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Research Article

Palindrome Mediated Translocation in Human: Where Do We Go from Here?

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Abstract

Palindromes are two groups of identical sequences which join each other in inverted direction. The palindrome mediated genomic instability contributes to a diverse group of genomic rearrangements like translocations, deletions, and amplifications. Palindrome involve in translocation have AT richness (PATRRs) and the best suited examples of this is t(11;22) translocation. PATRR22 is a hotspot of palindrome mediated translocation. Several molecular methods involve in identification of various PATRRs which modulate translocation by mechanism of double strand break (DSB), especially in gametogenesis. However, the precise mechanism of DSB, cloning of critical translocating factor PATRR22, enzymatic pathways and timing involved in formation of PATRRs translocations in gametogenesis is still undiagnosed.

Keywords: Palindrome; AT rich repeat; Translocation; Meiosis; Gametogenesis

Introduction

Palindromes are two units of identical sequences connected in an inverted position with respect to each other and can form specific secondary structure (non-B DNA)- (i) single-stranded (ss) hairpin or (ii) double- stranded (ds) cruciform DNA (Wang et al. 2014). Hairpin structures formed when the dsDNA is dissociated into ssDNA at the palindrome and this is during DNA or RNA replication or transcription. Cruciform formation starts from unwinding of the centre of the ds palindromic DNA, followed by extrusion at the centre of the palindrome to form an intra-strand base-paring of each strand.

A well-known palindrome mediated translocation is t(11;22)(q23;q11.2). Palindromic translocation occurs at AT rich regions (PATRRs). 22q11 region is a hotspot for nonrandom chromosomal rearrangements. The frequency of deletions, duplications and translocations at 22q11 region is greater than 1/3000–4000 live births [1]. PATRRs involving mostly 22q11 include the recurrent

t(11;22)(q23;q11.2), t(17;22)(q11.2;q11.2), t(8;22)(24.1;q11.2), and non-recurrent rearrangements like t(4;22)(q35.1;q11.2), and t(1;22)(p21.1;q11.2) (Table 1).

Therefore, Palindrome-mediated chromosomal translocation is one of the universal pathways of human genomic rearrangements.

Table (1): PATRRs and their mediated translocation

PATRR	AT Content	Location	Acc No	Karyotype	Reference
PATRR 22[a]	74%	22q11.1	ND	t(X;22)	[5]
PATRR 1	84.30%	1q21.1	ND	t(1;22)(p21;q11)	[6]
PATRR 4	61.10%	4q35.1	ND	t(4;22)(q35;q11)	[7]
PATRR 8	97.30%	8q24.13	ND	t(8;22)(q24;q11)	[8]
PATRR 17	80.20%	17q11	AB195812	t(17;22)(q11;q11	[9]
PATRR 11	93.00%	11q23	AF391129	t(11;22)(q23;11)	[10]
PATRR 22	74.10%	22q11.2	AB538236		
PATRR 3	75%	3q14.2	-	T(3;8)(p14.2;q24.1)	[11]

ND: Not Determined

[a]This reported PATRR22 translocation with partner chromosome that does not involve palindromic sequence

Translocation specific PCR (TSP), next generation sequencing (NGS), deep sequencing were used to observe the different PATRRs mediated translocation and double strand breakpoints (DSB) in human (Hidehito et al. 2016). Secondary structure of PATRR induce translocations during gametogenesis, especially spermatogenesis and the timing and mechanisms of secondary structure and translocation formation in male germ cells are potentially threefold- (i) before meiosis (ii) during meiosis, and (iii) post-meiosis. In humans, chromosomal abnormalities predominantly occur in the paternal germline because greater number of cell divisions occur during spermatogenesis [2] and spatial proximity of chromosomes during meiosis might play a role in generation of recurrent translocations [3].

Several difficulties have been related with PATRR like dilemma with PCR amplification, palindrome sequencing and cloning, therefore, proper mechanism of DSB, cloning of critical translocating factor PATRR22, enzymatic pathways and timing involved in formation of PATRRs translocations in gametogenesis, translocation through cruciform structure in meiosis remain undiagnosed. Thus, additional studies will be required to determine complex etiology of PATRRs which aid additional directional outputs related to palindrome mediated translocation in human beings.

Conclusion

PATRR is a unique phenomenon and hotspot for chromosomal rearrangements. Though several techniques and factors influencing the identification of PATRRs, yet several difficulties also encountered. Therefore, directional studies should be done in this field to signify the role of PATRRs in chromosomal translocation.

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