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Rebuttal: Adaptive Mutation in *Escherichia coli* (Foster)

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Foster (1) and we agree about most, if not all, of the fundamental aspects of adaptive mutation in the *Escherichia coli* Lac system, most notably, that the data provide strong support for hypermutation (HM) models in which the mutation rate increases generally in response to stress. There are just a few small apparent discrepancies, clarification of which might be helpful.

Whereas we state that 85% of point mutations require the special error-prone DNA polymerase DinB/Pol IV, Foster uses the figure of 50 to 80% (and thus attributes 50 to 20% of mutations to some other DNA polymerase, whereas we attribute only 15% to another polymerase). This discrepancy is caused partly by how each lab measures adaptive mutations. We measure point mutants separately from *lac*-amplified clones and have shown that 85% of point mutations require DinB/Pol IV whereas none of *lac* amplification does (2). Foster does not separate the point mutants and *lac*-amplified clones and therefore sees that the total number of Lac^+ colonies is decreased less than 85% by loss of DinB—this is because the number of *lac*-amplified clones is not reduced.

We note that Foster's proposal regarding the mechanism of antimutator activity of the *dnaE915* allele was made previously in reference 2.

As noted in both our (3) and Foster's (1) papers, there is not a consensus regarding whether all or some of Lac^+ adaptive revertant cells arise from the cells in the demonstrated hypermutable subpopulation (the reasons are reviewed in reference 3). However, here we wish to point out the fundamental agreement articulated in Foster's paper that all Lac^+ cells arise from cells experiencing higher mutation rates than "normal" cells. It is now articulated clearly that her model holds that both the "hypermutable subpopulation" and the remaining stressed cells are proposed to be more mutagenic per base pair replicated than growing cells. In this respect, her model diverges from that of Roth and Andersson (4). Thus, we both find that the data fit best with HM models.

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REFERENCES

1. **Foster, P. L.** 2004. Adaptive mutation in *Escherichia coli.* J. Bacteriol. **186:** 4846–4852.
2. **McKenzie, G. J., P. L. Lee, M.-J. Lombardo, P. J. Hastings, and S. M. Rosenberg.** 2001. SOS mutator DNA polymerase IV functions in adaptive mutation and not adaptive amplification. Mol. Cell **7:**571–579.
3. **Rosenberg, S. M., and P. J. Hastings.** 2004. Adaptive point mutation and adaptive amplification pathways in the *Escherichia coli* Lac system: stress responses producing genetic change. J. Bacteriol. **186:**4838–4843.
4. **Roth, J. R., and D. I. Andersson.** 2004. Adaptive mutation: how growth under selection stimulates Lac^+ reversion by increasing target copy number. J. Bacteriol. **186:**4855–4860.