

# An unusual derivative Y chromosome identified at prenatal diagnosis

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## Clinical Details

A CVS was taken from a 29 year old female at 12 weeks gestation following a combined nuchal translucency and first trimester biochemistry risk for trisomy 21 of 1 in 30. The nuchal translucency measurement was 2mm, free  $\beta$ HCG was 2.25MoM and PAPP-A was 0.27MoM. Fluorescence in situ hybridisation studies on uncultured interphase nuclei from the CV sample were consistent with one X chromosome signal, one Y chromosome signal and normal copy number for chromosomes 13, 18 and 21.

## Cytogenetic Studies

Chromosome analysis of the cultured chorionic villus showed one normal X chromosome and an abnormal Y chromosome derived from the translocation of most of the long arm of an X chromosome to the long arm of the Y chromosome at q11.2 in all cells examined (figure 1). FISH studies demonstrated that the XIST locus (Xq13.2) and the SRY locus (Yp11.3) were present on the derivative Y chromosome (figure 2). The presence of the derivative Y chromosome was confirmed in an amniotic fluid sample and parental karyotypes were normal.

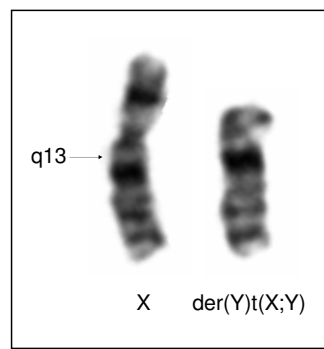


Figure 1: derivative Y chromosome composed of the Y chromosome short arm and proximal long arm (Ypter to q11.2) and most of the long arm of the X chromosome (Xq13 to Xqter)

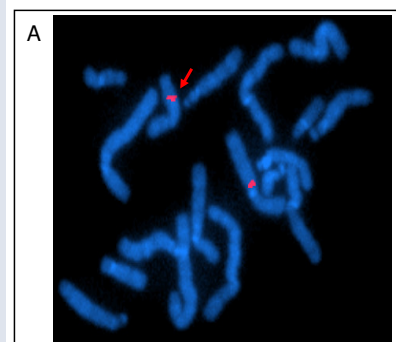


Figure 2A: **RP11-13M9** (XIST, Xq13) present on normal X and derivative Y chromosome (→).

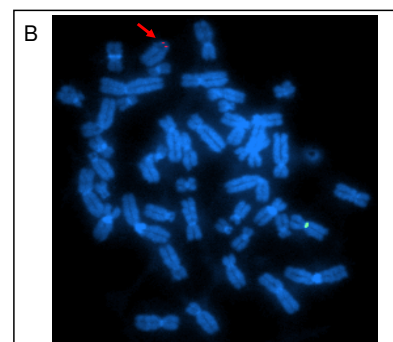


Figure 2B: **SRY** (Yp11.3) present on derivative Y chromosome (→).

**Full karyotype:** 46,X,der(Y)t(X;Y)(q13;q11.2)dn.ish der(Y)t(X;Y)(q13;q11.2)(SRY+,XIST+)

## Discussion

The presence of the SRY locus is usually associated with the development of a male fetus, however the abnormal Y chromosome in this case also contains the X inactivation centre (XIST), and would be expected to be subject to X chromosome inactivation. This inactivation may spread from the X chromosome segment into the Y chromosome short arm and affect the activity of the SRY locus. If this fetus develops as a female, the presence of Y chromosome derived material will increase the risk of germ cell tumours.

We have found one similar case in the literature (Lissoni et al., 2009). The female described showed no dysmorphism, no external or internal genital ambiguity, normal height, weight and mammary development. Further clinical features included the development of a germ cell tumour at age 10 and menarche at age 13 followed by ovarian failure a few months later.

Due to the scarcity of previous published cases, and the uncertainty over the extent of spreading of X inactivation, the outlook for this pregnancy, particularly with regards to gender, was unclear. However, the pregnancy is ongoing and on 2D and 3D ultrasound scanning at 28 weeks the fetal genitalia are clearly female and amniotic fluid, fetal growth and movements are normal.

**Reference:** Lissoni et al., Chromosome territories, X;Y translocation and premature ovarian failure: is there a relationship?, *Molecular Cytogenetics*, 2:19, 2009