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Bypassing Evolutionary Roadblocks: Phenotypic Diversity in Isogenic Population Bridges Tradeoff in Evolution of a New Function

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Introduction: A key problem in the development of life on Earth is the origin of novelty. How does evolution achieve the complex diversity of forms and functions we see today, starting from simpler precursors? In particular, how can selection transform one phenotype, optimized to provide a reproductive benefit, into a novel phenotype without sacrificing the original function? One traditional explanation resolving this conflict is a multistage process initiated by gene duplication. One copy preserves the original function, freeing the other to diverge until it finds new function. Cases of this process seem to explain the evolution of some protein families; however, the prevalence of this mechanism throughout evolutionary history is uncertain. It is unclear if both the frequency of spontaneous gene duplication and the availability of productive mutational paths for copied genes are sufficient to account for the incredible diversity of extant life. Instead, we predict that an alternative, more deterministic and repeatable mechanism for evolutionary innovation may play a role.

Key Finding: Recent observations during experimental evolution of a contemporary virus revealed a new mechanism for innovation that does not rely on gene duplication. The virus instead evolved a single copy of the host recognition gene (*J*), that partitions its protein products into populations with different phenotypes: some can carry out the new function, in this case binding to a novel cellular receptor on the bacterial host, and some have improved binding to the original receptor. This new mechanism, termed 'phenotypic stochasticity', relies on natural selection and not the remote chance of gene duplication. The phenotypic stochasticity arose as a side effect of selection favoring a faster reacting host recognition protein. Reaction rates were improved by creating an unstable and disordered protein that can fold into multiple conformations. Because fast reactivity is a property many enzymes experience selection for, it may be a common step on evolutionary paths toward innovation, and may be especially relevant for the earliest forms of simple life, which may have lacked mechanisms for gene duplication and the ability to accommodate expanded genomes.