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Mutation rates at 23 different short tandem repeat loci

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Abstract

In a collaborative study, we calculated mutation rates at 23 different STR loci after investigation of nearly 24,000 meioses including all Profiler™, Profiler Plus™, COfiler™, SGM Plus™ and Powerplex™ 16 loci except Penta D and Penta E and further loci, of which D12S391, D17S976 and SE33 are the most informative: CD4, CSF1PO, D2S1338, D3S1358, D5S818, D7S820, D8S1132, D8S1179, D12S391, D13S317, D16S539, D17S976, D18S51, D19S433, D21S11, F13A1, F13B, FES, FGA, SE33, TH01, TPOX and VWA. The alleles presumed to be taking part in mutations were sequenced. The possible origin and the possible structural variations of mutational events in microsatellites are discussed.

Keywords: STR; Mutation; Mutation rate; Microsatellite

1. Introduction

The investigation of short tandem repeat loci is a widely spread method for human genetics and forensics, but only a few reports on a large scale data on mutation rates of microsatellites exist up to now. In this collaborative study, we examined 31 mutations

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observed among 23.651 informative meioses (12.699 maternal and 10.952 paternal meioses) at 23 different microsatellite loci.

2. Materials and methods

Blood or buccal swab samples were either taken from members of a very large, five-generation family or from further parent/child duos or complete trios of Causcasoid origin living in Austria and Switzerland. Paternity was ascertained by using classical marker systems and/or a set of 0–5 minisatellite loci and 3–14 microsatellite loci, depending on the markers systems investigated by the contributing laboratories. They were analysed by singleplex or multiplex PCR (Profiler Plus™, SGM Plus™, Applied Biosystems or Geneprint™ Powerplex™, Promega), followed by native or denaturing horizontal polyacrylamide gel electrophoresis and subsequent silver staining or fragment analysis on an ABI 373, ABI PRISM 310, ABI PRISM 377 or an A.L.F. DNA sequencer. A mutation was considered to have occurred in cases of an isolated parent(s)/child mismatch, which appeared as non-Mendelian inheritance. The parenthood probability always exceeded 99.99% not taking the isolated mismatch into consideration. The shortest and most simple step of change in allelic size was assumed as the most

Table 1
Mutation rates at 23 different microsatellite loci

Locus	Number of meioses	Number of mutations	Mutation rate ($\times 10^{-3}$)	95% confidence limits
CD4	1091	0	<0.9	0–3.4
CSF1PO	271	0	<3.7	0–13.6
D2S1338	404	1	2.5	0.1–13.8
D3S1358	1041	0	<1.0	0–3.5
D5S818	795	0	<1.3	0–4.6
D7S820	795	0	<1.3	0–4.6
D8S1132	121	1	8.3	0.2–46.0
D8S1179	989	1	1.0	0–5.6
D12S391	433	0	<2.3	0–8.5
D13S317	795	1	1.3	0–7.0
D16S539	504	0	<2.0	0–7.3
D17S976	611	0	<1.6	0–6.0
D18S51	989	1	1.0	0–5.6
D19S433	404	0	<2.5	0–9.1
D21S11	1038	3	2.9	0.6–8.4
F13A1	382	0	<2.6	0–9.7
F13B	1374	0	<0.7	0–2.7
FES	1656	1	0.6	0–3.4
FGA	2055	6	2.9	1.1–6.4
SE33	1733	9	5.2	2.4–9.9
TH01	2735	0	<0.4	0–1.3
TPOX	271	0	<3.7	0–13.6
VWA	3164	7	2.2	0.9–4.6
Total	23,651	31	1.3	0.9–1.9

Table 2
Summary of characteristics of microsatellite mutations

	Gains	Losses	Gains or losses	Total
± 1 Repeats	10	13	3	26
± 2 Repeats	1	4	0	5
Maternal	3	5	1	9
Paternal	5	12	1	18
Maternal or paternal	2	1	1	4
Total	10	18	3	31

probable one. The alleles that were presumed to be involved in the mutational event were sequenced.

3. Results and discussion

The mutation rates of microsatellites observed in this study are given in Table 1. More losses than gains of one to two complete repeat units and more mutations in the male than in the female germline were observed (Table 2). The possible existence of a null allele could be ruled out by a second PCR with external primers, which showed true homozygosity in two cases and by sequencing which proved heterozygosity of two alleles of the same length but with different sequence variations in one case. Our results confirm the higher mutation rates of loci with longer uninterrupted repeats, which was already inferred elsewhere [1]. As mentioned above, our data were interpreted assuming that the shortest and most simple step in allelic size was the most probable one, according to the stepwise mutation model [2]. The possible origin and structural variations of mutational events in microsatellites discussed in this study must be considered with respect to these limitations. Further investigations on a larger set of samples will be necessary to solve this problem.

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