nature research

Corresponding author(s): Pascal Falter-Braun

Last updated by author(s): 08.4.2020

Reporting Summary

Nature Research wishes to improve the reproducibility of the work that we publish. This form provides structure for consistency and transparency in reporting. For further information on Nature Research policies, see Authors & Referees and the Editorial Policy Checklist .

Statistics

For all statistical analyses, confirm that the following items are present in the figure legend, table legend, main text, or Methods section.

n/a	Confirmed	
☐	☒	The exact sample size (*n*) for each experimental group/condition, given as a discrete number and unit of measurement
☐	☒	A statement on whether measurements were taken from distinct samples or whether the same sample was measured repeatedly
☐	☒	The statistical test(s) used AND whether they are one- or two-sided *Only common tests should be described solely by name; describe more complex techniques in the Methods section.*
☐	☒	A description of all covariates tested
☐	☒	A description of any assumptions or corrections, such as tests of normality and adjustment for multiple comparisons
☐	☒	A full description of the statistical parameters including central tendency (e.g. means) or other basic estimates (e.g. regression coefficient) AND variation (e.g. standard deviation) or associated estimates of uncertainty (e.g. confidence intervals)
☐	☒	For null hypothesis testing, the test statistic (e.g. *F*, *t*, *r*) with confidence intervals, effect sizes, degrees of freedom and *P* value noted *Give P values as exact values whenever suitable.*
☒	☐	For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings
☒	☐	For hierarchical and complex designs, identification of the appropriate level for tests and full reporting of outcomes
☒	☐	Estimates of effect sizes (e.g. Cohen's *d*, Pearson's *r*), indicating how they were calculated

Our web collection on statistics for biologists contains articles on many of the points above.

Software and code

Policy information about availability of computer code

Data collection	Data for PRS curation were downloaded from IntAct (August 2014) and BioGRID (version 3.2.115). Data for network comparisons were downloaded from the same databases in June 2016 (IntAct) and Nov 2016 (BioGrid ver 3.4.142). Hormone annotations for all analyses were downloaded from Arabidopsis hormone database version 2.0, and extracted from TAIR10 GO annotations (03/08/2018). Transcriptome data for edge score analysis were taken from the Supplementary material of the referenced paper.
Data analysis	The used public software packages are referred to in the materials and methods section. Custom scripts have been deposited in github as indicated in the code availability statement. Software and packages used for data analysis are Cytoscape 3.7.2, R 3.6.1; Fiji Software Simple Neurite Tracer (v 3.1.3), igraph 1.2.4; drc 3.0-1; topGO 2.36; Kallisto v0.45; FastQC v0.11.7; Trimmomatic v0.36;

For manuscripts utilizing custom algorithms or software that are central to the research but not yet described in published literature, software must be made available to editors/reviewers. We strongly encourage code deposition in a community repository (e.g. GitHub). See the Nature Research guidelines for submitting code & software for further information.

Data

Policy information about availability of data

All manuscripts must include a data availability statement. This statement should provide the following information, where applicable:

- Accession codes, unique identifiers, or web links for publicly available datasets
- A list of figures that have associated raw data
- A description of any restrictions on data availability

All functional, genetic, and interaction data generated in this study are available as supplementary information. The genes selected for interactome mapping (search space) are presented in Supplementary Information Table 1. All protein-protein interaction data acquired in this study can be found in Supplementary Information Table 2. The data for genetic validation assays can be found in Supplementary Information Table 5. The preliminary edge-scores for all interactions identified in this study are presented in Supplementary Information Table 6. Additionally, all protein interactions from this work have been submitted to the IMEx (http://www.imexconsortium.org) consortium through IntAct5 and assigned the identifier IM-27834.

Field-specific reporting

Please select the one below that is the best fit for your research. If you are not sure, read the appropriate sections before making your selection.

☒ Life sciences ☐ Behavioural & social sciences ☐ Ecological, evolutionary & environmental sciences

For a reference copy of the document with all sections, see nature.com/documents/nr-reporting-summary-flat.pdf

Life sciences study design

All studies must disclose on these points even when the disclosure is negative.

Sample size	For all network rewiring and bootstrapping analyses the number of iterations was set to n = 1,000 as this provides a reasonable balance between statstical power and computational effort. For all plant phenotyping experiments we aimed to get a total n of ~100 plants, which provides a good compromise between statistical power and experimental workload and is widely accepted in the community. We started with 40-50 plants for each of three repeats which were germinated in standard conditions. Subsequently, plants at a similar developmental stage were selected for transfer to the hormone or mock-control plates, respectively. The selection of similar developmtal stages is important to ensure comparability of results and exclude developmental stage as a confounding factor. Due to stochastic biological variabilty this selection led to moderately variable number of plants in each experiment, i.e. a variable n in each assay and repeat. For the germination assay, we also had the limitation that the seeds needed to fit onto a smaller plate that fit under the microscope, which is why the numbers are lower. For all plant assays the n of each repeat and each line is provided in the extended data tables.
Data exclusions	No data were excluded. During the phenotyping experiments, individual seedlings at similar developmental stage were selected to exlude developmental stage as a confounding variable. This was prior to observation of the outcome and even prior to start of treatment.
Replication	As part of the interaction mapping pipeline all Y2H interactions are verified at least three times. All functional genetic assays have at least three technical and three biological replicates. Cell biology data were repeated at least once (two repeats). For phenotypic assays we aimed for three, or two biological repeats.
Randomization	Network statistics are always checked against randomized networks to exclude pure effects due to network topology that may be independent of the measured biology.
Blinding	All in planta hormone validation assays, the yeast benchmarking using PRS/RRS and the validation assays were done and scored in a randomized design in which the experimenters were unaware of the identity of the samples.

Reporting for specific materials, systems and methods

We require information from authors about some types of materials, experimental systems and methods used in many studies. Here, indicate whether each material, system or method listed is relevant to your study. If you are not sure if a list item applies to your research, read the appropriate section before selecting a response.

Materials & experimental systems

n/a	Involved in the study
☐	☒ Antibodies
☒	☐ Eukaryotic cell lines
☒	☐ Palaeontology
☐	☒ Animals and other organisms
☒	☐ Human research participants
☒	☐ Clinical data

Methods

n/a	Involved in the study
☒	☐ ChIP-seq
☒	☐ Flow cytometry
☒	☐ MRI-based neuroimaging

Antibodies

Antibodies used	Only commercial anti-tag antibodies were used. Specifically M2 anti-Flag (Sigma), anti-GST (Amersham Biosciences) and anti-MBP (New England Biolabs)
Validation	We mostly relied on the quality control and many years of experimence of the scientific community with these standard regeants. We then only verified that the antibodies recognized the tags they were raised against. For the anti-Flag pull-down experiments negative controls were included to ensure specificity of the purification.

Animals and other organisms

Policy information about studies involving animals; ARRIVE guidelines recommended for reporting animal research

Laboratory animals	none, only plants from stock centers - numbers are provided in Supplementary Table 5
Wild animals	none, only plants from stock centers - numbers are provided in Supplementary Table 5
Field-collected samples	none, only plants from stock centers - numbers are provided in Supplementary Table 5
Ethics oversight	*Identify the organization(s) that approved or provided guidance on the study protocol, OR state that no ethical approval or guidance was required and explain why not.*

Note that full information on the approval of the study protocol must also be provided in the manuscript.