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TECHNICAL NOTE

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# A new Web site compiling forensic chromosome X research is now online

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**Abstract** We would like to announce the opening of a new Web site (http://www.chrx-str.org), which contains a database surveying current research on chromosome X markers used for forensic purposes, evolutionary anthropology and other genetic research. Currently, we summarise short tandem repeat data with regard to the physical and genetic localisation, repeat structure, allele nomenclature, mutation rates and population genetics. In the future, we may include diallelic markers. The results contained in this database come from published journal articles. The authors of published articles are invited to complement their own papers by submitting data obtained from follow-up studies here. Furthermore, population data which are not able to find space in journals may be published at this Web site. The growing field of ChrX haplotyping is producing an extensive amount of data, which requires a place that can complement journal publications.

**Keywords** X chromosome · Short tandem repeats · Haplotyping · Web site · Forensic DNA typing

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## Introduction

Typing of chromosome X (ChrX) markers has increasingly become an issue in kinship testing, especially in certain deficiency cases that can be solved by this technique rather than by using autosomal and Y-chromosome (ChrY) testing [6, 7]. However, this applies only to a minority of kinship cases, and consequently, there are only a few scientists currently dealing with this topic. Since the overall number of cases is low, the amount of available data for forensic and research purposes is increasing only slowly. On the other hand, forensic certainty is best achieved when expert testimony is based on information supported by a broad base of research. Therefore, it seems to be advisable to collect marker data such as allele distributions, null allele frequencies, mutation rates, etc. in an online database accessible to the entire forensic community. Thus, by combining a series of smaller studies, it may be possible to collectively accumulate enough data to sufficiently impact current research. Furthermore, with regard to other scientific disciplines such as evolutionary anthropology that also use ChrX markers in their research, they will need access to reliable ChrX marker data from different regions and racial groups. A worldwide survey of initial data regarding the variability of the markers can help to select markers of interest. Owing to the quite different mode of inheritance, ChrX typing will never reach the same level of significance in this field as ChrY research has obtained. Nevertheless, ChrX marker cluster haplotyping may complement the well-established disciplines of haploid DNA, ChrY and mitochondrial DNA marker research. In this sense the success of the Y chromosome haplotype reference database (YHRD) (http://www.yhrd.org/index.html) encouraged us to initiate this ChrX database.

Finally, ChrX marker investigations can have a clinical significance. Despite the fact that the whole human genome is now sequenced [2], linkage analysis is still important to identify specific disease-linked genes [3]. Furthermore,

some oncology ensemble marker panels for the investigation of microsatellite instability (MSI) and loss of heterozygosity (LOH) use ChrX short tandem repeats (STRs) [1, 4, 8].

## Web site architecture and data-submitting procedure

### ChrX marker localisation

Chromosome X typing in kinship testing requires good knowledge about the linkage between markers. Physical and genetic localisation of loci on the same chromosome are related, but this relationship is not strictly linear. Therefore, access to the special marker pages is guided via a ChrX ideogram, or alternatively, via a localisation table. The ideogram enables a survey of the marker distribution along the chromosome, while the localisation table gives numerals for physical and genetic localisations as exactly as possible. Although the human genome has already been completely sequenced [2], the currently available human DNA databases slightly differ in their localisations that are measured in base pairs. The Human Genome Browser of the Wellcome Trust Sanger Institute (http://www.ensembl.org/Homo_sapiens) and the National Center for Biotechnology Information (NCBI) (http://www.ncbi.nlm.nih.gov/) provide identical data for nearly all loci, and we have used them in the construction of our table. The NCBI presents additional data from the Celera database which we have also inserted. Our localisation table presents the physical locations of the STRs as the distance in base pairs from the Xp telomere according to the aforementioned databases.

The genetic localisations of most of the STRs considered here are shown in the database of the Marshfield Center for Medical Genetics (http://www2.marshfieldclinic.org/RESEARCH/GENETICS), which correlate with the results from the NCBI database. For markers which are not genetically located by the Marshfield database, we suggest figures for the genetic localisation, which are roughly estimated on the basis of physical localisation. All measurements are given as the distance from the Xp telomere in centimorgans (cM).

In many cases of forensic kinship testing, autosomal STR typing is the backbone of investigation, which can be supplemented by ChrX, ChrY or mtDNA testing. Therefore, our database also includes other cross-hyperlinks to well-established Web sites such as http://www.uni-duesseldorf.de/WWW/MedFak/Serology/database.html and http://www.cstl.nist.gov/div831/strbase.

### Short descriptions of ChrX markers

The descriptions of the STR markers are mainly based on papers published in forensic journals and include proposed primers for each marker but not complete PCR protocols. The amplicon lengths are indicated with regard to these primers. Allele designations are based on the presented typical repeat structures. To enable ladder calibration, lengths are indicated for four cell line DNAs, i.e. K562, NA9947A, 9948 and NA3657, as recommended [5] ABI007 may follow in the future.

### Population data of STRs

Population data on ChrX STRs have been collected from several papers. Although only peer-reviewed journals were considered for use in this Web site, not all publications were suitable to provide data. Simply stating that a method of ladder calibration was used does not guarantee the acceptance of a paper on population data because in some cases, the published data does not meet the recommendations by the International Society for Forensic Genetics (ISFG) regarding consensus allele nomenclature. In other cases, this situation is unclear. Such problems can be avoided when authors use at least two standard DNA cell lines for the ladder calibration. Population genetic parameters such as mutation rates, PIC, PD, MEC etc., which characterise the marker, are also indicated.

### Population data regarding STR haplotypes

In males, the ChrX marker appears in a hemizygous state. Hence, ChrX typing of marker clusters automatically provides haplotypes.

In certain pedigrees, ChrX haplotypes with two to four very closely linked STRs can be used in kinship testing instead of a single STR, in particular, when the expected crossing-over rate within the clusters is very low, and the STR haplotypes are transmitted as stable units. When the distance between two markers does not exceed 0.5 Mb, the recombination rate between two markers is not higher than the average mutation rate of a single STR. When two or more STR loci are used, the number of haplotypes may extend to several hundred or even more than 1,000 haplotypes. Since ChrX haplotyping may produce a flood of data, not all data will be able to find space in journals. Therefore, complementary data publication in other publishing media may be useful. Our Web site offers space for online publication of such data.

### Submitting data for online publication

The information currently found in this Web site was copied or transcribed from STR and haplotype data literature searches. To help facilitate the procedure in the future, authors are requested to copy their published data into our Web data sheet. Of course, unpublished data are also welcome. STR and STR haplotype data can be submitted.

The distance between the outer markers of the whole haplotype should not exceed a span of 5 cM. Submitted data must meet the following quality guidelines:

- Appropriate typing techniques must be used. STRs which have irregular alleles should always be typed using automated DNA sequencers.
- For ladder calibration, in general, at least two of the following standard DNA cell lines must be used: NA9947, NA9948, NA3657 and DNA ABI007. These standards can be purchased from the Coriell Institute for Medical Research, Camden, NJ; Promega, Madison, WI; and PerkinElmer, Foster City, CA. The cell line DNA K562 is not suitable for ladder calibration especially when ChrX STRs are to be typed [5].

Observations on mutation rates should survey at least 50 meioses and have to be separated into maternal and paternal meioses. Furthermore, when mutations are found, the age of the parents at conception of the mutant parents must be documented as well as the age profile (at conception) of the entire population sample. It is important that the negative results (i.e. no observed mutations in the sample) are also routinely reported; otherwise, a massive statistical reporting bias would make our mutation database useless.

The following population genetic parameters used in forensic science should be calculated and checked: MEC, PIC, HET, $PD_{female}$, $PD_{male}$ and the Hardy–Weinberg equilibrium. We have built a software into our Web site that can be used to calculate these genetic parameters.

As in many countries of the world, there is more than one population; it is not sufficient just to name the country, but also, metapopulation and further ethnic backgrounds should be indicated (e.g. North America, Idaho, Blackfoot Indians). The seven metapopulations are Europe, Asia, Latin America, North America, Africa, Oceania/Australia and the Arctic.

## Communication between users of ChrX STRs

To facilitate the current scientific communication we insert into our Web site a list of researchers dealing with ChrX STRs and related topics. If a scientist working with STRs for DNA typing purposes is not registered and would like to be added to this list, he may contact us. In such case he should cite his appropriate publications. Furthermore, the Web site will be equipped with a bibliography presenting relevant ChrX literature.

## Concluding remarks

The Web site reported here is operated by a loose connection of scientists linked by their common interest in forensic ChrX research. The group is founded by the authors of this communication, and we are not a corporate body. We will try to diligently maintain this page, exercising a high degree of care and scientific responsibility. We intend to accept all submissions which are within the scope of this Web site and which meet the required quality specifications. In some instances reasons may exist to reject a submission. In these situations legal consequences are excluded. However, if the author is able to obtain a letter of support from an advisory board member of the International Journal of Legal Medicine or Forensic Science International, the rejection may be reconsidered.

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