structure or other characteristics reported in the cited references. Sequence conflicts between references are also included in the feature table.

Note: The format descriptions make use of [POSIX ERE](#) syntax.

All [positional annotations](#) in the FT section historically referred to the [canonical sequence](#) that is shown in the UniProtKB entry.

The format is inspired by the [INSDC's feature table format](#) to enable code reuse:

```
FT <TYPE> <Location>
(FT /<Qualifier>{="

```

Where

- <TYPE> is a value from the controlled vocabulary of positional annotation types. A list of the currently defined feature types can be found [below](#).
- <Location> is a sequence location on the canonical or an isoform sequence. We only use a subset of the [INSDC Location](#) types: A <Location> must be either a single <Position> or a range of <Position> that may optionally be preceded by an [isoform ID](#). The < and > symbols may be used with begin and end positions to indicate that the begin or end point is beyond the specified amino acid position. Please note that we have to extend the INSDC Location format with the ? symbol to allow us to represent all existing UniProtKB locations. This symbol may precede a <Position> to indicate that the exact position is unsure, or it may substitute the <Position> when the position is unknown. Note that positions are always specified assuming a numbering of the listed sequence from 1 to n; this numbering is not necessarily the same as that used in the original reference(s).

```
(<IsoformId>:)?((<|\\?)?<Position>|\\?)(..(>|\\?)?<Position>|\\?))?
```

- /<Qualifier> may provide information in addition to that conveyed by the <TYPE> and <Location>. While we follow the format of the [INSDC Qualifiers](#), we introduce our own <Qualifier> types where necessary. For this format change, we represent the existing data with 3 qualifiers:
 - /note= presents additional information about the feature. For example, for a posttranslationally modified residue (type MOD_RES) the chemical nature of the modified residue is given, while for a sequence variation (type VARIANT) the nature of the variation is indicated.
 - /evidence= shows [evidence and source](#) of the annotation.
 - /id= contains a feature identifier (/FTId=, see [below](#)).

In the future, we may introduce more <Location> and <Qualifier> types to structure the description of positional annotations further.

Lines are wrapped at 80 characters.

An example of a feature table is shown below:

```
FT SIGNAL 1..15
FT /evidence="ECO:0000250"
FT CHAIN 16..360
FT /note="Alpha-2-HS-glycoprotein"
FT /id="PRO_0000008896"
FT DOMAIN 24..130
FT /note="Cystatin fetuin-A-type 1"
FT /evidence="ECO:0000255|PROSITE-ProRule:PRU00861"
FT DOMAIN 141..252
FT /note="Cystatin fetuin-A-type 2"
FT /evidence="ECO:0000255|PROSITE-ProRule:PRU00861"
FT MOD_RES 131
FT /note="Phosphoserine"
FT /evidence="ECO:0000250|UniProtKB:P02765"
FT MOD_RES 132
FT /note="Phosphothreonine"
FT /evidence="ECO:0000250|UniProtKB:P29699"
FT MOD_RES 135
FT /note="Phosphoserine"
FT /evidence="ECO:0000250|UniProtKB:P02765"
FT MOD_RES 312
FT /note="Phosphothreonine"
FT /evidence="ECO:0000250|UniProtKB:P02765"
FT MOD_RES 318
FT /note="Phosphoserine"
FT /evidence="ECO:0000250|UniProtKB:P02765"
FT MOD_RES 321
FT /note="Phosphoserine"
FT /evidence="ECO:0000250|UniProtKB:P02765"
FT MOD_RES 323
FT /note="Phosphoserine"
FT /evidence="ECO:0000250|UniProtKB:P02765"
FT CARBOHYD 96
```

```

FT          /note="N-linked (GlcNAc...) asparagine"
FT          /evidence="ECO:0000255"
FT  CARBOHYD 153
FT          /note="N-linked (GlcNAc...) asparagine"
FT          /evidence="ECO:0000255"
FT  DISULFID 29..351
FT          /evidence="ECO:0000255|PROSITE-ProRule:PRU00861"
FT  DISULFID 86..97
FT          /evidence="ECO:0000255|PROSITE-ProRule:PRU00861"
FT  DISULFID 111..129
FT          /evidence="ECO:0000255|PROSITE-ProRule:PRU00861"
FT  DISULFID 143..146
FT          /evidence="ECO:0000255|PROSITE-ProRule:PRU00861"
FT  DISULFID 205..216
FT          /evidence="ECO:0000255|PROSITE-ProRule:PRU00861"
FT  DISULFID 227..244
FT          /evidence="ECO:0000255|PROSITE-ProRule:PRU00861"
FT  CONFLICT 126
FT          /note="S -> P (in Ref. 1; BAA22653)"
FT          /evidence="ECO:0000305"

```

See also the notes concerning each of the feature types [below](#).

3.17.1. Feature identifiers

Some features are associated with unique and stable feature identifiers (FTId), which allows to construct links directly from position-specific annotation in the feature table to specialized protein-related databases.

Feature identifiers currently exist for the feature keys CARBOHYD, CHAIN, PEPTIDE, PROPEP, VARIANT and VAR_SEQ. Each of these feature types is associated with a 3-letter code feature identifier prefix, which is separated by an underscore from a 6 to 10-digit number. The format of the corresponding FTIds is shown in the following table:

Feature type	Format of the FTId	Availability
CARBOHYD	CAR_number	Currently only for residues attached to an oligosaccharide structure annotated in the GlyConnect database
CHAIN, PEPTIDE	PRO_number	Any mature polypeptide
PROPEP	PRO_number	Any processed propeptide
VARIANT	VAR_number	Currently only for protein sequence variants of Hominidae (great apes and humans)
VAR_SEQ	VSP_number	Any sequence with a VAR_SEQ feature

Examples of features with FTIds are given below:

```

FT  CHAIN      25..614
FT          /note="Uromodulin"
FT          /id="PRO_0000041671"
FT  CHAIN      25..587
FT          /note="Uromodulin, secreted form"
FT          /id="PRO_00000407909"
FT  PROPEP     615..640
FT          /note="Removed in mature form"
FT          /evidence="ECO:0000255"
FT          /id="PRO_0000041672"
FT  CARBOHYD   275
FT          /note="N-linked (GlcNAc...) asparagine"
FT          /id="CAR_000178"
FT  VAR_SEQ    29
FT          /note="A -> ARTKYNCPARSWRTPQRRGGDTEQGPDEDFTSQG (in isoform 5)"
FT          /evidence="ECO:0000303|PubMed:14702039"
FT          /id="VSP_054828"
FT  VAR_SEQ    67..199
FT          /note="Missing (in isoform 2)"
FT          /evidence="ECO:0000303|PubMed:14702039"
FT          /id="VSP_017565"

FT  PEPTIDE    20..57
FT          /note="Histatin-1"
FT          /id="PRO_0000021416"
FT  PEPTIDE    31..57
FT          /note="His1-(31-57)-peptide"
FT          /id="PRO_0000021417"

```

3.17.2. List of feature types

INIT_MET - Initiator methionine.

This feature key is associated with a 'I' value in the /Location field to indicate that the initiator methionine has been cleaved off:

```

FT   INIT_MET       1
FT   /note="Removed"
FT   /evidence="ECO:0000269|PubMed:7592317"

```

It is not used when the initiator methionine is not cleaved off.

SIGNAL - Extent of a signal sequence (prepeptide).

```

FT   SIGNAL         1..26
FT   /evidence="ECO:0000269|PubMed:11017100"

FT   SIGNAL         1..23
FT   /evidence="ECO:0000255"

```

PROPEP - Extent of a propeptide.

Examples of PROPEP key feature lines:

```

FT   PROPEP         20..53
FT   /note="Activation peptide"
FT   /evidence="ECO:0000269|PubMed:2334440,
FT   ECO:0000269|PubMed:8346912"
FT   /id="PRO_0000025974"

FT   PROPEP         550..574
FT   /note="Removed in mature form"
FT   /id="PRO_0000000016"

```

TRANSIT - Extent of a transit peptide (mitochondrion, chloroplast, thylakoid, cyanelle, peroxisome etc.).

Examples of TRANSIT key feature lines:

```

FT   TRANSIT        1..42
FT   /note="Chloroplast"
FT   /evidence="ECO:0000269|PubMed:1912506"

FT   TRANSIT        1..65
FT   /note="Cyanelle"
FT   /evidence="ECO:0000269|PubMed:8490125"

FT   TRANSIT        1..25
FT   /note="Mitochondrion"
FT   /evidence="ECO:0000250"

FT   TRANSIT        1..36
FT   /note="Glyoxysome"
FT   /evidence="ECO:0000269|PubMed:15670147, ECO:0000269|Ref.2"

FT   TRANSIT        1..?
FT   /note="Chloroplast"
FT   /evidence="ECO:0000255"
FT   TRANSIT        ?.77
FT   /note="Thylakoid"
FT   /evidence="ECO:0000269|PubMed:11719511,
FT   ECO:0000269|PubMed:11826309"

```

CHAIN - Extent of a polypeptide chain in the mature protein.

- In Swiss-Prot, it is present:
 1. For proteins that are not processed (those for which the mature protein sequence corresponds to the translated cDNA sequence) the CHAIN covers the whole protein sequence:

```

FT   CHAIN          2..334
FT   /note="COP9 signalosome complex subunit 5"
FT   /id="PRO_0000194835"

```

2. For processed proteins, it describes the mature part of the protein once preprotein parts such as propeptides and signal sequences have been removed:

```

FT   CHAIN          21..119
FT   /note="Beta-2-microglobulin"
FT   /id="PRO_0000018751"

FT   CHAIN          41..180
FT   /note="Factor X light chain"
FT   /id="PRO_0000027781"

```

- For TrEMBL, it is present only in those entries where the submitters to the nucleotide sequence databases have provided this information for processed proteins.

PEPTIDE - Extent of a released active peptide.

Examples of PEPTIDE key feature lines:

```

FT   PEPTIDE       1..9
FT   /note="Arg-vasopressin"
FT   /id="PRO_0000020507"

FT   PEPTIDE       235..239
FT   /note="Met-enkephalin"
FT   /id="PRO_0000024953"

```

TOPO_DOM - Topological domain.

Examples:

```

FT   TOPO_DOM      337..371
FT   /note="Cytoplasmic"

FT   TOPO_DOM      17..471
FT   /note="Mitochondrial matrix"
FT   /evidence="ECO:0000255"

```

TRANSMEM - Extent of a transmembrane region.

Examples:

```

FT   TRANSMEM      241..264
FT   /note="Helical"

FT   TRANSMEM      184..204
FT   /note="Helical"
FT   /evidence="ECO:0000255"

FT   TRANSMEM      171..191
FT   /note="Helical; Name=3"
FT   /evidence="ECO:0000255"

FT   TRANSMEM      1660..1677
FT   /note="Helical; Name=S5 of repeat IV"
FT   /evidence="ECO:0000250|UniProtKB:D0E0C2"

FT   TRANSMEM      490..516
FT   /note="Helical; Anchor for type IV membrane protein"
FT   /evidence="ECO:0000250"

FT   TRANSMEM      26..35
FT   /note="Beta stranded"

```

INTRAMEM - Extent of a region located in a membrane without crossing it.

Examples:

```

FT   INTRAMEM      306..320

FT   INTRAMEM      1145..1165
FT   /evidence="ECO:0000255"

FT   INTRAMEM      258..266
FT   /note="Helical"
FT   /evidence="ECO:0000250"

FT   INTRAMEM      260..282
FT   /note="Pore-forming; Name=P region"
FT   /evidence="ECO:0000255"

FT   INTRAMEM      500..514
FT   /note="Helical"
FT   /evidence="ECO:0000250"

FT   INTRAMEM      515..517
FT   /note="Note=Loop between two helices"
FT   /evidence="ECO:0000250"

FT   INTRAMEM      518..529
FT   /note="Helical"
FT   /evidence="ECO:0000250"

FT   INTRAMEM      530..534
FT   /note="Note=Loop between two helices"
FT   /evidence="ECO:0000250"

FT   INTRAMEM      412..423
FT   /note="Helical; Name=Pore helix"
FT   /evidence="ECO:0000250|UniProtKB:P63142"

```

DOMAIN - Extent of a domain, which is defined as a specific combination of secondary structures organized into a characteristic three-dimensional structure or fold.

The domain type is given in the description field. If there exist several copies of a domain, the domains are numbered. Examples of DOMAIN key feature lines:

```

FT  DOMAIN      27..128
FT              /note="Cadherin 1"
FT              /evidence="ECO:0000255|PROSITE-ProRule:PRU00043"

FT  DOMAIN      745..939
FT              /note="Ras-GAP"
FT              /evidence="ECO:0000255|PROSITE-ProRule:PRU00167"

FT  DOMAIN      746..805
FT              /note="SH3"
FT              /evidence="ECO:0000255|PROSITE-ProRule:PRU00192"

```

REPEAT - Extent of an internal sequence repetition.

Examples of REPEAT key feature lines:

```

FT  REPEAT      225..307
FT              /note="1"
FT  REPEAT      341..423
FT              /note="2"
FT  REPEAT      455..537
FT              /note="3; approximate"

```

CA_BIND - Extent of a calcium-binding region.

Example:

```

FT  CA_BIND      20..31
FT              /note="1"
FT  CA_BIND      56..67
FT              /note="2"

```

ZN_FING - Extent of a zinc finger region.

The zinc finger 'category' is indicated in the description field. Examples of ZN_FING key feature lines:

```

FT  ZN_FING      803..827
FT              /note="GATA-type"
FT              /evidence="ECO:0000255|PROSITE-ProRule:PRU00094"

FT  ZN_FING      560..580
FT              /note="NR C4-type"
FT              /evidence="ECO:0000255|PROSITE-ProRule:PRU00407"

```

DNA_BIND - Extent of a DNA-binding region.

The nature of the DNA-binding region is given in the description field. Examples of DNA_BIND key feature lines:

```

FT  DNA_BIND      335..415
FT              /note="ETS"
FT              /evidence="ECO:0000255|PROSITE-ProRule:PRU00237"

FT  DNA_BIND      69..128
FT              /note="Homeobox"
FT              /evidence="ECO:0000255|PROSITE-ProRule:PRU00108"

FT  DNA_BIND      44..67
FT              /note="H-T-H motif"
FT              /evidence="ECO:0000255|PROSITE-ProRule:PRU00625"

FT  DNA_BIND      133..207
FT              /note="TEA"
FT              /evidence="ECO:0000255|PROSITE-ProRule:PRU00505"

```

NP_BIND - Extent of a nucleotide phosphate-binding region.

The nature of the nucleotide phosphate is indicated in the description field. Examples of NP_BIND key feature lines:

```

FT  NP_BIND      182..189
FT              /note="ATP"

FT  NP_BIND      38..45
FT              /note="GTP"
FT              /evidence="ECO:0000255"

FT  NP_BIND      36..43
FT              /note="FAD"
FT              /evidence="ECO:0000269|PubMed:8114095"

```

REGION - Extent of a region of interest in the sequence.

Examples:

```

FT   REGION       620..631
FT   /note="Zymogen activation region"

FT   REGION       46..70
FT   /note="Possesses antibiotic activity"
FT   /evidence="ECO:0000269|PubMed:8506327"
```

COILED - Extent of a coiled-coil region.

Example:

```

FT   COILED       258..553
FT   /evidence="ECO:0000255"
```

MOTIF - Short (up to 20 amino acids) sequence motif of biological interest.

Examples:

```

FT   MOTIF        94..101
FT   /note="Nuclear localization signal"
FT   /evidence="ECO:0000269|PubMed:10894149"

FT   MOTIF        648..650
FT   /note="Microbody targeting signal"
FT   /evidence="ECO:0000255"
```

COMBIAS - Extent of a compositionally biased region.

Examples:

```

FT   COMBIAS      219..222
FT   /note="Poly-Ser"

FT   COMBIAS      22..124
FT   /note="Glu-rich (acidic)"
```

ACT_SITE - Amino acid(s) involved in the activity of an enzyme.

Examples of ACT_SITE key feature lines:

```

FT   ACT_SITE     238
FT   /note="Proton acceptor"

FT   ACT_SITE     1083
FT   /note="Charge relay system; for serine protease NS3
FT   activity"
FT   /evidence="ECO:0000255|PROSITE-ProRule:PRU01166"
```

METAL - Binding site for a metal ion.

The description field indicates the nature of the metal. Examples of METAL key feature lines:

```

FT   METAL        52
FT   /note="Iron (heme axial ligand); shared with dimeric
FT   partner"
FT   /evidence="ECO:0000255|PROSITE-ProRule:PRU00085,
FT   ECO:0000269|PubMed:17077480"

FT   METAL        28
FT   /note="Copper"
FT   /evidence="ECO:0000255"
```

BINDING - Binding site for any chemical group (co-enzyme, prosthetic group, etc.).

The chemical nature of the group is given in the description field. Examples of BINDING key feature lines:

```

FT   BINDING      15
FT   /note="Heme (covalent)"

FT   BINDING      132
FT   /note="Chloride"
```

SITE - Any interesting single amino-acid site on the sequence, that is not defined by another feature key. It can also apply to an amino acid bond which is represented by the positions of the two flanking amino acids.

Example:

```

FT   SITE         391..392
FT   /note="Cleavage; by thrombin"
```

NON_STD - Non-standard amino acid

This key describes the occurrence of non-standard amino acids selenocysteine and pyrrolysine. Note that we also display them in the [sequence data section](#) and use the IUPAC/IUBMB recommended one-letter codes 'U' for selenocysteine and 'O' for pyrrolysine

```

FT  NON_STD      52
FT                      /note="Selenocysteine"

FT  NON_STD      356
FT                      /note="Pyrrolysine"
FT                      /evidence="ECO:0000250"
```

MOD_RES - Posttranslational modification of a residue.

The chemical nature of the modified residue is given in the note.

The nature of the posttranslationally formed amino acid is annotated by using a controlled vocabulary; the currently defined list of controlled vocabulary, as well as other information such as the target amino acid, the related keyword, the species where the modification is annotated and the location of the mature protein are available in [ptmlist.txt](#) document. Links to example proteins and to the RESID database are also provided to help gain a better insight into every modification.

Modification	extent
ACETYLATION	N-terminal of some residues and side chain of lysine
AMIDATION	Generally at the C-terminal of a mature active peptide after oxidative cleavage of last glycine
BLOCKED	Unidentified N- or C-terminal blocking group
FORMYLATION	Generally of the N-terminal methionine
GAMMA-CARBOXYGLUTAMIC ACID	Of glutamate
HYDROXYLATION	Generally of asparagine, aspartate, proline or lysine
METHYLATION	Generally of N-terminal phenylalanine, side chain of lysine, arginine, histidine, asparagine or glutamate, and C-terminal cysteine
PHOSPHORYLATION	Of serine, threonine, tyrosine, aspartate, histidine or cysteine, and, more rarely, of arginine
PYRROLIDONE CARBOXYLIC ACID	N-terminal glutamine which has formed an internal cyclic lactam. This is also called 'pyro-Glu'. Very rarely, pyro-Glu can be produced by modification of a N-terminal glutamate
SULFATION	Of tyrosine, serine or threonine

Examples of MOD_RES key feature lines:

```

FT  MOD_RES      2
FT                      /note="N-acetylalanine"
FT                      /evidence="ECO:0000269|PubMed:3754823"

FT  MOD_RES      58
FT                      /note="Methionine amide"
FT                      /evidence="ECO:0000250"

FT  MOD_RES      52
FT                      /note="N6-methyllysine"
FT                      /evidence="ECO:0000255"
FT  MOD_RES      245
FT                      /note="N6-succinyllysine"
FT                      /evidence="ECO:0000250|UniProtKB:P48962"

FT  MOD_RES      206
FT                      /note="Phosphoserine; by CK1"
FT                      /evidence="ECO:0000269|PubMed:8999878"
FT  MOD_RES      217
FT                      /note="Sulfotyrosine"
FT                      /evidence="ECO:0000255"
```

Example of a feature where the identity of the amino acid is unknown (an X is shown at this position in the sequence):

```

FT  MOD_RES      1
FT                      /note="Blocked amino end (Xaa)"
```

LIPID - Covalent binding of a lipid moiety

The chemical nature of the bound lipid moiety is given in the /note.

The attached groups that are currently defined are listed below.

Attached group	Description
myristate	Myristate group attached through an amide bond to the N-terminal glycine residue of the mature form of a protein [1,2] or to an internal lysine residue. The myristate can also be attached through a thioester bond to an internal cysteine

palmitate	Palmitate group attached through an amide bond to the N-terminal cysteine of the mature form of a protein, or to an internal lysine. The palmitate can also be attached through a thioester bond to an internal cysteine or through an ester bond to a serine or threonine residue [1,2]
farnesyl	Farnesyl group attached through a thioether bond to a cysteine residue [3,4]
geranyl-geranyl	Geranyl-geranyl group attached through a thioether bond to a cysteine residue [3,4]
GPI-anchor	Glycosyl-phosphatidylinositol (GPI) group linked to the alpha-carboxyl group of the C-terminal residue of the mature form of a protein [5,6]
diacylglyceride	Glycerol group bearing two ester-linked fatty acids attached through a thioether bond to the N-terminal cysteine of the mature form of a prokaryotic lipoprotein [7]
archaeol	Archaeol (2,3-di-O-phytanyl-sn-glycerol) lipid group attached through a thioether bond to the N-terminal cysteine of the mature form of an archaeal lipoprotein [8]
n-octanoate	n-octanoate group linked through an ester bond to a serine residue
cholesterol	Cholesterol group attached through an ester bond to the C-terminal glycine of the mature form of a protein

References:

1. Grand R.J.A.
Biochem. J. 258:626-638(1989).
2. McIlhinney R.A.J.
Trends Biochem. Sci. 15:387-391(1990).
3. Glomset J.A., Gelb M.H., Farnsworth C.C.
Trends Biochem. Sci. 15:139-142(1990).
4. Sinensky M., Lutz R.J.
BioEssays 14:25-31(1992).
5. Low M.G.
FASEB J. 3:1600-1608(1989).
6. Low M.G.
Biochim. Biophys. Acta 988:427-454(1989).
7. Hayashi S., Wu H.C.
J. Bioenerg. Biomembr. 22:451-471(1990).
8. Nishihara M., Utagawa M., Akutsu H., Koga Y.
J. Biol. Chem. 267:12432-12435(1992).

Examples of LIPID key feature lines:

```

FT    LIPID          2
FT                                     /note="N-myristoyl glycine; by host"
FT                                     /evidence="ECO:0000250"

FT    LIPID          6
FT                                     /note="S-palmitoyl cysteine"
FT                                     /evidence="ECO:0000305|PubMed:10364453"

FT    LIPID          231
FT                                     /note="GPI-anchor amidated serine"
FT                                     /evidence="ECO:0000250|UniProtKB:P04273"

FT    LIPID          21
FT                                     /note="S-diacylglycerol cysteine"
FT                                     /evidence="ECO:0000255|HAMAP-Rule:MF_00843"

```

The nature of the posttranslationally formed amino acid is annotated by using a controlled vocabulary; the currently defined list of controlled vocabulary, as well as other information such as the target amino acid, the related keyword, the species where the modification is annotated and the location of the mature protein are available in [ptmlist.txt](#) document. Links to example proteins and to the RESID database are also provided to help gain a better insight into every modification.

CARBOHYD - Glycosylation site.

This key describes the occurrence of the attachment of a glycan (mono- or polysaccharide) to a residue of the protein:

- The type of linkage (C-, N-, O- or S-linked) to the protein is indicated.
- If the nature of the reducing terminal sugar is known, its abbreviation is shown between parenthesis. If three dots '...' follow the abbreviation, this indicates an extension of the carbohydrate chain. Conversely, the absence of dots means that a monosaccharide is linked.

Examples of CARBOHYD key feature lines:

```

FT    CARBOHYD       53
FT                                     /note="N-linked (GlcNAc...) asparagine"
FT                                     /evidence="ECO:0000269|PubMed:19159218"

FT    CARBOHYD       1486
FT                                     /note="O-linked (GlcNAc) threonine"
FT                                     /evidence="ECO:0000269|PubMed:1629228"
FT                                     /id="CAR_000155"

```



```

FT CARBOHYD 195
FT /note="O-linked (Glc...) tyrosine"
FT /evidence="ECO:0000244|PDB:3U2U, ECO:0000244|PDB:3U2V,
FT ECO:0000269|PubMed:22160680, ECO:0000269|PubMed:30356213"

FT CARBOHYD 41
FT /note="S-linked (Glc) cysteine"
FT /evidence="ECO:0000269|PubMed:21196935,
FT ECO:0000269|PubMed:21251913"

FT CARBOHYD 29
FT /note="C-linked (Man) tryptophan"
FT /evidence="ECO:0000269|PubMed:10551839"
FT CARBOHYD 32
FT /note="C-linked (Man) tryptophan; partial"
FT /evidence="ECO:0000269|PubMed:10551839"
FT CARBOHYD 38
FT /note="O-linked (Fuc...) threonine"
FT /evidence="ECO:0000305|PubMed:22267737"

FT CARBOHYD 152
FT /note="O-linked (Ara...) hydroxyproline"
FT /evidence="ECO:0000305|PubMed:666730"

```

The nature of the glycosylated amino acid is annotated by using a controlled vocabulary, which also includes information such as the target amino acid, the related keyword, the species where the modification is annotated and the location of the mature protein and is available in [ptmlist.txt](#) document. Links to example proteins and to the RESID database are also provided to help gain a better insight into every modification.

DISULFID - Disulfide bond.

The 'FROM' and 'TO' endpoints designate the two residues which are linked by an intra-chain disulfide bond. If only one position is given, the disulfide bond is an interchain one and the description field indicates the nature of the cross-link. Examples of DISULFID key feature lines:

```

FT DISULFID 5..103
FT /evidence="ECO:0000250"
FT DISULFID 23..84
FT /evidence="ECO:0000305"

FT DISULFID 30
FT /note="Interchain (between small and large chains, with C-
FT 101 in large chain)"

```

CROSSLNK - Posttranslationally formed amino acid bonds.

The 'FROM' and 'TO' endpoints designate the two residues, which are linked by an intrachain bond, and the /note field indicates the nature of the cross-link. If there is only one position, the amino acid bond is an interchain one. The name of the linked peptide is indicated in the description field. Examples of 'CROSSLNK' key feature lines:

```

FT CROSSLNK 1010..1013
FT /note="Isoglutamyl cysteine thioester (Cys-Gln)"

FT CROSSLNK 60..77
FT /note="Beta-methylanthionine (Cys-Thr)"
FT CROSSLNK 63..73
FT /note="Lanthionine (Ser-Cys)"
FT CROSSLNK 64..70
FT /note="Beta-methylanthionine (Cys-Thr)"
FT CROSSLNK 65..78
FT /note="Lysinoalanine (Ser-Lys)"

```

The nature of the posttranslationally formed amino acid bond is annotated by using a controlled vocabulary; the currently defined list of controlled vocabulary, as well as other information such as the target amino acid, the related keyword, the species where the modification is annotated and the location of the mature protein are available in [ptmlist.txt](#) document. Links to example proteins and to the RESID database are also provided to help gain a better insight into every modification.

VAR_SEQ - Description of sequence variants produced by alternative splicing, alternative promoter usage, alternative initiation and ribosomal frameshifting.

Examples of VAR_SEQ key feature lines:

```

FT VAR_SEQ 653..672
FT /note="VATSNPGKCLSFTNSTFTFT -> ALVSHHCPVEAVRAVHPTRL (in
FT isoform 2)"
FT /evidence="ECO:0000303|PubMed:12034717,
FT ECO:0000303|PubMed:12435728"
FT /id="VSP_003786"
FT VAR_SEQ 673..913
FT /note="Missing (in isoform 2)"
FT /evidence="ECO:0000303|PubMed:12034717,
FT ECO:0000303|PubMed:12435728"
FT /id="VSP_003787"

```

VARIANT - Authors report that sequence variants exist.

Examples of VARIANT key feature lines:

```

FT   VARIANT       214
FT   /note="V -> I (in dbSNP:rs111642750)"
FT   /evidence="ECO:0000269|Ref.9"
FT   /id="VAR_009122"

FT   VARIANT       237
FT   /note="I -> L (in strain: B293, Z3524, Z3910, Z3915 and
FT   Z3918)"

FT   VARIANT       21..22
FT   /note="Missing (in 35% of the chains)"
FT   /id="VAR_006353"

FT   VARIANT       265..296
FT   /note="Missing (in allele D4.2)"
FT   /evidence="ECO:0000269|PubMed:1840645"
FT   /id="VAR_003465"

FT   VARIANT       156
FT   /note="I -> V (in RNA edited version)"
FT   /id="VAR_010166"

```

Explicit links are present in protein sequence entries of Hominidae to the Single Nucleotide Polymorphism database (dbSNP) (Nucleic Acids Res. 29:308-311(2001); PMID: [11125122](https://pubmed.ncbi.nlm.nih.gov/11125122/)). The dbSNP identifiers in human FT VARIANT lines are prefixed by "rs". NCBI/dbSNP has rs and ss numbers, but we only refer to SNPs with rs numbers. The format of such links is:

```

FT   VARIANT       location
FT   /note=description (in dbSNP:rsaccession_number).
FT   /id=VAR_number.

```

Example of a feature with a link to dbSNP:

```

FT   VARIANT       246
FT   /note="S -> A (in dbSNP:rs2228541)"
FT   /evidence="ECO:0000269|PubMed:15489334"
FT   /id="VAR_024350"

```

MUTAGEN - Site which has been experimentally altered by mutagenesis.

Examples of MUTAGEN key feature lines:

```

FT   MUTAGEN       119
FT   /note="C->R,E,A: Loss of cADPr hydrolase and ADP-ribosyl
FT   cyclase activity."
FT   /evidence="ECO:0000269|PubMed:7961800"

FT   MUTAGEN       169..177
FT   /note="Missing: Abolishes ATP-binding."

```

UNSURE - Uncertainties in the sequence

Used to describe region(s) of a sequence for which the authors are unsure about the sequence assignment.

```

FT   UNSURE        12
FT   /note="V or Y"

```

CONFLICT - Different sources report differing sequences.

Examples of CONFLICT key feature lines:

```

FT   CONFLICT       728
FT   /note="Missing (in Ref. 4; AAH40259 and 5; AAL15446)"
FT   /evidence="ECO:0000305"

FT   CONFLICT       802
FT   /note="Q -> K (in Ref. 2; no nucleotide entry and 3;
FT   AAA35793/AAA35794)"
FT   /evidence="ECO:0000305"

FT   CONFLICT       6..10
FT   /note="GSDSE -> RIRLR (in Ref. 2; AAD51365)"
FT   /evidence="ECO:0000305"

FT   CONFLICT       405
FT   /note="V -> A (in Ref. 10; AAF71067)"
FT   /evidence="ECO:0000305"

```

NON_CONS - Non-consecutive residues.

Indicates that two residues in a sequence are not consecutive and that there are a number of unsequenced residues between them. Example of a NON_CONS key feature line:

```

FT   NON_CONS      52..53
FT   /evidence="ECO:0000305"

```

NON_TER - The residue at an extremity of the sequence is not the terminal residue.

If applied to position 1, this means that the first position is not the N-terminus of the complete molecule. If applied to the last position, it means that this position is not the C-terminus of the complete molecule. There is no description field for this key. Examples of NON_TER key feature lines:

```

FT   NON_TER      1
FT   NON_TER     29

```

Secondary structure (HELIX, STRAND, TURN) - The feature table of sequence entries of proteins whose tertiary structure is known experimentally contains the secondary structure information corresponding to that protein. The secondary structure assignment is made according to DSSP (see Kabsch W., Sander C.; Biopolymers, 22:2577-2637(1983)) and the information is extracted from the coordinate data sets of the Protein Data Bank (PDB).

In the feature table only three types of secondary structure are specified: helices (key HELIX), beta-strands (key STRAND) and turns (key TURN). Residues not specified in one of these classes are in a 'loop' or 'random-coil' structure. Because the DSSP assignment has more than the three common secondary structure classes, we have converted the different DSSP assignments to HELIX, STRAND and TURN as shown in the table below.

DSSP code	DSSP definition	Swiss-Prot assignment
H	Alpha-helix	HELIX
G	3(10) helix	HELIX
I	Pi-helix	HELIX
E	Hydrogen-bonded beta-strand (extended strand)	STRAND
B	Residue in an isolated beta-bridge	STRAND
T	H-bonded turn (3-turn, 4-turn or 5-turn)	TURN
S	Bend (five-residue bend centered at residue i)	Not specified

One should be aware of the following facts:

- Segment length. For helices (alpha and 3-10), the residue just before and just after the helix as given by DSSP participates in the helical hydrogen-bonding pattern with a single H-bond. For practical purposes, one can extend the HELIX range by one residue on each side, e.g. HELIX 25-35 instead of HELIX 26-34. Also, the ends of secondary structure segments are less well defined for lower-resolution structures. A fluctuation of one residue is common.
- Missing segments. In low-resolution structures, badly formed helices or strands may be omitted in the DSSP definition.
- Special helices and strands. Helices of length three are 3-10 helices, those of length four and longer are either alpha-helices or 3-10 helices (pi helices are extremely rare). A strand of one residue corresponds to a residue in an isolated beta-bridge. Such bridges can be structurally important.
- Missing secondary structure. No secondary structure is currently given in the feature table in the following cases:
 - No sequence data in the PDB entry;
 - Structure for which only C-alpha coordinates are in PDB;
 - NMR structure with more than one coordinate data set;
 - Model (i.e. theoretical) structure.

Examples:

```

FT   HELIX      3..12
FT   /evidence="ECO:0000244|PDB:1HB6"
FT   HELIX     13..15
FT   /evidence="ECO:0000244|PDB:1HB6"
FT   STRAND    16..18
FT   /evidence="ECO:0000244|PDB:1ACA"
FT   HELIX    22..36
FT   /evidence="ECO:0000244|PDB:1HB6"
FT   HELIX    50..61
FT   /evidence="ECO:0000244|PDB:1HB6"
FT   TURN     62..64
FT   /evidence="ECO:0000244|PDB:1HB6"
FT   HELIX    67..85
FT   /evidence="ECO:0000244|PDB:1HB6"

```

3.18. The SQ line

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The SQ (SeQuence header) line marks the beginning of the sequence data and gives a quick summary of its content.

The format of the SQ line is:

```
SQ   SEQUENCE XXXX AA; XXXXX MW; XXXXXXXXXXXXXXXX CRC64;
```

The line contains the length of the sequence in amino acids ('AA') followed by the molecular weight ('MW') rounded to the nearest mass unit (Dalton) and the sequence 64-bit CRC (Cyclic Redundancy Check) value ('CRC64').

The molecular weight (MW) indicated on the SQ line is not meant to be that of the mature processed and posttranslationally modified protein. The MW of the mature protein can be predicted by the program [Compute pI/MW tool](#) on the ExPASy server.

The algorithm to compute the CRC64 is described in the ISO 3309 standard. The generator polynomial is $x^{64} + x^4 + x^3 + x + 1$.
Reference: Press W.H., Flannery B.P., Teukolsky S.A. and Vetterling W.T. "Numerical recipes in C", 2nd ed., pp896-902, Cambridge University Press (1993). (See <http://library.lanl.gov/numerical/>)

It should be noted that while, in theory, two different sequences could have the same CRC64 value, the likelihood that this would happen is extremely low.

An example of an SQ line is shown here:

```
SQ  SEQUENCE  486 AA;  55639 MW;  D7862E867AD74383 CRC64;
```

The information in the SQ line can be used as a check on accuracy or for statistical purposes. The word 'SEQUENCE' is present solely for readability.

3.19. The sequence data line

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The sequence data line has a line code consisting of two blanks rather than the two-letter codes used until now. The sequence counts 60 amino acids per line, in groups of 10 amino acids, beginning in position 6 of the line.

The characters used for the amino acids are the standard IUPAC one letter codes (see [Amino-acid codes section](#)).

An example of sequence data preceded by the corresponding SQ line is shown here:

```
SQ  SEQUENCE  97 AA;  9110 MW;  E3C20C259858B830 CRC64;
MTILASICKL GNTKSTSSSI GSSYSSAVSF GSNSVSCGEC GGDGPSFPNA SPRTGVKAGV
NVDGLLGAIG KTVNGMLISP NGGGGGMGMG GSGCGCI
```

3.20. The // line

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The // (terminator) line contains no data or comments and designates the end of an entry.

Appendix A : Amino-acid codes

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The one-letter and three-letter codes for amino acids used in the knowledgebase are those adopted by the commission on Biochemical Nomenclature of the IUPAC-IUB (see the reference listed below).

One-letter code	Three-letter code	Amino-acid name
A	Ala	Alanine
R	Arg	Arginine
N	Asn	Asparagine
D	Asp	Aspartic acid
C	Cys	Cysteine
Q	Gln	Glutamine
E	Glu	Glutamic acid
G	Gly	Glycine
H	His	Histidine
I	Ile	Isoleucine
L	Leu	Leucine
K	Lys	Lysine
M	Met	Methionine
F	Phe	Phenylalanine
P	Pro	Proline
S	Ser	Serine
T	Thr	Threonine
W	Trp	Tryptophan
Y	Tyr	Tyrosine
V	Val	Valine
O	Pyl	Pyrrolysine
U	Sec	Selenocysteine
B	Asx	Aspartic acid or Asparagine
Z	Glx	Glutamic acid or Glutamine
X	Xaa	Any amino acid

Reference

IUPAC-IUB Joint Commission on Biochemical Nomenclature (JCBN).
Nomenclature and Symbolism for Amino Acids and Peptides. Recommendations 1983.
Eur. J. Biochem. 138:9-37(1984).

See also: <http://www.chem.qmw.ac.uk/iupac/AminoAcid/>

Appendix B : Format differences between the Swiss-Prot and EMBL databases

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B.1 Generalities

The format of Swiss-Prot follows as closely as possible that of the EMBL database. The general structure of an entry is identical in both databases. The status are the same except though Swiss-Prot does not make use of the data classes and uses the 'reviewed' status instead. One line type used in Swiss-Prot does not exist in the EMBL database (see this [section](#)); conversely Swiss-Prot does not currently make use of every EMBL line type (see this [section](#)).

B.2 Differences in line types present in both databases

B.2.1 The ID line (IDentification)

Differences with the EMBL database ID line format are:

- The entry name can be up to 10 characters long (instead of 9 in EMBL) and can begin with a numerical character;
- EMBL entry ID lines have an additional three-letter taxonomic division 'token' inserted between the status and the molecule type;
- The molecule type is not listed;
- The length of the molecule is followed by 'AA' (Amino Acid) instead of 'BP' (Base Pairs).

B.2.2 The AC line (ACcession number)

The format of this line type is identical to that defined by the EMBL database. Swiss-Prot and TrEMBL accession numbers do not overlap those used in the EMBL/GenBank/DBJ nucleotide sequence database. However, it should be noted that there are differences in the format of the accession numbers themselves. In Swiss-Prot and TrEMBL accession numbers consist of 6 alphanumerical characters in the following format:

1	2	3	4	5	6
[A-N,R-Z]	[0-9]	[A-Z]	[A-Z, 0-9]	[A-Z, 0-9]	[0-9]
[O,P,Q]	[0-9]	[A-Z, 0-9]	[A-Z, 0-9]	[A-Z, 0-9]	[0-9]

Examples: P01234; Q1AA12.

In EMBL, two different types of accession numbers co-exist:

1. Accession numbers with 6 alphanumerical characters, where the first character is any letter with the exception of O,P or Q and the five other characters are numbers (example: M23765);
2. Accession numbers with 8 alphanumerical characters, where the first two characters are letters and the following six characters are numbers (example: AB001084).

B.2.3 The DT line (DaTe)

Differences with the EMBL database DT line format are:

- In EMBL there are two DT lines per entry whereas there are three in Swiss-Prot;
- In EMBL the format of the DT line that indicates when an entry was created is identical to that defined in Swiss-Prot; but the two DT lines that convey information relevant to the updating of an entry are replaced by a single line in EMBL. This is shown in the example below.

DT lines in a Swiss-Prot entry:

```
DT 01-OCT-1989, integrated into UniProtKB/Swiss-Prot.
DT 01-OCT-1989, sequence version 1.
DT 07-FEB-2006, entry version 76.
```

DT lines in an EMBL database entry:

```
DT 10-MAR-1990 (Rel. 22, Created)
DT 12-APR-1990 (Rel. 23, Last updated, Version 3)
```

B.2.4 The DE line (DEscription)

- In the UniProt Knowledgebase the species of origin is not included in the description;
- In EMBL the last DE line is not terminated by a period.

B.2.5 The OS line (Organism Species)

- In EMBL the last OS line is not terminated by a period.

B.2.6 The OG line (OrGanelle)

- EMBL makes a distinction between 'Mitochondrion', and 'Kinetoplast', while Swiss-Prot does not use the latter designation;
- EMBL makes a distinction between 'Chloroplast' and 'Plastid', while Swiss-Prot does not use the latter designation;
- In EMBL the OG line is not terminated by a period.

B.2.7 The RP and RC lines

- In EMBL, unlike Swiss-Prot, the RC line precedes the RP line;
- In EMBL the RC line is in free format and is generally not used.

B.2.8 The RT line (Reference Title)

In EMBL the reference title is not terminated by a period, a question mark or an exclamation mark.

B.2.9 The FT line (Feature Table)

The format of this line is totally different from that currently defined for the EMBL database. The format used in Swiss-Prot is similar to that which was used in older versions of the EMBL database, prior to the introduction of the common EMBL/GenBank/DDBJ feature table.

B.2.10 The CC line (Comment)

The comment lines, which are free text and can appear anywhere in an EMBL entry, are grouped together in the Swiss-Prot database. They are always listed below the last reference line, and follow a precise syntax (see section [3.22](#)).

B.2.11 The SQ line (SeQuence header)

Although the rough format and purpose of this line type is conserved, its exact content differs from that of the EMBL database. The numerical length of the sequence is listed, followed by 'AA' (Amino Acid) instead of 'BP' (Base Pairs). Rather than indicating the sequence composition which, for protein sequences, would not fit in a single line, the molecular weight and the 64-bit CRC (Cyclic Redundancy Check) value of the sequence are indicated.

B.3 Line types defined by Swiss-Prot but currently not used by EMBL

Presently, there are two line types in Swiss-Prot, which are not used in the EMBL database: the GN and OX lines.

B.4 Line types defined by EMBL but currently not used by Swiss-Prot

There are three line types in the EMBL database, which are not used in Swiss-Prot:

- FH and XX. The FH and XX lines contain no data and are present in EMBL only to improve readability of an entry when it is printed or displayed on a terminal screen. These lines are not included in Swiss-Prot so as to keep it as compact as possible and thereby facilitate its use on small computer systems.
- SV. The SV (Sequence Version) line contains an identifier specific to nucleic acid sequences. It has no meaning in the context of Swiss-Prot.

Appendix C : Documentation files

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The knowledgebase is distributed with a large number of documentation files, which are available on the [web](#) and [ftp](#) sites.

Appendix D : UniProt Knowledgebase

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The UniProt Knowledgebase is a non-redundant and complete protein sequence database consisting of two components:

1. Swiss-Prot
2. TrEMBL

At every release, two files are completely rebuilt and made available on our [FTP server](#). These files are named: uniprot_sprot.dat.gz and uniprot_trembl.dat.gz. As indicated by their '.gz' extension, these are gzip-compressed files which, when decompressed, produce ASCII files in Swiss-Prot format.

The same data is available in fasta and xml format. The fasta files are useful for building the databases used by FASTA, BLAST and other sequence similarity search programs. Please do not use these files for any other purpose, as you will lose all annotations by using this stripped-down format.

Additional notes:

- The Swiss-Prot file continuously grows as new annotated sequences are added.
- The TrEMBL file slightly decreases in size as sequences are moved out of TrEMBL after being annotated and moved into Swiss-Prot. However, at the same time, TrEMBL increases on a much larger scale by the new coding sequences submitted to the nucleotide sequence databases.
- Swiss-Prot and TrEMBL share the same system of accession numbers. Therefore you will not find any primary accession number duplicated between the two sections. A TrEMBL entry (and its associated accession number(s)) can either move to Swiss-Prot as a new entry or be merged with an existing Swiss-Prot entry. In the latter case, the accession number(s) of that TrEMBL entry are added to that of the Swiss-Prot entry.
- While these two files allow you to build what we call a 'non-redundant' database, the UniProt Knowledgebase, it must be noted that this is not completely a true statement. Without going into a long explanation we can say that this is currently the best attempt in providing a complete selection of protein sequence entries while trying to eliminate redundancies (2 or more entries for the same gene of a species). While Swiss-Prot is non-redundant, TrEMBL is far from being non-redundant and the addition of Swiss-Prot + TrEMBL is even less so.

- To describe to your users the version of the UniProt Knowledgebase that you are providing them with, you should use a statement of the form "UniProtKB release 2011_07 of Jun 28, 2011".

Appendix E : Relationships between Swiss-Prot and some biomolecular databases

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The current status of the relationships (cross-references) between Swiss-Prot and some biomolecular databases is shown in the following schema:

