Evolutionary significance and the genetic basis of starvation-induced quiescence (G0) in *Saccharomyces cerevisiae*

Saccharomyces cerevisiae, baker's yeast, is one of the best model organisms, for biological and biomedical research. Many evolutionary conserved genes and metabolic pathways are shared between yeast and other eukaryotes, including humans [1] . Yeast can sense the quality of their environment and respond appropriately by tuning their physiology. In the absence of available nutrients, about ~ 75% of the yeast population become quiescent (Q), while the rest of the population stays as non-quiescent (NS) cells. Quiescent (Q) cells stop divisions and accumulate storage materials such as glycogen and trehalose instead. Q cells have distinct phenotype, with thick cell wall, condensed chromatin, but their most important feature is ability to survive long-term starvation and other environmental stresses. Because ~ 60% of all microorganisms on Earth are in a quiescence state, and microbial ability to extremely long-term survival is associated presence of spores and quiescence cells, the subjects are of top interest for scientists.

In the project we are interested in genetics and evolution of yeast quiescence as a model for other fungi and eukaryotes. As a result of the previous evolutionary experiment, we created a unique collection of strains which, when starved produce changed NQ /Q cells proportion comparing to the wild type strain [2]. Analysis of the genome sequences of these 96 strains allowed us to identify gene mutations that have been accumulated during ~ 300 generations in the evolutionary experiment. Among these, ~100 various mutations, there are several that we recognised as probably important for the yeast quiescence. These include, for example, multiple mutations in genes *SSY1-PTR3-SSY5* identified in the cell lines with increased NS cell production. These genes are forming the SPS pathway responsible for amino acids sensing in the environment. We also identified genes influencing chromatin conformation: *SIR3* and *FAS1*, in the lines with increased the proportion of S cells production. To ultimately confirm the impact of the mutation, we want to introduce it into the ancestor genome (which has no other mutated mutation) and test the phenotype (S/NS cell production) of modified strains. We also want to test the Q/NQ cell balance in the clones that were not checked before and compare these results with the sequence analysis of mutations acquisition during evolution experiment (trees of the phylogenetic mutation in [2]. In addition, we plan to analyse transcripts of selected clones with altered Q/NQ balance, because the observed phenotype is probably related to changes in the activity of specific genes that we hope to identify.

Single-cell microorganisms are self-sufficient, but most often live in colonies, biofilms - multi-generational populations. In such communities, all individuals interact and often synchronize their reactions. Many yeast behaviour can be treated as social features or division of labour [3, 4] We are planning experiments that will provide evidence to answer the evolutionary questions: Why do starved yeast populations in the event of environmental stress produce phenotypically differentiated cells? Is this the effect of maximizing the fitness of one of the phenotypes? Will this diversity provide the benefits for all individuals in this colony? Can it be classified as a "division of labour"? Does the corresponding Q/NQ cell balance increase the immunity of the biofilm-producing population to fungicides?

Do you want to know more? Literature:

1. Duina, A. A., Miller, M. E. and Keeney, J. B. (2014). Budding yeast for budding geneticists: a primer on the Saccharomyces cerevisiae model system. *Genetics* **197,** 33-48.
2. Wloch-Salamon, D. M., Tomala, K., Aggeli, D. and Dunn, B. (2017). Adaptive Roles of SSY1 and SIR3 During Cycles of Growth and Starvation in Saccharomyces cerevisiae Populations Enriched for Quiescent or Non-quiescent Cells. *G3: Genes|Genomes|Genetics*. g3. 117.041749.
3. Wloch-Salamon, D. M. (2014). Sociobiology of the budding yeast. *Journal of biosciences* **39,** 225-236.
4. Wloch-Salamon D. M., Fisher R.M., Regenberg B., (2017) Division of labour in Saccharomyces cerevisiae. YEAST accepted for publication.