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LETTER TO THE EDITOR

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Comments on the paper entitled "Polymorphism of nine X chromosomal STR loci in Koreans" by Jin Young Son et al. (2002) Int J Legal Med 116:317–321

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Dear Sir,

We highly appreciate that more and more forensic research groups are focusing their attention on the X chromosome (ChrX) to increase the number of established ChrX markers. We therefore read the paper by Jin Young Son et al. (2002) with great interest, however we find it difficult to agree with them on several points.

The authors suggest that the allele distributions in the Korean sample do not differ from those of other populations, and cite our investigations in Europe with reference to DXS6789 (Hering et al. 2001) and DXS9898 (Hering and Szibor 2000). However, the results obtained by Jin Young Son et al. (2002) do seem to show considerable differences to our findings, e.g. for DXS9898 we found the allele 8.3 on about 25% of the chromosomes examined in Germany but for the Korean publication the allele 8.3 is not described. We established a frequency of about 16% for the allele 13, whereas the Korean colleagues indicate a frequency of 1%.

Discrepancies can be also found in other loci, such as DXS6789, DXS7133, DXS7132, DXS8378, etc. (Edelmann et al. 2001), and as they are obvious we do not consider it necessary to prove them by means of a statistical method. As no reference is given to the use of any international standard DNA, such as K562 or 9947A, it cannot be verified whether the allele designation as suggested corresponds to that of other publications.

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Jin Young Son et al. (2002) report 29 mutations they found in 303 families: "The number of mutations found was 13 in DXS6803, 2 in DXS8378, 4 in GATA164A09, 3 in DXS7132, 2 in DXS7133, 1 in DXS9895, 2 in DXS9898, 1 in DXS6789, and 1 in DXS6795. ..... Mutations usually occurred at one locus in a family, but in two families mutations were noted in three loci simultaneously. In two cases, both paternal and maternal alleles were transmitted abnormally..." They refer to 2 cases of a 2-repeat shift and 2 cases of a 4-repeat shift. In particular, the high apparent mutation rate found for DXS6803, mainly as a single 0.1 repeat shift, would seem to warrant closer scrutiny. We appreciate that it is difficult for an outsider to criticise or provide a reliable explanation for such unusual findings without having seen the raw data. However, from the paper it seems as if the authors did not choose adequate conditions for their DXS6803 analyses. As we know from our experience with STRs, such as TH01, DXS981 and DXS6803, the conventional PAGE and silver staining method is rather unsafe in discriminating between alleles differing in length by 1 bp only. Here, special care must be exercised, even when applying an automated fragment analysis evaluation. Moreover, the results were obtained by using multiplex PCRs. If the conditions for multiplex PCR analyses are not really optimal, phenomena such as allelic drop-out or unspecific additional bands may cause assignment errors. We would therefore recommend that all apparent mutations should be double checked using a single-plex amplification regime, if this has not already been done.

Jin Young Son et al. (2002) found deviations from the regular allele distribution in markers GATA164A09, DXS9895 and DXS6789. As the authors correctly stated the Hardy-Weinberg allele distribution test can be used to indicate whether or not the population investigated is panmixed. However, another aspect should be emphasised: if the allele distribution of a panmixed population was demonstrated using an unreliable method, the result may be in conflict with the Hardy-Weinberg law. Again, to be on the safe side, we recommend to use the single-plex amplification method for all markers which do not meet the

criteria of the Hardy-Weinberg law. Basically however, a gene scanner should be used for any problematic marker.

Using the PE value calculations as suggested by Desmarais et al. (1998), we obtained different results based on the allele frequencies published in the paper, e.g. 0.60 instead of 0.34 for DXS6803, 0.52 instead of 0.15 for DXS8378 and 0.75 instead of 0.33 for GATA164A09.

It is not only the possible methodological shortcomings which make us feel doubtful about the results of the paper, but also their marked contradiction to publications in the literature and to our own results. As can be found in the literature, single-(repeat)step mutations account for about 90% of STR mutation events, followed by double-step mutations. Multistep mutations are very rare (Brinkmann et al. 1998). In light of these previously established guidelines it is not only the average mutation rate which is unusually high, but also the mutation type statistics must be considered dramatically unusual, unless this is a population-specific phenomenon.

Apart from GATA164A09 and DXS6795, our group also carried out investigations into the mutability of the ChrX markers mentioned above as well as other ChrX markers (Szibor et al. 2003). The data we obtained for 16 ChrX markers suggest an average mutation rate of 2.09×10^{-3} per meiosis, i.e. a rate similar to that of human autosomal STRs. Also the mutation rate for DXS6803 in our sample showed no unusual tendencies as we did not detect any mutations in our analysis comprising 135 family trios with female children (Edelmann and Szibor 2003).

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