RECOMBINATION IMPEDES THE SPREAD OF MUTATOR ALLELES IN EXPERIMENTAL POPULATIONS OF *E. COLI*. B. Galeota-Sprung[1*], Y. Raynes[2†], B. Martino[1], M. Hyun[1], P.D. Sniegowski[1], [1]University of Pennsylvania, [2]Brown University, [*]gbe@sas.upenn.edu , [†]yevgeniy_raynes@brown.edu

Background: Complex genetic systems whose function is to reduce the error rate of the replication of genetic information are ancient and pervasive in bacteria and eukaryotes. Yet, when two asexual microbial lineages differing only in their mutation rate are competed against one another, the high-mutation-rate ("mutator") lineage generally wins the competition [1]. Furthermore, in long-term evolution experiments, mutator lineages have been observed to arise spontaneously and fix in populations [2]. In both cases, the rise of mutators in frequency is thought to be driven by linkage disequilibrium between the mutator allele and newly arising beneficial mutations, a process termed hitchhiking [3].

The implications of this substantial body of experiment—that higher mutation rates are generally advantageous—are contrary to the observation of generally low mutation rates in nature. A key difference may be that while experimental populations (of *E. coli* for example) are truly asexual, in nature all or nearly all microbial populations recombine to at least some degree, by one of several mechanisms of horizontal gene transfer. Such recombination is expected to interfere generally with hitchhiking [4], and thus with the spread of mutator alleles in particular, although the latter prediction has been little investigated.

Methods: We examined the fate of mutator alleles in two *E. coli* backgrounds: one in which genetic exchange via conjugation is relatively frequent, and one in which the population is strictly asexual. We conducted replicate competitions in which mismatch repair mutators were seeded into populations at a starting frequency of ~2%. We propagated replicate populations in flasks by daily 1/100 dilution, and tracked the frequency of the mutator allele over hundreds of generations using an antibiotic resistance marker.

Results: We found that in both backgrounds, mutators usually spread to fixation, but that the time to fixation of mutator alleles was greater in the recombining populations than in the asexual populations. Follow-up assays showed that many of our recombining populations had evolved away the ability to donate DNA over the course of the experiment. There was a strong association between a population retaining a substantial portion of its recombining ability and a delayed time to fixation of the mutator allele.

Conclusions: This result has implications for our understanding of mutation rate evolution in natural populations. Many natural microbial populations have been shown to harbor mutator sub-populations: our results imply that one factor preventing mutators from fixing in such cases is the exchange and recombination of genetic material mediated by horizontal gene transfer.

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