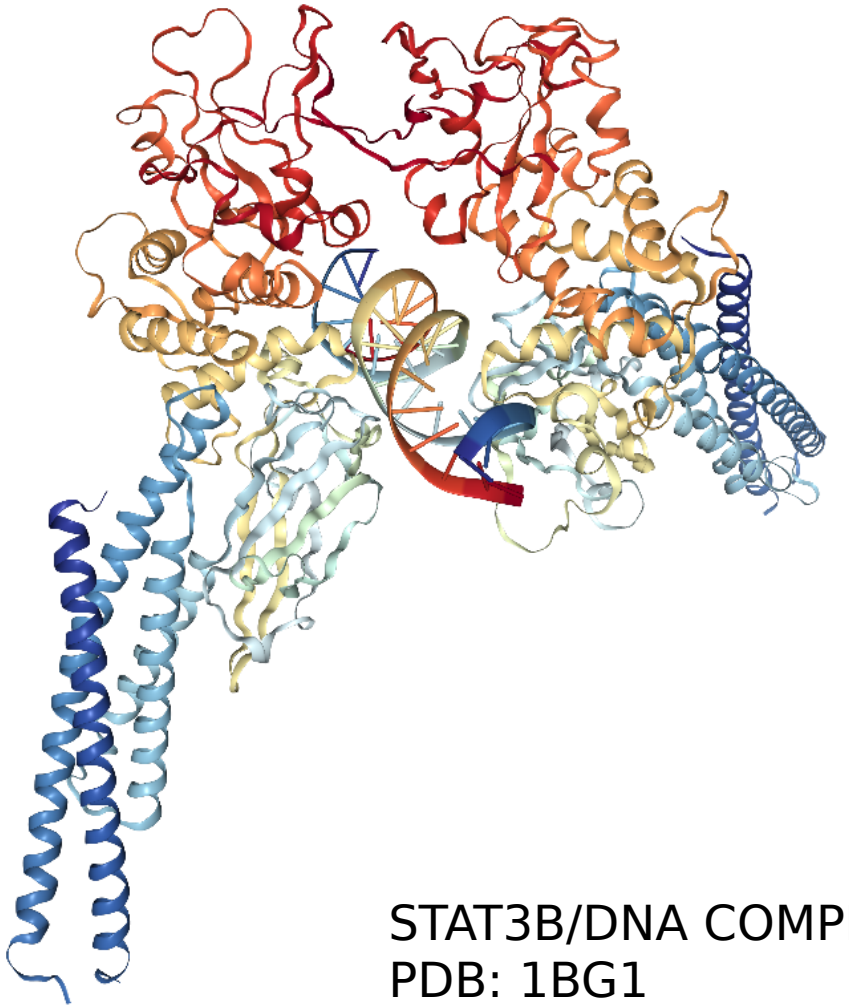
TFClass – a classification of transcription factors

Jürgen Dönitz, Edgar Wingender

Transcription factors, the proteins for regulation of transcription

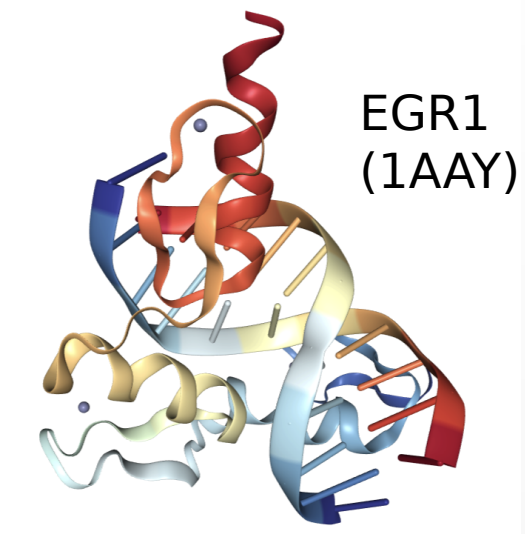


STAT3B/DNA COMPLEX
PDB: 1BG1

„Transcription factors are proteins that regulate transcription by binding to specific sequence elements in regulatory genome regions such as promoters, enhancers etc.“

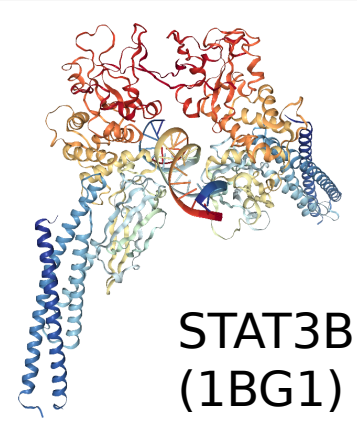
TFClass: a hierarchy of TFs according their DNA binding domain (DBD)

- Proteins are built by modules, protein domains
- Most TF have at least one DBD
- The DBDs can be sorted into a few groups, e.g.
  - Zinc finger
  - Helix-turn-helix
  - alpha-helices exposed by beta-structures
  - Immunoglobulin fold


EGR1
(1AAY)

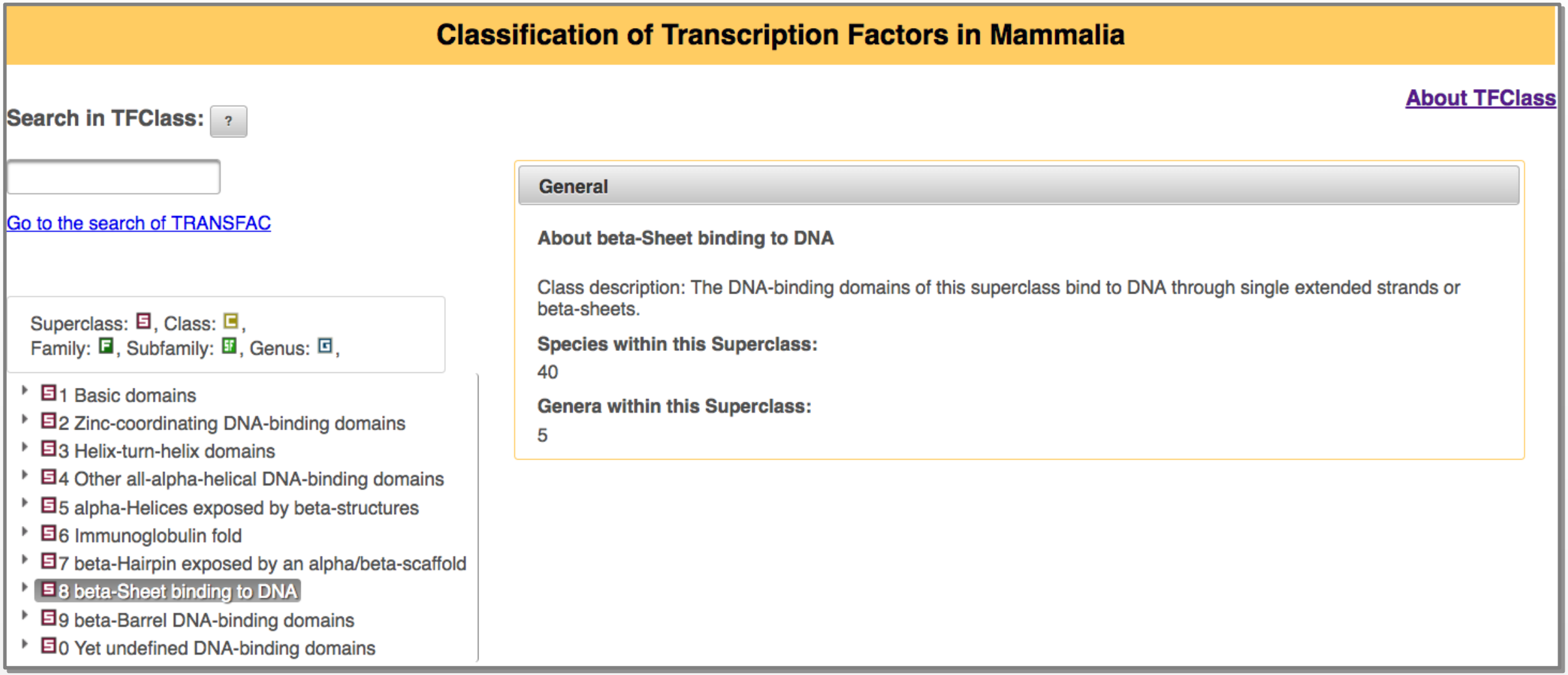
CDX2
(5LTY)

MEF2A
(1C7U)

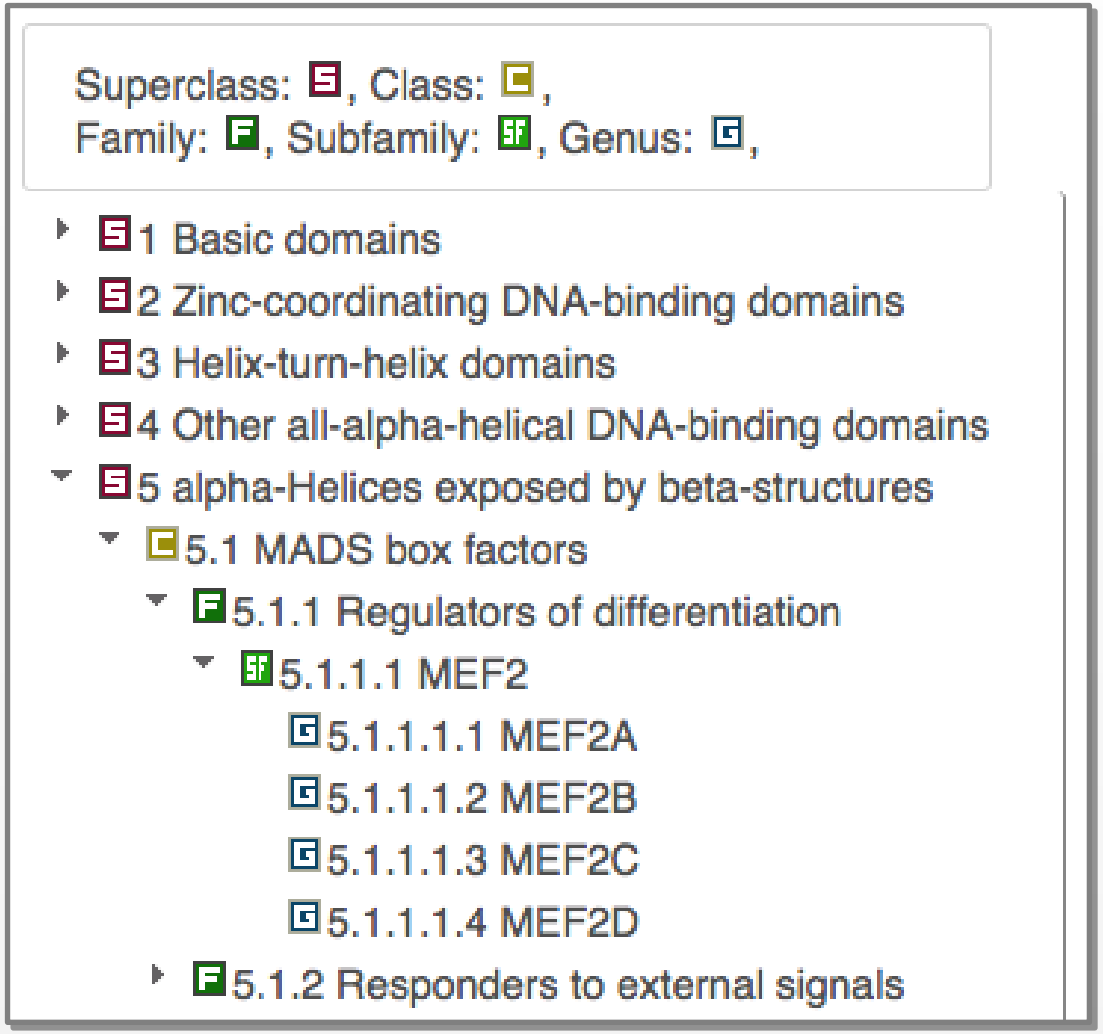

STAT3B
(1BG1)

Images taken from RCSB PDB, IDs in parentheses

TFClass: The top level Superclasses

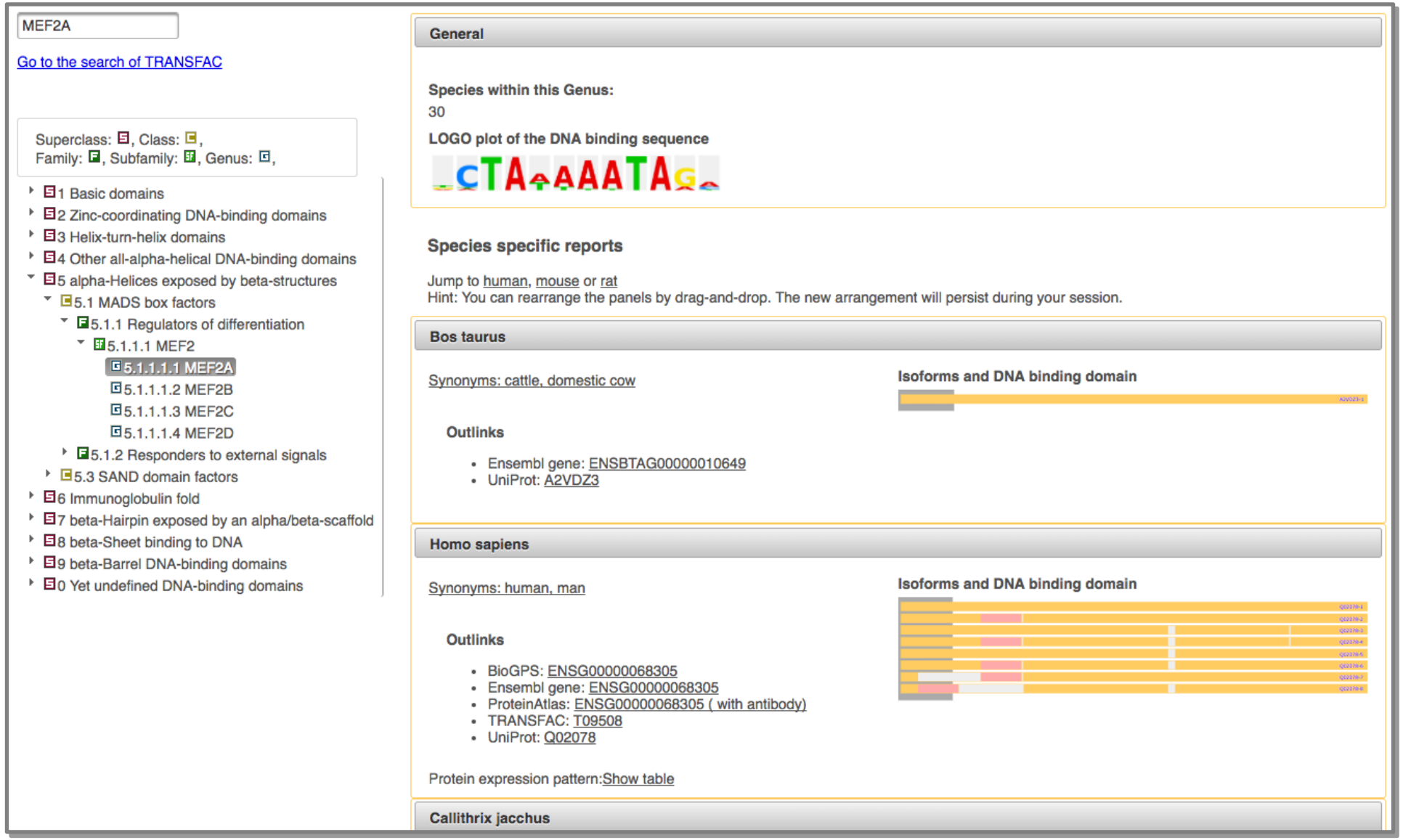


The five levels of TFClass

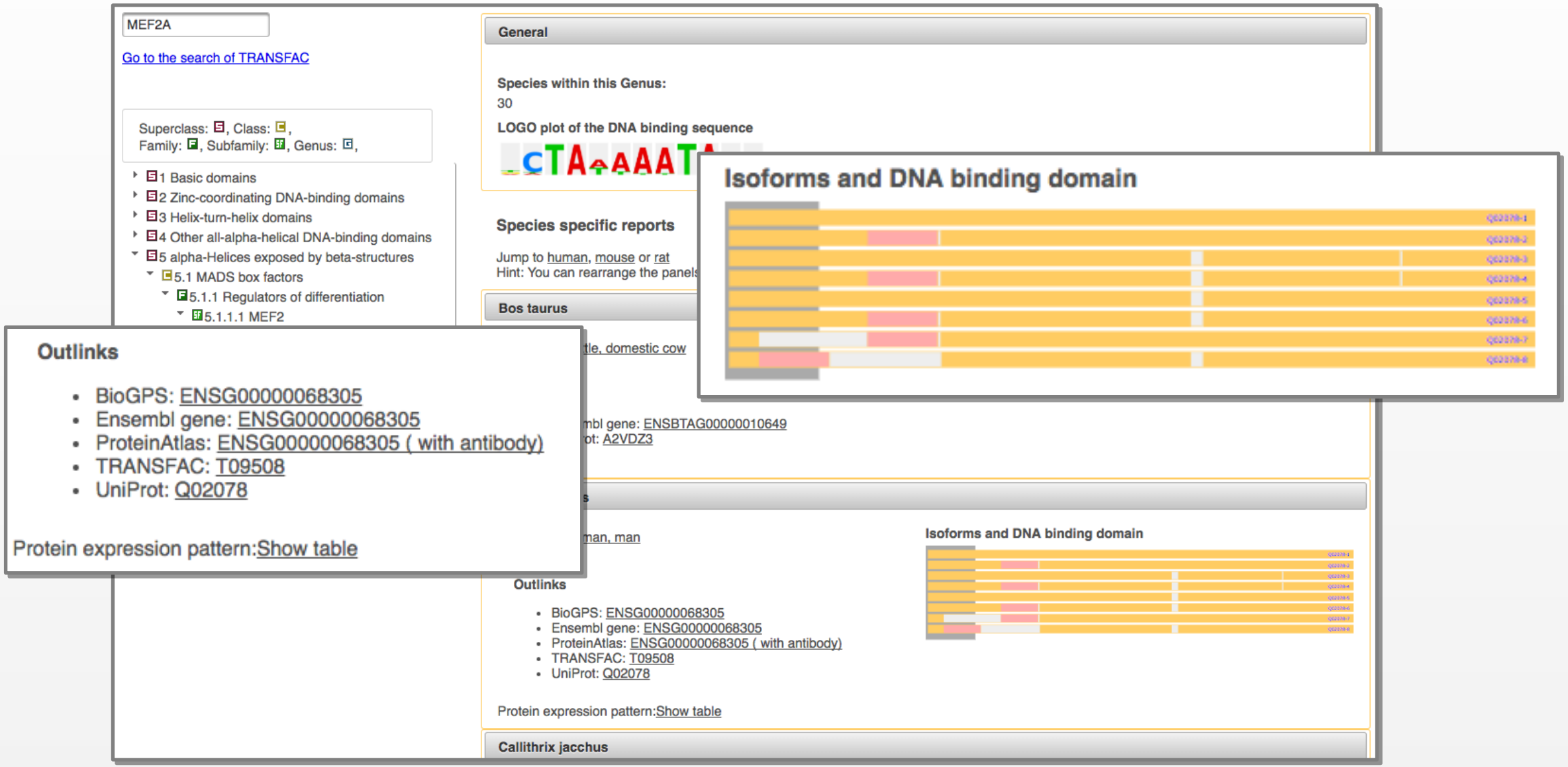


- Names of the levels similar to the biological taxonomy
- Levels 1 – 4 are abstract, Genus relates to a gene
- Mammalian orthologs of human TFs
- Pattern of the IDs similar to the EC numbers
- One number for each level, separated by a dot

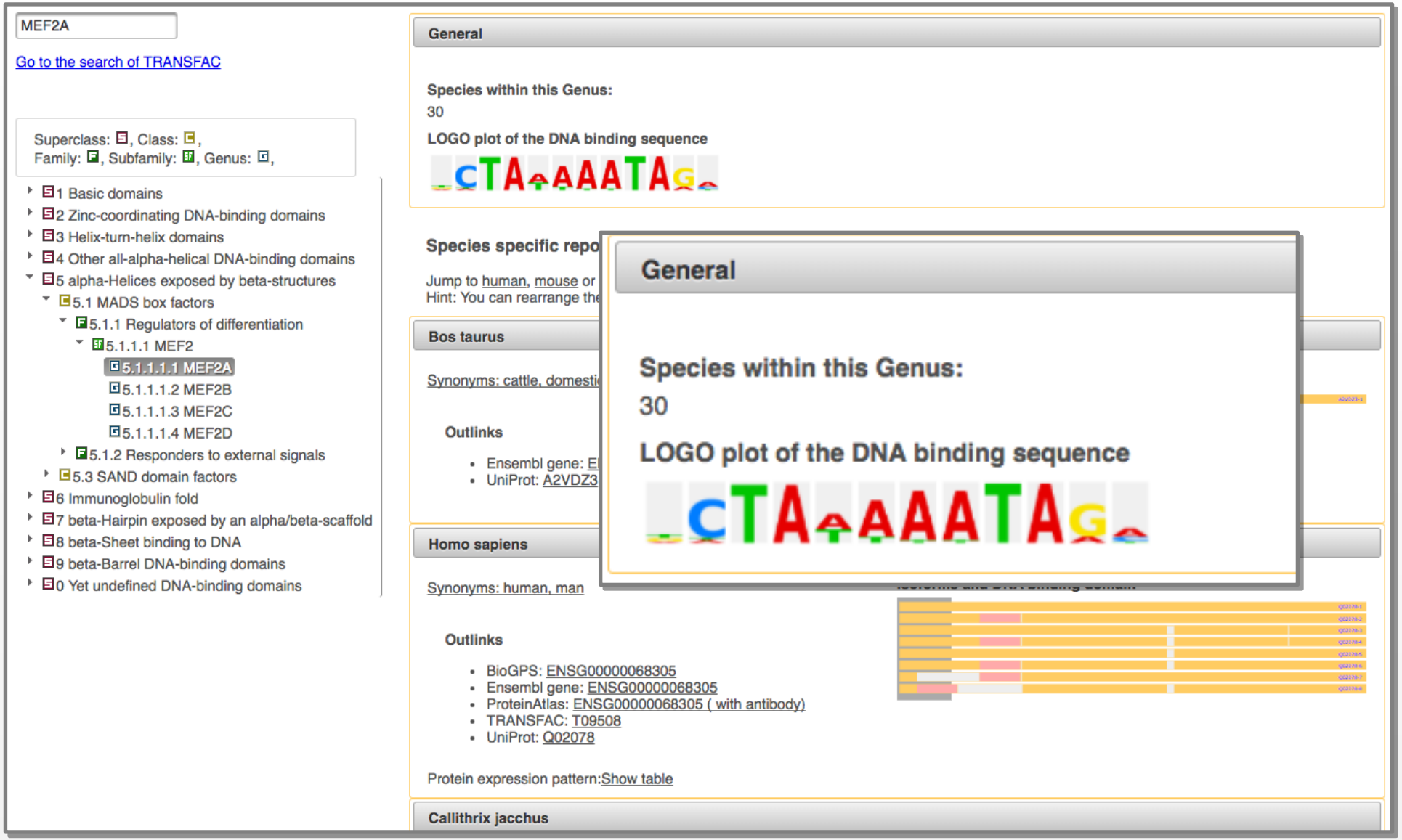
The species reports



The DBD in the Isoforms

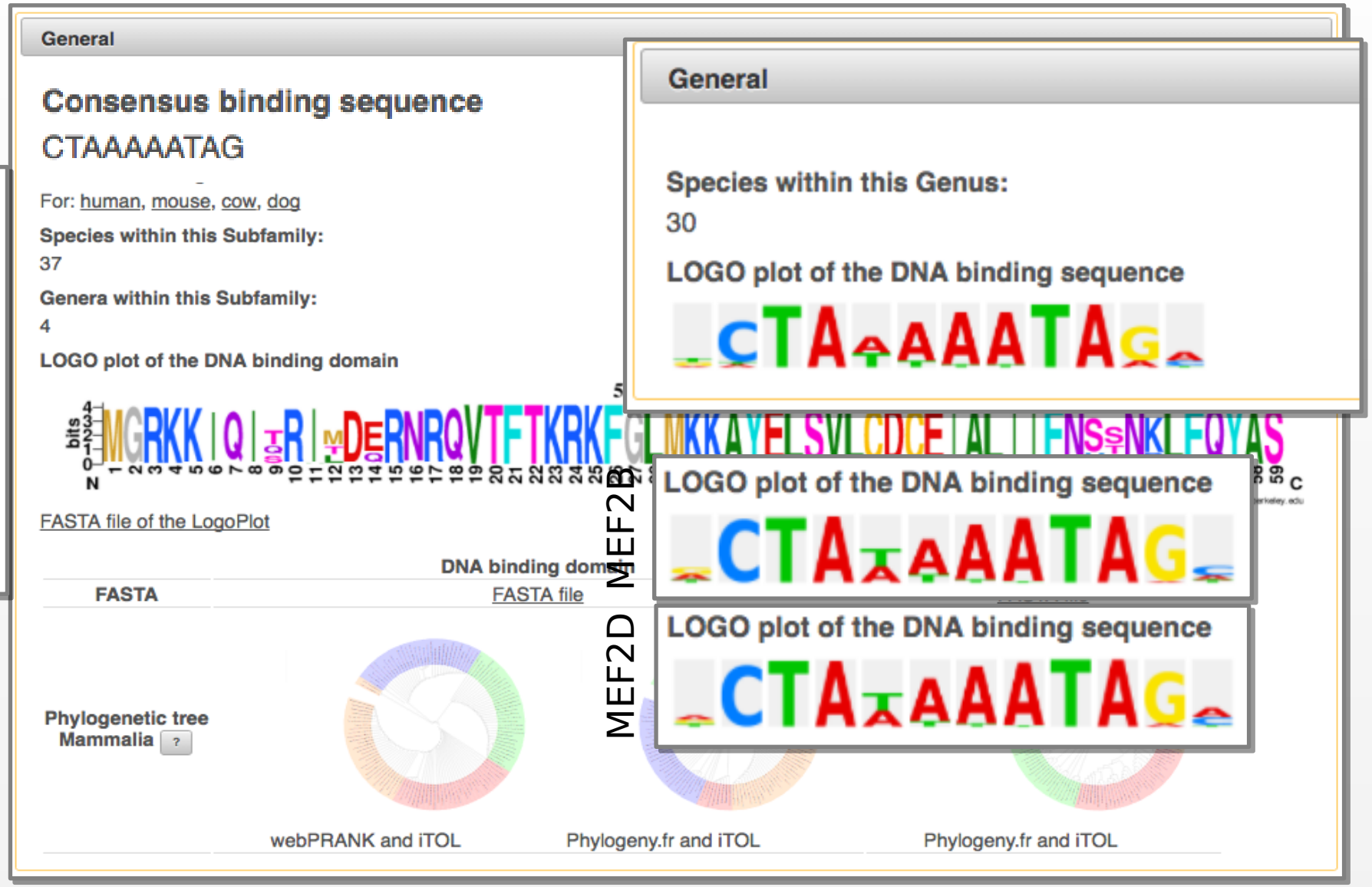


General information and LOGO plot of DNA binding site



Consensus sequence

- 1 Basic domains
- 2 Zinc-coordinating DNA-binding domains
- 3 Helix-turn-helix domains
- 4 Other all-alpha-helical DNA-binding domains
- 5 alpha-Helices exposed by beta-structures
  - 5.1 MADS box factors
    - 5.1.1 Regulators of differentiation
      - 5.1.1.1 MEF2
        - 5.1.1.1.1 MEF2A
        - 5.1.1.1.2 MEF2B
        - 5.1.1.1.3 MEF2C
        - 5.1.1.1.4 MEF2D
    - 5.1.2 Responders to external signals



The upper levels of the hierarchy

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        - 5.1.1.1.2 MEF2B
        - 5.1.1.1.3 MEF2C
        - 5.1.1.1.4 MEF2D
    - 5.1.2 Responders to external signals

General

Consensus binding sequence
CTAAAAATAG

Predicted binding sites
For: human, mouse, cow, dog

Species within this Subfamily:
37

Genera within this Subfamily:
4

LOGO plot of the DNA binding domain

FASTA file of the LogoPlot

	DNA binding domain	Whole protein
FASTA	FASTA file	FASTA file
Phylogenetic tree Mammalia ?	webPRANK and iTOL	Phylogeny.fr and iTOL	Phylogeny.fr and iTOL

LogoPlot of the DBD

- 1 Basic domains
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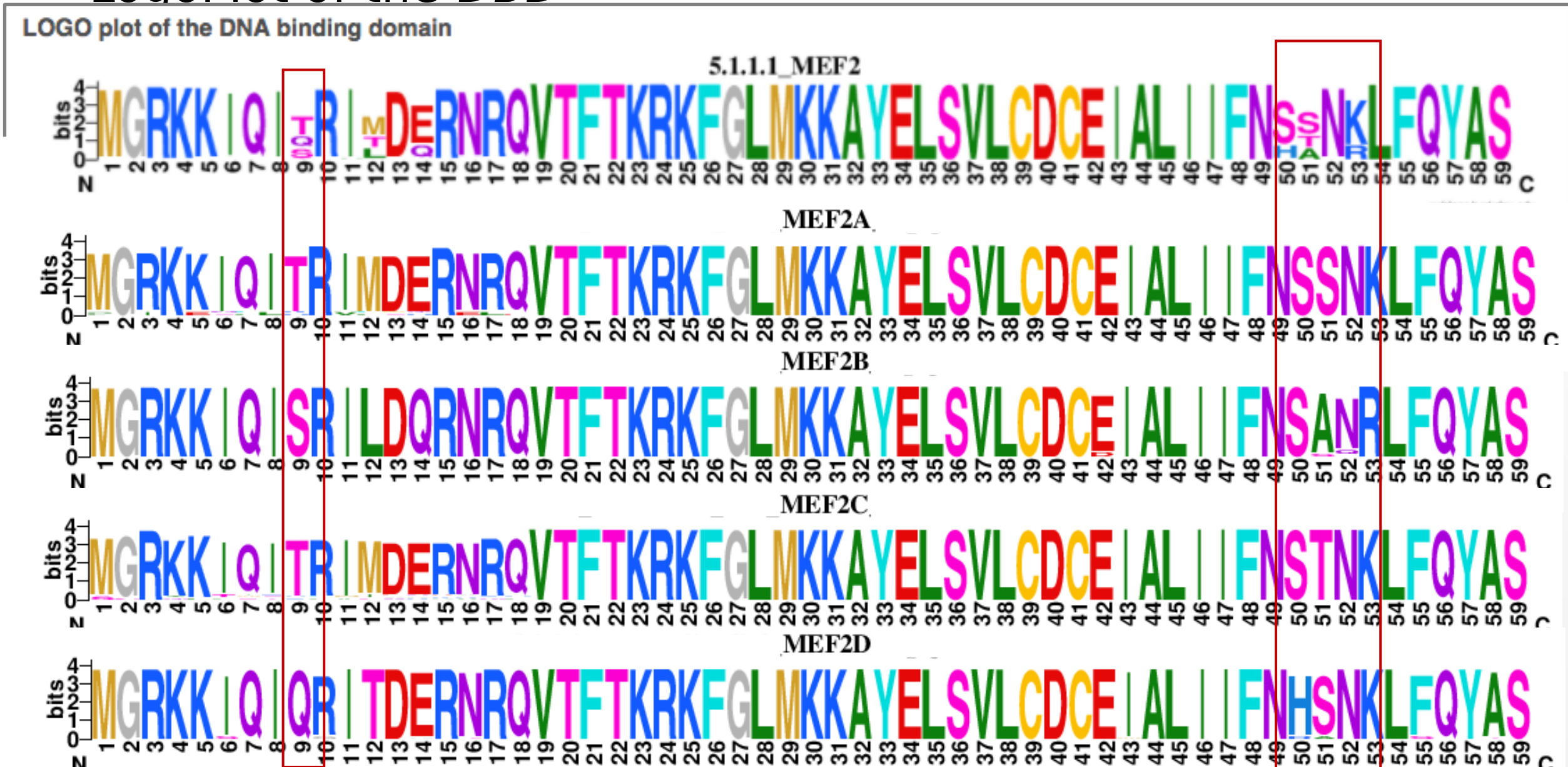
UMG

LogoPlot of the DBD



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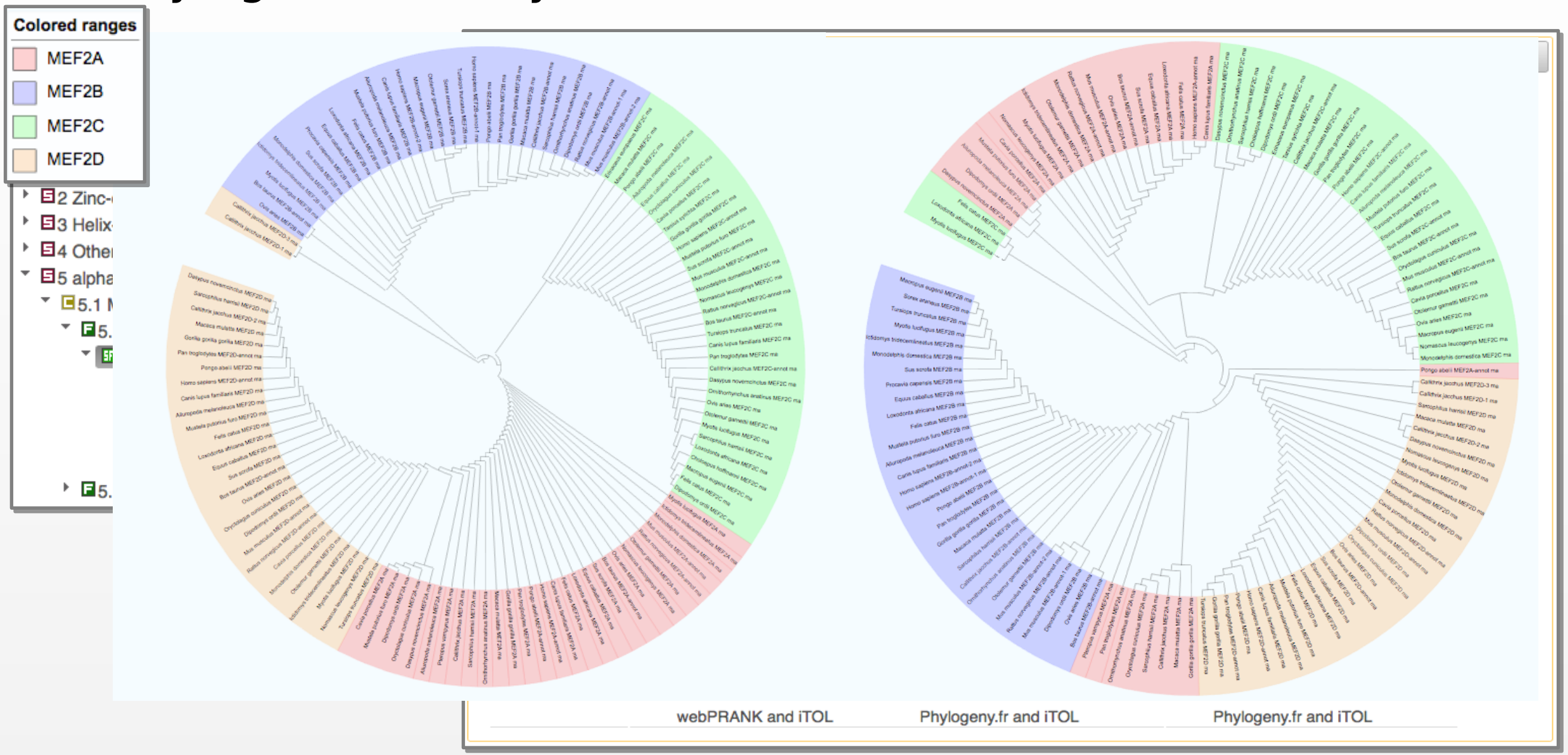
Phylogenetic analysis



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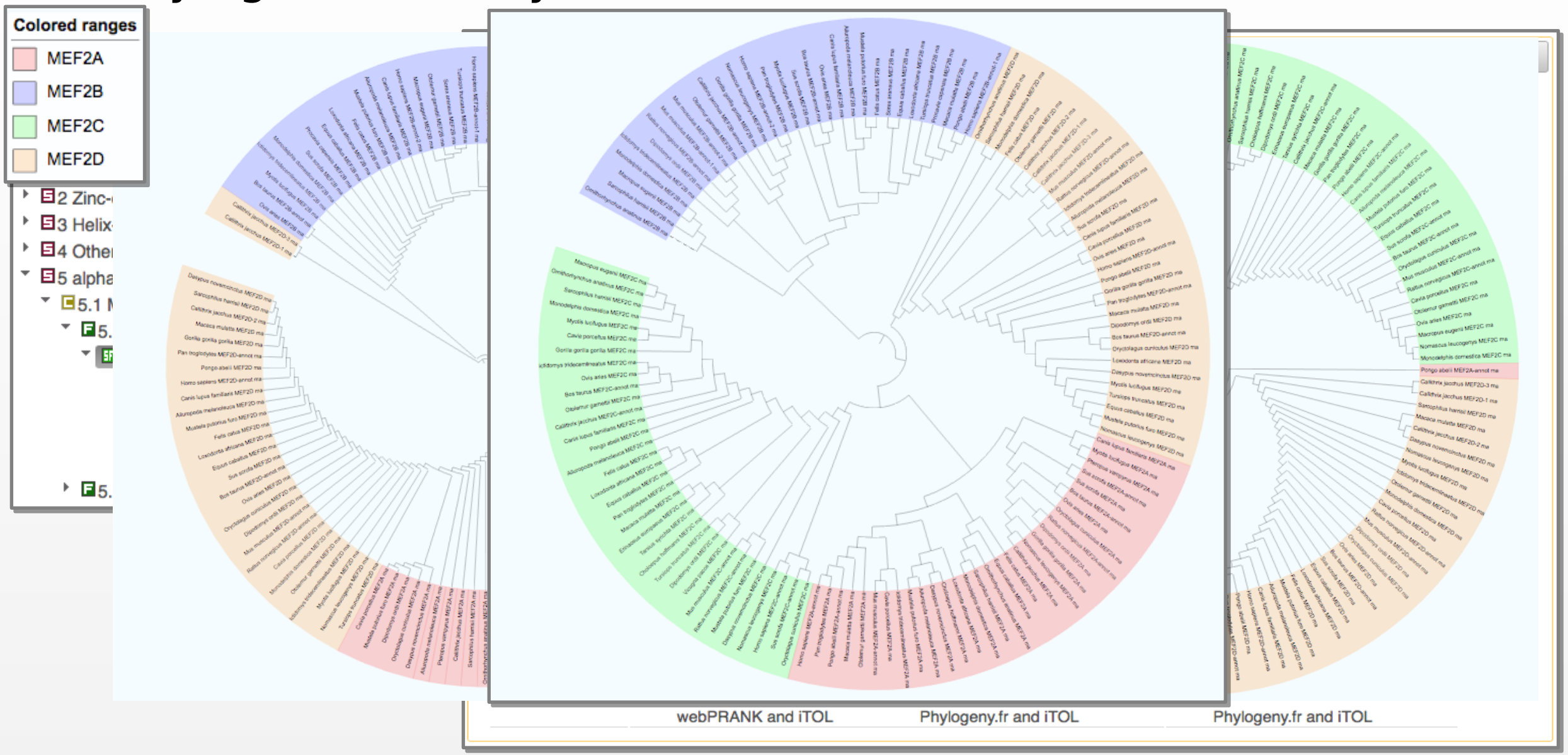
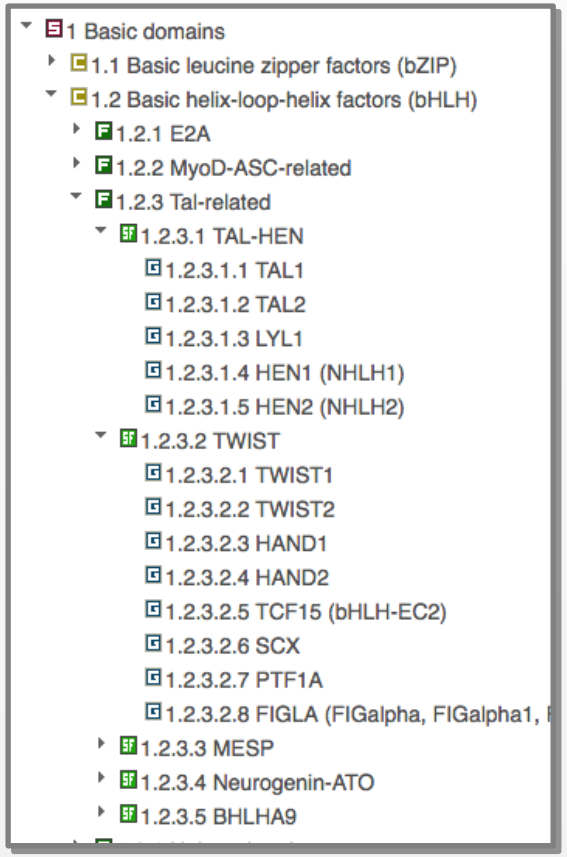
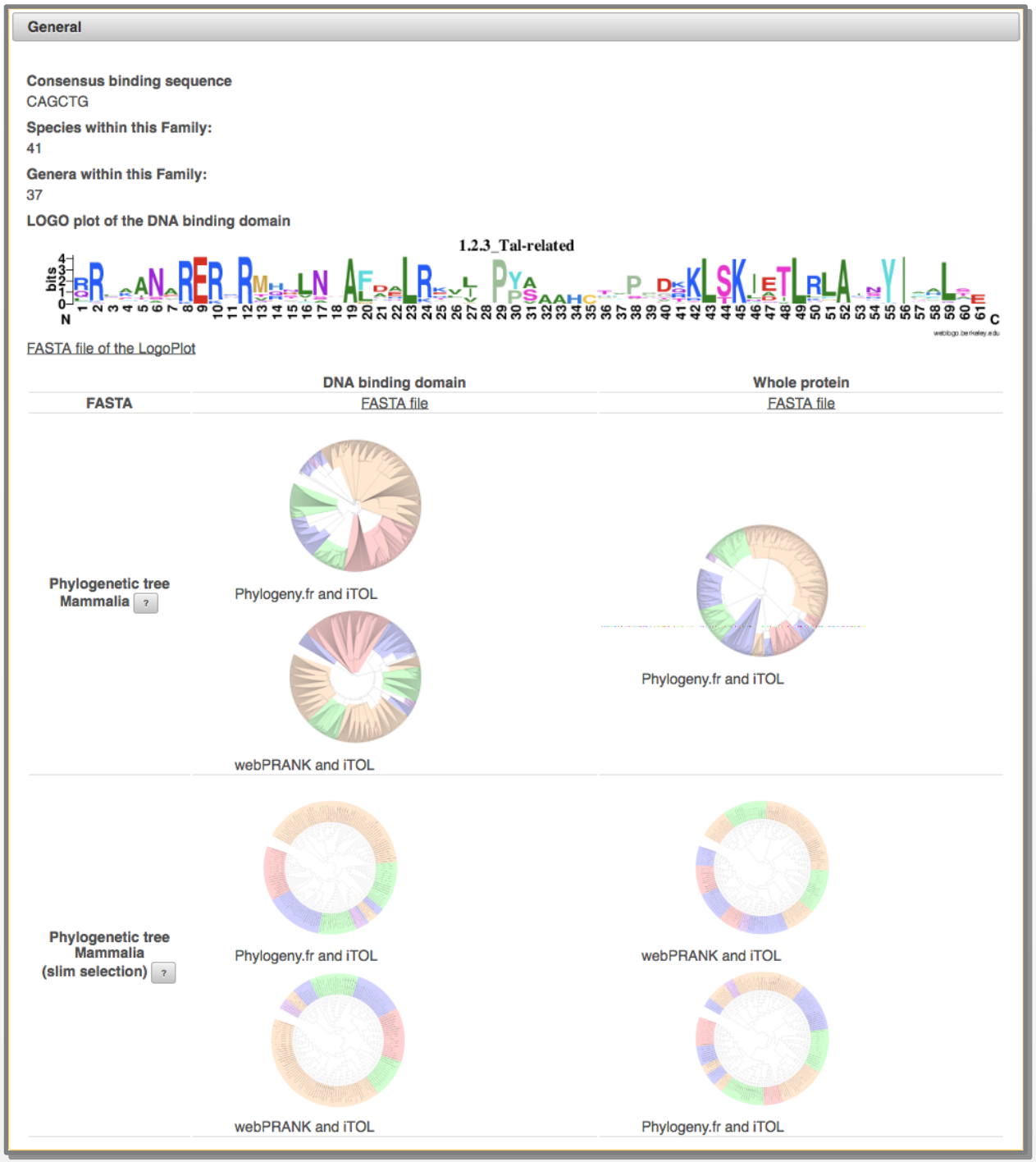


Upstream nodes

- Phylogenetic trees, LOGO plot combined from the lower level
- Slim selection to control amount data



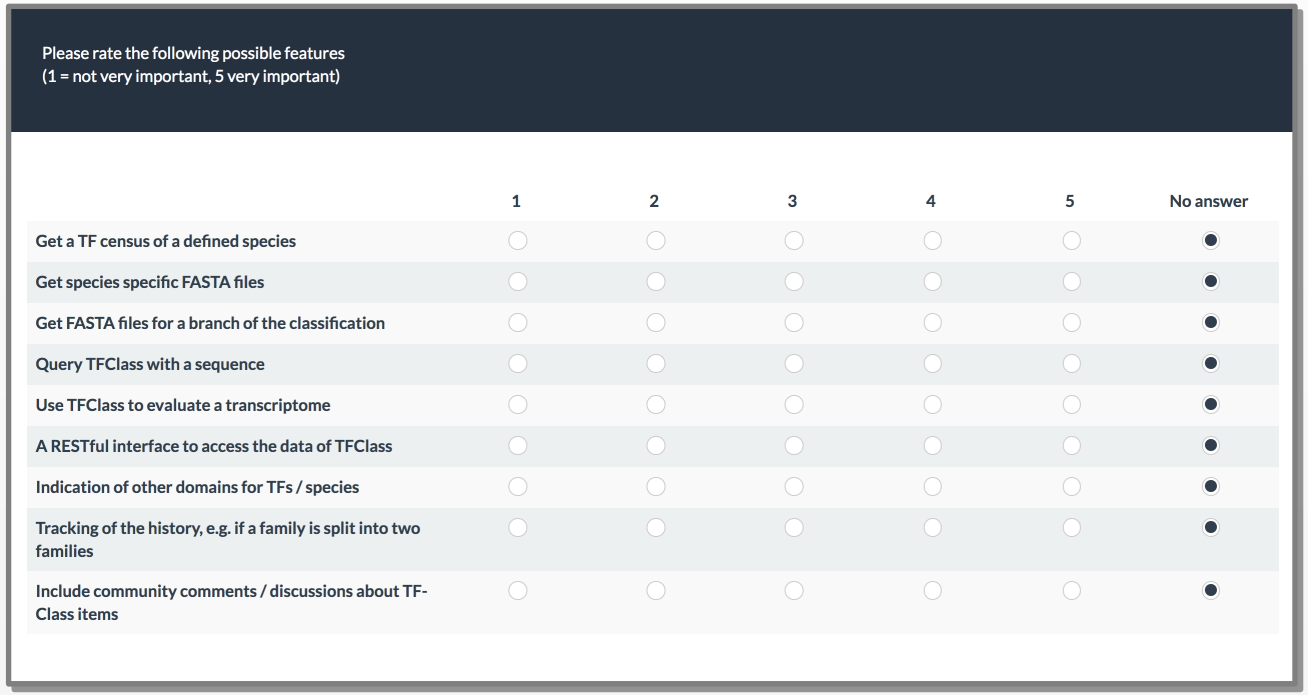


Future plans

- Recent publications:
  Wingender et al. Nucleic Acids Res
  (2013, 2015, 2018)

- Adding more species
- Data based backend
- More functions

- Funding to achieve
  - long time operating
  - new features
  ␣ Please fill out the survey



Please rate the following possible features
(1 = not very important, 5 very important)

	1	2	3	4	5	No answer
Get a TF census of a defined species	○	○	○	○	○	●
Get species specific FASTA files	○	○	○	○	○	●
Get FASTA files for a branch of the classification	○	○	○	○	○	●
Query TFClass with a sequence	○	○	○	○	○	●
Use TFClass to evaluate a transcriptome	○	○	○	○	○	●
A RESTful interface to access the data of TFClass	○	○	○	○	○	●
Indication of other domains for TFs / species	○	○	○	○	○	●
Tracking of the history, e.g. if a family is split into two families	○	○	○	○	○	●
Include community comments / discussions about TF-Class items	○	○	○	○	○	●

- http://tfclass.bioinf.med.uni-goettingen.de

Thank you!

TFClass is available at
http://tfclass.bioinf.med.uni-goettingen.de