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***Research Article***

# EXCLUSION OF REPLICATIVE TRANSPOSONS FROM LINEAR CHROMOSOME: AN INTERESTING OBSERVATION

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## ABSTRACT
Exclusion of replicative tansposons (RTs) from linear eukaryotic chromosomes may be an obvious phenomenon. But, surprisingly, there are no references documenting the negative role of chromosomal geometry on RTs' maintenance in eukaryotes as well as in prokaryotes possessing linear genomes. Here we summarize a simple observation considering importance of documenting this phenomenon from the view of transposon evolution.

***Key Words:*** *Replicative Transposon, Resolvase, Site-specific Recombination, Chromosome Geometry*

## INTRODUCTION
DNA transposons are nucleotide sequences capable of moving from one location to another in the genome. These are identified in both prokarya and eukarya and comprise a high proportion of species's genome that play pivotal role in shaping genomes (Muñoz-López and García-Pérez, 2010). DNA transposons are classified into two types namely (i) cut and paste transposons (CPT) and (ii) replicative transposons (RT) (Watson *et al*., 2006). There are distinctive features that set apart CPT from RT.
Details about CPT transposition can be found in many references (Bender and Kleckner, 1986; Craig, 1996; Reznikoff *et al*., 1999; Peters and Craig, 2001) and we will be primarily dealing with RT transposition events in this study. During transposition, RT makes a copy of it at the site of transposition and possesses an internal resolution system of which resolvase form an important component (Kleckner, 1981). This result in two copies of transposons where one half of each possesses newly synthesized segment and the other half retains older part (Figure 1). Resolvases, unique to RTs, are site-specific type-1 topoisomerase enzymes which effect site specific recombination at *res* (recombination site) sites (Reed, 1981; Krasnow and Cozzarelli, 1983). Examples of resolvase utilizing RT include Tn3, γδ etc. Unlike detailed regulation systems known for CPT (Simons and Kleckner, 1983; Kleckner *et al.*, 1996; Jaillet *et al*., 2012; Bouuaert and Chalmers, 2013) elaborate regulation mechanisms for RT transposition is wanting.
Previously, several investigators have reviewed different types of transposons and their evolutionary dynamics in different genomes (Feschotte and Pritham, 2007; Touchon and Rocha, 2007). By reviewing these publications we observed that DNA transposons in eukaryotes are only CPT types and there is no report of RT type transposon existence in eukaryotes. We were also surprised by the observation that there is no statement in the literature stating this fact. We started looking for the possible explanation. The first thing that drew our attention is the geometry of eukaryotic chromosome, which is linear whereas prokaryotic genome is circular. When we started drawing a possible transposition event between two linear genomes, it was obvious to observe that the transposition event is leading to translocation. As depicted in Figure1 replicative transposition in linear chromosomes results in reciprocal translocation ahead of resolvase acting over it. Reciprocal translocation in turn can lead to di-centric chromosome formation and may end up in mis-pairing amongst chromosomes during meiosis event. Both episodes are disastrous for cell's survivability.
Peering into this fact prompted us to inquire upon if there exists any correlation between linear chromosome geometry and RT's frequency of occurrence and maintenance across genomes. Further, it is

known that resolvase is necessary for resolution of co-integrates after RT transposition in circular chromosomes (Gill *et al.*, 1978; Reed, 1981; Grindley *et al.*, 1982) and its absence leads to stable co-integrate formation without resolved products. Considering the above fact we contemplated that absence of resolvase will be an important clue for lack of RT from linear genomes. Therefore, we performed searches for the presence of resolvase gene association with transposon in linear chromosomes of three bacteria i.e. *Borrelia burgdorferi* (a member of *Spirochaete* phyla), *Streptomyces* genus, *Agrobacterium tumefaciens* and three representative eukaryotes *Homo sapiens*, *Saccharomyces cerevisiae* and *Arabidopsis thaliana* in NCBI database (www.nlm.nih.gov.in). During our investigation we could not detect presence of resolvase gene nearby any transposase gene in linear chromosomes of above mentioned genomes. In one occasion, in *A. tumefaciens* str. C58 (recent name *A. fabrum* str. C58), we could locate Atu3849 resolvase gene in a linear chromosome. At protein level this showed some homology with *tnpR-tn3* resolvases of *Escherichia coli*, but, showed no association with any transposon/transposase. Lastly, we looked for homologous resolvase sequence of Tn3, γδ, phage Mu in the database by doing a BlastP (Altschul *et al.*, 1997). In this case too, no homologous sequences were observed in linear chromosomes of above representative species (Table 1). This study could not reveal resolvase association with RT in linear chromosomes of both prokaryotic and eukaryotic species under consideration. Im is pertinent to note that studies relating to effect of chromosome geometry on genetic diversity and implications of linear genomes in bacterial survivability have also been discussed by different authors (Cui *et al.*, 2007; Galperin, 2007; Marri *et al.*, 2008). However in none of these studies the role of linear chromosomal geometry's influence on RT abundance has been discussed.

Considering linear bacterial chromosomes and eukaryotic chromosomes, it is apparent that RTs are not obligatory for these. Then, why there is persistence of RT in some organisms? This remains to be investigated! RT's inherent capability to replicate and migrate bypassing biased proof-reading mechanisms (Kleckner, 1981) should have been advantageous for genomes, yet they have been eliminated from these. In eukaryotic genomes, similar feature is manifested by 'retrotransposons' like Ty1-copia, Ty3-gypsy etc. The shift from RT type to retrotransposon type in eukaryotic linear genomes is intriguing and whether there is any role of chromosome geometry for such a shift has never been considered. How in the long run of evolution, by attaining linear geometry and still keeping CPT intact, genomes could get rid of RT is a fascinating enigma! May and Craig (1996) reported Tn7 (a CPT) transoposon's plasticity to behave as RT just by alteration of an element encoded amino acid. We do not know if this is the case for other CPT transposons too! This certainly compels us to think about possible CPT to RT conversion or vice versa during evolution and linear chromosome might have preferred to harbor transposons as CPT rather than RT. But, that will be too early to assume at this moment!

Shifting from circular to linear geometry accompanied by variations of genetic elements within genome to accomplish stability and advancements might have resulted in elimination of components like RT from evolving genomes. Prevalence of linear chromosomes in certain prokaryotes has already opened up new windows in genomic research. Lastly, we hope our approach of looking at RT distribution in linear chromosomes will elicit critical experimental investigations from concerned faculties in this regard so that we can have an acceptable answer for this in near future. Illustration of a replicative transposition between two linear DNA molecules. This is a modification of the events shown in circular chromosomes (Watson *et al*. 2004). Drawn in black and blue are two double-stranded DNA (dsDNA) molecules with labeled polarity. Upper dsDNA (drawn in black) harbors a transposon (yellow block) delimited by two inverted repeats shown as red blocks. Transposase acts at the ends of the transposon, generating OH-groups at 3'-ends in both the strands (drawn in black). 3'-OH ends then attacks phosphate groups in the lower dsDNA (drawn in blue) and joins them (1). DNA synthesis occurs from the 3'- OH ends generated in the lower strand utilizing the previously connected strands as template and joins the free phosphate groups present in the upper dsDNA molecule; in this step duplication of the transposon occurs followed by reciprocal translocation (2). Resolvase then acts on the *res* sites of both the copies of transposons

bringing about site-specific recombination within the duplicated transposons (3). Finally, partition occurs giving rise to two independent dsDNA molecules with each harboring a copy of transposon containing a half of newly synthesized and another half of old fragment of the transposon in each strand (shown in different colors) (4).

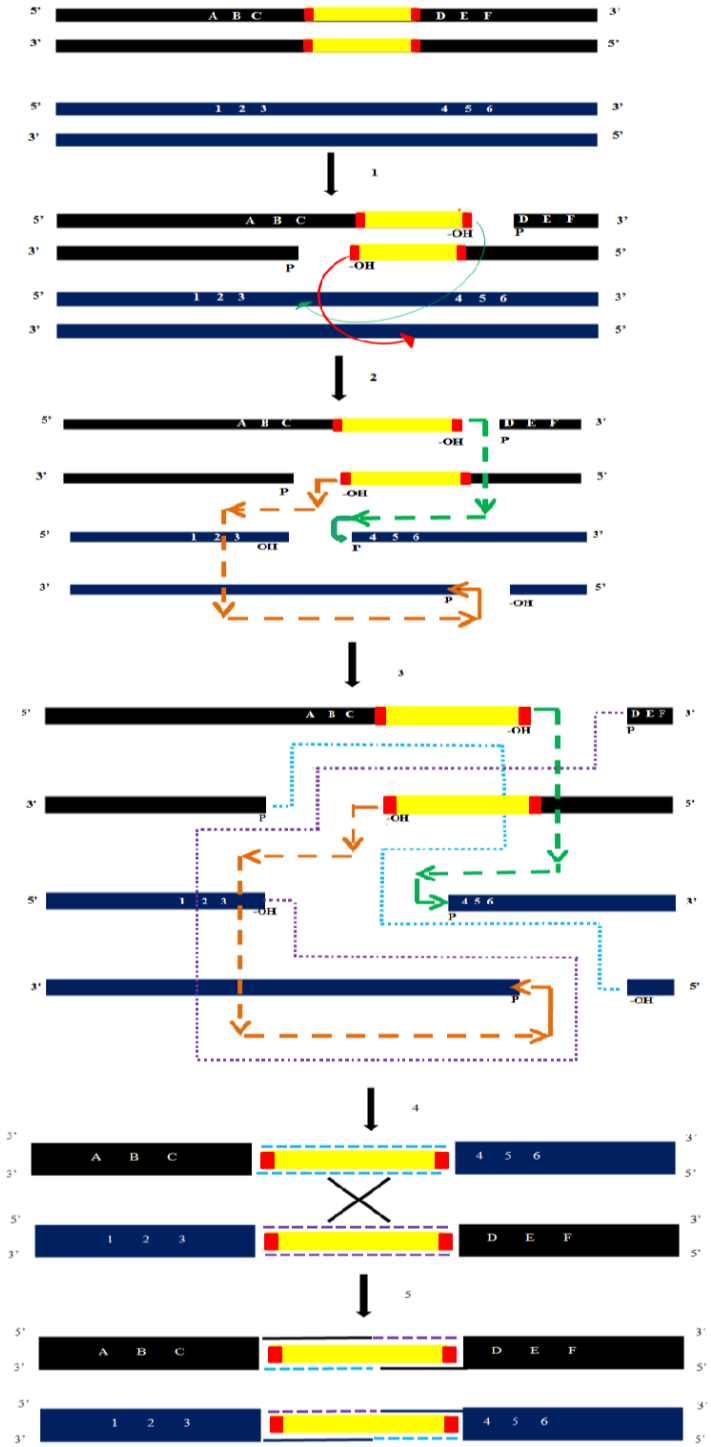


**Figure 1: Schematic representation of replicative transposition between linear chromosomes.**

**Table 1:**
**Outcomes of comparative homology search for representative RT sequences in genomes of the representative organisms considered in this study, using BlastP**

| RT type | Organism | Constitutive genes | *A. tumefaciens* | *B. burgdorferi* | *Streptomyces* sps. | *H. sapiens* | *S. cerevisiae* | *A. thaliana* |
|---|---|---|---|---|---|---|---|---|
| ϒδ Transposon | *E. coli* K-12 | tnA transposase (NP_061389.1) | Absent | Absent | Absent | Absent | Absent | Absent |
| | | tnR resolvase (NP_061388.1) | Absent | Absent | Absent | Absent | Absent | Absent |
| Tn3 Transposon | *E. coli* | tnA transposase (YP_003108100.1) | Absent | Absent | Absent | Absent | Absent | Absent |
| | | tnR resolvase (YP_003108101.1) | Absent | Absent | Absent | Absent | Absent | Absent |
| Phagemu Transposon | *Shigella flexneri* 2a str. 2457T | phage transposase (NP_836362.1) | Absent | Absent | Absent | Absent | Absent | Absent |
| Bacteriophage Mu Transposon | *E. coli* E24377A | bacteriophage Mu transposase MuA (YP_001462167.1) | Absent | Absent | Absent | Absent | Absent | Absent |
| Transposon | *Enterobacteria* phage Mu | transposase (NP_050607.1) | Absent | Absent | Absent | Absent | Absent | Absent |
| | | DNA transposition protein (NP_050608.1) | Absent | Absent | Absent | Absent | Absent | Absent |
| Bacteriophage Mu Transposon | *Gallibacterium anatis* UMN179 | bacteriophage Mu transposase (YP_004420511.1) | Absent | Absent | Absent | Absent | Absent | Absent |
| | | Mu B transposition protein, C terminal protein (YP_004420513.1) | Absent | Absent | Absent | Absent | Absent | Absent |

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