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Assessment of transposable elements: A review

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Abstract
Transposable elements (TEs) are mobile DNA segments that produce duplicate copies of itself and gets incorporated into another chromosomal location. TEs are found in both prokaryotes and eukaryotes. They are the largest elements and constitute significant proportion of the plant genome and by transposition they can lead a way to evolution by altering the structure and function of the chromatin. They interrupt the genetic codon by insertion and drive heterogeneity in the framework of the expression of genes as well as generate the adaptability. Mutations occurred by transposition can be reversible or irreversible depending upon the type of elements. Transposons are categorized into two groups, the one that makes the replica of DNA through reverse RNA transcriptase and these copies of DNA gets incorporated into new location in the genome and the another is DNA transposons that move via DNA and about 3% of human genome comprise of DNA transposons. These mobile elements encode for the enzyme transposase that initiate the process of transposition and have recognition site (inverted repeats) and target site (integration site). Transposons also carry the genes that are resistance to antibiotics and can move from DNA segment to another.

Keywords: DNA segments, plant genome, mobile elements, mutations, transcription

Introduction
The chunk of DNA (Deoxyribonucleic acid) that can swap its position from one location to another are designated as Transposable elements (TEs). These TEs have been multifariously called as jumping genes, mobile elements, insertion sequences, transposons, cassettes, and selfish DNA. TEs were also called as "Junk DNA", a label formulated by Susumo Ohno in the 1970s (Graur, 2013; Palazzo and Gregory, 2014) [13, 24]. The displacements of these genetic units can generate functional changes by interrupting the coding sequence and structural changes of chromosomes like translocations, inversions as well as various chromosomal rearrangements (Levan and Moran. 2011) [19]. TEs accounts for more than 45% of the human genome and are considered as the largest part of the eukaryotic genome (Lander E.S., 2001) [18]. Barbara McClintock was first to locate transposable elements while analyzing the genetic instability in maize (corn) in the year 1965. She reported that the genetic agents, which can move were responsible for the altered pigmentation of maize kernels and named it as controlling elements. In 1983, she was honored with the noble prize for her work. A few years later, a new group of mutant *Escherichia coli* (Intestinal bacteria) was spotted. The aforesaid novel mutant was caused by introduction of certain DNA fragments into the genome of the bacteria and was named as IS elements or insertion sequences (Malamy *et al*., 1972) [21].
Sequencing of eukaryotic genome has unveiled that substantial portion is composed of the mobile elements (Pappalardo AM *et al*., 2021) [25]. Transposases is the enzyme coded by transposons that is essential for the transposition of the mobile elements. Moreover, this enzyme has two activities, excise from one site and insert to another site. During the process of substitution, the original copy of transposable element remains in the place while the replicated one appears at the target site on the host genome. There is no homology between the site of insertion and the transposons. They can fit at any site in the host chromosome. The action of TEs is virtually reckoned as exploitative to the host along with large detrimental effects at the micro-level. However, the significance of TEs in bringing genetic diversity and modulation of the expression of genes has been extensively realized in recent times (Hollister *et al*., 2011) [14]. They help in shaping the structure and function of human genome according to the evolution (Chu, C *et al*., 2021) [5]. The recent findings on the transposable elements reveal that they have an important role in the ordinance of gene expression (Adam G. Diehl *et al*., 2020).
Transposable elements are assorted into two-classes based on the process of transposition. The foremost class is Class I retrotransposons (RTs), and the secondary class is Class II DNA transposons (Slotkin and Martienssen., 2007) [29].

RTs incorporates by means of an RNA as intermediary through a two-phase mechanism i.e., copy and paste and are fringed on both sides by terminal inverted repeats. On the other hand, the displacement of DNA transposons needs the implication of various transposase enzymes without the participation of an RNA intermediate (Dombroski *et al*., 1994; Chen *et al*., 2007) [9, 4].

Insertion sequences

Insertion sequence or an IS element is a small DNA sequences that are part of transposons and can relocate themselves to a new location within a genome. They are comparatively shorter than other transposable elements and typically ranges from 800 bp to 2500 bp in length. The coding region of IS elements have inverted repeats (about 30 bp in length) flanked by both sides of insertion sequence and carries only the hereditary information required for their transposition i.e., the enzyme transposase. The integration of IS elements at new site in the genome can cause mutations plus can terminate the function of the genes due to nonsense codon. However, the changes can be reversed by excision of the IS element. Insertion sequences are entitled as IS 1, IS 2, IS 3, IS 10, IS 50 etc.

Transposons (Tn) are like IS elements but carry more complex structure. They are the elements that can code for the enzyme transposase as well as contain one or more accessory genes, which are antibiotic resistance. There are two types of transposons namely composite transposons and non-composite transposons. Composite transposons comprise of the central portion flanked by two IS elements, which provides transposase and ITR recognition signals. The transposition activity is initiated when enzyme recognizes the inverted repeats of insertion sequences. There are various composite transposons such as Tn 9, Tn 10, Tn *5* etc. Non-composite transposons are type of prokaryotic transposons that are like composite transposons but do not terminate with an IS elements. However, they have repeated sequence at their ends as well as have the genes that code for antibiotic resistance like composite transposons. Example of non-composite transposons are Tn 3 and Tn 21.

Transposons via RNA intermediates (class I)

Transposons by means of RNA as intermediate are a sort of genetic constituents that makes the copies of DNA by reverse RNA transcriptase and position them at another location of the genome. This event allows the original elements to remain in place whereas duplicated copies pile up in another place (Dombroski BA *et al*., 1994) [9]. Because of duplication, retrotransposons can enlarge the proportion speedily in relation to genetic makeup of eukaryotes. Furthermore, depending on the existence and non-existence of long terminal repeats (LTR) i.e., flanking terminal repeats, retroelements are of two categories (Xiong Y *et al*., 1990) [33]. The genetic sequence in which long terminal repeats (LTR) is present are human endogenous retroviruses (HERV) and mammalian apparent LTR-retrotransposons (MaLR). The genome of maize largely composes of LTR-retrotransposons while only about 8% of the human genome contains LTR sequences (Cordaux R *et al*., 2009) [6]. LTR-retrotransposons have direct long terminal repeats that are a few hundred base pair long (ranges from 100 bp to 5 kb). In the middle of long terminal repeats (LTRs) two genes are present i.e., gag and pol that are important for duplication. A virus like particles is transcribed by gag gene (Sandmeyer *et al*., 2010) [26]. The pol gene encodes for three enzymes, a reverse transcriptase (accomplishes reverse transcription); a protease (processes functional gene products); an integrase, it assimilates retrotransposons DNA into eukaryotic genetic sequence (Wicker, Thomas *et al*., 2007) [32].

Non-LTR retrotransposons also includes genes for nuclease and reverse transcriptase like LTR-retrotransposons except the long terminal repeats (Yadav VP *et al*., 2009) [34]. However, these retrotransposons have short, inverted repeats of genetic sequences instead of direct repeats. Additionally, non- LTR retrotransposons are unable to do reverse transcription by utilizing an RNA intermediate as LTR-retrotransposons carry out due to the absence of t-RNA binding site. Non-LTR retrotransposons can be subclassified into two types. *viz*. Long Interspersed Nuclear Elements (LINE) and Short Interspersed Nuclear Elements (SINE) and constitutes around 30% of the human genome (Lander ES *et al*., 2001) [18].

Line (Long Interspersed Nuclear Element) is predominant in the genetic makeup of numerous eukaryotes and accounts for about 21% of the human genome (Schumann GG *et al*., 2010) [27]. Firstly, mRNA is transcribed from LINEs and then it is translated into proteins that function as reverse transcriptase. Subsequently, DNA copies transcribed from LINE RNA are incorporated at a new site which are rich in AT region. During the process of transcription RNA polymerase II act as a promoter and numerous adenines are present at the termination of LINE transcription to prevent degradation (Liang KH *et al*., 2013) [20].

SINE (Short Interspersed Nuclear Element) are non-coding and non-autonomous elements that are considerably shorter than LINEs (Stansfield WD, King RC. 1997) [30]. They are around 100 to 800 bp in length and make up to about 12% of the eukaryotic genome (Ishak, Charles A *et al*., 2020) [15]. SINE do not code for the enzyme on their own for reverse transcriptase instead they depend upon the LINEs (Dewannieux M *et al*., 2003) [8]. The transcription of short interspersed nuclear elements (SINEs) is carried out by RNA polymerase III. Moreover, they are unable to code for SINE transcripts consequently, they are incapable of transposing themselves. However, SINEs show resemblance to LINEs with regards to sequence therefore, it provides basis to LINE for integrating SINE transcript (Singer MF. 1982) [28].

DNA transposons (Class II)

DNA Transposons are categorized under the Class II Transposable elements, and they can be found in both prokaryotes and eukaryotes (Almojil, D *et al*., 2021) [2]. They make up about 3% of the human genome. DNA transposons do not replicate like Class I retrotransposons instead, they move via "cut and paste" mechanism. (Craig, Nancy L. 1995) [7]. Furthermore, they consist of the genes that code for enzyme transposase and are flanked by terminal inverted repeats on both sides. Transposase recognize the terminal repeats and binds to it then after his enzyme will detach the segment from the original site and excise it to new target site. The gaps created by insertion are then filled by DNA ligase (Berg and Howe, Douglas E and Martha M, 1989) [3]. Based on movement, DNA transposons can be classified as autonomous and non-autonomous. Autonomous elements are those that can translocate themselves and the mutations produced by them are reversible. In contrast, non-autonomous

elements lack transposition genes and rely on presence of another Tn elements and mutations caused by them is stable.

AC-DS system in maize

Activator (AC) and Dissociation (DS) elements were first discovered in maize by Barbara MC Clintock. The "AC" is autonomous transposon that control "DS" which is non-autonomous, and they transpose only during the process of DNA replication and do not leave the copies behind. Both AC and DS shares two properties in common. Firstly, a short DNA segments that are 8 BP long are present at the site of insertion. Secondly, these both elements end up with inverted terminal repeats (Doring HP, Starlinger P. 1984) [10].

Different levels of expression are observed in maize kernel color based on the absence and presence of elements (McClintock B. 1950) [22]. When both AC and DS are present at their original places then it expresses the normal purple color of the maize kernels. Furthermore, colorless kernels are expressed when AC activates DS, afterwards DS interrupts in the normal expression of gene that produces purple pigmentation and because of this disruption, colorless kernels are observed. Spotted kernels are expressed when AC again activates DS, and it gets excised out of the gene expressing normal pigmentation. As a result, the spotted kernel with pigmentation is observed.

P elements in drosophila

P elements were first discovered in *Drosophila melanogaster* that leads to hybrid dysgenesis. Hybrid dysgenesis is a type of genetic trait that induce high proportion of mutation, chromosomal breakages, and sterility in fruit flies. The enzyme transposase, which is responsible for transposition only occurs in germline cells and the transposition of P element causes change in the phenotypic expression. Hybrid dysgenesis occurs in offspring when a male with autonomous P element is crossed with normal female. However, when the female with P strain is crossed with M strain males the resultant progeny will be normal because of the presence of repressor protein contained in eggs of P strain females (Ghanim GE *et al*., 2020) [12].

ALU elements in human

Alu element is the most copious transposable element present in the genome of human and it is reckoned that about 10 percent of the human genome contains Alu elements. They are characterized under the retrotransposons and regulates tissue specific genes. The insertion of Alu elements causes various inheritable diseases and mutations. They interrupt the normal gene expression and causes methylation in about 30 percent of the human genome. Alu elements begin to move and replicate after interacting with SRPs (Signal recognition particles), which enable Alu's bind to ribosomes and begin the process of reverse transcriptase. The various disorders associated with Alu elements are breast cancer, lung cancer, leigh syndrome, macular degeneration, Alzheimer's disease, hemophilia, Alport syndrome (Wanding Zhou *et al*., 2020) [31].

Conclusion

Transposable elements have played a major role in evolution of eukaryotic as well as prokaryotic genome. They are present in high ratio in the genomes and are characterized based on transposition. However, every variation is not considered useful as some causes detrimental effects on the organisms leading to drastic changes in phenotype. The various new tools are coming into consideration to study the behavior of the mobile elements and tackling the difficulties which leads to various abnormalities.

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