Release Factor One Is Nonessential in Escherichia coli.

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**Public Summary:**
Recoding a stop codon to an amino acid may afford orthogonal genetic systems for biosynthesizing new protein and organism properties. Although reassignment of stop codons has been found in extant organisms, a model organism is lacking to investigate the reassignment process and to direct code evolution. Complete reassignment of a stop codon is precluded by release factors (RFs), which recognize stop codons to terminate translation. Here we discovered that RF1 could be unconditionally knocked out from various Escherichia coli stains, demonstrating that the reportedly essential RF1 is generally dispensable for the E. coli species. The apparent essentiality of RF1 was found to be caused by the inefficiency of a mutant RF2 in terminating all UAA stop codons; a wild type RF2 was sufficient for RF1 knockout. The RF1-knockout strains were autonomous and unambiguously reassigned UAG to encode natural or unnatural amino acids (Uaas) at multiple sites, affording a previously unavailable model for studying code evolution and a unique host for exploiting Uaas to evolve new biological functions.

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