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The dynamics of adaptive genetic diversity during the early stages of clonal evolution

The dynamics of genetic diversity in large clonally-evolving cell populations are poorly understood, despite having implications for the treatment of cancer and microbial infections. Here, we combine barcode lineage tracking, sequencing of adaptive clones, and mathematical modelling of mutational dynamics to understand diversity changes during experimental evolution. We find that, despite differences in beneficial mutational mechanisms and fitness effects between two environments, early adaptive genetic diversity increases predictably, driven by the expansion of many single-mutant lineages. However, a crash in diversity follows, caused by highly-fit double-mutants fed from exponentially growing single-mutants, a process closely related to the classic Luria-Delbruck experiment. The diversity crash is likely to be a general feature of clonal evolution, however its timing and magnitude is stochastic and depends on the population size, the distribution of beneficial fitness effects, and patterns of epistasis.