

Epistasis describes the phenomenon that mutations at different loci do not have independent effects with regard to certain phenotypes/characteristics. Its understanding is vital for many genetic and evolutionary processes. Epistasis can be positive (alleviating), or negative (aggravating), when a combination of deleterious mutations shows a phenotype value that is higher, or lower, than expectation, respectively. As biological systems in nature have to face multiple genetic and environmental perturbations, understanding the dynamics of epistasis under these perturbations remains an important issue in the evolutionary field. The main objective of this project is to broaden our understanding of how dynamics of epistasis changes under different environmental conditions.

The dynamics of epistasis will be studied with model multicellular organism *Caenorhabditis elegans*. *C. elegans* is free-living, small (~1mm) soil nematode. Its life cycle is only three days long and it lives up to 3 weeks. It was the first organism to have its genome sequenced. Because it is easy to rear in a laboratory, small and transparent (what makes it easy to see its internal structure under microscope), it became one of the model organisms widely used in biological studies. There are many strains of *C. elegans* with single gene mutations available. Moreover by feeding *C. elegans* especially genetically engineered *Escherichia coli* bacteria we can selectively turn off their chosen genes (RNA interference method).

In this project genetic interactions between genes involved in DNA repair and in response to oxidative stress, for which single mutant strains are available (total of 100 genes), will be studied. To identify pairwise interactions among genes, each of those genes will be inactivated by RNA interference or mutation. This approach enables high-throughput construction of double mutants. Single mutant data will be used to compute an expected phenotypic score for the double mutant. Then two genes will be inactivated simultaneously by applying RNA interference to mutant strains and we will examine whether the observed double mutant phenotype is significantly different than the expected value. Simultaneously, the same set of genetic interactions will be scored in standard laboratory condition, and in six harsh conditions (under treatment with three different concentrations of genotoxic agent and three different concentrations of chemical causing oxidative stress). Fitness (population growth) will be scored to quantify epistasis. This will generate 7 static epistatic maps of 10 000 genetic interactions each. The dynamics of epistasis will be quantified based on differences between static interaction maps.

To our knowledge it will be the first high-throughput study of dynamics of epistasis carried out in multiple environments in a whole multicellular organism. This will broaden our understanding of how dynamics of epistasis under environmental perturbations can affect evolutionary processes. It will allow as well comparison of the dynamics of epistasis between unicellular and multicellular organisms.