GRECO TFBS Benchmarking Initiative

Towards a representative set of TFs

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Slides

https://github.com/oriolfornes/GRECO

Outline

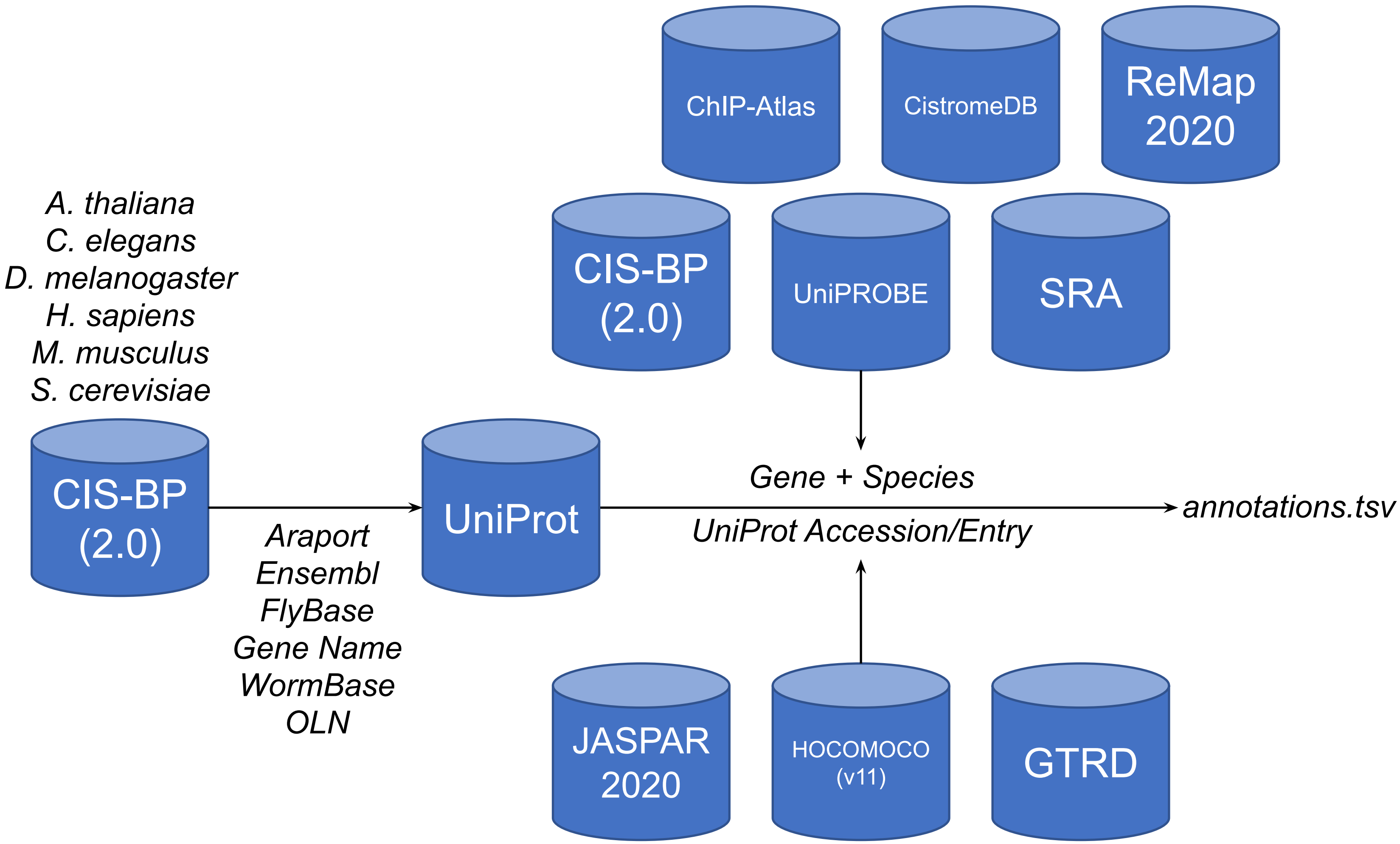
- Aim
- Annotation
- Clustering
- Results
- Next steps

Aim

- Obtain a representative set of TFs:

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

Annotation


ChIP-Atlas
CistromeDB
ReMap 2020
A. thaliana
C. elegans
D. melanogaster
H. sapiens
M. musculus
S. cerevisiae
CIS-BP (2.0)
UniPROBE
SRA
CIS-BP (2.0)
UniProt
Gene + Species
annotations.tsv
UniProt Accession/Entry
Araport
Ensembl
FlyBase
Gene Name
WormBase
OLN
JASPAR 2020
HOCOMOCO (v11)
GTRD

Annotation

https://raw.githubusercontent.com/oriolfornes/GRECO/master/annotations.tsv

Clustering

- For each TF (*i.e.* query)… (sort by amount of experimental evidence):

1. Identify the query's Pfam DBD(s) using hmmscan with the "--domtblout" option and E-value thresholds for models and domains of 10^{-5} and 10^{-2}, respectively;

2. Search for TFs homologous to the query using BLAST+;

3. Select homologs:
   - ■ with the same DBD composition than the query; and
   - ■ whose BLAST+ alignment with the query is above the Rost's sequence identity curve;

4. For each selected homolog, if the amino acid sequence identity of the query and homolog DBDs is greater than the DBD-specific motif inference thresholds from CIS-BP, cluster the TFs together.

Clustering

https://github.com/oriolfornes/GRECO/blob/master/Data/Clusters/TFs.json

Results

- Triads: *i.e.* TFs with support by *in vivo* and **at least two** *in vitro* methods

- Species:

1. Drosophila melanogaster **1**
2. Homo sapiens **57**
3. Mus musculus **28**

- Families:

1. C2H2 ZF **15**
2. C2H2 ZF,MADF **1**
3. CUT,Homeodomain **1**
4. DM **1**
5. E2F **1**
6. Ets **4**
7. Forkhead **6**
8. GATA **2**
9. Homeodomain **13**
10. Homeodomain,POU **1**
11. Homeodomain,Paired box **1**
12. Nuclear receptor **14**
13. RFX **2**
14. Rel **2**
15. SAND **1**
16. Sox **4**
17. bHLH **9**
18. bZIP **8**

Results

- Duos: *i.e.* TFs with support by *in vivo* and *in vitro* methods
- Species:

   1. Arabidopsis thaliana **98**
   2. Caenorhabditis elegans **30**
   3. Drosophila melanogaster **39**
   4. Homo sapiens **279**
   5. Mus musculus **130**
   6. Saccharomyces cerevisiae **32**

- Families: **62**

Results

- Multiple evidence: *i.e.* TFs with support by **at least two** methods
- Species:

  1. Arabidopsis thaliana **98**
  2. Caenorhabditis elegans **30**
  3. Drosophila melanogaster **40**
  4. Homo sapiens **290**
  5. Mus musculus **141**
  6. Saccharomyces cerevisiae **32**

- Families: **62**

Next steps

- Ensure that the representative set of TFs contains only sequence-specific DNA-binding TFs

- For each representative TF, ensure that the mapped experimental data correspond to that TF