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Chromosome X haplotyping in deficiency paternity testing principles and case report

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Abstract

This paper presents an example of deficiency paternity testing by using 15 chromosome X (ChrX) markers. The special power of ChrX typing in deficiency kinship testing is demonstrated. In the case of investigation, ChrX haplotyping confirmed the claim of the disputed offspring to be related to the deceased putative father.

Keywords: X chromosome; STR; Kinship testing; Haplotyping

1. Introduction

The analysis of deficiency paternity cases belongs to the special challenges in kinship testing.

For solving cases, in which the disputed child is a boy, the procedure of Y chromosome haplotyping is well established. When the disputed child is female, the testing of chromosome X markers may be successful. This paper presents an example of deficiency paternity testing.

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The special power of chromosome X (ChrX) typing in deficiency kinship testing can be explained by summarising the following facts:

Males carry only one ChrX, hence:

- Chromosome X typing in males automatically reveals their haplotype.
- Males transmit their whole chromosome X to their daughters. The paternal ChrX haplotype can be detected in their daughters.
- All sisters share their paternal ChrX haplotype.
- All ChrX alleles not shared by sisters must be of maternal origin.
- ChrX typing of two ore more sisters reveals both their father's ChrX haplotype and large parts of their mother's ChrX genotype.
- ChrX typing of two ore more brothers yields large parts of their mother's ChrX genotypes.
- Furthermore, it is very likely that haplotypes of linkage groups remain stable throughout many generations. Consequently, they are a powerful means to demonstrate kinship.

2. Materials and methods

We were asked to perform a deficiency kinship test as shown in Fig. 1.

To this end, we divided the pedigree into three branches, sections A, sections B and sections C. All members were renamed using names which start with the corresponding initial letters A, B or C.

Claire claimed to be the daughter of the deceased putative father Chris.

Blood samples were available from Claire and her mother Carmen.

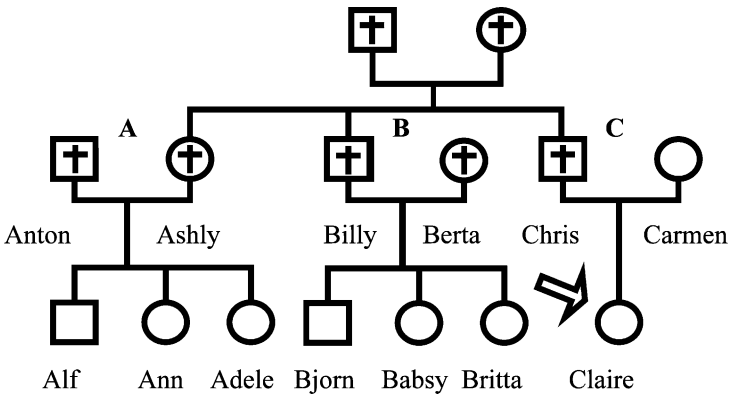

Fig. 1. Pedigree of the family tree investigated. Claire claimed to be the daughter of the deceased father Chris. The pedigree is divided the into three branches, sections A, sections B and sections C. All members were renamed using names which start with the corresponding initial letters A, B and C.

Furthermore, we got samples from Alf, Ann and Adele. These are the children of Ashley who is the deceased sister of Chris. Further samples came from Bjorn, Babsy and Britta. They are the children of Billy. He is the deceased brother of Chris.

All markers used here are shown in the idiogram in Fig. 2 and in the table on top of Fig 3. The appropriate population data were elaborated and published [1].

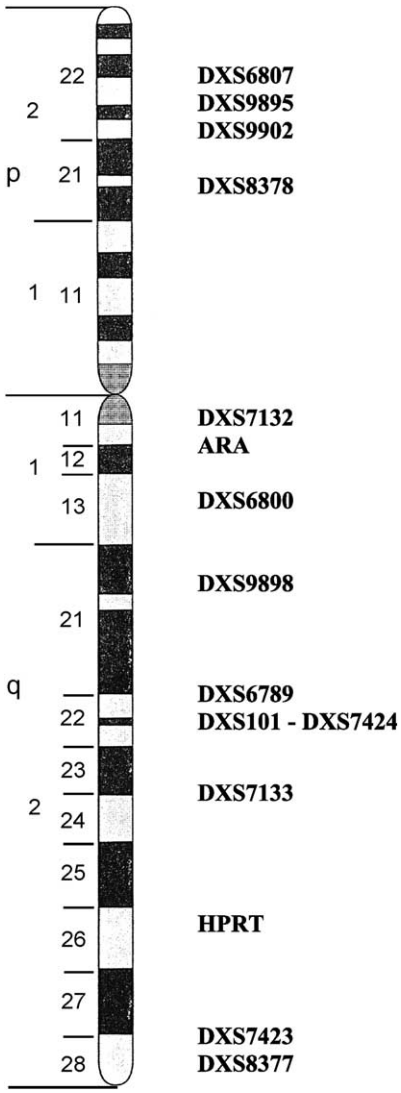

Fig. 2. Chromosome X idiogram containing all markers used in the present case.

3. Results and discussion

We start the explanation of our results with the regions Xq 21.3 to Xq22 since here we have a very transparent situation. The markers located here are DXS101[J] and

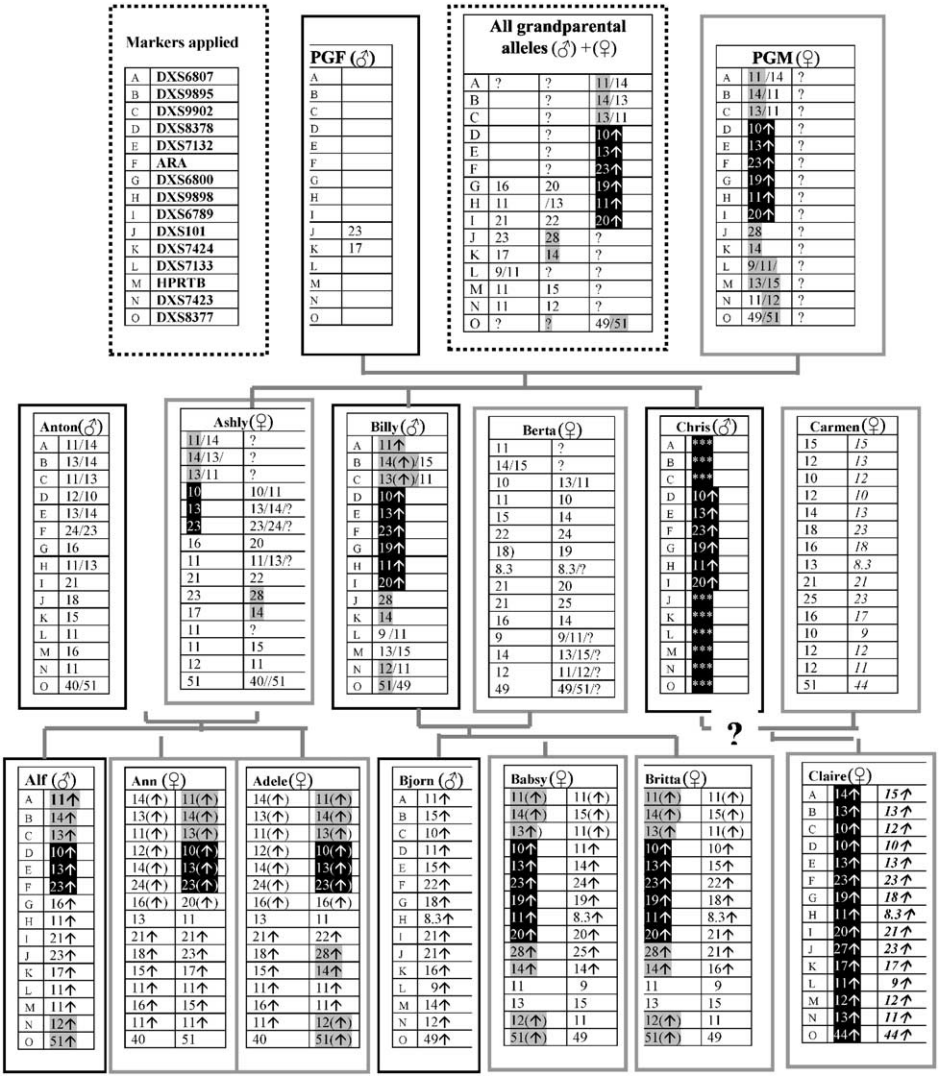

Fig. 3. Kinship testing using ChrX haplotyping. The examination of the pedigree depicted here proved that the disputed offspring (Claire) and two putative cousins (Babsy and Britta) share the same ChrX haplotype spanning the region Xp21 to Xq21 (marked black). All ChrX markers used are listed in alphabetical order, Symbol: ↑ [phase known]; (↑) [assumed phase]; black marked figures [Claire's paternally inherited haplotype]; grey marked figures [grandmaternally inherited haplotype assumed]; slash between allele numbers (e.g. 11/14) [two different alleles are possible (e.g. 11 or 14)].

DXS7424^{K}. They are closely linked, and are separated only by about 1 cM, resulting in very stable haplotypes. Claire inherited the haplotype $27^{J}-17^{K}$ from her father. None of Claire's alleged cousins carry this haplotype. Hence, there is no indication of any relationship. We can reconstruct the grandmaternal genotype to check it for a relationship exclusion.

Babsy and Britta share the $28^{J}-14^{K}$ haplotype. Therefore, this haplotype must be a haplotype of the grandmother passed on via Billy. The different haplotypes $25^{J}-14^{K}$ and $21^{J}-16^{K}$ were inherited by Berta.

In branch A, Ann and Adele share the haplotype $18^{J}-15^{K}$ which must have been passed on by their father Anton. The different haplotypes $23^{J}-17^{K}$ and $28^{J}-14^{K}$ must have been inherited by Ashly. This is partially confirmed by Alf. He carries the haplotype $23^{J}-17^{K}$ which must be maternal. As can be seen, we can only find two of the three grandparental haplotypes and cannot exclude a relationship between Claire and their alleged cousins. Analysis of the region Xp22 which contains the markers DXS6807^{A}, DXS9895^{B} and DXS9902^{C} are shown below. Unfortunately, Babsy and Britta carry identical alleles in all STRs^{A-C}. Hence, we cannot easily distinguish between their inherited paternal and maternal haplotypes. In addition, we do not know the phase. Claire's paternal DXS9902^{C} allele is 10^{C}. Only Bjorn carries allele 10^{C}, but Bjorn inherited his ChrX from his mother Berta who is not related to the alleged father Chris.

All cousins in section A and section B, who are related to Chris via an X chromosomal line, carry the rare allele 13. Its frequency is less than 1%. This indicates that the grandmother probably gave the DXS9902^{C} allele 13^{C} to Ashly and to Billy. Billy transferred it to Babsy and Britta. Ashly passed it on to all her children. Thus, it is very likely that one of the grandmaternal allele is 13^{C}, and the grandmaternal haplotype is $11^{A}-14^{B}-13^{C}$. As the grandmother transmitted the same Xp22 haplotype to branch A and branch B, we are not able to identify both Xp22 hapolotypes. Summarising the results from the Xp22 analysis, there is no indication of any relationship between Claire and her alleged cousins, but a relationship cannot be excluded as one of the grandmaternal haplotypes has remained unidentified.

The region Xq26 to Xq28 was analysed by typing four markers (markers L–O in Fig. 3). Again, the typing results were not indicative of a relationship; however, such relationship cannot be excluded.

The data suggest that the grandmother transferred the same haplotype to Ashly and to Billy. Therefore, one of the grandparental haplotypes of this region remains unknown. Due to crossing-overs occurring in this region, the situation cannot be fully clarified.

For examining the region Xp21 to Xq21.6, markers (D–I) were typed. In Fig. 3, Claire's paternally inherited haplotype is flagged black. In section B, we could completely identify all haplotypes involved. Babsy and Britta share the haplotype marked black. This must be their grandmaternal haplotype passed on via Billy. All markers involved in this haplotype are not influenced by a linkage disequilibrium (this is a fact we could establish by studying 210 male X chromosomes). Consequently, the haplotype frequency can be calculated by multiplying the frequencies of the single alleles. Allele frequencies of a German sample are published for all X chromosomal markers used in the present case [1].

The haplotype frequency in German X chromosomes is 0.00035 or about 1 in 2800. ChrX haplotyping in the case under investigation confirmed the claim of Claire to belong to the deceased putative father's relationship.

Reference

[1] J. Edelmann, S. Hering, M. Michael, R. Lessig, D. Deichsel, G. Meier-Sundhausen, L. Roewer, I. Plate, R. Szibor, 16 X chromosomal STR loci frequency data from a German population, Forensic Sci. Int. (in press).