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SÉMINAIRE

Congruent evolution of genetic and environmental robustness in microRNA.

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Genetic robustness, the preservation of an optimal phenotype in the face of mutations, is critical to the understanding of evolution as phenotypically expressed genetic variation is the fuel of natural selection. The origin of genetic robustness, whether it evolves directly by natural selection or it is a correlated byproduct of other phenotypic traits, is, however, unresolved. Examining micro-RNA (miRNA) genes of several eukaryotic species, Borenstein and Ruppin (Borenstein E, Ruppin E. 2006. Direct evolution of genetic robustness in microRNA. Proc Natl Acad Sci USA. 103: 6593) showed that the structure of miRNA precursor stem loops exhibits significantly increased mutational robustness in comparison with a sample of random RNA sequences with the same stem-loop structure. The observed robustness was found to be uncorrelated with traditional measures of environmental robustness--implying that miRNA sequences show evidence of the direct evolution of genetic robustness. These findings are surprising as theoretical results indicate that the direct evolution of robustness requires high mutation rates and/or large effective population sizes only found among RNA viruses, not multicellular eukaryotes. We demonstrate that the sampling method used by Borenstein and Ruppin introduced significant bias that lead to an overestimation of robustness. Introducing a novel measure of environmental robustness based on the equilibrium thermodynamic ensemble of secondary structures of the miRNA precursor sequences, we demonstrate that the biophysics of RNA folding induces a high level of correlation between genetic (mutational) and environmental (thermodynamic) robustness, as expected from the theory of plastogenetic congruence introduced by Ancel and Fontana (Ancel LW, Fontana W. 2000. Plasticity, evolvability, and modularity in RNA. J Exp Zool. 288: 242-283). In light of theoretical considerations, we believe that this correlation strongly suggests that genetic robustness observed in miRNA sequences is the byproduct of selection for environmental robustness.