Decision-making in paternity diagnostics using SLPs

Evaluation based on a three-year material

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INTRODUCTION

A number of factors represent a challenge to the establishment of a sound theoretical statistical basis for decision-making in paternity diagnostics with hyperpolymorphic minisatellite loci; for example the degree of variation itself, the "pseudo-continous" allele distribution, the choice of matching criteria, the influence of kinship, and the presence of considerable mutation rates (see e.g. Cohen 1990, Chakraborty 1991, Lewontin and Hartl 1991, Morton 1992, Roeder 1994).

We wanted to use empirical data to test if the product rule, applied on match/nonmatch typing results obtained with hyperpolymorphic SLPs, is invalidated. If it is not, and if a sufficient number of extremely informative markers is chosen, the power of this typing approach could pave the way for considerable reductions in the tedious casework evaluation procedures in common use.

MATERIAL AND METHODS

Material: Blood samples from 3431 (mother)/child/man pairs or triplets in consecutive paternity cases in Norway (1992, 1993, and 1994). Cases where case information indicated cosanguinity between the man and the true father (6 cases) were excluded.

Genetic markers: 5 SLPs: D2S44 (probe YNH24), D7S21 (g3), D7S22 (MS31), D12S11 (MS43A), and D14S13 (CMM101).

Methodology: DNA extraction (Miller 1988), Southern technique using EDNAP standards, HinfI and chemiluminescence/p32 detection.

Typing procedure: Typing as match (M) or nonmatch (NM) was performed independently by two experienced persons, by a manual procedure. Visual comparison between fragments in adjacent lanes was employed, using fragment gel positions within 0.5 mm as match criterion.

Subdivision of material: The material described was divided into one of nonfathers (921 men), and one of fathers (2510 men) by the following procedure: Cases with the type combinations 4M1MN, 3M2MN, and 2M3MN were analysed with three more SLPs (probes MS1, B6.7 and MS205) and/ or a battery of STRs), whereby an unambigous establishment of the paternity state was obtained in each of these 103 cases. Having experienced no nonfathers among 82 men with the 4M1MN combination, we assumed that there were no nonfathers among the 2424 men with 5M either. Similarly, since there were no fathers among 16 men with 2M3NM, we ascertained all 175 with 1M4NM and all 729 with 5NM to the group of fathers.

RESULTS AND DISCUSSION

In table 1 is shown the typing results with each of the SLPs in the 2510 fathers. Studies indicate that the probability that a true match is typed a nonmatch by the present procedure is less than one in one thousand, and more than 80 of the 89 nonmatches in fathers have been shown to represent true mutations (data not given here). The narrow limits for a match is

therefore not to a noticeable degree influenced by such "false nonmatches". They do, however, leed to a relative high number of nonmatches caused by small mutations.

Table 1 TYPING RESULTS OF EACH SLP IN 2510 FATHERS						
SLP	D2S44	D7S21	D7S22	D12S11	D14S13	AVG.
NONMATCH	10	22	32	5	20	18
NM RATE	0,004	0,009	0,013	0,002	0,008	0,007

Table 2 demonstrates the results in the 921 nonfathers. Applying the present matching criteria yields a high power of detecting allele differences. The probability that a nonfather has at least one SLP with a NM result is extremely high (0.99999984).

Table 2 TYPING RESULTS OF EACH SLP IN 921 NONFATHERS						
SLP	D2S44	D7S21	D7S22	D12S11	D14S13	AVG.
NONMATCH	884	885	879	856	891	879
NM RATE	0,960	0,961	0,954	0,929	0,967	0,954

Combined typing results in the total material of 3431 man/child pairs as well as in each of the two subgroups of fathers and nonfathers are given in Table 3. For the latter two groups are also given the expected distribution of type combinations, applying the product rule on average match-/nonmatch rates in each of the five loci applied.

Table 3 TYPING RESULTS IN 3431 MAN/CHILD PAIRS WITH 5 SLPs: D2S44, D7S21, D7S22, D12S11, AND D14S13

MATCH/NONMATCH COMBINATION	NO. OF PAIRS	FATHERS		NONFATHERS	
		obs.	exp.	obs.	exp.
5 M, 0 NM	2424	2424	2422	0	10^{-4}
4 M, 1 NM	82	82	87	0	10^{-2}
3 M, 2 NM	5	4	1.15	1	0.75
2 M, 3 NM	16	0	10^{-2}	16	16
1 M, 4 NM	175	0	10^{-5}	175	175
0 M, 5 NM	729	0	10^{-8}	729	729

In the group of fathers, there is a statistically not significant surplus og 3M2NM pairs. The typing of the 82 4M1NM pairs in three additional SLPs, however, did not give indication of any tendencies towards multiple mutation (independence in mutation rate between these loci) (data not shown). Expected numbers in each type group in nonfathers are in very good accordance with expectations.

The present evaluation indicates that the use of the product rule is not grossly invalidated when applied to SLP locus specific average match- and nonmatch rates in fathers and nonfathers. This may allow for a simple decision-making procedure in paternity casework. In Table 4, paternity indices are based on the theoretical frequency of each match/nonmatch combination in the present groups of fathers and nonfathers, and by applying the product rule. Nothing else known about the typing results, the paternity index of a 5M combination is about 6 millions. Observations of the distribution of individually calculated paternity indices (based on allele frequencies) indicate that the individual paternity index of a 5M type practically never will be less than 10^5 (data not shown). In our opinion, this type combination - occuring in 71% of the man/child pairs - could ordinarily make a sound basis for establishing paternity. Similarly, the nonpaternity indices in the 1M4NM and 5NM combinations could make the basis for a decision of nonpaternity. This means that 97% of the cases is solved by employing the match/nonmatch combination of the five SLPs. For the 4M1NM (2% of the cases) and 2M3NM (0.5% of the cases) combination the addition of for instance the STR triplex analysis with a combined nonmatch rate in nonfathers of 99.77% (Dupuy and Olaisen, this conference), would raise indices to the level found in the former combinations. The 2M3NM combination is obviously practically noninformative as to the paternity status of the man, and must be solved using additional genetic markers (about 2 cases a year in the present material) .

Table 4 PATERNITY INDEX AND "NON-PATERNITY INDEX" WITH 5 SLPs: D2S44 D7S21 D7S22 D12S11 D14S13

MATCH/NONMATCH COMBINATION	PATERNITY INDEX	NON-PATERNITY INDEX	PERCENT OF MEN
5 M, 0 NM	**$6*10^6$**		71
4 M, 1 NM	$2*10^3$		2
3 M, 2 NM	0,6	1,8	0,2
2 M, 3 NM		$6*10^3$	0,5
1 M, 4 NM		**$3*10^7$**	5
0 M, 5 NM		**10^{11}**	21

CONCLUSIONS

The present evaluation of a large paternity case material shows that the distribution of match/nonmatch combinations in 5 SLP is in good accordance with expectations based on match/nonmatch typing rates of each SLP and the use of the product rule. We argue that paternity diagnostics could be performed without any fragment sizing, allele frequency determinations or further individual case statistics.

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