

## Evolving strategies for life in an uncertain world

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Molecular processes are fundamentally stochastic. Randomness is the rule in transcription, translation, cell-to-cell variation in protein levels, and heterogeneity in interactions. One common assumption is that such phenotypic variation is simply noise, and scientists often appeal to the statistics of large numbers when developing deterministic theories, ignoring any potentially adaptive role of stochasticity. Yet evidence is accumulating that phenotypic variance constitutes an evolutionary driving force across diverse biological processes, including the adaptive immune system, the development of cancerous neoplasms, and the persistence of pathogens under drug pressure. All these systems are fundamentally characterized by high levels of environmental change and uncertainty: either persistent, global, temporal fluctuations in selection pressure, or local, micro-environmental and spatially-defined selective forces. Can evolution prepare organisms for this environmental stochasticity? I will talk about the genetic signatures of this commonplace yet unpredictable environmental variation. I will particularly focus on exploring the evolutionary advantage of alleles that confer the ability to express a range of phenotypes, a type of evolutionary bet-hedging that need not confer a direct benefit to a single individual, but can increase the chance of long-term survival of a lineage. I will also discuss implications of these results in the context of therapies designed to eradicate populations of pathogens or aberrant cellular lineages.

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