GRECO TFBS Benchmarking Initiative

Selection, curation, and preparation of benchmarking data

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Outline

- Aim
- Experiments
- TF Families
- Model Organisms
- Annotation
- Clustering

Aim

- Obtain a representative set of TFs:

    1. Supported by high-quality experimental data;
    2. From different structural families; and
    3. For several model organisms.

Experiments

- In vivo:

  1. ChIP-seq (from GTRD); and
  2. DAP-seq (plants; PMID 27203113; SRA SRP045296)

- In vitro:

  1. HT-SELEX (PMIDs 23332764 and 28473536; SRAs ERP001824 and ERP010942);
  2. PBM (UniPROBE and CIS-BP); and
  3. SMiLE-seq (PMID 28092692; SRA SRP073361).

- *Should we consider additional sources of uniformly processed ChIP-seq data? (e.g. ReMap, ChIP-Atlas, CistromeDB, ModERN)*

- *Should we consider additional experiment types? Which?*

TF Families

- Examples of TF family classification:

  1. Pfam → TFs can be assigned multiple Pfam IDs
  2. OrthoDB → Zinc fingers are grouped in a single (huge) family
  3. TFClass → Great, but limited to mammals

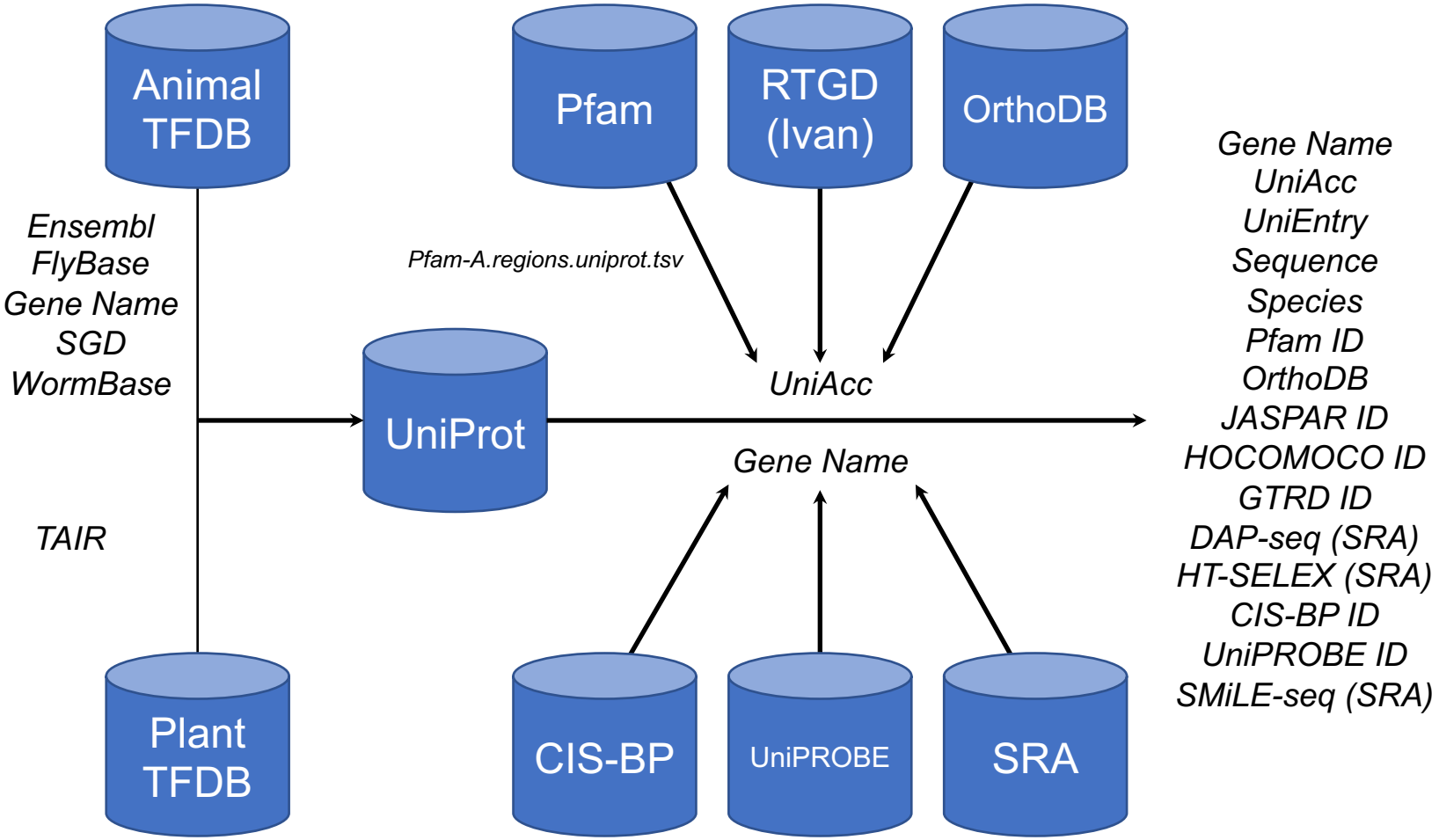
- *Should we automate the TF family assignment? (e.g. CIS-BP)*

Model Organisms

- Arabidopsis thaliana (1,693 TFs from the PlantTFDB 4.0)
- Caenorhabditis elegans (745 TFs from the AnimalTFDB 3.0)
- Danio rerio (2,414 TFs from the AnimalTFDB 3.0)
- Drosophila melanogaster (650 TFs from the AnimalTFDB 3.0)
- Homo sapiens (1,635 TFs from the AnimalTFDB 3.0)
- Mus musculus (1,548 TFs from the AnimalTFDB 3.0)
- Saccharomyces cerevisiae (180 TFs from the AnimalTFDB 3.0)
- Xenopus tropicalis (1,001 TFs from the AnimalTFDB 3.0)

- *Anyone can confirm these numbers? (e.g. zebrafish)*

Annotation


Animal TFDB
Pfam
RTGD (Ivan)
OrthoDB
Ensembl
FlyBase
Gene Name
SGD
WormBase
Pfam-A.regions.uniprot.tsv
UniAcc
UniProt
Gene Name
TAIR
Plant TFDB
CIS-BP
UniPROBE
SRA
Gene Name
UniAcc
UniEntry
Sequence
Species
Pfam ID
OrthoDB
JASPAR ID
HOCOMOCO ID
GTRD ID
DAP-seq (SRA)
HT-SELEX (SRA)
CIS-BP ID
UniPROBE ID
SMiLE-seq (SRA)

Annotation

- GTRD: 840 (~80%) out of 1,047 TFs mapped
- DAP-seq: 400 (~75%) out of 536 TFs mapped
- HT-SELEX: 668 (~96%) out of 697 TFs mapped
- CIS-BP: 851 (~80%) out of 1,065 TFs mapped
- UniPROBE: 537 (~93%) out of 576 TFs mapped
- SMiLE-seq: 54 (~92%) out of 59 TFs mapped

- *Should we manually check those cases that could not be mapped directly? (e.g. DAP-seq)*

Clustering

- For each Pfam id:

  1. Make a FASTA database with all TF sequences that have assigned that Pfam ID; and
  2. Clustering of the sequences using MMseqs2 “easy-cluster” with options “--min-seq-id 0.3 -c 0.5”

- From the MMseqs2 user’s guide:

  “We are using MMseqs2 to regularly update versions of the UniProtKB database clustered down to 30% sequence similarity[1] threshold”

  [1]Most likely, authors refer to sequence identity.

Clustering

Classification of Transcription Factors in Mammalia

About TFClass

Search in TFClass: ?

SOX1

Go to the search of TRANSFAC

Superclass: , Class: , Family: , Subfamily: , Genus: ,

- 1 Basic domains
- 2 Zinc-coordinating DNA-binding domains
- 3 Helix-turn-helix domains
- 4 Other all-alpha-helical DNA-binding domains
  - 4.1 High-mobility group (HMG) domain factors
    - F 4.1.1 SOX-related
      - 4.1.1.1 Group A
        - 4.1.1.1.1 SRY
      - 4.1.1.2 Group B
        - 4.1.1.2.1 SOX1
        - 4.1.1.2.2 SOX2
        - 4.1.1.2.3 SOX3
        - 4.1.1.2.4 SOX14
        - 4.1.1.2.5 SOX21
      - 4.1.1.3 Group C
        - 4.1.1.3.1 SOX4
        - 4.1.1.3.2 SOX11
        - 4.1.1.3.3 SOX12
      - 4.1.1.4 Group D
        - 4.1.1.4.1 SOX5
        - 4.1.1.4.2 SOX6
        - 4.1.1.4.3 SOX13
      - 4.1.1.5 Group E
        - 4.1.1.5.1 SOX8
        - 4.1.1.5.2 SOX9
        - 4.1.1.5.3 SOX10
      - 4.1.1.6 Group F
        - 4.1.1.6.1 SOX7
        - 4.1.1.6.2 SOX17
        - 4.1.1.6.3 SOX18
      - 4.1.1.7 Group G
        - 4.1.1.7.1 SOX15
      - 4.1.1.8 Group H
        - 4.1.1.8.1 SOX30
      - 4.1.1.9 Further SOX-related
        - 4.1.1.9.1 CIC
        - 4.1.1.9.2 HBP-1
        - 4.1.1.9.3 BBX
    - F 4.1.2 TOX-related
    - F 4.1.3 TCF7-related
    - F 4.1.4 PBRM1-related
    - F 4.1.5 WHSC1-related
    - F 4.1.6 UBF-related

Sox100B HMG_box 11
sox-4 HMG_box 19
Sox15 HMG_box 26
SOX15 HMG_box 30
Sox15 HMG_box 30
SOX13 HMG_box 31
SOX5 HMG_box 31
SOX6 HMG_box 31
Sox13 HMG_box 31
Sox5 HMG_box 31
Sox6 HMG_box 31
sox13 HMG_box 31
sox13 HMG_box 31
sox13 HMG_box 31
sox5 HMG_box 31
sox5 HMG_box 31
sox6 HMG_box 31
sox6 HMG_box 31
Sox21a HMG_box 33
Sox14 HMG_box 36
Sox21b HMG_box 39
SoxN HMG_box 39

Sox102F HMG_box 43
sox9b HMG_box 46
SOX1 HMG_box 47
SOX14 HMG_box 47
SOX2 HMG_box 47
SOX21 HMG_box 47
SOX3 HMG_box 47
Sox1 HMG_box 47
Sox14 HMG_box 47
Sox2 HMG_box 47
Sox21 HMG_box 47
Sox3 HMG_box 47
sox-3 HMG_box 47
sox14 HMG_box 47
sox14 HMG_box 47
sox1a HMG_box 47
sox1a HMG_box 47
sox1a HMG_box 47
sox1b HMG_box 47
sox2 HMG_box 47
sox2 HMG_box 47
sox21 HMG_box 47
sox21a HMG_box 47
sox21a HMG_box 47
sox21b HMG_box 47
sox3 HMG_box 47
sox3 HMG_box 47

SOX11 HMG_box 48
SOX12 HMG_box 48
SOX4 HMG_box 48
Sox11 HMG_box 48
Sox12 HMG_box 48
Sox4 HMG_box 48
sox11a HMG_box 48
sox11b HMG_box 48
sox12 HMG_box 48
sox12 HMG_box 48
sox17a HMG_box 48
sox17b.1 HMG_box 48
sox17b.2 HMG_box 48
sox4a HMG_box 48
sox4b HMG_box 48
SOX30 HMG_box 50
Sox30 HMG_box 50
sox-2 HMG_box 53
sox1 HMG_box 53
sox19a HMG_box 53
sox19a HMG_box 53
sox19b HMG_box 53
sox32 HMG_box 53

SOX10 HMG_box 56
SOX17 HMG_box 56
SOX18 HMG_box 56
SOX7 HMG_box 56
SOX8 HMG_box 56
SOX9 HMG_box 56
Sox10 HMG_box 56
Sox17 HMG_box 56
Sox18 HMG_box 56
Sox7 HMG_box 56
Sox8 HMG_box 56
Sox9 HMG_box 56
sox10 HMG_box 56
sox10 HMG_box 56
sox17 HMG_box 56
sox18 HMG_box 56
sox7 HMG_box 56
sox7 HMG_box 56
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sox8a HMG_box 56
sox8b HMG_box 56
sox9 HMG_box 56
sox9a HMG_box 56