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Usefulness of X-chromosome markers in resolving relationships: Report of a court case involving presumed half sisters

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Abstract. A deficiency case of inheritance dispute involved two women that were either half sisters or unrelated. Using 16 standard forensic markers, the likelihood ratio (LR) in favour of the first hypothesis was 701.1 ($P=0.9986$); using four unlinked X-chromosome (chr-X) markers (DXS101, HPRTB, STRX1, DXS8377), the LR was 495.8 ($P=0.9980$). The increase of power in discriminating relationships among females using chr-X markers was investigated by calculating the expected value of the posterior probability that two true half-sisters were half-sisters rather than unrelated for these chr-X marker and autosomal markers with equivalent allele frequency distribution. The mean increase of the posterior probability was included between 19% (HPRTB) and 37% (DXS8377), and was correlated with locus heterozygosity. © 2005 Published by Elsevier B.V.

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1. Introduction

The use of X-chromosome (Chr-X) markers in forensic practice has played a minor role so far, probably because of its peculiar transmission rules, which reduce their potential use in forensic analyses to cases involving females only [1]. However, the probability of

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Table 1
Formulas for computing the likelihood ratio (LR) that two women are half sisters rather than non-relatives for autosomal and Chr-X markers, and cumulative LRs obtained in our case

Genotype configuration	Autosomal markers LR	Chr-X markers LR
AA,AA	$1/2+1/2p_A$	$1/p_A$
AA,AB	$1/2+1/4p_A$	$1/2p_A$
AA,BB	1/2	0
AB,AB	$1/2+1/8p_A1/2+1/8p_B$	$1/4p_A+1/4p_B$
AA,BC	1/2	0
AB,AC	$1/2+1/8p_A$	$1/4p_A$
AB,CD	1/2	0
Actual values in our casework study	701.1[a] ($P=0.9986$)	495.8[b] ($P=0.9980$)

[a] Using 16 forensic markers: D3S1358, vWA, FGA, D8S1179, D21S11, D18S51, D5S818, D13S317, D7S820, D16S539, THO1, TPOX, CSF1PO, SE33, YNZ22, D1S80.
[b] Using four Chr-X markers: DXS101, HPRTB, STRX1, DXS8377.

excluding a false father in standard trios is higher for Chr-X markers than for autosomal loci with comparable values of polymorphic information content, and there are special circumstances in which they may resolve cases with deficiencies more efficiently than conventional loci [2]. Therefore, Chr-X genotyping can efficiently complement the analysis of other genetic markers, and may resolve cases that otherwise would remain inconclusive.

2. Case report

The following deficiency case of inheritance dispute has come to our attention recently. Subjects S1 and S2, both females, had different mothers; the father F of S1 had died, and S2 claimed also to be a child of F. Then, we were interested in the likelihood ratio (LR) that S1 and S2 were half sisters rather than unrelated, based on the genotypes of S1 and S2 only. We first typed 16 autosomal markers commonly used in forensic practice (see legend to Table 1), and obtained a cumulative LR of 701.3, in favour of the hypothesis that they were half sisters and corresponding to a P value of 0.9986 assuming equal priors. As we usually present more compelling evidence in court cases, we typed the four Chr-X markers DXS101, HPRTB, STRX1, DXS8377 [3]. Formulas needed for calculating likelihood ratios for X-chromosome markers in this instance (Table 1) were obtained by Bayesian analysis and were verified computationally. The LR of the four Chr-X markers alone was 495.8, corresponding to a P value of 0.9980, not much lower of the probability value

Table 2
Expected values of the posterior probability that two true half-sisters are half-sisters rather than non-relatives using Chr-X or autosomal markers and their ratio

Locus	Heterozygosity	$\langle P\rangle_{\text{Chr-X}}$	$\langle P\rangle_{\text{autosomal}}$	Ratio
HPRTB	0.734	0.632	0.531	1.19
STRX-1	0.831	0.68	0.54	1.26
DXS8377	0.913	0.778	0.658	1.37
DxS101	0.879	0.739	0.558	1.33

Table 3
Power of exclusion of the four Chr-X markers in half sisters with common father

Locus	PE	Cumulative
HPRTB	0.3316	0.3316
STRX-1	0.4905	0.6595
DXS8377	0.6996	0.8977
DXS101	0.6121	0.9603

attained with 16 autosomal markers The final (combined) probability value was 0.999997, thus providing sufficient proof.

3. A more general analysis

We were interested in comparing the power of discriminating relationships between Chr-X and autosomal markers in more general terms. Considering the case at hand, the question is: what is the expected increase of power deriving from the use of Chr-X markers instead of autosomal markers of equivalent informativeness, before performing any typing?

We addressed this question by calculating the mean value, over all possible genotype configurations, of the posterior probability that two true half-sisters were half-sisters rather than unrelated. All possible pairs of genotypes were listed for each of the four Chr-X markers, and the LR that each pair was composed by half sisters rather than by non-relatives was calculated. We applied separately the autosomal and the Chr-X formulas (table above), and converted the obtained LRs into probabilities as usual [$P = \mathrm{LR}/(\mathrm{LR}+1)$]; then, the mean value of these probabilities, $\langle P \rangle_{\text{autosomal}}$ and $\langle P \rangle_{\text{Chr-X}}$ respectively, was compared as a measure of discriminating power. Table 2 shows the results of this analysis. All Chr-X markers were more efficient than autosomes with the same distribution of allele frequencies; the mean increase of the posterior probability of assignment was included between 19% (HPRTB) and 37% (DXS8377). The increase of power was correlated with locus heterozygosity.

A further property of Chr-X markers is that they may generate incompatibilities in the case of half sisters with common father (this cannot occur for autosomal markers). We therefore calculated the power of exclusion (PE) of these four markers, noting that it has the same value of the PE of autosomal markers observed in duos father–son. Table 3 shows both the single locus PE and its cumulative value over the four loci.

Thus, the present results confirm the superior statistical power of Chr-X markers in resolving relationships when female subjects are concerned. A more general treatment considering other relationships and other gender combinations will be shown elsewhere.

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