INTERPLAY OF GENOME STRUCTURE AND METABOLIC NETWORK IN ADAPTATION (ADAGE)

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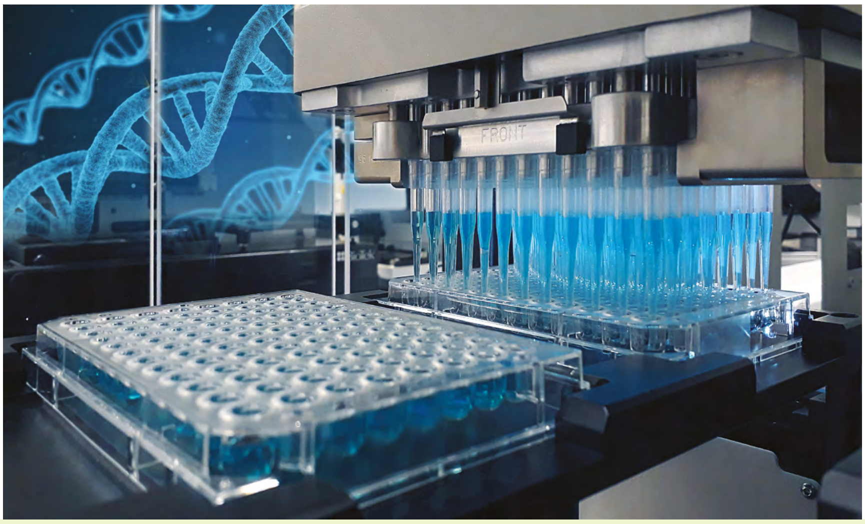
All proliferating cells, from tumor cells to microbes used in industrial biotechnology production, evolve. In adaptive evolution the genotypic underpinnings of the fittest phenotypes, selected in a given environment, are influenced by metabolic network. Simultaneously, the adaptability of a particular genotype depends on genome structure. **Yet, the interplay of genome structure and metabolic network in cellular adaptive evolution has been overlooked so far.** In Adage -project this interplay will be elucidated by **combining eukaryotic synthetic biology, genome-scale metabolic modelling, adaptive laboratory evolution (ALE), evolutionary data analysis, and machine learning.**

Synthetic biology tools enable engineering structural and metabolic network variant strains of yeast *Saccharomyces cerevisiae*, a eukaryotic model organism and common industrial production host. By subsequently exposing the variant strains to ALE, the contributions of genome structure and metabolic network become dissectible. The nutritional conditions for ALE allowing disclosing differential adaptive potentials will be designed using genome-scale metabolic model simulations. The resulting evolved lineages will be phenotyped and analysed using deep next-generation sequencing for uncovering the differential adaptive potentials and de novo mutations. The de novo mutations specific for a particular engineered variant reveal the interplay between the genome structure and metabolic network. Associated responses of cellular regulatory circuitry will be uncovered with machine learning on omics data (metabolomics, gene expression) of the evolved lineages.

By revealing fundamental information on the links between genome structure, metabolic network, and other cellular regulation, Adage-project will provide a substantial leap towards predicting adaptive evolution and controlling evolutionary trajectories with chemical environments or genome engineering. The project outcomes will contribute towards tackling global grand challenges. Effectively steering adaptive evolution would allow, for example, crop and food fermentation process improvement for food security. Understanding the regulation of adaptability will enable developing more stable industrial biotechnology microbes promoting sustainable use of resources.



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Twitter account of the project: https://twitter.com/AdaGe_project