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REVIEW

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Maize *Mutator* transposon

Abstract Transposable elements are widely distributed in eukaryotes. Due to its high copy numbers, high forward mutation rate and preferential insertion into low-copy DNA sequences, among others, the *Mutator* system has been widely used as a mutagen in genomic research. The discovery, classification, transposition specificity and epigenetic regulation of *Mutator* transposons were described. The application of *Mutator* tagging in plant genomic research was also presented. The role of *Mu*-like elements in genome evolution was briefly depicted. Moreover, the direction of *Mutator* transposon research in the future was discussed.

Keywords maize, *Mutator* transposon, transposon tagging, epigenetic modification, exon shuffling, genome evolution

1 Introduction

The discovery of transposition can be traced to January of 1949 from Barbara McClintock's unpublished manuscript (Fedoroff, 2001). Transposable elements, or 'jumping genes', are DNA fragments which can move from one genomic site to another. Transposons are widely distributed in plants, animals, fungi and bacteria (Okamoto and Hirochika, 2001).

More and more researchers have shifted their attention from structural genomics to functional genomics. The mutant library is the platform of functional genomics research. There are many ways to construct the library, including T-DNA insertion and transposon tagging (Jeong et al., 2002; Kumar et al., 2005). Although *Ac*-*Ds* and *Spm* (*En*)-*dSpm* (*I*) mobile elements were first discovered in maize, these two transposon tagging elements have been developed and widely used in exploiting gene function in heterogeneous plants (Aarts et al., 1993; Jones et al., 1994).

To date, *Mutator* (*Mu*) transposon has the highest transposition frequency and mutagenicity in the plant kingdom. *Mutator* transposon already existed in plants 60–70 million years ago when the differentiation of the ancestor of rice and maize occurred (Bennetzen, 1996). Since the discovery of the *Mutator* system, several large-scale genomic projects, such as the trait utility system for corn (TUSC) (Brutnell, 2002), the maize targeted mutagenesis (MTM) project (May et al., 2003), the maize gene discovery project (MGDP) using *RescueMu* (Lunde et al., 2003), the *Mu*Array/*Mu*ID protocol based on fluorescent labeling technique (Edwards et al., 2002), and the maize endosperm development project by Uniform*Mu* (McCarty et al., 2005), have been initiated. Details of these programs can be obtained from the website (http://www.mutransposon.org). Moreover, *Mutator* transposon tagging has proven to be a powerful and reliable tool for exploiting gene function in genomics research. *Mu*-like elements (MULEs) are capable of reshuffling the host genome by capturing host genes and gene fragments during evolution (Jiang et al., 2004). The interaction between MULEs and their hosts provides a window for investigating the mode and temple of genome evolution.

2 Discovery of the *Mutator* system

The *Mutator* system was first identified and characterized by Robertson in 1978 (Robertson, 1978). The inbred line containing active *Ac* transposon and inbred line W23 were used as backcross parents. In advanced backcross populations, Dr. Brink found that some lines lost transposition activity. Dr. Brink transferred these lines to Dr. Kermicle. A pale-yellow endosperm mutant was identified by Dr. Kermicle in self population. Dr. Robertson obtained this endosperm mutant in 1961. Robertson named the locus controlling the endosperm color as *y9*. The line containing *y9* was first crossed with some maize lines to generate F_1. F_1 was selfed. In a selfed population, some mutant

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phenotypes during seedling were identified, such as albino, pale-yellow, pale-green, and spotted leaf. Further results indicate that the mutation frequency of populations containing *y9* locus was 30 times higher than that of the common line without *y9*. Most importantly, somatic reverse mutation was observed in populations containing the *y9* locus. Robertson speculated that there was a new kind of mobile element in the population containing *y9*. Robertson named the line containing *y9* locus as "*Mutator*". Because this new mobile element was from the maize *Mutator* line, the new transposable element was referred to as *Mutator*, short title *Mu* (Bennetzen et al., 1993).

3 Classification of *Mutator* family

The *Mutator* family can be divided into some subfamilies, including *Mu1*/*Mu2*, *Mu3*, *Mu4*, *Mu6*/*Mu7*, *Mu8* and *Mu9*/*Mu5*. All subfamilies share 170–220 bp conservative terminal inverted repeats (TIRs), and their internal sequences are distinct (Lisch, 2002). The 1367-bp *Mu1* has the highest copy number and mutation rate (Barker et al., 1984). The *Cy*/*bz-rcy* locus first identified by Schnable and Peterson (1989) is classified as the *Mu7* subfamily. The 4942-bp *Mu9* missing 3748-bp sequences near its TIRs generated the *Mu5* subfamily. To honor Dr. Donald Robertson for his outstanding contribution to *Mutator* system research, the autonomous mobile elements are all named *MuDR* (Bennetzen et al., 1993).

MuDR, the master element of the *Mutator* family, has two genes *mudrA* and *mudrB* (Fig. 1). The transcription initiation sites of *mudrA* and *mudrB* are located in TIRs. Two genes transcribe convergent from opposite strands and mainly generate 2.8 kb and 1.0 kb transcripts (Lisch, 2002). *mudrA* encodes 120 kDa transposase MURA, which is highly similar to bacterial transposases. The 32-bp binding sites of MURA lie in the highly conservative TIRs (Benito and Walbot, 1997). *mudrB* encodes 23 kDa MURB, which is essential for *Mu* transposition activity and specially in maize (Jane Hershberger et al., 1995). The internal sequence of *MuDR* tends to delete. When 2.8-kb transcripts were deleted, all transposition behavior will disappear (Lisch et al., 1999).

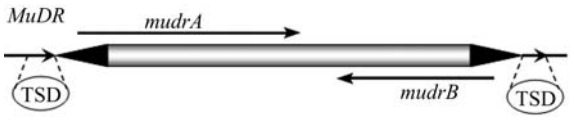

Fig. 1 General structure of *MuDR*
Note: *MuDR* has 220 bp TIRs (black triangles) at both ends and two genes *mudrA* and *mudrB*. The 9-bp target site duplications (TSDs) are encompassed by ellipses in Fig. 1. Structures are not drawn to scale.

How is a *Mutator* subfamily generated? One hypothesis is that *Mutator* subfamilies originate from deletion or rearrangement of *MuDR* sequences (Bennetzen et al., 1993). Additionally, MULEs transport host DNA sequences and place these 'borrowed' sequences between their TIRs. Many new types of *Mutator* subfamilies are formed this way. It is very useful for mobile elements to enhance their diversity and viability during evolution. Transposon *Mu1.7* research provides the first evidence of the capture behavior. The ancestor of *Mutator* subfamily *Mu1.7* is derived from the functional domain *MRS-A* (*Mu*-related sequence) in combination with *Mu* TIRs (Talbert and Chandler, 1988).

4 Characteristics of *Mutator* transposition

Mu transposes during the late developmental stage of reproductive cells (Robertson, 1980). *Mu* transposes in a replicative manner in premeiotic cells and gametes (Lisch et al., 1995). The transposition frequency of *Mu* is 10^{-3}–10^{-5} per gene per generation. The 9-bp TSDs are diagnostic of *Mu* insertion (Alleman and Freeling, 1986). Different *Mutator* subfamilies have different transposition frequencies. The *Mu1* and *Mu2* subfamilies transpose at least once each generation. On the contrary, the *Mu4* subfamily is not mobile (Bennetzen, 1996). *Mu* preferentially inserts into low-copy and unmethylated DNA sequences. *Mu* is able to jump in promoter, exon, intron, 5′ leader region and 3′ untranslated region (Hanley et al., 2000). To a certain gene, *Mutator* subfamilies may show the site bias. The site bias may be related with chromatin structure and DNA methylation (Hardeman and Chandler, 1993). The frequency of germinal excision of *Mu* is very low ($< 10^{-4}$ per gene per generation) (Bennetzen et al., 1993). The *Mu* insertion mutant is mainly recessive (Bennetzen, 1996).

5 Epigenetic modification of *Mutator* transposons

Mutator transposons and their hosts have a variety of strategies for their survival during genome evolution. First, hosts trigger *Mu* transposition specificity and frequency validly at transcriptional and post-transcriptional level. Many methods are employed as a defensive system to restrain *Mu* transposon 'flooding' (Fig. 2) (Lisch, 2002). Of any, DNA methylation modification plays an important role in modulating *Mu* transposition activity. The methylation of cytosine residues, which are located in the 5′ termini of TIRs, is the hallmark of *Mu* transposition activity loss. Hypomethylation generally contributes to the restoration of mobile ability (Chandler and Walbot, 1986). Lisch and coworkers found that methylation elimination does not cause immediate reactivation of the silenced *Mu* transposons. A likely explanation for this

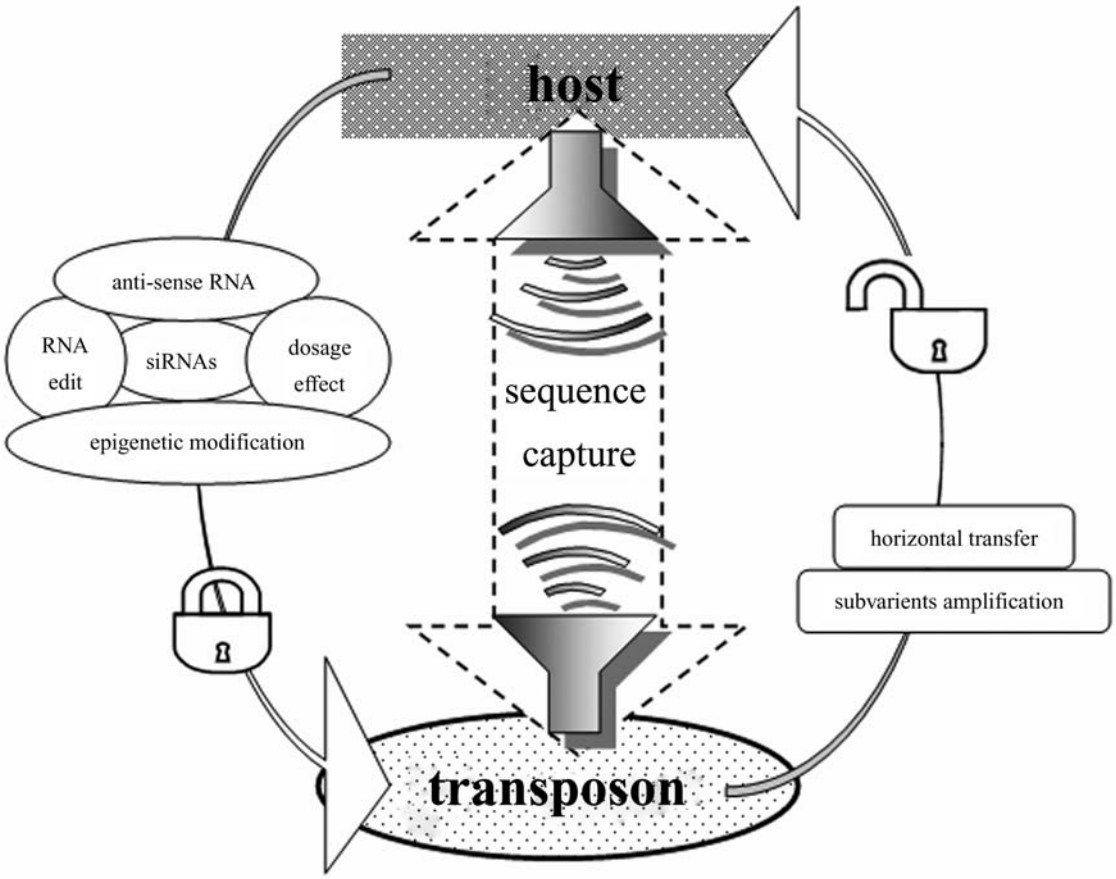

Fig. 2 *Mutator* transposon and host interaction during genome evolution
Note: Many strategies, including co-suppression mediated by siRNAs, are adopted by the host to suppress *Mu* transposition activity. To avoid extinction, *Mu* transposons must keep their mobile ability. Rapid amplification and horizontal transfer of subvarients are useful for maintaining mobile ability. Sequence capture, an important way to communicate, enhances the diversity of genomes.

phenomenon is that complex and particular pathways are involved in *Mu* transposon silencing (Lisch et al., 2002).

Paramutation is a heritable change in gene expression induced by an allelic interaction. The *mediator of paramutation1* (*mop1*) gene, an RNA-dependent RNA polymerase gene, is required for paramutation in maize (Alleman et al., 2006). The *mop1* mutant is not inclined to change the methylation state of other transposons except for *Mu* elements. In other words, only silenced *Mu* elements are demethylated and reactived in *mop1* mutants (Woodhouse et al., 2006a, 2006b).

6 Maintenance and loss of *Mutator* transposition activity

The maintenance of genomic integrity is partly ascribed to the optimal self-regulation of transposons. The significance of optimal self-regulation is that transposable elements transpose and expand with the minimum, even without 'detriment and cost', to their hosts. During genome evolution, there is a lasting struggle between the *Mu* transposon and its host. To avoid extinction, *Mu* transposable elements have no choice but to maintain their transposition activity. However, negative selective pressures from their host are against their transposition. *Mu* transposons are always in an 'embarrassed' state. The first way to overcome host repression is rapid amplification of *Mu* subvariants. One massively amplifying *Mu* transposon subfamily is subject to the host suppression. Simultaneously, variants of this *Mu* transposon subfamily (subvariants) escape the host triggering by chance. Although many subvariants of the *Mutator* family have been found in maize and rice, knowledge on their transposition behavior remains limited (Lisch et al., 2001). A second way to keep *Mu* transposition activity is by horizontal transfer, where genes shift between reproductively isolated species. *Mu* transposons hop into some hosts, which belong to neutral selection, and do not constrain their transposition. Diao et al. (2006) found that some MULEs are capable of horizontal transfer between *Setaria* and rice lineages. This marks the first report demonstrating that nuclear-encoded genes can horizontal transfer between higher plants.

The loss of *Mu* transposition activity is mainly attributed to hybrid segregation, internal sequence deletion and

epigenetic silencing (Bennetzen et al., 1993). A single dominant loci *Mu killer* (*Muk*) capable of silencing autonomous mobile element *MuDR* was also identified in a minimal line. *Muk* is the derivative of *MuDR* element. *Muk* results in the methylation of *MuDR* TIRs. About 26 bp siRNAs are produced during *MuDR* silencing, indicating that RNA-dependent DNA methylation is involved in *MuDR* silence (Keith Slotkin et al., 2003). Additionally, *Muk* is unlinked with *mop1* and does not influence the methylation state of centromere and rRNA. It implies that chromatin remodeling caused by *Muk* does not occur at the whole genome level (Woodhouse et al., 2006a, 2006b). This is similar to the *DDM1* gene in *Arabidopsis* (Jeddeloh et al., 1998). Moreover, *hMuDR* (homologous *MuDR* sequence) is the product of point mutation and Indel (insertion and deletion) of *MuDR*. Although *hMuDR* cannot transpose, it is able to transcript and translate normally. The functional defect proteins generated by *hMuDR* translation negatively regulate *MuDR* transposition activity (Rudenko and Walbot, 2001).

7 Genes cloned by *Mutator* transposon tagging

Mutator transposon tagging has been widely used for exploiting gene function in functional genomics research. Genes cloned by *Mutator* transposon tagging in maize are listed in Table 1. These genes play roles in the growth and development of organisms such as affecting plant morphogenesis, pigment accumulation, carbohydrate biosynthesis, and cell programmed death.

8 MULEs and genome evolution

MULEs are widely distributed in grasses, such as rice, wheat, barely, oat, sorghum, and bamboo (Lisch et al., 2001). After a genome-wide survey of MULEs in *Arabidopsis thaliana*, Hoen et al. (2006) identified some ubiquitin-like protein-specific protease (ULP). ULP-like genes have been recruited into non-TIRs regions to form the autonomous MULEs. Captured ULP-like genes are found to be used to generate new MULEs in rice and melon genome as well (van Leeuwen et al., 2007). The diversity of MULEs is also discovered through database minings in *Arabidopsis thaliana* (Yu et al., 2000). The structure of MULEs is polymorphic in different species. Structural diversity may represent functional diversity. The presence of MULEs in rice and *Arabidopsis thaliana* also implies that previous MULEs have the ability to transpose in dicotyledonous and monocotyledonous plants. There is evidence supporting the ability of MULEs (*AtMu1*) to transpose in *DDM1* mutant in *Arabidopsis thaliana* (Singer et al., 2001). The transposition behavior of MULEs (*Hop1*) is observed in fungi (Chalvet et al., 2003). To date, MULEs have not been found in animals (Bennetzen, 2005).

Many MULEs are capable of reorganizing host genes or gene fragments. Jiang et al. (2004) referred these chimeric elements to Pack-MULEs. There are more than 3000 Pack-MULEs in rice containing gene fragments from over 1000 host genes. Genes capture occurs at DNA level. Intriguingly, some MULEs have the ability to fish gene fragments from multiple chromosomal loci and fuse them together (Fig. 3). By genome sequence shuffling and duplication, many distinct genes with novel biological functions are generated. The mechanism and frequency of gene shuffling are not well known to date. It is presumed that DNA replication errors in repairing double broken strands caused by transposon excision contribute to gene capturing (Dooner and Weil, 2007).

9 Possibility of *Mutator* system used as transformation vector

The *P* element has been successfully used in increasing transgenic efficiency in *Drosophila* (Ryder and Russell, 2003). The *Mutator* system has high transposition activity and is very similar to the *P* element. It implies that the system can be adopted as a transformation vector to increase transgenic efficiency in maize. Unfortunately, *MuDR* tends to lose its transposion activity in *E. coli* and *Agrobacterium*. *mudrA* gene encoding transposase MURA produces frameshift and point mutation in *E. coli*. Moreover, *mudrA* containing introns is toxic in *E. coli* (Rudenko and Walbot, 2001). This makes it difficult to transfer the *Mutator* system to heterogenous plants. One way to solve this problem is to modify the *mudrA* gene. By adding regulatory sequence into *mudrA* gene, it makes transposase MURA express in the transformation receptor, not in *E. coli*.

10 Perspectives

There is no doubt that the discovery of autonomous mobile element *MuDR* is a landmark in *Mutator* system research. Some problems concerning the *MuDR* element need to be further investigated, including the mechanism of *MuDR* high transposition frequency and epigenetic silencing. How to suppress *MuDR* transposition activity by *Muk* also needs to be analyzed at transcriptional level. The application of *Mutator* systems in heterogenous plants is a challenging proposition. The interaction of MULEs and their hosts during genome evolution is the hotspot in *Mutator* system research. To date, there are still many unanswered questions relating to the functions and

Table 1 List of genes cloned by *Mutator* tagging in maize

gene or allele	*Mutator* subfamily tagging	putative function	references
ae1 (*amylose extender1*)	*Mu1*	encoding starch branching enzyme II	Stinard et al., 1993
An1 (*Anther ear1*)	*Mu2*	*ent*-kaurene synthesis	Bensen et al., 1995
Bk2 (*Brittle stalk2*)	*Mu7*	affecting stalk strength	Ching et al., 2006
Bsd2 (*Bundle sheath defective2*)	*Mu8*	ribulose-1,5-bisphosphate carboxylase/oxygenase (Rubisco) accumulation	Brutnell et al., 1999
Bz2 (*Bronze2*)	*Mu1*	anthocyanin synthesis	McLaughlin and Walbot, 1987
Cr4 (*Crinkly4*)	*Mu1*	affecting leaf epidermis differentiation	Becraft et al., 1996
Crp1 (*Chloroplast RNA processing1*)	*MuDR*	chloroplast mRNA processing and translation	Fisk et al., 1999
D3 (*Dwarf3*)	*Mu8*	gibberellin biosynthesis	Winkler and Helentjaris, 1995
Dsc1 (*Discolored1*)	*Mu1*, *MuDR*	early kernel development	Scanlon and Myers, 1998
Du1 (*Dull1*)	*Mu1*	encoding starch synthase	Gao et al., 1998
Emp2 (*Empty pericarp2*)	*Mu1*	maize embryogenesis	Fu et al., 2002
Et1 (*Etched1*)	*Mu1*, *Mu8*	plastid transcription elongation	da Costa et al., 2004
Fea2 (*Fasciated ear2*)	*Mu8*	meristem size regulation	Taguchi-Shiobara et al., 2001
Gl1 (*Glossy1*)	*Mu1*	cuticular wax accumulation	Hansen et al., 1997
Gl8 (*Glossy8*)	*Mu8*	cuticular wax biosynthesis	Xu et al., 1997
gn1 (*gnarley1*)	*Mu*	affecting cell shape and identity	Foster et al., 1999
*Hcf*106* (*high chlorophyll fluorescence*106*)	*Mu1*	photosynthetic membrane organization	Martienssen et al., 1989
Ij (*Iojap*)	*Mu1*	affecting plastid development	Han et al., 1992
les22 (*lesion mimic22*)	*Mu1*	encoding uroporphyrinogen decarboxylase	Hu et al., 1998
Lg2 (*Liguleless2*)	*Mu8*	leaf cell differentiation	Walsh et al., 1997
Lg3 (*Liguleless3*)	*Mu*	blade-to-sheath transformation	Muehlbauer et al., 1999
Lls1 (*Lethal leaf spot1*)	*Mu8*	cell death suppressor	Gray et al., 1997
Pac1 (*Pale aleurone color1*)	*Mu1*	anthocyanin synthesis	Carey et al., 2004
Rf2 (*Restoring fertility 2*)	*Mu1*, *Mu7*	nuclear restorer of T-cytoplasm maize	Schnable and Wise, 1994
rs1 (*rough sheath1*)	*Mu*	sheath-like tissue proliferation	Becraft and Freeling, 1994
rs2 (*rough sheath2*)	*Mu1*, *MuDR*	*knox* gene family regulation	Timmermans et al., 1999
Sal1 (*Supernumerary aleurone layers1*)	*Mu1*, *Mu8*	determining the number of aleurone cell layers	Shen et al., 2003
Sbe1 (*Starch-branching enzyme1*)	*Mu*	encoding starch-branching enzyme1	Blauth et al., 2002
Sbe2a (*Starch-branching enzyme2a*)	*Mu*	affecting plant development	Blauth et al., 2001
Sil (*Silky1*)	*MuDR*	determining floral organ specification	Ambrose et al., 2000
Slr1, Slr2 (*short lateral roots1* and *2*)	*Mu*	lateral root-specific cell elongation	Hochholdinger et al., 2001
Su1 (*Sugary1*)	*Mu1*	determining starch composition in kernels	James et al., 1995
Tan1 (*Tangled1*)	*Mu1*	spatial control of cytokinesis	Smith et al., 2001
Td1 (*Thick tassel dwarf1*)	*Mu1*	affecting inflorescence meristem size and vegetative development	Bommert et al., 2005
Te1 (*Terminal ear1*)	*Mu8*	regulating leaf initiation	Veit et al., 1998
Vp1 (*Viviparous1*)	*Mu1*	regulating abscisic acid response and anthocyanin metabolism	McCarty et al., 1989
Vp10, Vp13 (*Viviparous1* and *13*)	*Mu1*	molybdenum cofactor biosynthesis	Porch et al., 2006
Vp14 (*Viviparous14*)	*Mu1*	abscisic acid biosynthesis	Tan et al., 1997
Vp15 (*Viviparous15*)	*Mu1*	encoding the molybdopterin synthase small subunit	Suzuki et al., 2006
Y1 (*Yellow1*)	*Mu3*	β-carotene biosynthesis	Buckner et al., 1990
Zag1 (*Zea mays agamous1*)	*Mu*	floral organ determinacy	Mena et al., 1996

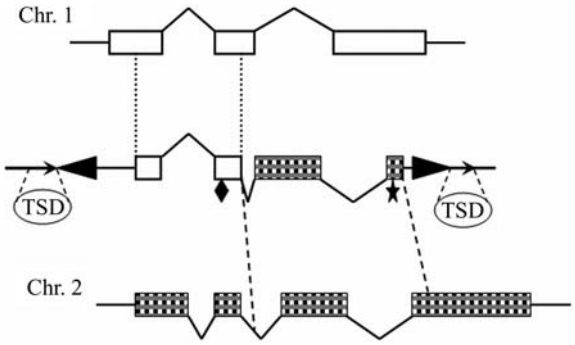

Fig. 3 Schematic diagram of gene capture from multiple loci Note: Pack-MULEs capture gene fragments of Chr. 1 and Chr. 2, then combine them together. Exons are indicated by open boxes in Chr. 1 and griddings in Chr. 2, respectively. Introns are shown by single lines. Start codon and stop codon are denoted by diamond and star, respectively. TIRs at both ends are figured by black triangles. 9-bp TSDs are circled by ellipses in Fig. 3.

fates of captured genes and gene fragments. One hypothesis is that most captured gene spieces belong to pseudogenes (Gupta et al., 2005). Only a few captured gene segments, which express under certain environmental conditions, may be involved in the regulation of exiting gene expression (Juretic et al., 2005). In such a scenario, these pseudogenes will be lost from the host genome within a few million years due in part to the 'dilution' effect. Alternatively, there is an increasing body of evidence that these chimeric transcripts have novel functions, including cell defence and signal transduction (Jiang et al., 2004; Lisch, 2005). The functions of chimeric genes need to be further verified by experimental methods such as mutagenesis or other methodology. Microcolinearity violation does exist within the species (Lai et al., 2004, 2005). Taking into account the capturing behavior of transposons, it is reasonable to reassess the microcolinearity violation (Bennetzen, 2005). Evidently, sequence information derived from large-scale sequencing projects is invaluable for elucidating the mechanism of microcolinearity violation. It is obvious that the *Mutator* system is mature enough for genome research. However, somatic insertion, cosuppression and low frequency of germinal excision increase the complexity of *Mutator* system research.

References

Aarts M G M, Dirkse W G, Stiekema W J, Pereira A (1993). Transposon tagging of a male sterility gene in *Arabidopsis*. Nature, 363(6431): 715–717

Alleman M, Freeling M (1986). The *Mu* transposable elements of maize: evidence for transposition and copy number regulation during development. Genetics, 112(1): 107–119

Alleman M, Sidorenko L, McGinnis K, Seshadri V, Dorweiler J E, White J, Sikkink K, Chandler V L (2006). An RNA-dependent RNA polymerase is required for paramutation in maize. Nature, 442(7100): 265–298

Ambrose B A, Lerner D R, Ciceri P, Padilla C M, Yanofsky M F, Schmidt R J (2000). Molecular and genetic analyses of the *Silky1* gene reveal conservation in floral organ specification between eudicots and monocots. Mol Cell, 5(3): 569–579

Barker R F, Thompson D V, Talbot D R, Swanson J, Bennetzen J L (1984). Nucleotide sequence of the maize transposable element *Mu1*. Nucleic Acids Res, 12(15): 5955–5967

Becraft P W, Freeling M (1994). Genetic analysis of *Rough sheath1* developmental mutants of maize. Genetics, 136(1): 295–311

Becraft P W, Stinard P S, McCarty D R (1996). CRINKLY4: A TNFR-Like receptor kinase involved in maize epidermal differentiation. Science, 273(5280): 1406–1409

Benito M I, Walbot V (1997). Characterization of the maize *Mutator* transposable element MURA transposase as a DNA-binding protein. Mol Cell Biol, 17(9): 5165–5175

Bennetzen J L (1996). The *Mutator* transposable element system of maize. Curr Top Microbiol Immunol, 204(1): 195–229

Bennetzen J L (2005). Transposable elements, gene creation and genome rearrangement in flowering plants. Curr Opin Genet Dev, 15(6): 621–627

Bennetzen J L, Springer P S, Cresse A D, Hendrickx M (1993). Specificity and regulation of the *Mutator* transposable element system in maize. Crit Rev Plant Sci, 12(1): 57–95

Bensen R J, Johal G S, Crane V C, Tossberg J T, Schnable P S, Meeley R B, Briggs S P (1995). Cloning and characterization of the maize *An1* gene. Plant Cell, 7(1): 75–84

Blauth S L, Kim K N, Klucinec J, Shannon J C, Thompson D, Guiltinan M (2002). Identification of *Mutator* insertional mutants of starch-branching enzyme 1 (*sbe1*) in *Zea mays* L. Plant Mol Biol, 48(3): 287–297

Blauth S L, Yao Y, Klucinec J D, Shannon J C, Thompson D B, Guilitinan M J (2001). Identification of *Mutator* insertional mutants of starch-branching enzyme 2a in corn. Plant Physiol, 125(3): 1396–1405

Bommert P, Lunde C, Nardmann J, Vollbrecht E, Running M, Jackson D, Hake S, Werr W (2005). *Thick tassel dwarf1* encodes a putative maize ortholog of the *Arabidopsis CLAVATA1* leucine-rich repeat receptor-like kinase. Development, 132(6): 1235–1245

Brutnell T P (2002). Transposon tagging in maize. Funct Integr Genomics, 2(1): 4–12

Brutnell T P, Sawers R J H, Mant A, Langdale J A (1999). BUNDLE SHEATH DEFECTIVE2, a novel protein required for post-translational regulation of the *rbcL* gene of maize. Plant Cell, 11(5): 849–864

Buckner B, Kelson T L, Robertson D S (1990). Cloning of the *y1* locus of maize, a gene involved in the biosynthesis of carotenoids. Plant Cell, 2(9): 867–876

Carey C C, Strahle J T, Selinger D A, Chandler V L (2004). Mutations in the *pale aleurone color1* regulatory gene of the *Zea mays* anthocyanin pathway have distinct phenotypes relative to the functionally similar *TRANSPARENT TESTA GLABRA1* gene in *Arabidopsis thaliana*. Plant Cell, 16(2): 450–464

Chalvet F, Grimaldi C, Kaper F, Langin T, Daboussi M J (2003). *Hop*, an active *Mutator*-like element in the genome of the fungus *Fusarium oxysporum*. Mol Biol Evol, 20(8): 1362–1375

Chandler V L, Walbot V (1986). DNA modification of a maize transposable element correlates with loss of activity. Proc Natl Acad Sci USA, 83(6): 1767–1771

Ching A, Dhugga K S, Appenzeller L, Meeley R, Bourett T M, Howard R J, Rafalski A (2006). *Brittle stalk 2* encodes a putative glycosylphosphatidylinositol-anchored protein that affects mechanical strength of maize tissues by altering the composition and structure of secondary cell walls. Planta, 224(5): 1174–1184

da Costa e Silva O, Lorbiecke R, Garg P, Müller L, Waβmann M, Lauert P, Scanlon M, Hsia A P, Schnable P S, Krupinska K, Wienand U (2004). The *Etched1* gene of *Zea mays* L. encodes a zinc ribbon protein that belongs to the transcriptionally active

chromosome (TAC) of plasmids and is similar to the transcription factor TFII S. Plant J, 38(6): 923–939
Diao X M, Freeling M, Lisch D R (2006). Horizontal transfer of a plant transposon. PLoS Biol, 4(1): e5
Dooner H K, Weil C F (2007). Give-and-take: interactions between DNA transposons and their host plant genomes. Curr Opin Genet Dev, 17(1): 1–7
Edwards D, Coghill J, Batley J, Holdsworth M, Edwards K J (2002). Amplification and detection of transposon insertion flanking sequences using fluorescent *Mu*AFLP. Biotechniques, 32(5): 1090–1097
Fedoroff N V (2001). How jumping genes were discovered. Nat Struct Biol, 8(4): 300–301
Fisk D G, Walker M B, Barkan A (1999). Molecular cloning of the maize gene *crp1* reveals similarity between regulators of mitochondrial and chloroplast gene expression. EMBO J, 18(9): 2621–2630
Foster T, Yamaguchi J, Wong B C, Veit B, Hake S (1999). *Gnarley1* is a dominant mutation in the *knox4* homeobox gene affecting cell shape and identity. Plant Cell, 11(7): 1239–1252
Fu S, Meeley R, Scanlon M J (2002). *empty pericarp2* encodes a negative regulator of the heat shock response and is required for maize embryogenesis. Plant Cell, 14(12): 3119–3132
Gao M, Wanat J, Stinard P S, James M G, Myers A M (1998). Characterization of *dull1*, a maize gene coding for a novel starch synthase. Plant Cell, 10(3): 399–412
Gray J, Close P S, Briggs S P, Johal G S (1997). A novel suppressor of cell death in plants encoded by the *Lls1* gene of maize. Cell, 89(1): 25–31
Gupta S, Gallavotti A, Stryker G A, Schmidt R J, Lal S K (2005). A novel class of *Helitron*-related transposable elements in maize contain portions of multiple pseudogenes. Plant Mol Biol, 57(1): 115–127
Han C, Coe E H Jr, Martienssen R A (1992). Molecular cloning and characterization of *iojap* (*ij*), a pattern striping gene of maize. EMBO J, 11(11): 4037–4046
Hanley S, Edwards D, Stevenson D, Haines S, Hegarty M, Schuch W, Edwards K J (2000). Identification of transposon-tagged genes by the random sequencing of *Mutator*-tagged DNA fragments from *Zea mays*. Plant J, 22(6): 557–566
Hansen J D, Pyee J, Xia Y, Wen T J, Robertson D S, Kolattukudy P E, Nikolau B J, Schnable P S (1997). The *glossy1* locus of maize and an epidermis-specific cDNA from *KIeinia odora* define a class of receotor-like proteins required for the normal accumulation of cuticular waxes. Plant Physiol, 113(4): 1091–1100
Hardeman K J, Chandler V L (1993). Two maize genes are each targeted predominantly by distinct classes of *Mu* elements. Genetics, 135(4): 1141–1150
Hochholdinger F, Park W J, Feix G H (2001). Cooperative action of *SLR1* and *SLR2* is required for lateral root-specific cell elongation in maize. Plant Physiol, 125(3): 1529–1539
Hoen D R, Park K C, Elrouby N, Yu Z H, Mohabir N, Cowan R K, Bureau T E (2006). Transposon-mediated expansion and diversification of a family of *ULP*-like genes. Mol Biol Evol, 23(6): 1254–1268
Hu G S, Yalpani N, Briggs S P, Johal G S (1998). A porphyrin pathway impairment is responsible for the phenotype of a dominant disease lesion mimic mutant of maize. Plant Cell, 10(7): 1095–1105
James M G, Robertson D S, Myers A M (1995). Characterization of the maize gene *sugary1*, a determinant of starch composition in kernels. Plant Cell, 7(4): 417–429
Jane Hershberger R, Benito M I, Hardeman K J, Warren C, Chandlert V L, Walbot V (1995). Characterization of the major transcripts encoded by the regulatory *MuDR* transposable element of maize. Genetics, 140(3): 1087–1098
Jeddeloh J A, Bender J, Richards E J (1998). The DNA methylation locus *DDM1* is required for maintenance of gene silencing in *Arabidopsis*. Genes Dev, 12(11): 1714–1725
Jeong D H, An S, Kang H G, Moon S, Han J J, Park S, Lee H S, An K, An G (2002). T-DNA insertional mutagenesis for activation tagging in rice. Plant Physiol, 130(4): 1636–1644
Jiang N, Bao Z R, Zhang X Y, Eddy S R, Wessler S R (2004). Pack-MULE transposable elements mediate gene evolution in plants. Nature, 431(7008): 569–573
Jones D A, Thomas C M, Hammond-Kosack K E, Balint-Kurti P J, Jones J D (1994). Isolation of the tomato *Cf-9* gene for resistance to *Cladosporium fulvum* by transposon tagging. Science, 266(5186): 789–793
Juretic N, Hoen D R, Huynh M L, Harrison P M, Bureau T E (2005). The evolutionary fate of MULE-mediated duplications of host gene fragments in rice. Genome Res, 15(9): 1292–1297
Keith Slotkin R, Freeling M, Lisch D R (2003). *Mu* killer causes the heritable inactivation of the *Mutator* family of transposable elements in *Zea mays*. Genetics, 165(2): 781–797
Kumar C S, Wing R A, Sundaresan V (2005). Efficient insertional mutagenesis in rice using the maize *En*/*Spm* elements. Plant J, 44(5): 879–892
Lai J S, Li Y B, Messing J, Dooner H K (2005). Gene movement by *Helitron* transposons contributes to the haplotype variability of maize. Proc Natl Acad Sci USA, 102(25): 9068–9073
Lai J S, Ma J X, Swigoňová Z, Ramakrishna W, Linton E, Llaca V, Tanyolac B, Park Y J, Jeong O Y, Bennetzen J L, Messing J (2004). Gene loss and movement in the maize genome. Genome Res, 14(10): 1924–1931
Lisch D R (2002). *Mutator* transposons. Trends Plant Sci, 7(11): 498–504
Lisch D R (2005). Pack-MULEs: theft on a massive scale. Bioessays, 27(4): 353–355
Lisch D R, Carey C C, Dorweiler J E, Chandler V L (2002). A mutation that prevents paramutation in maize also reverses *Mutator* transposon methylation and silencing. Proc Natl Acad Sci USA, 99(9): 6130–6135
Lisch D R, Chomet P, Freeling M (1995). Genetic characterization of the *Mutator* system in maize: behavior and regulation of *Mu* transposons in a minimal line. Genetics, 139(4): 1777–1796
Lisch D R, Freeling M, Langham R J, Choy M Y (2001). *Mutator* transposase is widespread in the grasses. Plant Physiol, 125(3): 1293–1303.
Lisch D R, Girard L, Donlin M, Freeling M (1999). Functional analysis of deletion derivatives of the maize transposon *MuDR* delineates roles for the MURA and MURB proteins. Genetics, 151(1): 331–341
Lunde C F, Morrow D J, Roy L M, Walbot V (2003). Progress in maize gene discovery: a project update. Funct Integr Genomics, 3(1): 25–32
Martienssen R A, Barkan A, Freeling M, Taylor W C (1989). Molecular cloning of a maize gene involved in photosynthetic membrane organization that is regulated by Robertson's *Mutator*. EMBO J, 8(6): 1633–1639
May B P, Liu H, Vollbrecht E, Senior L, Rabinowicz P D, Roh D, Pan X K, Stein L, Freeling M, Alexander D, Martienssen R A (2003). Maize-targeted mutagenesis: a knockout resource for maize. Proc Natl Acad Sci USA, 100(20): 11541–11546
McCarty D R, Carson C B, Stinard P S, Robertson D S (1989). Molecular analysis of *viviparous-1*: an abscisic acid insensitive mutant of maize. Plant Cell, 1(5): 523–532
McCarty D R, Mark Settles A, Suzuki M, Tan B C, Latshaw S, Porch T, Robin K, Baier J, Avigne W, Lai J S, Messing J, Koch K E, Curtis Hannah L (2005). Steady-state transposon mutagenesis in inbred maize. Plant J, 44(1): 52–61

McLaughlin M, Walbot V (1987). Cloning of a mutable *bz2* allele of maize by transposon tagging and differential hybridization. Genetics, 117(4): 771–776

Mena M, Ambrose B A, Meeley R B, Briggs S P, Yanofsky M F, Schmidt R J (1996). Diversification of C-function activity in maize flower development. Science, 274(5292): 1537–1540

Muehlbauer G J, Fowler J E, Girard L, Tyers R, Harper L, Freeling M (1999). Ectopic expression of the maize homeobox gene *Liguleless3* alters cell fates in the leaf. Plant Physiol, 119(2): 651–662

Okamoto H, Hirochika H (2001). Silencing of transposable elements in plants. Trends Plant Sci, 6(11): 527–534

Porch T G, Tseung C W, Schmelz E A, Mark Settles A (2006). The maize *Viviparous10*/*Viviparous13* locus encodes the *Cnx1* gene required for molybdenum cofactor biosynthesis. Plant J, 45(2): 250–263

Robertson D S (1978). Characterization of a *Mutator* system in maize. Mutat Res, 51(1): 21−28

Robertson D S (1980). The timing of *Mu* activity in maize. Genetics, 94(4): 969–978

Rudenko G N, Walbot V (2001). Expression and post-transcriptional regulation of maize transposable element *MuDR* and its derivatives. Plant Cell, 13(3): 553–570

Ryder E, Russell S (2003). Transposable elements as tools for genomics and genetics in *Drosophila*. Brief Funct Genomic Proteomic, 2(1): 57–71

Scanlon M J, Myers A M (1998). Phenotypic analysis and molecular cloning of *discolored-1* (*dsc1*), a maize gene required for early kernel development. Plant Mol Biol, 37(3): 483–493

Schnable P S, Peterson P A (1989). Genetic evidence of a relationship between two maize transposable element systems: *Cy* and *Mutator*. Mol Gen Genet, 215(2): 317–321

Schnable P S, Wise R P (1994). Recovery of heritable, transposon-induced, mutant alleles of the *rf2* nuclear restorer of T-cytoplasm maize. Genetics, 136(3): 1171–1185

Shen B, Li C, Min Z, Meeley R B, Tarczynski M C, Olsen O A (2003). *sal1* determines the number of aleurone cell layers in maize endosperm and encodes a class E vacuolar sorting protein. Proc Natl Acad Sci USA, 100(11): 6552–6557

Singer T, Yordan C, Martienssen R A (2001). Robertson's *Mutator* transposons in *A. thaliana* are regulated by the chromatin-remodeling gene *Decrease in DNA Methylation* (*DDM1*). Genes Dev, 15(5): 591–602

Smith L G, Gerttula S M, Han S, Levy J (2001). TANGLED1: a microtubule binding protein required for the spatial control of cytokinesis in maize. J Cell Biol, 152(1): 231–236

Stinard P S, Robertson D S, Schnable P S (1993). Genetic isolation, cloning, and analysis of a *Mutator*-induced, dominant antimorph of the maize *amylose extender1* locus. Plant Cell, 5(11): 1555–1566

Suzuki M, Mark Settles. A, Tseung C W, Li Q B, Latshaw S, Wu S, Porch T G, Schmelz E A, James M G, McCarty D R (2006). The maize *viviparous15* locus encodes the molybdopterin synthase small subunit. Plant J, 45(2): 264–274

Taguchi-Shiobara F, Yuan Z, Hake S, Jackson D (2001). The *fasciated ear2* gene encodes a leucine-rich repeat receptor-like protein that regulates shoot meristem proliferation in maize. Genes Dev, 15(20): 2755–2766

Talbert L E, Chandler V L (1988). Characterization of a highly conserved sequence related to *Mutator* transposable elements in maize. Mol Biol Evol, 5(5): 519–529

Tan B C, Schwartz S H, Zeevaart J A D, McCarty D R (1997). Genetic control of abscisic acid biosynthesis in maize. Proc Natl Acad Sci USA, 94(22): 12235–12240

Timmermans M C P, Hudson A, Becraft P W, Nelson T (1999). ROUGH SHEATH2: A Myb protein that represses *knox* homeobox genes in maize lateral organ primordia. Science, 284(5411): 151–153

van Leeuwen H, Monfort A, Puigdomenech P (2007). *Mutator*-like elements identified in melon, *Arabidopsis* and rice contain ULP1 protease domains. Mol Genet Genomics, 277(4): 357–364

Veit B, Briggs S P, Schmidt R J, Yanofsky M F, Hake S (1998). Regulation of leaf initiation by the *terminal ear1* gene of maize. Nature, 393(6681): 166–168

Walsh J, Waters C A, Freeling M (1997). The maize gene *liguleless2* encodes a basic leucine zipper protein involved in the establishment of the leaf blade-sheath boundary. Genes Dev, 11(2): 208–218

Winkler R G, Helentjaris T (1995). The maize *Dwarf3* gene encodes a cytochrome P450-mediated early step in gibberellin biosynthesis. Plant Cell, 7(8): 1307–1317

Woodhouse M R, Freeling M, Lisch D R (2006a). Initiation, establishment, and maintenance of heritable *MuDR* transposon silencing in maize are mediated by distinct factors. PLoS Biol, 4(10): e339

Woodhouse M R, Freeling M, Lisch D R (2006b). The *mop1* (*mediator of paramutation1*) mutant progressively reactivates one of the two genes encoded by the *MuDR* transposon in maize. Genetics, 172(1): 579–592

Xu X, Dietrich C R, Delledonne M, Xia Y, Wen T J, Robertson D S, Nikolau B J, Schnable P S (1997). Sequence analysis of the cloned *glossy8* gene of maize suggests that it may code for a β-ketoacyl reductase required for the biosynthesis of cuticular waxes. Plant Physiol, 115(2): 501–510

Yu Z H, Wright S I, Bureau T E (2000). *Mutator*-like elements in *Arabidopsis thaliana*: structure, diversity and evolution. Genetics, 156(4): 2019–2031