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Distal cis-regulatory elements regulate tissue-specific water-deficit response

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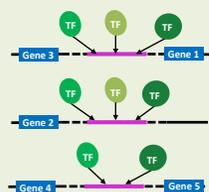
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Introduction

Understanding the molecular bases of crops response to environment is crucial for adapting cultivated varieties to climate change. Crops response to environment is mainly driven by developmental modifications and determined by a complex interaction between genetic background and environment. However, these GxE interaction remain largely unknown. Distal *cis*-regulatory elements (dCRE), including enhancers and silencers, are key players in the spatio-temporal coordination of gene expression during development and in response to environment. They activate complex genome-wide regulatory networks. While annotating dCRE in a genome is now largely feasible, identifying the target genes of these elements in non-model species is challenging. Functional biology experiments are costly, and dCRE can target different genes in different cell types, and not necessarily the closest genes. For these reasons, the contribution of dCRE-articulated regulatory networks to crops response to the environment remains poorly understood. **Here we aim to address two questions: (1) What role plays the dCRE in the regulating gene expression in response to water deficit in crops? (2) Are the regulatory networks of some tissues more impacted by water deficit than others?** Using maize and its response to water deficit as a model, we investigate the extent of the gene regulatory network rewiring in response to environment in several tissues. We first generated RNA-Seq data from seven tissues of the inbred line B73 grown in two watering conditions. Using the NetZoo software suite, we integrated these data with genomic and DNA methylation data to model the tissue- and condition-specific regulatory networks between transcription factors binding the dCRE and their potential target genes.

Methods

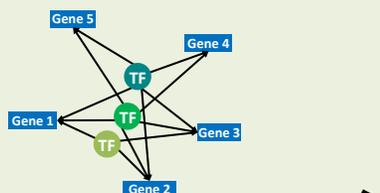
Annotation of TFBS & Potential target genes



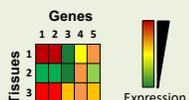
Gene Potential target genes
Gene Non-target genes
Gene True target genes

TFBS = transcription factor binding sites

« Prior » GRN



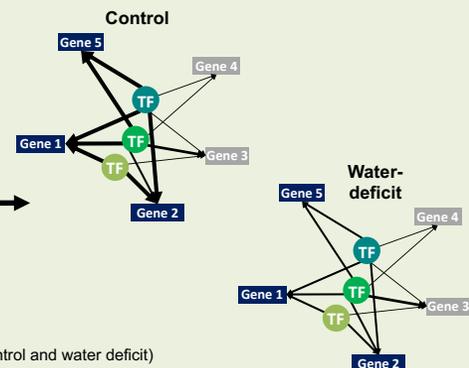
Co-expression data



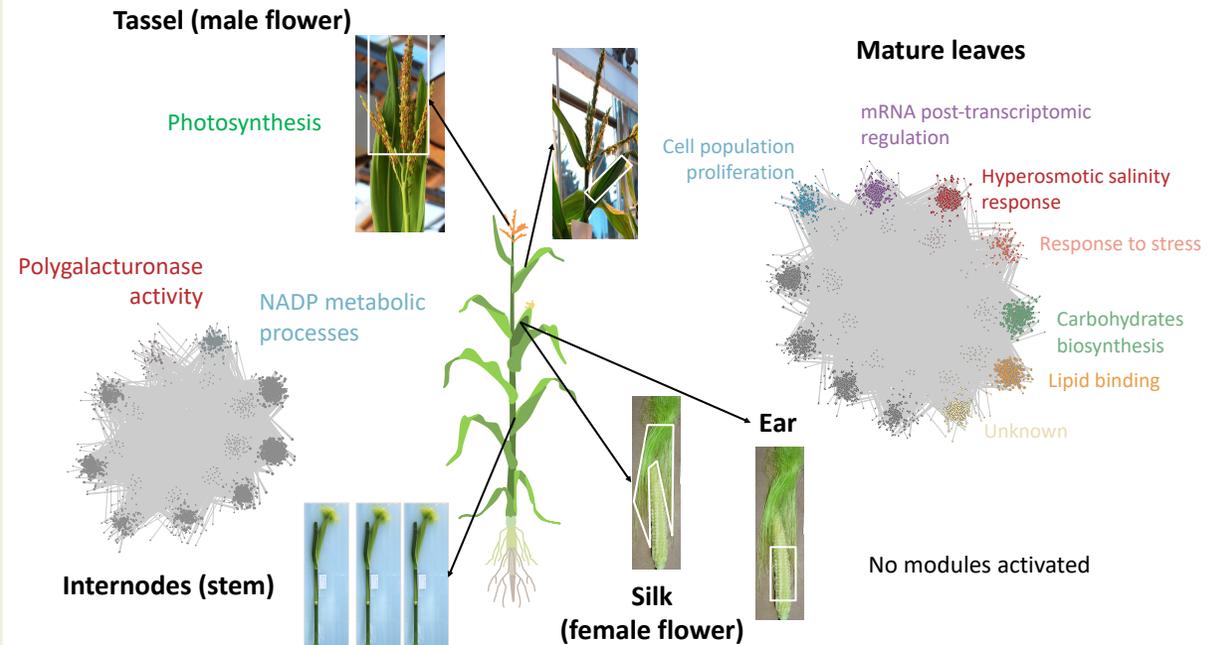
B73 (model maize line)

- ✓ 7 tissues
- ✓ 2 watering condition (control and water deficit)

Tissue-specific networks (NETZOOPIY - <https://netzoo.github.io/>)



Results



Conclusions

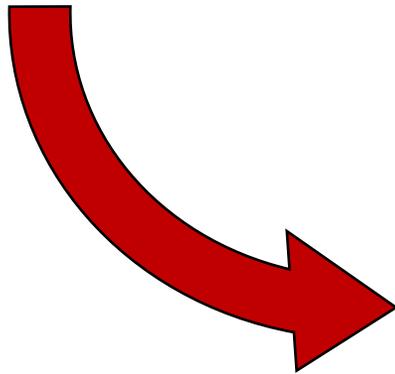
We show that gene regulatory network inference methods are efficient tools to identify target genes of dCRE involved in maize response to water deficit. This varies across tissues in terms of both magnitude of regulatory network rewiring and categories of biological functions activated. Maize response to water deficit involves, at the molecular level, a profound rewiring of the gene regulatory networks articulated by dCRE. Mutation at these elements could thus play a crucial role in determining tolerance to water deficit in maize.

Fundings



Introduction

Climate change

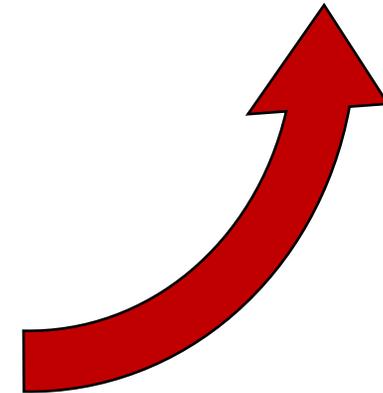


Dry maize field
Mid-August 2022, France



Yield loss:

- **Smaller Crops**
- **Less biomass**
- **Less grain**



➤ **Slowed or stopped development**

➤ **What are the molecular bases of this response?**



A role for distal *cis*-regulatory elements

Location of developmental QTL/GWAS



Target genes?

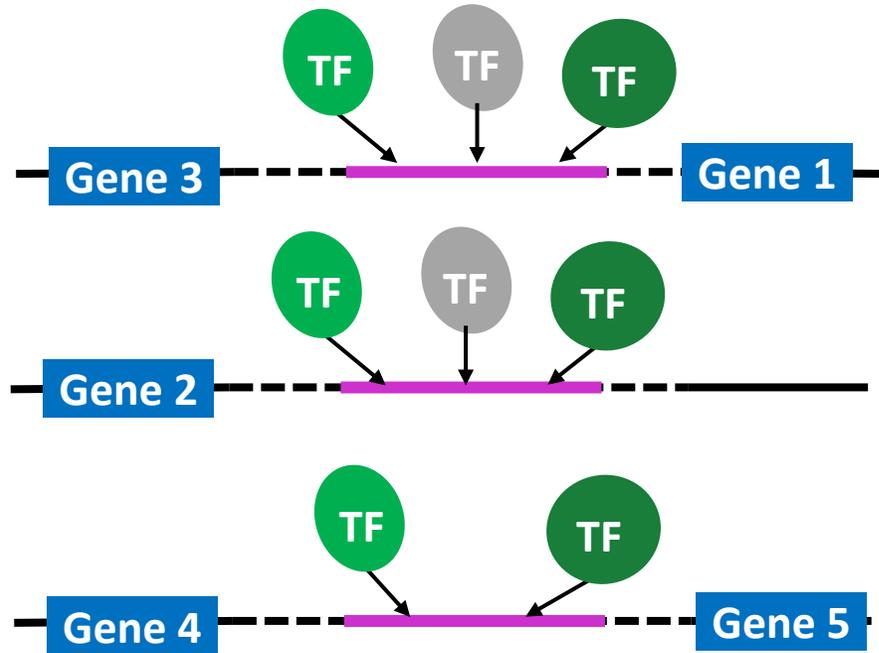
Adapted from Wallace *et al.*, *PLoS Genetics*, 2014

- What is the role of dCRE in regulating crops gene expression in response to water deficit?

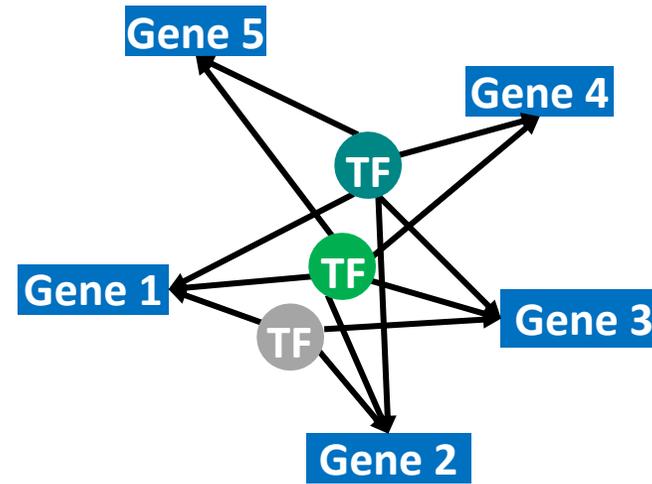


Inferring tissue- and condition-specific regulatory networks

Annotation of TFBS & Potential target genes



« Prior » GRN



Gene Potential target genes

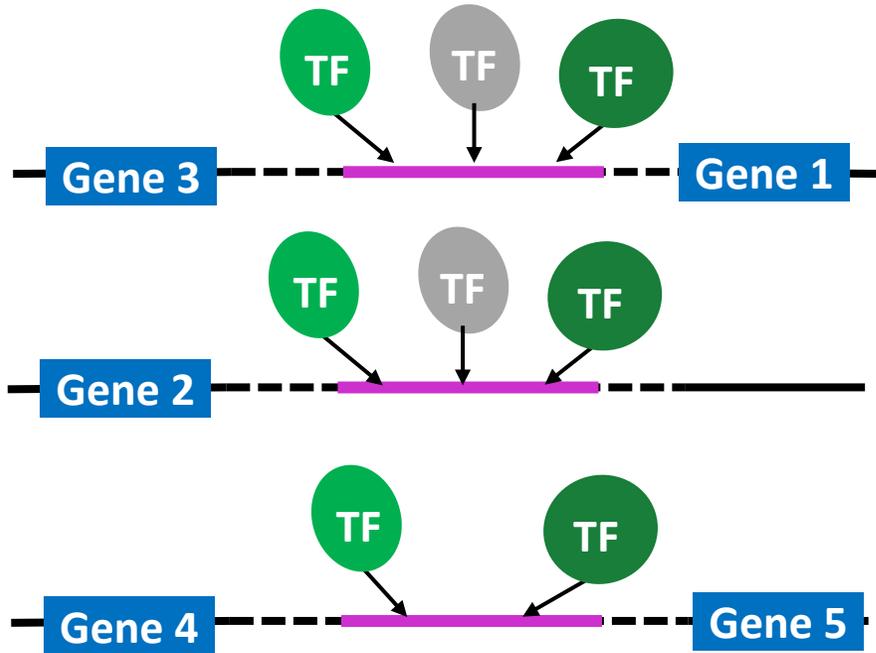
Gene Non-target genes

Gene True target genes



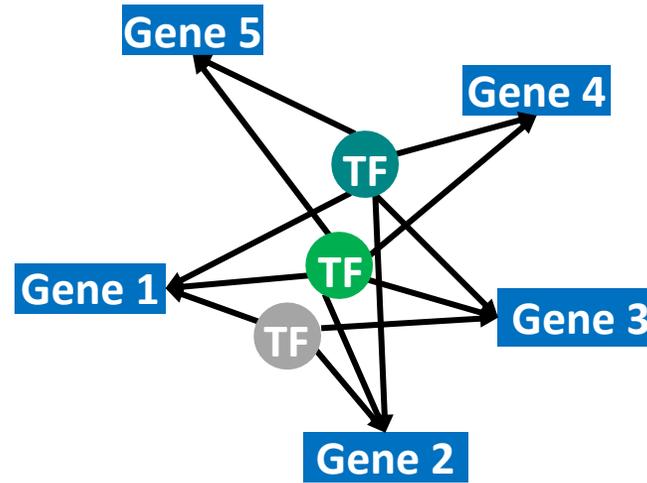
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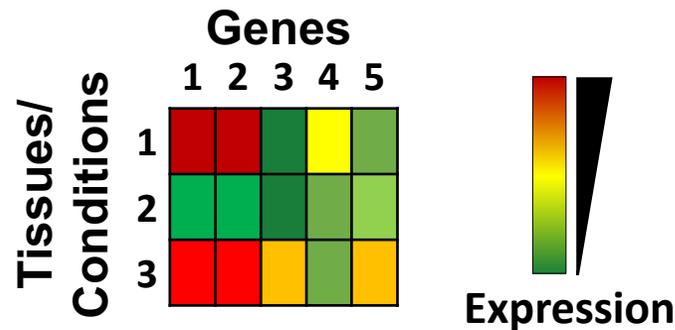


- Gene** Potential target genes
- Gene** Non-target genes
- Gene** True target genes

« Prior » GRN



Co-expression data

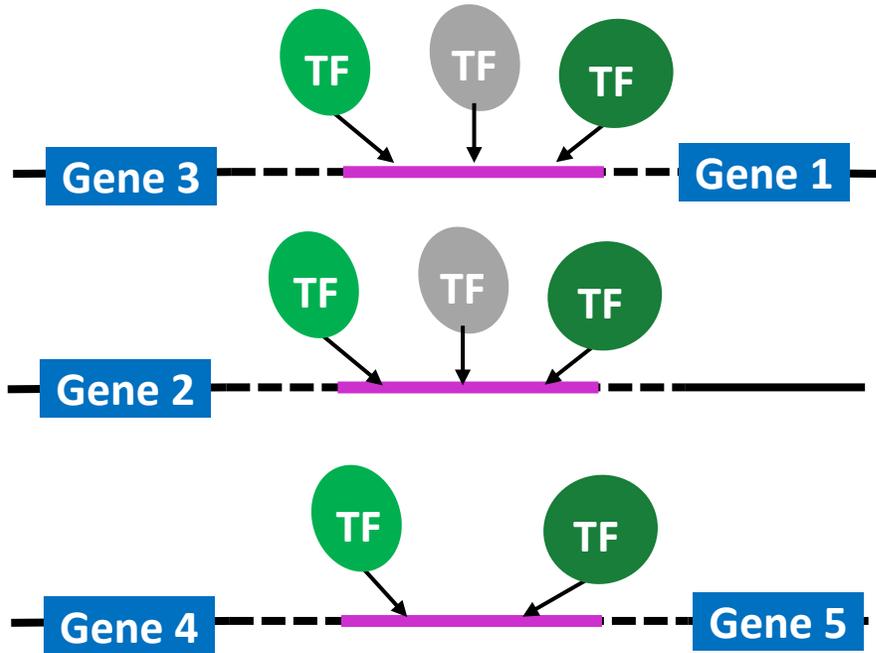


[\(https://netzoo.github.io/\)](https://netzoo.github.io/)



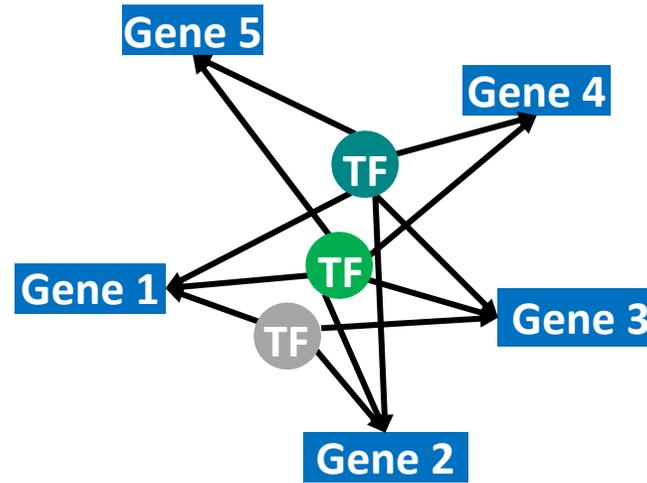
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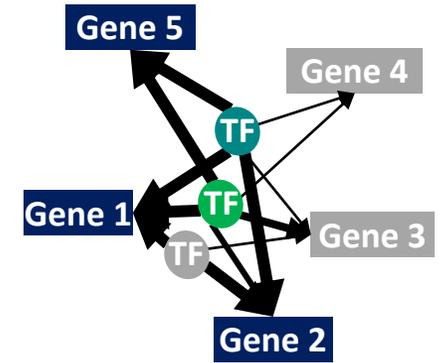
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« Prior » GRN



Tissue/Condition-specific networks

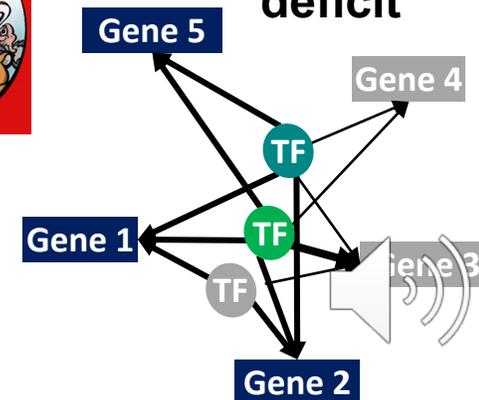
Control



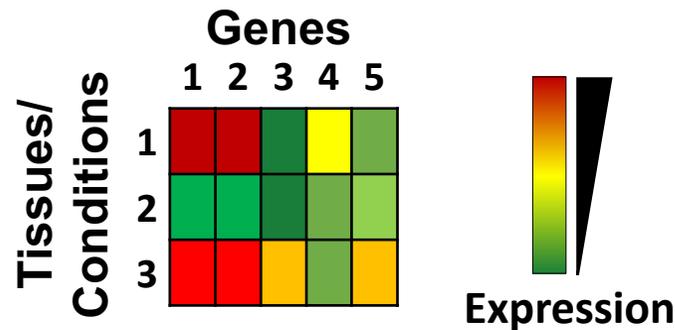
(<https://netzoo.github.io/>)



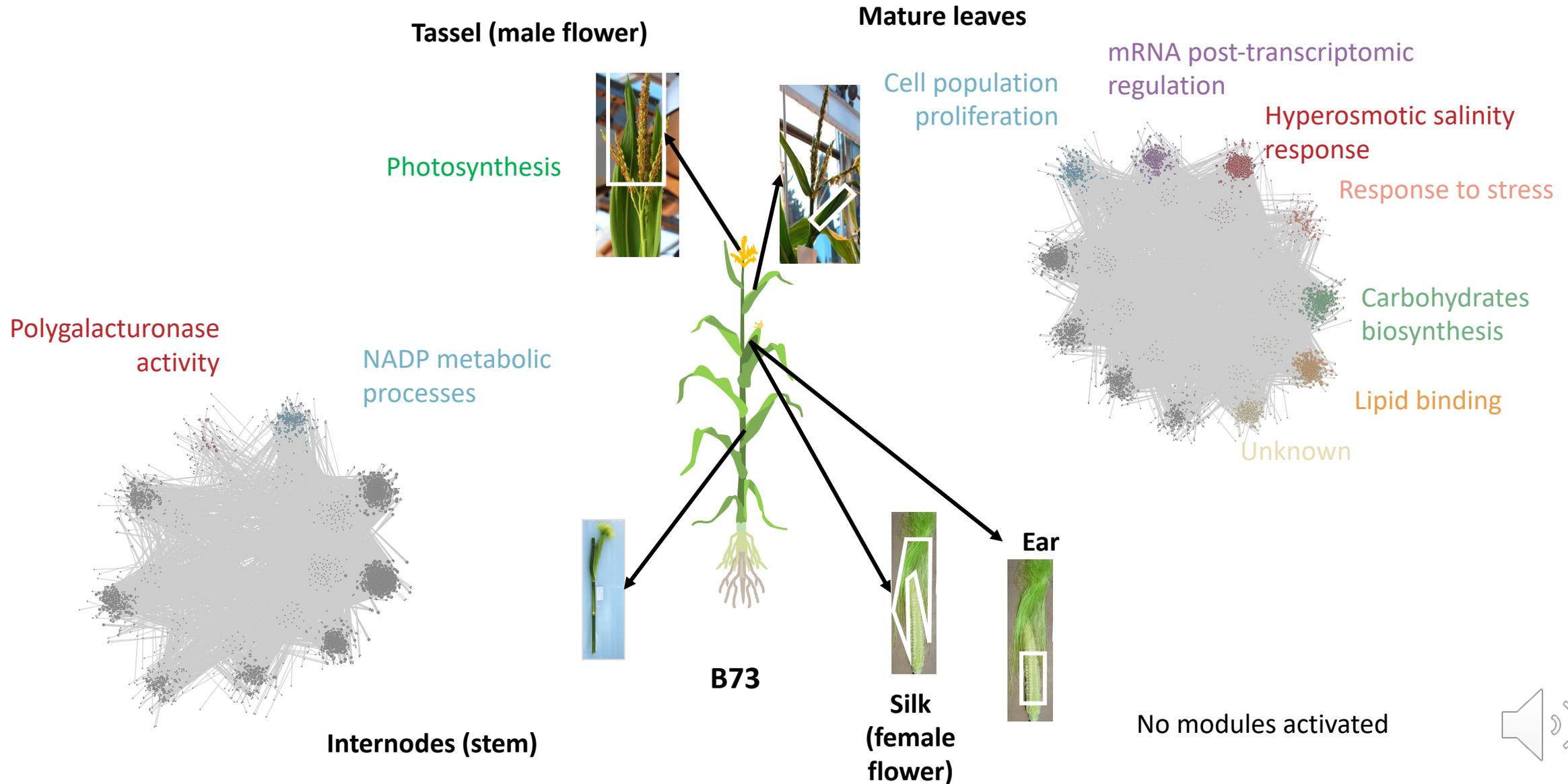
Water-deficit



Co-expression data



Tissues display widely different rewiring after water-deficit



Take-home message

- PANDA/LIONESS from the netzoo suite allows us to identify likely targets of distal *cis*-regulatory elements
- dCRE are playing an important role in rewiring the gene expression regulatory networks in response to water-deficit
- The extent of the rewiring is strongly tissue-dependent, with a strong response from leaves and internodes, and no response from ear and silks.

