

# Mutation Analysis of STR Locus on 23 Autosomes in Hainan Population

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## Abstract

[Objective] To analyze the mutation signature and regularity of STR locus on 23 autosomes in paternity testing cases in Hainan. [Methods] A total of 2715 paternity testing cases accepted by the Forensic Medical Identification Centre of our hospital from 2017 to 2020 derived from counties and cities in Hainan Province were collected, the cases containing gene mutations were selected, the mutation rate and details of each locus were counted, and the mutation regularity of 23 STR loci was analyzed. [Results] Of the 2715 cases identified as “support”, 1487 were triplet cases and 1640 were dyad cases, totaling 4614 meioses; There were 50 gene mutation events (including 17 triplet mutations and 33 dyad mutations), with an average mutation rate of 0.0047% and a cumulative mutation rate of 1.0837%. A total of 19 of the 23 STR loci were mutated, with a mutation rate of 0.1301% at the D12S391 locus and 0.0217% at five loci, TPOX, D1S1656, D2S441, D22S1045, and PentaD, while no mutation events were found at four loci, D19S433, TH01, D13S317, and D7S820. Of the 50 mutation events, 47 were one-step mutations, 1 was two-step, and 2 were three-step. There were 35 paternal mutations (13 triplets and 22 dyads), 6 maternal mutations (4 triplets and 2 dyads), and 9 indeterminate paternal/maternal mutations, with a paternal to maternal mutation ratio of 5.83:1. [Conclusion] The mutation rate of D12S391 locus is the highest, and the mutation rate of TPOX, D1S1656, D2S441, D22S1045 and PentaD loci is the lowest in Hainan population, and paternal mutations are more than maternal mutations. In the paternity test, if 1 - 3 STR loci do not conform to the genetic law, especially when the mutant locus is homozygous or the next of kin is identified, it is necessary to use other kits to review and increase the number of loci or use the second-generation sequencing technology to confirm, carefully determine the mutation and ensure the accuracy of the identification conclusion.

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## Keywords

STR Locus, Paternity Testing, Mutation

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## 1. Introduction

Short tandem repeat (STR) refers to the core repeat formed by tandem connection with relatively constant 2 - 6 bases as repeat units, also known as satellite DNA, the most commonly used genetic marker in forensic physical evidence identification. Because STR typing technology has the characteristics such as high sensitivity, standardization and automatic typing, it has become the leading technology for forensic physical evidence identification. In this study, the mutation signature of STR loci on 23 autosomes in 2715 paternity cases from counties and cities in Hainan Province were analyzed to provide a reference for STR mutation data of Hainan regional and nationwide.

## 2. Materials and Methods

### 2.1. Sample Material

A total of 2715 (8274) paternity testing cases determined as “support” conclusions of the identification opinions in the Forensic Medical Identification Centre of Hainan Provincial People’s Hospital from 2017 to 2020 were taken as the statistical objects, and the samples of all cases were blood spots on FTA sample cards.

China Platinum Kit (Applied Biosystems, USA).

X-filer or Y-filer kits (both are Peoplespot (Beijing) Co., Ltd.).

### 2.2. STR Locus Genotype

According to DNA laboratory test specifications of forensic science (GA/T383-2014), the sample DNA is mainly amplified (not extracted) with China Platinum kit (Applied Biosystems, USA). The kit contains 23 loci including D3S1358, vWA, D16S539, CSF1PO, TPOX, D8S1179, D21S11, D18S51, PentaE, D2S441, D19S433, TH01, FGA, D22S1045, D5S818, D13S317, D7S820, D6S1043, D10S1248, D1S1656, D12S391, D2S1338 and PentaD. The amplified products are detected and typed by fluorescence with ABI-3500DX Genetic Analyzer (Applied Biosystems, USA) to obtain the genotypes of each locus.

### 2.3. Determination of Mutated Genes

When 1 - 3 loci failed to conform to the genetic law, after kin identification was excluded, it should be considered that the locus had a mutation. Another kit could be used for validation (Peoplespot (Beijing) Co., Ltd.), and X-filer or Y-filer kit (Peoplespot (Beijing) Co., Ltd.) was added for detection. If cumulative paternity index (CPI) > 10,000 and X or Y kit genotypes were consistent, it could be judged as supporting the parent-child relationship.

## 2.4. Data Processing

Calculation of mutation rate at STR locus: Locus mutation rate = (number of mutations detected at the locus/total number of meioses observed at the locus) × 100%.

## 3. Results

### 3.1. Analysis of Mutation Rate Results of STR Locus

Of the 2715 cases judged to be “support” identification opinions, 1487 were triplet cases, and 1640 were dyad cases (including 1173 father-child cases and 467 mother-child cases), with a total of 4,614 meioses and a total of 50 gene mutation events (including 17 triplet mutations and 33 dyad mutations), with a cumulative mutation rate of 1.0837% and an average mutation rate of 0.0047% at 23 loci. Mutations occurred in 19 of the 23 STR loci. The mutation rate of D12S391 was the highest, the mutation rate of TPOX, D1S1656, D2S441, D22S1045 and PentaD was the lowest, and no mutation was found at D19S433, TH01, D13S317 and D7S820. See **Table 1**.

### 3.2. Detailed Analysis of STR Locus Mutations

Of the 50 mutation events, 47 were one-step mutations, 1 was two-step, and 2 were three-step. In a one-step mutation, one repeat unit was increased 22 times, one repeat unit was decreased 15 times, and one repeat unit was indefinitely increased or decreased 10 times. In addition, among the 50 mutation events, there were 35 paternal mutations (13 triplets and 22 dyads), 6 maternal mutations (4 triplets and 2 dyads), and 9 indeterminate paternal/maternal mutations, with a paternal to maternal mutation ratio of 5.83:1, and see **Table 2**.

**Table 1.** Mutation rate of 23 STR loci ( $n = 4614$ ).

No.	Locus	Number of mutations (times)	Mutation rate (%)	No.	Locus	Number of mutations (times)	Mutation rate (%)
1	D3S1358	2	0.0433	13	FGA	3	0.0651
2	vWA	4	0.0867	14	D22S1045	1	0.0217
3	D16S539	4	0.0867	15	D5S818	4	0.0867
4	CSF1PO	2	0.0433	16	D13S317	0	0
5	TPOX	1	0.0217	17	D7S820	0	0
6	D8S1179	3	0.0650	18	D6S1043	4	0.0867
7	D21S11	5	0.1084	19	D10S1248	2	0.0433
8	D18S51	2	0.0433	20	D1S1656	1	0.0217
9	Penta E	2	0.0433	21	D12S391	6	0.1301
10	D2S441	1	0.0217	22	D2S1338	2	0.0433
11	D19S433	0	0	23	Penta D	1	0.0217
12	TH01	0	0		Total	50	1.0837

**Table 2.** Details of mutations at 23 STR loci.

Locus	one-step mutations			two-step mutations +2	three-step mutations +3	Source of mutation		
	+1	-1	+ 1 or -1			Paternal origin	Maternal origin	Indetermination
D3S1358	1	1	0	0	0	2	0	0
vWA	1	3	0	0	0	4	0	0
D16S539	3	0	1	0	0	3	0	1
CSF1PO	2	0	0	0	0	1	1	0
TPOX	1	0	0	0	0	1	0	0
D8S1179	0	3	0	0	0	2	1	0
D21S11	2	1	2	0	0	3	0	2
D18S51	2	0	0	0	0	1	1	0
Penta E	0	0	1	1	0	1	0	1
D2S441	1	0	0	0	0	1	0	0
D19S433	0	0	0	0	0	0	0	0
TH01	0	0	0	0	0	0	0	0
FGA	2	1	0	0	0	3	0	0
D22S1045	0	0	0	0	1	1	0	0
D5S818	0	2	2	0	0	3	0	1
D13S317	0	0	0	0	0	0	0	0
D7S820	0	0	0	0	0	0	0	0
D6S1043	3	0	0	0	1	2	2	0
D10S1248	1	0	1	0	0	1	0	1
D1S1656	1	0	0	0	0	0	0	1
D12S391	1	2	3	0	0	3	1	2
D2S1338	0	2	0	0	0	2	0	0
Penta D	1	0	0	0	0	1	0	0
Total	22	15	10	1	2	35	6	9

#### 4. Discussion

Mutation rate refers to the probability of a certain mutation event of a cell under specific conditions in one generation or other specified time of each organism. It is a reliability indicator for assessing the stability of genetic markers and paternity testing. Therefore, in the design of paternity testing kit, the genetic marker with a lower mutation rate, such as STR locus, should be selected. In order to avoid falsely excluded paternity as the mutation of loci, the pedigree investigation must be performed for loci selecting of forensic paternity testing with the observation of at least 500 meioses and the mutation rate of the selected loci should be less than 0.2% [1]. In this study, we observed that the mutation rate of 23 mutated STR loci ranged from 0.0217% to 0.1301%, and the mutation rates of the loci were less than 0.2% so that they can be used as loci for forensic paternity

testing.

Replication slippage is the main reason for the formation of mutations in STR loci. Replication slippage mutations are characterised mainly by one repeat unit increase or decrease in alleles. In the 50 mutation events of this study, 47 were one-step mutations, 1 was two-step, and 2 were three-step. This result shows that one-step mutations are significantly more than multi-step mutations, consistently with the results of literature studies [2] [3]. In addition, the phenomenon of increasing one repeat unit in a one-step mutation was 22 times, the phenomenon of decreasing one repeat unit was 15 times, the uncertainty increases or decreases one repeat unit was 10 times, and the proportion of increasing and decreasing one repeat unit in a one-step mutation is similar. STR gene mutations are also associated with gender, and reports have shown [4] [5] that the proportion of paternal mutations is more significant than that of maternal mutations since the number of division of sperm cells is 10 times more than egg cells, and the accumulation of base substitutions in sperm chromosomes is twice that of egg cells. The results of this study showed that the ratio of paternal mutation to maternal mutation was 5.83:1, with a significant gender difference, which was consistent with the literature reports.

A relatively specific mutation, called uniparental diploid mutation, refers to replacing a chromosomal region/segment from one parent with a homologous part from the other, or both homologous chromosomes of an individual come from the same parent. The phenomenon of non-conforming genetic law caused by this mutation can be confirmed by SNP technology in conditional laboratories [6]. In addition, some kits suffer from allele loss due to the inability of the same primer to anneal during amplification, and the phenotype is that both parents and offspring are homozygous and do not conform to the genetic law, which is easily mistaken for locus mutations. However, when another kit is used for the retest, it is found that both parents and offspring are heterozygous and conform to the genetic law [7], and the possibility of mutation can be excluded at this time.

## 5. Conclusion

In summary, the mutation of 23 STR loci in Hainan population counted in this study showed that the mutation rate of D12S391 locus was the highest, which was similar to that reported by domestic and foreign scholars [3] [8]; Five loci, TPOX, D1S1656, D2S441, D22S1045 and PentaD, had the lowest mutation rates, with paternal mutations substantially more than maternal mutations. When 1 - 3 STR loci in paternity testing do not conform to the genetic rule, it must be rechecked with other kits, increase the number of loci or be confirmed with the second-generation sequencing technology. Dyad cases should be supplemented and identified as triplet cases as far as possible. Biological parents should be added to the identification as far as possible in next of kin identification cases [9], or X and Y chromosomes should be added to improve the accuracy and re-

liability of identification conclusions.

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### Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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