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Meiotic mutation rates of mini- and microsatellites in a Spanish population sample

M.J. Farfán*, M. López-Soto, V. Prieto, Y. Torres, J. García-Hirschfeld, P. Sanz

Servicio de Biología, Instituto Nacional de Toxicología, PO Box 863, E-41080 Seville, Spain

Abstract

We report an estimation of meiotic mutation rates at 6 minisatellites and 15 Short Tandem Repeats (STRs) deduced from the results obtained in the course of the filiation analyses carried out in our institute. At the six minisatellites, we observed 13 mutational events out of 2473 meioses, leading to a calculated overall mutation rate of 5.3×10^{-3}. Only 3 paternal mutations out of 3283 meioses were found at the 15 STRs under study, leading to an overall mutation rate of 0.9×10^{-3}. According to the stepwise mutation model, in these three cases the mutations could be due to the gain or loss of one repeat.

Keywords: Meiotic mutation rate; Minisatellite; Microsatellite

1. Introduction

Knowledge about mutation rates of DNA markers used in forensic genetics is important for the interpretation of results. Although rare, transmission incompatibilities in paternity testing or single mismatches in DNA profiles obtained during forensic investigations may occur due to germline or somatic mutation.

In paternity testing, differences at genetic loci between the alleged parent and the child would lead to exclusion of biological paternity. Thus, it is necessary to know the rates at which the different DNA markers commonly used in filiation investigations mutate.

Here we report an estimation of meiotic mutation rates at 6 minisatellites (D1S7, D7S21, D2S44, D5S43, D7S22 and D12S11) and 15 Short Tandem Repeats (STRs) (D3S1358,

* Corresponding author. Tel.: +34-954-371-233; fax: +34-954-370-262.
E-mail address: farfan@cica.es (M.J. Farfán).

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vWA, FGA, D8S1179, D21S11, D18S51, D5S818, D13S317, D7S820, TH01, TPOX, CSF1PO, D16S539, FES/FPS and F13A01) deduced from the results obtained in the course of the filiation analyses carried out in our institute.

2. Material and methods

Blood or saliva samples were collected from individuals from Andalusia, Extremadura and Canary Islands (S and SW Spain). DNA was extracted either by the phenol/chloroform standard method or through GFX™ genomic purification columns (Amersham-Pharmacia-Biotech, Piscataway, NJ, USA). DNA was quantitated by hybridization with a primate probe D17Z1 (Quantiblot® Human Quantitation kit, Applied BioSystems, Foster City, CA, USA).

For minisatellite analyses, DNA was restricted with *Hin*fI and electrophoresed in 0.7% agarose gel running in TBE for 18 h. For hybridization, alkaline phosphatase conjugated single locus probes YNH24 (Promega, Madison, WI, USA), MS43a, MS31, G3, MS8 and MS1 (Cellmark Diagnostics, Oxon, UK) were sequentially used. Results were analysed with software Bioimage (Millipore).

For STRs, PCR amplification was carried out according to manufacturer's instructions for kits GenePrint™ STR Multiplex System FFV (Promega), AmpF*l*STR Blue™, Green™, Yellow™, Profiler™, Profiler Plus™ and COfiler™ (Applied Biosystems). Detection was made by capillary electrophoresis in an ABI PRISM™ 310 Genetic Analyzer (Applied

Table 1
Genotypes of mismatched loci in cases of filiation analyses with a single exclusion

Locus	Mother	Child	Father	P/M probability[a] (%)
D1S7	10.13–5.26	5.15–4.92	4.18–4.08	99.99999978
	6.37–5.80	7.19–6.39	7.45–3.99	99.9999986
	4.22–4.10	7.08–4.12	6.70–3.81	99.99999976
	8.89–5.53	8.89–5.49	6.37–3.73	99.999999997
	5.26–2.11	3.91–1.99	11.78–3.90	99.99687209
	6.77–4.32	8.35–2.62	unknown	99.99999993
D7S21	5.98–5.52	6.99–5.52	6.79–6.31	99.999926
	7.19–5.84	5.83–3.95	5.35–4.90	99.9999999999
	6.67–5.48	5.48–5.22	5.66–4.55	99.99999986
	8.95–1.77	5.58–1.78	6.58–4.80	99.99781
D2S44	4.14–2.66	4.94–2.48	4.96–3.52	99.9999845
	4.57–2.84	4.39–3.03	unknown	99.99997937
D7S22	7.45–4.09	9.82–6.67	unknown	99.99973022
D12S11	10.03–7.76	8.61–8.20	8.81–3.45	99.99988834
D3S1358	unknown	14–18	15–17	99.999991
vWA	16–18	18–20	16–19	99.9999999999996
F13A01	5–6	6–6	5–5	99.997739251

[a] Paternity (P) or maternity (M) probability depending on whether the origin of the mutation is paternal or maternal, respectively, based on the markers analyzed in each case and ruling out the mutated locus.

Biosystems). For the analysis of results, software 310 Genescan® 2.1 and Genotyper® 2.0 (Applied Biosystems) were used.

3. Results and discussion

A mutation was assumed when a single exclusion was observed in paternity cases where the parenthood probability calculated ruling out the mismatched locus was higher than 99.99% (Table 1). At minisatellites, we detected 13 mutational events out of 2473 meioses, leading to a calculated overall mutation rate of 5.3×10^{-3} (Table 2). A ratio of 1.6:1 for mutations of paternal/maternal origin, respectively, was found. At the 15 STRs under study, only 3 paternal mutations out of 3283 meioses were found, leading to an overall mutation rate of 0.9×10^{-3} (Table 2). These results are in agreement with previously reported data [1–3]. The overall mutation rate for the 13 STRs CODIS loci was estimated in 6.6×10^{-4}. According to the stepwise mutation model, the three mutations found at STRs can be explained by gain or loss of one repeat (see Table 1). The mutation rate estimated for microsatellites was approximately six times lower than for minisatellites.

Table 2
Mutation rates at minisatellite and microsatellite loci

Locus	Number of meioses (mutations)			Mutation rate $\times 10^{-3}$ (95% confidence limits)
	Paternal	Maternal	Total	
D1S7	138 (4)	172 (2)	310 (6)	19.4 (7.1–42)
D7S21	211 (4)	267	478 (4)	8.4 (2.3–22)
D2S44	200	240 (1)	440 (1)	2.3 (0.1–13)
D5S43	196	238	434	<2.3 (0–8.5)
D7S22	151	182 (1)	333 (1)	3.0 (0.1–17)
D12S11	217	261 (1)	478 (1)	2.1 (0.1–12)
Minisatellites	1113 (8)	1360 (5)	2473 (13)	5.3 (2.8–9.2)
D3S1358	112 (1)	138	250 (1)	4.0 (0.1–22)
vWA	152 (1)	198	350 (1)	2.9 (0.1–16)
FGA	111	137	248	<4.0 (0–15)
D8S1179	73	90	163	<6.1 (0–22)
D21S11	73	90	163	<6.1 (0–22)
D18S51	72	89	161	<6.2 (0–23)
D5S818	77	95	172	<5.8 (0–21)
D13S317	80	98	178	<5.6 (0–21)
D7S820	80	98	178	<5.6 (0–21)
TH01	156	196	352	<2.8 (0–11)
TPOX	152	189	341	<2.9 (0–11)
CSF1PO	146	183	329	<3.0 (0–11)
D16S539	66	75	141	<7.1 (0–26)
FESFPS	54	77	131	<7.6 (0–28)
F13A01	52 (1)	74	126 (1)	7.9 (0.2–43)
Microsatellites	1456 (3)	1827	3283 (3)	0.9 (0.2–2.7)

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