⊐ **TECHNOLOGY**

ADAM and evolution

Bacteria are often used to study evolution on a laboratory timescale owing to their ability to adapt quickly to changing environments. Modern sequencing technologies make locating genetic differences between a parental and evolved strain straightforward, but uncovering which of these changes confer a selective advantage is a labour-intensive process. Goodarzi *et al.* have overcome this limitation with a new technique, array-based discovery of adaptive mutations (ADAM), which can search an entire bacterial genome for adaptive mutations.

In ADAM, a transposon from a parental bacterial strain is transferred and replaces the corresponding DNA in the evolved strain. Occasionally, this DNA swap causes a mutation in the evolved strain to be reverted to the parental genotype. If the reverted mutation was beneficial, fitness will be lower in the bacteria containing the transposon compared with bacteria from the original evolved strain. These differences are detected using an array hybridization technique, which is followed by computational techniques to determine the likely locations for the adaptive mutations.

As proof of principle, the authors chose an *Escherichia coli* strain with a chloramphenicol resistance (Cml^R) cassette in the *LacZ* locus as the 'evolved' strain; the parental strain lacked the Cml^R cassette. Therefore, when parental DNA was transferred into an evolved bacterium at a site near the *LacZ* locus, the recipient was rendered sensitive to chloramphenicol. After transfection, half of the bacterial population that was transfected with the transposon library was grown in selective medium containing chloramphenicol and the other half was grown in medium lacking the antibiotic. DNA adjacent to the transposon was extracted from both subpopulations and labelled with either Cy3 or Cy5. The samples were hybridized to an *E. coli* ORF array to determine which transposon insertions caused loss of fitness. As expected, transposon insertions close to the *LacZ* locus were significantly depleted under selective conditions.

The authors also used ADAM to identify adaptive mutations in two new laboratory evolved strains — the first is able to use Asn as the sole carbon source and the second is ethanol tolerant. Their results indicated that ADAM is a sensitive and highly specific assay.

ADAM could be combined with whole-genome or comparative sequencing to reveal the exact locations of the mutations and their relevance to a phenotype of interest. The technique can be easily adapted for use in other bacteria, providing researchers with a faster method to address numerous questions in bacterial evolution, including mechanisms of adaptation in industrial engineering and infectious disease.

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ORIGINAL RESEARCH PAPER Goodarzi, H., Hottes, A. K. & Tavazoie, S. Global discovery of adaptive mutations. *Nature Methods* 13 Jul 2009 (doi:10.1038/nmeth.1352)
FURTHER READING Eyre-Walker, A. & Keightley, P. D. The distribution of fitness effects of new mutations. *Nature Rev. Genet.* **8**, 610–618 (2007)