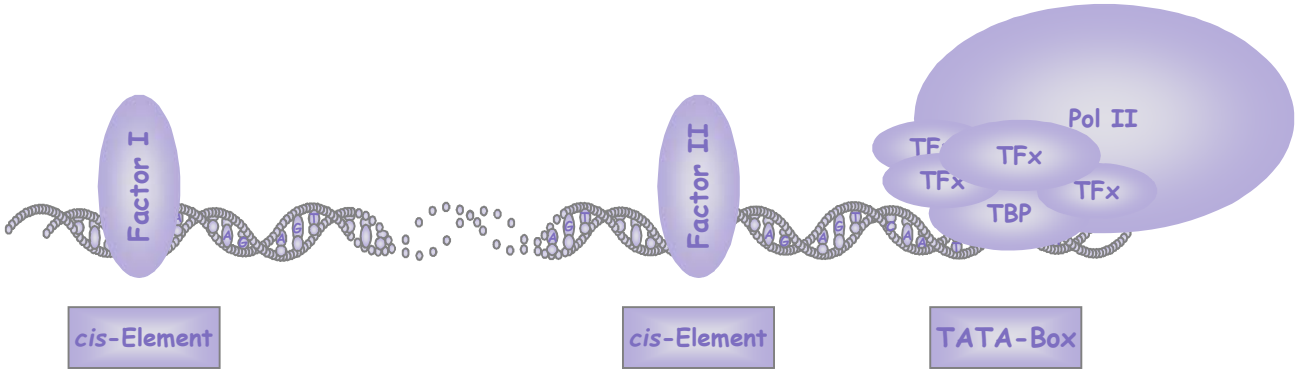
Mining metadata for meaningful information

The combination of 'OMICS' data from different sources provides novel insights into transcription factor function



Dierk Wanke
dierk.wanke@zmbp.uni-tuebingen.de

Principle of functional genomics

„Central Dogma of Molecular Biology“

DNA → **RNA** → **Protein** → **Metabolism** → **Physiology**

„Central Dogma of functional Genomics“

Genome → **Transcriptome** → **Proteome** → **Metabolome**

Besides the four classical ‚**omes**‘, a number of derived omes exist:

with **Interactome** being probably the most important one!

There is high interdependency between the different ‚omes‘

Quantitative *vs.* qualitative analyses in Biology

Qualitative Analysis → ***empirical data*** ⇨ Yes / No / Maybe

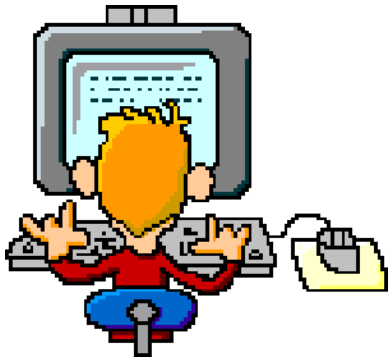
The biologist is an expert in his field and
defines the scientific question!

Quantitative *vs.* qualitative analyses in Biology

Qualitative Analysis → ***empirical data*** → Yes / No / Maybe

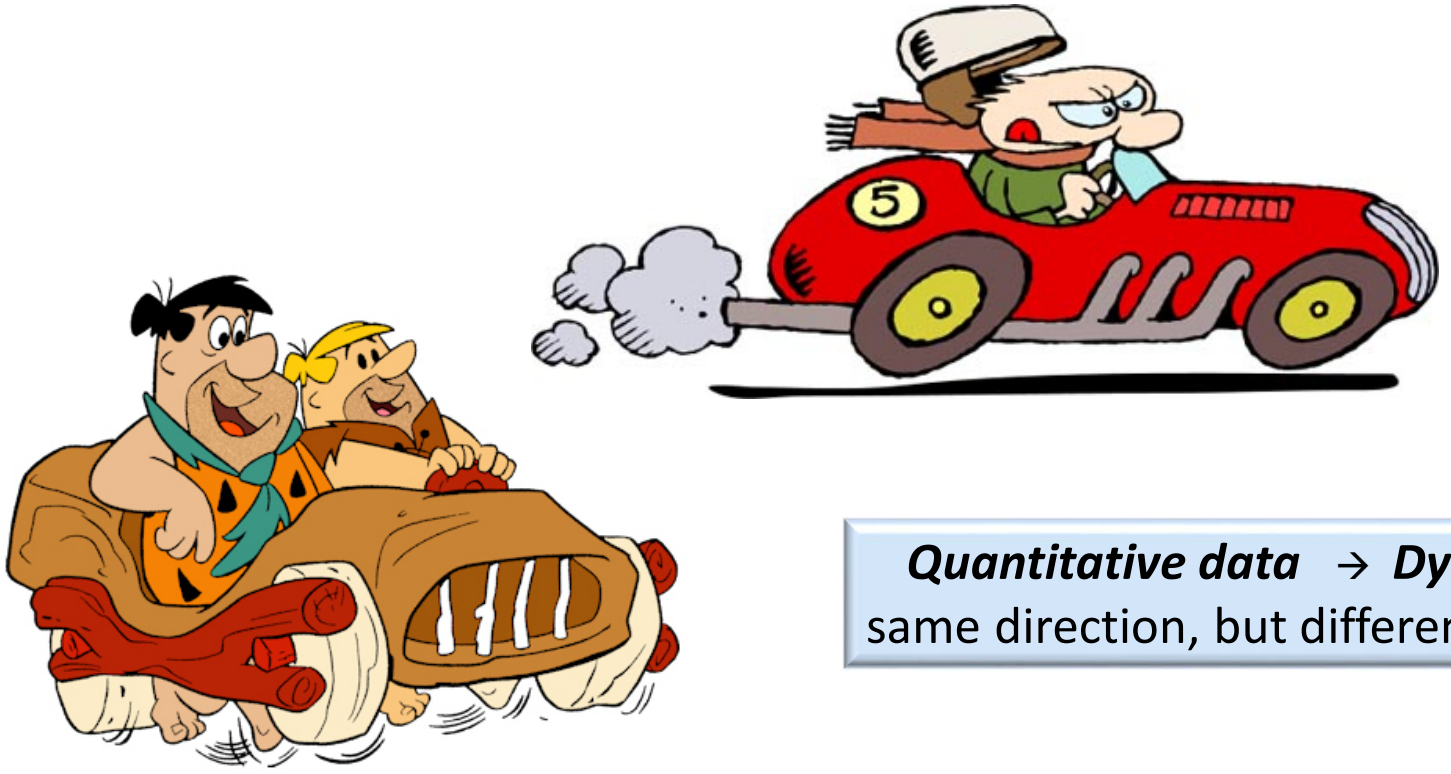
experimental validation of hypothesis

Quantitative Analysis → ***metric data*** → significance



Quantitative *vs.* qualitative analyses

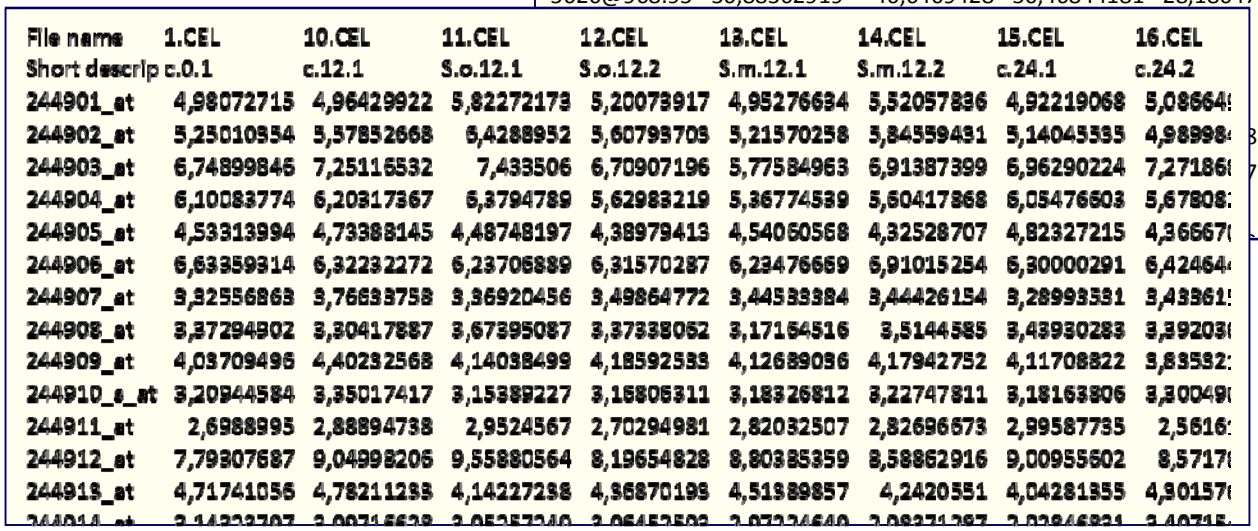
Acquiring of quantitative data of subcellular processes with high spatio-temporal resolution in living (plant) cells in their native tissue environment



Quantitative data → ***Dynamics***
same direction, but different speed!

All quantitative data come as (huge) tables

Genome → **Transcriptome** → Proteome → **Metabolome**



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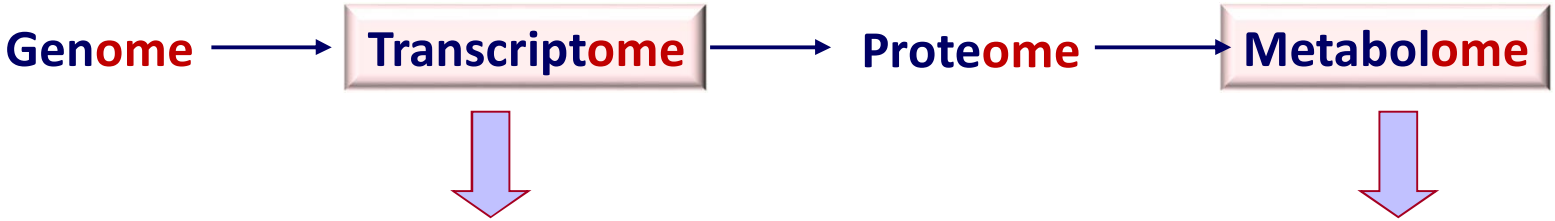
244911_at	2,6988995	2,88894738	2,9524567	2,70294981	2,82032507	2,82696573	2,99587735	2,5616
244912_at	7,79307687	9,04998206	9,55880564	8,19654828	8,80385359	8,58862916	9,00955602	8,5717
244913_at	4,71741056	4,78211293	4,14227238	4,36870193	4,51389857	4,2420551	4,04281355	4,30157

Cluster_Te	11102if_3	11105if_3	11109if_3	11102if_4	11102if_5	11105if_4	11105if_5
6899@966.62	9,636363636	12,78787879	7,272727273	16,3030303	18,84848485	21,51515152	23,09090909
8524@966.95	NA	NA	NA	NA	NA	NA	NA
2394@967.86	NA	NA	0,229984618	NA	NA	0,857215394	0,522692313
6996@968.45	4,655609189	11,77601487	9,100354804	6,541623297	11,43663281	27,39333191	29,77458115
5620@968.95	36,88362919	46,6469428	50,46844181	28,18047337	27,71203156	57,32248521	58,85108481
					NA	61,85185185	80
					NA	80,39215686	91,50326797
					NA	5,40192926	6,495176849
				3738	NA	13,41301461	17,26427623
				7863	1,988351075	9,03795943	10,14259892
					NA	21,13482935	30,81940925

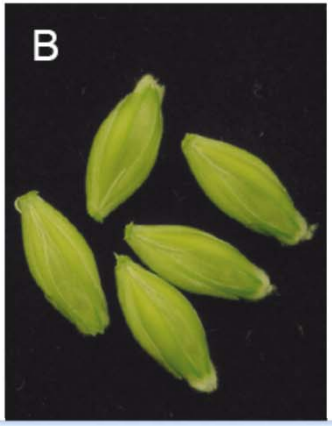
Quantitative data come as (huge) tables

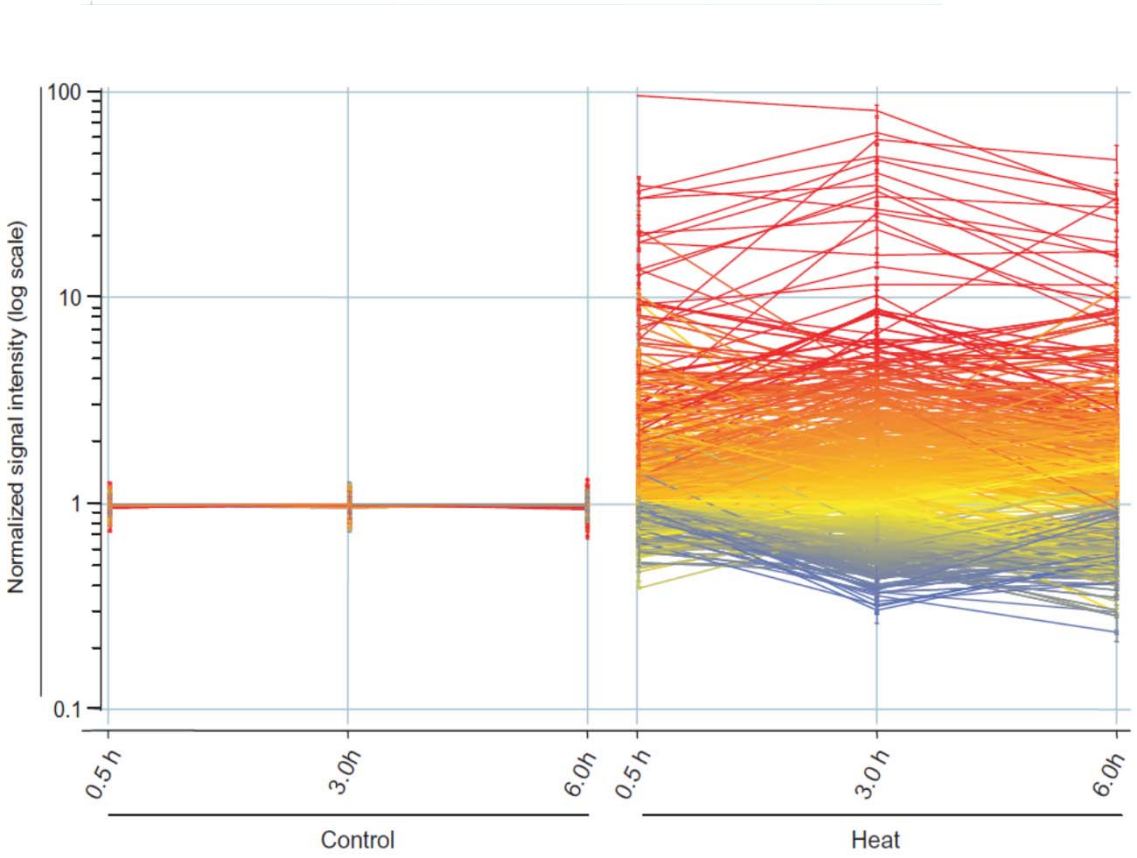


Interestingly, due to the quantitative nature of the data types, both OMICS analyses **use similar programs** for analysis and **cope with similar problems**

Analysis of developing barley caryopses

Genome → **Transcriptome** → Proteome → Metabolome



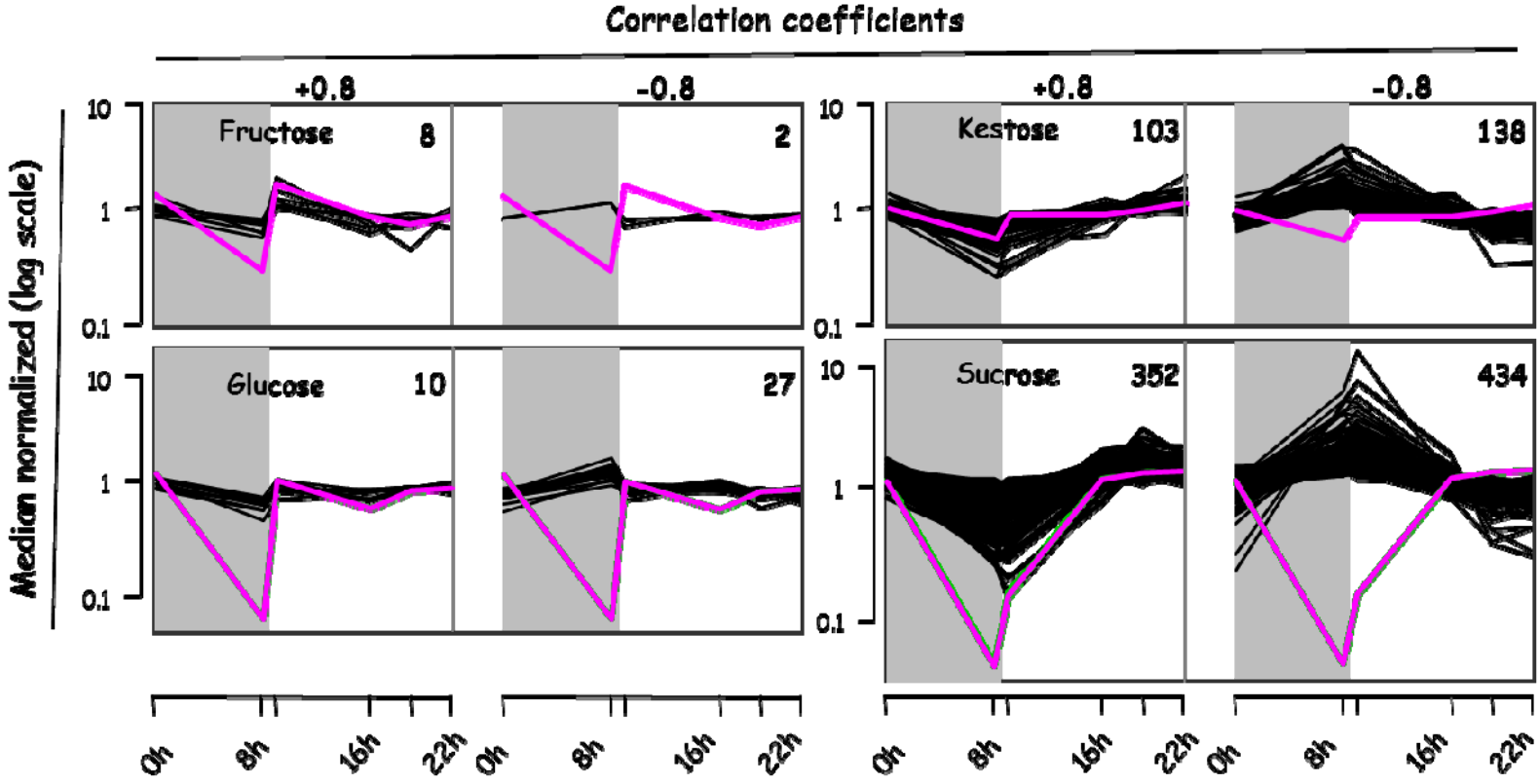


Transcriptome changes during heat stress and diurnal (day/night) cycle

Mangelsen et al., 2010a; Mangelsen et al., 2010b

Analysis of developing barley caryopses

Genome → **Transcriptome** → Proteome → **Metabolome**



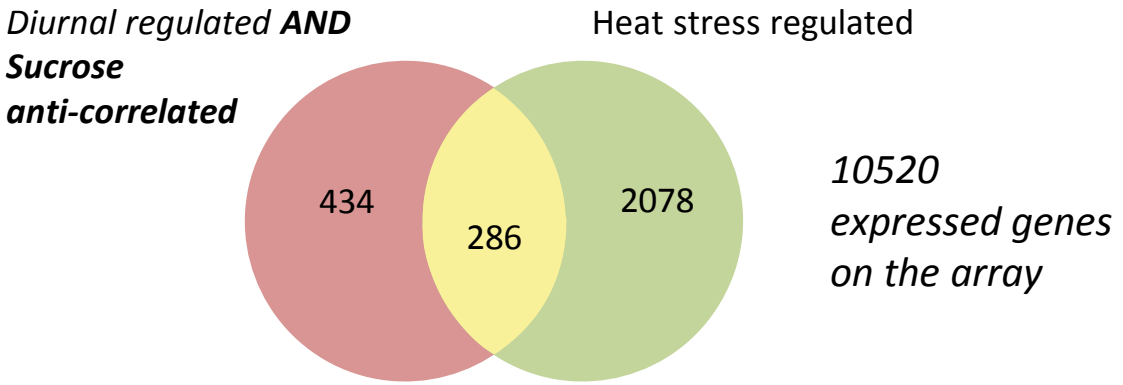
Combined analysis of Transcriptome and Metabolome
→ high temporal correlation between transcripts and certain metabolites

Mangelsen et al., 2010a; Mangelsen et al., 2010b

Analysis of developing barley caryopses

Genome → **Transcriptome** → **Proteome** → **Metabolome**

Use the **hypergeometric distribution** to check whether the overlap is significant, or not!



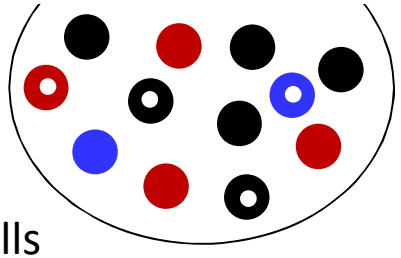
Gene list overlap is a typical application to compute the probability of occurrence by **hypergeometric distribution**.

Mangelsen et al., 2010a; Mangelsen et al., 2010b

Hypergeometric distribution

$$p(x,N,n,m) = \frac{\binom{m}{x}\binom{N-m}{n-x}}{\binom{N}{n}}$$

- **N** is the population size
- **m** is the number of success states in the population
- **n** is the number of draws
  (i.e. quantity drawn in each trial)
- **x** is the number of observed successes



13 balls

4 red → 4/13

2 blue → 2/13

4 have a white dot → 4/13

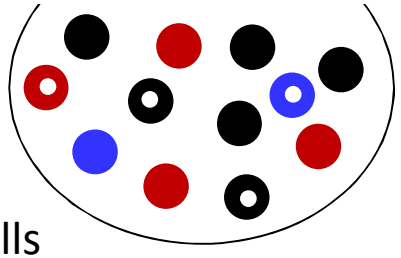
After sampling 4 balls from the bowl,

I gained 2 red ones! Was this expected on average?

Hyper.Dist. returns the probability (P_{hyp}) of successes (x) in a sample (n), without replacement, from a finite population (N), in which the total number of successes is known (m).

Hypergeometric distribution

$$p(x,N,n,m) = \frac{\binom{m}{x}\binom{N-m}{n-x}}{\binom{N}{n}}$$



- **13** is the population size
- **4** is the number of success states in the population
- **4** is the number of draws
  (i.e. quantity drawn in each trial)
- **2** is the number of observed successes

13 balls

4 red → 4/13

2 blue → 2/13

4 have a white dot → 4/13

After sampling 4 balls from the bowl,

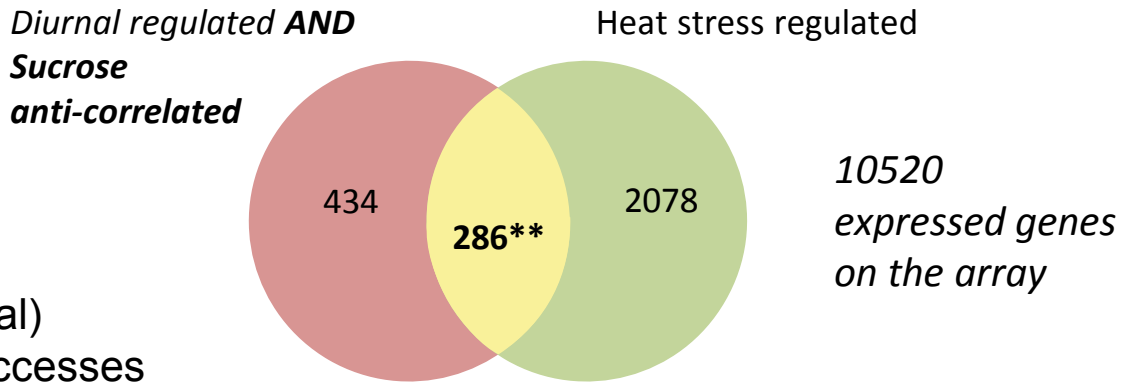
I gained 2 red ones! Was this expected on average? $P_{hyp} = 0.30$

Hyper.Dist. returns the probability (*Hyp P*) of successes (x) in a sample (n), without replacement, from a finite population (N), in which the total number of successes is known (m).

Analysis of developing barley caryopses

Genome → **Transcriptome** → Proteome → **Metabolome**

- **10520** is the population size
- **2364** is the number of success states in the population
- **720** is the number of draws (i.e. quantity drawn in each trial)
- **286** is the number of observed successes



10520 expressed genes on the array

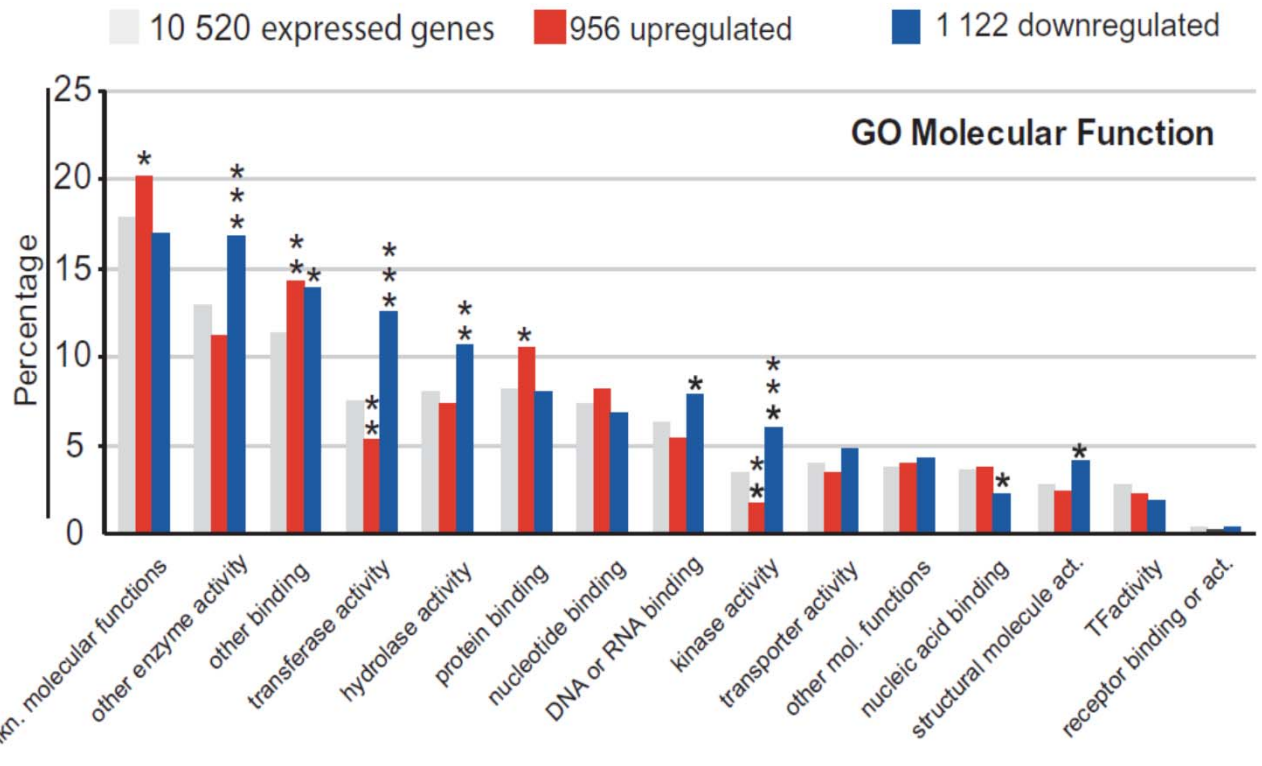
Are 286 genes a significant overlap between the two gene lists?

Answer:
Yes, a P_{hyp} = 1,58 10^{-27} supports a highly significant difference from what could be expected on average.

Mangelsen et al., 2010a; Mangelsen et al., 2010b

Analysis of developing barley caryopses

Genome → **Transcriptome** → **Proteome** → **Metabolome**



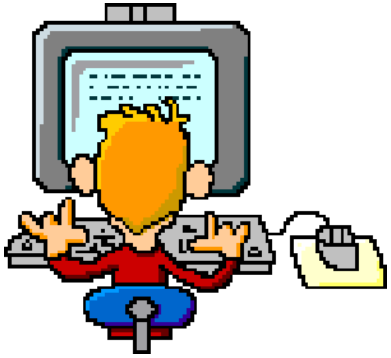
Gene Ontology (GO) analysis → compare ***your*** gene-list-of-interest with lists of genes with already known molecular function

Mangelsen et al., 2010a; Mangelsen et al., 2010b

Quantitative data come as (huge) tables

Genome → Transcriptome → Proteome → Metabolome

Quantitative Analysis → *metric data* → significance



experimental validation ← *infer a mechanistic model (e.g. logic connections)*

Quantitative *vs.* qualitative analyses

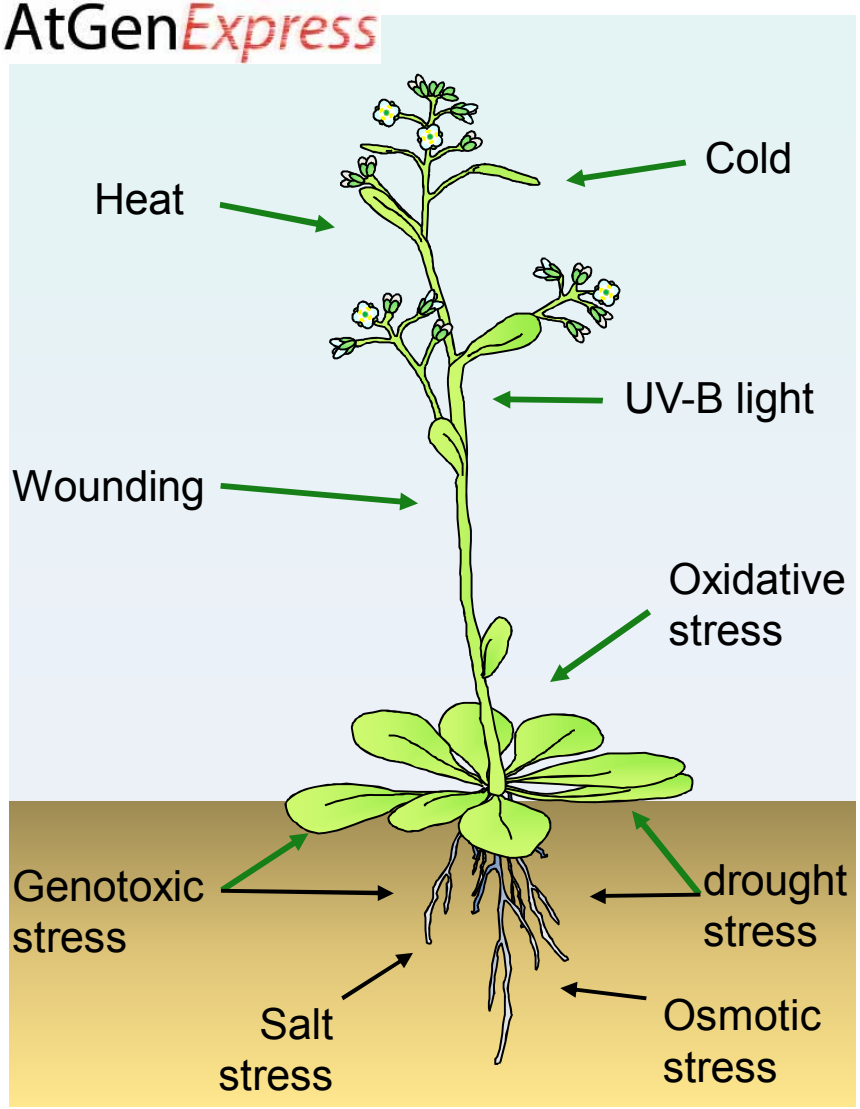
Acquiring of quantitative data of subcellular processes with high spatio-temporal resolution in living (plant) cells in their native tissue environment

Dynamics: spatio - temporal resolution

high resolution imaging

Time course

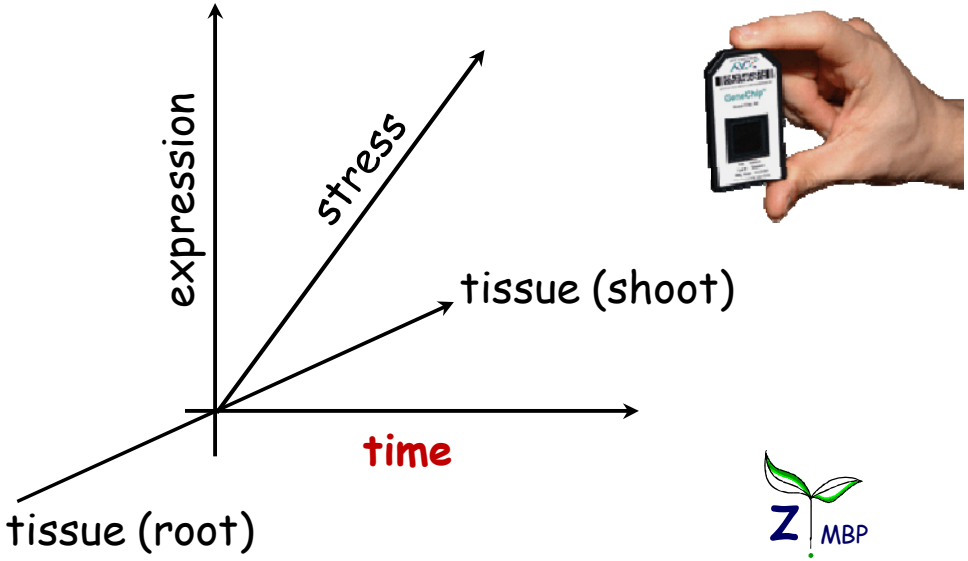
Transcriptome of the abiotic stress response in *Arabidopsis thaliana*



Kilian *et al*., 2007

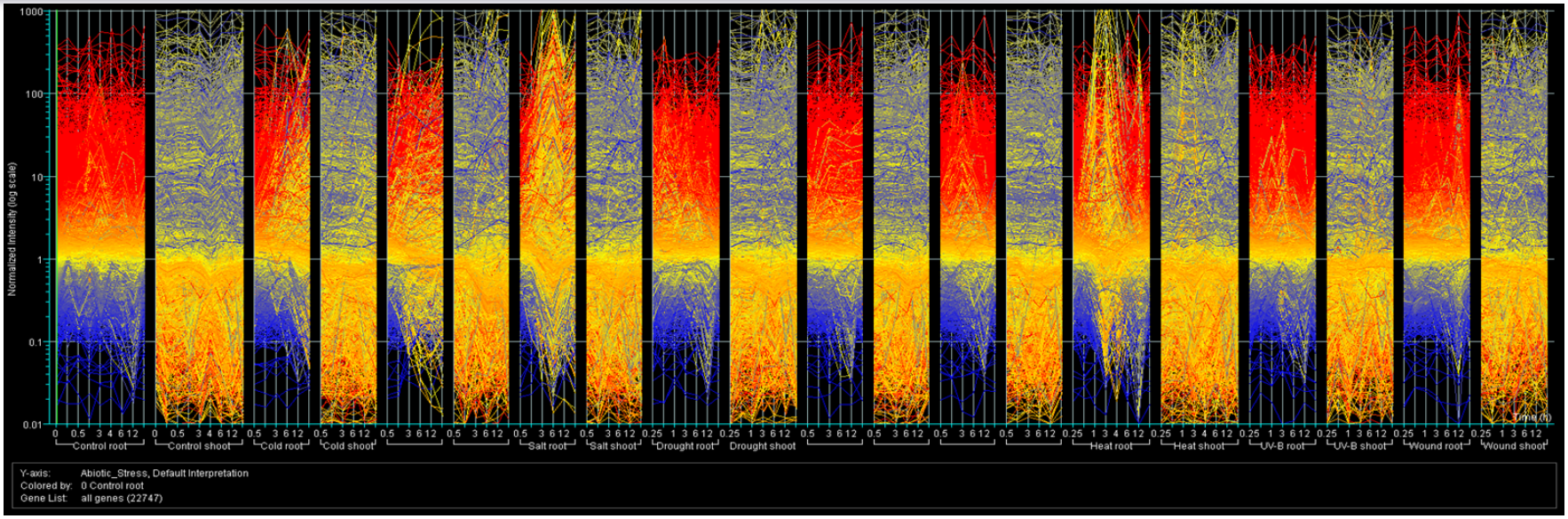
→ first 4-dimensional transcriptome analysis (gene – time – stress - tissue)

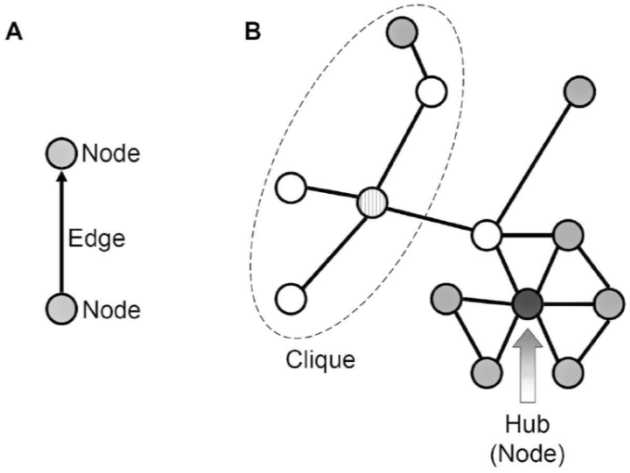
→ provides insights into gene expression dynamics at high comparability between the stress treatments

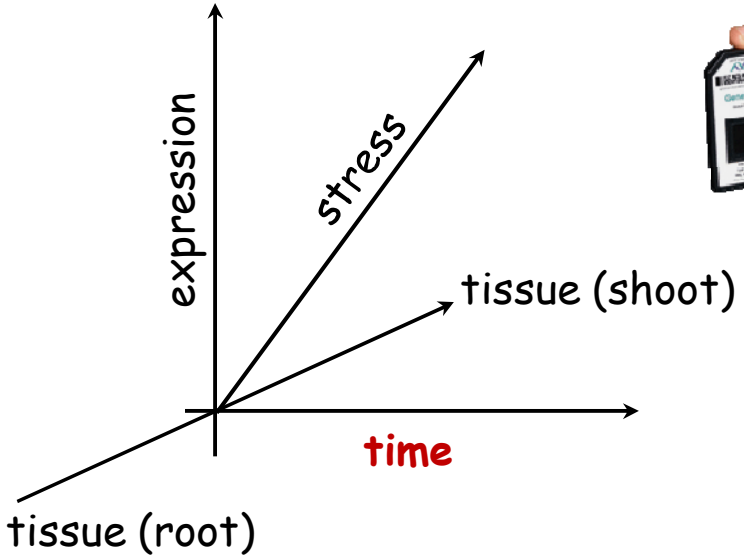


MBP

Transcriptome of the abiotic stress response in *Arabidopsis thaliana*







Kilian *et al*., 2007 Wanke et al.,2009

The AtGenExpress expression atlas comprises 1295 microarray experiments

AtGenExpress

…was a multinational effort designed to uncover the transcriptome of the multicellular model organism *Arabidopsis thaliana*

All 41 different experimental core-conditions have been finished in time:

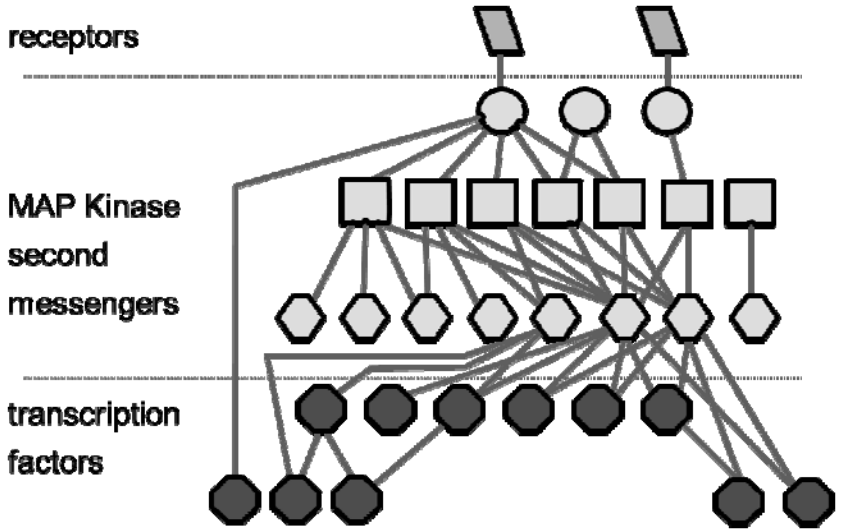
- Development
- Biotic Stress Treatment
- Abiotic Stress Treatment
- Nutrient Experiment
- Hormone Treatment

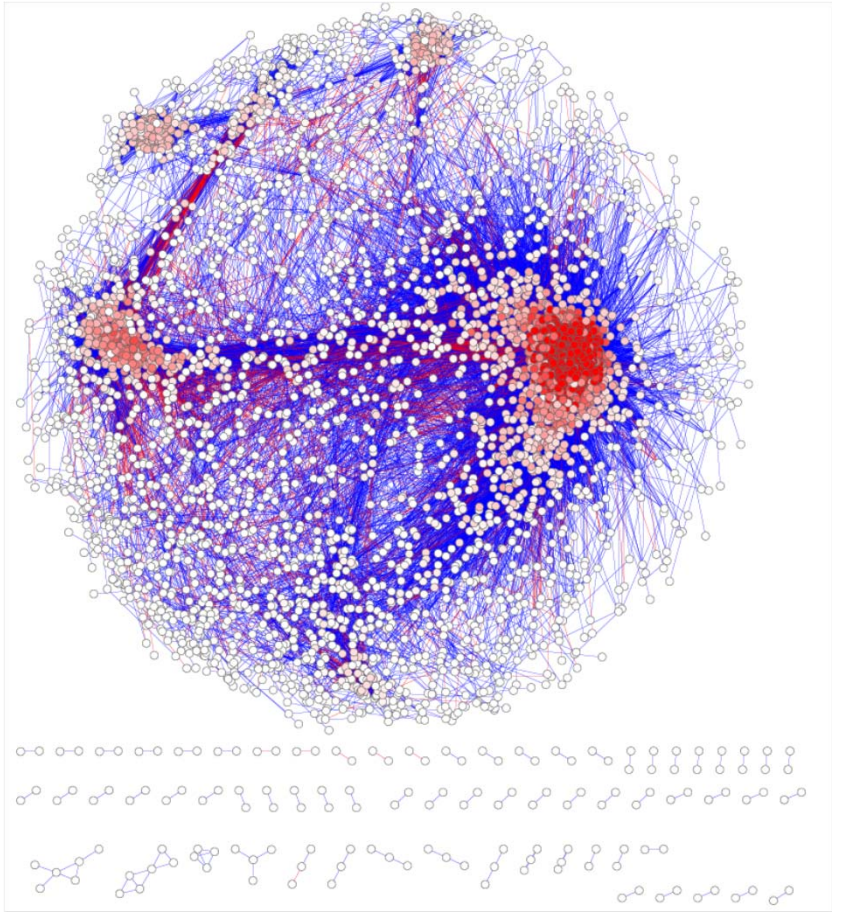
We contributed the abiotic stress experiments

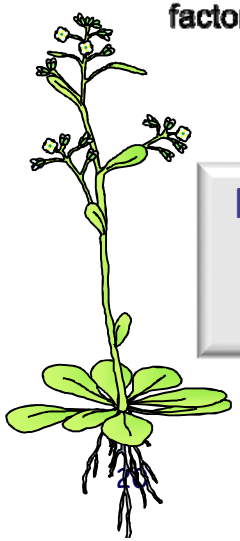
Currently, there are more than 3000 highly comparable microarray expression profiles in the database

Temporal resolution provides a dynamical insight into stress responses

Transcriptome





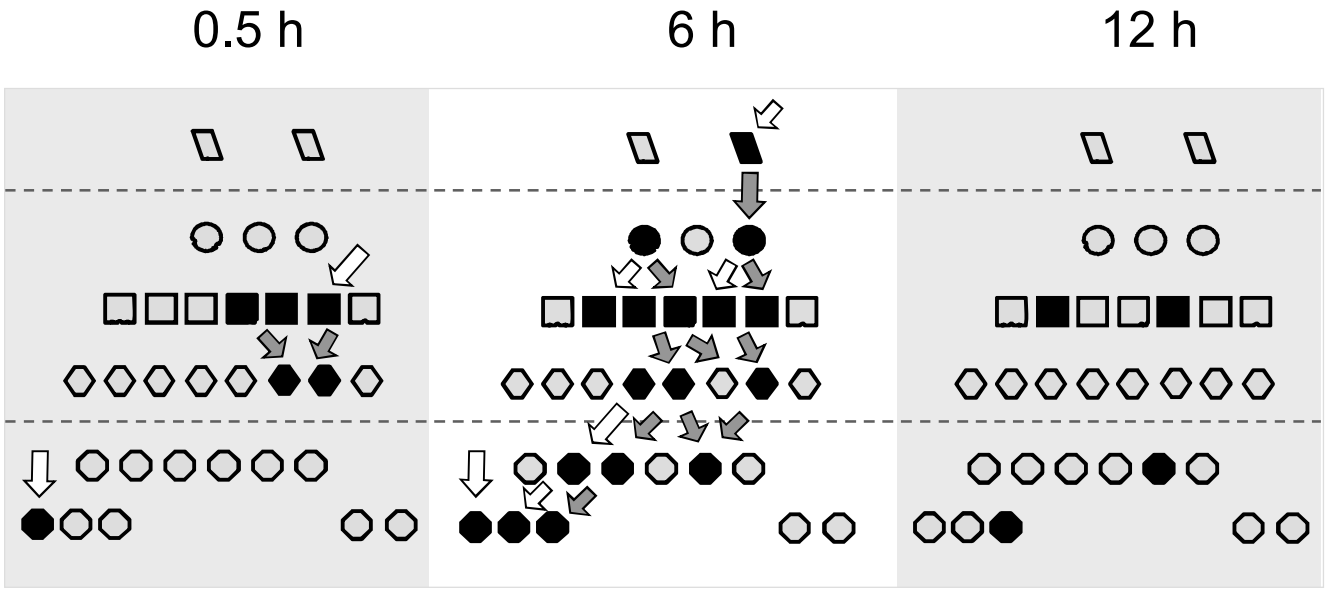


Regulatory networks of all genes (right) or of a subset (left) help to derive functional models

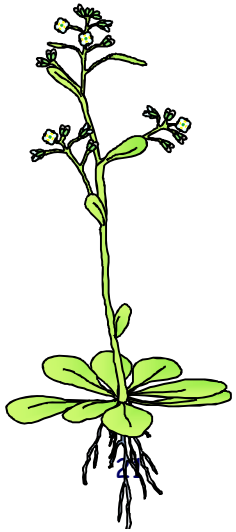
Wanke et al.,2009

Temporal resolution provides a dynamical insight into stress responses

Transcriptome

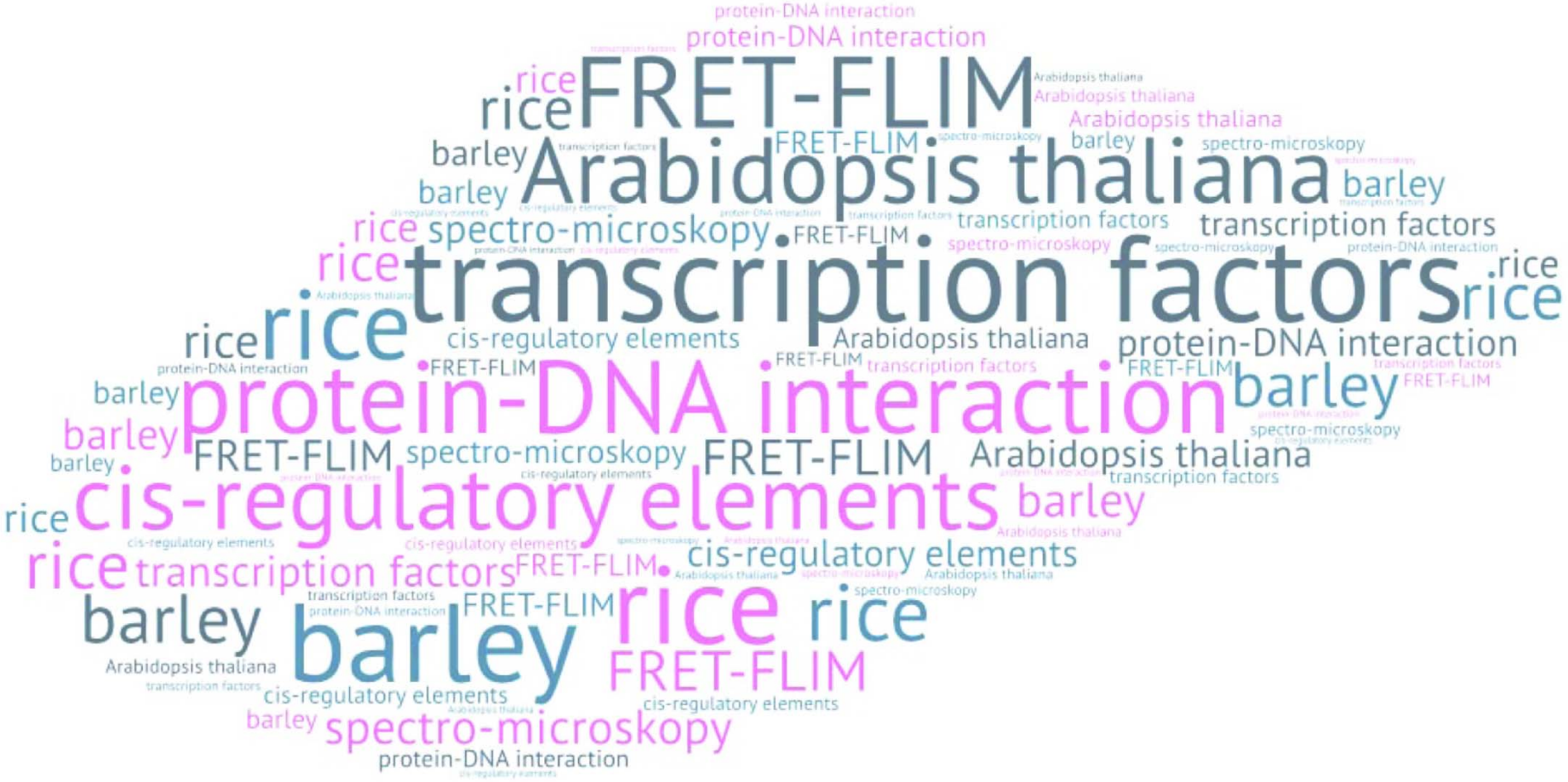


UV-B light stress



→ including the time trajectory in regulatory network analyses uncovers information flow and dynamics of stress responses

Wanke et al.,2009


protein-DNA interaction
protein-DNA interaction
rice
FRET-FLIM
rice
Arabidopsis thaliana
Arabidopsis thaliana
Arabidopsis thaliana
barley
FRET-FLIM
barley
spectro-microskopy
barley
Arabidopsis thaliana
barley
rice
spectro-microskopy
FRET-FLIM
transcription factors
transcription factors
rice
transcription factors
spectro-microskopy
rice
rice
rice
cis-regulatory elements
Arabidopsis thaliana
protein-DNA interaction
rice
FRET-FLIM
FRET-FLIM
transcription factors
FRET-FLIM
barley
protein-DNA interaction
barley
FRET-FLIM
spectro-microskopy
barley
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Arabidopsis thaliana
transcription factors
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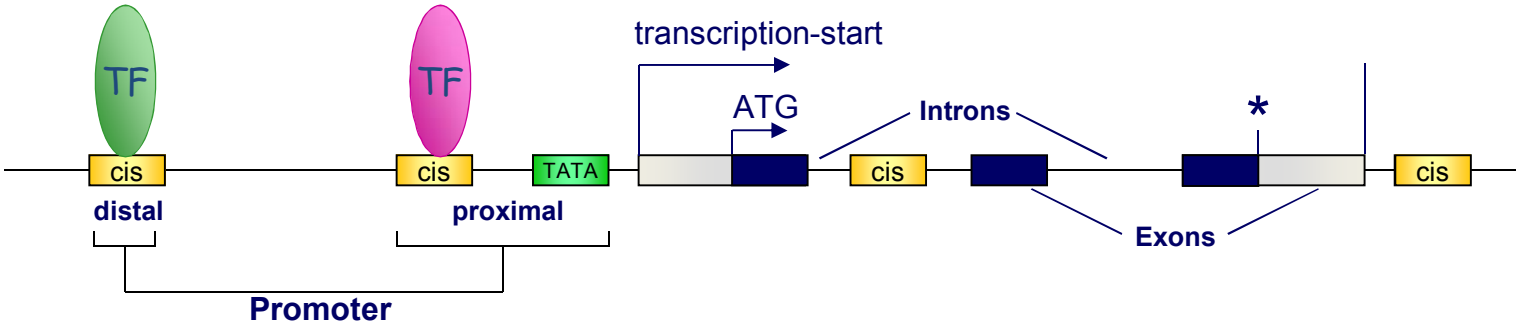
transcription factors
FRET-FLIM
spectro-microskopy
barley
rice
rice
FRET-FLIM
Arabidopsis thaliana
cis-regulatory elements
cis-regulatory elements
barley
spectro-microskopy
protein-DNA interaction

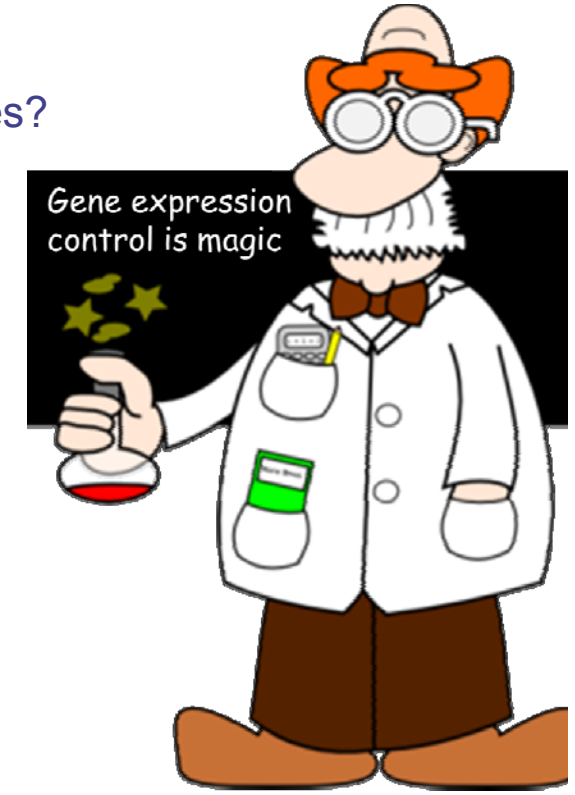
My research interest: Gene expression control



Genome → Can we infer putative binding sites in genomes?

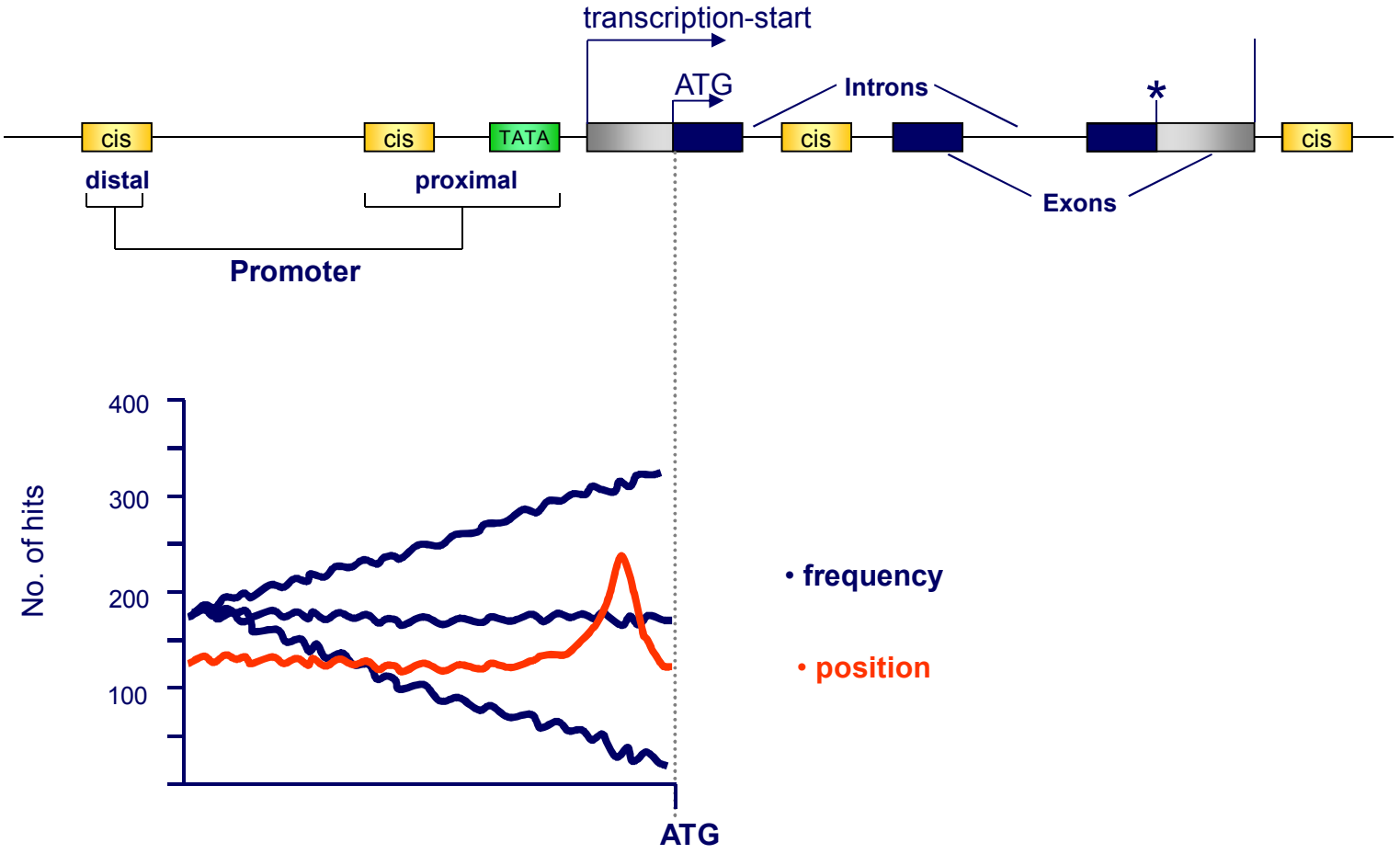
Transcriptome → What are the effects of transcription factor (TF) binding?

Proteome → Which are the TF binding sites *in vivo*?
→ Which protein partners act together?



Is there a cryptic code in non-coding regulatory sequence?

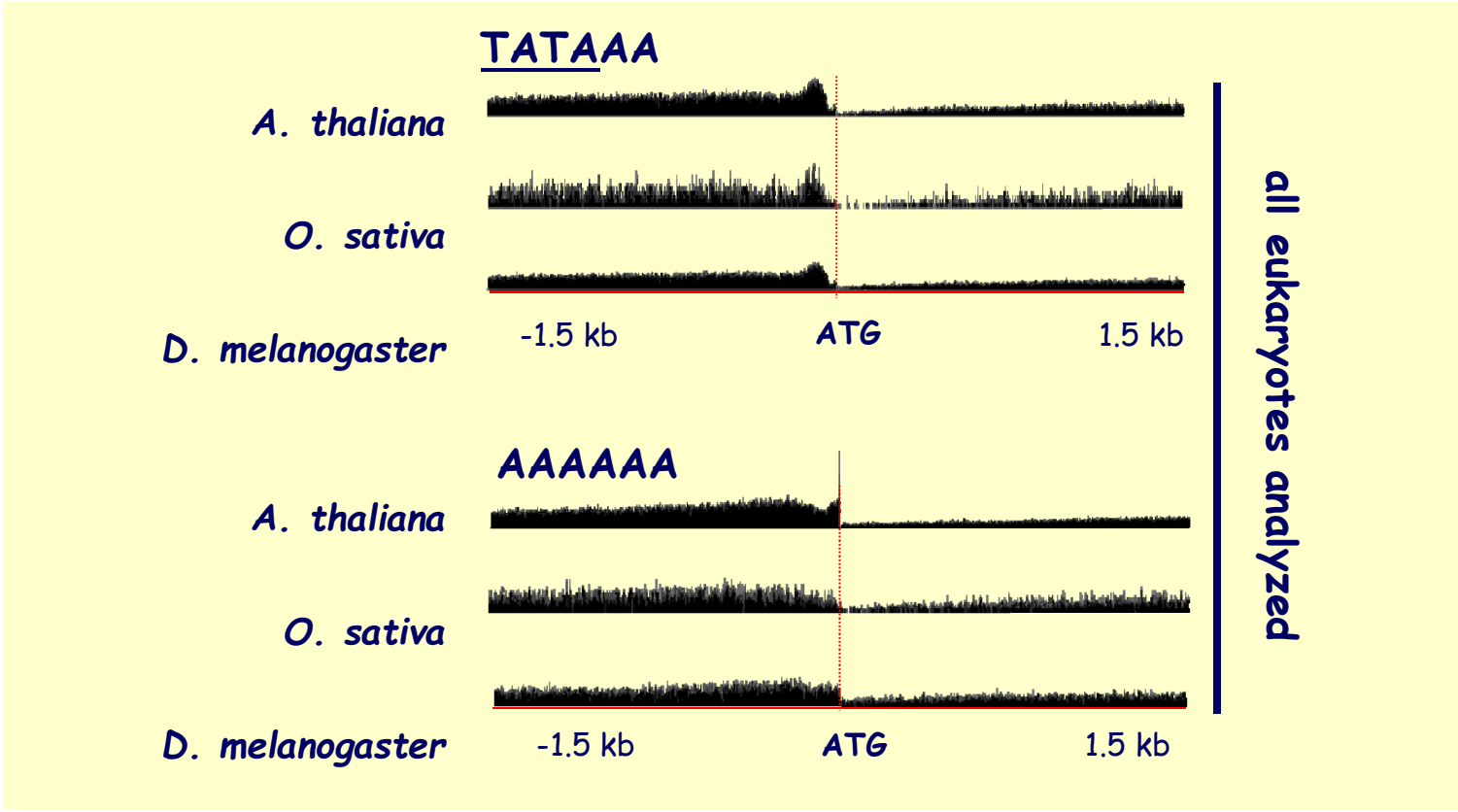
Genome



Berendzen et al., 2006

Motif-distribution in promoters

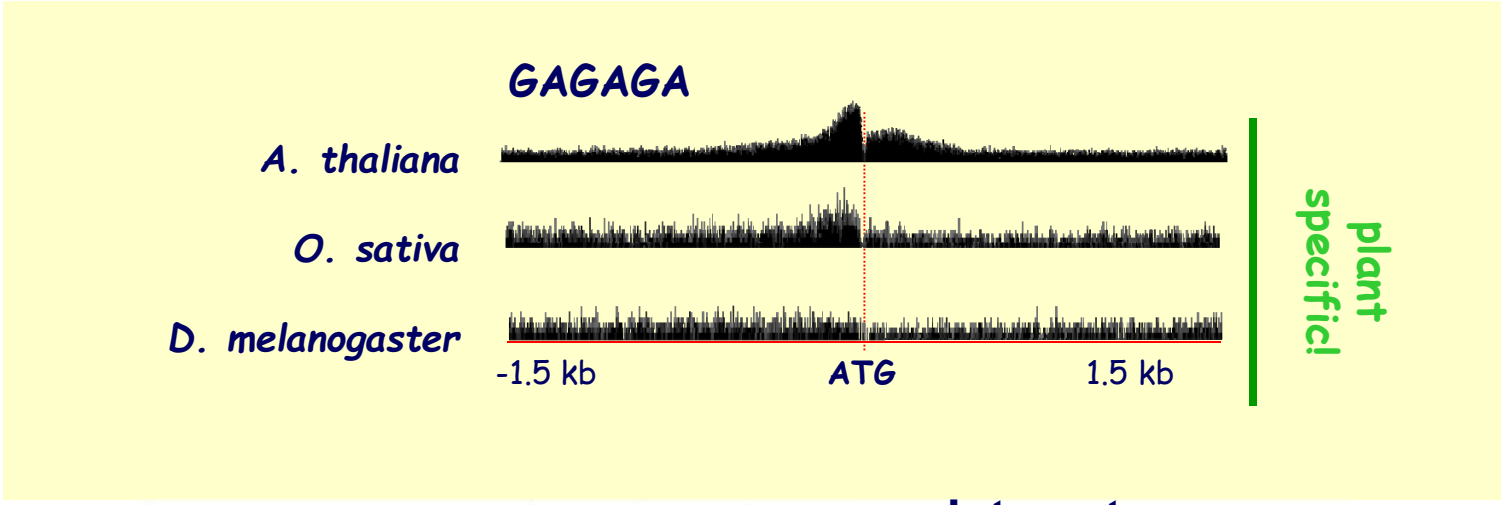
Genome



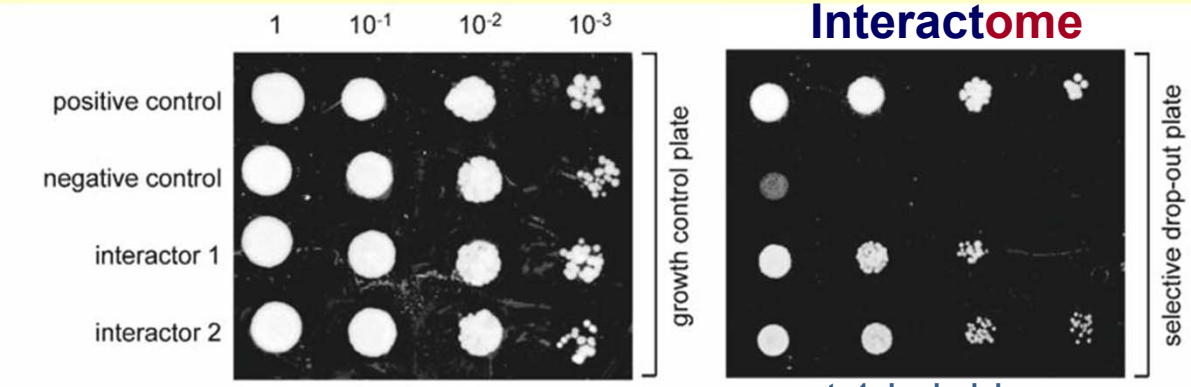
BPC proteins are plant GAGA-binding proteins

Genome

We identified unique GAGA-frequency characteristics in plant promoters by bioinformatics



Interactome

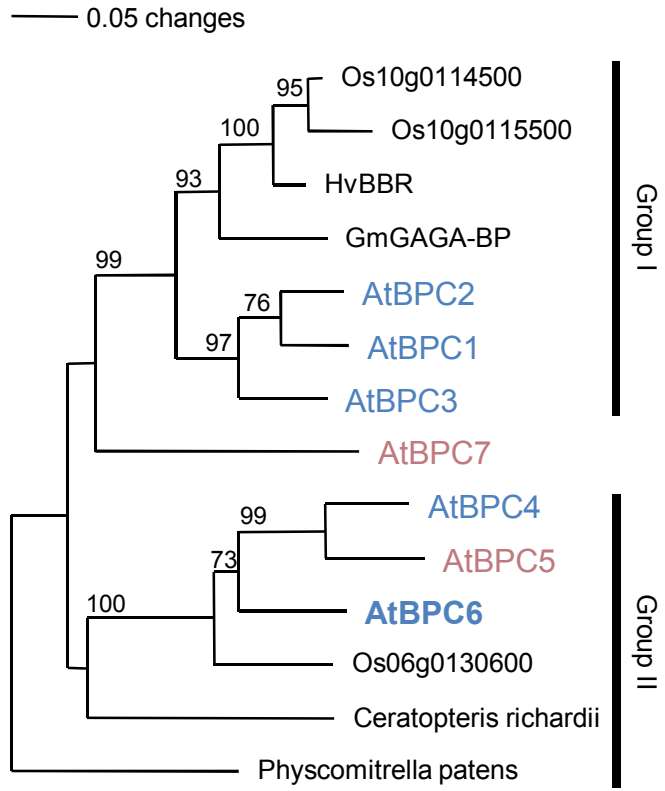


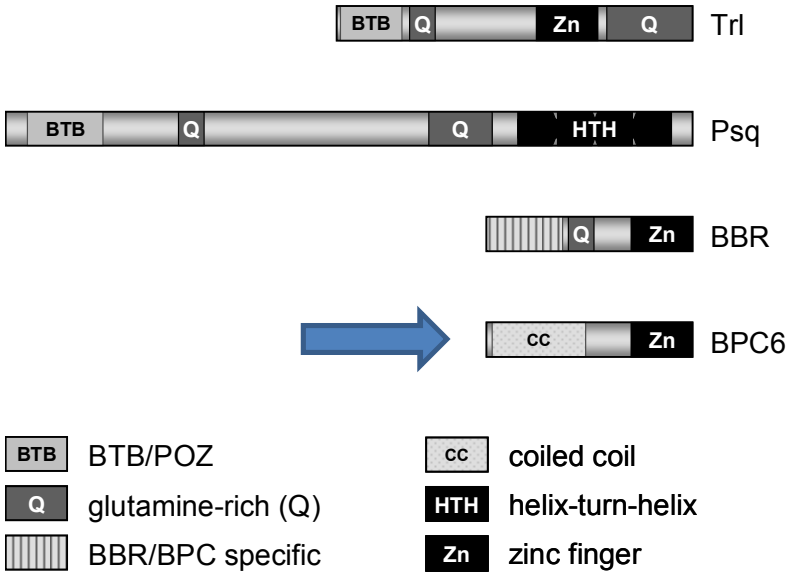
yeast 1-hybrid screen

Wanke & Harter, 2009; Berendzen et al., 2006, Santi et al., 2003

Plant and animal *GAGA*-factors are unrelated

Genome





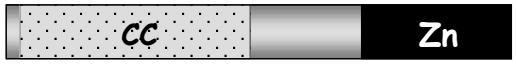
Although plant and animal GAGA-binding factors recognize GAGA-motifs, they appear to be phylogenetically unrelated and functionally distinct

Wanke et al., 2011; Santi et al., 2003

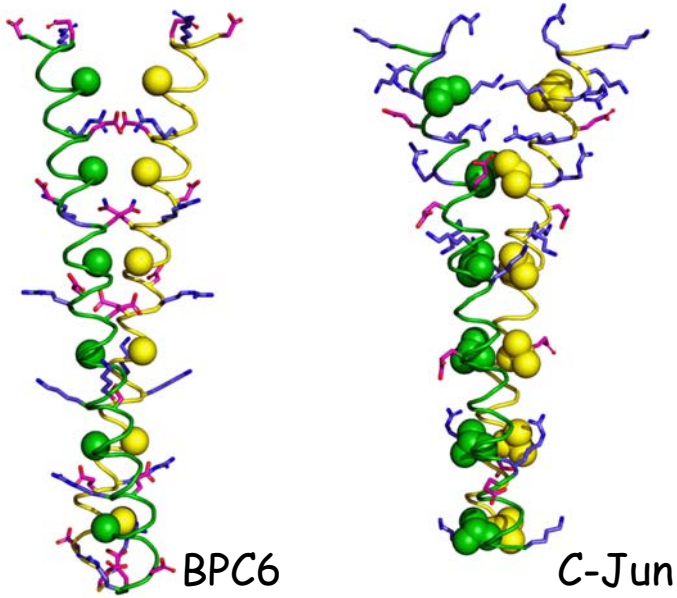
A unique Alanine-zipper domain in BPC6

Interactome

Question: Is the N-terminal Coiled-Coil domain important for homodimerization?




```
BPC6      ERDAAIQERNLAISEKKAAVAERDMAFLQRDTAIAERNNAI
C-Jun     SRKRKLERIARLEEKVKTLKAQNSELASTANMLREQVAQLKQKVM
```



- Use the available structural information of c-Jun to derive a predicted model structure for BPC6
- Apply **Molecular Dynamics simulations** to compare the different domains

Wanke et al., 2011

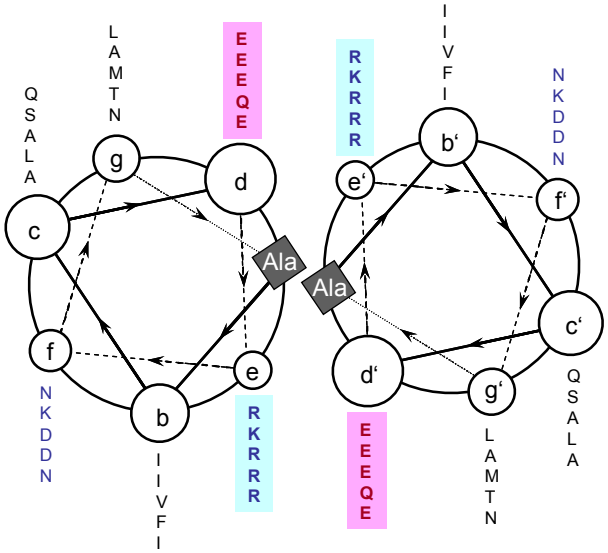
A unique Alanine-zipper domain in BPC6

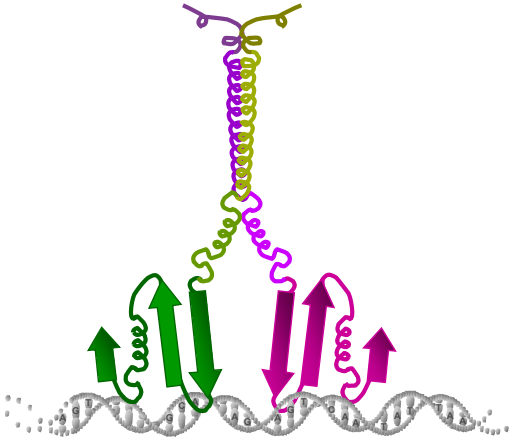
Interactome

Genome

```
C-Jun          SRKRKLERIARLEEKVKTLKAQNSELASTANMLREQVAQLKQKVM
BPC6           ERDAAIQERNLAISEKKAAVAERDMAFLQRDTAIAERNNAI

Physcomitrella AFKDRHKAAIEREQAIKEKAQAEREKMQAEREKAQVE
Microcystis    AQQERNQAQQERNQAQQERNQAQQERDRAFARLRELG
Azorhizobium   AQTYRNAAETFRNDASRFRNEAETFRNQAAQSAANAA
Aspergillus    ARKERELAEIARDAAEKERVAAENERKEAAAERQRA
Homo           LCQELKEALQEADVAKCRRDWAFQERDKIVAERD
Sus              LEQKGRALEQRDTAQEQKEKA
```





Answer:

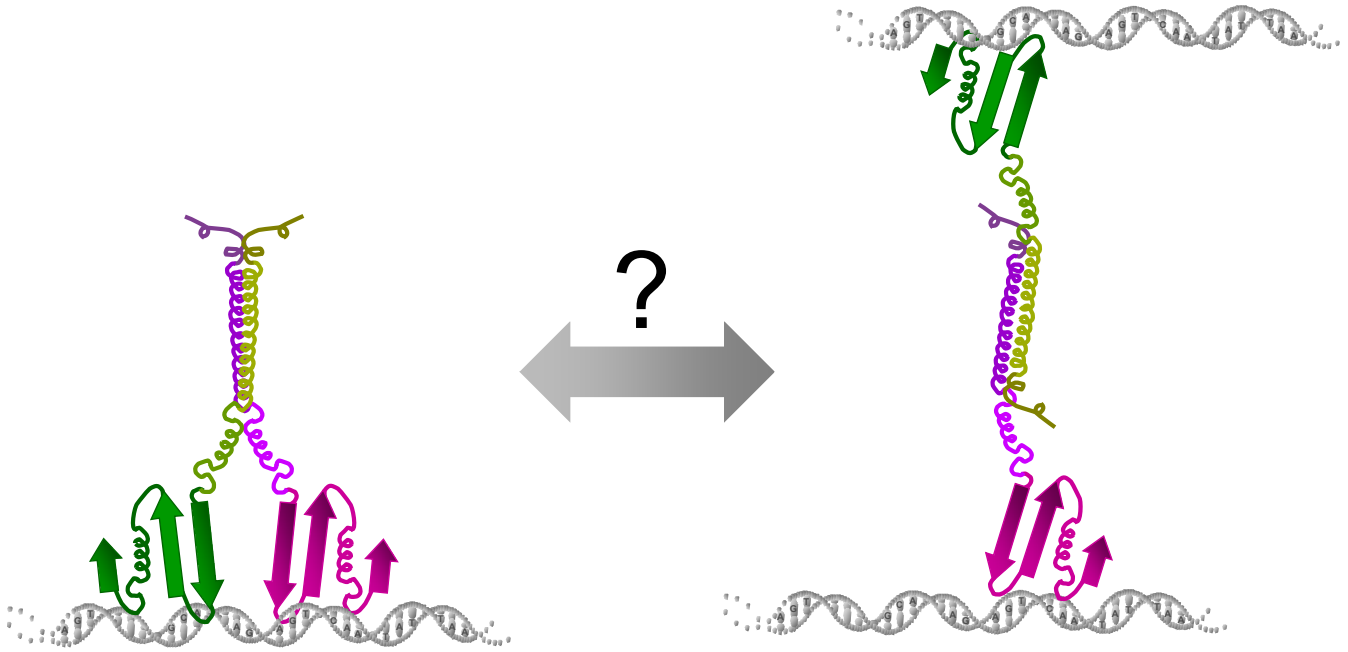
- Yes, the CC-domain can form dimers that are stabilized by salt bridges between the monomers
- **Molecular Dynamics simulations** propose that parallel dimers are formed.

Wanke et al., 2011

BPC6 forms homotypic dimers

Interactome

Experimental validation: Is the model correct?
→ Important functional implications for DNA-binding



parallel orientation
→ neighboring DNA-motifs on the same strand

anti-parallel orientation
→ DNA-motifs on different strands of DNA

Quantitative *vs.* qualitative analyses

Acquiring of quantitative data of subcellular processes with high spatio-temporal resolution in living (plant) cells in their native tissue environment

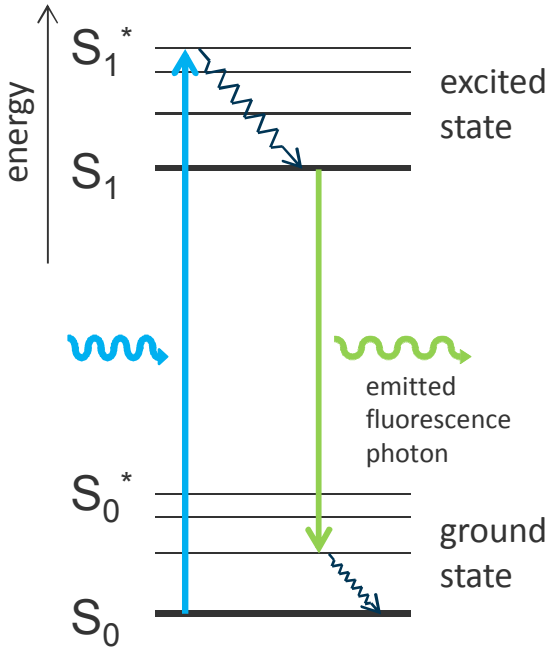
Dynamics: spatio - temporal resolution

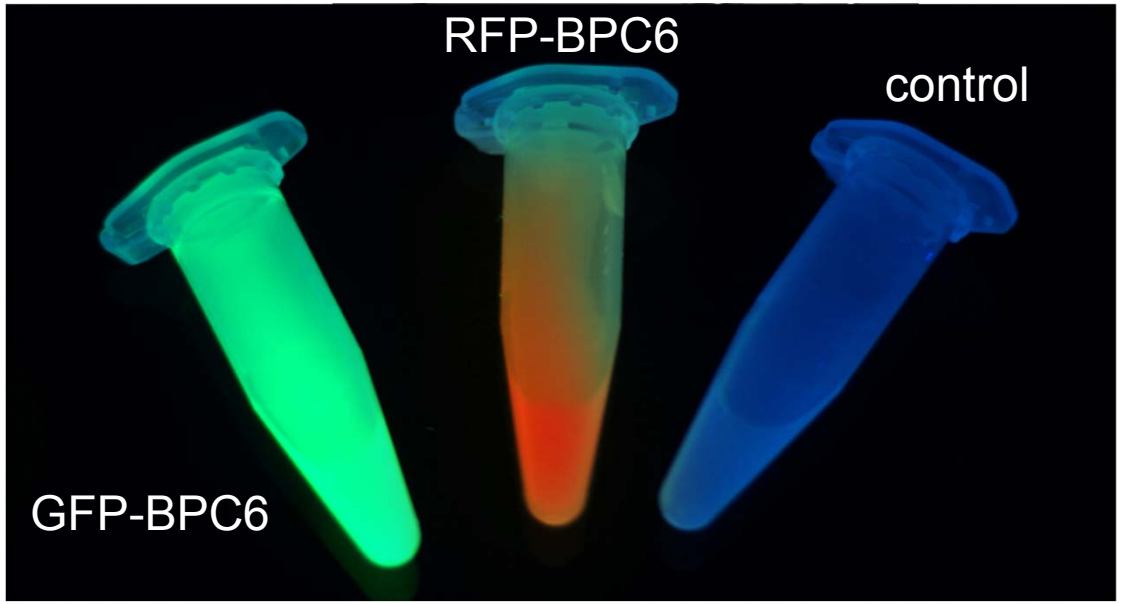
fluorescence lifetime imaging

Time course

Fluorescence Lifetime Imaging Microscopy (FLIM)

Interactome



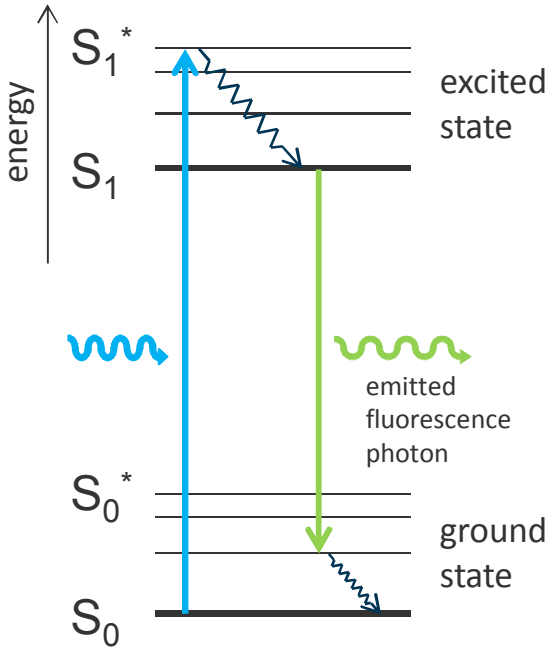


Green- and Red- fluorescent protein fusions
under UV excitation light

Wanke et al., 2011; Elgass et al., 2010

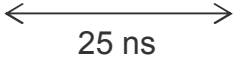
Fluorescence Lifetime Imaging Microscopy (FLIM)

Interactome



Fluorescence is not instantaneous:
Excited state has a certain lifetime

TCSPC
(time correlated single photon counting)



chromophore excited by short pulsed laser (~100 ps)

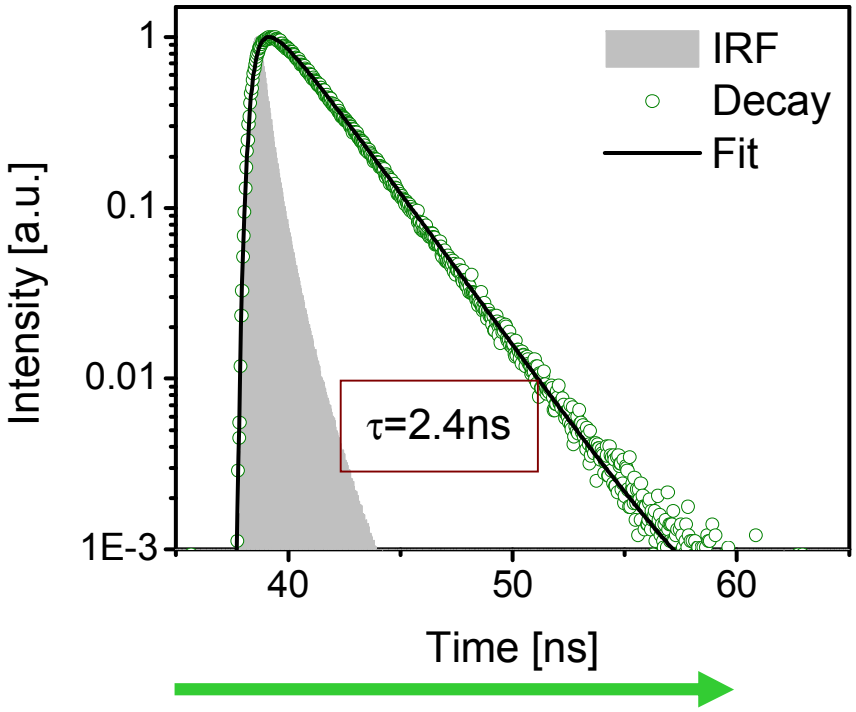
stop-watch:
starts with each laser pulse
stops with first detected fluorescence photon

Wanke et al., 2011; Elgass et al., 2010

Fluorescence Lifetime Imaging Microscopy (FLIM)

Interactome

in plasma membrane



Fluorescence-decay shape depends on the cellular environment!

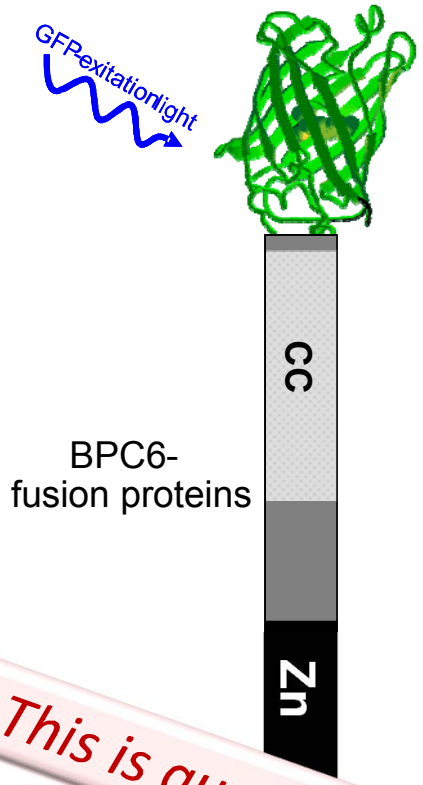
If possible ‚acceptors' are present, the **lifetime decreases**

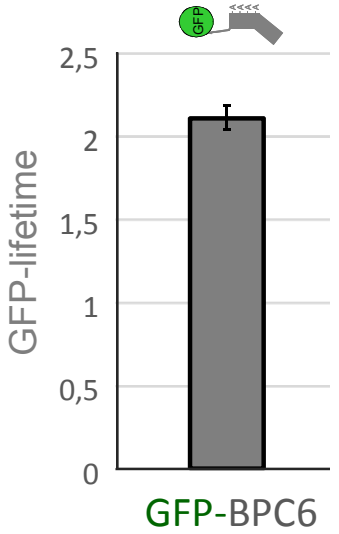
Time with detectable GFP signal **AFTER** the excitation light was switched off!

Wanke et al., 2011; Elgass et al., 2010

Fluorescence Lifetime Imaging Microscopy (FLIM)

Interactome





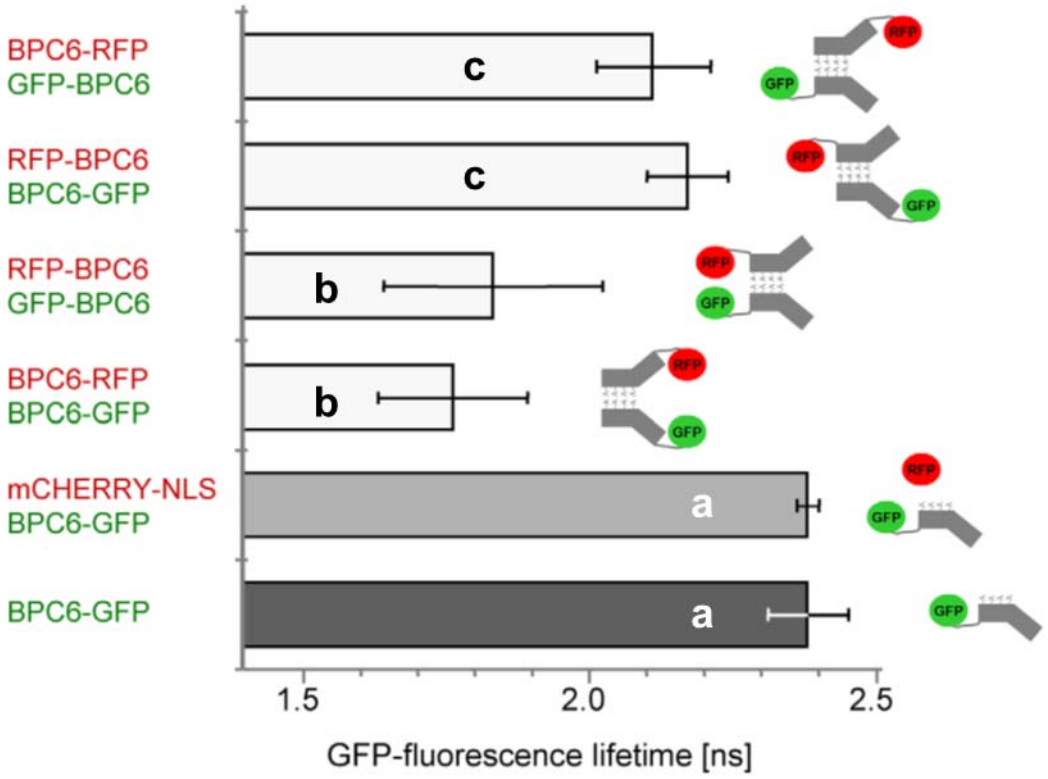
The closer **donor** chromophore and **acceptor** chromophore are positioned towards each other, the **shorter** will be the **lifetime of the donor** (GFP)

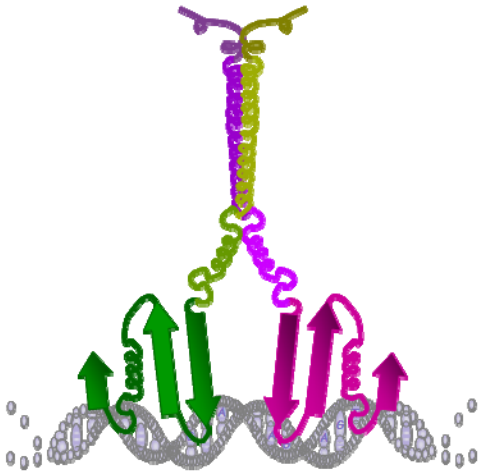
This is quantitative data!

Wanke et al., 2011; Elgass et al., 2010

FLIM provides quantitative data!

Interactome





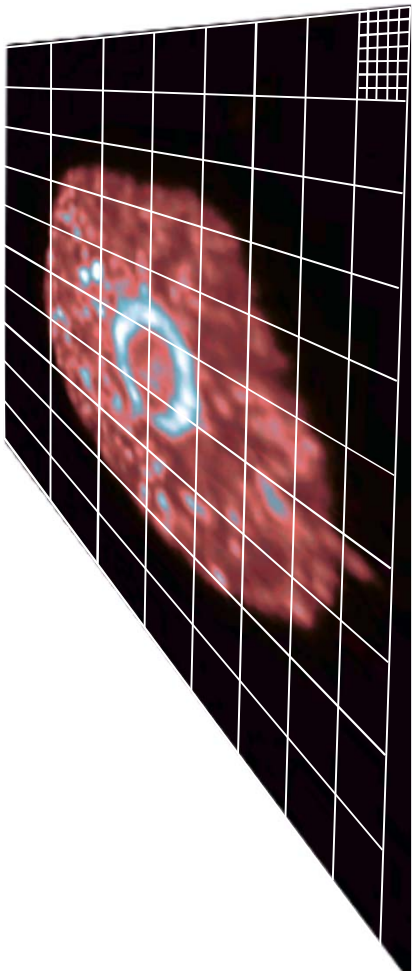
- FRET-FLIM validates that parallel homotypic dimers are formed *in vivo*
- First experiment to study protein conformation in a living eukaryote cell

Wanke et al., 2011; Elgass et al., 2010

WHY is that an Interactome? - FLIM data is generated for all pixels ('Pixelome')

Pixelome

All GFP-lifetime data of all pixels of a spectro-microscopic image



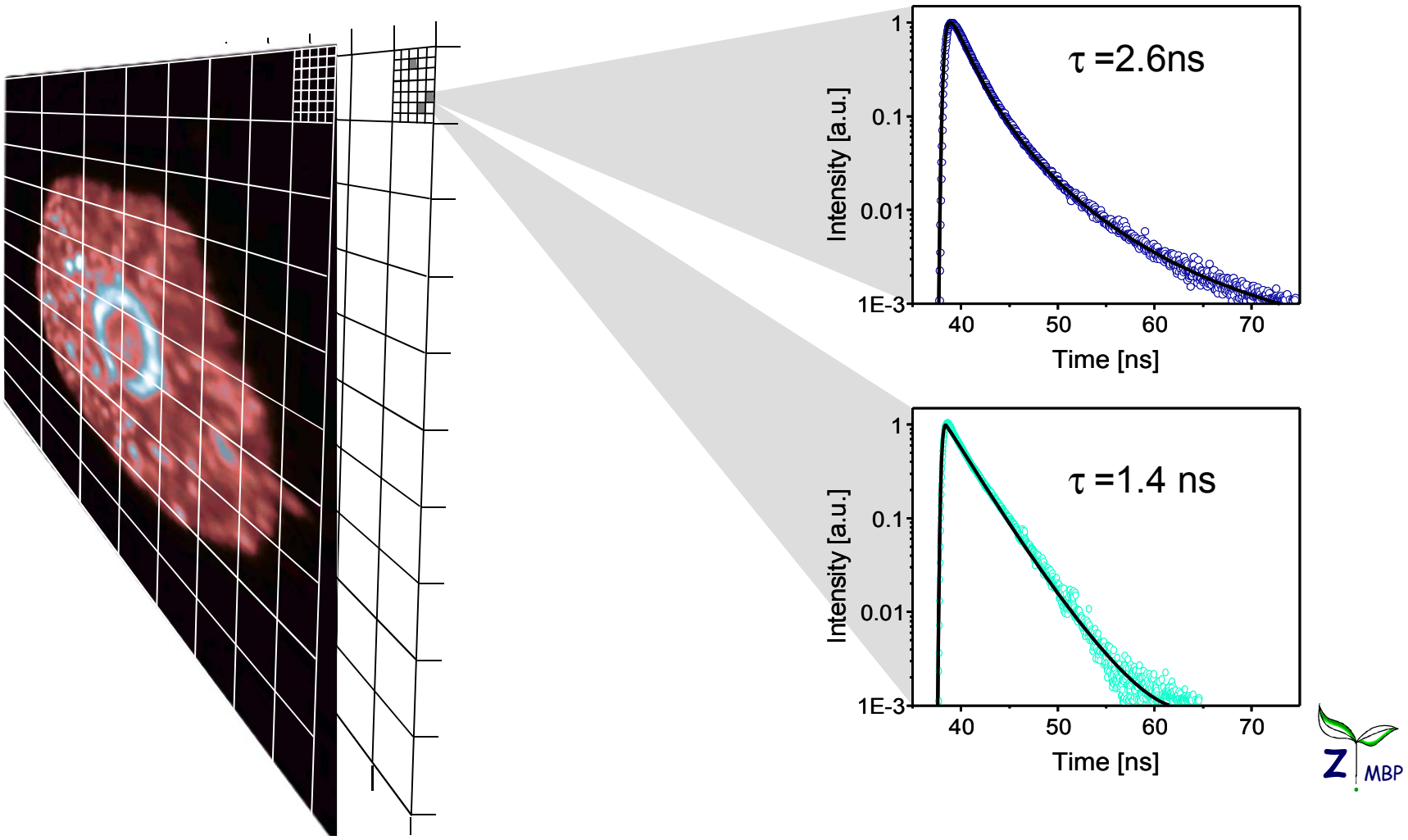
The pixel-wise information of an image is a **qualitative** 'ome' already!

MBP

pixel-wise FLIM is an 'Pixelome' OMICS

Pixelome

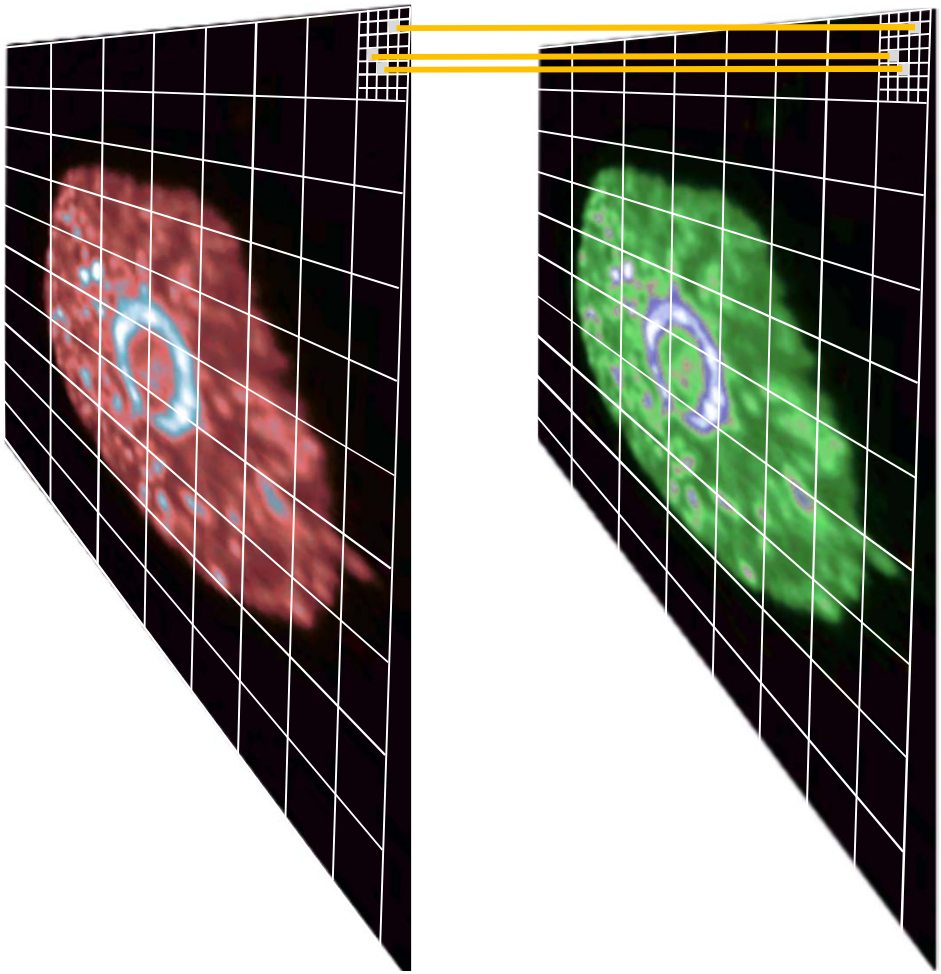
All GFP-lifetime data at all pixels of a spectro-microscopic image



pixel-wise FLIM is an 'Pixelome' OMICS

Pixelome

Pixel-wise comparison between different fluorescence signal of the same image



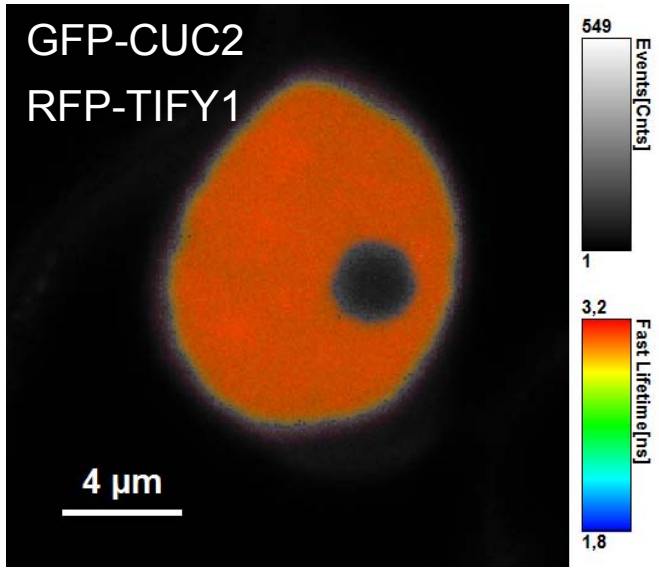
Comparison of **quantitative** fluorescence information between different channels

→ spacial signal information

→ lifetime (LT) changes in microdomains

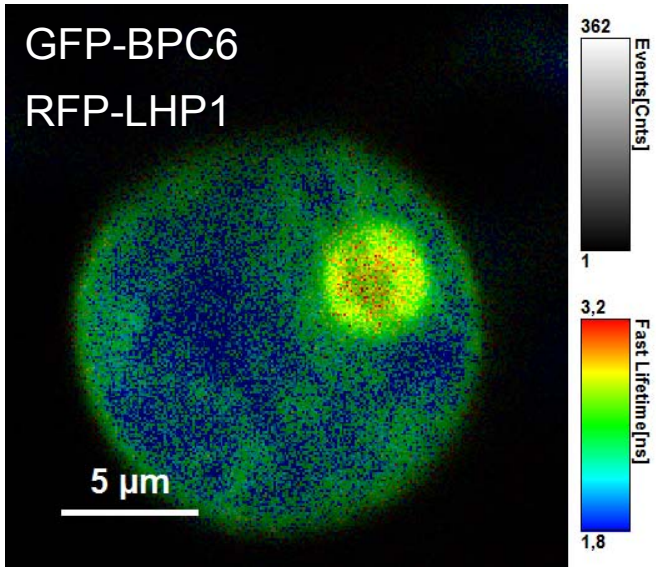
→ *in vivo* interaction data

Spatial analysis of protein – protein interaction by FLIM



no interaction

Quantitative analysis of donor-fluorescence lifetime *in vivo*



LT change in the nucleolus, LHP1

BPC6 and LHP1 interact in the nucleoplasm

→ spacial signal information
→ lifetime (LT) changes in microdomains
→ *in vivo* interaction data

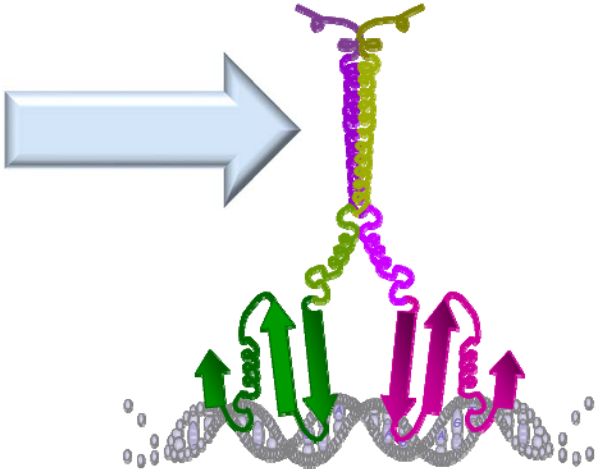
MBP

FLIM provides quantitative data!

Interactome

Question: Are there more proteins interacting with BPC6?

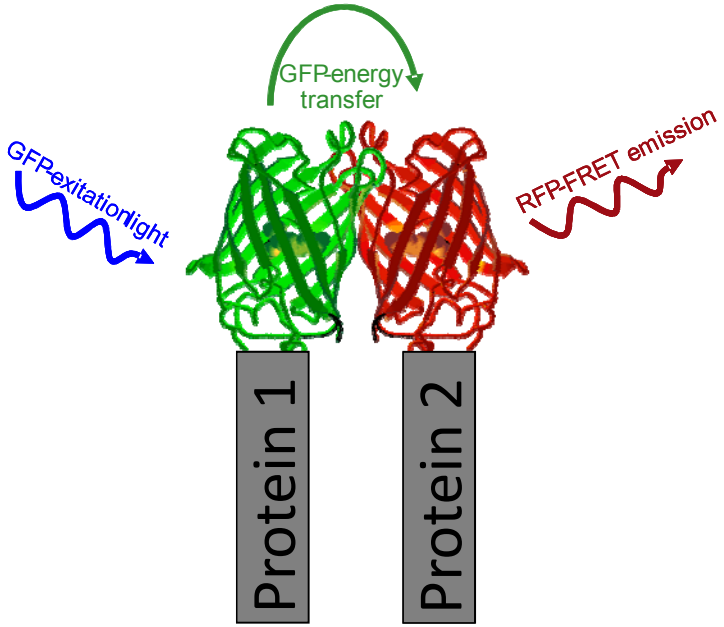
Answer: Yes!

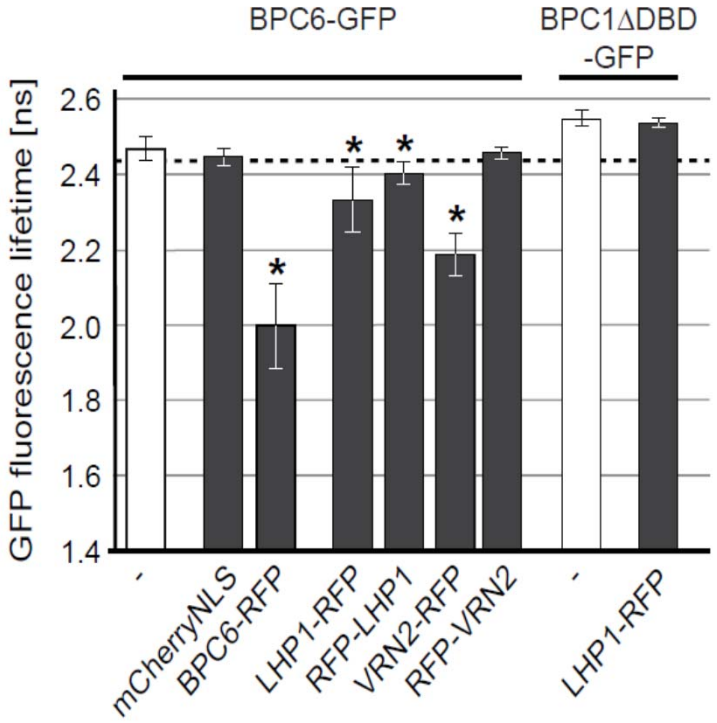


Wanke et al., 2011; Elgass et al., 2010

Group II BPCs interact with LHP1 and VRN2 and others…

Interactome



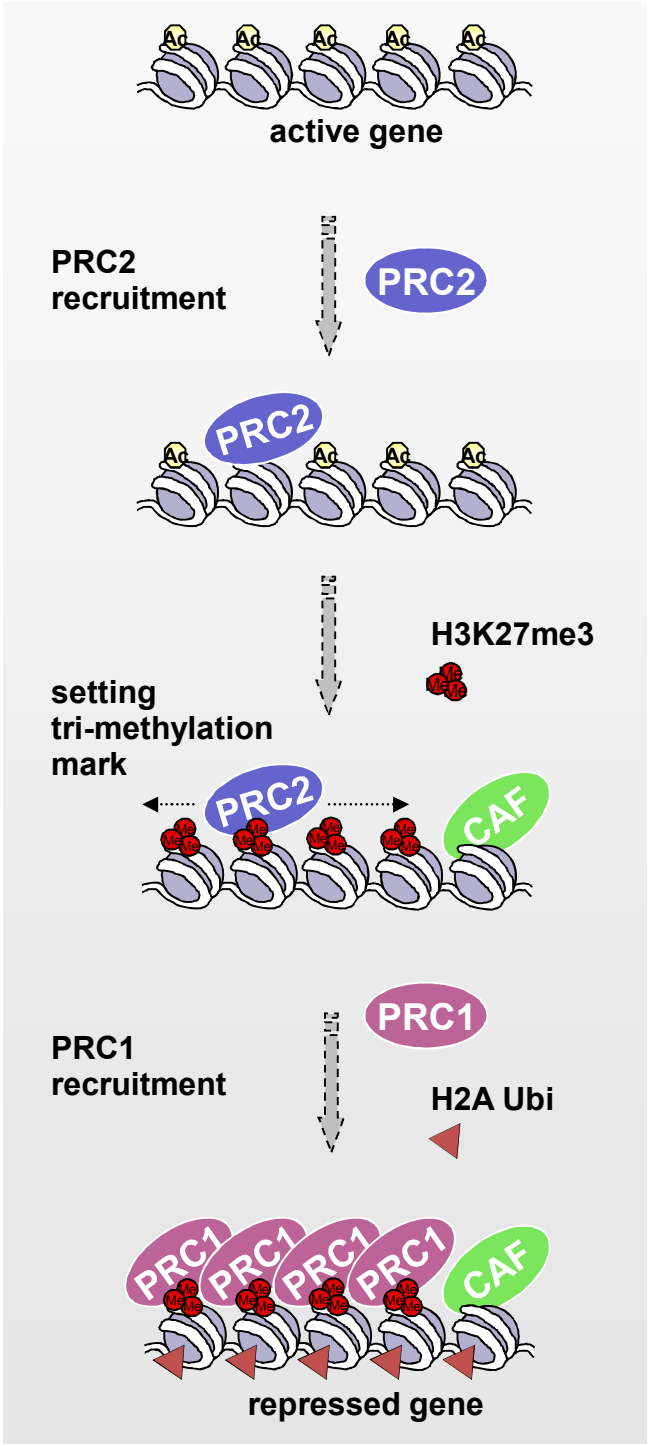


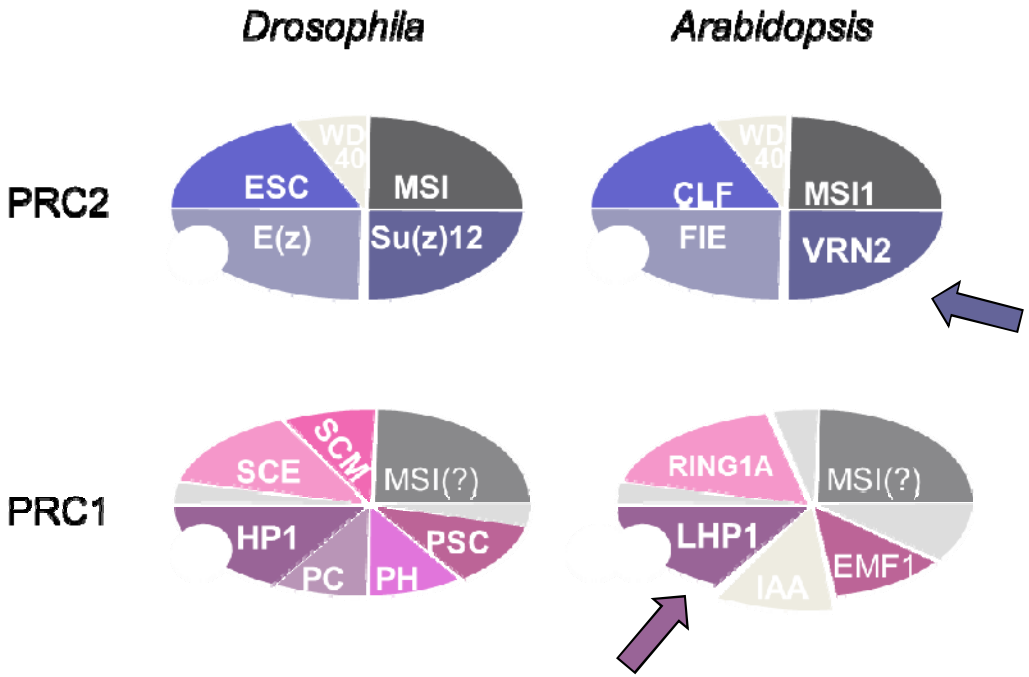
FLIM uncovered that a larger BPC6 dependent complex exists in the nucleoplasm:

LHP1 (part of PRC1) and **VRN2** (part of PRC2) associate with **BPC6** *in vivo*

Wanke et al., 2011; Hecker et al., 2015

PRC1 and PRC2 are involved in gene silencing





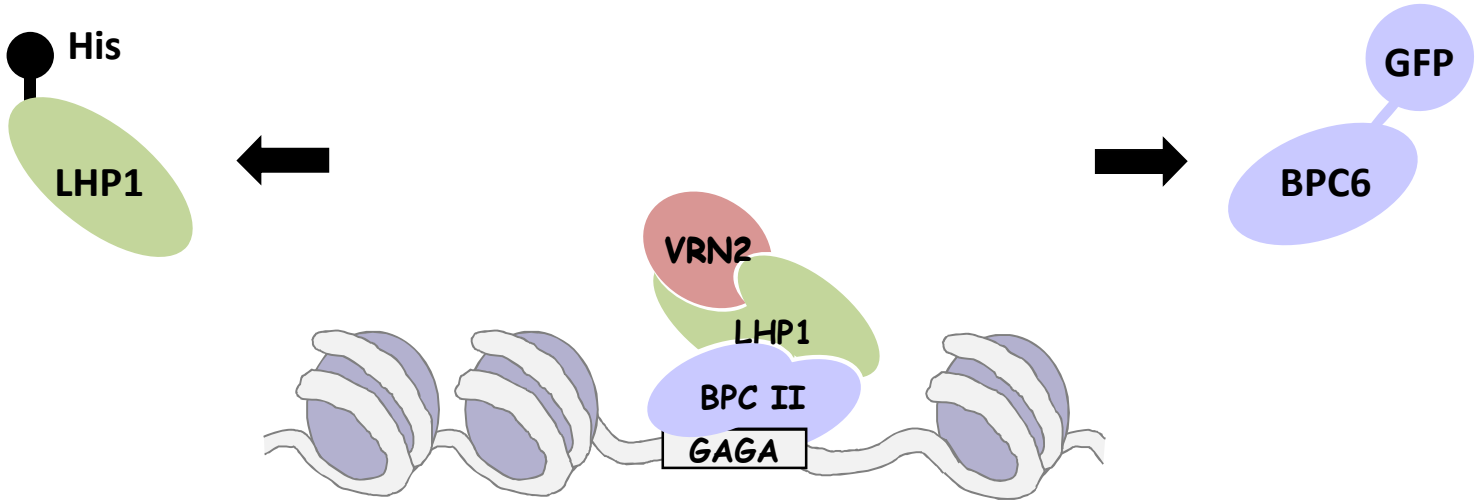
Our data suggest a role for BPC6 in gene silencing *via* Histone 3 trimethylation (H3K27me3)

Hecker et al., 2015

Does BPC6 recruit LHP1 to GAGA-motifs?

Interactome

Question: Does BPC6 recruit LHP1 to GAGA-motifs?



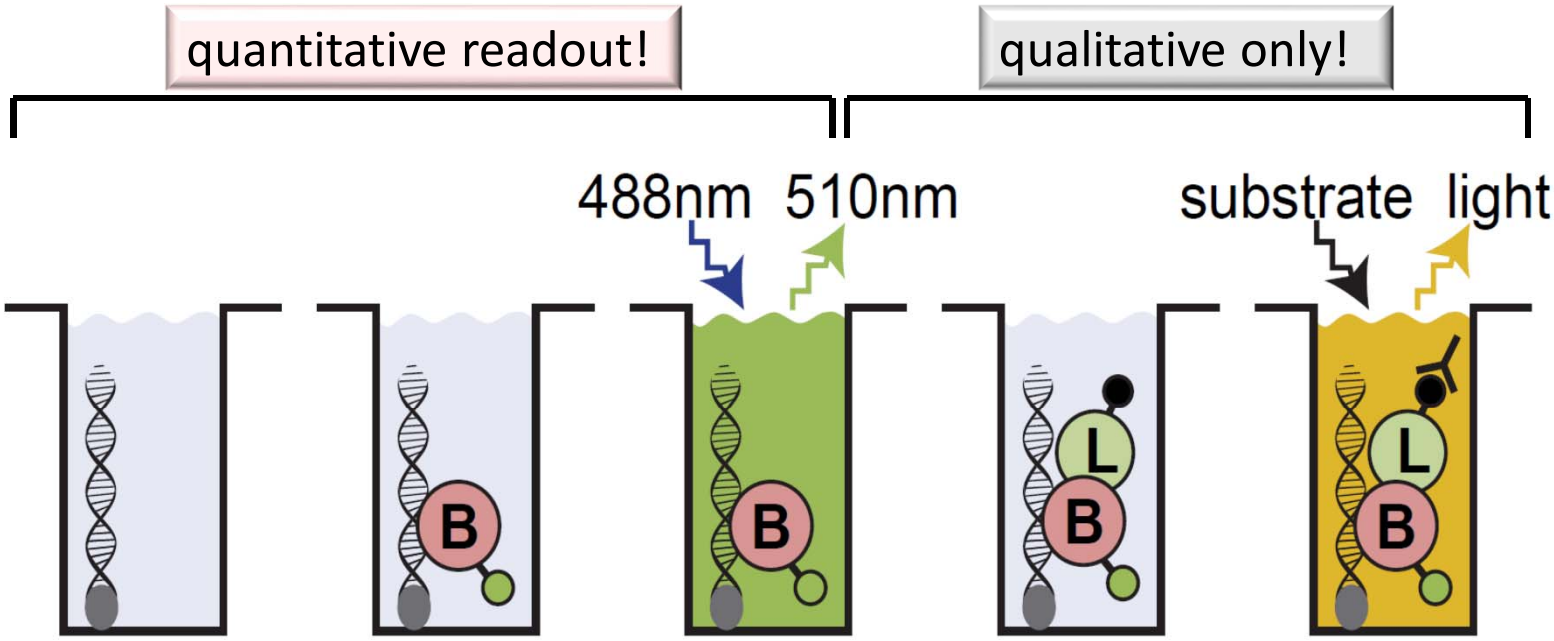
Recombinant LHP1-His and GFP-BPC6 are extracted from E.coli
→ DPI-R-ELISA (DNA-Protein-Interaction - Recruitment-ELISA)

Hecker et al., 2015

MBP

Does BPC6 recruit LHP1 to GAGA-motifs?

Interactome



Recombinant LHP1-His and GFP-BPC6 are extracted from E.coli
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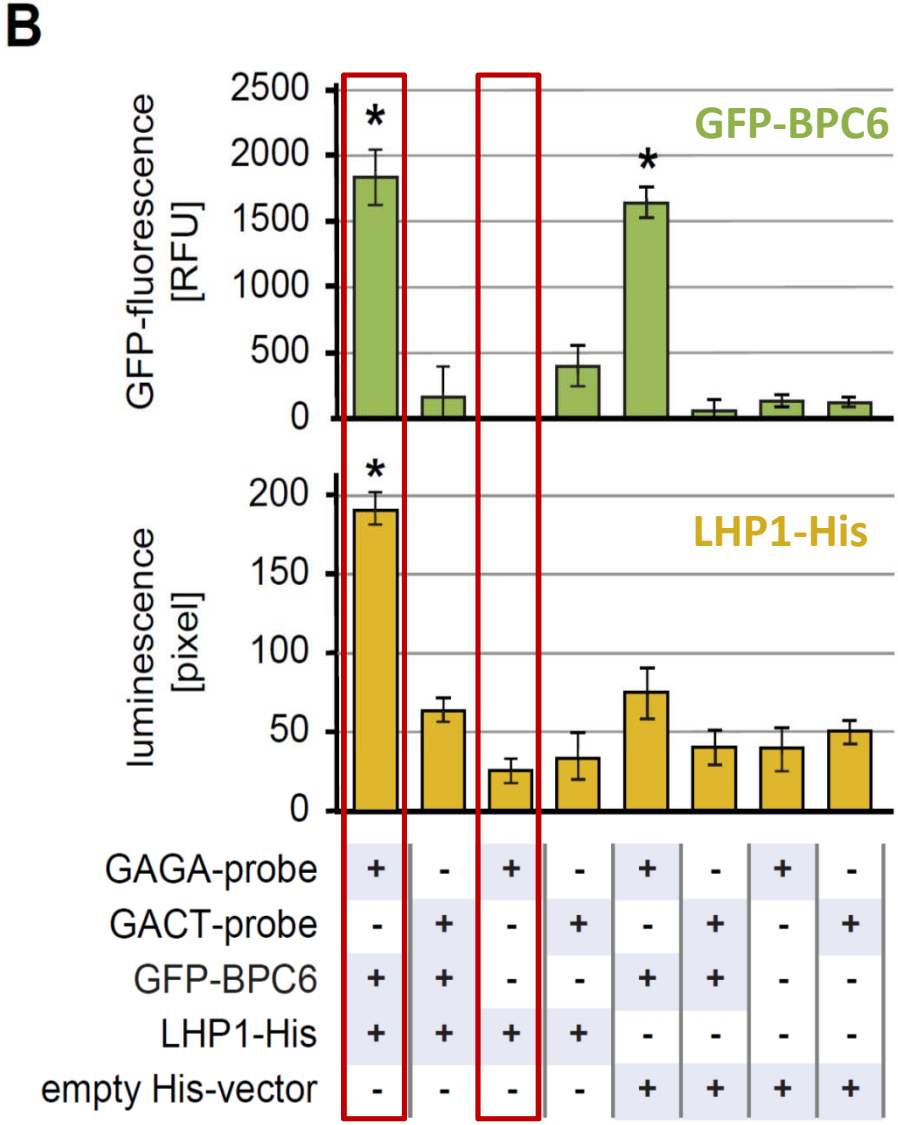
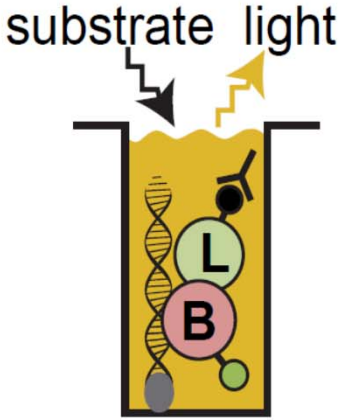
Hecker et al., 2015

BPC6 recruits LHP1 to GAGA-motifs!

Interactome





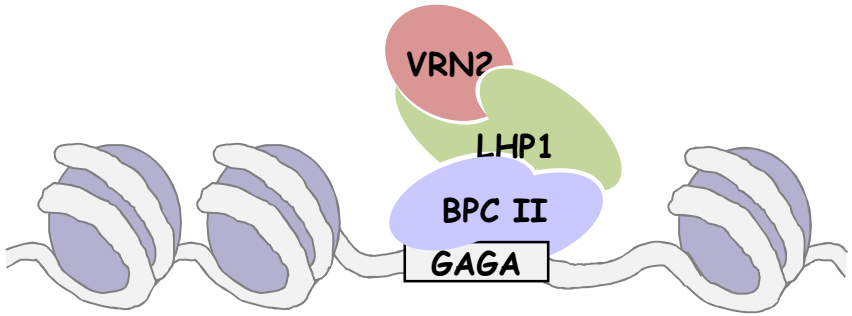
GFP-BPC6 binds GAGA-motifs

GFP-BPC6 is required for LHP1 recruitment to DNA

Hecker et al., 2015

DNA-binding studies using quantitative DPI-ELISA

Interactome



Answer: Yes, BPC6 is sufficient to recruit LHP1 to GAGA-motifs.

Fischer et al., 2016

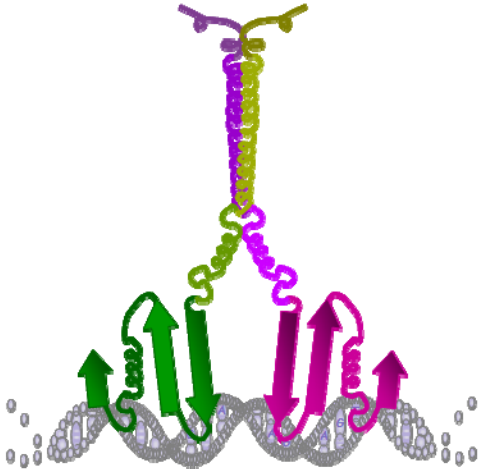
Meta-Proteomics using the Rosetta-Algorithm

Proteome

Rosetta@home
Protein Folding, Design, and Docking

Rosetta (David Baker Lab) uses all available data on protein structures to identify 'lead'-signatures for the de novo model structure prediction.

Question:
Can we propose a structure for the DNA-binding domain that consolidates our data on the
Interactome (protein-DNA, dimerization)
Genome (GAGA-distribution)?



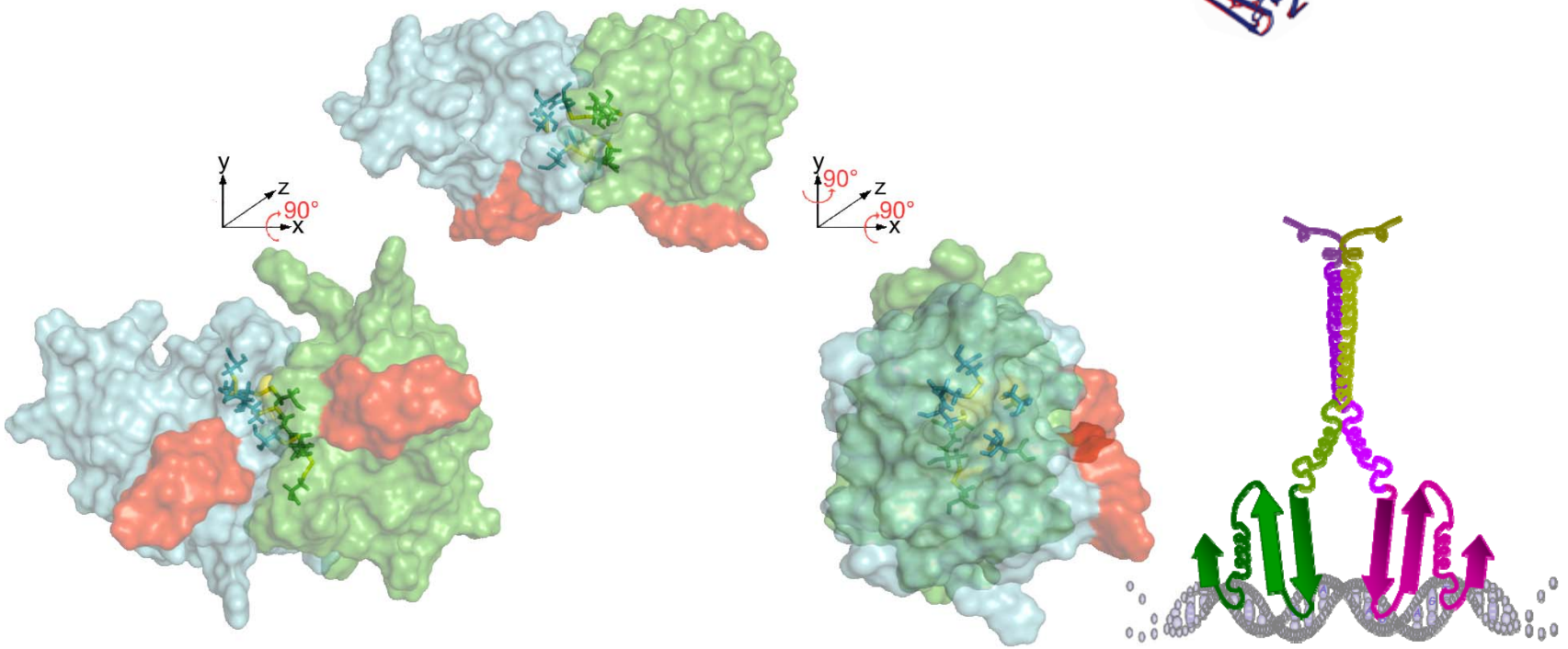
Theune et al., 2017

MBP

Meta-Proteomics using the Rosetta-Algorithm

Rosetta@home
Protein Folding, Design, and Docking

Proteome



Answer:
Yes, a conclusive model structure was derived for BPC-DNA-binding domains
The DNA-binding domains were proposed to interact strongly *via* disulfide bonds

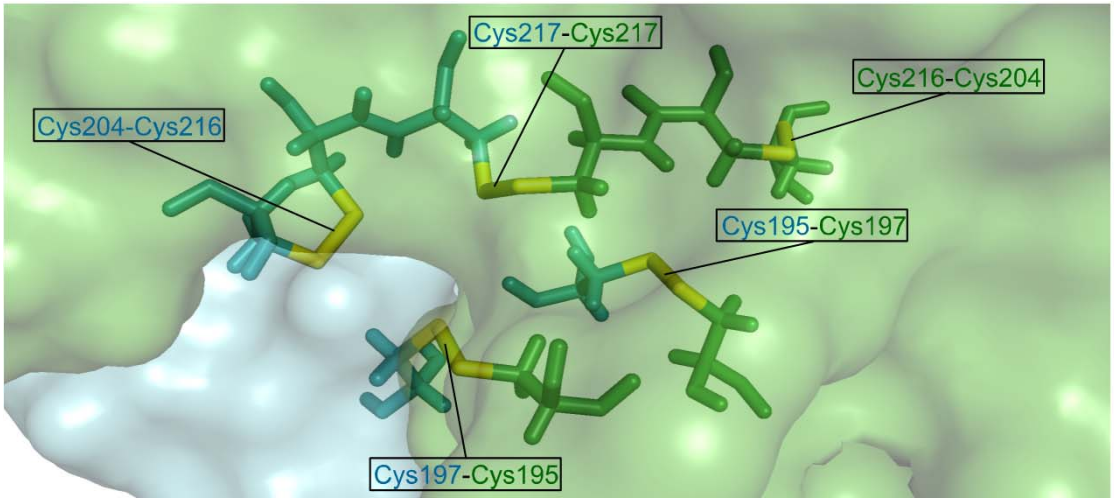
Theune et al., 2017

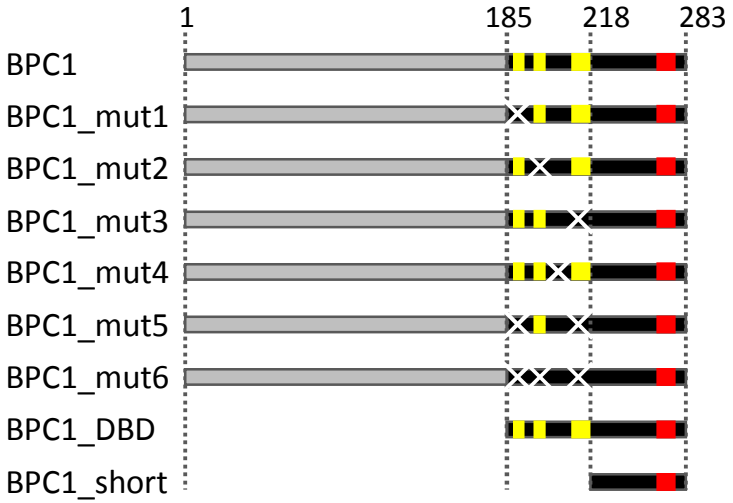
Z MBP

Meta-Proteomics using the Rosetta-Algorithm

Proteome

Question: Are the disulfide bonds important for DNA-binding?





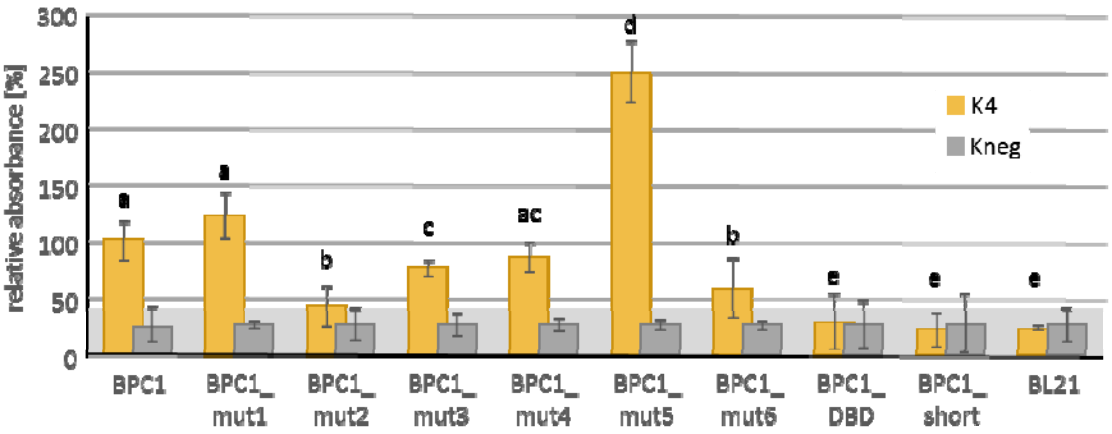
Inter- and intramolecular disulfide binds are formed

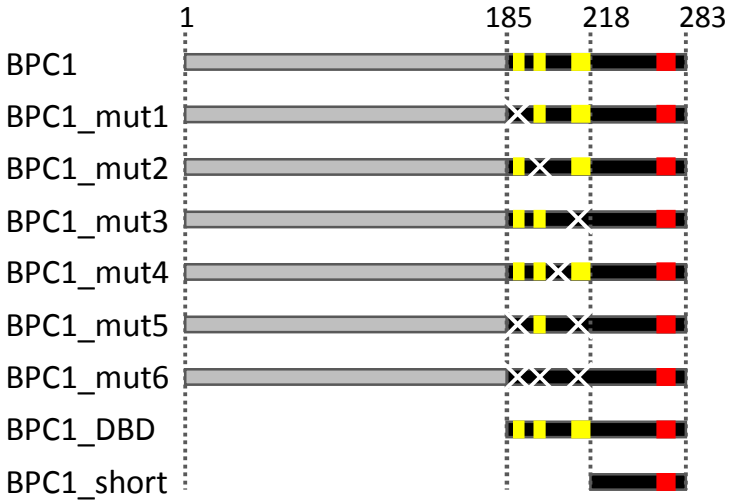
Theune et al., 2017

Meta-Proteomics using the Rosetta-Algorithm

Proteome

Question: Are the disulfide bonds important for DNA-binding?





Answer:
Yes, they modulate binding specificity, but do not contact the DNA-bases directly.
Deletion of all five Cysteins did not prevent GAGA-motif binding.

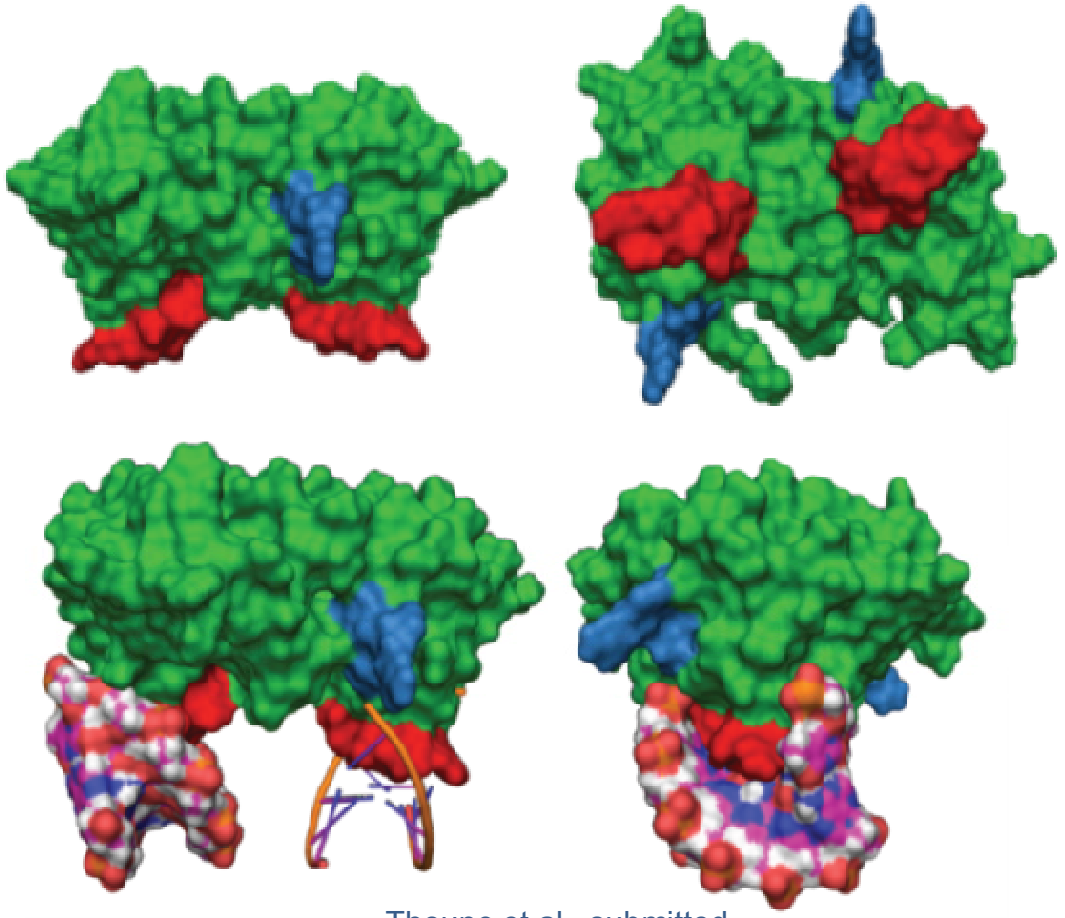
Theune et al., 2017

Meta-Proteomics using the Rosetta-Algorithm

Rosetta@home
Protein Folding, Design, and Docking

Proteome

Question: If not the Cysteins are making contact with the DNA, which residues might bind to GAGA-motifs then?

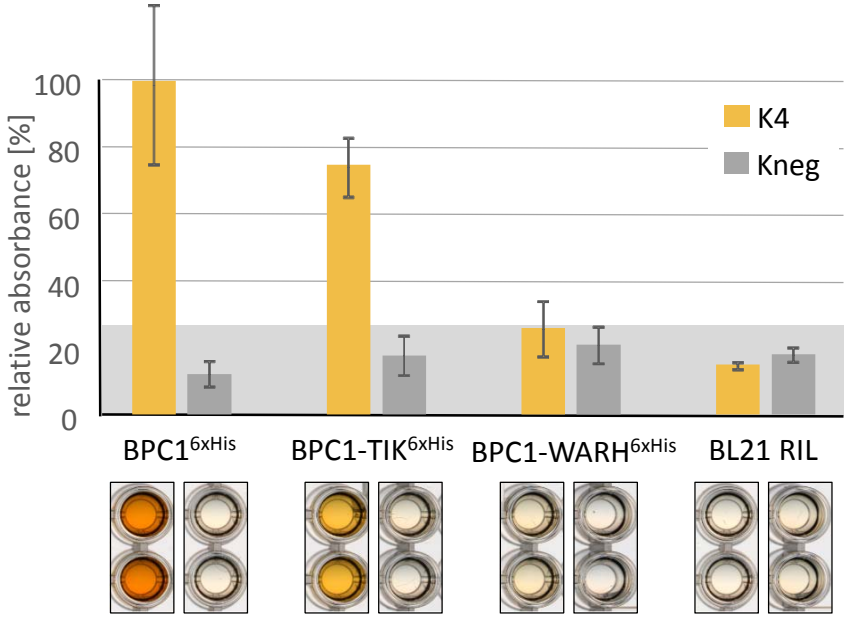


Theune et al., submitted

Meta-Proteomics using the Rosetta-Algorithm

Proteome

Question: If not the Cysteins are making contact with the DNA, which residues might bind to GAGA-motifs then?

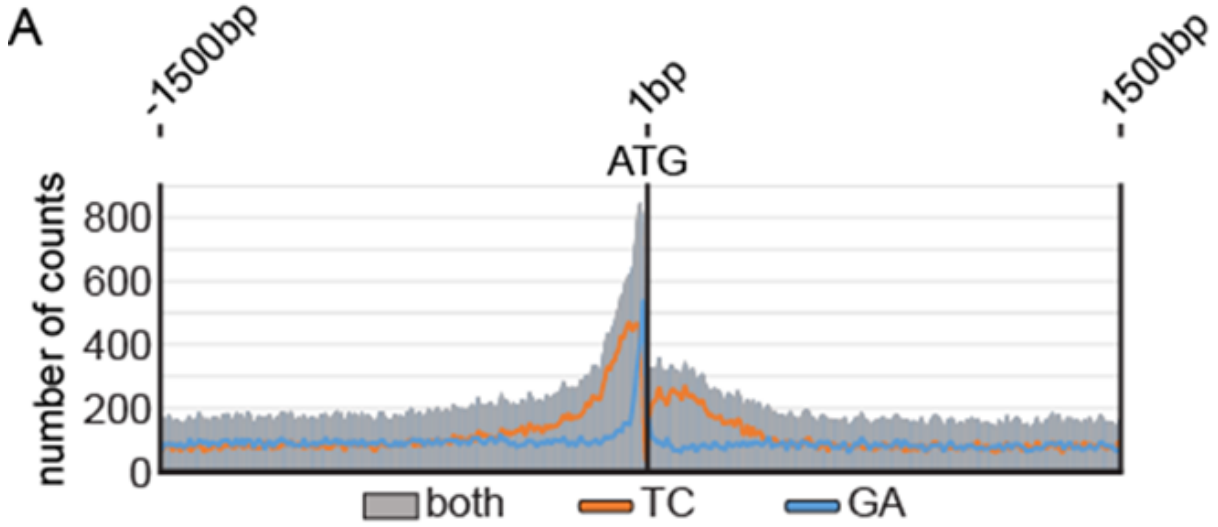


Answer:
The very N-terminus with its conserved WAKHGTN and TIK peptide signatures is required for GAGA-motif recognition.

Theune et al., submitted

Where do we find GAGA-motifs?

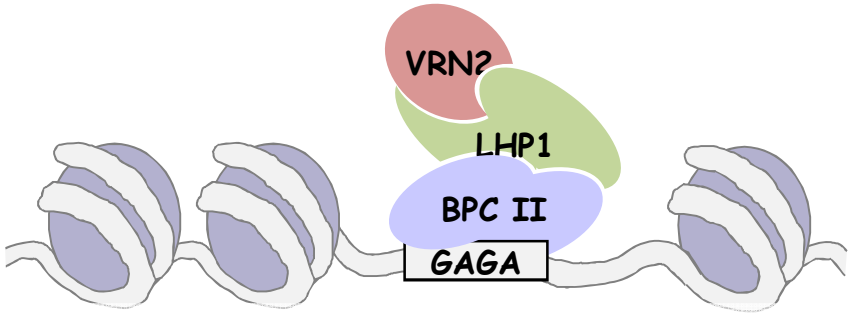
Genome

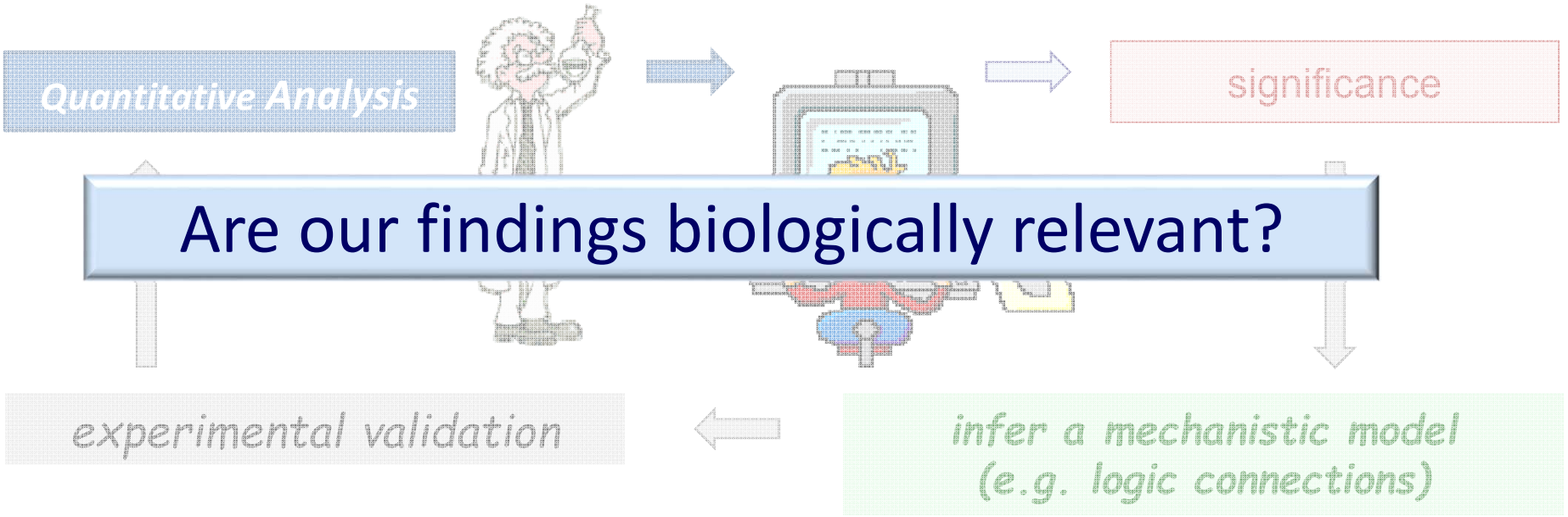


GAGA-motifs are significantly enriched close to the translation start site!

Hecker et al., 2015

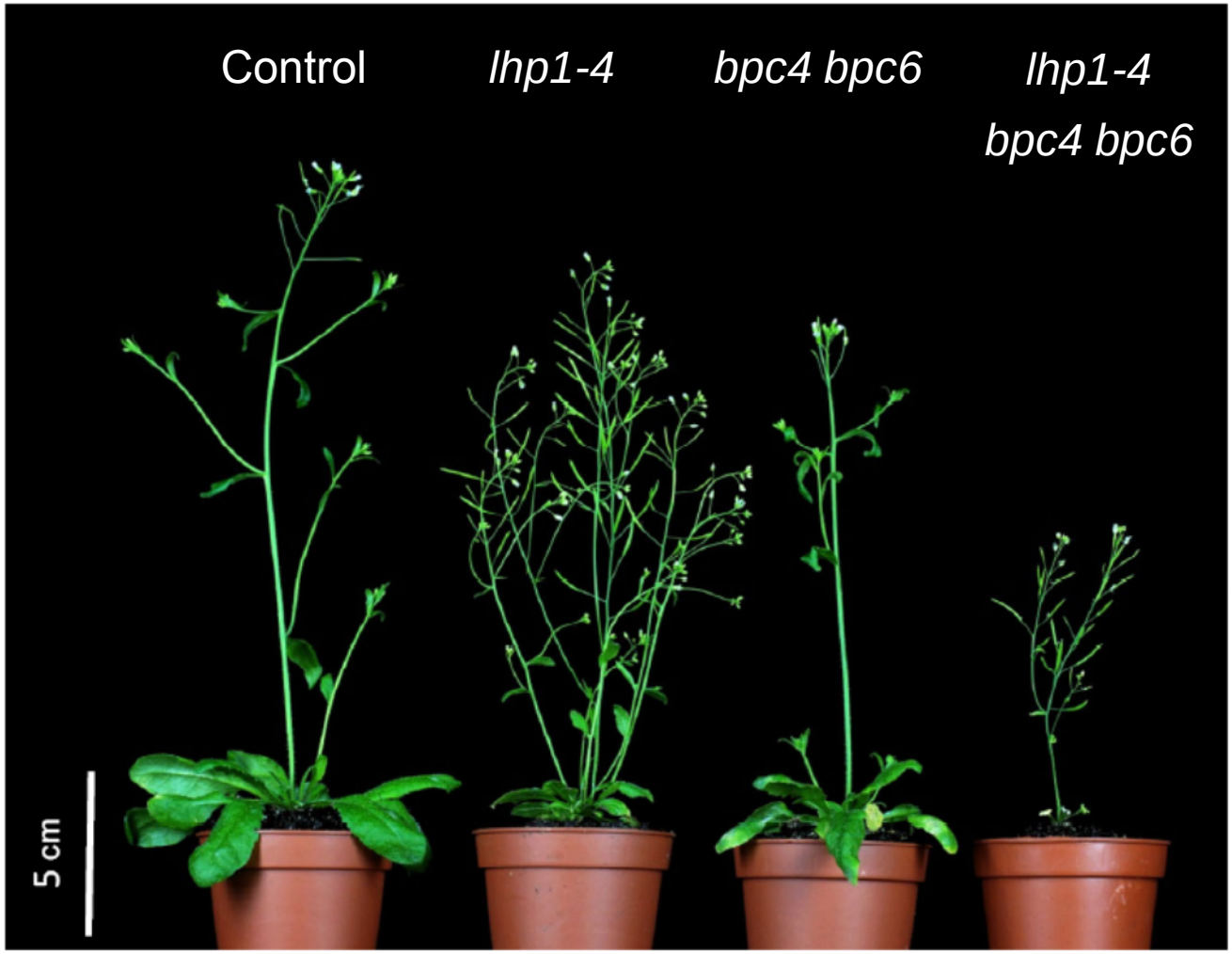
Quantitative data come as (huge) tables



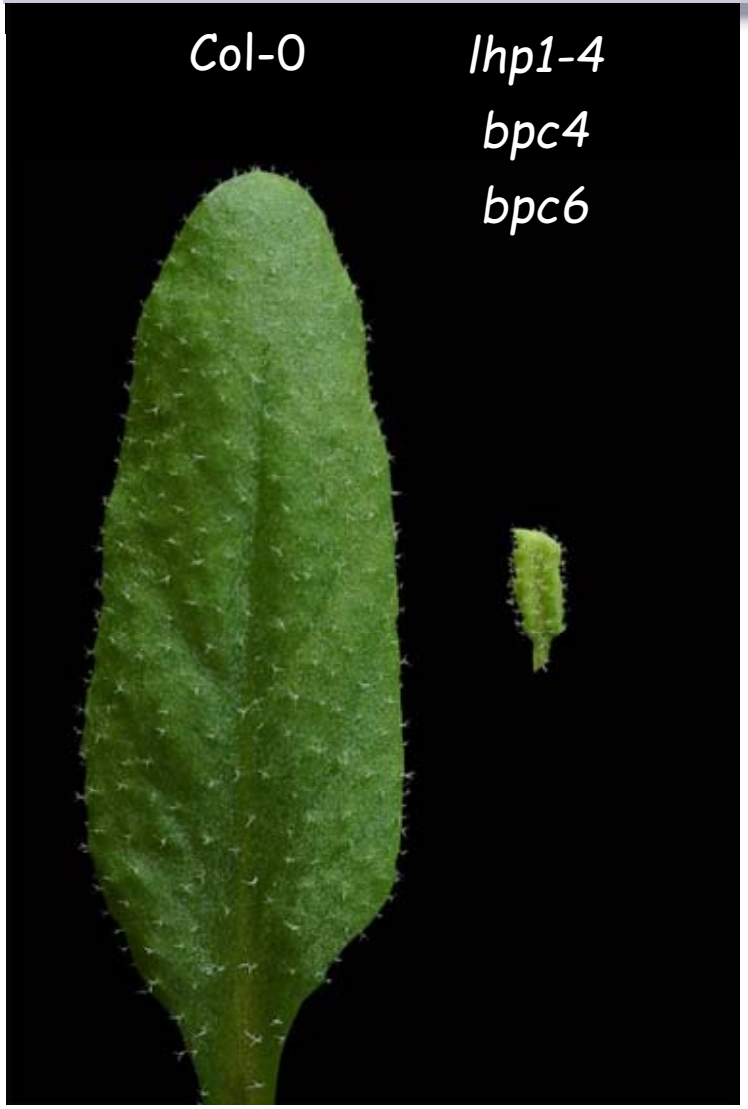


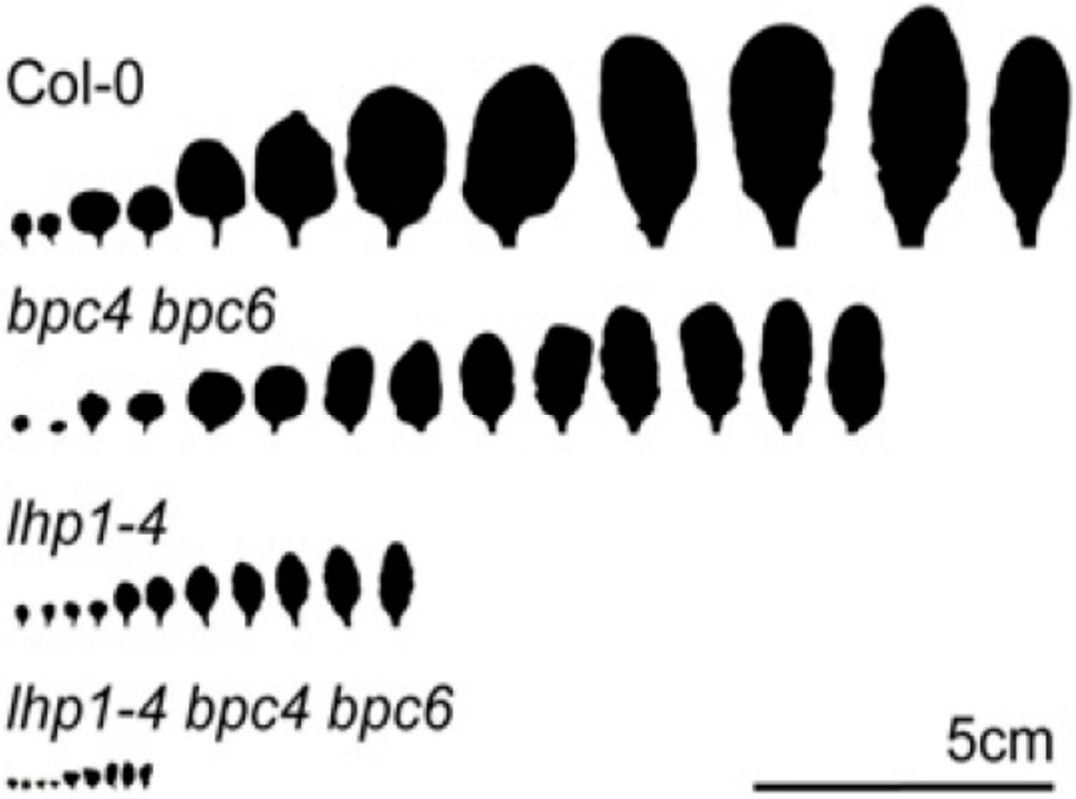
Biological relevance of our findings

Mutants in transcription factor genes exhibit differences in development



Biological relevance of our findings



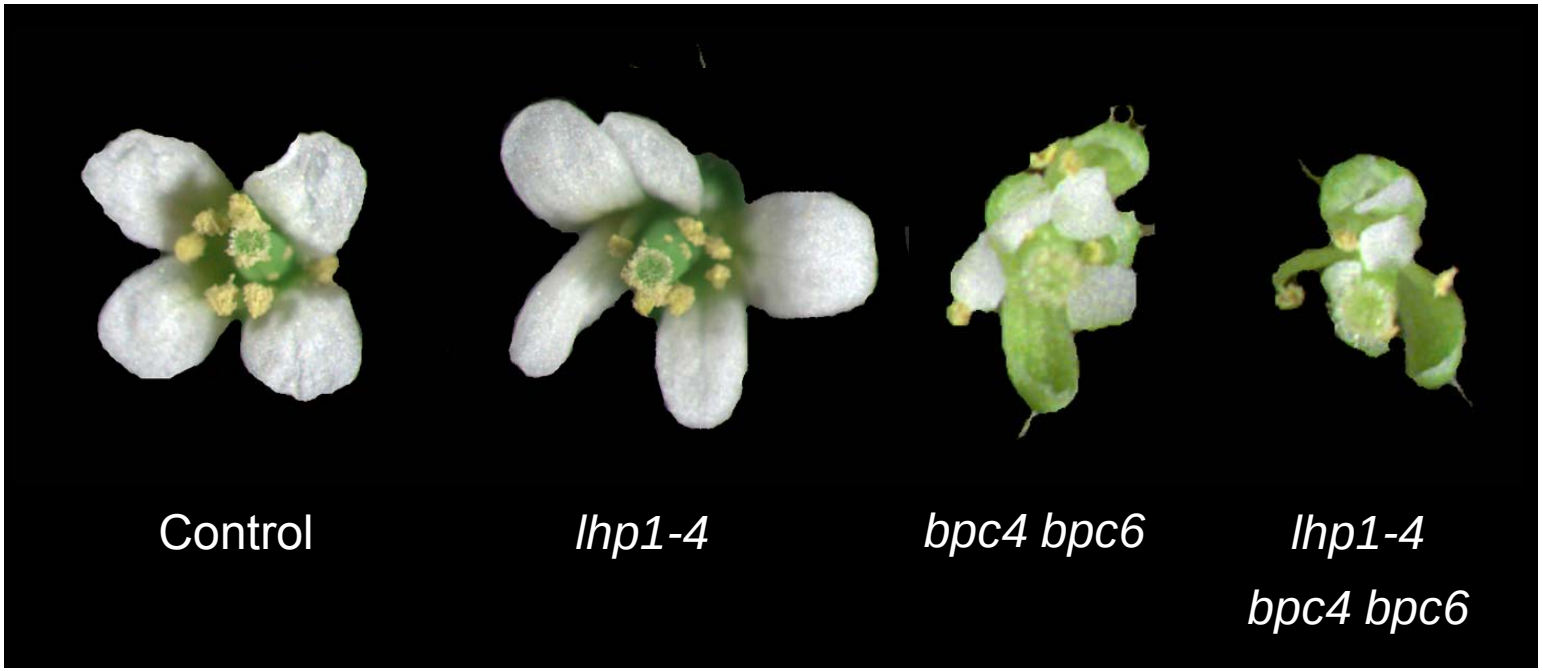


Hecker et al., 2015

Biological relevance of our findings

Transcriptome

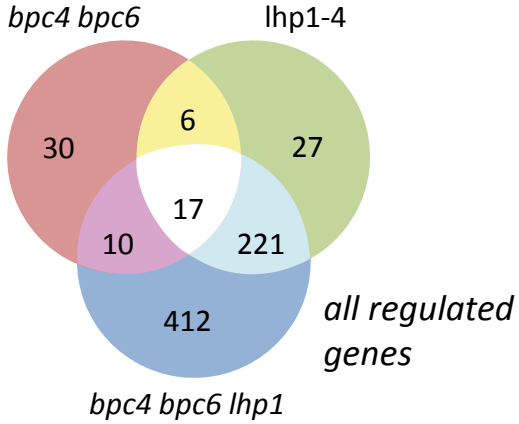
Strong developmental defects!



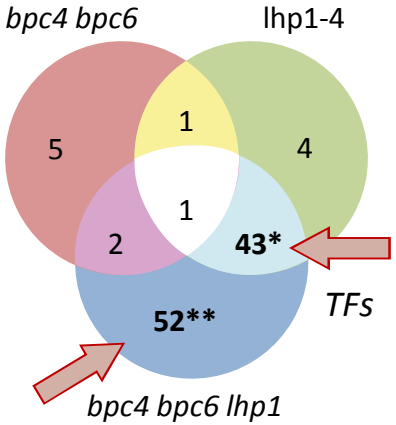
⇒ **Transcriptome** (microarray) analysis to understand what is wrong!

Transcriptome uncovered a synergistic function for LHP1 and BPC6

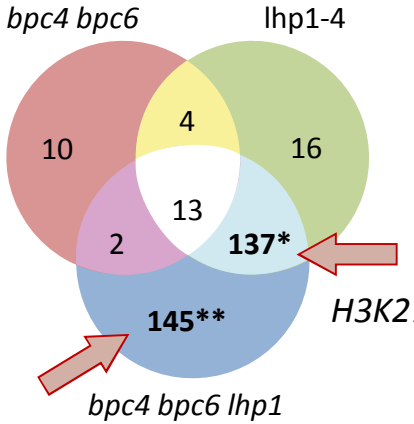
Transcriptome



all regulated genes



TFs



H3K27me³

Problem:

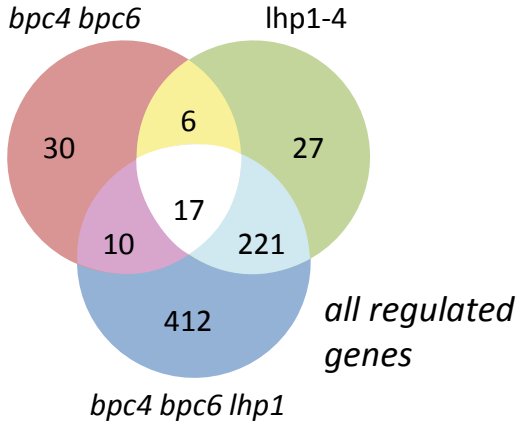
The hypergeometric distribution works only between two gene lists and their overlap.

But not for 3! → 3 consecutive analyses

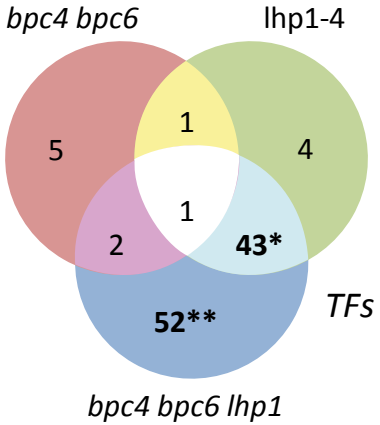
Hecker et al., 2015

Transcriptome uncovered a synergistic function for LHP1 and BPC6

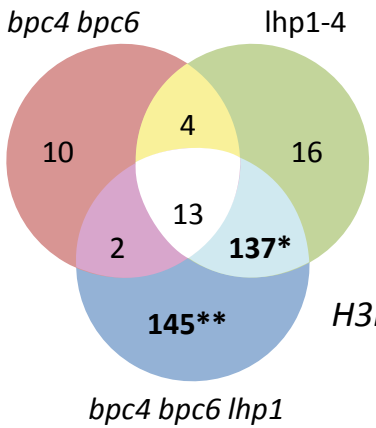
Transcriptome



all regulated genes



TFs

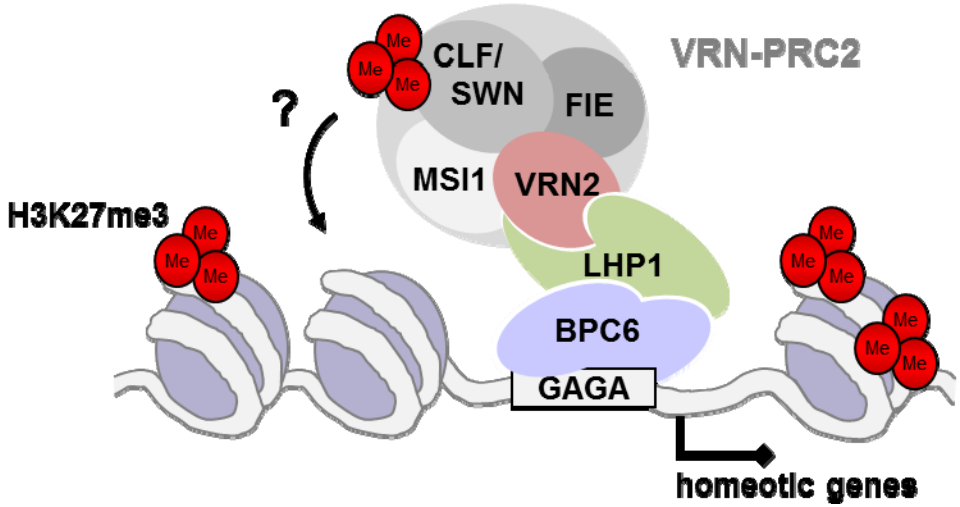


H3K27me³

- more induced genes in the mutants → function as repressor proteins
- repression coincides with already known repressive H3K27me3 marks

Hecker et al., 2015

Transcriptome data consolidated our model



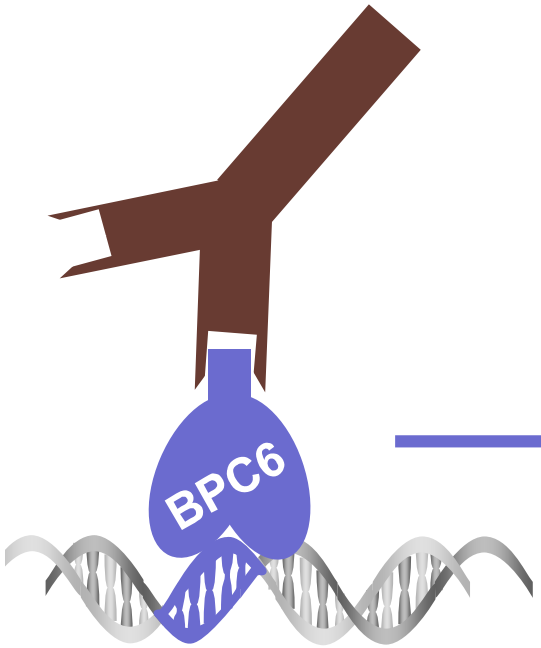
BPC6 recruits LHP1 to Polycomb-repressive element (PRE)-like GAGA-Motifs

Hecker et al., 2015

MBP

Which genes are BPC6-targets? → ChIP-seq

Genome - Interactome



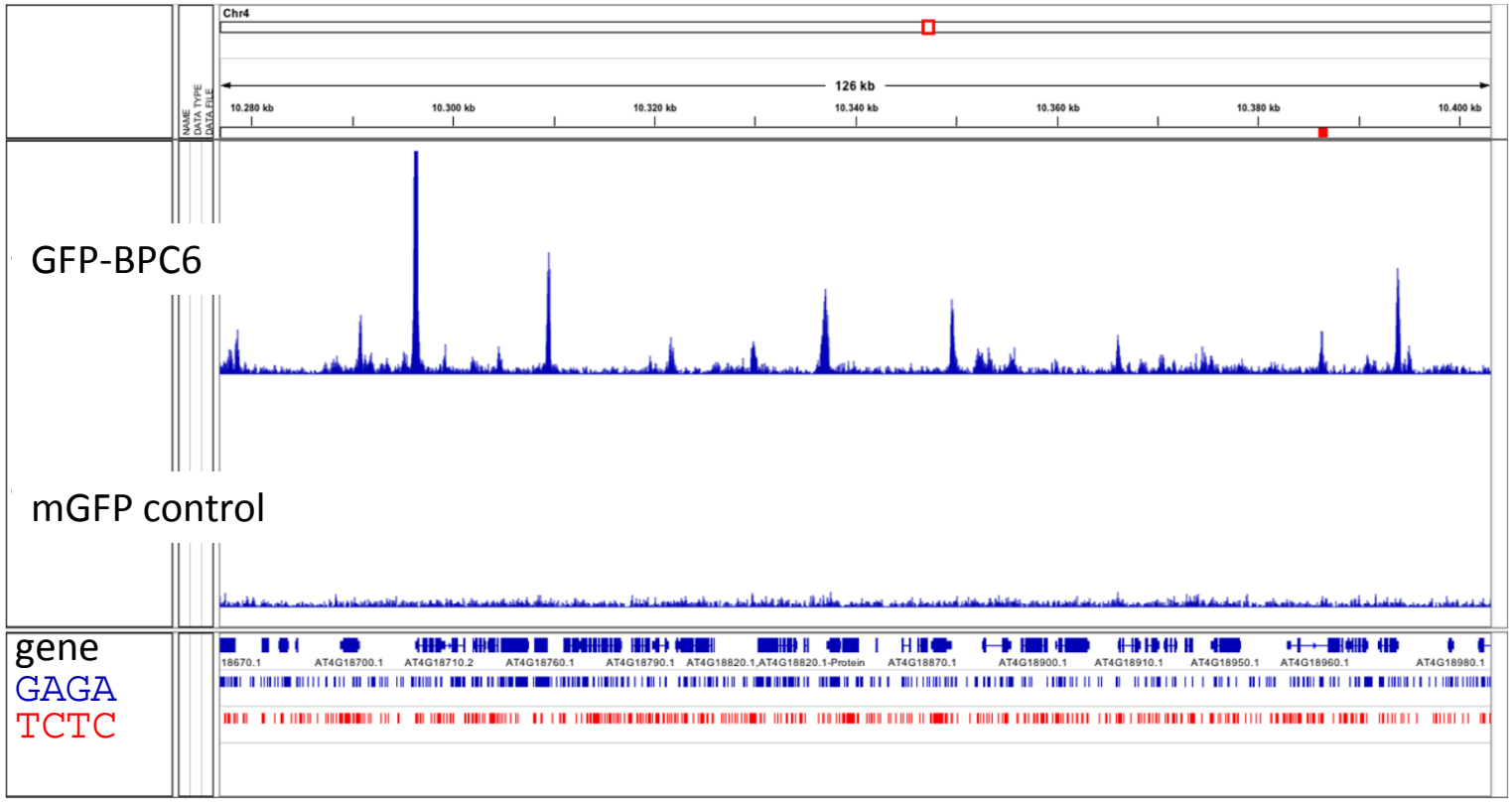
- two replicate libraries from BPC6-expressing plants
- single end reads
- ~ 50 Mio analyzable reads each

Isolation of target DNA → **Sequencing by NGS**

⇒ **Interactome** (ChIP-seq) analysis to identify direct target genes!

Which genes are BPC6-targets? → ChIP-seq

Interactome

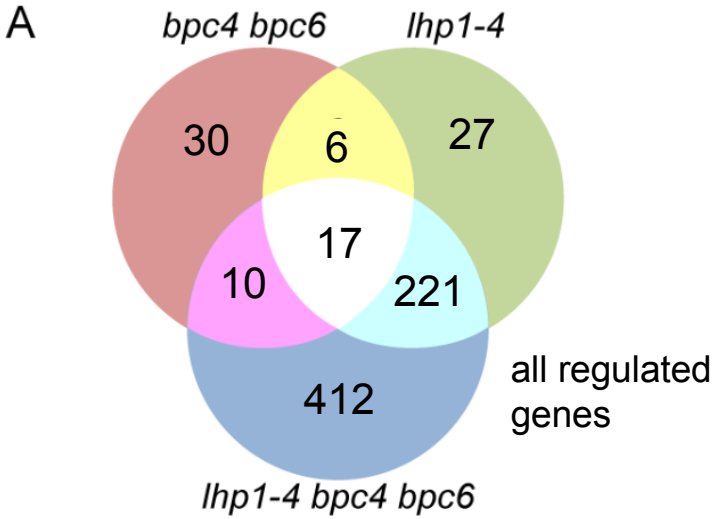


- we could identify 4032 unambiguous peaks that coincide with GAGA motifs

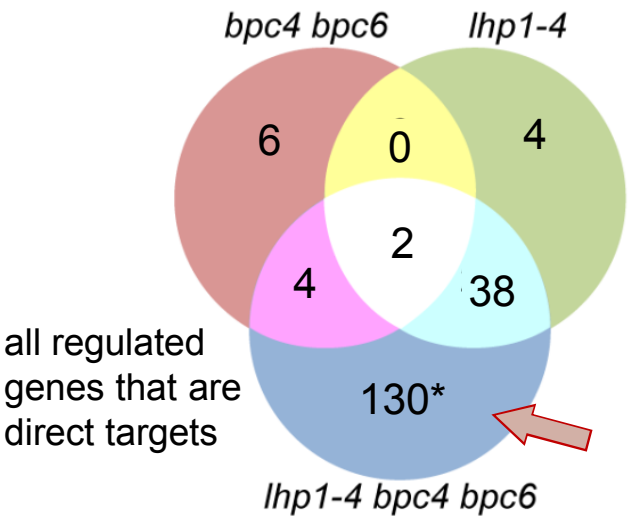
Shanks et al., 2018

Microarray vs. ChIP-seq

Transcriptome - Interactome



microarray

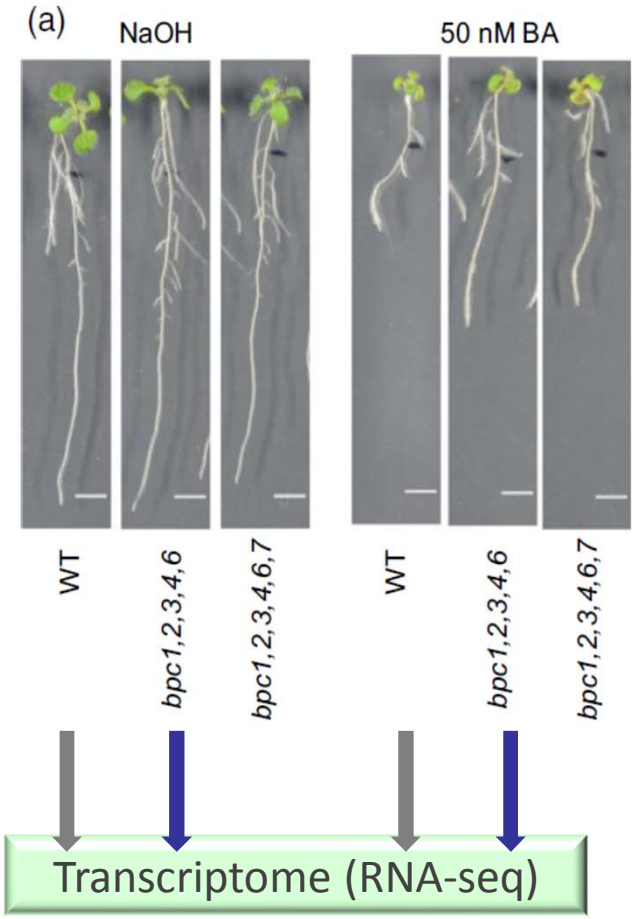


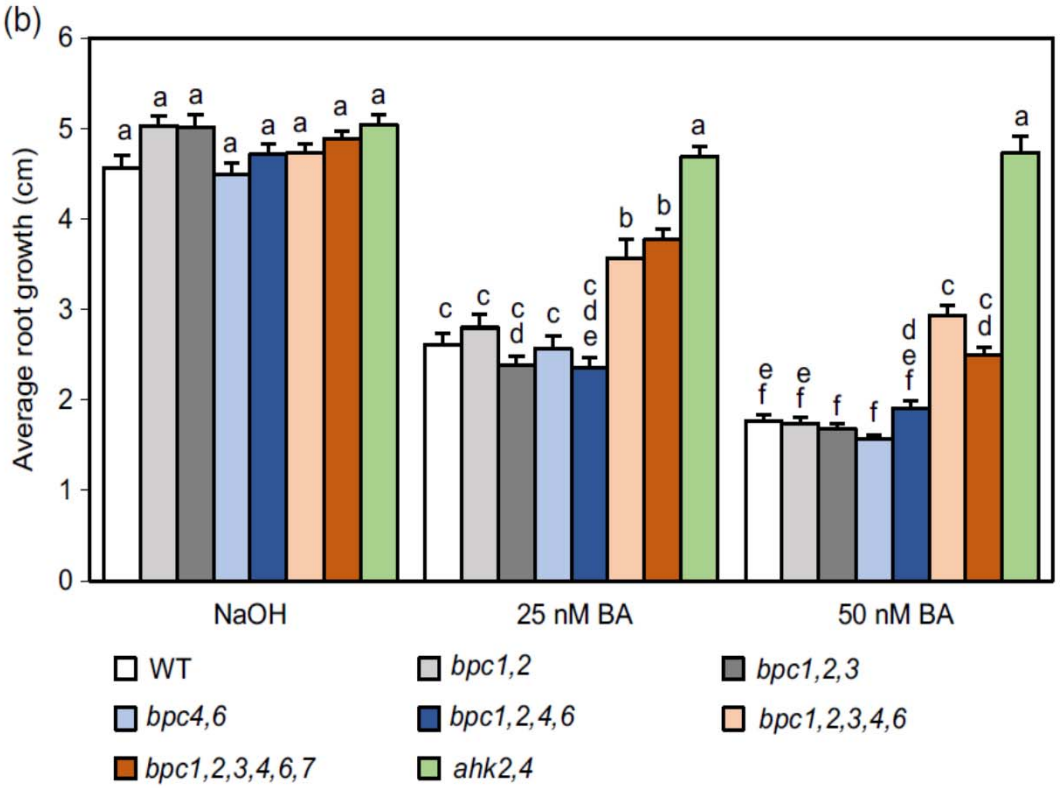
ChIP-seq

- significant overlap between expression in the triple mutant and ChIP data

In which processes are BPC-proteins involved in?

Transcriptome



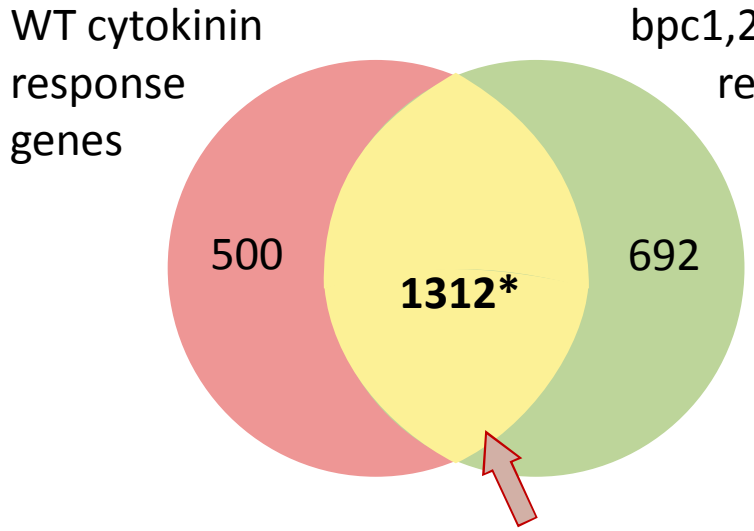


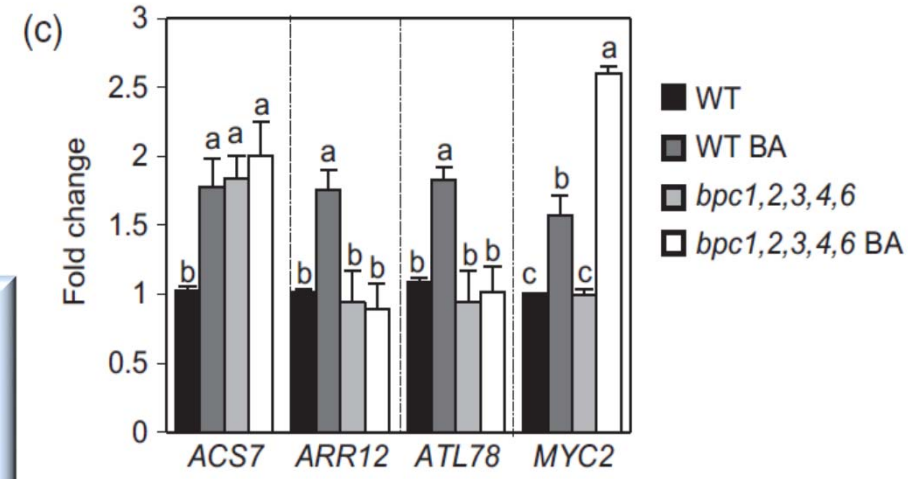
Answer:
Mutants with multiple loss-of-function mutants in *BPC* genes are less sensitive to a the plant hormone Cytokinin. Involvement in hormone homeostasis!

Shanks et al., 2018

A subset of cytokinin responses are BPC dependent

Transcriptome



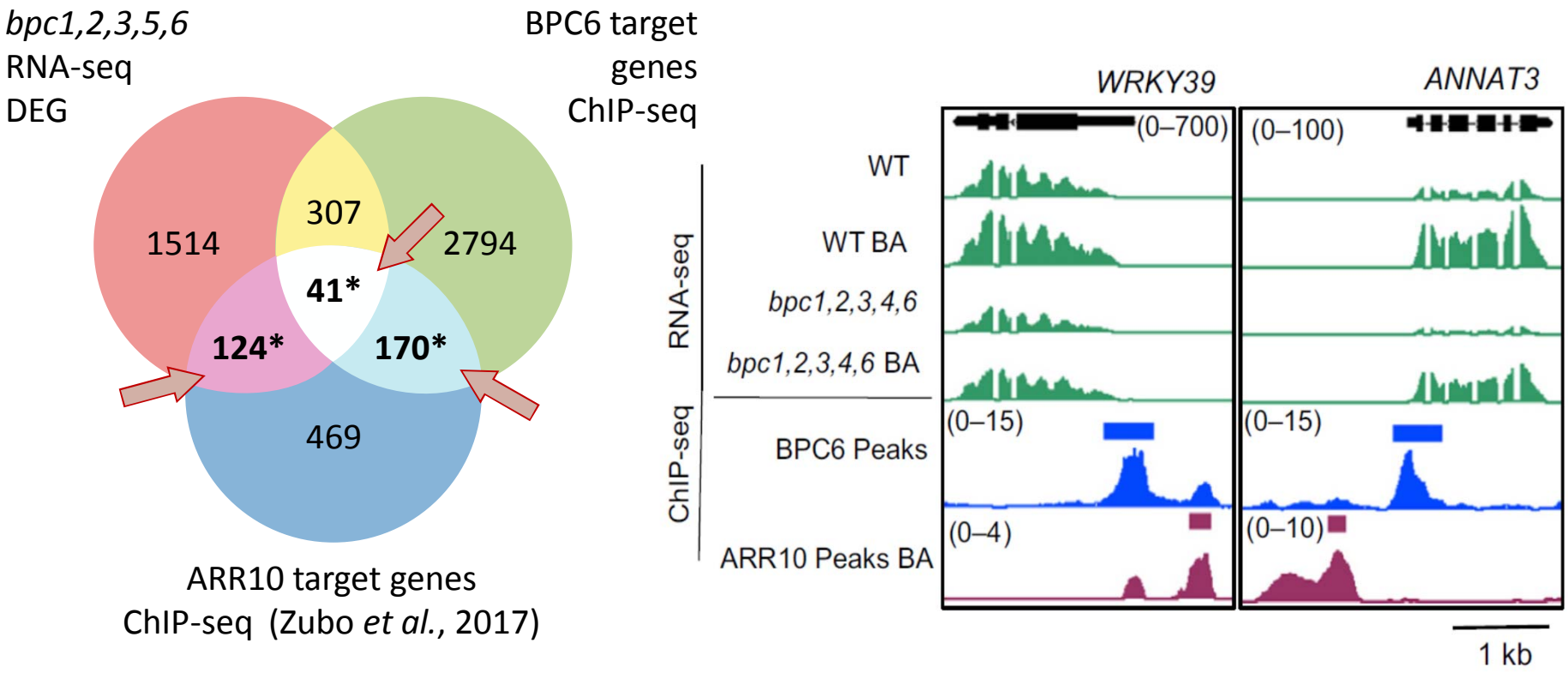


Answer:
Mutants with multiple loss-of-function mutants in *BPC* genes are less sensitive to a the plant hormone Cytokinin.
Involvement in hormone homeostasis!

Shanks et al., 2018

BPC6 and ARR10 target the same subset of cytokinin response genes

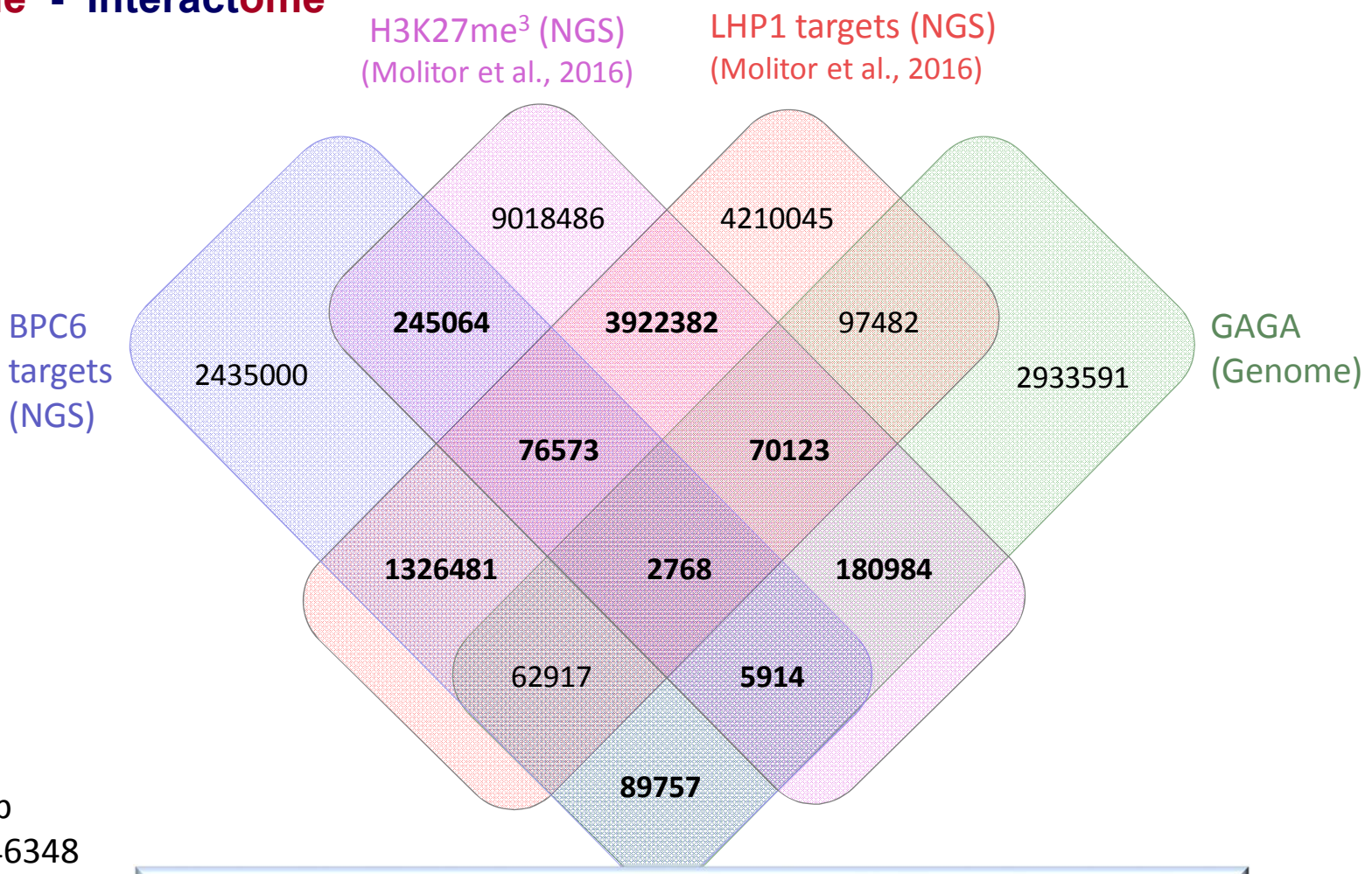
Transcriptome - Interactome



Answer:
Differentially expressed genes (DEGs) in the mutant are not direct targets of BPC6. But a subset of hormone responsive genes are targeted by ARR10 (cytokinin signal integrator) and BPC6 simultaneously.

Do BPC6 and LHP1 target the same genes?

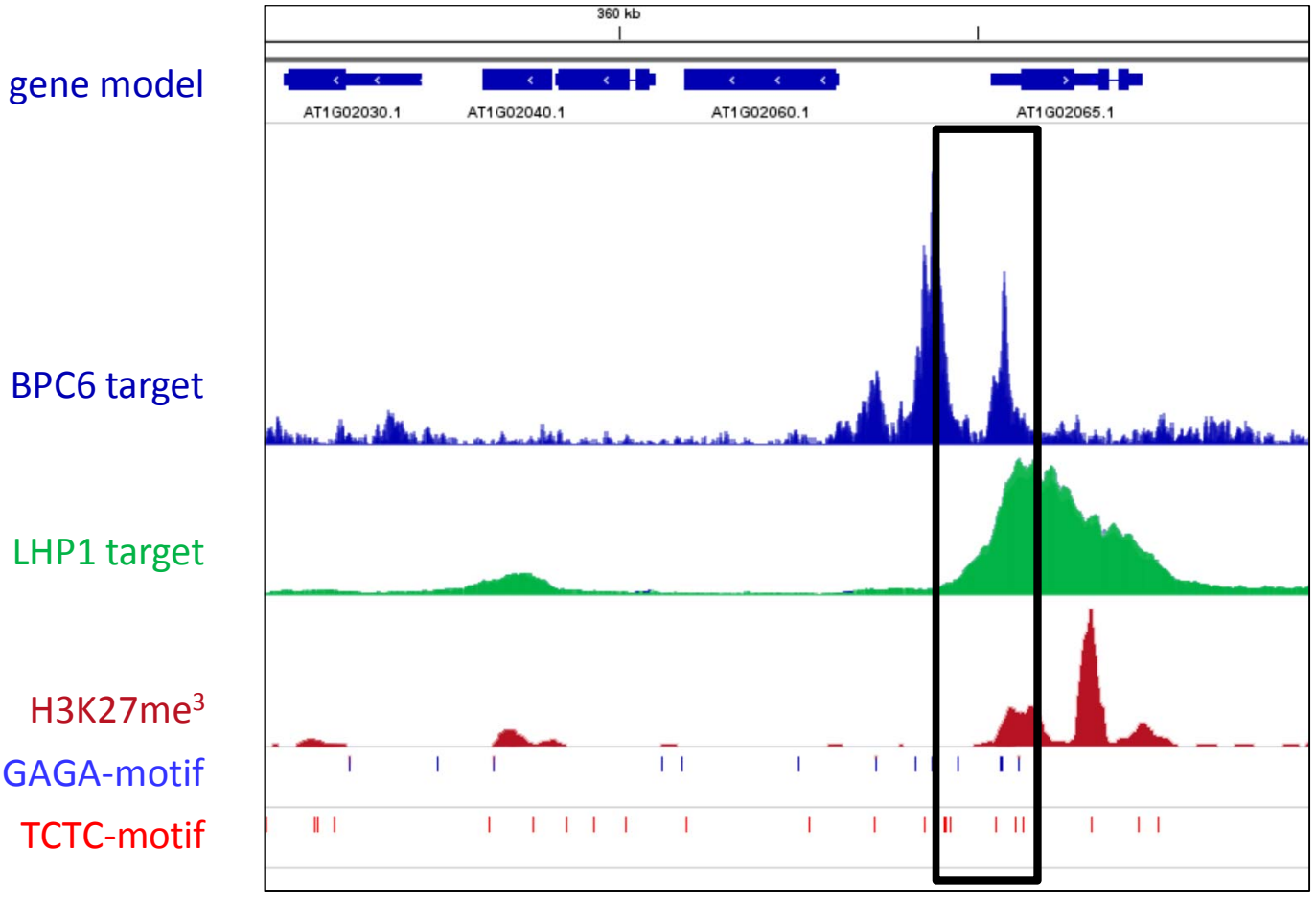
Genome - Interactome



Ref. bp
119146348

Answer:
Yes, about 25% of the sequences are targeted simultaneously!

Do BPC6 and LHP1 target the same genes?

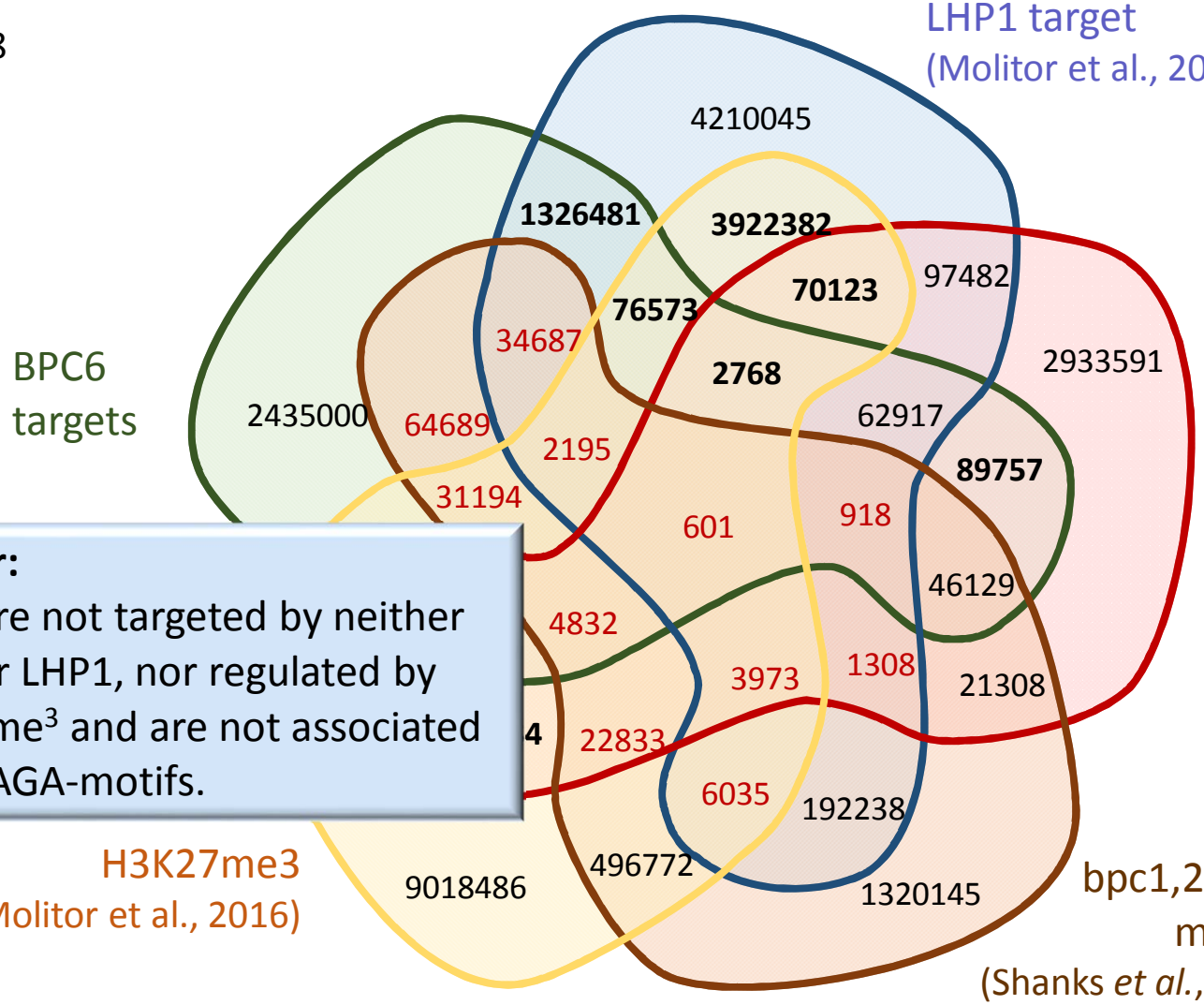


Answer:
Yes, about 25% of the sequences are targeted simultaneously!

What about *bpc*-dependent gene expression?

Genome - Transcriptome - Interactome

Ref. bp
119146348



Answer:
DEGs are not targeted by neither BPC6 or LHP1, nor regulated by H3K27me^3 and are not associated with GAGA-motifs.

The AtGenExpress expression atlas comprises 1295 microarray experiments

AtGenExpress

...was a multinational effort designed to uncover the transcriptome of the multicellular model organism *Arabidopsis thaliana*

All 41 different experimental core-conditions have been finish

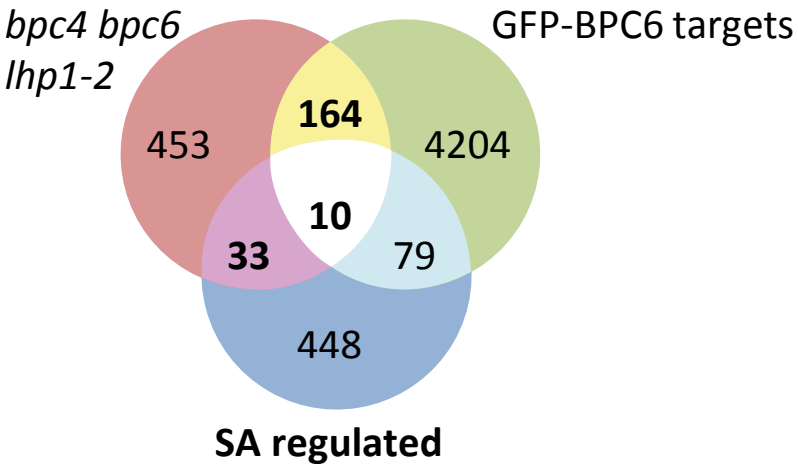
- Development

More than 1300 gene lists were compiled over the last 10 years that contain either specific gene expression responses after a treatment (e.g. heat responsive) or hand-curated gene ontology lists (e.g. all cell-cycle genes)

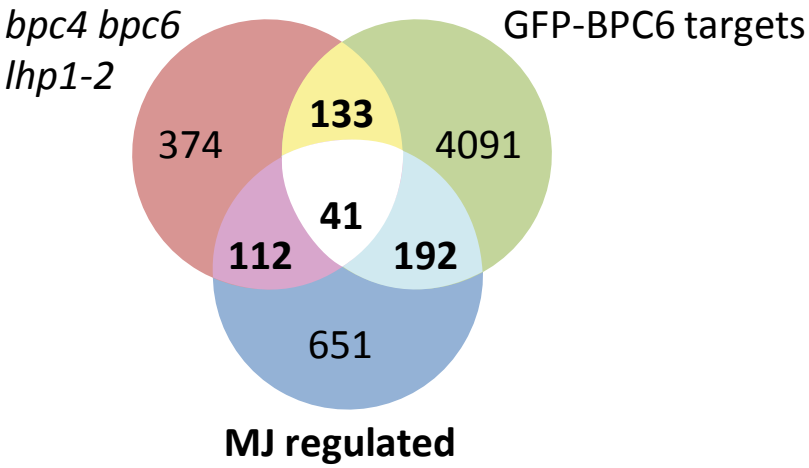
...ed the abiotic stress experiments

Currently, there are more than 3000 highly comparable microarray expression profiles in the database

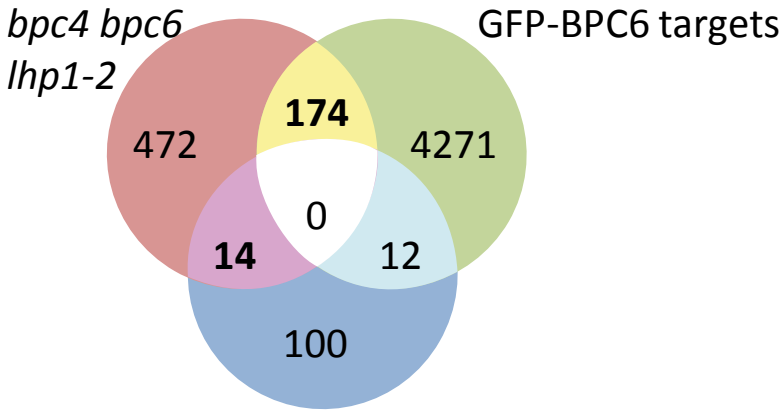
What else is targeted by BPC6?



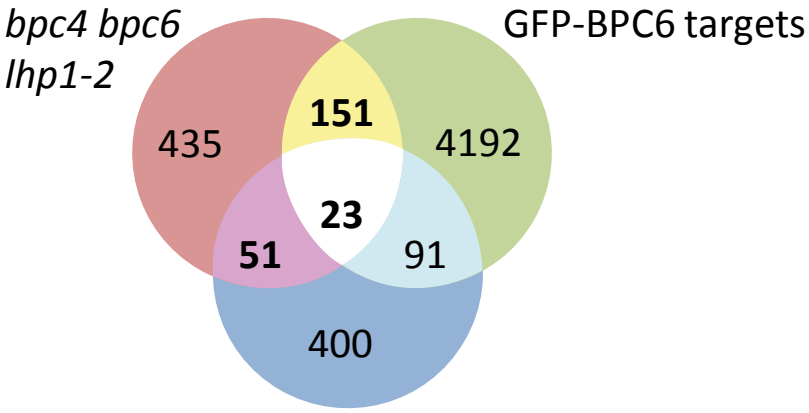
SA regulated



MJ regulated



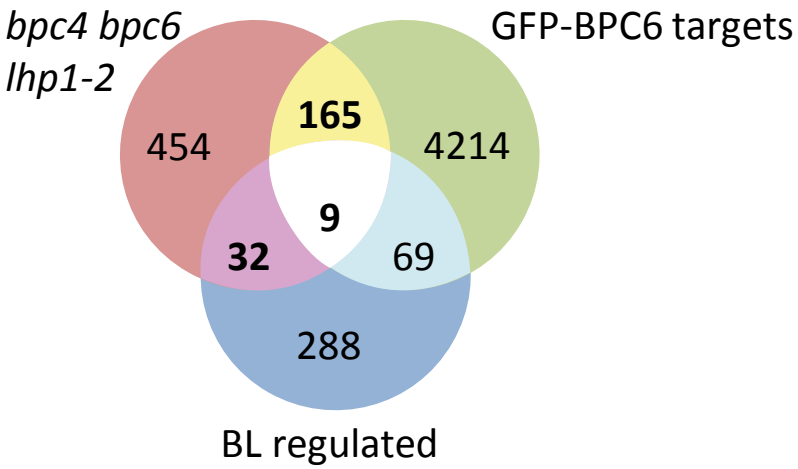
GA regulated

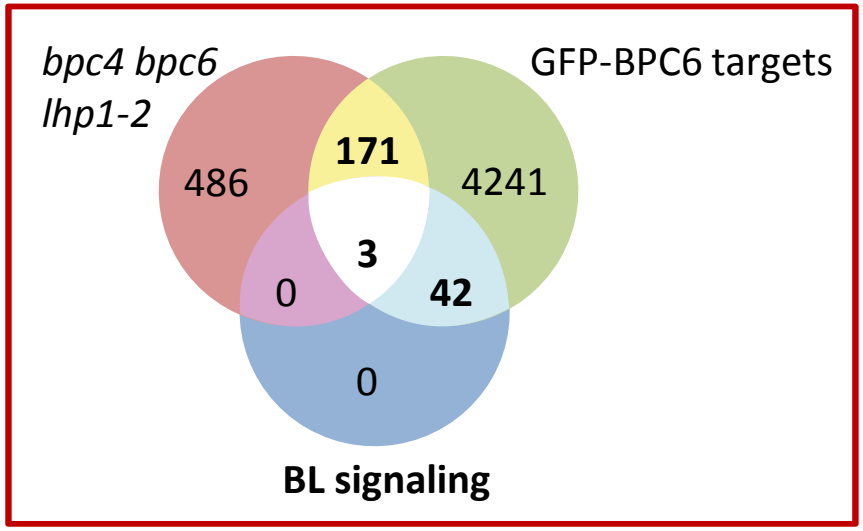


IAA regulated

24747
all genes

What are the other target genes targeting?



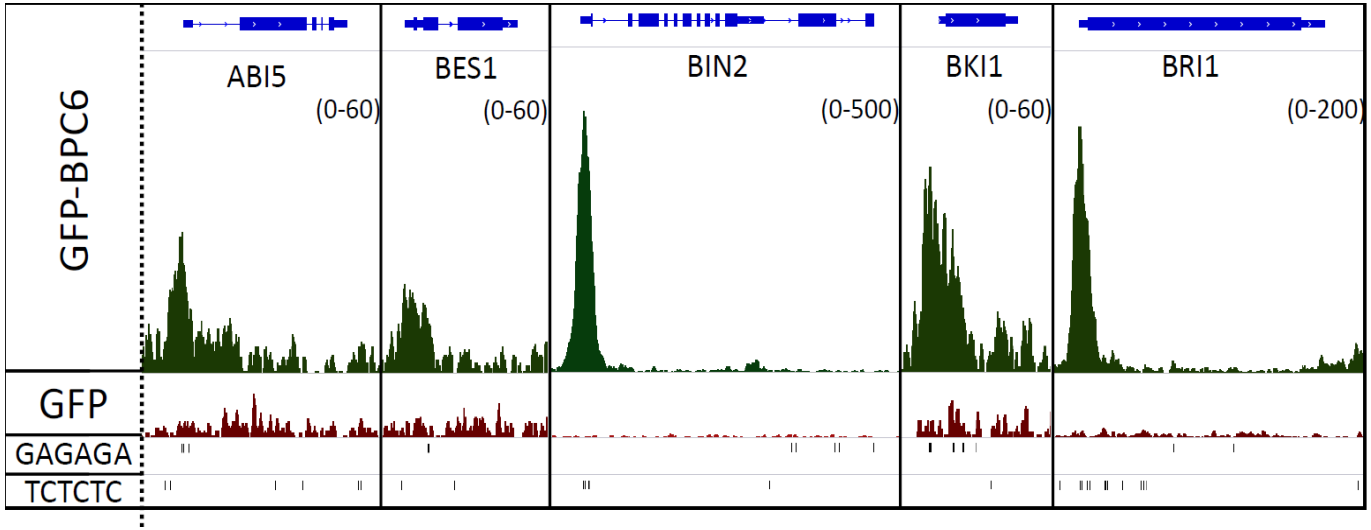


Answer:

ALL known brassinosteroid ***signaling*** components are targeted by BPC6 in vivo! This finding is exclusive for brassinosteroid and not found for any other hormone signaling pathway!

The use of brasinosteroids as a plant hormone has evolved 'recently' in land plant evolution!

The targeting of the BL-pathway gene occurs at very different levels!



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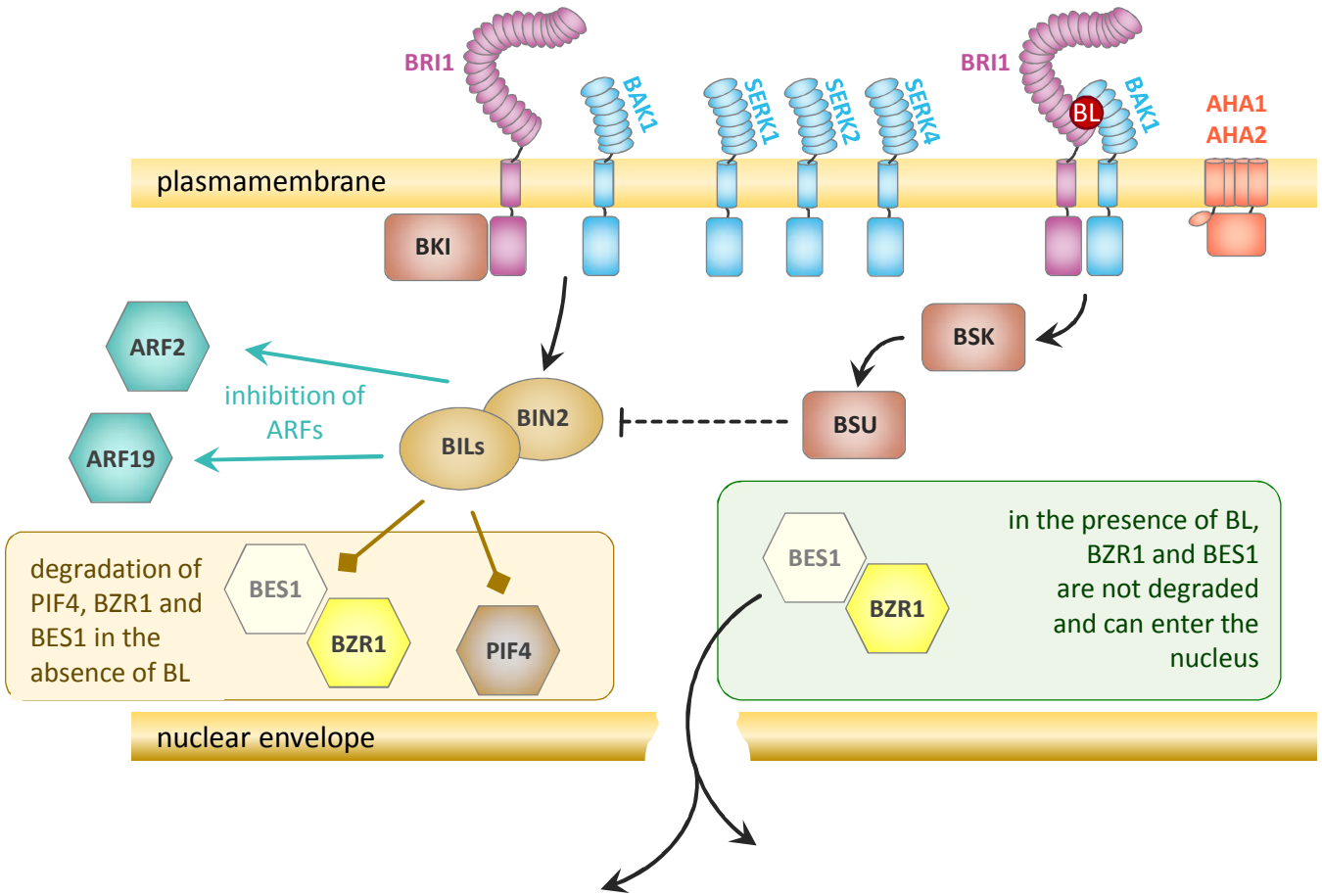
MBP

The targeting of the BL-pathway gene occurs at very different levels!

BL-dependent signaling processes in the cytosol



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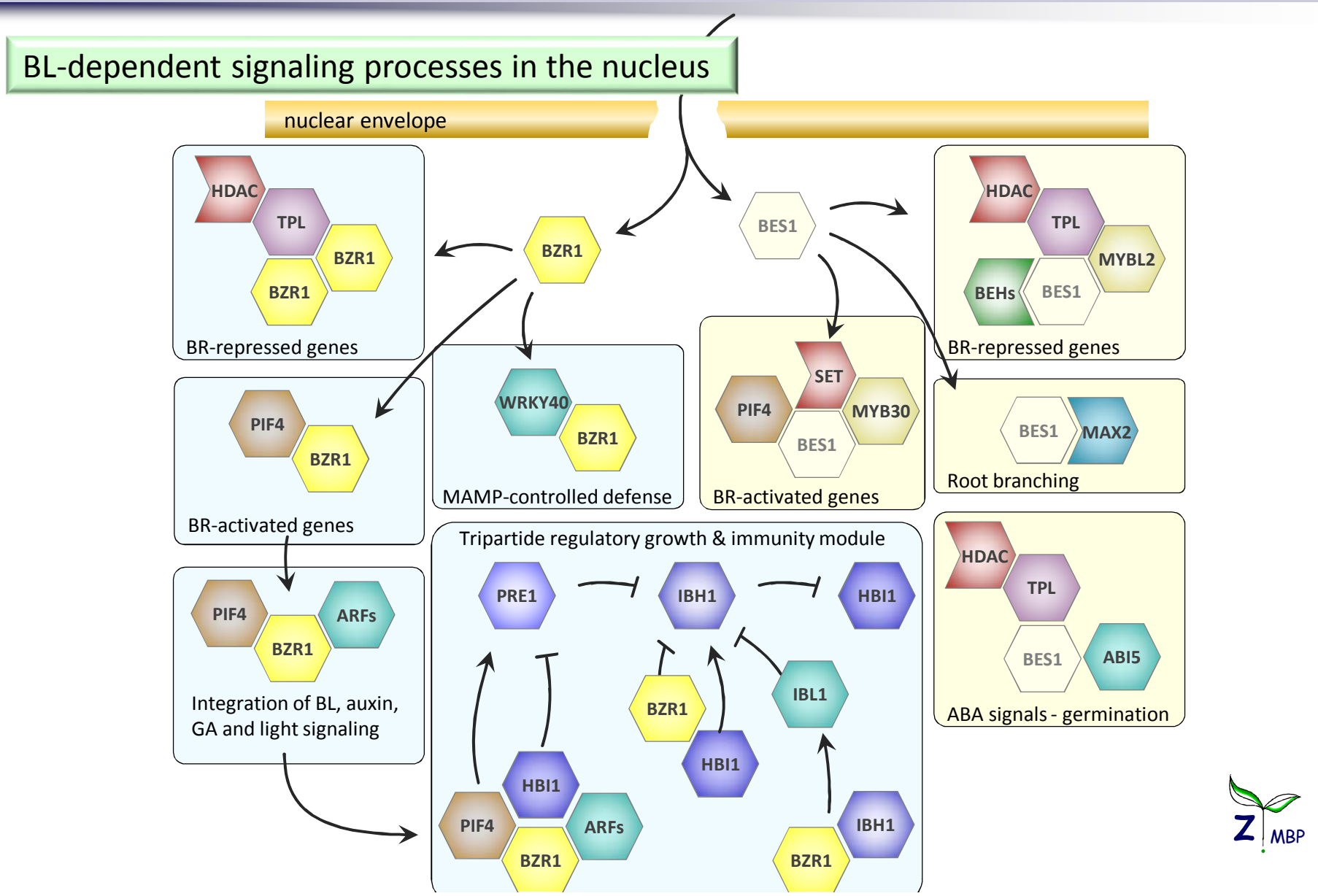

What are the 'take-home-messages'?

Combined 'Omics' analyses are a powerful resource of in functional biology!

- Integration of novel quantitative interactome methods (protein-DNA or protein-protein-…. interaction) is highly desirable

- Try to apply simulations to gain novel insights into the functional mechanistic of your research object

- Be clear in the scientific questions you are asking and check whether your experiment will provide you with an answer

- don't stay with significance – validate your results independently!

Thank you!

Tübingen

Andreas Hecker

Carl Zeiss Stiftung

Rebecca Dautel
Joachim Kilian

Saarland

Marius Theune
Tobias Bardhun
Christine Zehren
Angelika Anna

Umeå University
Markus Schmid
Silvio Collani

Uni Chapell Hill
Joe Kieber

INRA Versailles
Valerie Gaudin

ETH Zürich
Sam Zeeman

Uni Würzburg
Wolfgang Dröge-Laser

Observatoire Océanologique de Banyuls/Mer 1882

Reinhold-und-Maria-Teufel-Stiftung Tuttlingen

AWI Alfred-Wegener-Institut Helmholtz-Zentrum für Polar- und Meeresforschung

DFG Deutsche Forschungsgemeinschaft

Baden-Württemberg

ZMBP