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Mutants of *aspA* and *yhbC* increase IS903 Transposition

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Transposition is a tightly regulated process, as insertion into important genes can be lethal or deleterious to the host. However, there are times during cell growth when transposon-promoted rearrangements are likely to be advantageous by activating or creating new genes. To identify host factors that may regulate transposition, we have carried out a screen of a library of 20,000 independent host mutants for effects on transposition of the bacterial insertion element IS903. One class of host mutants increase transposition suggesting those gene products negatively regulate transposition. From the initial screen three up-mutants were identified that inactivated the *yhbC* and *aspA* genes of *E. coli*. A series of assays were performed, including mating-out assays and complementation assays to confirm that these genes are involved in transposition. Disruption of the *yhbC* gene caused a 74,000-fold increase in transposition frequency. This phenotype can be suppressed by addition of a copy of the wild-type *yhbC* gene in trans. The function of *yhbC* is currently unknown, but it is found in an operon with *nusA*, which encodes a transcription elongation factor, and *infB*, which encodes the translation initiation factor IF2. Two independent *aspA* mutants were found to not only cause an increase in the transposition frequency, but also to cause transposition events to occur earlier in the growth of colonies, suggesting a direct link between transposition and the status of cell metabolism. The *aspA* gene encodes aspartase, which is known to convert aspartate into fumarate. The elevated transposition phenotype is suppressed both by the wild-type *aspA* gene and by the addition of exogenous fumarate. In the next step in the pathway, fumarate is converted into succinate by fumarate reductase. The addition of exogenous succinate to the media also suppresses the elevated or early transposition phenotype. This correlation of cell metabolism and transposition is consistent with the hypothesis that activation of transposition occurs during cell stress to enhance survival of the population.