InterPro and InterProScan 5.0

EMBL-EBI

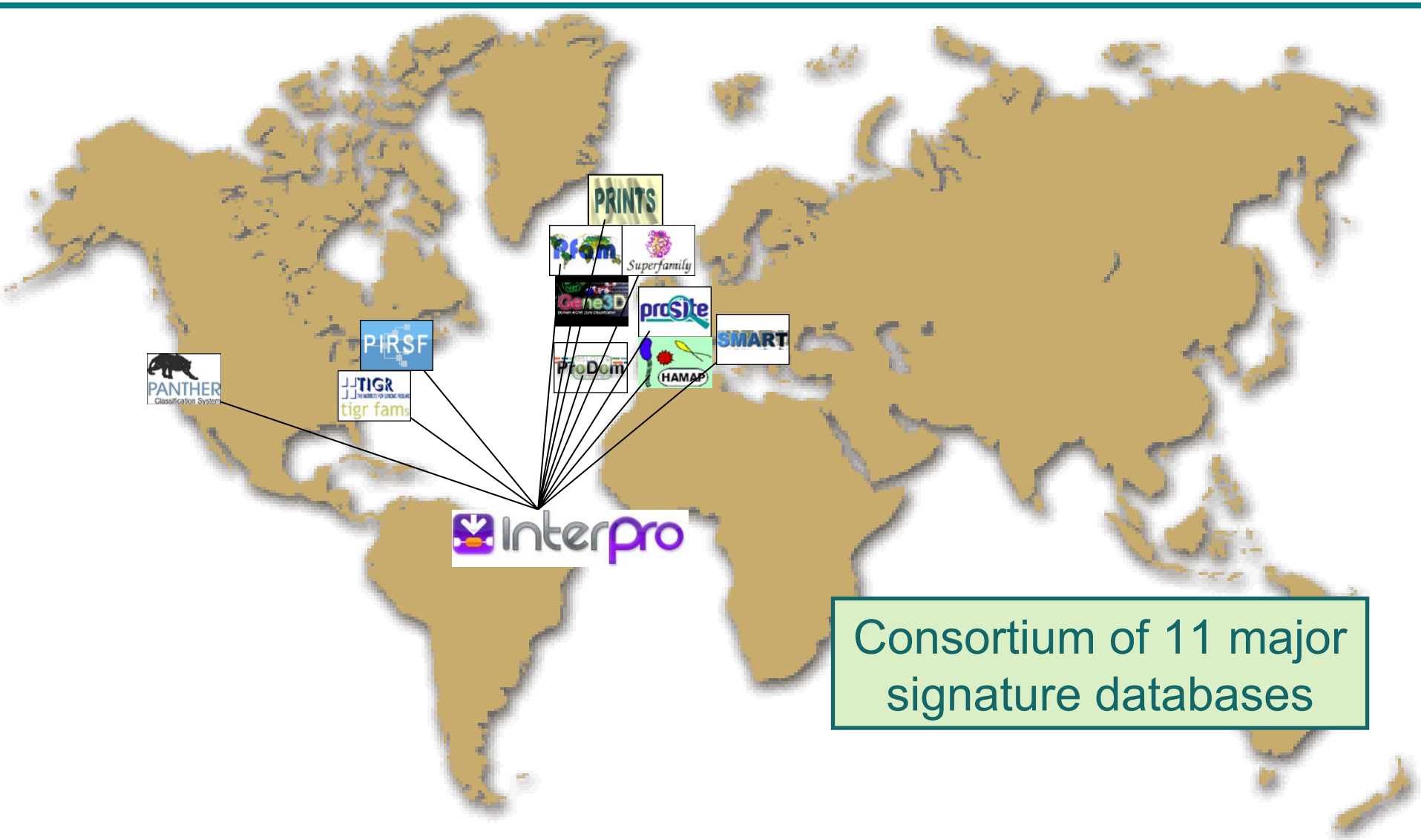
EBI is an Outstation of the European Molecular Biology Laboratory.

InterPro

- is a database that groups predictive protein signatures together
- 11 member databases

- single searchable resource
- provides functional analysis of proteins by classifying them into families and predicting domains and important sites
- Enables whole genome analysis

InterPro Consortium



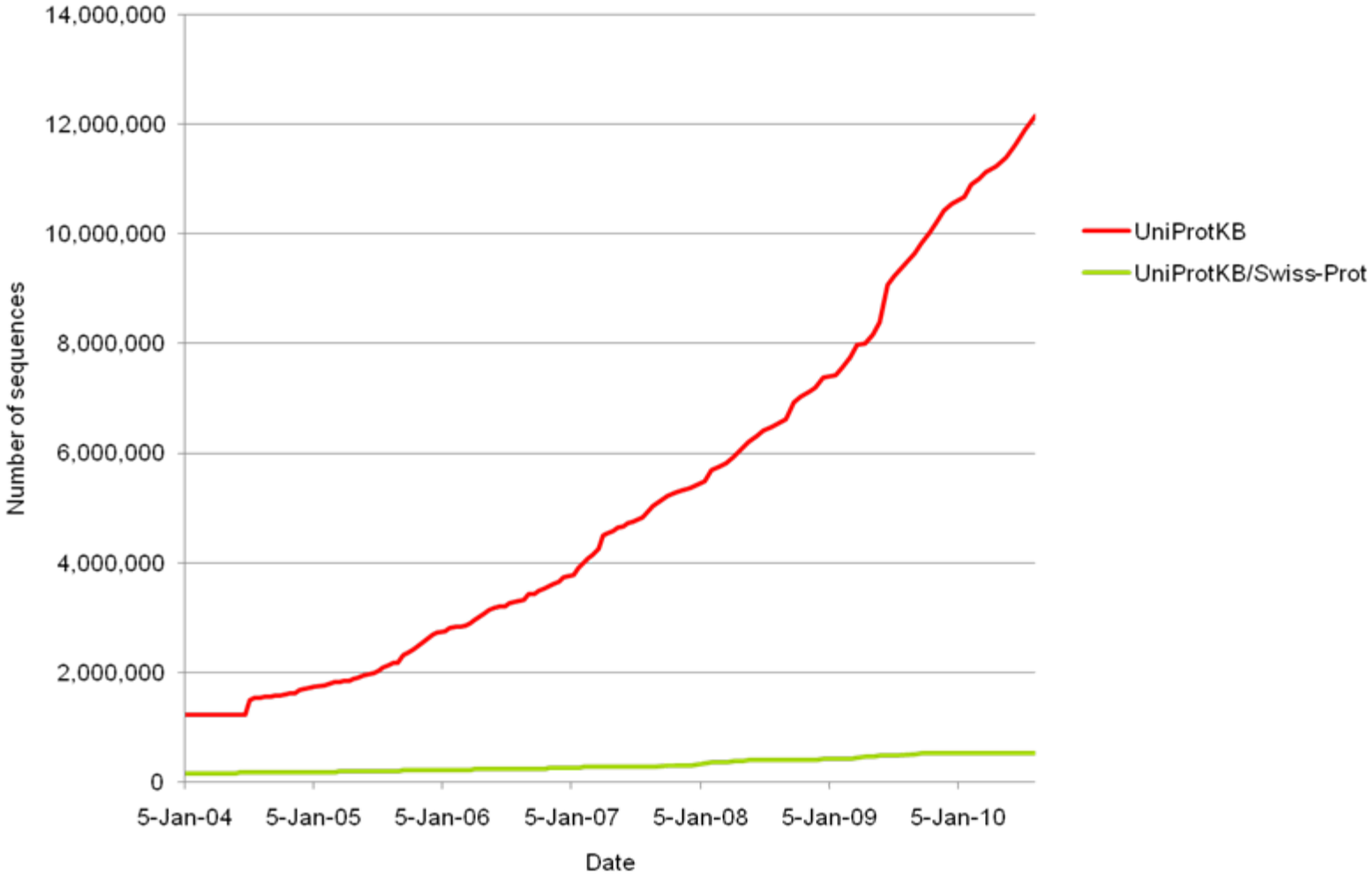
Consortium of 11 major signature databases

Protein signatures

- More sensitive homology searches

- Each member database creates signatures using different methods and methodologies:
  - manually-created sequence alignments
  - automatic processes with some human input and correction
  - entirely automatically.

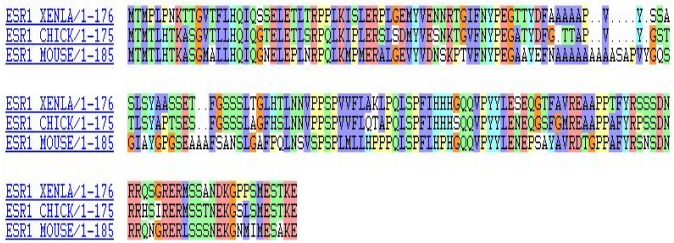
Why do we need predictive annotation tools?



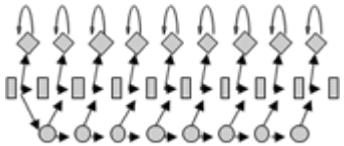
What are protein signatures?

Protein family/domain

Multiple sequence alignment



Build model



Search

it.

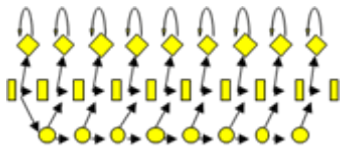
UniProt

Protein analysis

ITWKGPVCGLDGKTYRNECALL

AVPRSPVCGSDDVTYANECELK

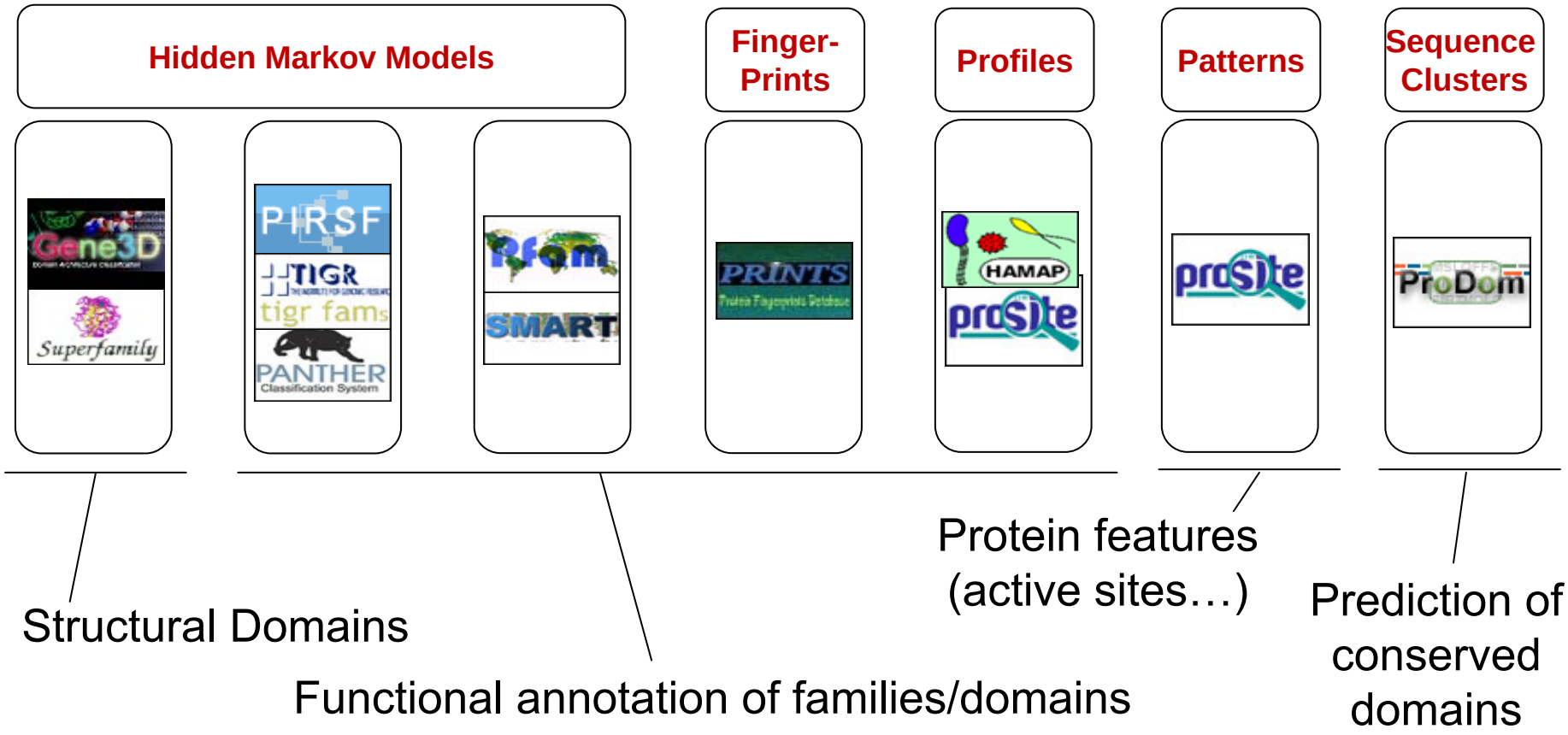
Mature model



Significant match

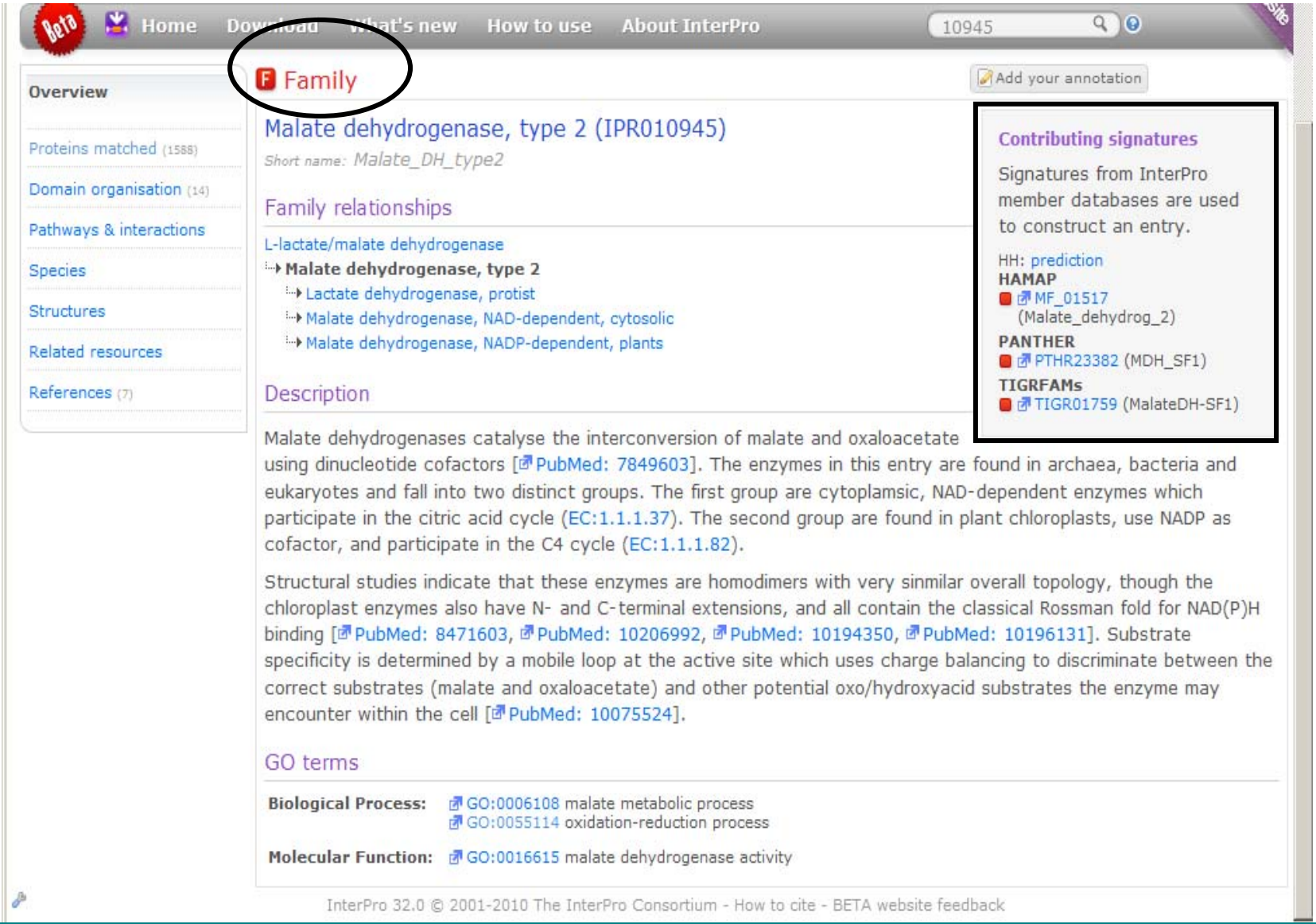
Member databases

METHODS

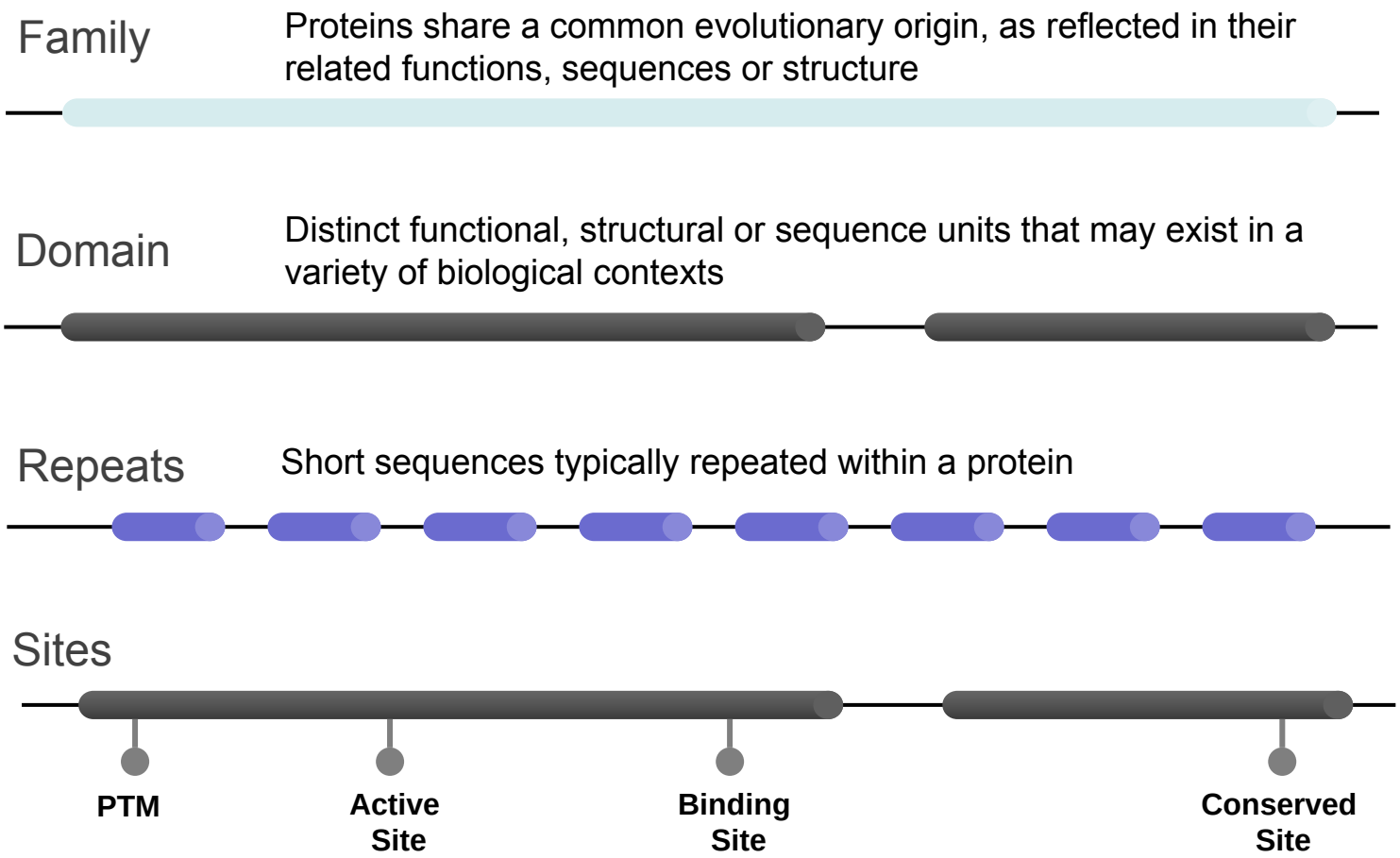


InterPro entry

InterPro entry



The InterPro entry: types



InterPro Entry

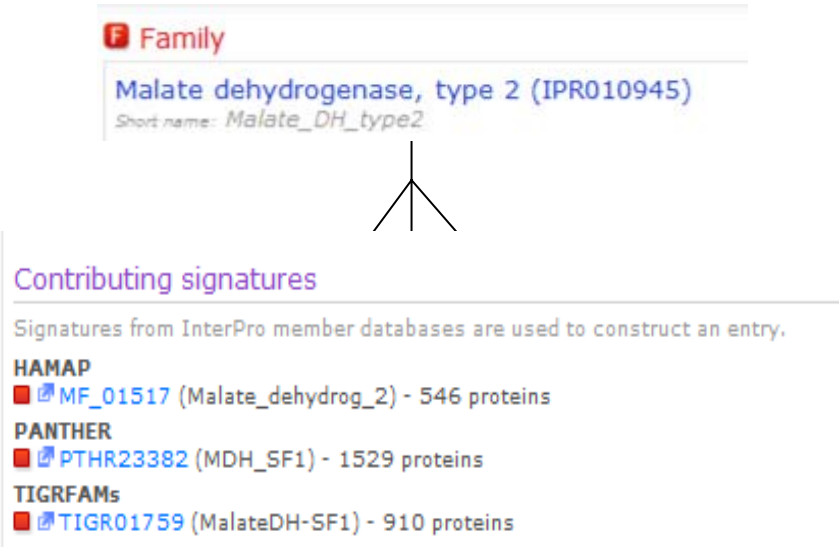
Groups similar signatures together

Adds extensive annotation

Links to other databases

Structural information and viewers

- Quality control
- Removes redundancy



InterPro Entry

Groups similar signatures together

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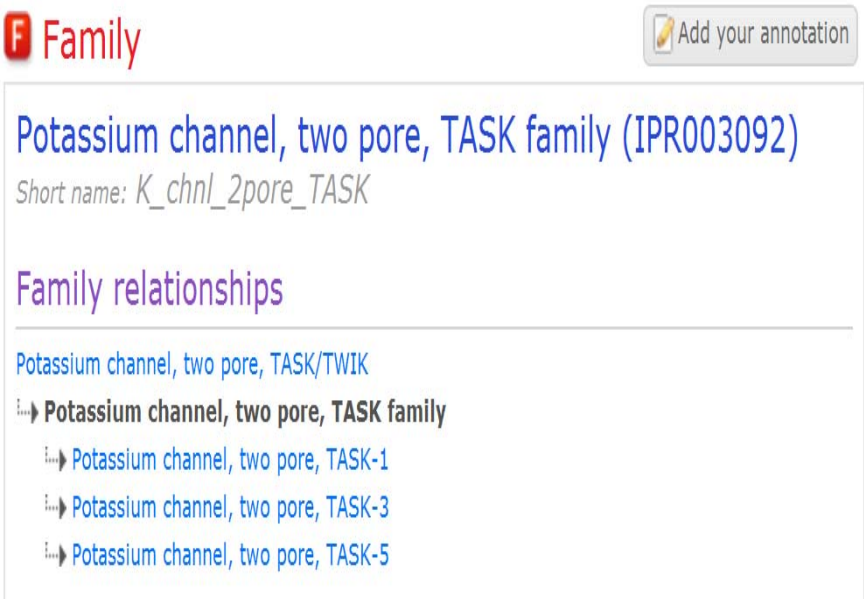
Links to other databases

Structural information and viewers

- Hierarchical classification

Interpro hierarchies: Families

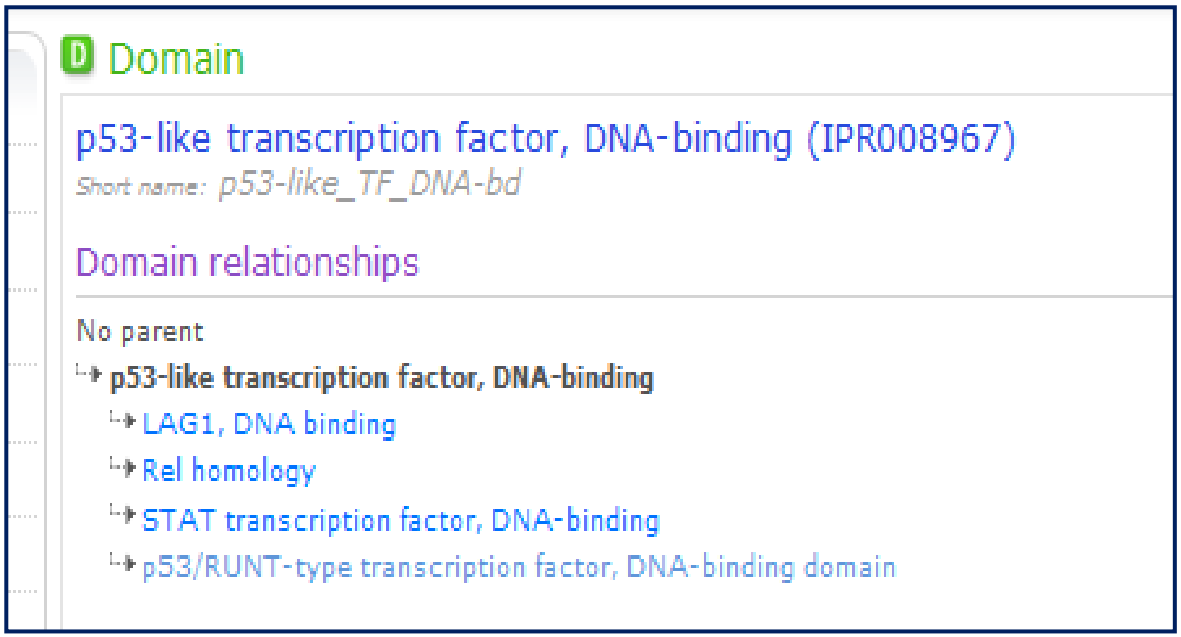
FAMILIES can have **parent/child** relationships with other Families



Parent/Child relationships are based on:

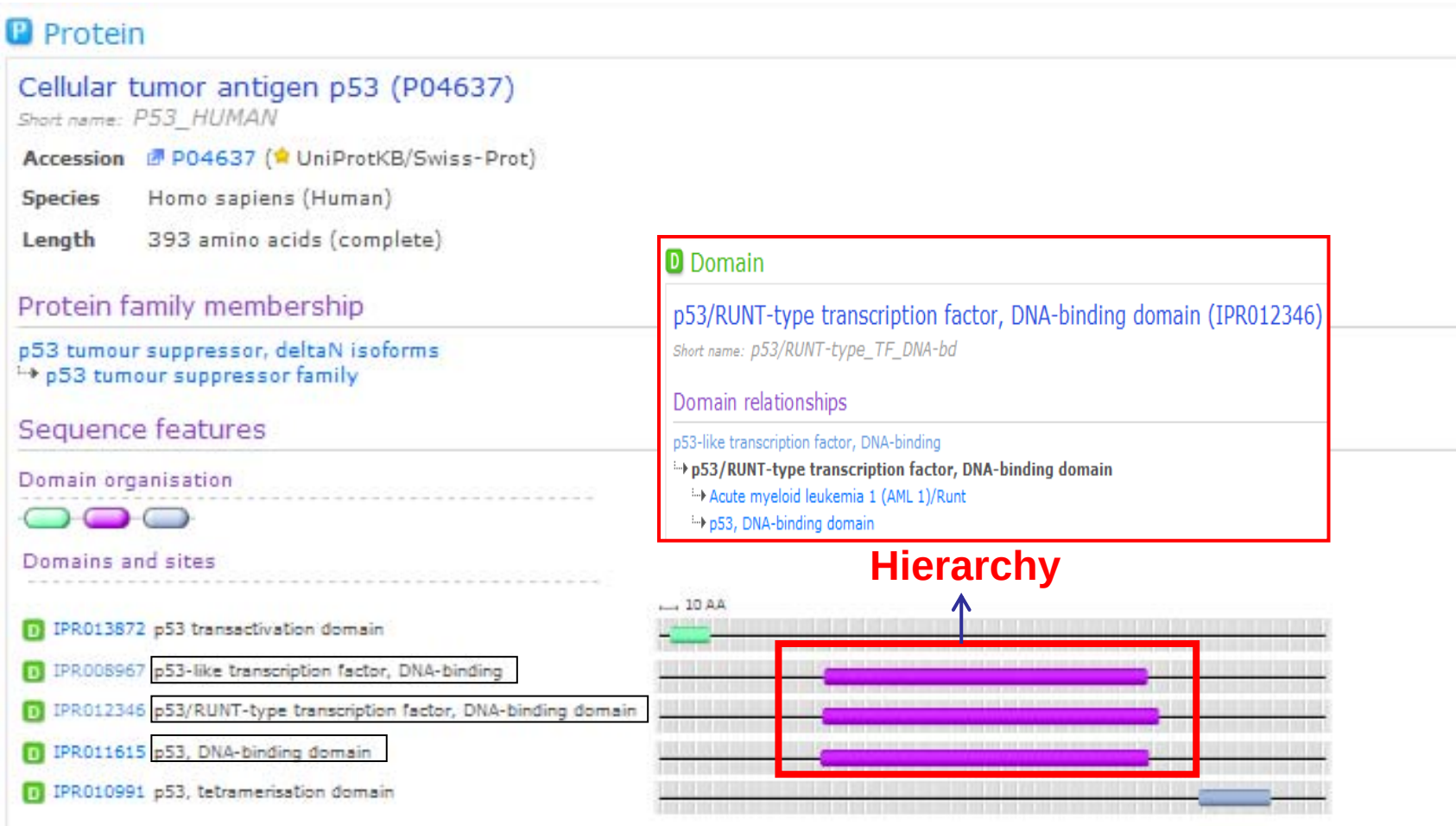
- **Comparison of protein hits**
  - child should be a subset of parent
  - siblings should not have matches in common
- **Existing hierarchies in member databases**
- **Biological knowledge of curators**

InterPro hierarchies: Domains



DOMAINS can have **parent/child** relationships with other domains

Domains and Families may be linked through Domain Organisation



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Structural information and viewers

Family

Malate dehydrogenase, type 2 (IPR010945)

Short name: *Malate_DH_type2*

Description

Malate dehydrogenases catalyse the interconversion of malate and oxaloacetate using dinucleotide cofactors [PubMed: 7849603]. The enzymes in this entry are found in archaea, bacteria and eukaryotes and fall into two distinct groups. The first group are cytoplamsic, NAD-dependent enzymes which participate in the citric acid cycle (EC:1.1.1.37). The second group are found in plant chloroplasts, use NADP as cofactor, and participate in the C4 cycle (EC:1.1.1.82).

Structural studies indicate that these enzymes are homodimers with very sinmilar overall topology, though the chloroplast enzymes also have N- and C-terminal extensions, and all contain the classical Rossman fold for NAD(P)H binding [PubMed: 8471603, PubMed: 10206992, PubMed: 10194350, PubMed: 10196131]. Substrate specificity is determined by a mobile loop at the active site which uses charge balancing to discriminate between the correct substrates (malate and oxaloacetate) and other potential oxo/hydroxyacid substrates the enzyme may encounter within the cell [PubMed: 10075524].

InterPro Entry

Groups similar signatures together

Adds extensive annotation

Links to other databases

Structural information and viewers

The Gene Ontology project provides a controlled vocabulary of terms for describing gene product characteristics

InterPro Entry

Groups similar signatures together

Adds extensive annotation

Links to other databases

Structural information and viewers

→ UniProt

→ KEGG ... Reactome ... IntAct ...

→ UniProt taxonomy

→ PANDIT ... MEROPS ... Pfam clans ...

→ Pubmed

InterPro Entry

Groups similar signatures together

Adds extensive annotation

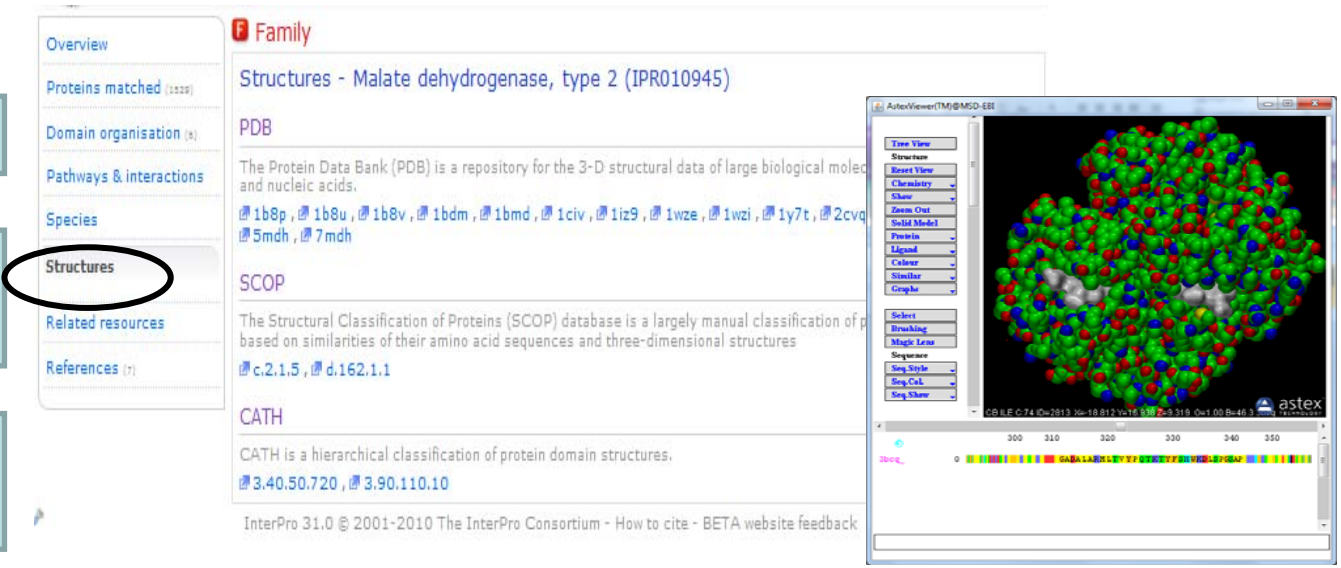
Links to other databases

Structural information and viewers

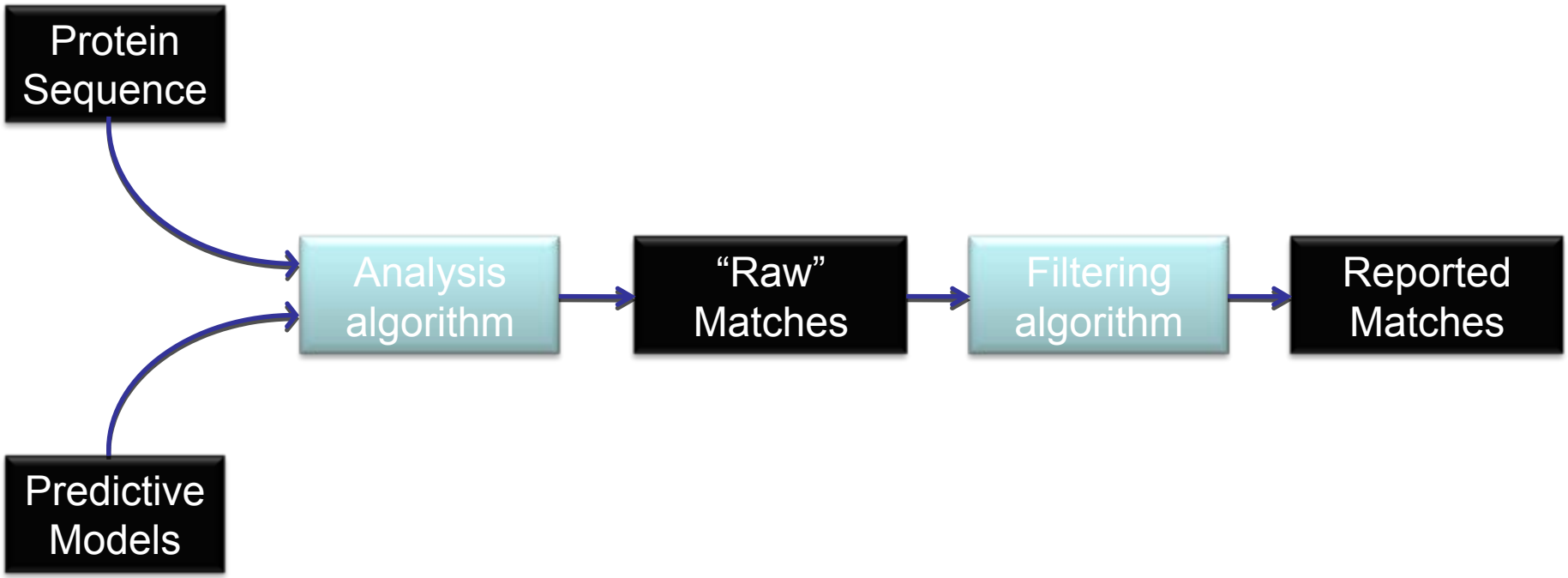
PDB 3-D Structures

SCOP Structural domains

CATH Structural domain

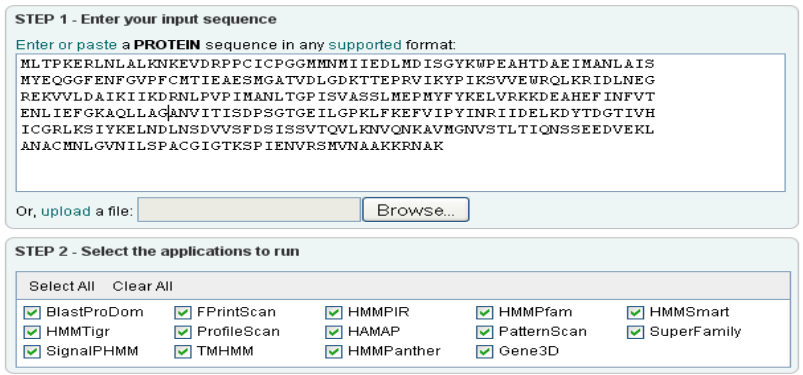


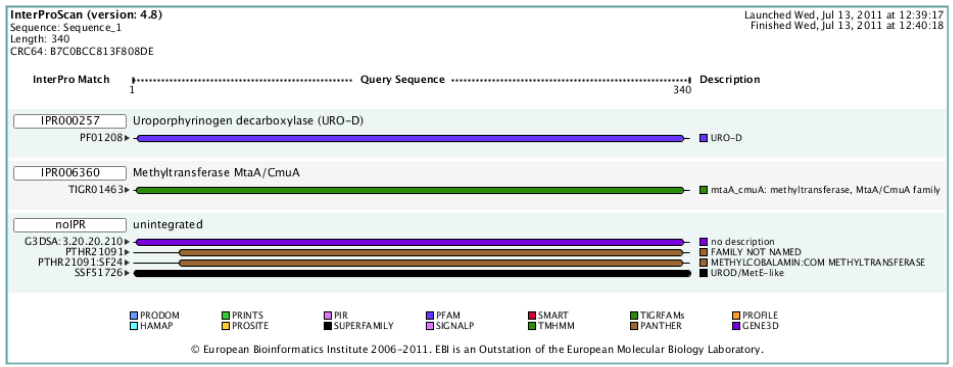
InterProScan



InterProScan access

Interactive:
http://www.ebi.ac.uk/Tools/pfa/iprscan/





Webservice (SOAP and REST):
http://www.ebi.ac.uk/Tools/webservices/services/pfa/iprscan_rest
http://www.ebi.ac.uk/Tools/webservices/services/pfa/iprscan_soap

Downloadable:
ftp://ftp.ebi.ac.uk/pub/software/unix/iprscan/

Why redesign InterProScan?

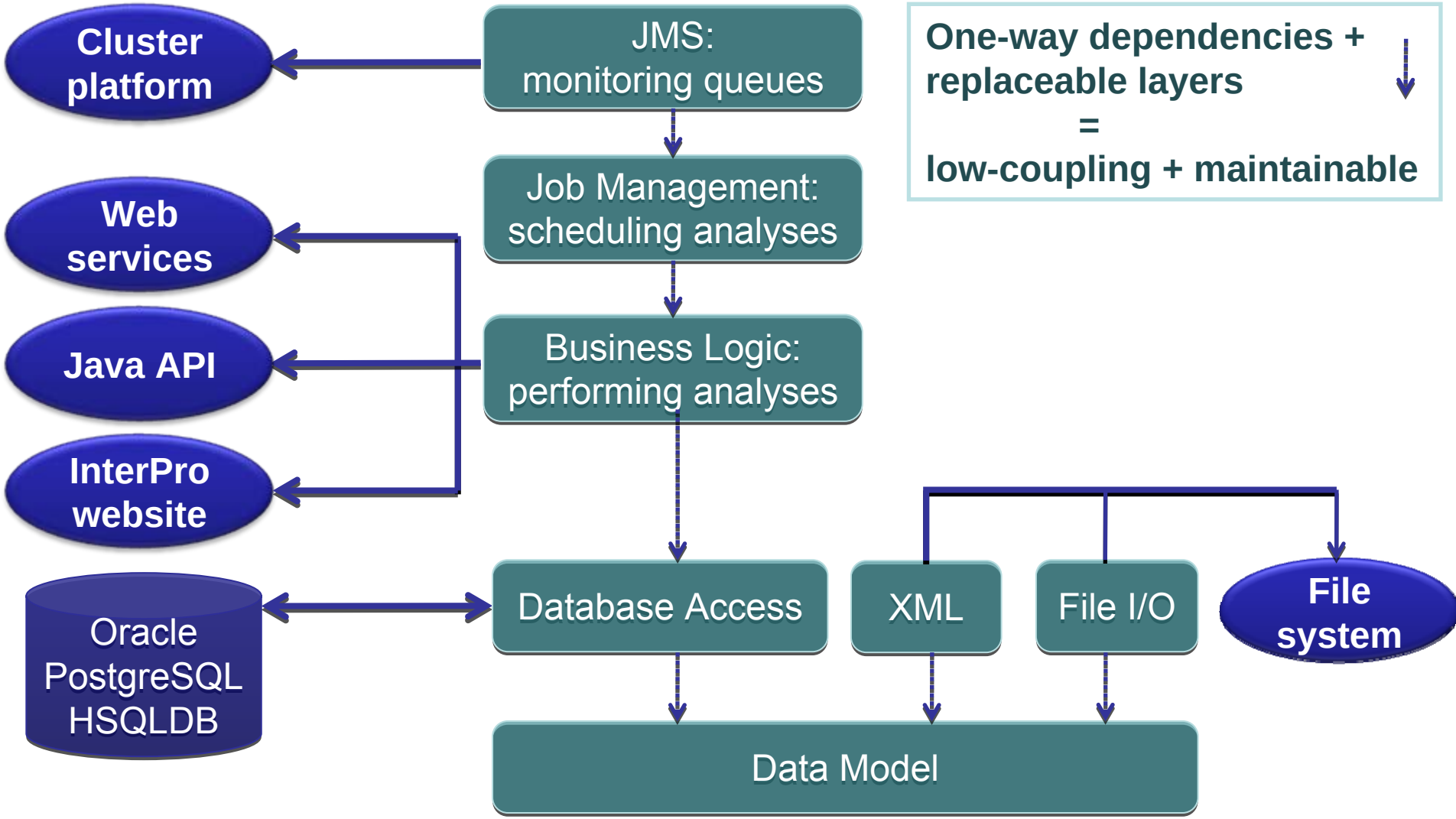
- InterProScan 4
  - complicated installation
  - complicated update
  - limited queuing system
    - Only guaranteed with LSF
  - limited configurability
  - reliability

InterProScan 5.0 aims

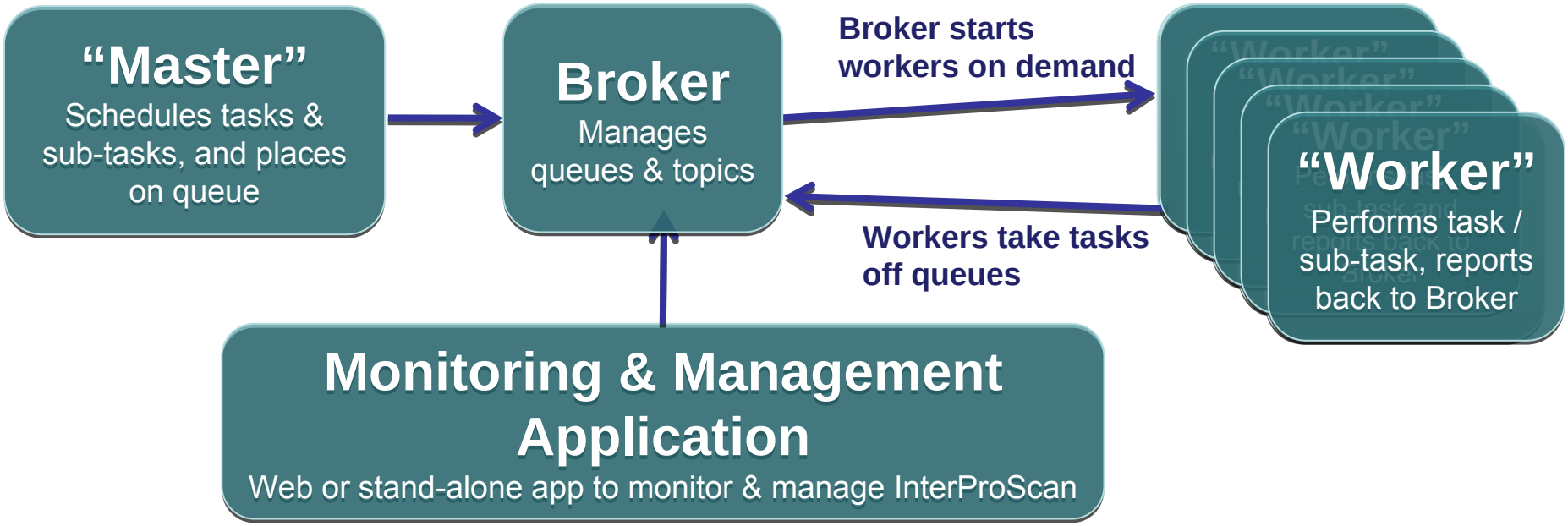
- Easy install and configuration
- Modular
- Expandable
- Easily integrated into existing pipelines
- Incorporate new data model / XML exchange format
- Easy to port on to different architectures:
  - Desktop machine
  - Simple **LAN**
  - **LSF**
  - **PBS**
  - **Sun Grid Engine** ...cloud? GRID?
- Reliablity

InterProScan 5 Technology

Architecture



Java Messaging Service



- Simple and robust programming model
- Mature and stable standard – current JMS version released in 2002
- Guaranteed message delivery to a single worker
- Easy to monitor
- Flexible – easy to implement on multiple platforms

Beta release functionality

Installation

- Requirements
  - Java 1.6
  - Linux
  - Perl
- Installation process

```
wget ftp://ftp.ebi.ac.uk/pub/software/unix/iprscan/i5-dist.tar.gz

tar -xzf i5-dist.tar.gz
```

  - ready to use

```
./interproscan.sh -i test_proteins.fasta -o test_proteins.tsv --goterms
```

```
A2YIW7  f927b0d241297dcc9a1c5990b58bf3c4        122     Pfam    PF00085 Thioredoxin     9       112     1.3E-28
T       08-07-2011      IPR013766       Thioredoxin domain      Biological Process:cell redox homeostasis
(GO:0045454)
A2YIW7  f927b0d241297dcc9a1c5990b58bf3c4        122     ProSitePatterns PS00194 Thioredoxin family active site.
32      50      -       T       08-07-2011      IPR017937       Thioredoxin, conserved site     Biological
Process:cell redox homeostasis (GO:0045454)
A2YIW7  f927b0d241297dcc9a1c5990b58bf3c4        122     PIRSF   PIRSF000077     null    4       113
1.50000307E-27  T       08-07-2011      IPR005746       Thioredoxin     Molecular Function:protein disulfide
oxidoreductase activity (GO:0015035), Biological Process:glycerol ether metabolic process (GO:0006662),
Biological Process:cell redox homeostasis (GO:0045454), Molecular Function:electron carrier activity
(GO:0009055)
A2YIW7  f927b0d241297dcc9a1c5990b58bf3c4        122     PRINTS  PR00421 Thioredoxin family signature    39
48      -       T       08-07-2011      IPR005746       Thioredoxin     Molecular Function:protein disulfide
oxidoreductase activity (GO:0015035), Biological Process:glycerol ether metabolic process (GO:0006662),
Biological Process:cell redox homeostasis (GO:0045454), Molecular Function:electron carrier activity
(GO:0009055)
A2YIW7  f927b0d241297dcc9a1c5990b58bf3c4        122     PRINTS  PR00421 Thioredoxin family signature    78
89      -       T       08-07-2011      IPR005746       Thioredoxin     Molecular Function:protein disulfide
oxidoreductase activity (GO:0015035), Biological Process:glycerol ether metabolic process (GO:0006662),
Biological Process:cell redox homeostasis (GO:0045454), Molecular Function:electron carrier activity
(GO:0009055)
A2YIW7  f927b0d241297dcc9a1c5990b58bf3c4        122     PRINTS  PR00421 Thioredoxin family signature    31
39      -       T       08-07-2011      IPR005746       Thioredoxin     Molecular Function:protein disulfide
oxidoreductase activity (GO:0015035), Biological Process:glycerol ether metabolic process (GO:0006662),
Biological Process:cell redox homeostasis (GO:0045454), Molecular Function:electron carrier activity
(GO:0009055)
```

Default tab-separated values output

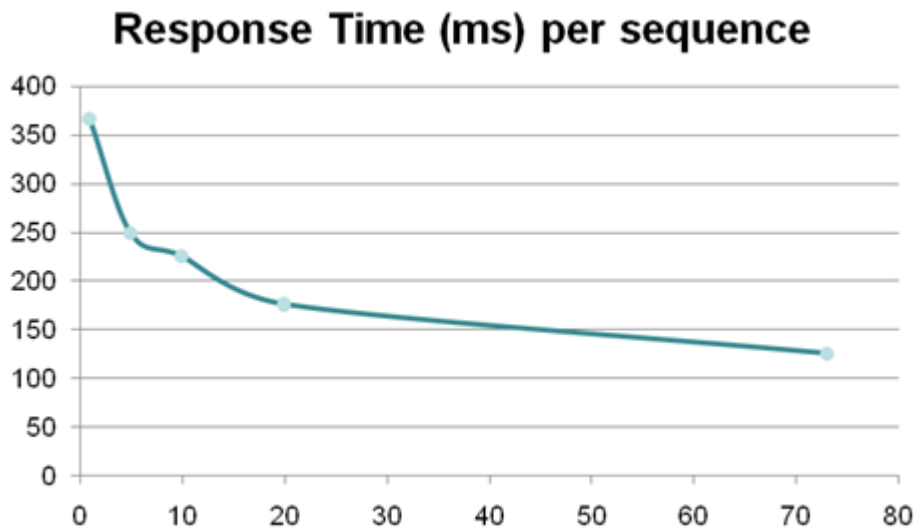
```
./interproscan.sh -i test_proteins.fasta -o test_proteins.xml --goterms -F xml
```

```
<?xml version="1.0" encoding="UTF-8" standalone="yes"?>
<protein-matches xmlns="http://www.ebi.ac.uk/schema/interpro">
    <protein>
        <sequence
md5="f927b0d241297dcc9a1c5990b58bf3c4">MAAEEGVVIACHNKDEFDAQMTKAKEAGKVVIIDFTASWCGPCRFIAPVFAEYAKKFPGAVFLKVDVDELKEV
AEKYNVEAMPTFLFIKDGAEADKVVGARKDDLQNTIVKHVGATAASASA</sequence>
        <xref id="A2YIW7"/>
        <matches>
            <fingerprints-match graphscan="III" evalue="2.500000864E-7">
                <signature name="THIOREDOXIN" desc="Thioredoxin family signature" ac="PR00421">
                    <models>
                        <model name="THIOREDOXIN" desc="Thioredoxin family signature" ac="PR00421"/>
                    </models>
                    <signature-library-release version="41.1" library="PRINTS"/>
                </signature>
                <locations>
                    <fingerprints-location score="0.0" pvalue="0.0" motifNumber="3" end="48" start="39"/>
                    <fingerprints-location score="0.0" pvalue="0.0" motifNumber="2" end="89" start="78"/>
                    <fingerprints-location score="0.0" pvalue="0.0" motifNumber="1" end="39" start="31"/>
                </locations>
            </fingerprints-match>
            <hmmer2-match score="100.5" evalue="-INF">
                <signature name="Thioredoxin" ac="PIRSF000077">
                    <models>
                        <model name="Thioredoxin" ac="PIRSF000077"/>
                    </models>
                    <signature-library-release version="2.74" library="PIRSF"/>
                </signature>
                <locations>
                    <hmmer2-location hmm-length="0" hmm-end="108" hmm-start="1" evalue="1.50000307E-27"
score="0.0" end="113" start="4"/>
                </locations>
            </hmmer2-match>
...etc
```

XML output

Pre-calculated match lookup

- BerkeleyDB-backed **REST** web service
- Includes matches for all of UniParc (27 million sequences)
- 250 million matches
- Fast response
- Integrated into i5.



Other functionality

- Increased reliability
- Precalculated match lookup
- Configuration
  - simple properties file
- Nucleotide sequence
  - getOrf
  - map matches to nucleotide coordinates
- Pathway mapping
  - KEGG, Reactome, MetaCyc, Unipathway

Future functionality

- Webservice
- Interact directly with architecture:
  - LAN
  - LSF
  - PBS
  - Sun Grid Engine
- Database persistence
  - Oracle
  - MySQL
  - Postgres
  - etc
- Graphical output
- Other functionality
  - ask!

InterProScan 5 timeline

- Beta release
  - August 2011
  - InterProScan 4 still maintained
- Full release
  - Early 2012
  - InterProScan 4 deprecated

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Acknowledgements

Team leader

Sarah Hunter

Developers

Matthew Fraser

Anthony Quinn

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Bioinformaticians

Craig McAnulla

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Curators

Alex Mitchell

Amaia Sangrador

Any Questions → Stand 302

Come and see us at booths 9 and 10!

- Job opportunities
- PhD and postdoc positions
- Training in person and online
- Services
- Industry programme

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