

REPs, genetic insulators that enable differential regulation of gene expression in bacteria

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Background: Repetitive Extragenic Palindromic elements (REPs) are short palindromic sequences, commonly found in enteric bacteria. REPs (i) are almost exclusively found in the intergenic space, often arranged in repeats (BIMEs); (ii) occur in high abundance and; (iii) are highly conserved within a genome. Various biological roles have been proposed, however none of them provides a common functional denominator. We therefore decided to investigate the commonality using a comparative genomics approach.

Results: *E.coli* REPs were identified using the related 29bp conserved sequence. We observed a biased distribution of REPs with respect to the ORFs: REPs are not found between divergent gene-pairs and predominantly located between convergent gene-pairs. A set of 465 publicly available microarrays (M3D) was used to explore the effects of REPs on transcription under various conditions. This analysis revealed an association between REP-related gene-pairs and higher expression levels. This association is also evident when Codon Adaptation Index values were compared. We identified microarrays with significant effects on gene-REP-gene pair (co-) expression. These arrays all represented the transcriptional response to certain kinds of stress such as biofilm formation and aerobiosis.

Conclusions: This study shows that REPs potentially have a global role in regulation of differential expression. Our results imply that REPs enable differential expression specifically in cases where transcription-driven DNA supercoiling can arise, i.e. expression of convergent gene-pairs and transcription regulated by an alternative promoter. Our findings suggest that the phenomenon of REP-enabled differential expression is linked to the bacterial stress response in *E. coli*.