



THE EUKARYOTIC LINEAR MOTIF RESOURCE - ELM REGULATORY SITES IN PROTEINS

What are Linear Motifs?

Protein linear motifs (LMs) describe **short**, common stretches of polypeptide chains (typically peptides between **3 and 8 amino acid residues** long) that embody a distinct molecular function independent of a larger sequence/structure context.

The LMs are nearly always involved in **regulation**. Their function is often mediated by interactions with one or more globular domain classes. Linear motifs **bind** to their interaction partners with **low affinity**, usually between 1.0 and 150 micromolar.

They often reside in **disordered** or low-complexity sequence regions within proteins, and often becoming **ordered upon binding** to another protein or domain.

Instances of linear motifs seem to arise or disappear as a result of **point mutations**. Unrelated proteins are likely to contain similar linear motif if sharing functional feature (i.e. convergent evolution of linear motifs).



Classification of Linear Motif

Binding/Ligand	PDZ, SH2, SH3, EH domain-binding motifs
Localisation/Targeting	KDEL, NLS, NES, Peroxisomal Targeting signal
PTM	Phosphorylation, methylation, glycosylation
Cleavage	Protease cleavage targets in secretion, apoptosis

Overprediction and context information

Experimentally LMs are often neglected because the **biochemical** verification of the linear motif is **difficult**: e.g. some sites are only transiently used, thus difficult to capture by molecular methods.

Bioinformatically the linear motifs suffer severe **overprediction**: traditional detection methods, regular expressions, profiles and hidden markov models, usually give statistically **insignificant** results.

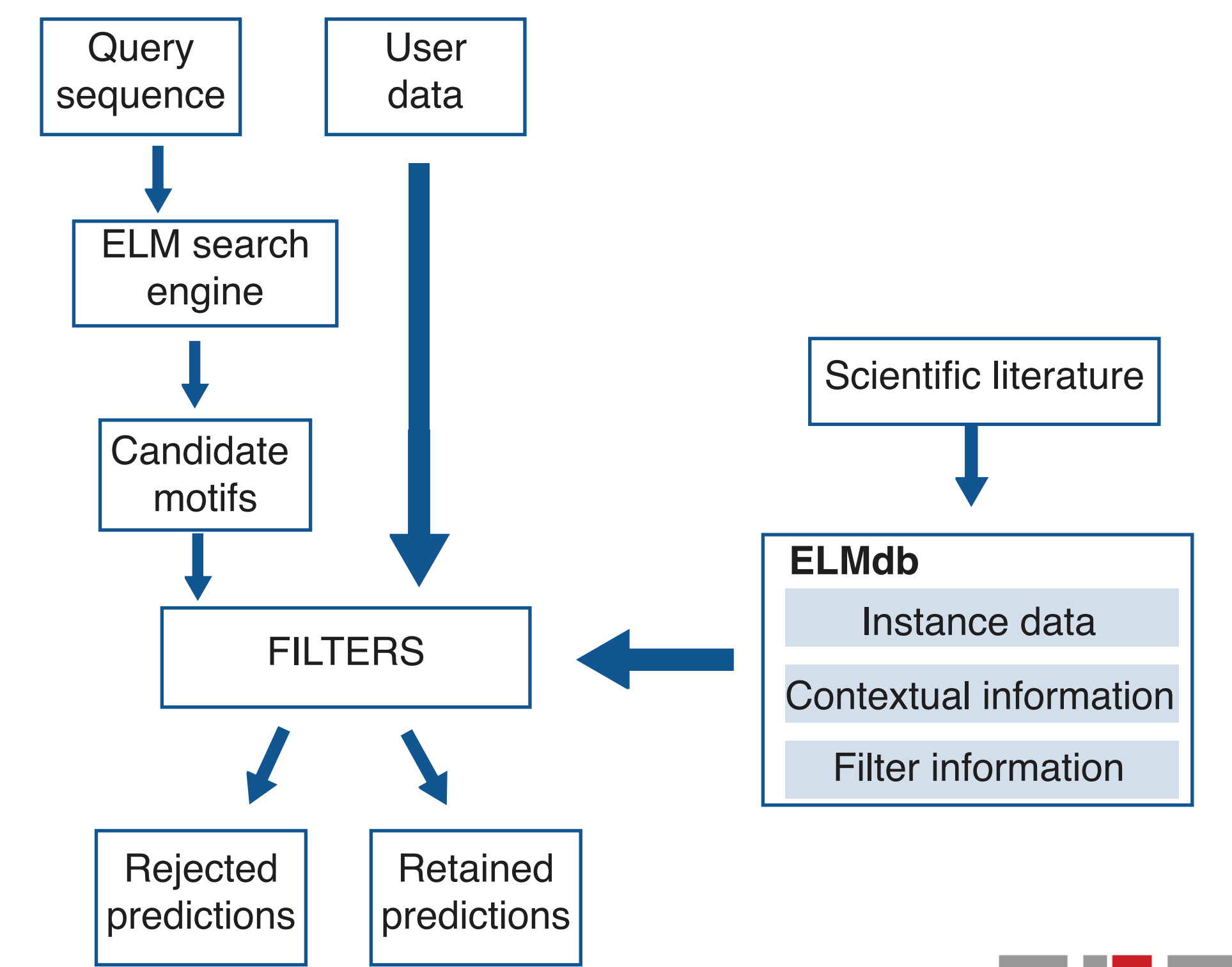
To be functional the linear motifs must occur in the proper biological context. Therefore **contextual information**, like cellular localisation and taxonomical distribution, can be used to filter out false matches, i.e. **improve their prediction**.



The Eukaryotic Linear Motif Resource

ELM is both a knowledgebase and discovery tool:

- Repository of information about short linear motif, including experimentally reported instances
- Motif-based query tool to find possible new functional sites



The ELM server

<http://elm.eu.org/>

The Eukaryotic Linear Motif resource for Functional Sites in Proteins

server browse links about usage news help

Functional site prediction

Protein sequence
 Enter SWISS-PROT/EMBL identifier or accession number:

Or paste the sequence (Single letter code sequence or FASTA format):

Context information

Species
 Select from list:

Cell compartment (one or several):

Submit / Reset Form

Please be patient! The ELM server collects the SMART-Pfam information through the SMART public queue.

NEW
 ELM Structure Filter 1.0 functionality added to ELM Server. To enable remote tool integration, a web-service for the structure filter pipeline is also available here.

Release Notes
 The current release of the ELM database (Nov 2009) contains 133 ELMs.

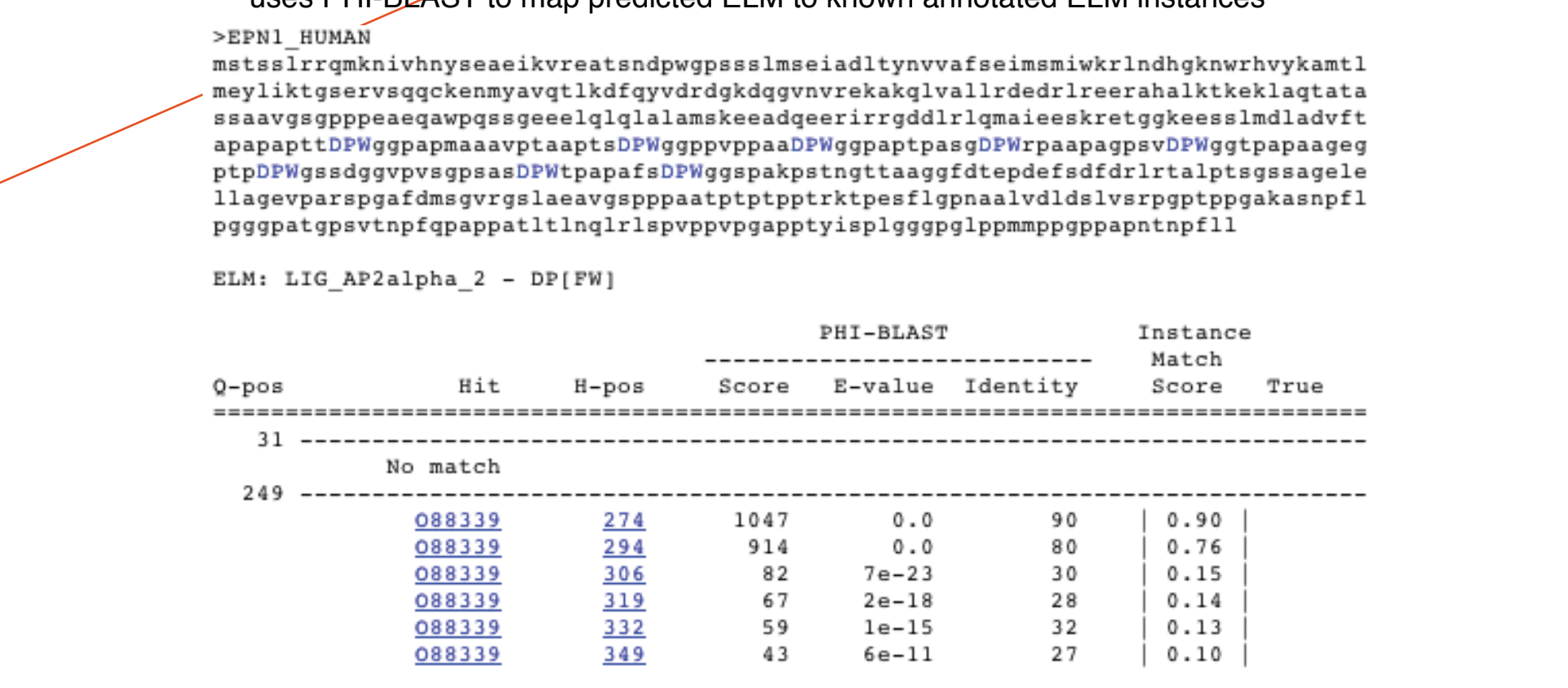
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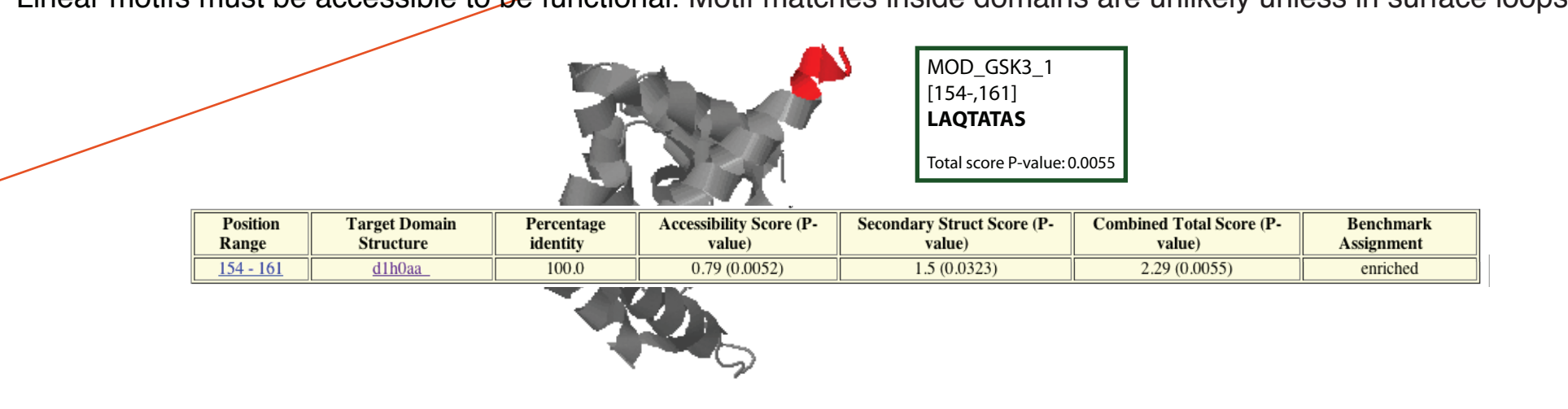
Graphical output



ELM instances mapper:



Structural filter



Detailed information on known instances annotated from the literature

Sequence	Position	Subsequence	Instance Logic	PDB	MINT	Gene Name	Protein Description	Organism	Length
EPN1_HUMAN	377-386	FDTEPEFSDPDRILATFTS	true positive	-	-	Name=EPN1;	ReName: Full-Epna-1; AName: Full-EPN-15-interacting protein 1; AName: Full-EH domain-binding motif; group=protein;	Homo sapiens (Human)	551

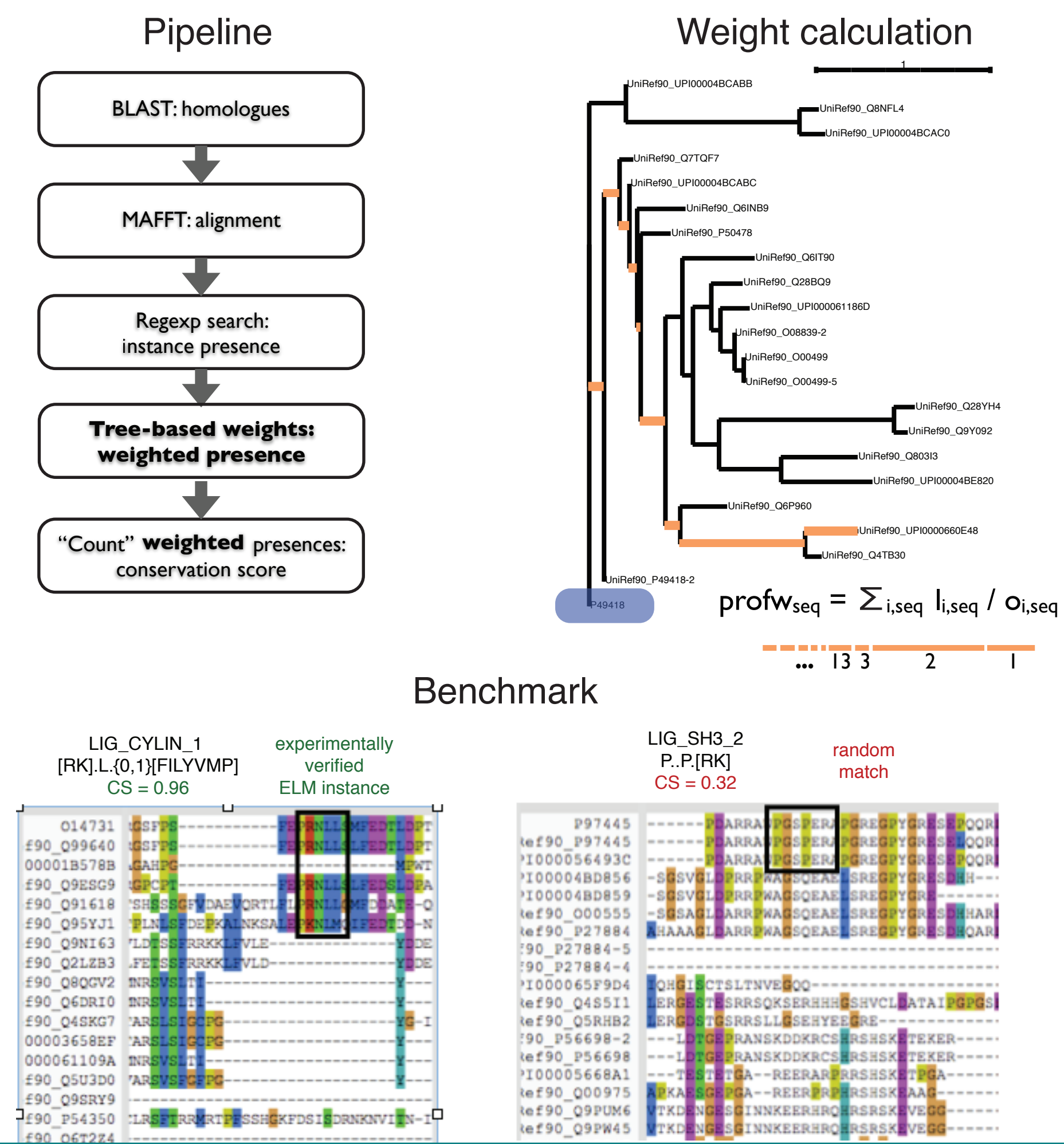
Instance evidence

Evidence class	Method	PubMed	Evidence Logic	Reliability
experimental	mutation analysis (M:0074)	16516836	support	certain
experimental	yeast 2 hybrid assay	16516836	support	certain
experimental	gst pull down (M:0059)	16516836	support	certain
experimental	ITC (M:0065)	16516836	support	certain



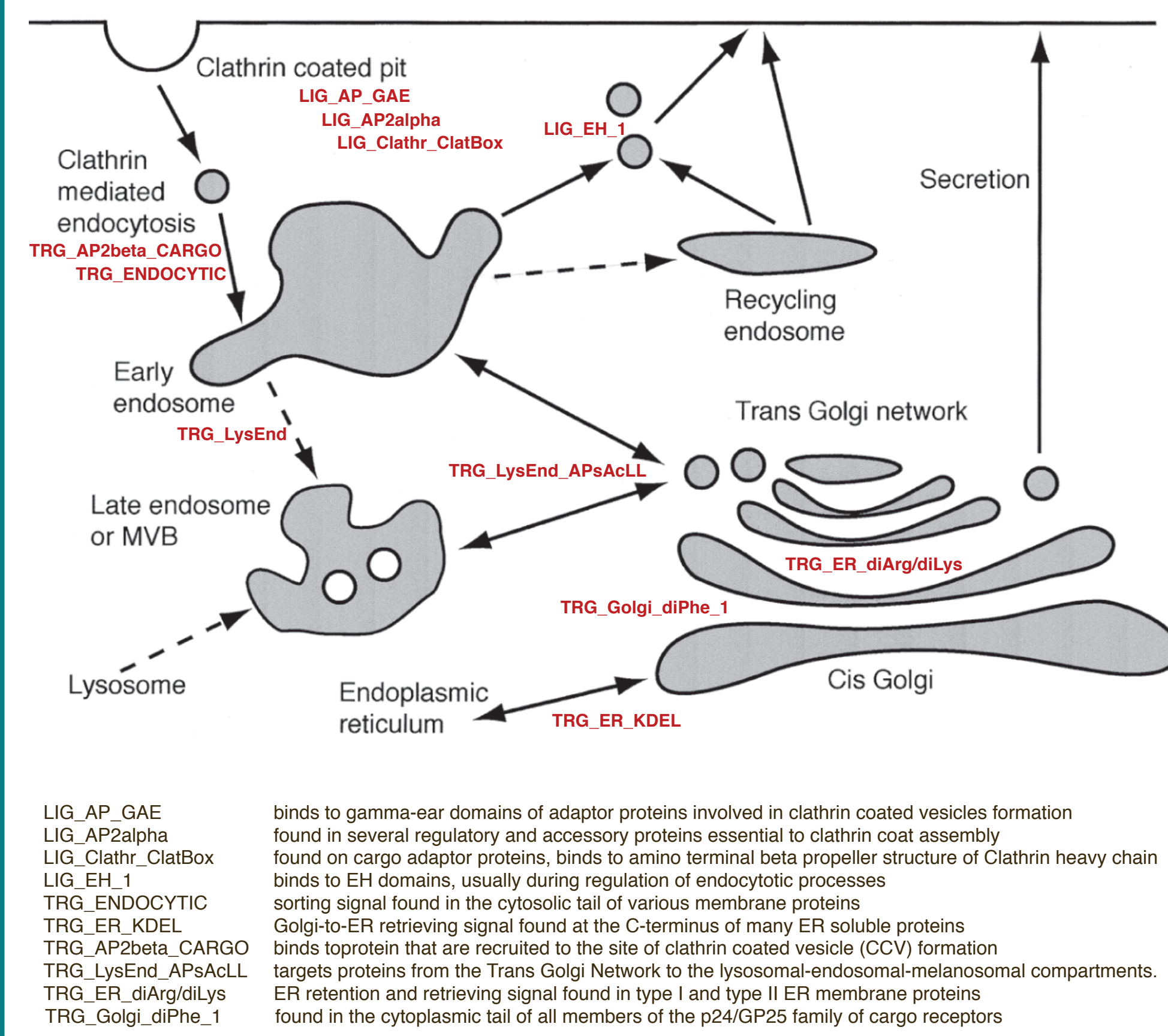
Conservation Score (CS)

Conservation has been shown to be an essential factor in the prediction of functional sites.



Linear Motifs in Endocytic and Recycling Pathway

Linear motifs play a key role in the regulation of many cellular processes. Clathrin-mediated endocytosis typifies the role of linear motifs in the fast and specific co-ordination of a wide range of connections between proteins.



Phospho.ELM

<http://phospho.elm.eu.org>

The Phospho.ELM database contains a collection of experimentally verified Serine, Threonine and Tyrosine sites in eukaryotic proteins. The entries, manually annotated and based on scientific literature, provide information about the phosphorylated proteins, the exact position of the phosphorylated instances and the kinases responsible for the modification (where known). Phospho.ELM is developed as part of the ELM resource.

