Global Rebalancing of Cellular Resources by Pleiotropic Point Mutations Illustrates a Multi-scale Mechanism of Adaptive Evolution - DTU Orbit (09/11/2017)

Global Rebalancing of Cellular Resources by Pleiotropic Point Mutations Illustrates a Multi-scale Mechanism of Adaptive Evolution

Pleiotropic regulatory mutations affect diverse cellular processes, posing a challenge to our understanding of genotype-phenotype relationships across multiple biological scales. Adaptive laboratory evolution (ALE) allows for such mutations to be found and characterized in the context of clear selection pressures. Here, several ALE-selected single-mutation variants in RNA polymerase (RNAP) of Escherichia coli are detailed using an integrated multi-scale experimental and computational approach. While these mutations increase cellular growth rates in steady environments, they reduce tolerance to stress and environmental fluctuations. We detail structural changes in the RNAP that rewire the transcriptional machinery to rebalance proteome and energy allocation toward growth and away from several hedging and stress functions. We find that while these mutations occur in diverse locations in the RNAP, they share a common adaptive mechanism. In turn, these findings highlight the resource allocation trade-offs organisms face and suggest how the structure of the regulatory network enhances evolvability.

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