Detection of fetal cells in transcervical samples using X22 marker

Editor—The presence of trophoblastic cells in the endocervical canal of pregnant women between 5 and 13-15 weeks of gestation has been repeatedly confirmed.1,2 Using fluorescence in situ hybridisation (FISH) or the polymerase chain reaction (PCR) assay, chromosome Y derived sequences have been detected in transcervical cells (TCCs) retrieved from mothers with male fetuses. Although small tandem repeats (STRs) and quantitative fluorescent PCR (QF-PCR) have also been used to monitor the presence in TCC samples of fetal DNA sequences inherited from the father and absent in the mothers,1,3 the direct and unequivocal demonstration of trophoblastic cells derived from female fetuses has been hampered by the unavailability of highly polymorphic markers specific for the X and Y chromosomes.

In this pilot study, we have assessed the diagnostic value of using a new X/Y chromosome marker, X22,4 for the detection of trophoblastic cellular elements released into the endocervical canal by female fetuses. After receiving verbal consent, samples were retrieved by cervical mucus aspiration1 from four pregnant women, at about 10 weeks of gestation, before termination of pregnancy. Maternal peripheral blood and chorionic tissues were also collected. Aliquots of TCC samples were suspended in phosphate buffered saline (PBS) and analysed under an inverted microscope in order to isolate clumps of cells with the morphological characteristics of syncytial or cytotrophoblastic cellular elements.

DNA extracted from chorionic tissue, individual clumps of TCC cells, and maternal blood samples, was then tested using single or multiplex QF-PCR assay and STRs specific for chromosomes 21, 18, and 13 besides the amelogenin (AMXY) and hypoxantine-guanine-phosphoribosyl transferase (HPRT) markers for sexing.5 All samples were tested with the highly polymorphic X22 pentanucleotide (AAATA) repeat that maps in the PAR2 region of homologous chromosomes.

Table 1: Maternal blood, CVS, and TCC samples tested by QF-PCR with X22 and other STR markers. All the mixed (fetal + maternal) clumps have skewed fluorescent peak ratios between the STRs alleles.

| Sample          | AMXY | X22 | HPRT | D21S1411 | D13S634 | D18S386 | Comments            |
|-----------------|------|-----|------|----------|---------|=========|---------------------|
| HW (mat blood)  | XX   | 223 | 284  | 282      | 474-488 | 352-376 |                    |
| CVS             | XX   | 218-223 | 276-284 | 282      | 474-482 | 350-376 |                    |
| TCC clumps 1,2,5,6 | XX   | 223 | 284  | 282      | 474-488 | 352-376 |                    |
| TCC clumps 3,4  | XX   | 218-223 | 276-284 | 282      | 474-482 | 350-376 |                    |
| P G (mat blood) | XX   | 223 | 284  | 282      | 474-482 | 372     |                    |
| CVS             | XX   | 203-228 | 284-288 | 290-298 | 478-482 | 372     | Maternal           |
| TCC clumps 1,3  | XX   | 223-233 | 284-288 | 290      | 466-478 | 372-376 | Fetal              |
| TCC clamp 2     | XX   | 203-228-223 | 284-288 | 290-298 | 466-478 | 372-376 | Fetal + maternal   |
| TCC clamp 4     | XX   | 203-228 | 284-288 | 290      | 466-478 | 372-376 | Fetal              |
from these clumps can be used for the prenatal diagnosis of inherited single gene disorders. The X22 pentanucleotide repeat is also of diagnostic value for the detection of cells present in maternal blood derived from female fetuses.

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Figure 1  (A) Electrophoretogram of maternal, CVS, and TCC clump tested with X22, AMXY, and HPRT markers and other autosomal STRs (see text). (B) Electrophoretogram of maternal, CVS, and TCC clump tested with X22 and HPRT markers.

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J Med Genet 2000 37: e1
doi: 10.1136/jmg.37.5.e1

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