

Systems Biology for wheat improvement



Grain

Spike

Leaves

5 cm

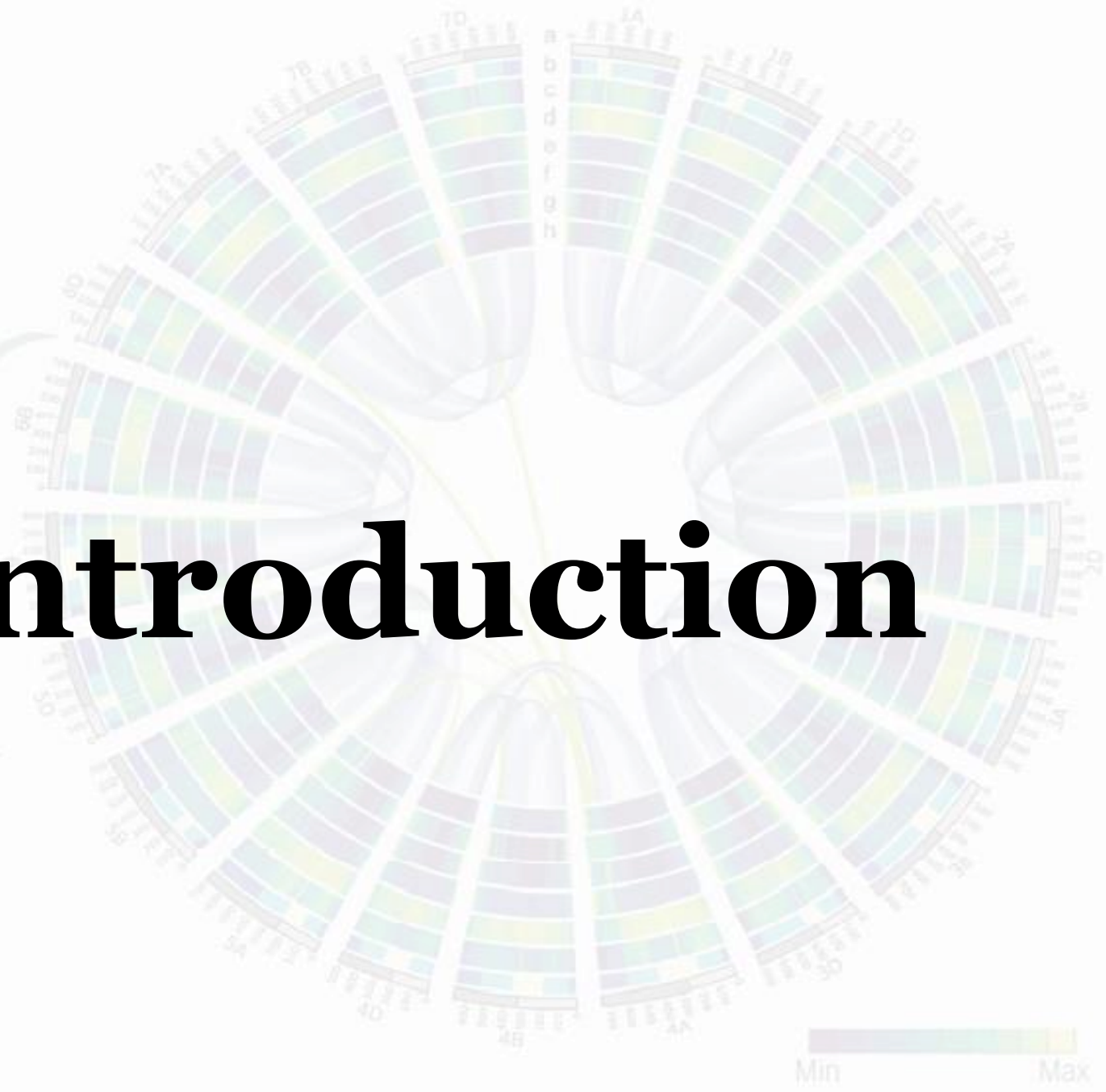
Roots

Max

IWGSC (2018)



Introduction



Wheat production has grown tremendously in the past six decades

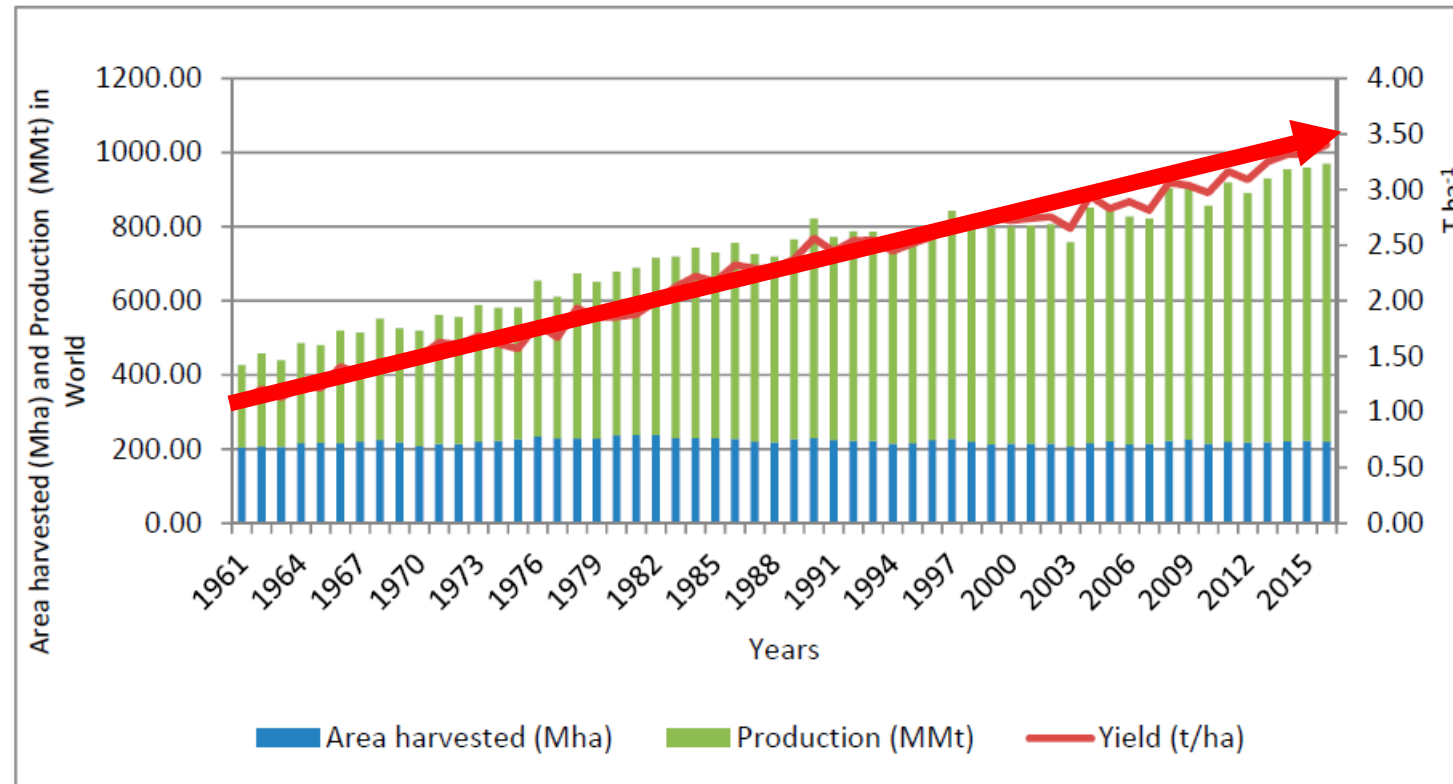
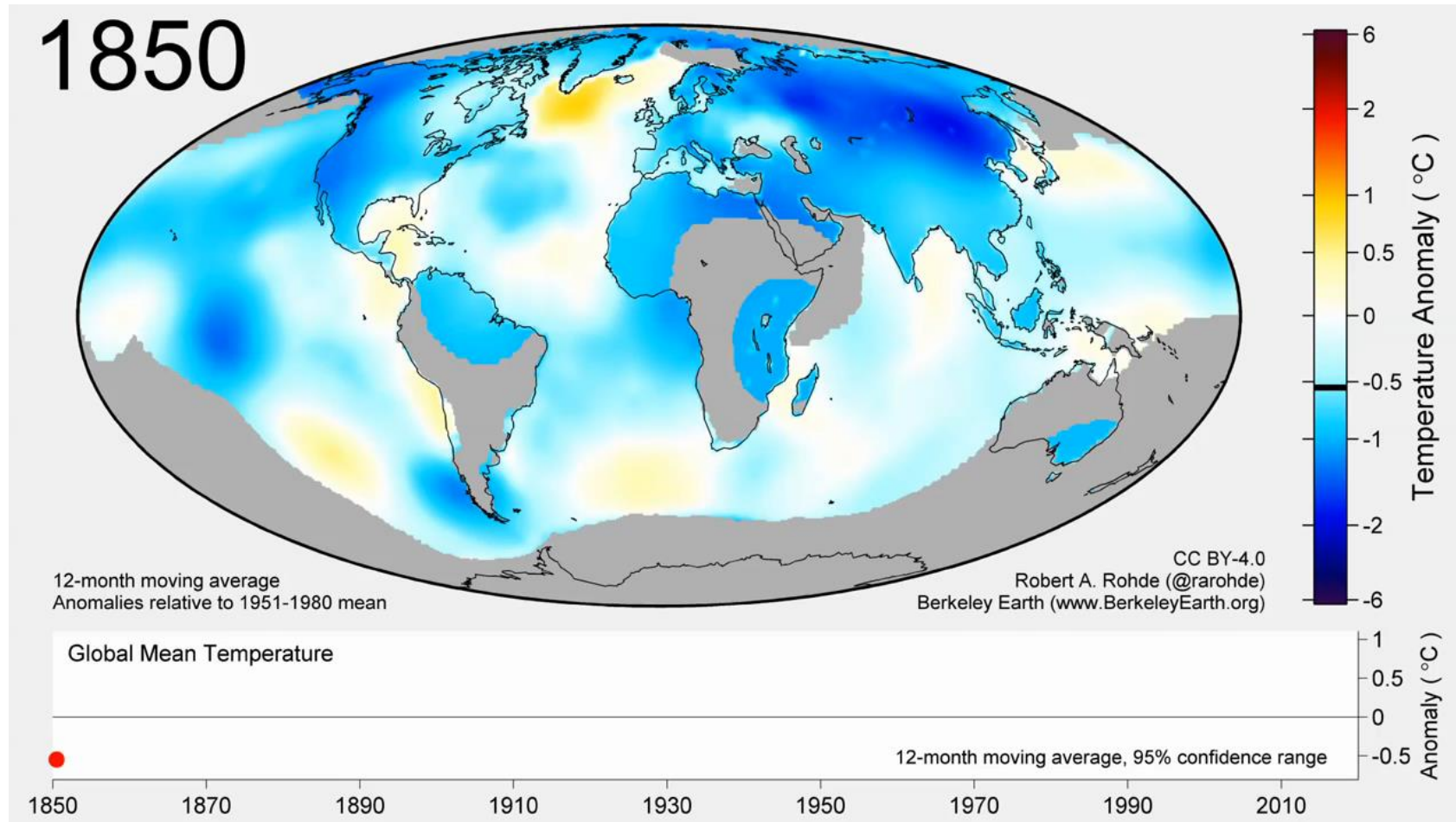


Figure 1. World wheat yield, production and area from 1961 to 2016 (FAO, 2018).

Global warming- the history of temperature anomaly between 1850 to 2018



Though most of potential wheat crop yield is lost to abiotic stresses

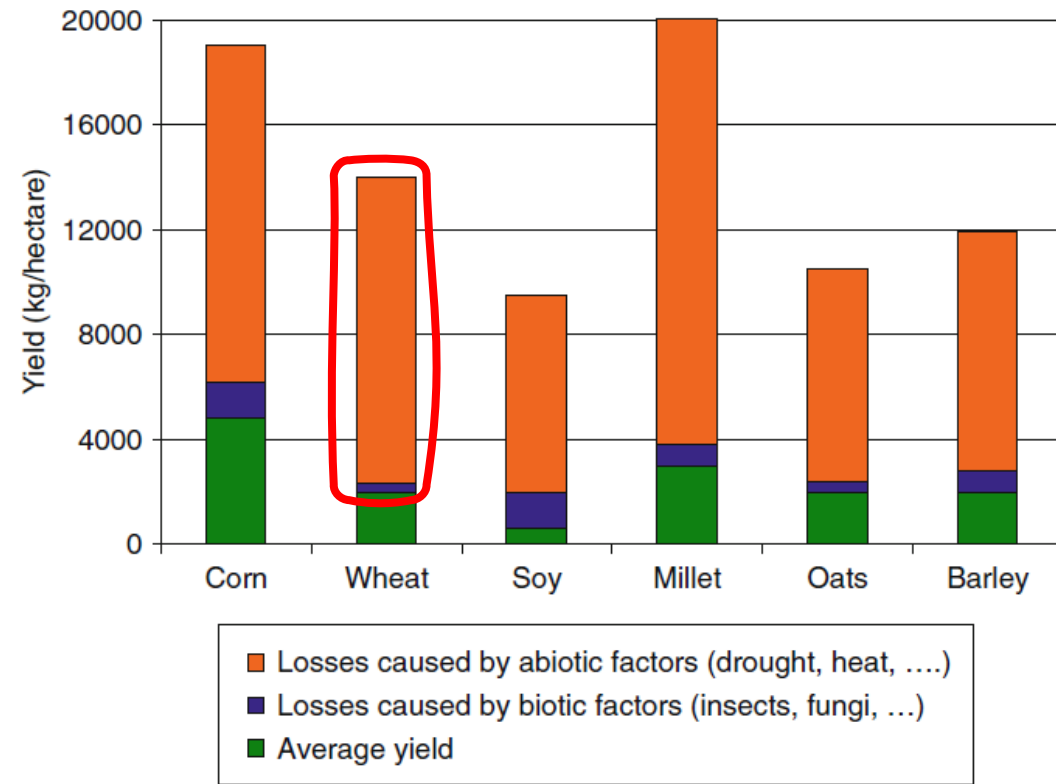
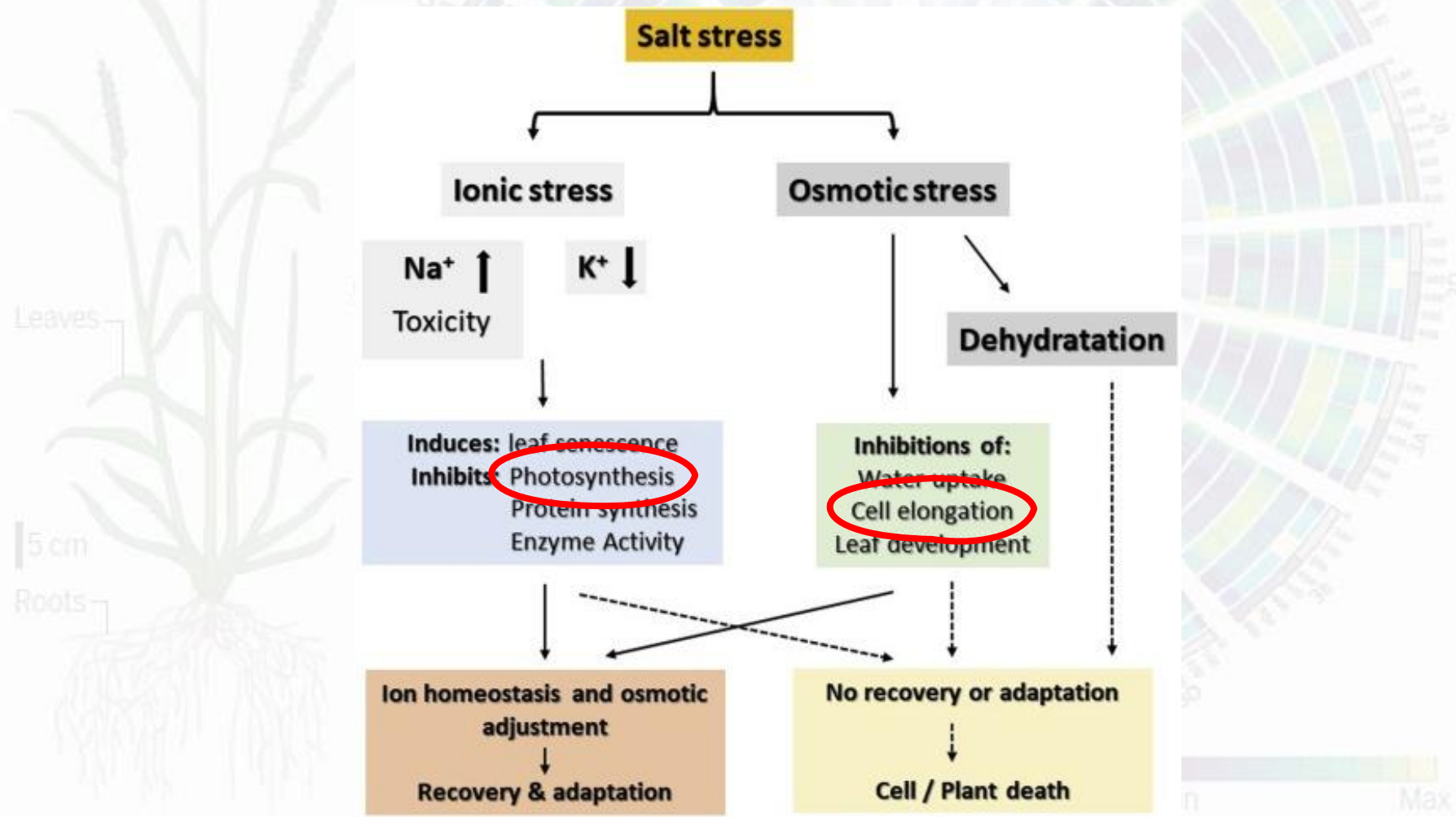
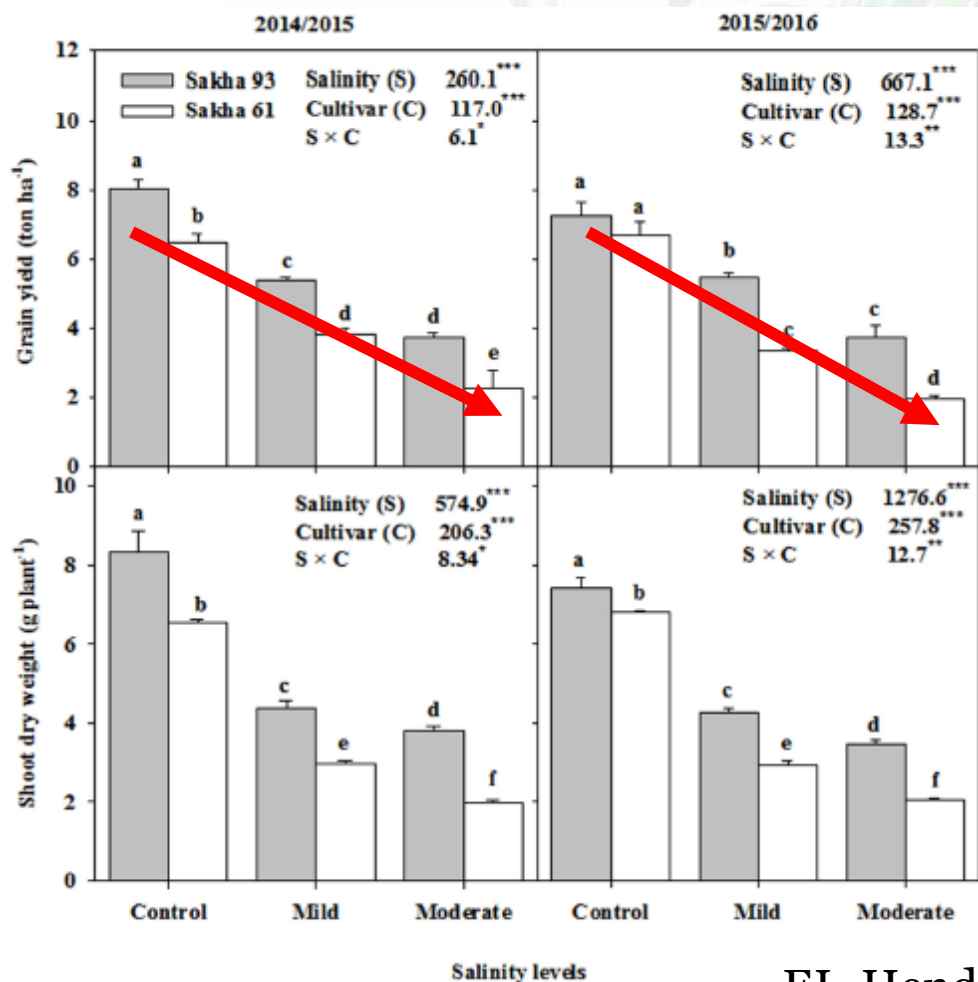


Fig. 1.7 Estimated crop losses due to biotic and abiotic stresses (Bayer Crop Science 2008, <http://www.seedquest.com/News/releases/2008/october/23973.htm>)

Drought and Salinity specifically limit photosynthesis and growth (**common and unique pathways**)



Drought and Salinity cause reduction of up to 92% and more than 50%, respectively



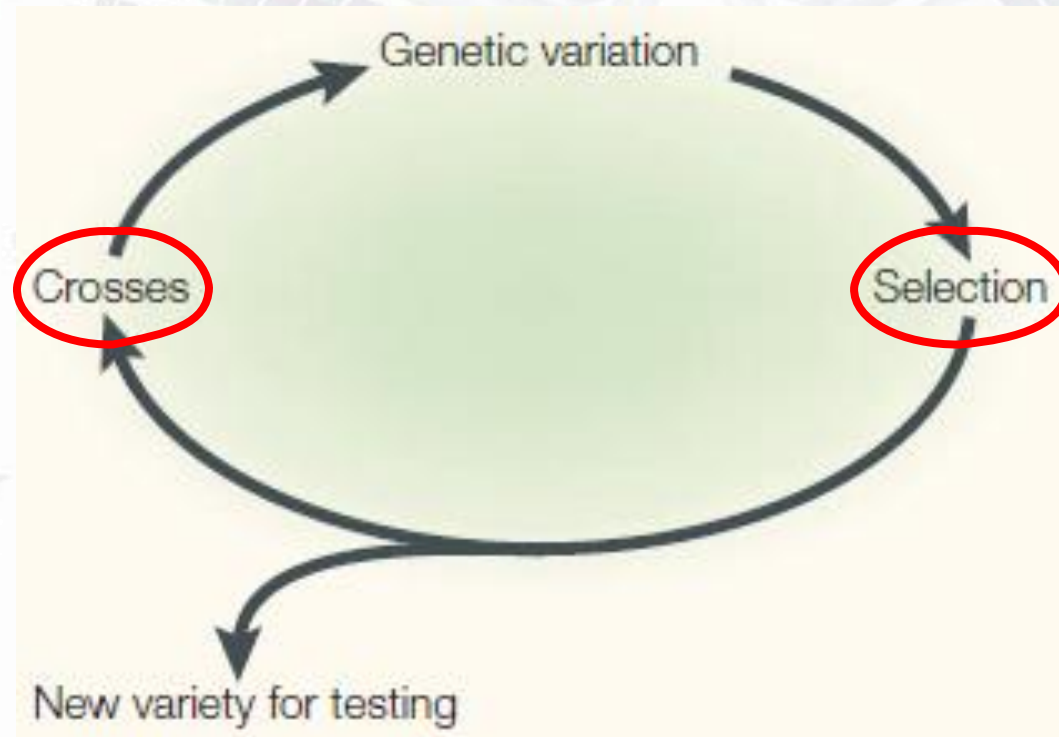
EL-Hendawy et al. (2017)

TABLE 1
Reductions in grain yield in wheat caused by drought stress

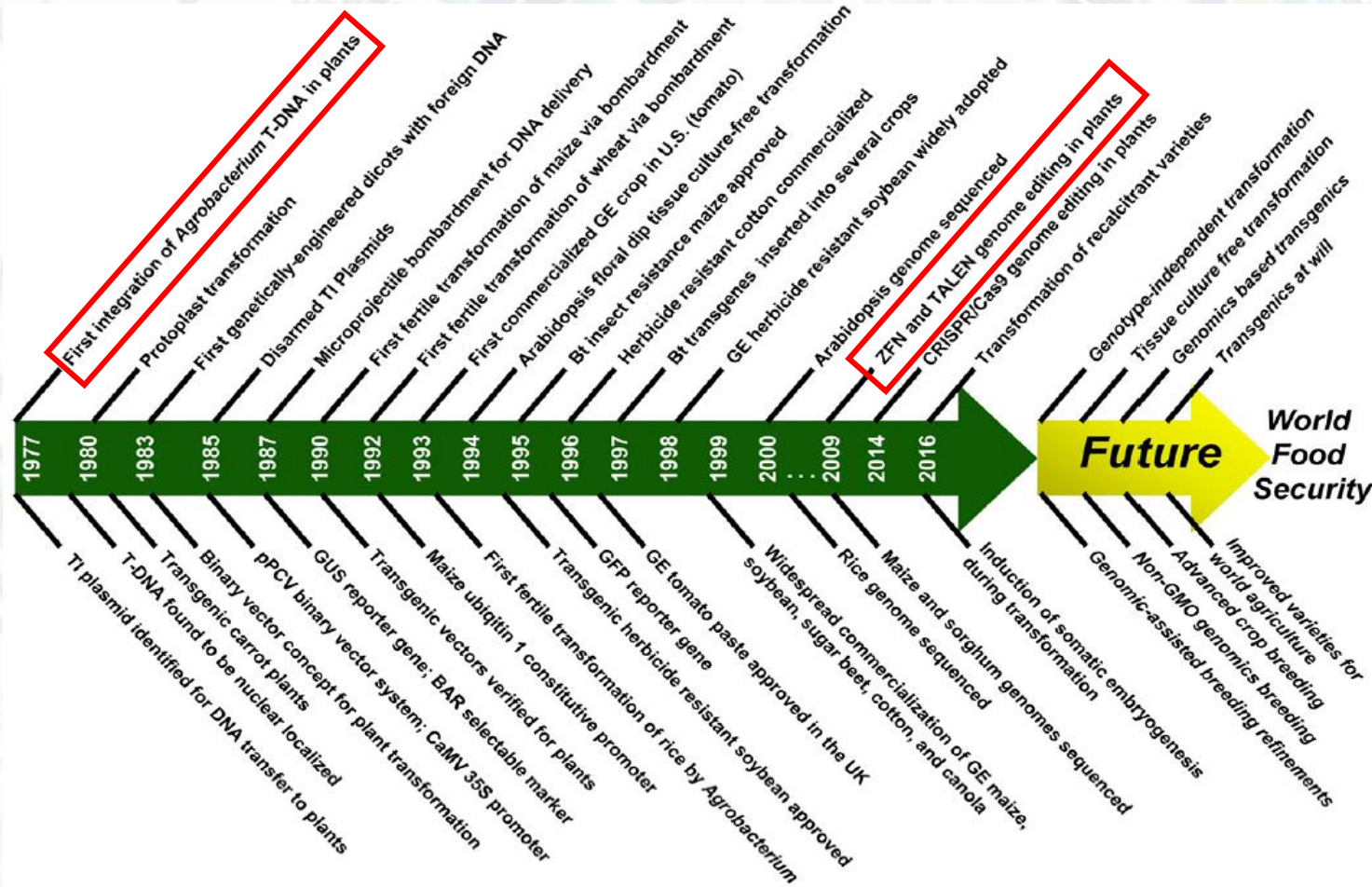
Growth stage	Stress type	Yield reduction	Reference
Booting to maturity	Severe stress	37%	Shamsi <i>et al.</i> (2010)
Booting to maturity	Severe stress	27%	Shamsi and Kobraee (2011)
Heading	Mild stress	57%	Balla <i>et al.</i> (2011)
Heading to maturity	Severe stress	44%	Prasad <i>et al.</i> (2011)
Heading and grain filling	Prolonged mild stress	58–92%	Dhanda and Sethi (2002)
Pre-anthesis	Prolonged mild stress	18–53%	Majid <i>et al.</i> (2007)
Anthesis	Mild stress	8%	Akram (2011)
Anthesis	Mild stress	19%	Sangtarash (2010)
Anthesis	Severe stress	11–39%	Jatoi <i>et al.</i> (2011)
Anthesis	Severe stress	43–51%	Gupta <i>et al.</i> (2001)
Post-anthesis	Mild stress	1–30%	Eskandari and Kazemi (2010)
Post-anthesis	Prolonged mild stress	13–38%	Majid <i>et al.</i> (2007)
Grain filling	Severe stress	9–78%	Guóth <i>et al.</i> (2009)
Grain filling to maturity	Severe stress	31%	Shamsi <i>et al.</i> (2010)
Grain filling to maturity	Severe stress	35%	Shamsi and Kobraee (2011)

Farooq et al. (2014)

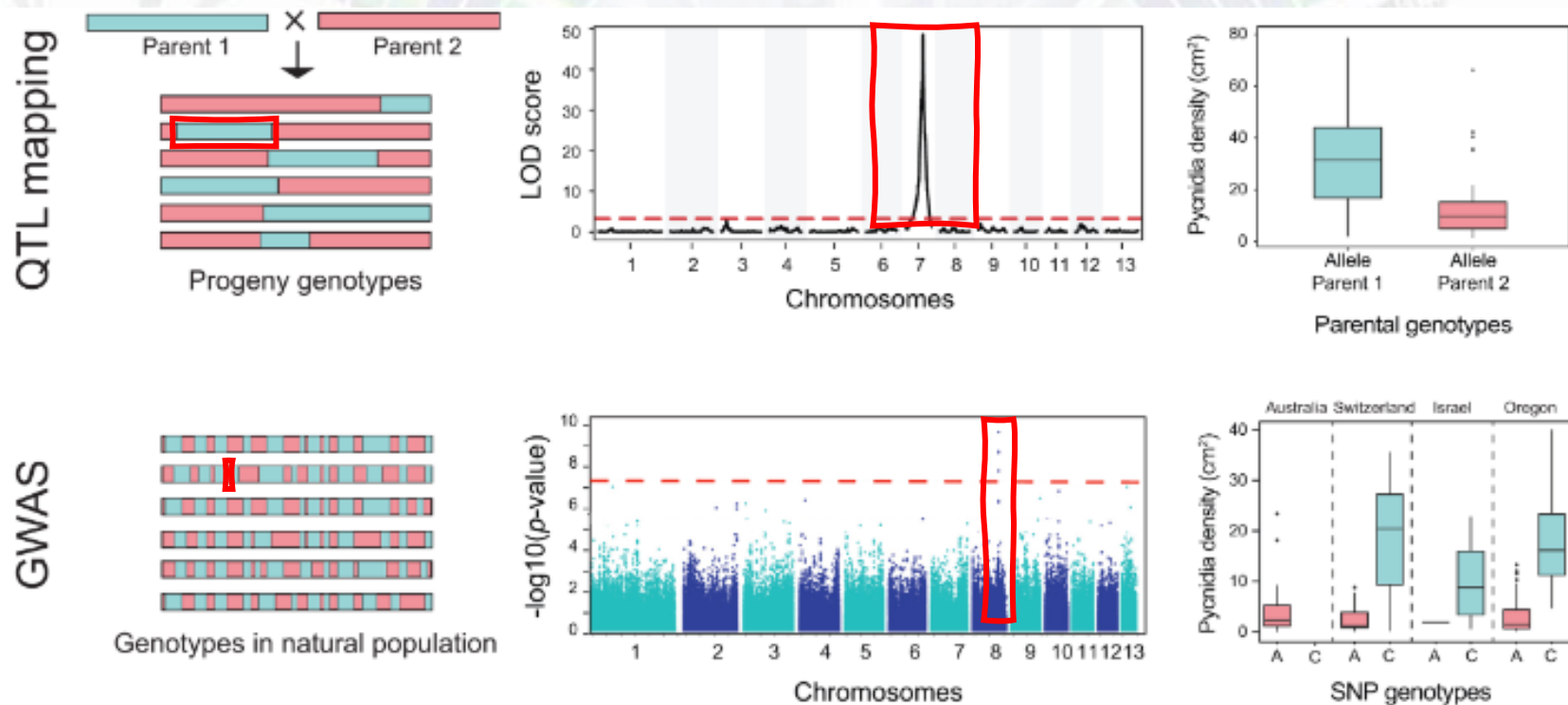
The original (conventional) breeding model for plant improvement consists of cross-breeding and selection



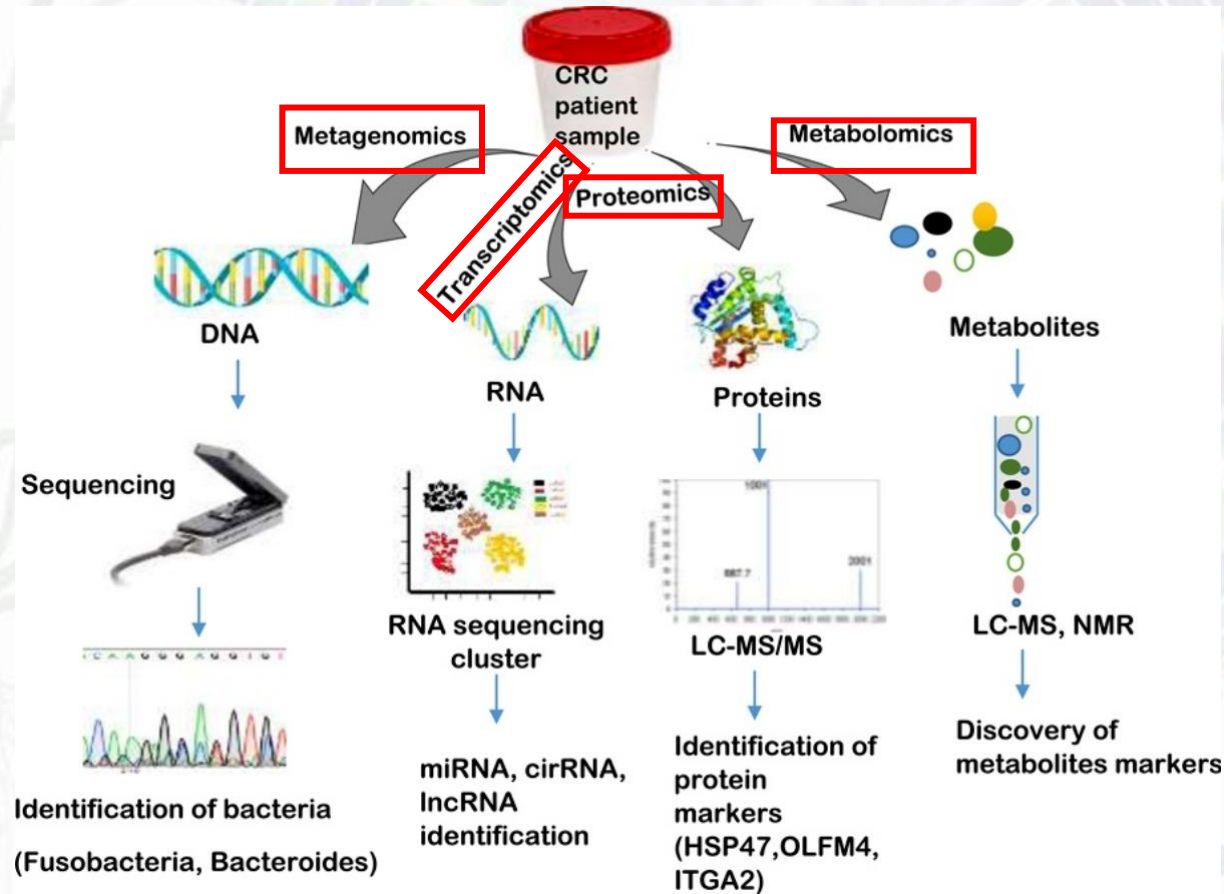
But transformation and genome editing expedited the genetic integration



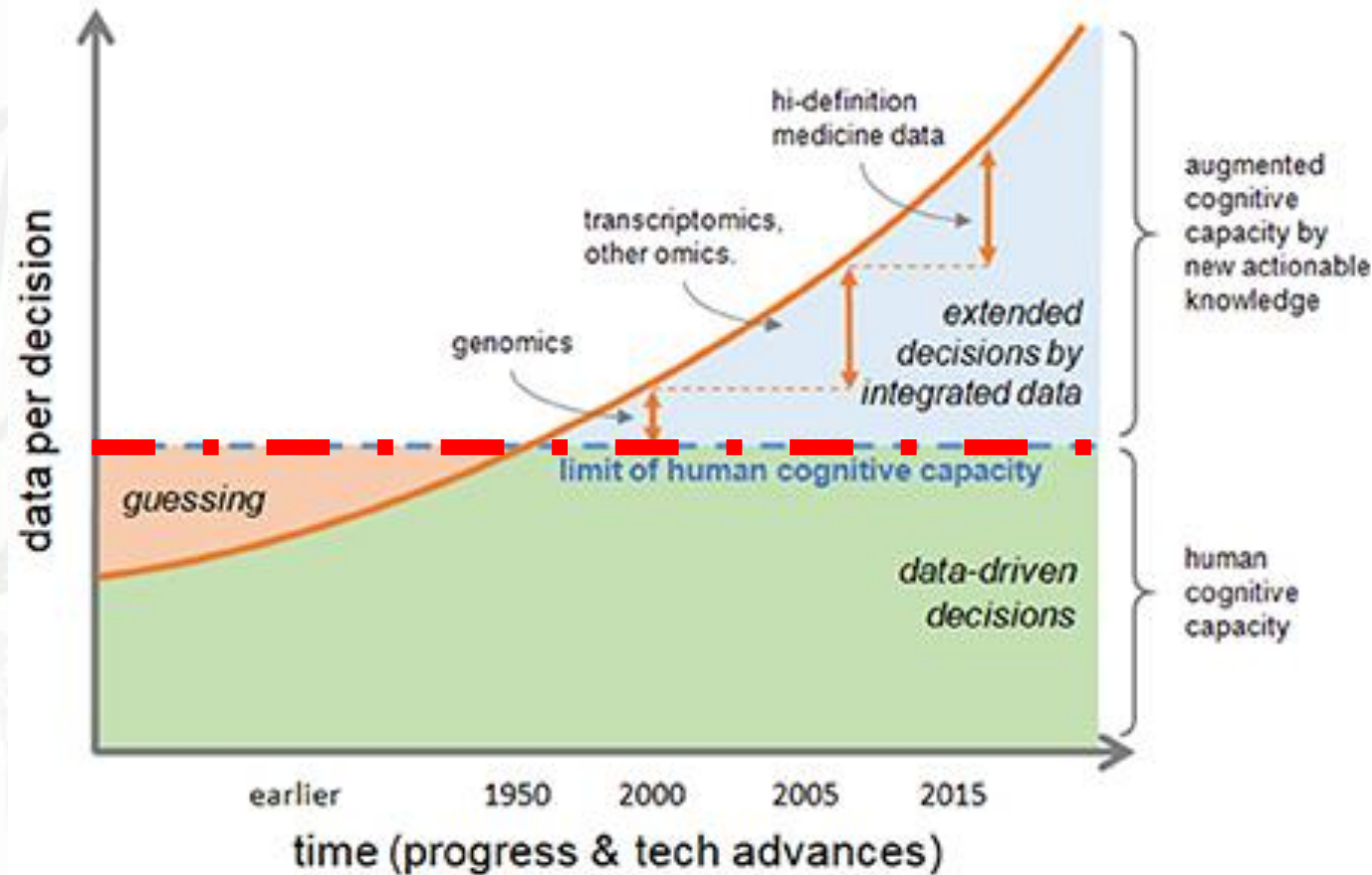
QTL mapping (fragment markers) and GWAS (SNP markers) are relatively modern tools to discover relevant genes



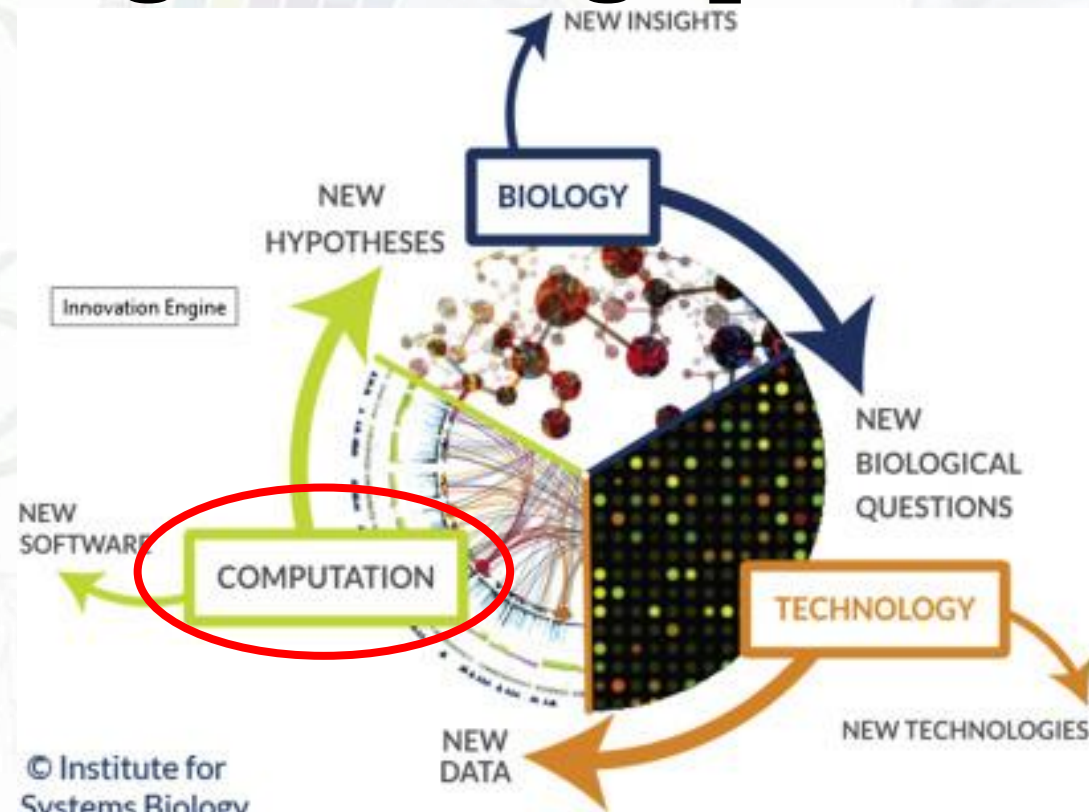
Omics recently became the newest method for relevant gene discovery



The problem is that the amount of data from Omics exceeds human capacity and requires computational methods

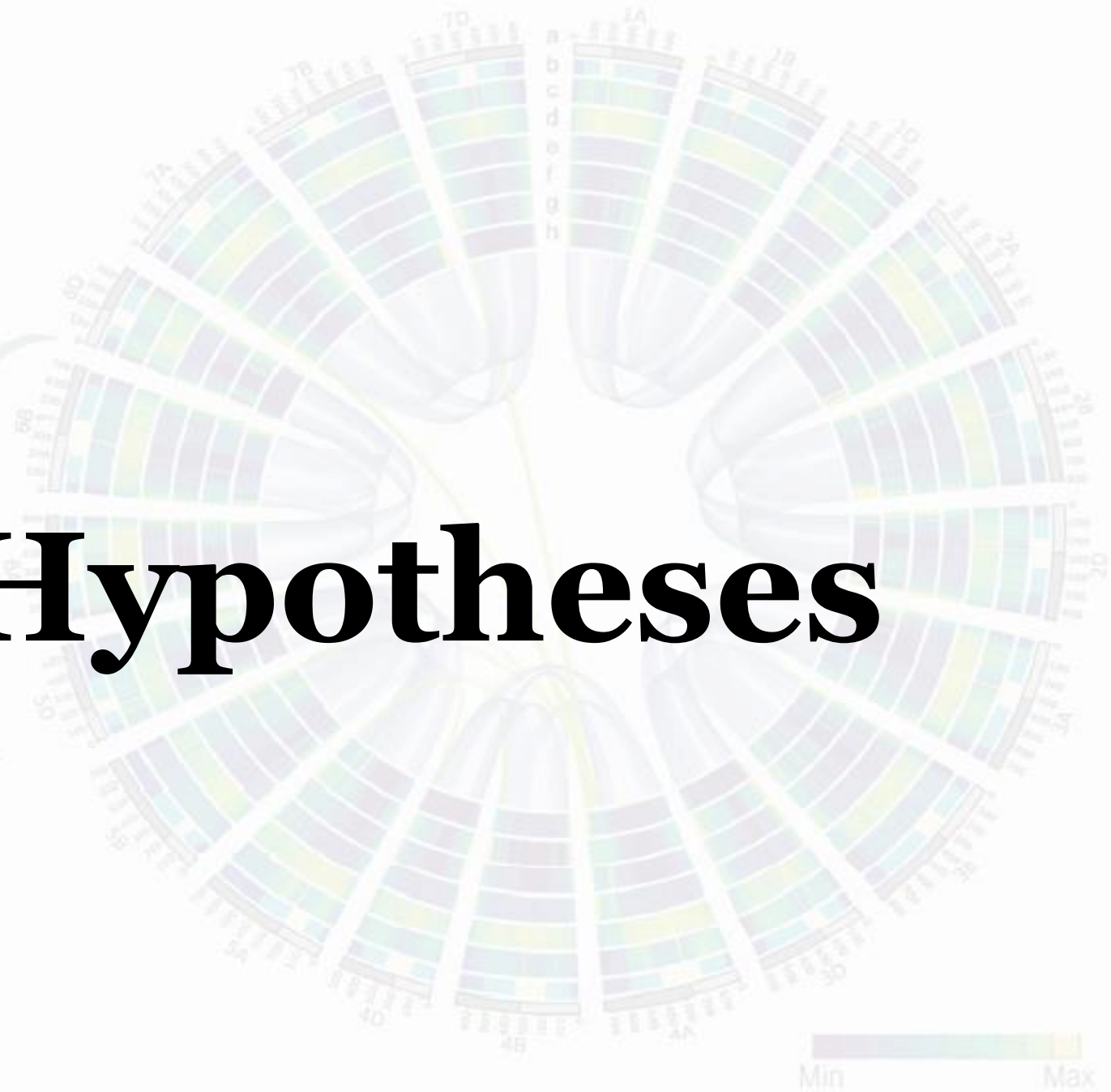


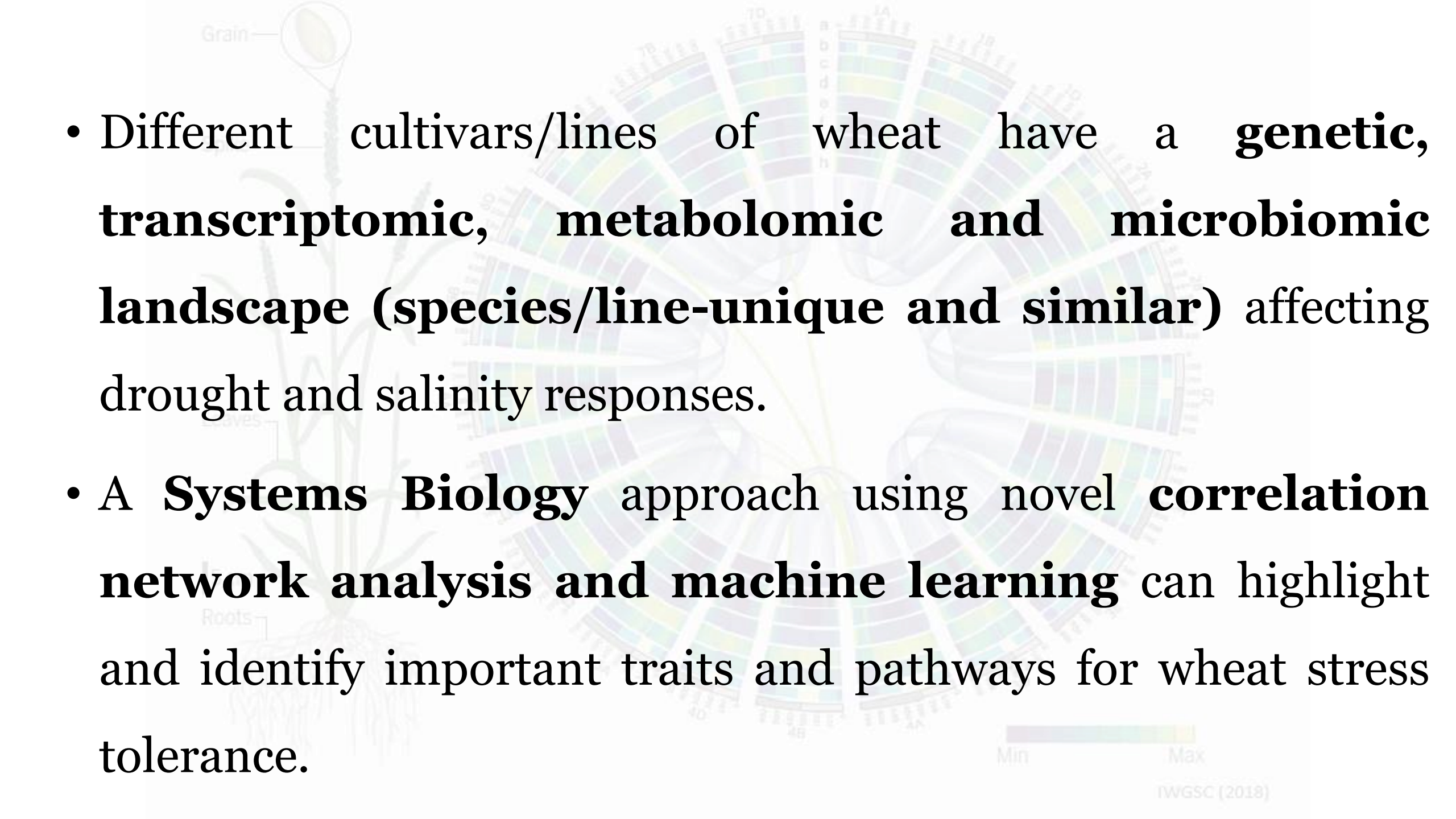
Systems biology does exactly that- the use of computational methods in deciphering biological-derived technology-enabled high-throughput data





Hypotheses



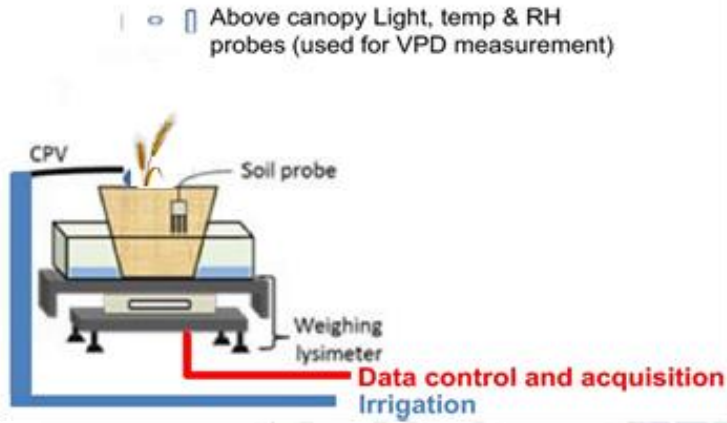
- 
- Different cultivars/lines of wheat have a **genetic, transcriptomic, metabolomic and microbiomic landscape (species/line-unique and similar)** affecting drought and salinity responses.
 - A **Systems Biology** approach using novel **correlation network analysis and machine learning** can highlight and identify important traits and pathways for wheat stress tolerance.



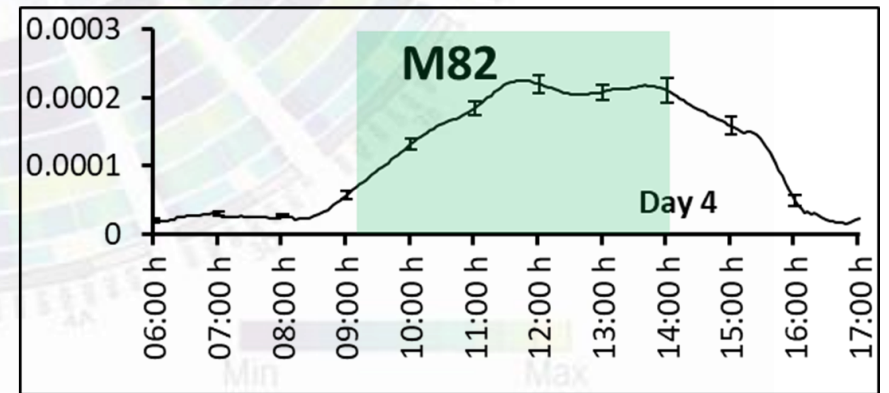
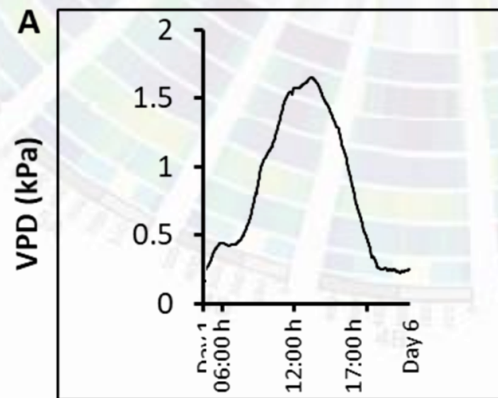
1) Whole-plant in-depth physiological growth experiments under control, drought and salinity

Whole plant physiological analysis

B



C



Whole-



Physiology (phenomics)
Biochemistry
Metabolomics
Microbiomics
Transcriptomics

Correlation Network Analysis
Machine learning

Future work (possible AI with Menachem)

experiments

Control



Drought

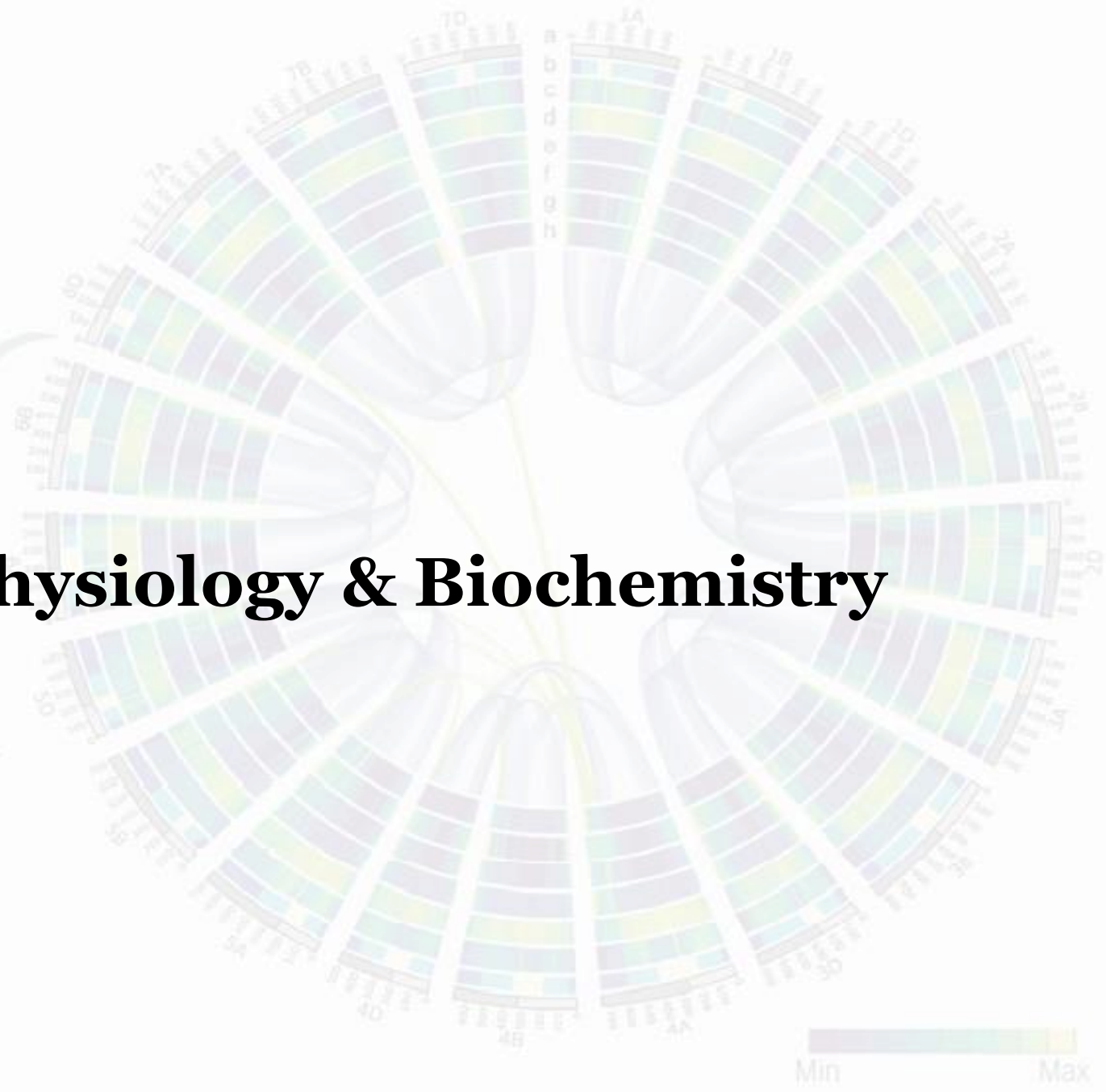


Salinity

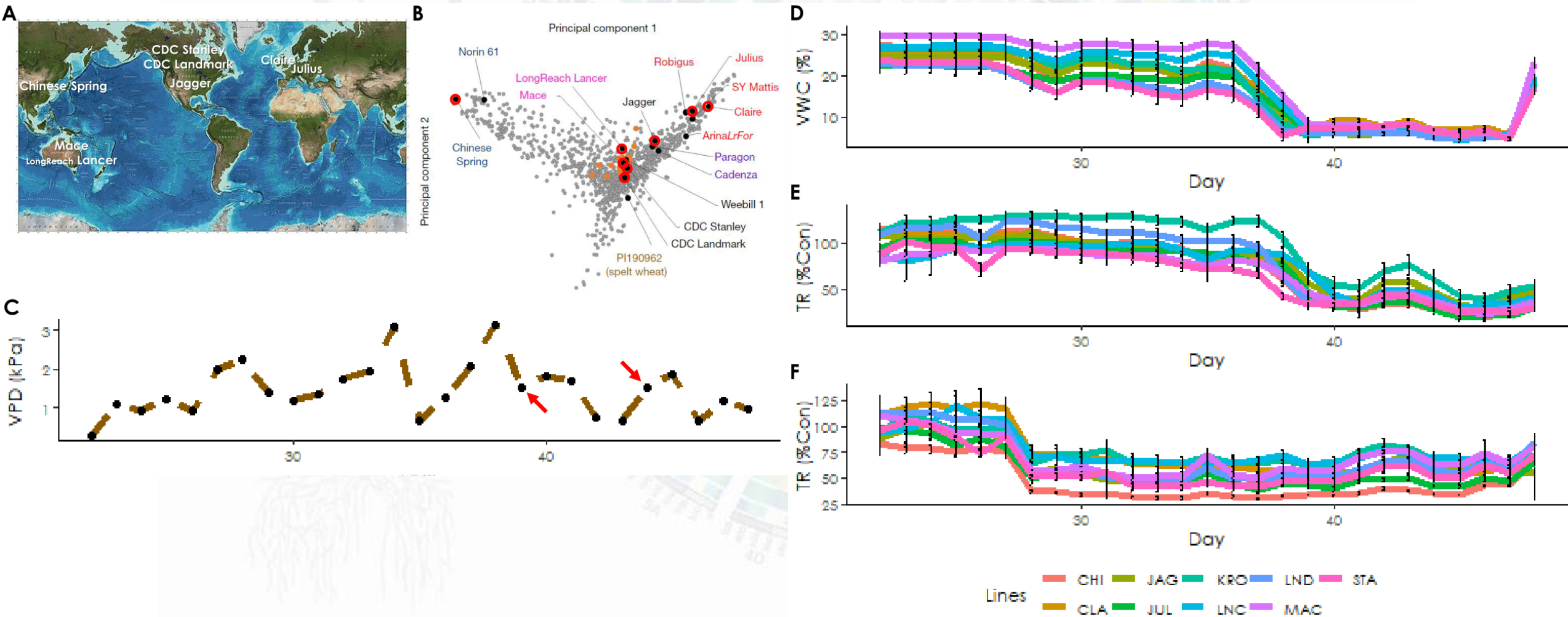


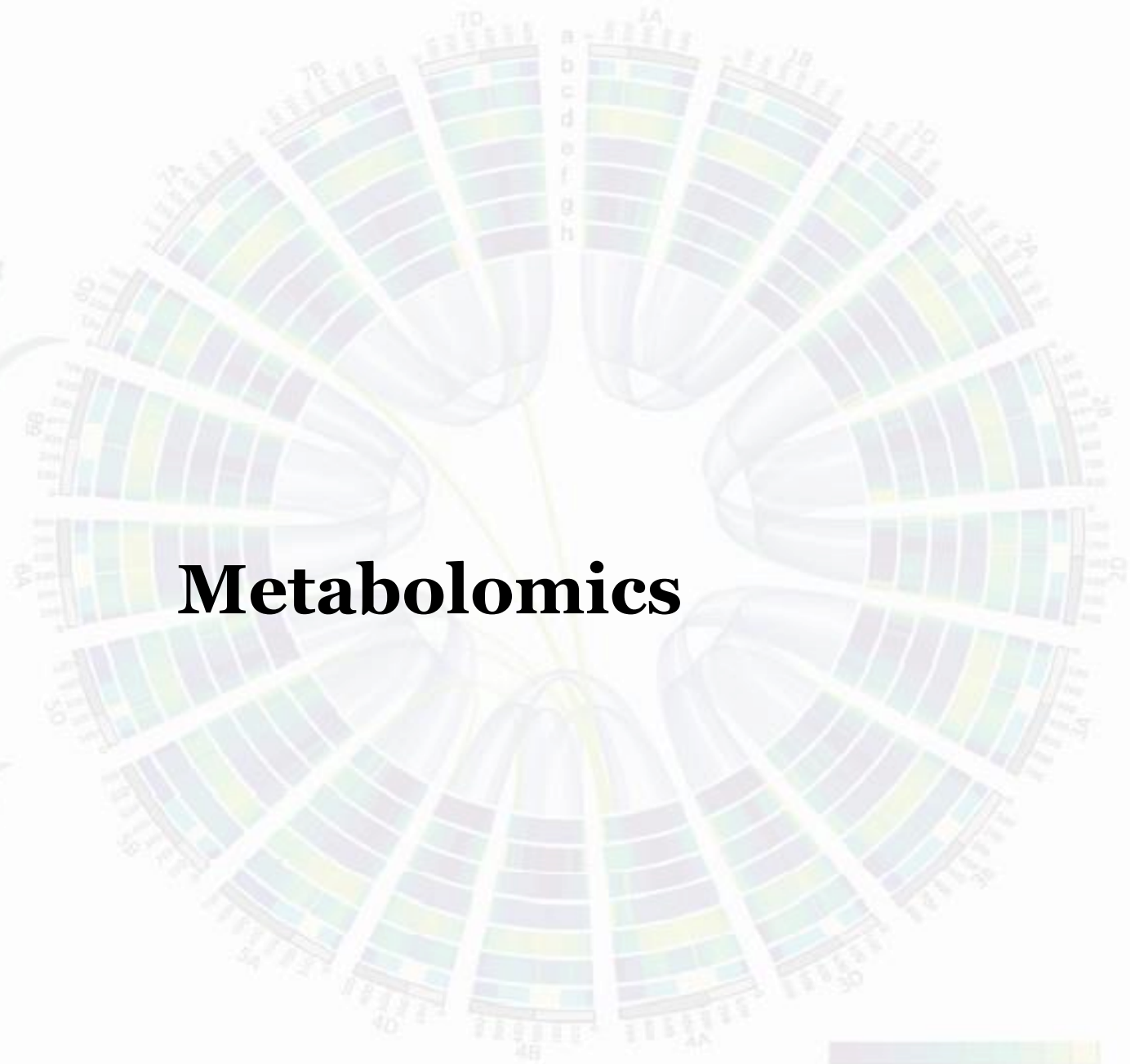


Physiology & Biochemistry

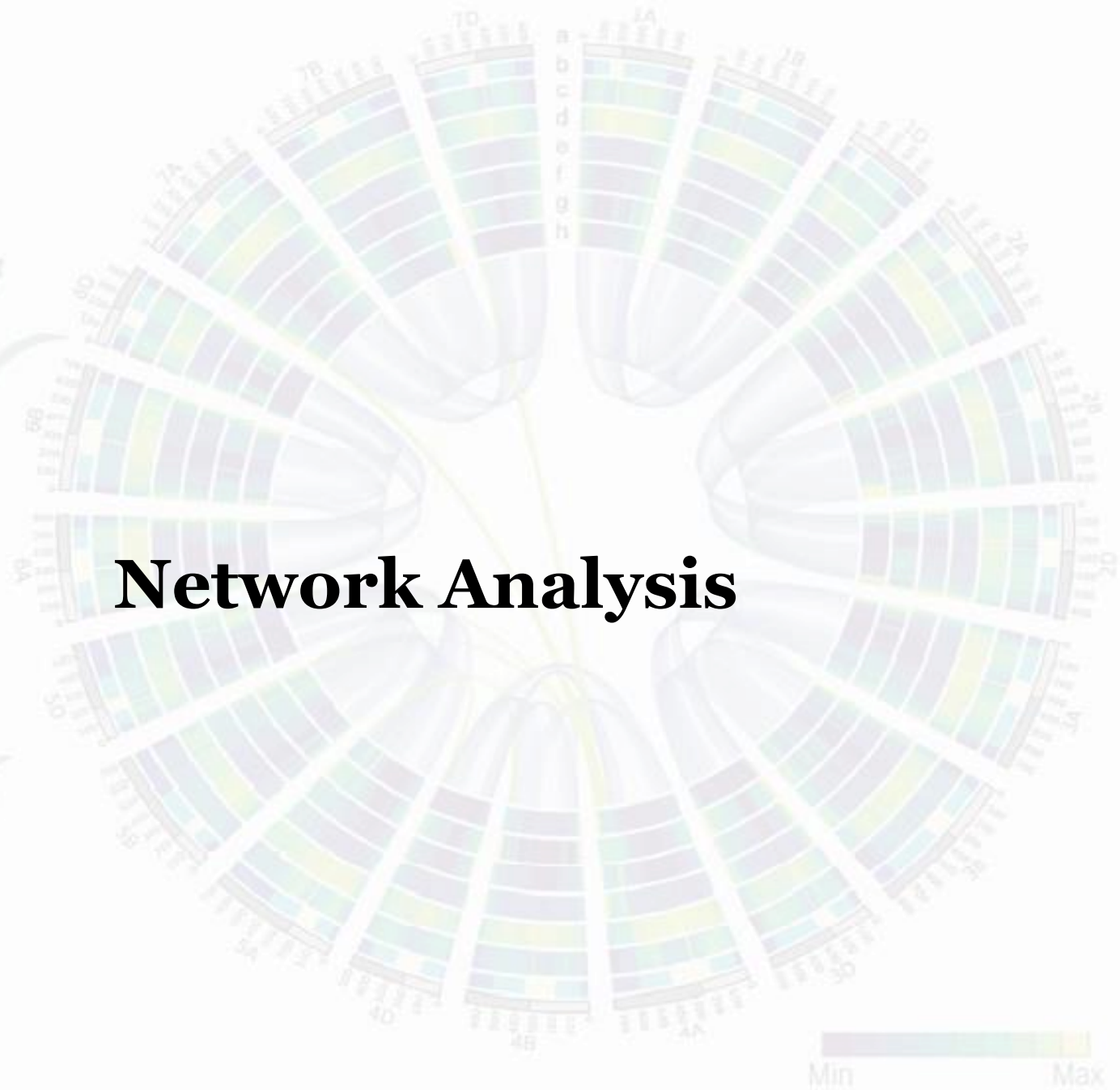


Diversity and variation in 2nd experiment





Metabolomics



Network Analysis

Creating metabolomic networks and metabolic pathway predictions

	A	B	C	D	E	F	G
1		4-hydroxy	alanine	asparagine	asparagine	aspartic	citric
2	694_C1	302	369822	213	9748	201281	45
3	694_C2	217	301062	220	43495	313091	74
4	694_C3	368	694476	427	65052	523714	80
5	1144_C1	599	960712	778	103950	555819	141
6	1144_C2	436	644878	420	113314	458236	106
7	1144_C3	387	944438	1178	890038	416620	90
8	2059_C1	1175	699272	1033563	4341067	1170484	93
9	2059_C2	311	588344	925594	2722994	720483	69
10	2059_C3	1703	650614	850293	3107527	924745	99

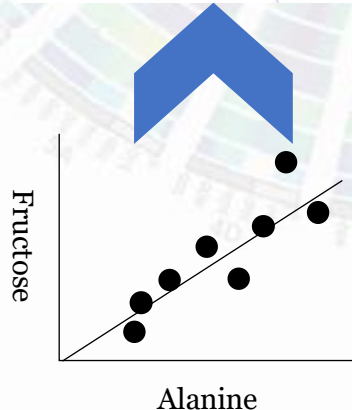
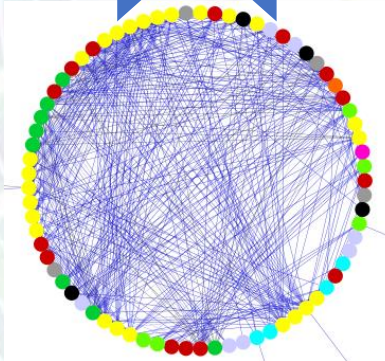
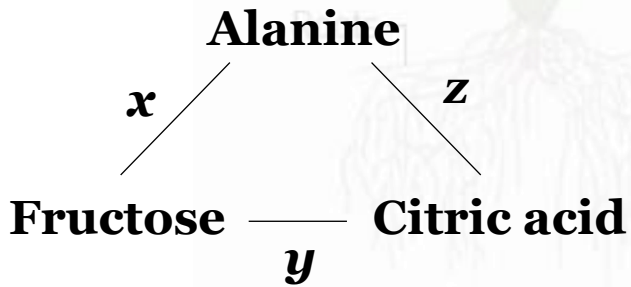
ML train

Positive pathways	PlantCyc
Negative pathways	MetaCyc
Negative	Random metabolites



ML test
(known plant pathways)

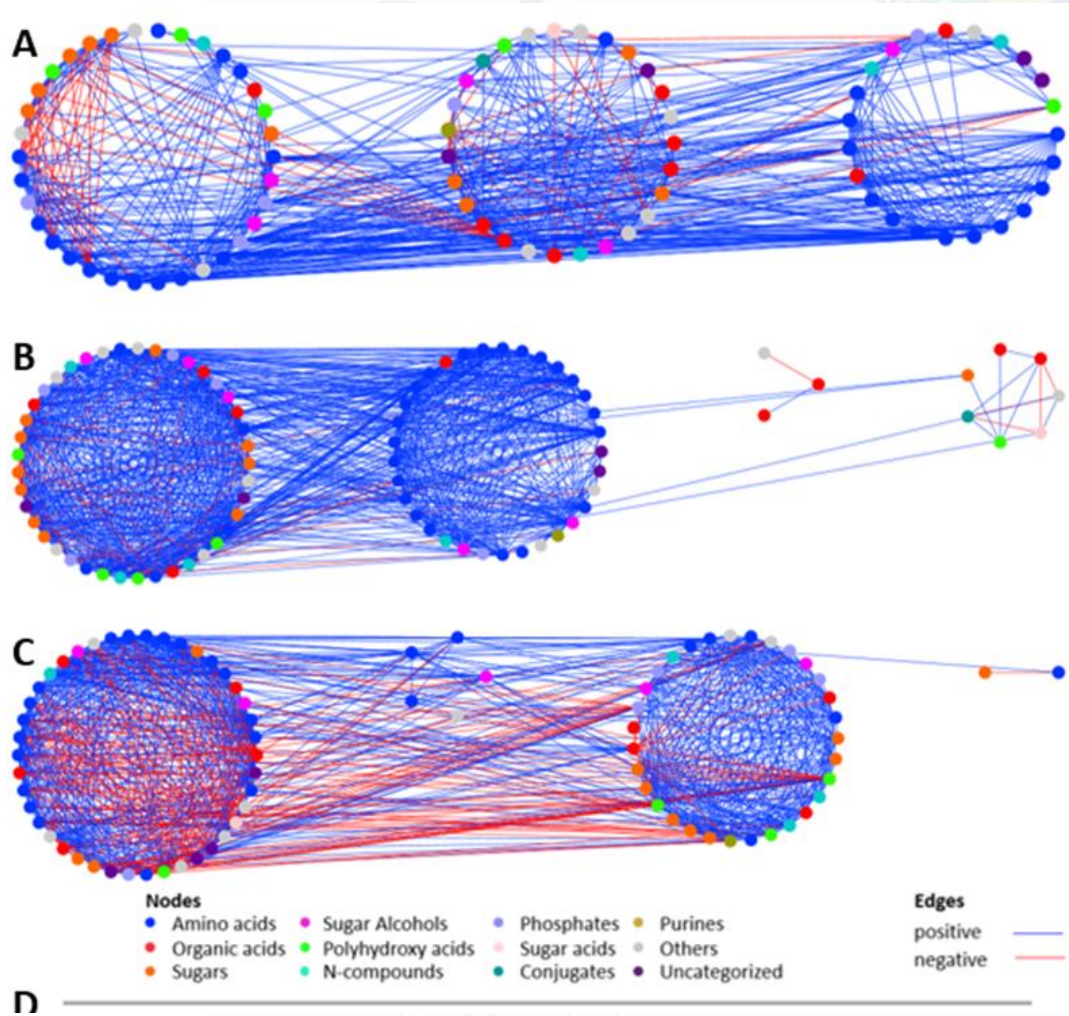
Data Calibration



Metabolic pathway predictions

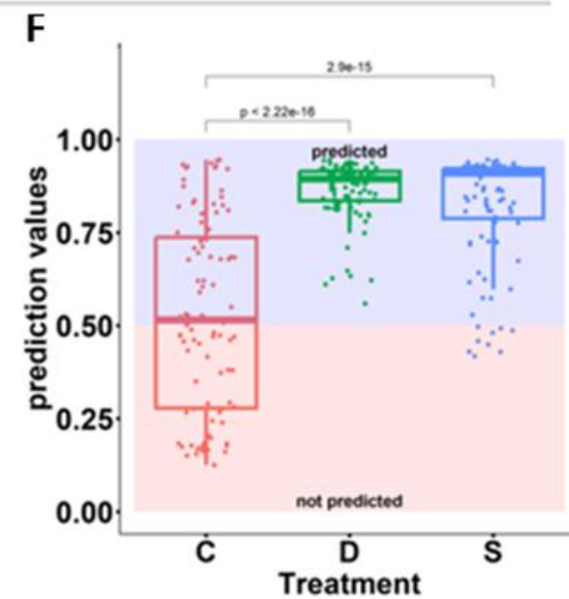
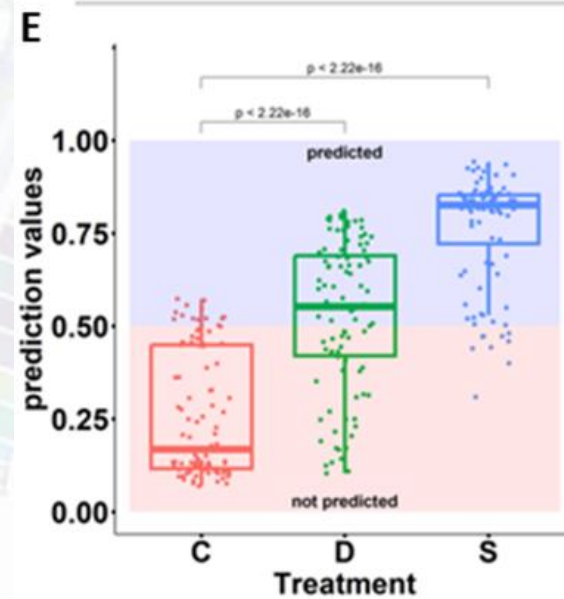
Prediction sensitivity test

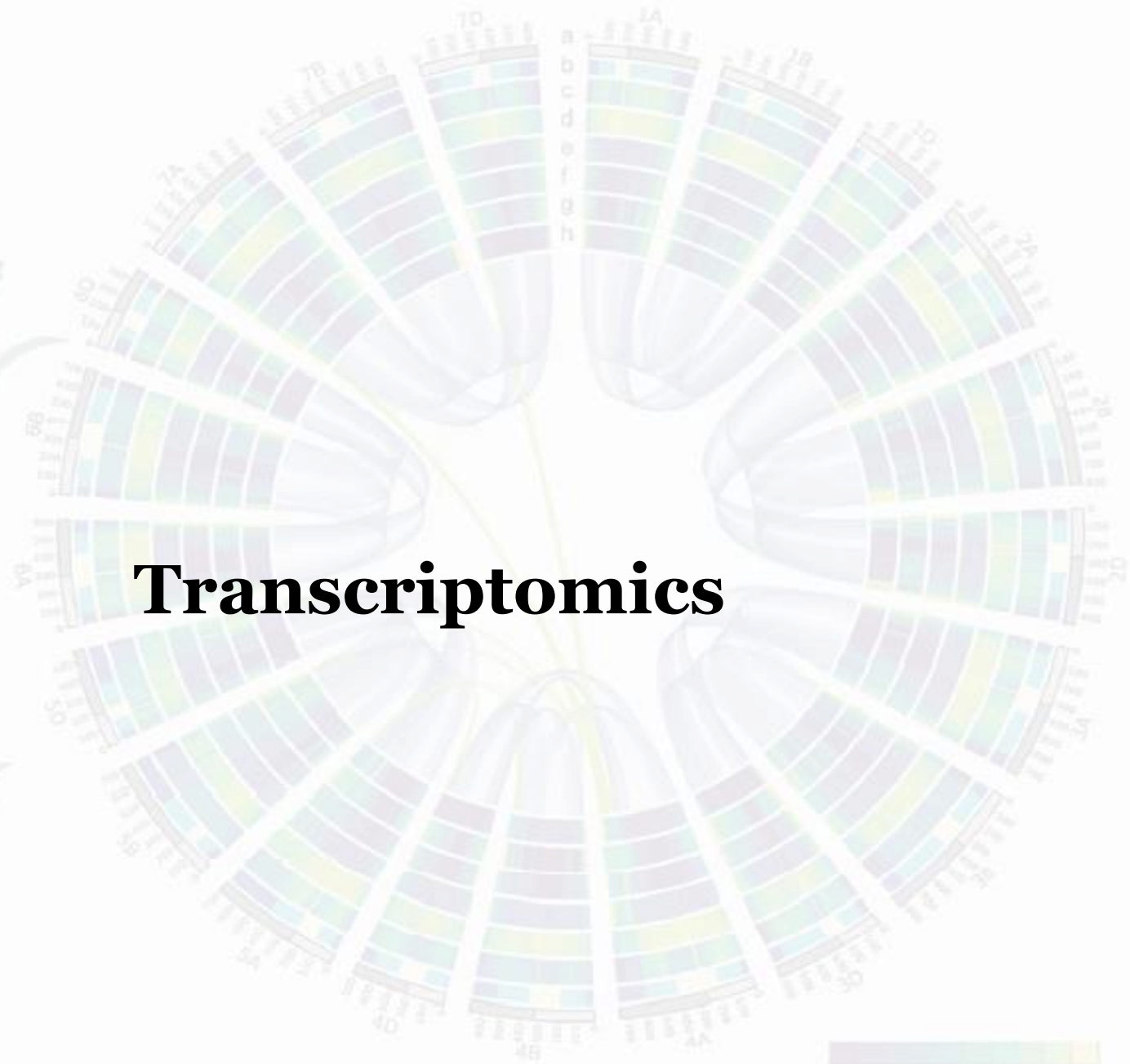




D

Pathway	Con Pred	Con Sens	Dro Pred	Dro Sens	Sal Pred	Sal Sens
L-carnitine biosynthesis	0.497	0.257	0.697	0.532	0.859	0.765
L-arginine biosynthesis I (via L-ornithine)	0.155	0.452	0.927	0.888	0.570	0.562
indole-3-acetate inactivation VIII	0.155	0.527	0.927	0.863	0.928	0.822
glycine biosynthesis III	0.497	0.374	0.697	0.586	0.859	0.764
nitric oxide biosynthesis II (mammals)	0.497	0.375	0.801	0.703	0.928	0.749





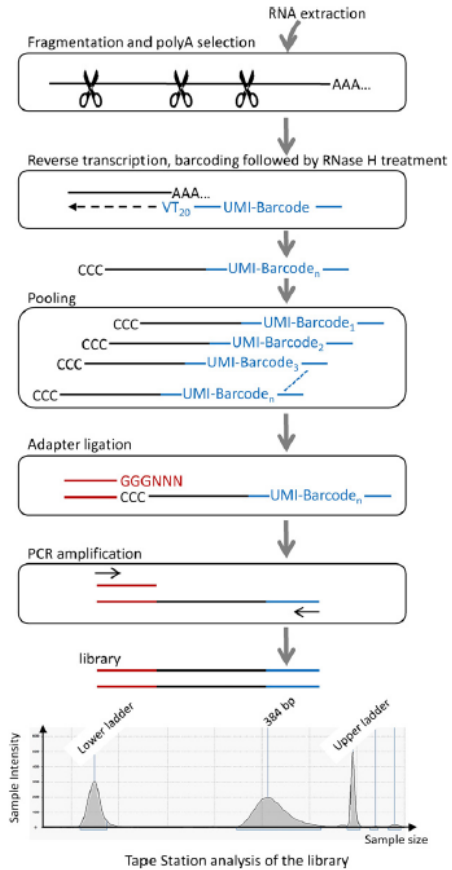
Transcriptomics



IRGSC (2018)

Pipeline for Transcriptomics

MARS-Seq



Tzfadia et al. (2018)

WGCNA

Construct a gene co-expression network
Rationale: make use of interaction patterns among genes
Tools: correlation as a measure of co-expression

Identify modules
Rationale: module (pathway) based analysis
Tools: hierarchical clustering, Dynamic Tree Cut

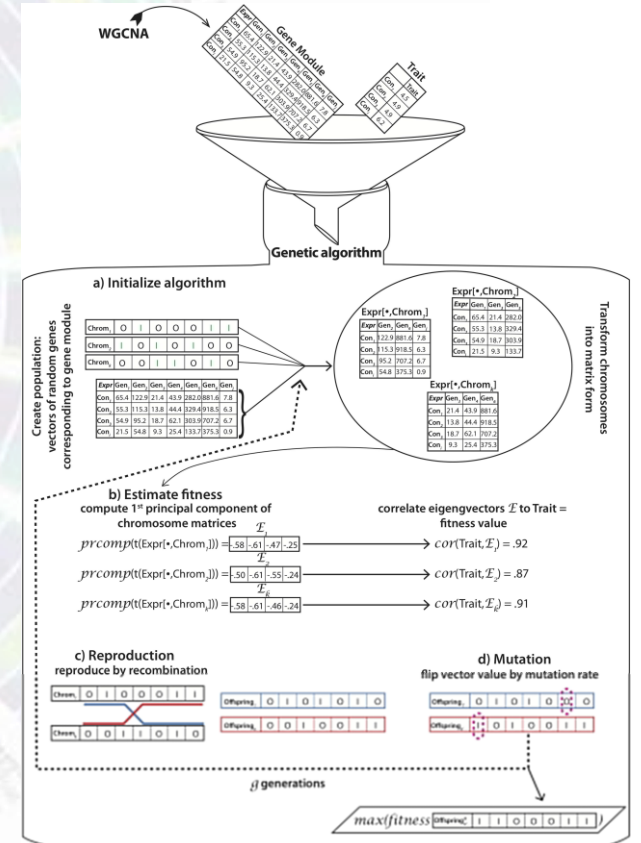
Relate modules to external information
 Array Information: clinical data, SNPs, proteomics
 Gene Information: ontology, functional enrichment
Rationale: find biologically interesting modules

Study module relationships
Rationale: biological data reduction, systems-level view
Tools: Eigengene Networks

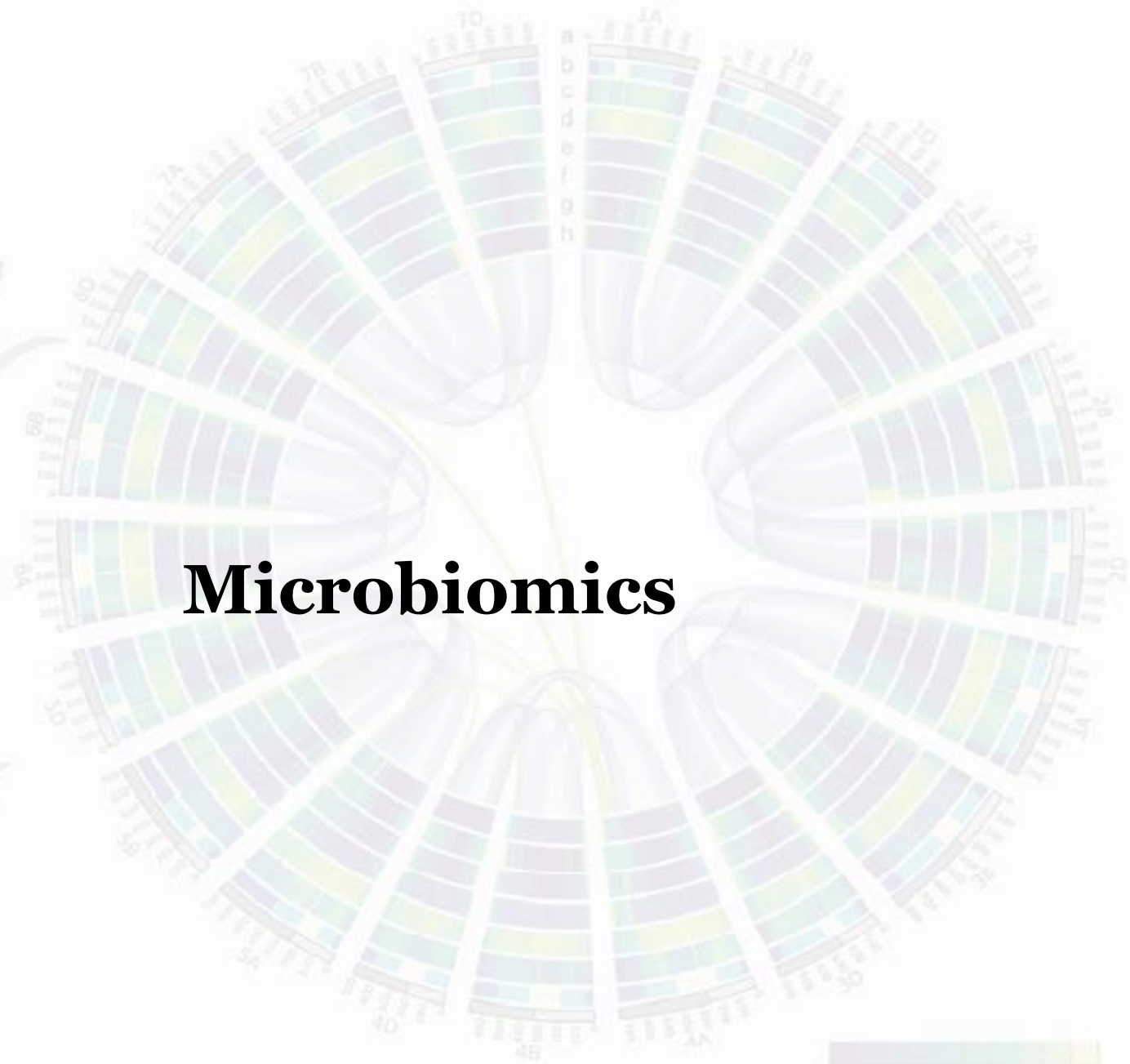
Find the key drivers in interesting modules
Rationale: experimental validation, biomarkers
Tools: intramodular connectivity, causality testing

Langfelder and Horvath (2008)

GA



Toubiana et al. (2019)

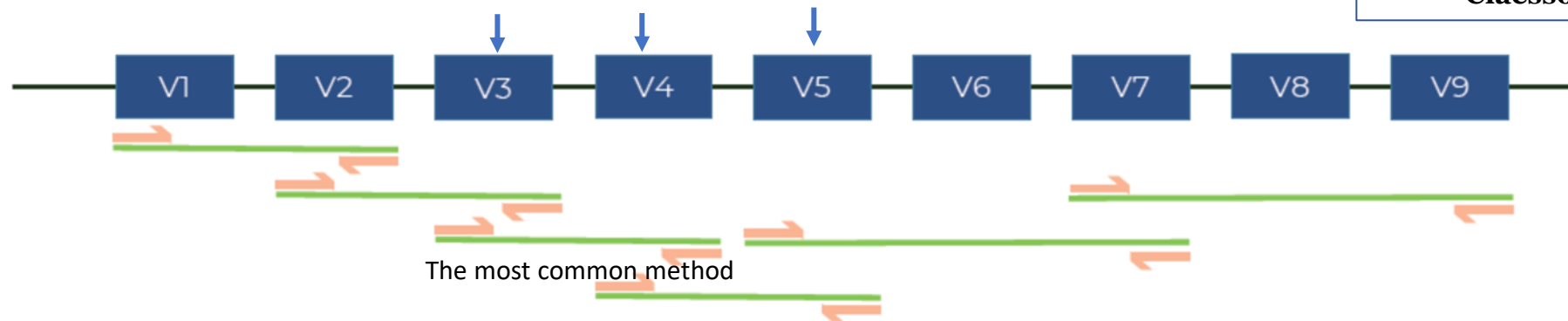


Microbiomics

Microbiomics – classical approach

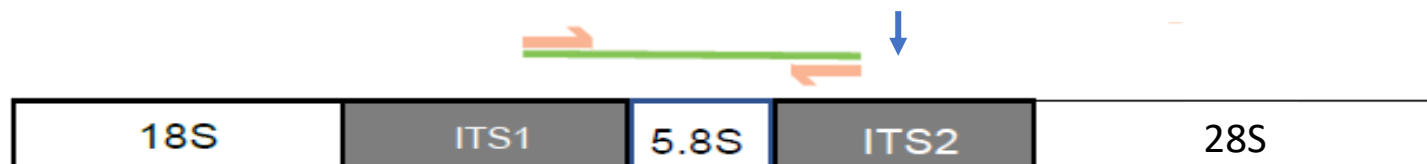
16S rRNA Gene Amplicons

Multiple region amplification of the 16S gene



V3, V4 and V5 provide sufficient classification accuracy.
(Liu et al., 2008;
Claesson et al., 2010)

ITS1 and ITS2 Amplicons (Fungal)

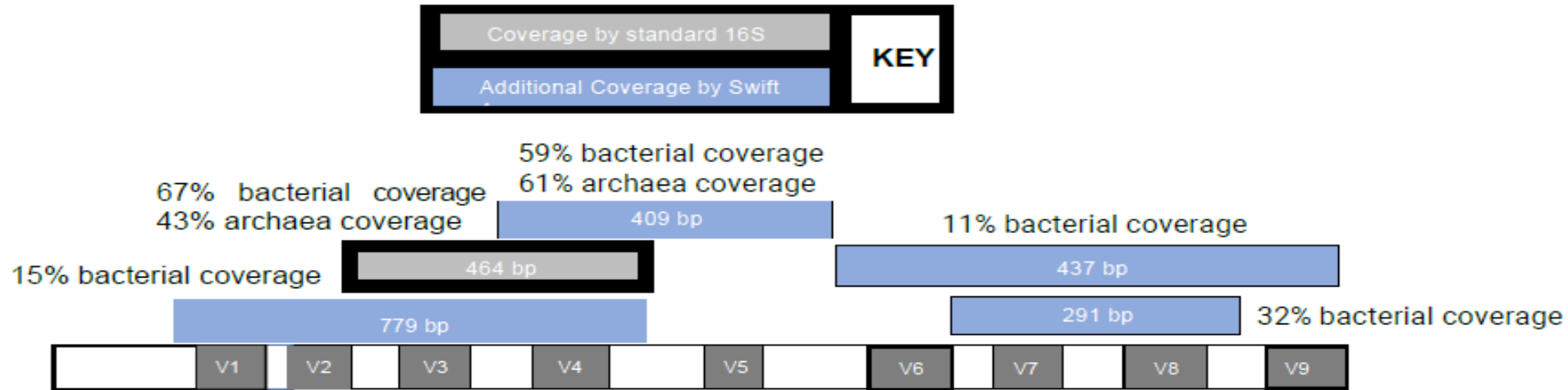


Recently been suggested as a better suited target to extend the coverage of fungal kingdom.
(Nilsson et al., 2019)

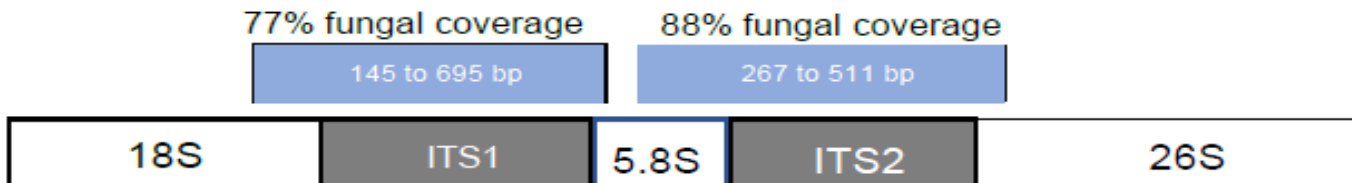


Microbiomics – novel approach

16S rRNA Gene Amplicons



ITS1 and ITS2 Amplicons (Fungal)



Microbiomics – novel approach

Provides Superior Representation of a Diverse Microbial Community Versus V3-V4 Only

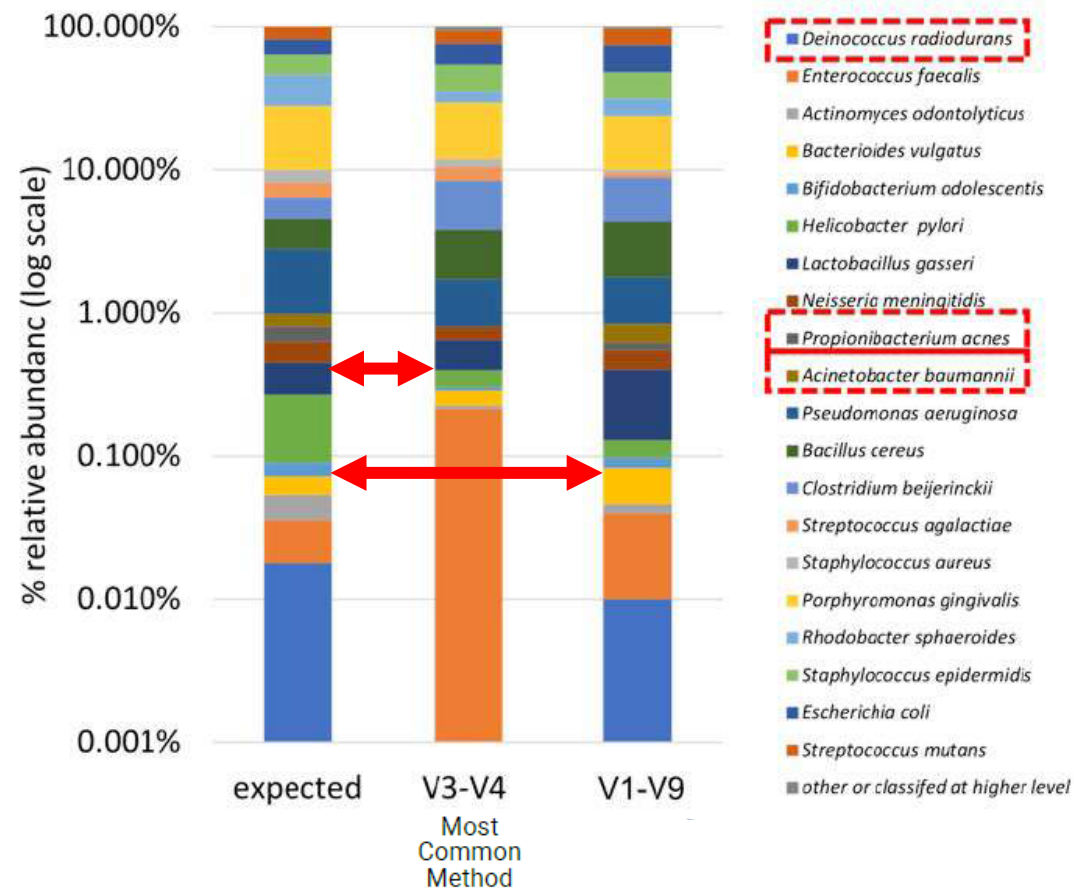
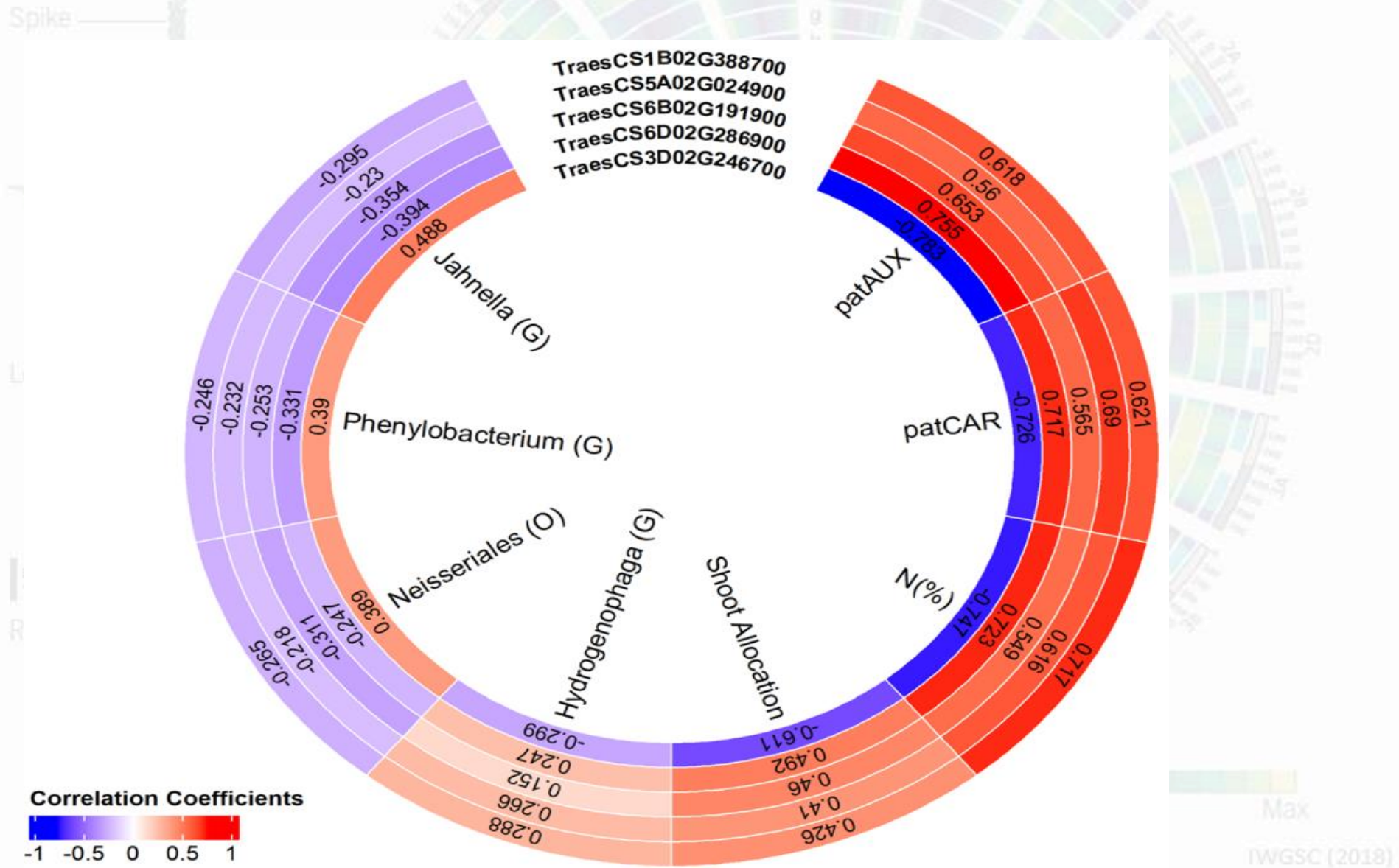
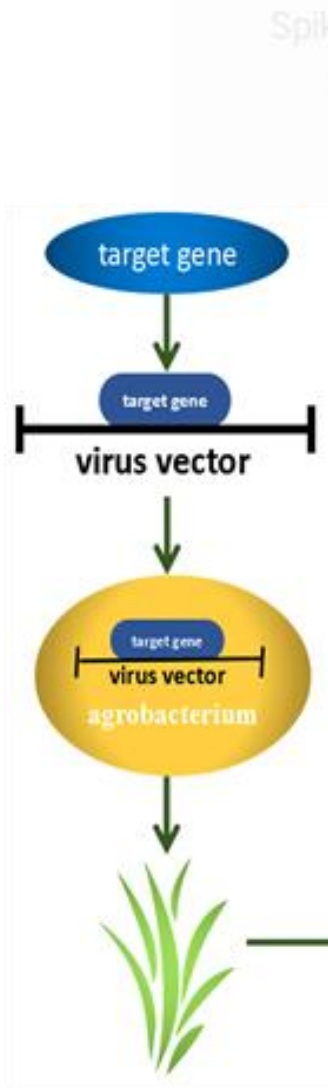


Figure 2. The Swift Amplicon 16S+ITS Panel covering all V1-V9 regions provides sensitive detection and accurate representation of each species in the sample compared to standard methods interrogating the V3-V4 region alone. Organisms marked in red were underrepresented by V3-V4 only method. Input DNA was a mix of 20 bacterial species (ATCC[®] MSA-1003[™]) tested with the Swift Amplicon 16S+ITS Panel, sequenced with Illumina[®] MiSeq[®] V3 (2x300bp reads).

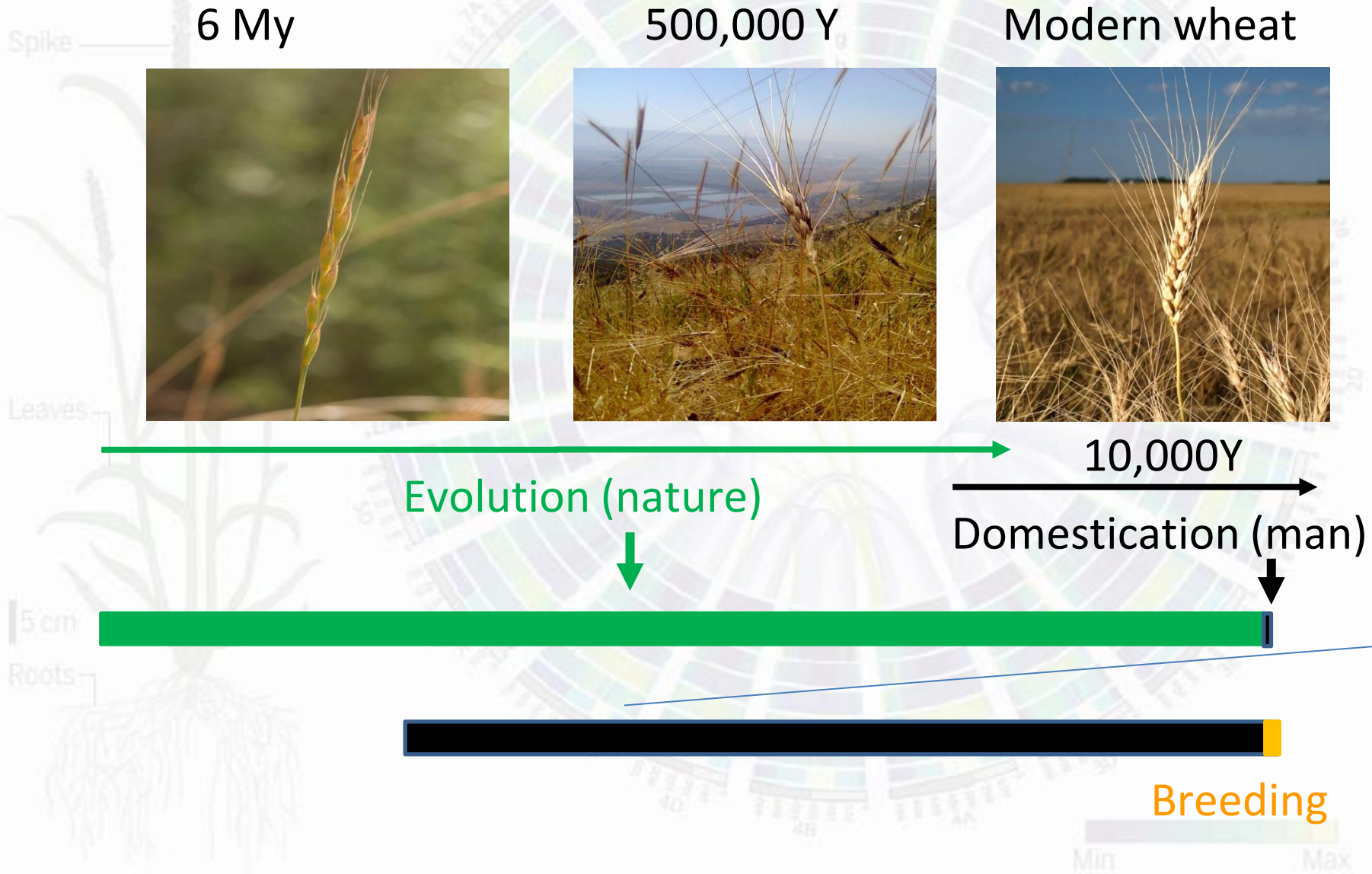
Correlation heatmap between post-GA genes' expression data and physiological, biochemical and microbiome parameters



The effect of Virus-Induced Gene Silencing on L-carnitine biosynthesis under salinity conditions



Modern wheat has evolved over >6,000,00 years



Non-shattering;

Uniform;

High yield



Loss of natural diversity



Climate, environment, pests, diseases, nutrition.....





The Lieberman Okinow Genebank

20 species

~16,000 accessions

~900 sites

Wild wheat 2,500

Goat grasses
(11 species) 8,500

Barley
(4 species) 3,000

Oat 1,500

Rye 50

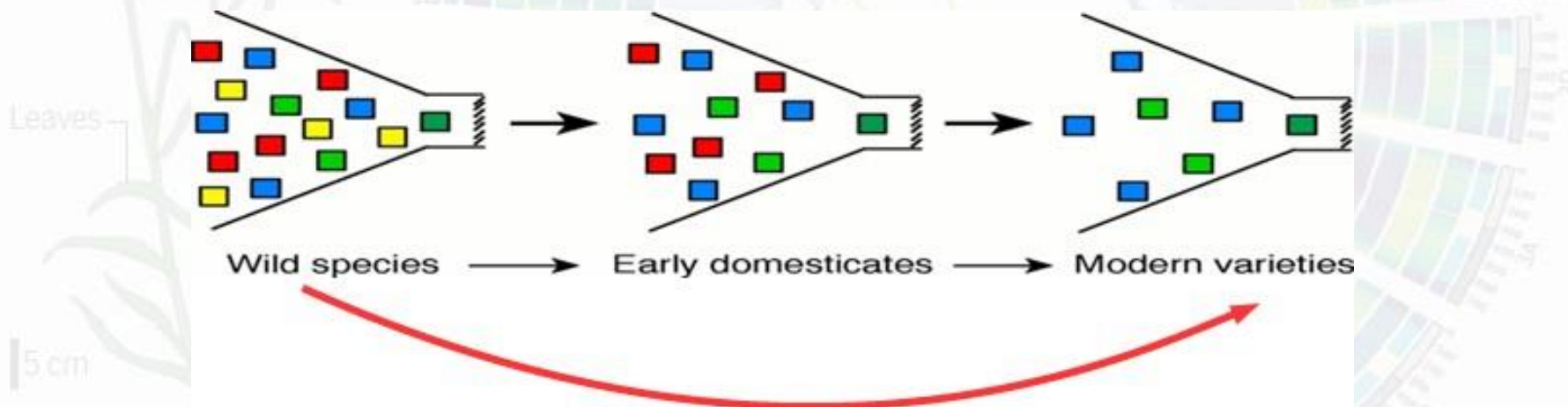
Brachypodium 400



ICCR Mission

Utilization of the collection to produce better cereals

Diseases, Climate, Pests, Quality, Yield



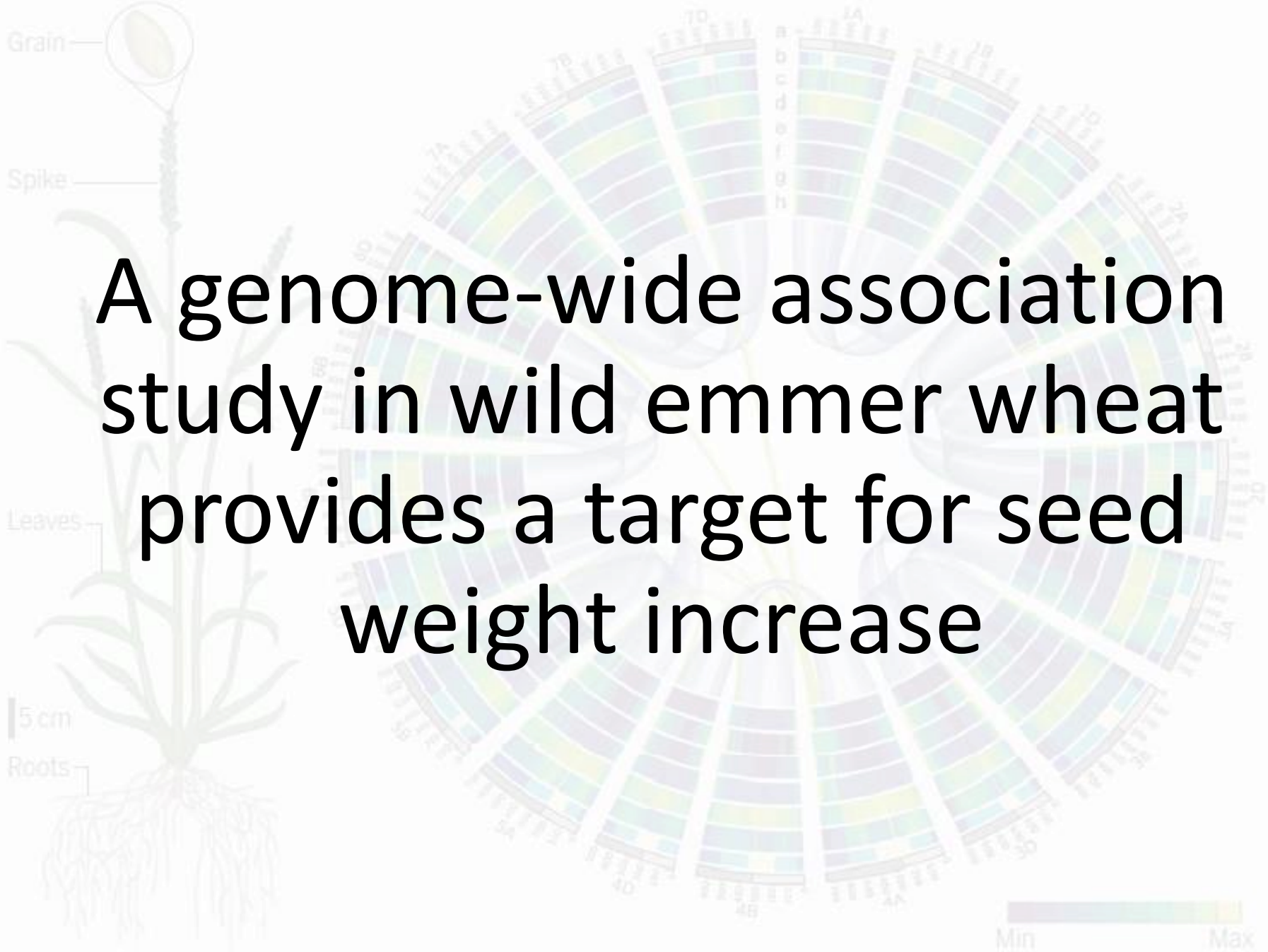
5 cm

Roots



Our goal is to produce super wheat for a better future

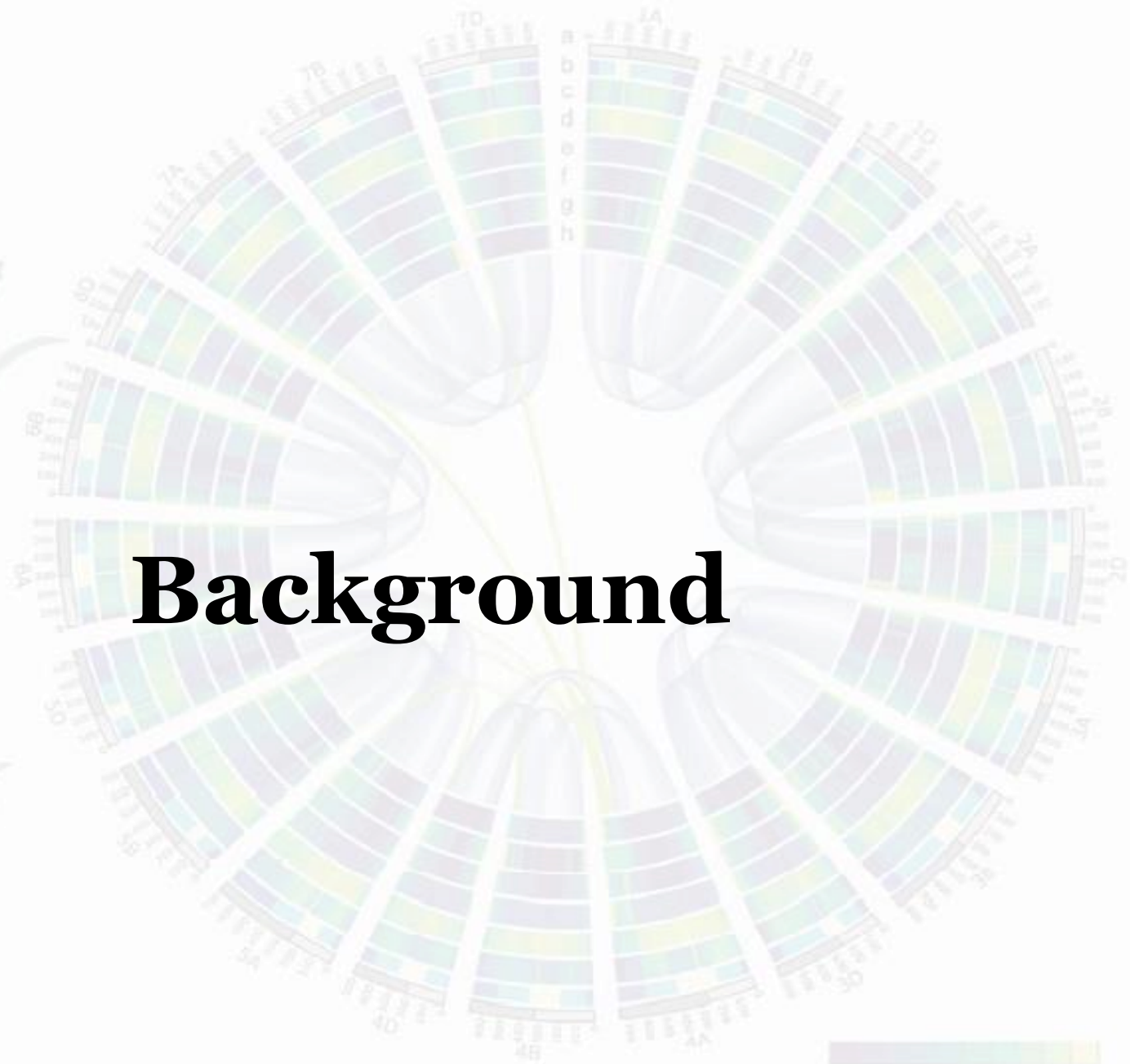




A genome-wide association study in wild emmer wheat provides a target for seed weight increase

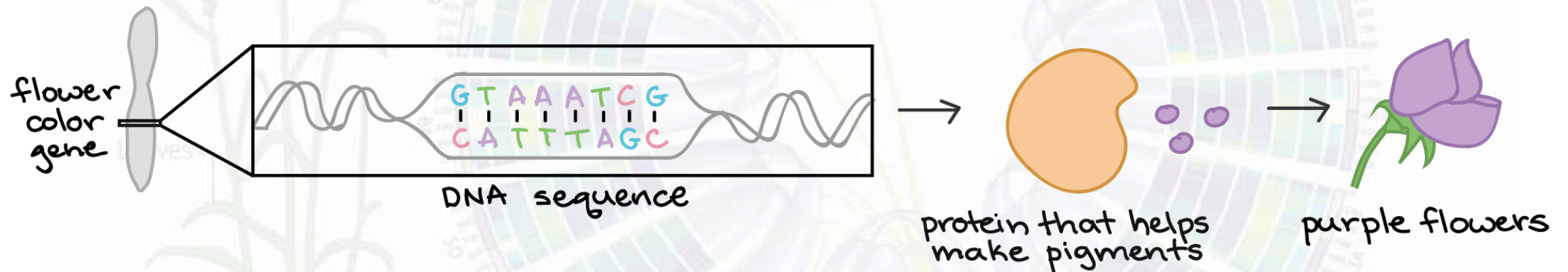
Min Max

IWGSC (2018)

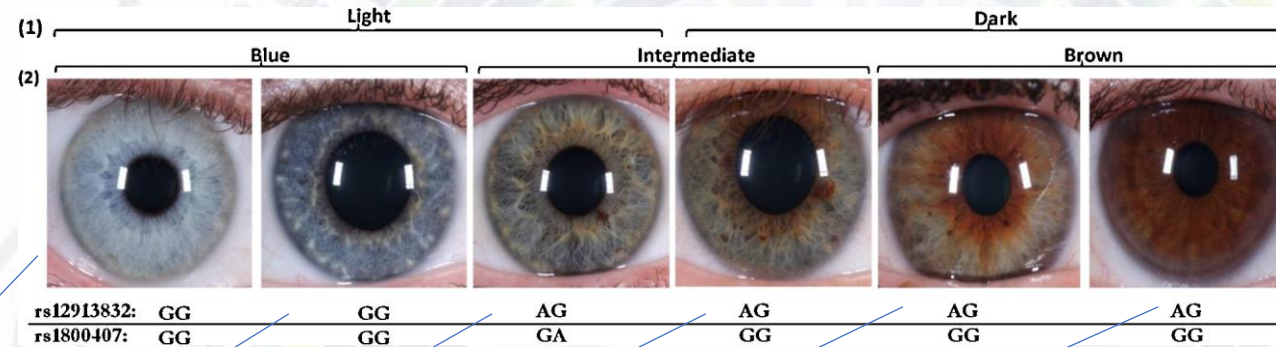


Background

The central dogma – the DNA sequence (“genotype”) dictates the protein sequence which dictates the physical characteristics (“phenotype”)



Even changes in single nucleotides (SNPs) cause phenotypic changes

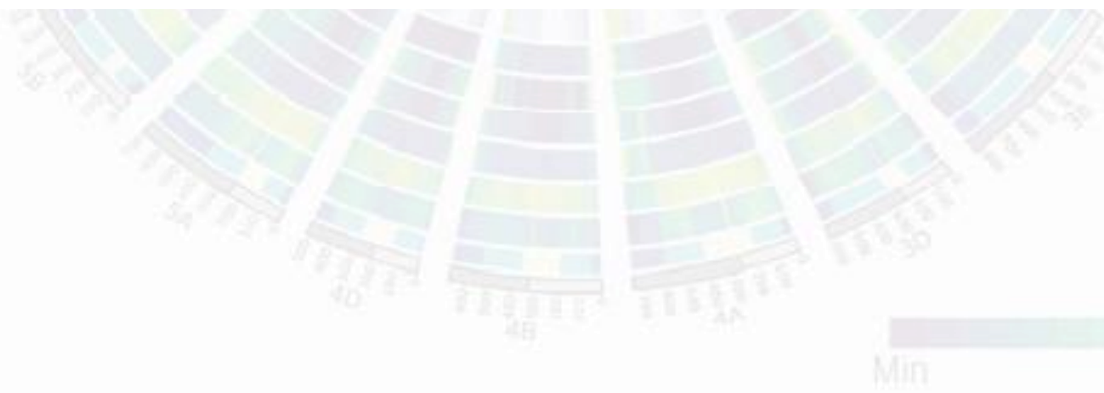
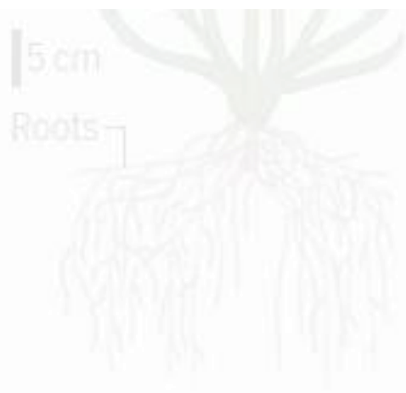
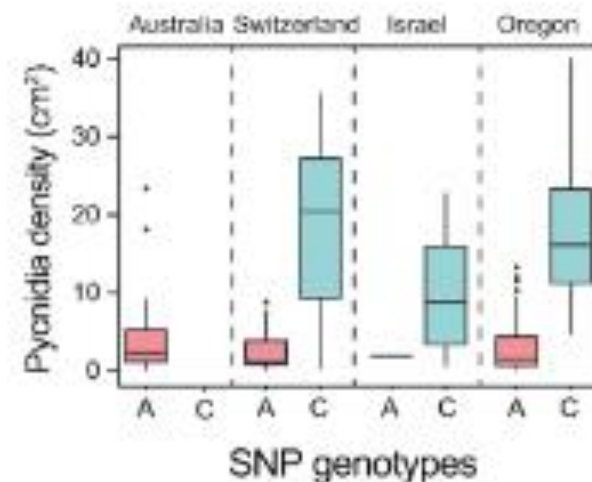
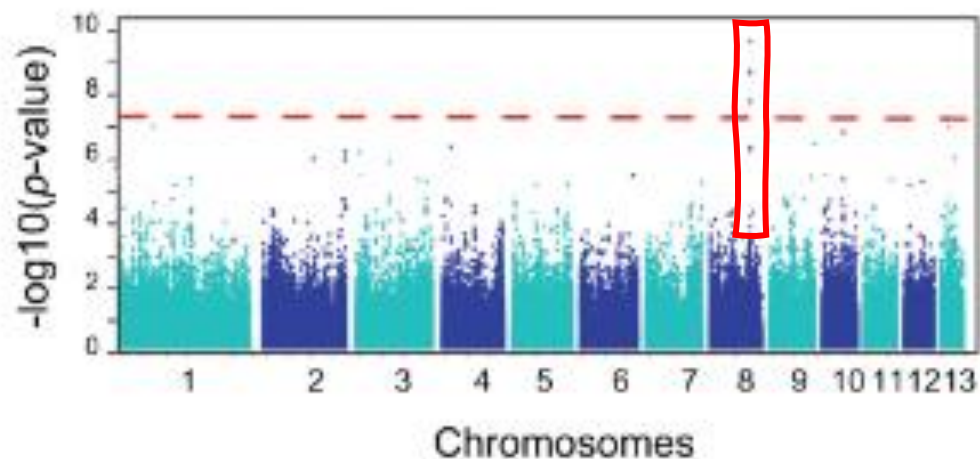
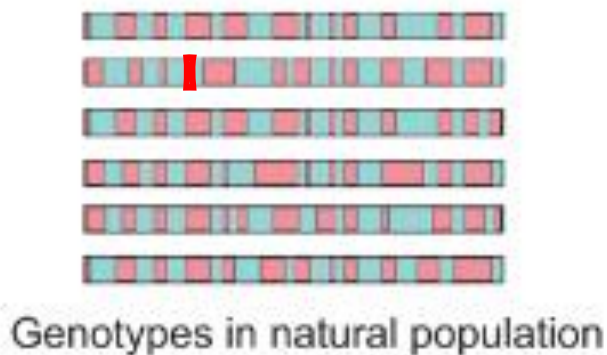


Subject 1: ACTCGCTA**GG**TCGATC ACTAGCTACT**GG**AATCGCTTGCA
 Subject 2: ACTCGCTA**GG**TCGATC ACTAGCTACT**GG**AATCGCTTGCA
 Subject 3: ACTCGCTA**AG**TCGATC ACTAGCTACT**GA**AATCGCTTGCA
 Subject 4: ACTCGCTA**AG**TCGATC ACTAGCTACT**GG**AATCGCTTGCA
 Subject 5: ACTCGCTA**AG**TCGATC ACTAGCTACT**GG**AATCGCTTGCA
 Subject 6: ACTCGCTA**AG**TCGATC ACTAGCTACT**GG**AATCGCTTGCA

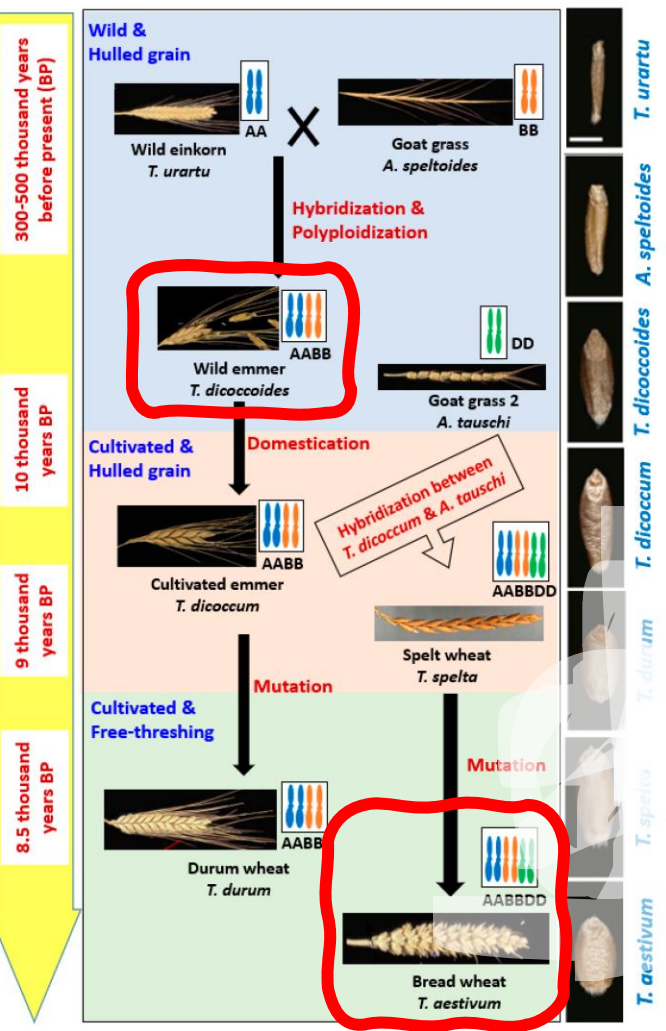


GWAS (genome-wide association study) uses SNPs to discover relevant genes

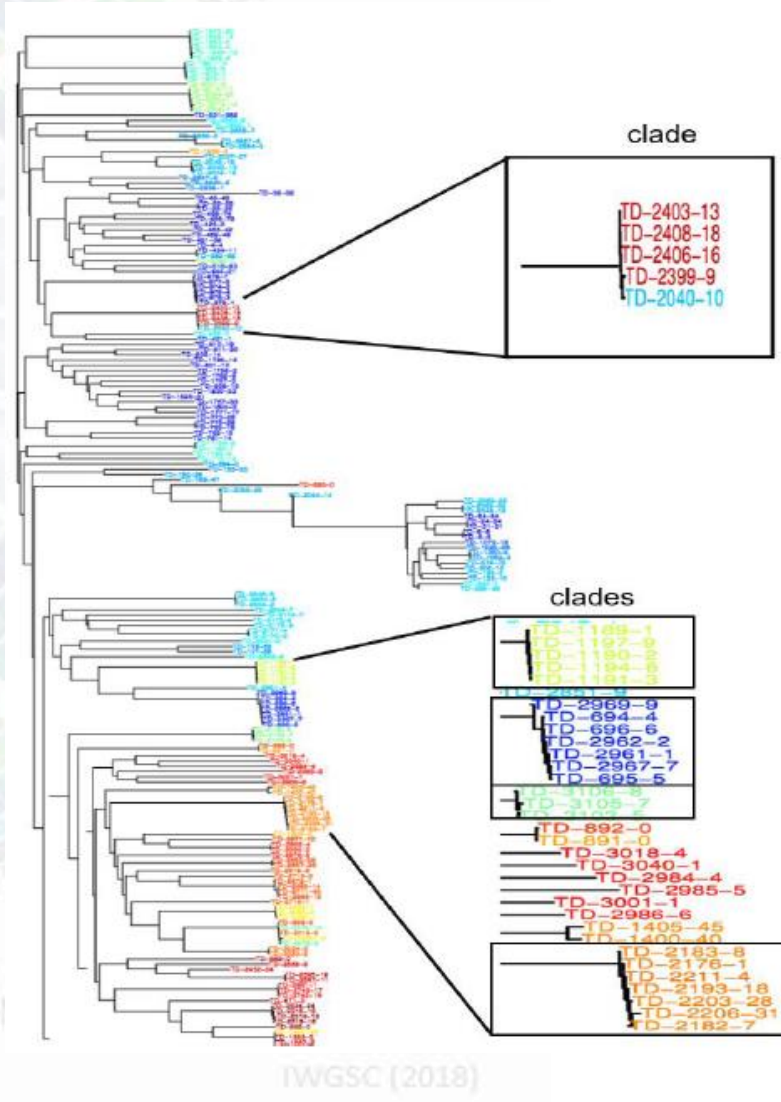
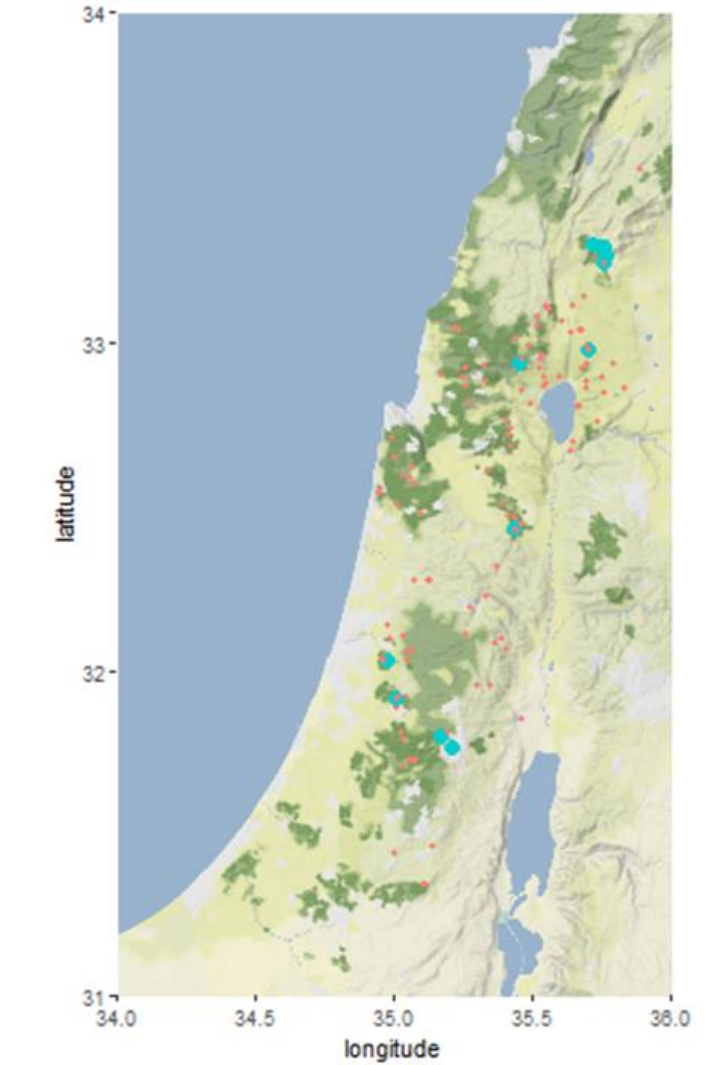
GWAS



A population of Td (an ancient progenitor of Ta; bread wheat) from all over Israel was used in a GWAS

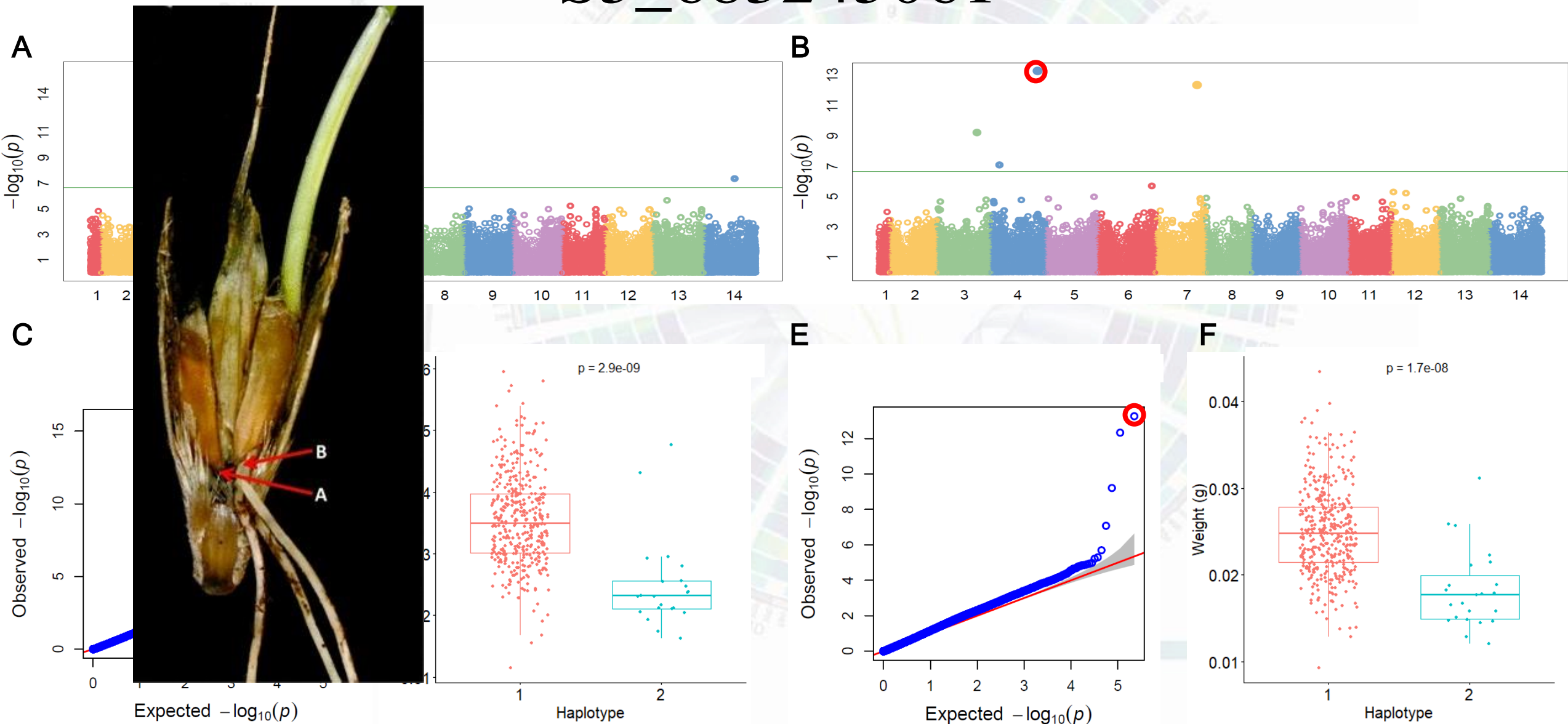


Rahman et al. (2020)

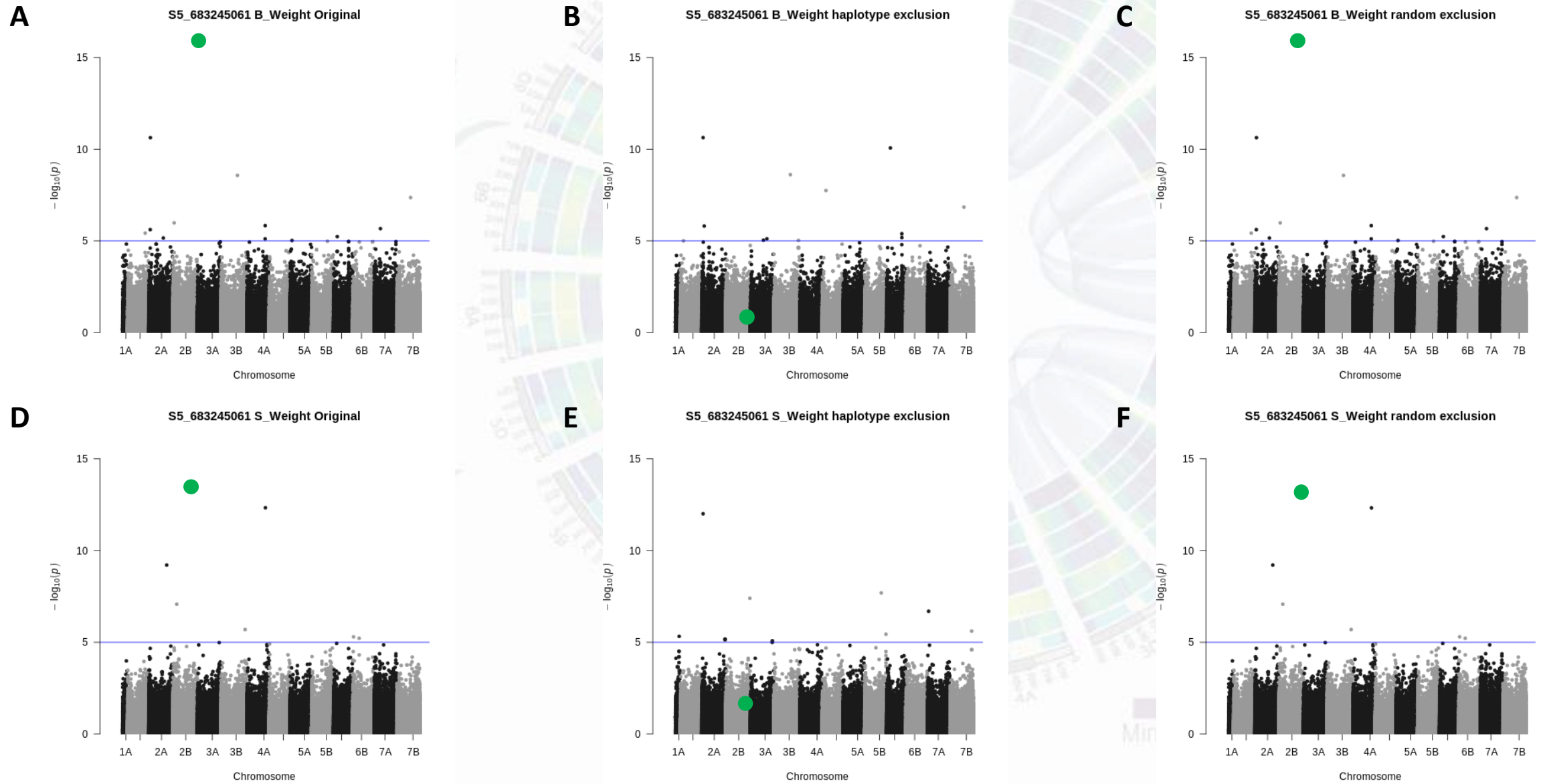


IWGSC (2018)

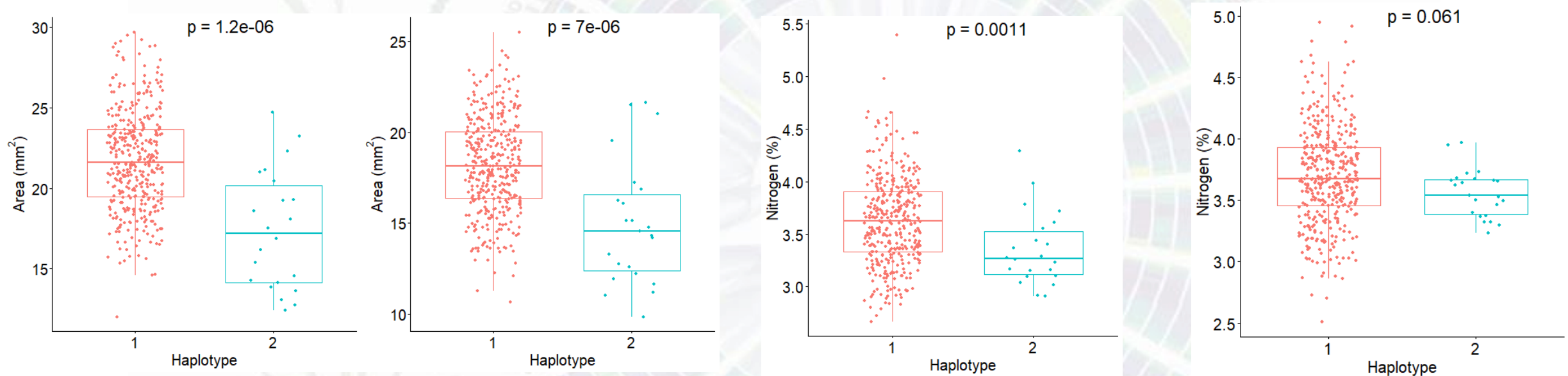
Seed weight is differential for haplotypes of S5_683245061



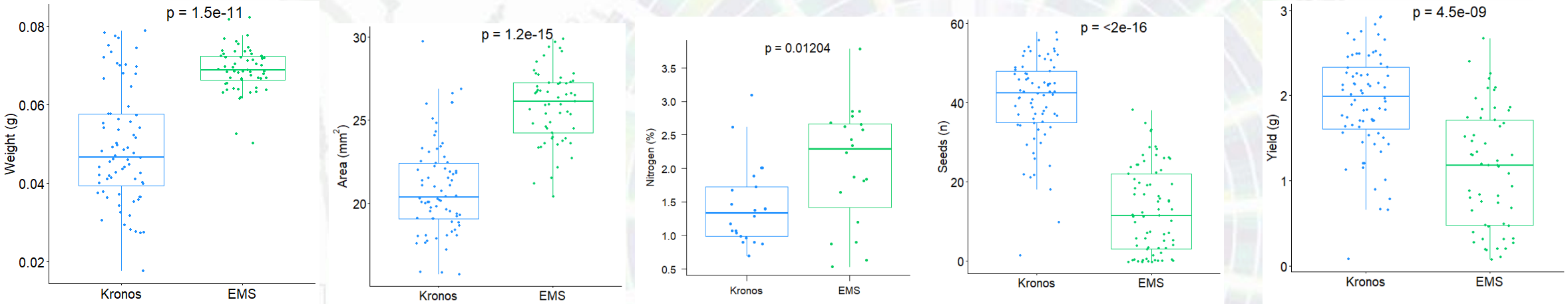
The SNP results passed a permutation test



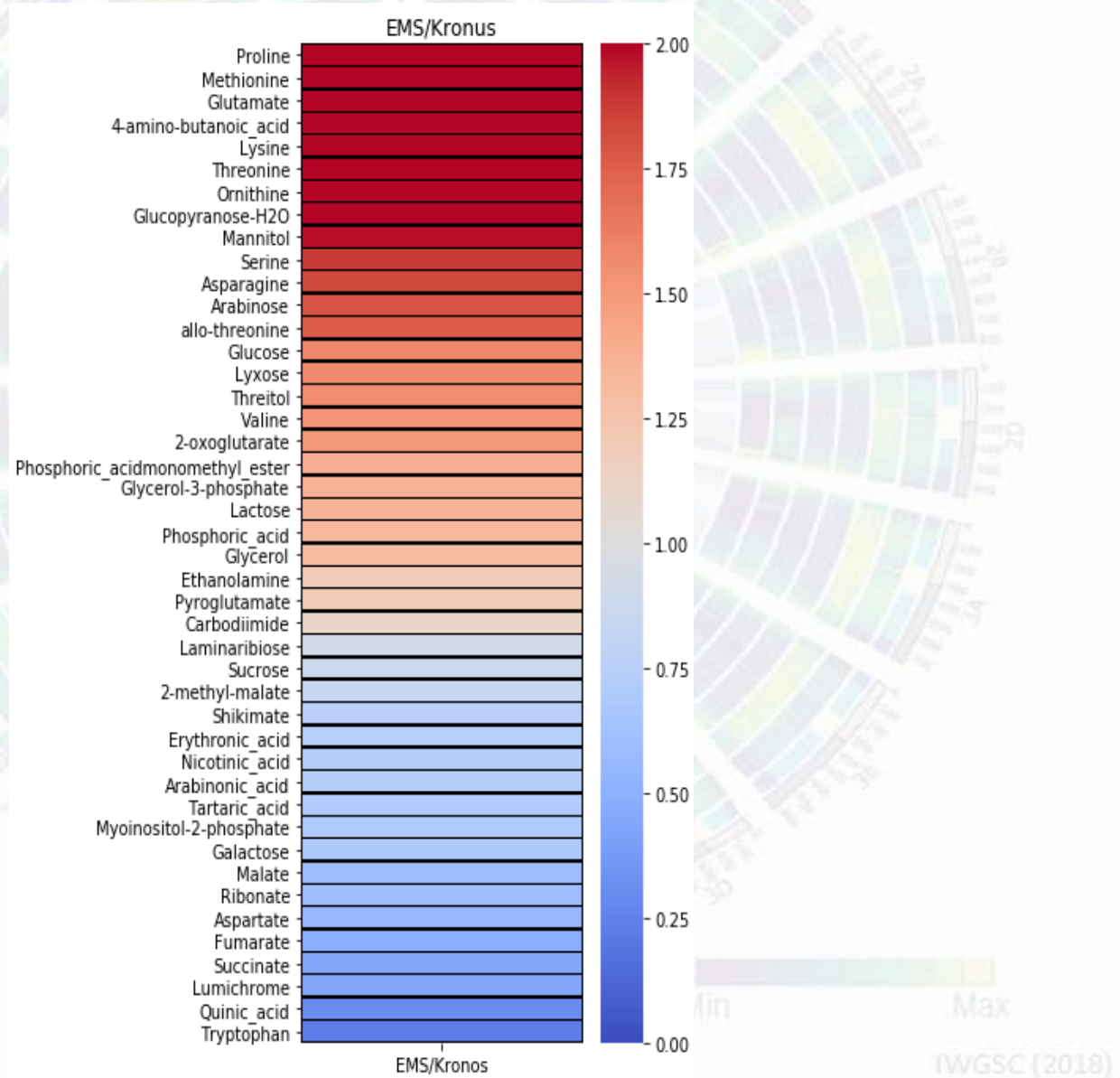
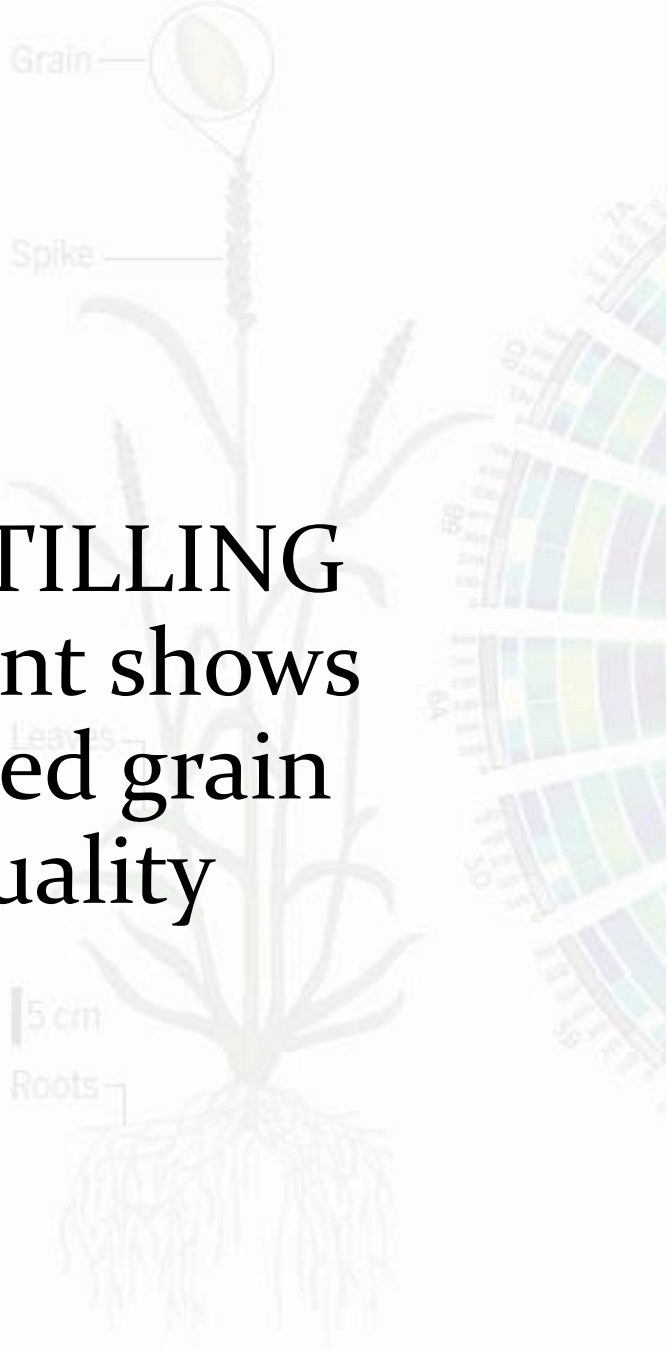
The area and nitrogen content were differential for haplotypes of S5_683245061



The TILLING mutant shows higher seed weight and seed area, higher nitrogen content while *showing* lower seed number and lower yield per spike



The TILLING mutant shows altered grain quality



References

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