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Y-chromosomal microsatellite mutation rates: differences in mutation rate between and within loci

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Abstract. We have studied 1766 father–son pairs of confirmed paternity (a total of 15 894 meioses) in nine Y-STR loci. The fathers were also analysed in five biallelic markers defining haplogroups (Hg) 1, 2, 3, 4, 9 and 16. A total of 36 fragment length mutations were observed. Our data demonstrate a significant surplus of gains and a bias towards increase in allele length upon mutational events. Overall, the mutation rate is correlated to STR repeat length, and there is a significant excess of losses in long alleles and gains in short alleles. Significant differences in mutation rate between and within loci are verified as is differences in mutation rates between haplogroups. Our findings clearly demonstrate the necessity of not only locus-specific but even allele-specific mutation rate estimates for forensic and population genetic purposes.

Keywords: Y-STR mutation rate; Microsatellite mutation rate; Father–son pair; Norway

1. Introduction

Precise estimates of mutation rates at Y-chromosomal microsatellite (Short Tandem Repeat) loci make an important basis for paternity diagnostics and dating of Y-chromosome lineage origins. There are indications of considerable locus mutation rate variability between (inter) and within (intra) loci. In light of these observations, we have studied Y-chromosomal microsatellite mutation in a large material of father–son pairs, giving access to direct observation and characterization of the individual mutations, and to individual STR locus mutation rate estimates even at the haplotype level.

2. Material and methods

The material consists of 1766 consecutive father–son pairs from a paternity case material in Norway. Paternity was confirmed at five minisatellite loci. DNA was extracted

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Table 1
Y-STR loci structure and individual STR mutation rates

Locus sorted by increasing mutation rates	Genome database (GDB)	Number of mutations		Locus-specific mutation rate	Average mutation rate
		Simple	Complex compound		
DYS392 (trinucleotide)	456509	0		0	Simple:
DYS388 (trinucleotide)	365729	1		5.70×10^{-4}	3.78×10^{-4}
DYS393	456649	1		5.70×10^{-4}	
DYS19	121409		3	1.70×10^{-3}	
DYS389I (C/D)	366108		4	2.26×10^{-3}	Complex:
DYS389II (A/B)	366108		4	2.26×10^{-3}	3.21×10^{-3}
DYS385	316257		7	3.96×10^{-3}	
DYS391	366118		8	4.53×10^{-3}	
DYS390	366115		8	4.53×10^{-3}	

from venous blood samples by the salting out method [1]. PCR conditions are as described in Ref. [2] and Ref. [3]. The repeat number nomenclature is according to the ISFH guidelines Ref. [4] and Refs. [5,6]. Mutations are identified by electrophoresis as allele length differences between father and son. They are confirmed by reanalysis and DNA sequence analysis.

3. Results

In 1766 father–son pairs (15 894 meioses in total), fragment length analysis demonstrated 36 mutations: 24 gains and 12 losses; thus, there is a surplus of gains [7]. Our data demonstrated significant correlation between STR size and mutation rate. We found relatively more gains in short alleles and more losses in long alleles. We observed one double mutation displaying two mutations at two different loci: DYS389I and DYS389II. These loci are located within 50 base pairs apart, and in addition, changes in both repeat motifs in DYS389II have occurred. Speculations regarding dependency in this particular case might therefore seem appropriate. However, the present data seem to exclude any strong dependency between loci with respect to mutation events. No noteworthy correlation between mutation rate and the father's age at the birth of child is observed. We observed a significant difference between individual STR mutation rate estimates ($p = 0.007$, Fisher's Exact Test) ranging from 0 in DYS392 to 4.53×10^{-3} in DYS390 and DYS391 (Table 1). Differences in mutation rates between the haplogroups (Hg) studied were demonstrated, a phenomenon which is a reflection of the dependence of mutation rate on allele size.

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