

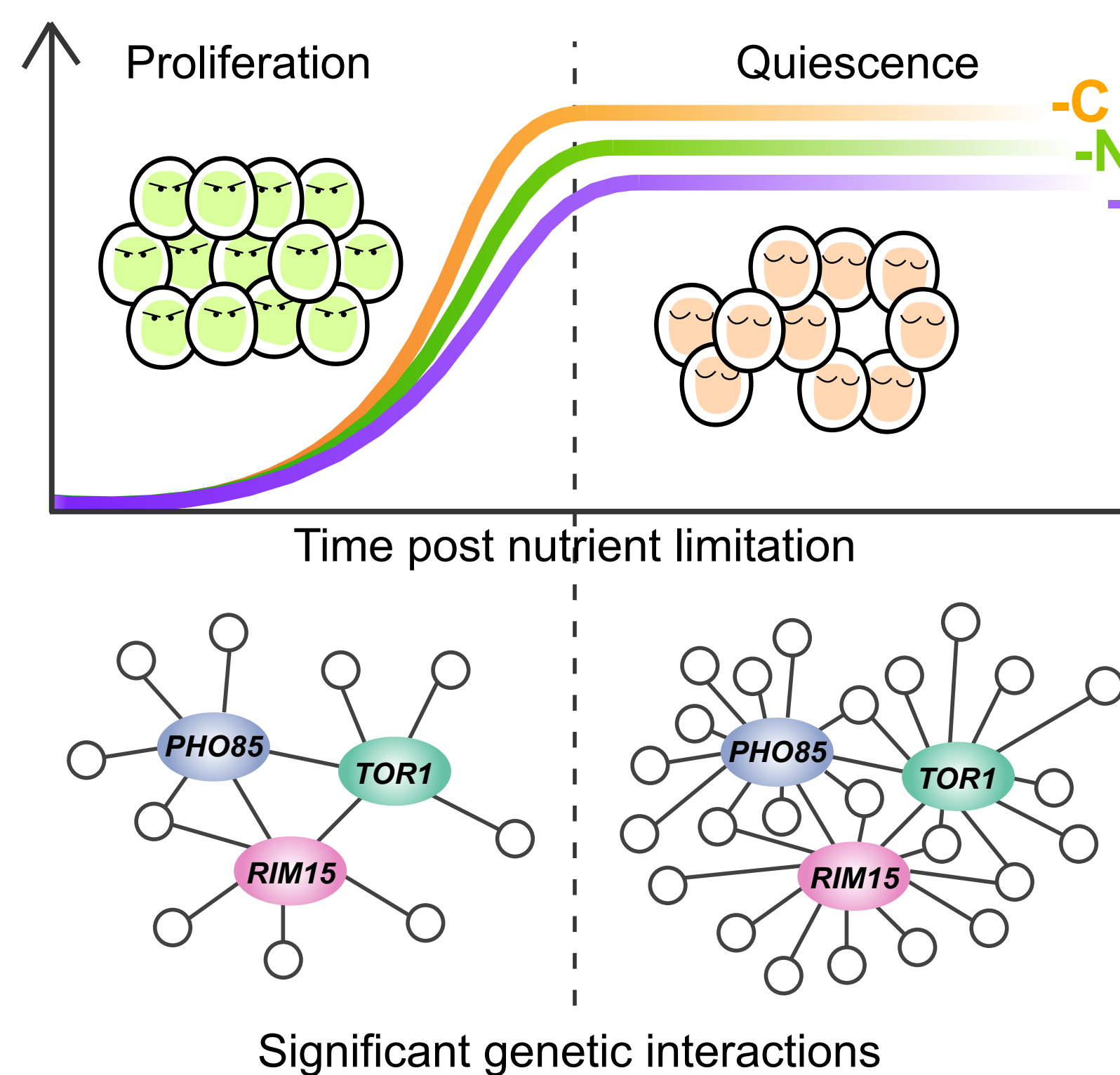
# Genetic interaction profiles of regulatory kinases differ between environmental conditions and cellular states

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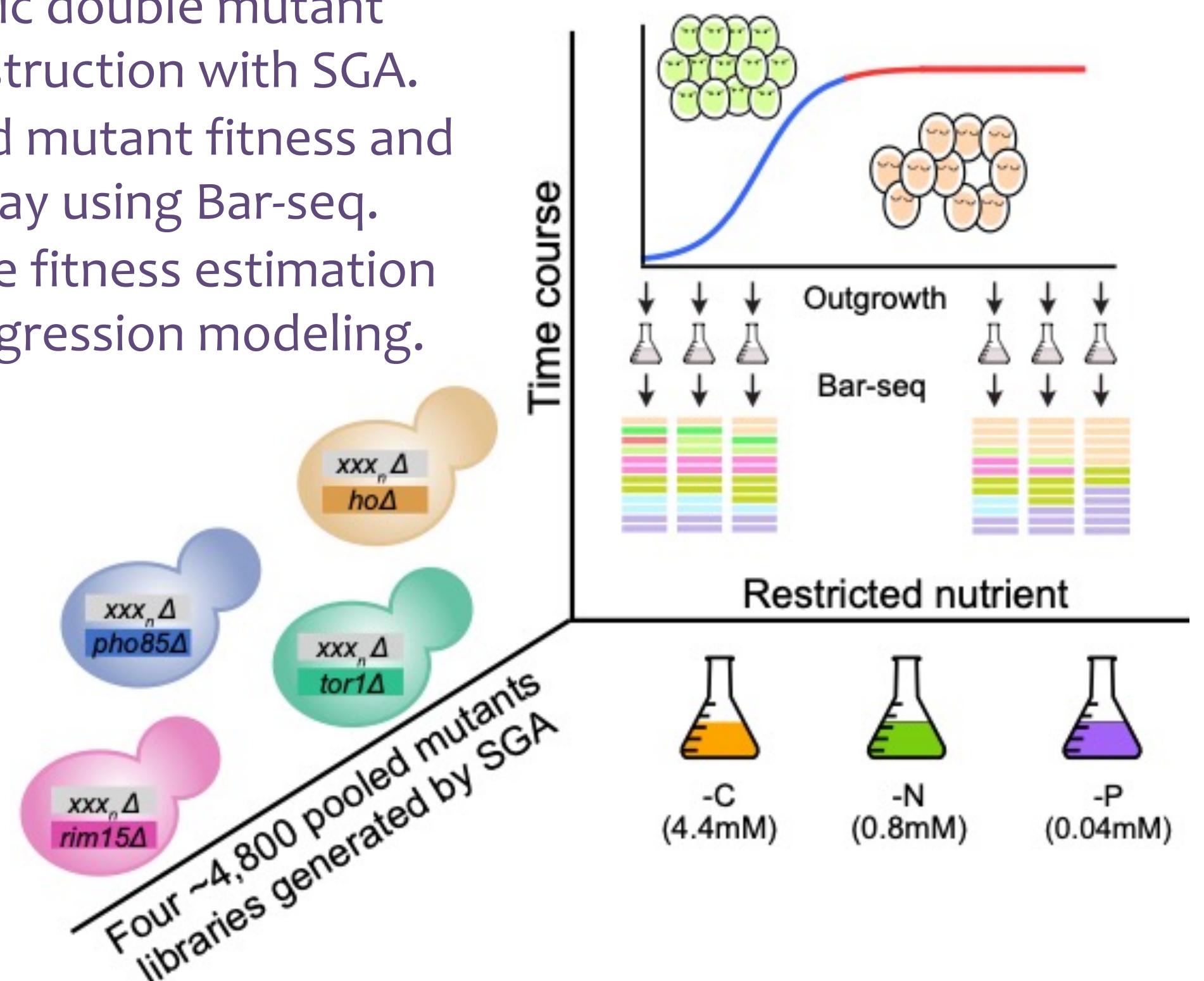
## ABSTRACT



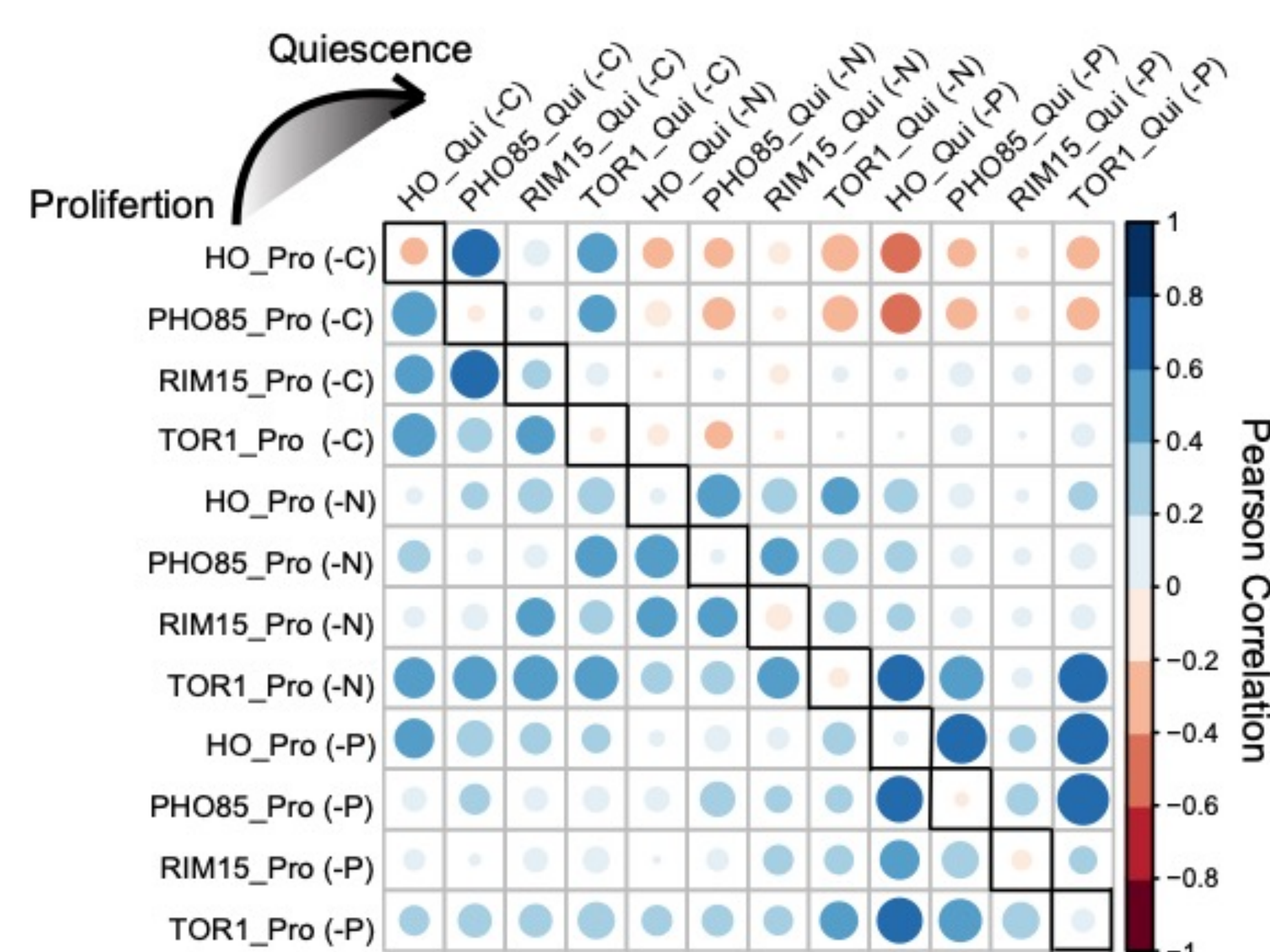
- Additional phenotypic readouts are used for quantifying genetic interaction (GI) in different cellular states. E.g. survival of nutrient starvations (-C: carbon limitation, -N: nitrogen limitation, -P phosphorous limitation).
- The GIs of signaling kinase genes *TOR1*, *RIM15*, *PHO85* vary between different environmental conditions and cellular states.
- *RIM15* interacts with similar functional classes of genes in different starvations conditions.
- Unique and cohesive positive GIs between *RIM15* and *ERAD-L* genes in nitrogen starved quiescent cells.

## EXPERIMENTAL DESIGN

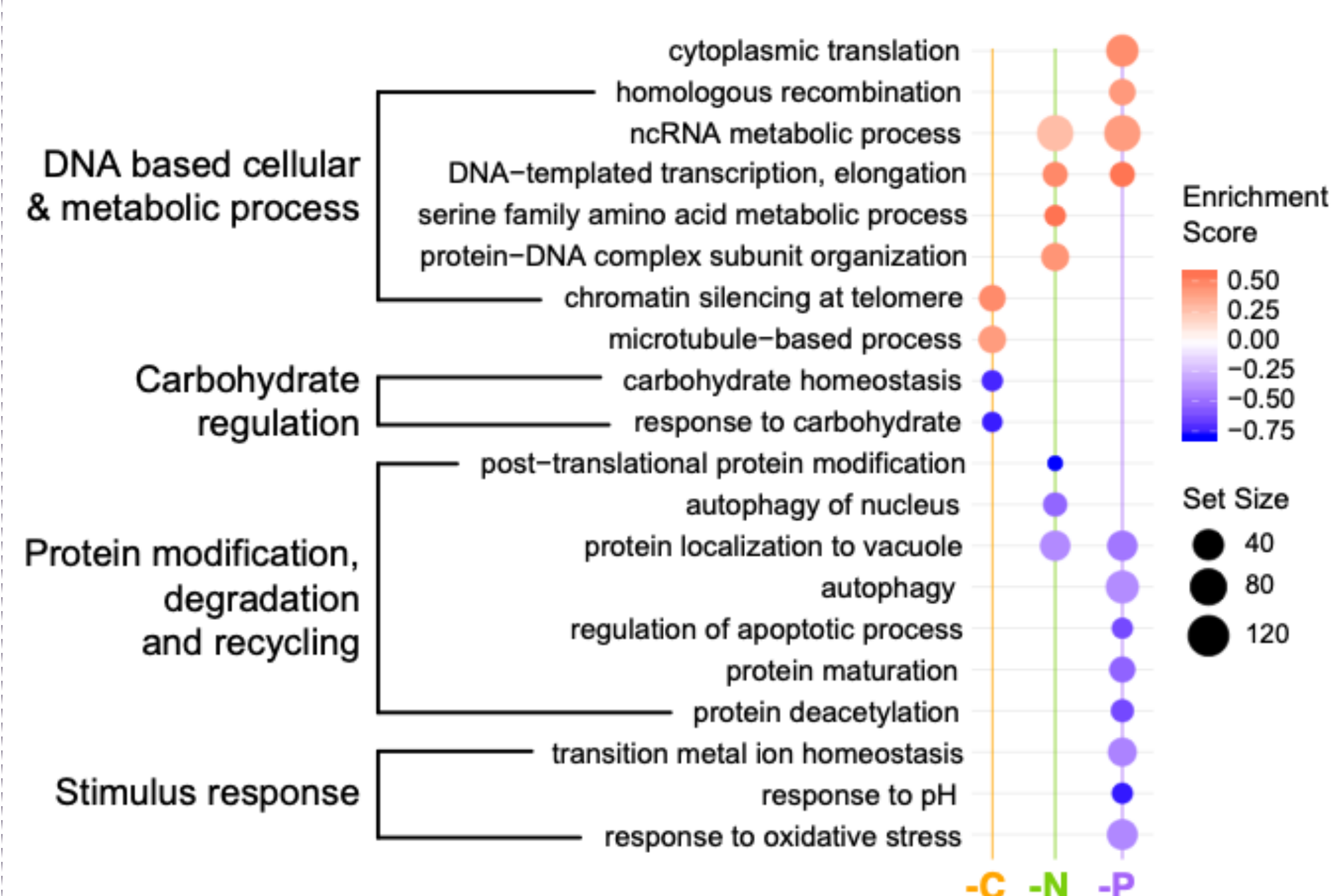
- Prototrophic double mutant library construction with SGA.
- Multiplexed mutant fitness and survival assay using Bar-seq.
- Time-course fitness estimation by linear regression modeling.



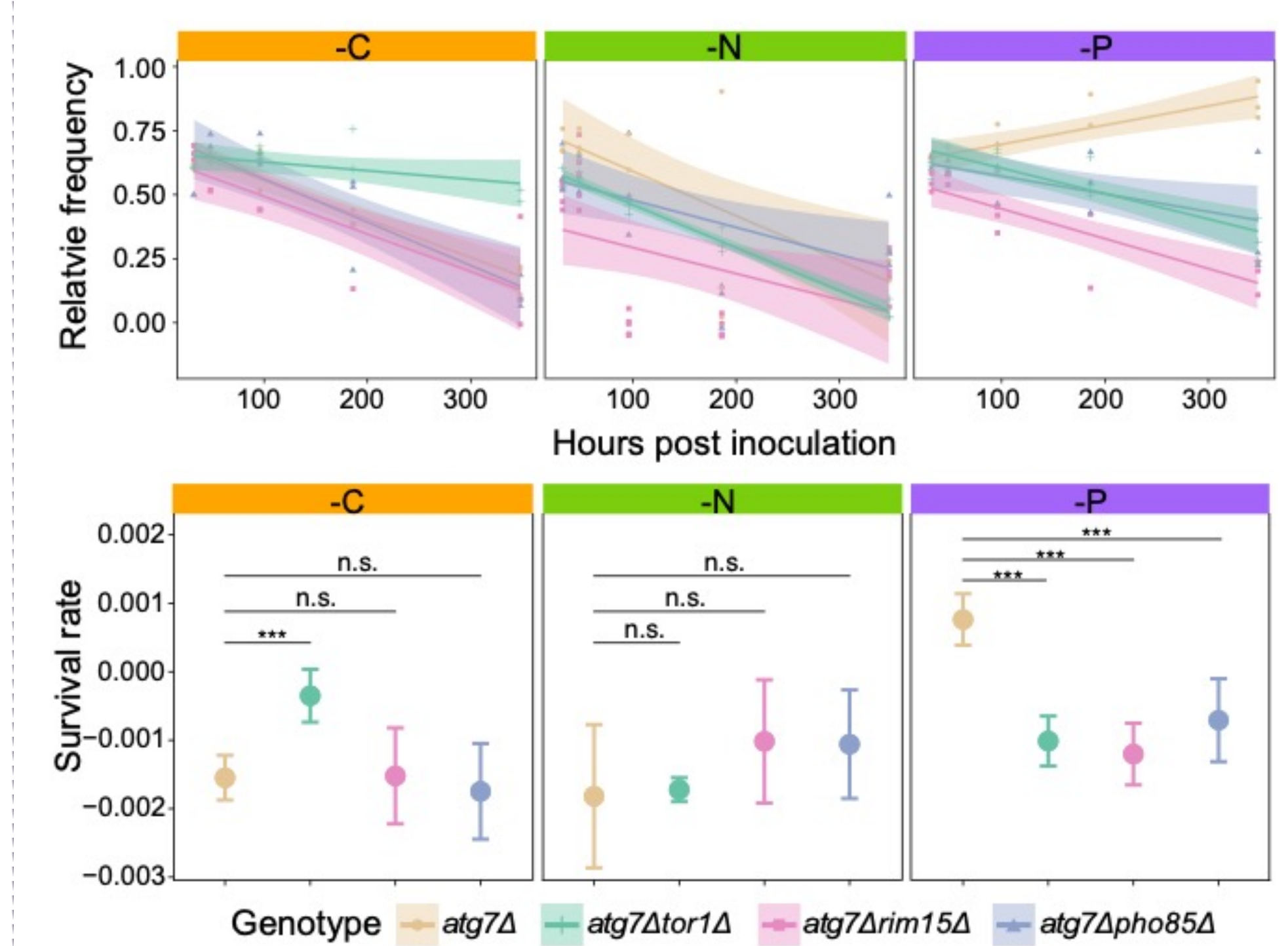
## RESULTS



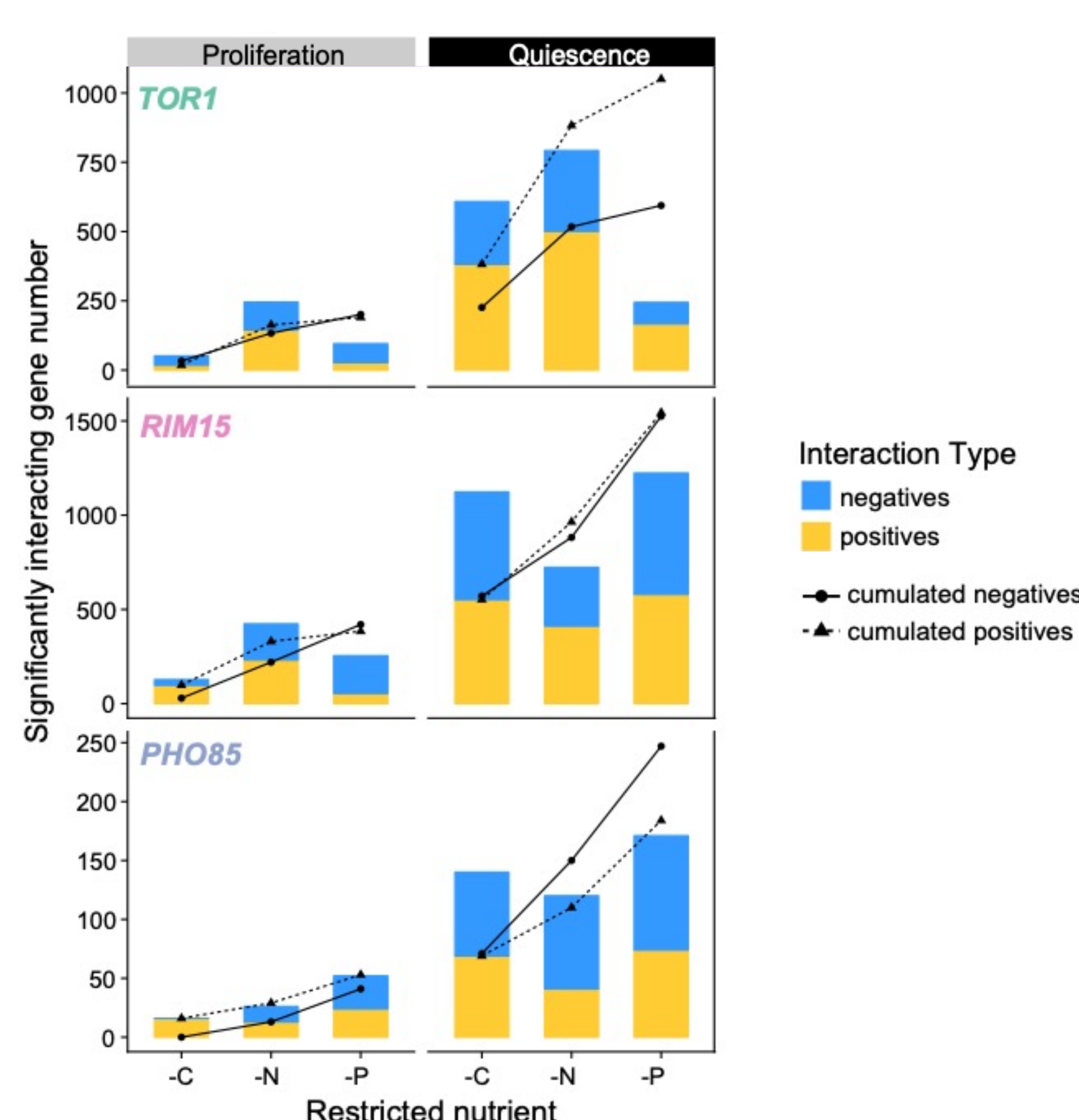
Nutrient type is the primary determinant of survival profiles in quiescent cell



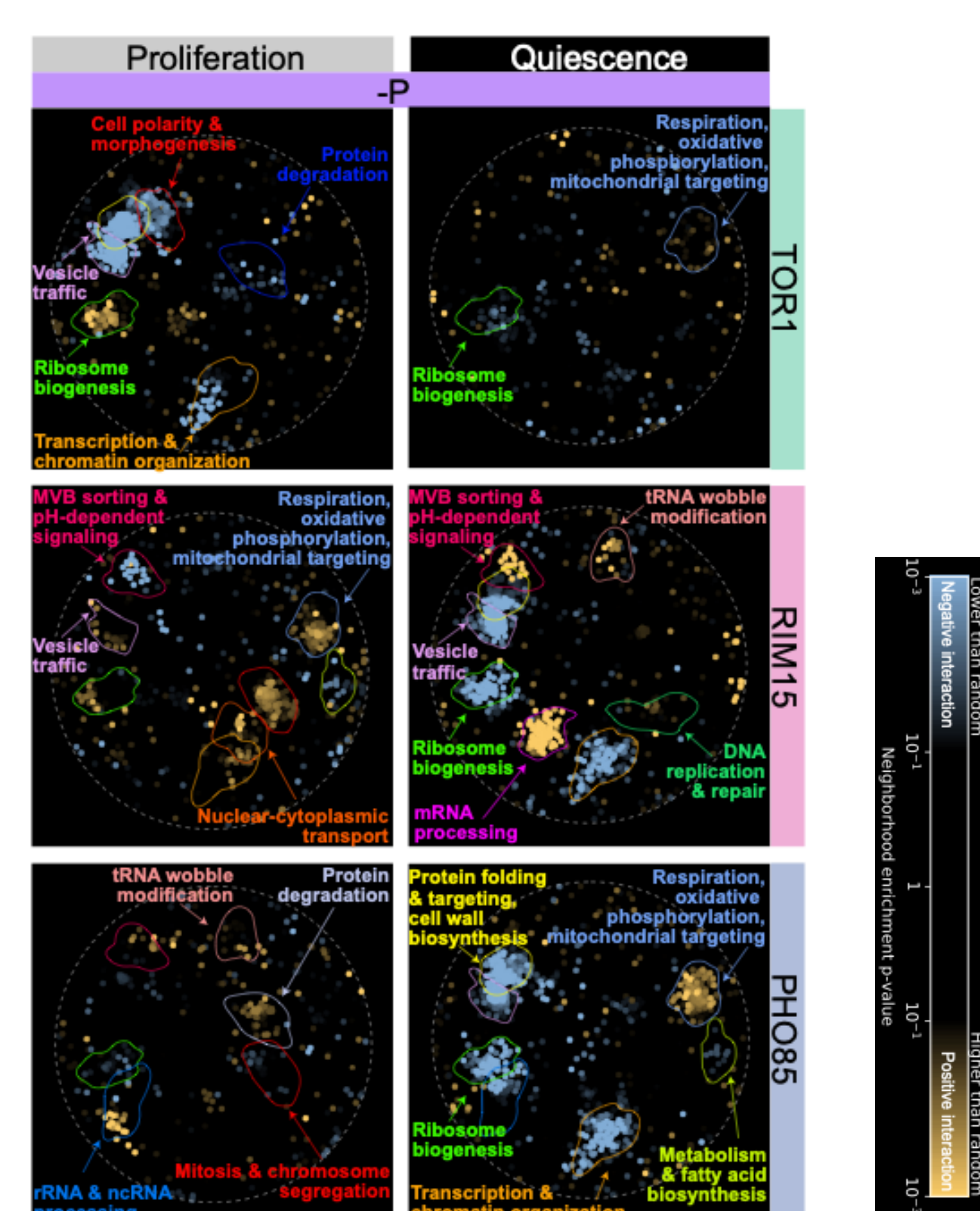
### Distinct cellular functions are required for quiescence in response to different nutrient starvation signals



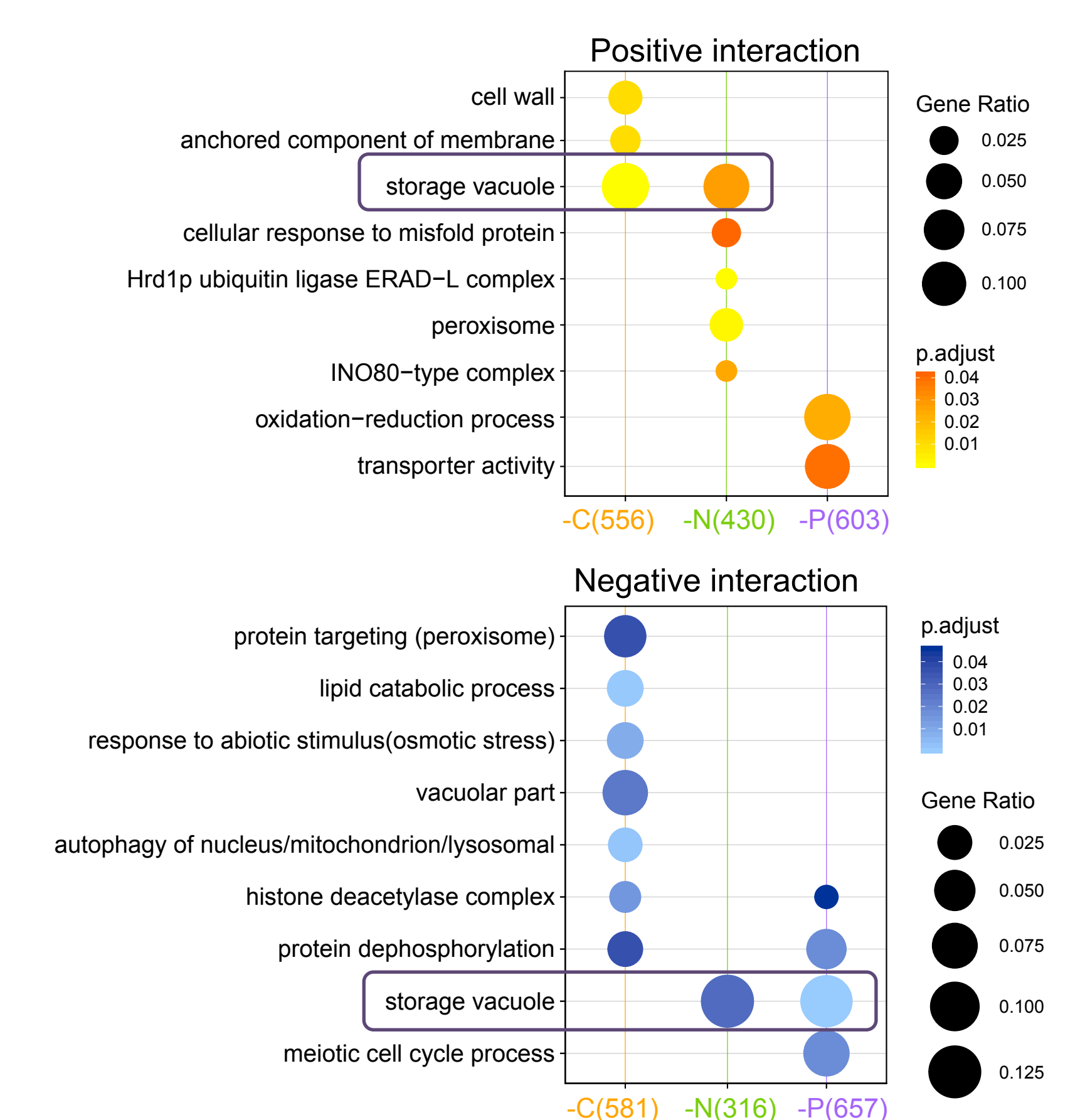
### Genetic interactions quantified using pooled assays between gene pairs are condition dependent



More genetic interactions are detected in quiescent cells regardless of the starvation signal



## Genetic interaction profiles of kinases differ between cellular states and are functionally coherent (SAFE)



RIM15 interacts with similar functional classes of genes in different starvations conditions.

## CONCLUSION

1. QUIESCENT SPECIFIC GENETIC INTERACTION CAN BE DETECTED BY HIGH-THROUGHPUT DNA BARCODE SEQUENCING AND FITNESS MODELING OVER TIME.
2. UNDER STRINGENT SELECTIVE CONDITION, NON-ESSENTIAL GENES BECOME NECESSARY FOR MAINTAINING VIABILITY.
3. GENETIC NETWORK MAPPING UNVEILS CONDITION SPECIFIC INTERACTIONS FOR DIFFERENT NUTRIENT AND PHYSIOLOGICAL STAGES.
4. SUPPRESSION INTERACTION BETWEEN RIM15 AND ERAD-L MEDIATED UNFOLDED PROTEIN RESPONSE UNDER NITROGEN RESTRICTED QUIESCENCE.

## ACKNOWLEDGEMENTS & PUBLICATION

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Peer reviewed publication associated with this study has been accepted by Molecular and System Biology.