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The Editors

Current Biology 28/05/2024

Dear Editors,

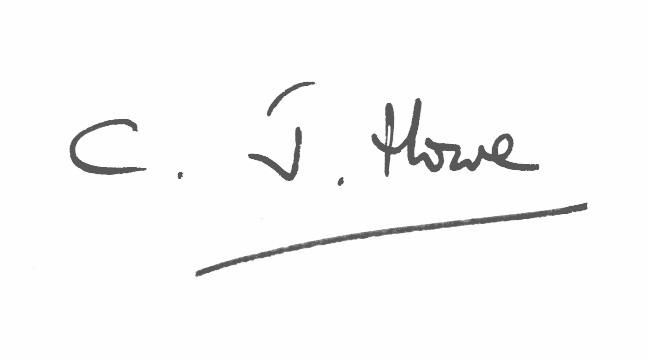
We are contacting you with a presubmission enquiry for our manuscript entitled "Polyploid cyanobacterial genomes provide a reservoir of mutations allowing rapid evolution of herbicide resistance” as an Article in Current Biology. We show that the highly polyploid nature of cyanobacteria allows wild type strains to maintain low levels of mutant genes. This in turn allows rapid evolution of resistance to external selective agents (in this case the herbicide methyl viologen). Our observations contrast dramatically with the textbook picture of bacteria being haploid or partially diploid, and resistance to selection occurring as a result of rare spontaneous mutations occurring at the time of selection with mutant cells surviving. Instead, a range of mutations are already present in highly polyploid cells, and relevant ones are rapidly selected and fixed.

Our paper provides a significant advance in our understanding of how cyanobacteria (responsible for at least a quarter of global oceanic primary productivity) adapt to stresses, including xenobiotic chemicals. This mode of evolution is likely to extend beyond cyanobacteria, as an increasingly wide range of prokaryotes has been identified as polyploid, and therefore in principle able to evolve in a similar way (eg Soppa, Nature Microbiology (2021) 7:186-188 <https://doi.org/10.1038/s41564-021-01034-3>). Retaining pools of mutations in polyploid genomes may provide a mechanism for bacteria to evolve antimicrobial resistance rapidly, and to retain a pool of AMR genes without the need for lateral transfer from other strains (eg Adam et al., BMC Evol Biol (2008) <https://doi.org/10.1186/1471-2148-8-52>; Wilmaerts & Michiels Curr. Biol. (2021) https://doi.org/10.1016/j.cub.2021.03.072).

Our work will therefore be of great interest to a wide readership, including those working on a very broad range of topics, including microbiology, antimicrobial resistance, evolutionary biology, photosynthesis, plant physiology, and bioelectrochemistry. It should promote widespread discussion, as it contrasts with the textbook model of bacterial evolution. We therefore believe it is particularly appropriate for the wide readership of Current Biology.

We confirm that the article is original and not under consideration for publication by another journal. Assuming you invite us to submit it, we would expect to be able to do so within a week or two. We very much hope you will invite a full submission, and I look forward to hearing from you. The Abstract is below.

Yours sincerely,



Prof Christopher Howe

**Polyploid cyanobacterial genomes provide a reservoir of mutations allowing rapid evolution of herbicide resistance**   
  
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**Abstract**

Microbial adaptation allows the evolution of a population towards a phenotype that best fits the surrounding environment. As currently understood, adaptive mechanisms in bacteria, which are widely assumed to be haploid or partially diploid, mostly rely on the emergence of spontaneous mutations, or lateral gene transfer from a reservoir of pre-existing variants within the surrounding environment, and which become established in the population upon exposure to selective pressures. In contrast, we show here that the model freshwater cyanobacterium, *Synechocystis sp.* PCC 6803, which is highly polyploid, can adapt very rapidly to the potent herbicide methyl viologen (MV) and that the variants that are responsible for the adapted phenotypes are already present, at low allelic frequencies, in wild type populations supported by the high ploidy levels.

We performed several independent adaptive laboratory evolution experiments starting from two phenotypically distinct parent substrains. We isolated 8 MV-adapted strains, showing tolerance to MV concentrations up to 30 times higher than the parental strains. We showed that the resistance persisted after long-term removal of selection pressure and we performed whole genome deep sequencing on all strains to identify the genetic mutations responsible. Surprisingly, a number of mutations (in genes for membrane transporters) were observed in multiple independently adapted strains and at low frequencies in the parental genomes. This indicates that wild type (highly polyploid) genomes contain a reservoir of mutations that can become rapidly enriched and fixed upon selection by methyl viologen. MV-resistant strains could still perform oxygenic photosynthesis in the presence of MV, unlike wild type strains. However, MV-resistant strains performed oxygenic photosynthesis less efficiently than wild types when MV was absent, suggesting trade-offs in cellular fitness associated with the evolution of MV resistance, and a possible role for balancing selection in the maintenance of the MV-resistance alleles in the absence of MV.

Our results indicate that genome polyploidy can provide a reservoir of conditionally beneficial mutations in some bacteria, facilitating rapid adaptation to stressful conditions. These may include xenobiotics, environmental stresses, and antibiotics.