What do cells do when they are not dividing? Most living cells on Earth spend their lives in a state of rest called quiescence. Quiescence is a reversible, deliberate halt in cell division, from which cells can resume dividing. Studying quiescence is technically challenging, so despite its prevalence, it is much less studied than cell growth and division. Recent research shows that, contrary to traditional views, quiescent cells are not like a frozen "Sleeping Beauty" but more like "Little Red Riding Hood" – energy-demanding, living systems that interact, communicate, and respond to both biotic and abiotic factors. Ecological factors, such as temperature changes, nutrient availability, the presence of toxins, and interactions with other cells and organisms, contribute to the diversity of quiescent cells in populations. Over time, the characteristics of quiescent cells change. Quiescent cells can age, eventually losing their ability to divide, leading to their death.

To fully understand the dynamics of quiescence and its adaptive capacity, we plan to conduct research at both the single-cell and population levels. We use baker's yeast, *Saccharomyces cerevisiae*, as our model organism. It is the only well-studied eukaryotic organism from which we can relatively easily obtain both individual quiescent cells and their multimillion-cell populations. Thus, yeast is an ideal organism for studying quiescence at both cellular and population levels.

The aim of the project is to investigate how environmental factors, both biotic and abiotic, affect quiescent cells and their interactions with other cells in the population. This study aims to fill gaps in knowledge about how these cells respond to different environmental elements and adapt to them. We aim to answer research questions such as: How do the internal structures of individual cells change, and how does this affect the entire population in quiescence for varying lengths of time? How do cell interactions and nutrient recovery from the environment affect diversity during quiescence? What are the genetic bases for adaptation to long and short periods of quiescence? What are the evolutionary trade-offs associated with population heterogeneity in the context of long and short quiescence? How does individual cell survival depend on population density? What ecological conditions lead to the evolution of increased phenotypic diversity?

To answer the main questions of the project, an interdisciplinary team of biologists, biochemists, bioinformaticians, and mathematicians will use a combination of techniques. At the cellular level, these will include fluorescent microscopy, flow cytometry, and microfluidics; at the population level, spectrophotometry and experimental evolution. We plan to use genome modification techniques (homologous transformations) and next-generation sequencing (NGS). The results will form the basis for developing a phenomenological mathematical model describing and predicting population dynamics of diversity in quiescence.

The project has significance for:

Basic research: The results will help us understand the genetic basis for the decision between cell division and entering quiescence, as well as phenotypic diversity within a population.

Health: *Saccharomyces cerevisiae* is a model for eukaryotic cells; homologs of identified genes could be tested in the context of quiescent cancer cells, which increase the risk of metastasis and treatment failure.

Evolutionary ecology: The mathematical model could be extended to populations of prokaryotic microorganisms to address the general ecological question: Which strategy (rapid multiplication vs. quiescence) is optimal under which ecological conditions? Integrating unique scientific teams, specialists in experimental research at the cellular and population levels with mathematical modeling, will allow us to understand the ecological conditions that shape quiescent cell heterogeneity and provide a deeper understanding of aging processes.