

# The Insertion Sequence Excision Enhancer (IEE): a PrimPol-based system for Immobilizing Transposon-Transmitted Antibiotic Resistance Genes?

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June 9, 2023

## Abstract

Evolutionary studies often identify genes that are shared between different organisms and the phrase Lateral or Horizontal Gene Transfer is often used in this context. However, they rarely provide any mechanistic information concerning how these gene transfers might have occurred. With the astonishing increase in the number of sequences in the public databases over the past two or three decades, identical antibiotic resistance genes have been identified in many different sequence contexts. One explanation for this would be that genes are initially transmitted by transposons which have subsequently decayed and can no longer be detected. Here, we provide an overview of a protein, IEE (Insertion Sequence Excision Enhancer) observed to facilitate high frequency excision of IS *629* from clinically important *Escherichia coli* O157:H7 and subsequently shown to affect a large class of bacterial insertion sequences which all transpose by using the copy-out-paste-in transposition mechanism. Excision depends on both IEE and transposase indicating association with the transposition process itself. We review genetic and biochemical data and propose that IEE immobilizes genes carried by compound transposons by removing the flanking IS copies. The biochemical activities of IEE as a primase with the capacity to recognize DNA microhomologies and the observation that its effect appears restricted to IS families which use copy-out-paste-in transposition, suggests IS deletion occurs by abortive transposition involving strand switching during the copy-out step. This reinforces the proposal made for understanding loss of IS *Apl1* flanking *mcr-1* in the compound transposon Tn *6330* which we illustrate with a detailed model.

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