

A complex rearrangement involving chromosomes 7, 11 and 13 which became an apparently balanced 7;13 translocation in one generation.

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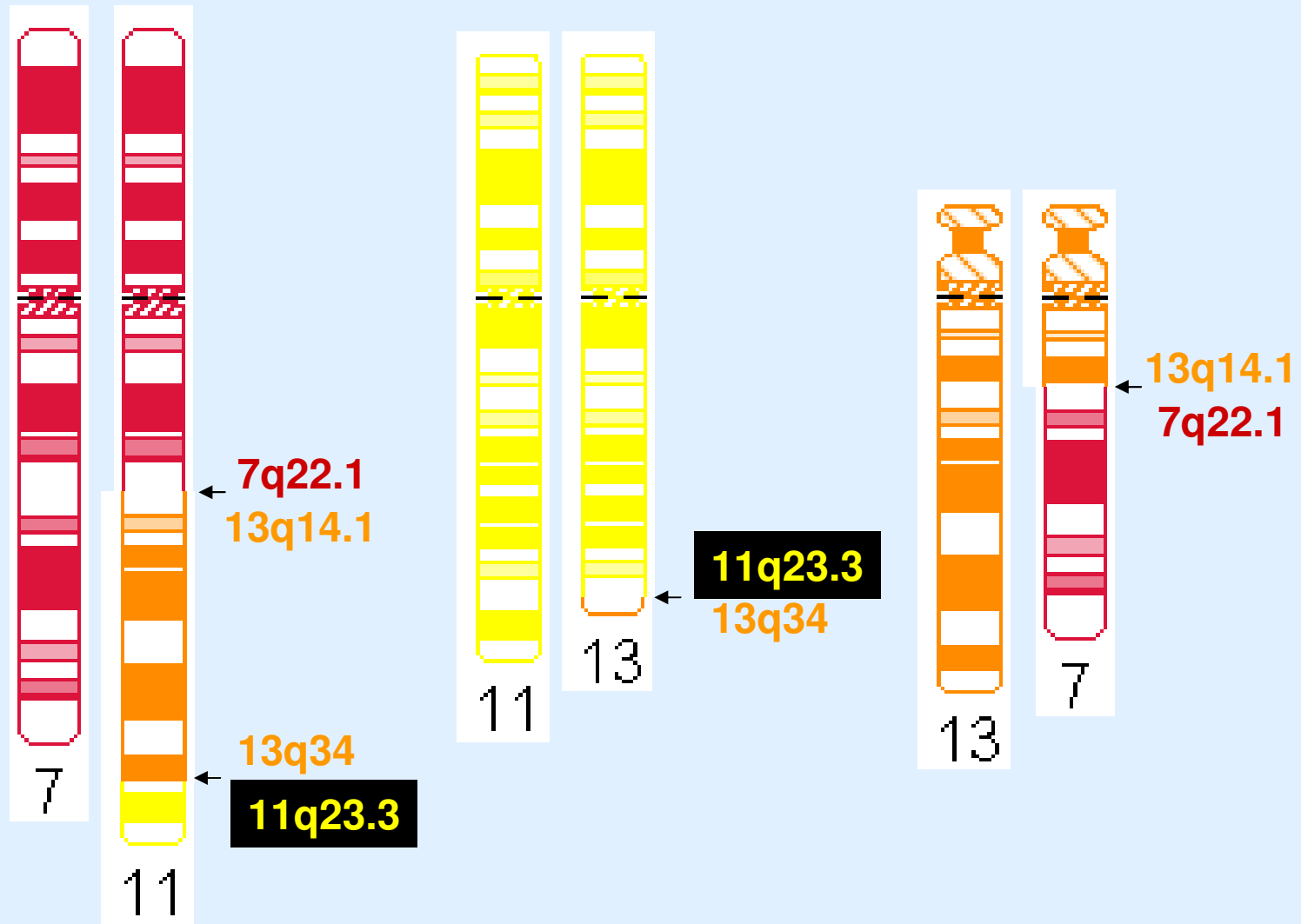
Patient AB

- Referred in 1998 at age 24 years having had seven early (<8 weeks) miscarriages over four years
- Blood karyotype showed a complex chromosomal rearrangement involving chromosomes 7, 11 and 13

Patient AB



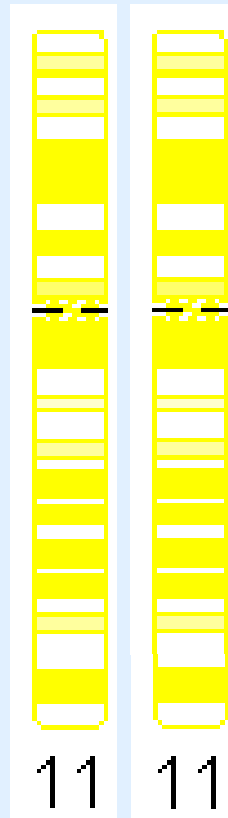
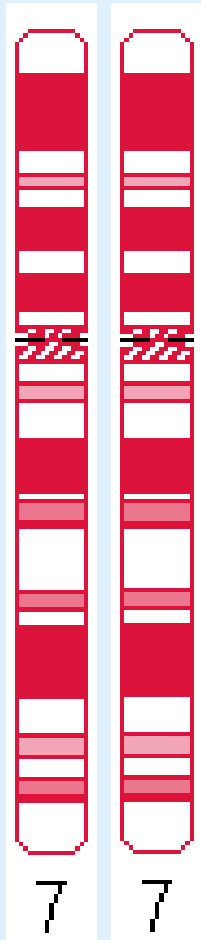
Patient AB



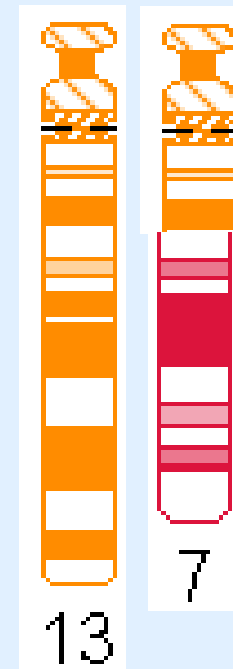
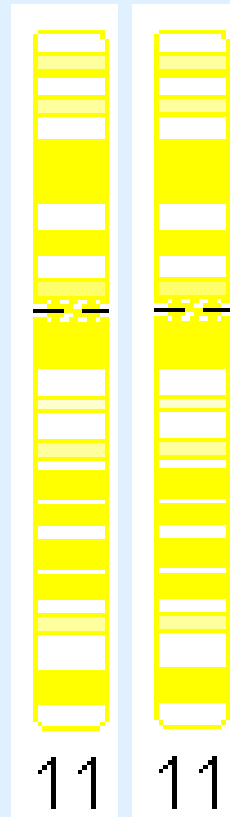
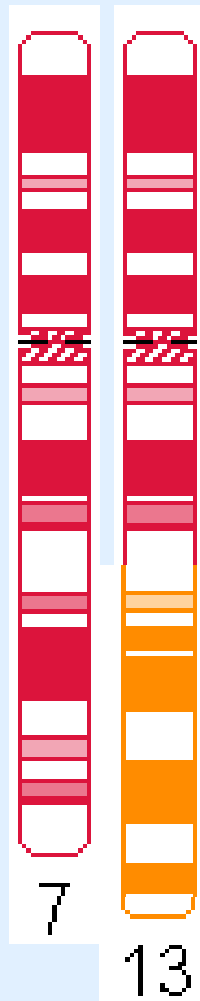
Complex chromosomal rearrangements

- Rare
- Three or more chromosomes or breaks
- Cause problems at meiosis
- May be balanced or unbalanced
- Three major categories:
 - Three-way exchange (three breakpoints)
 - Double two-way exchange (four breakpoints)
 - More complicated rearrangements

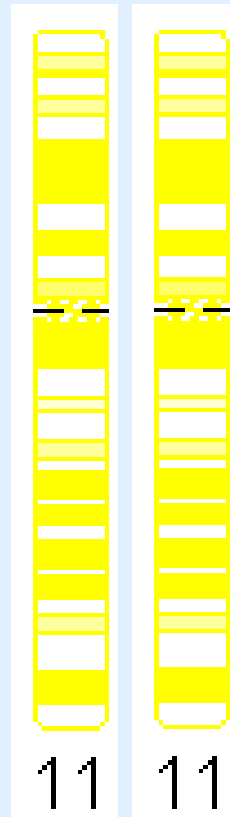
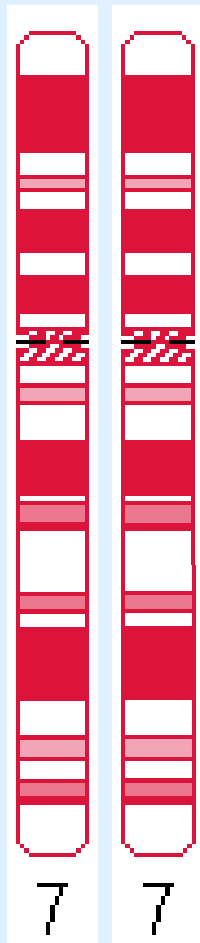
Double two-way exchange “a”



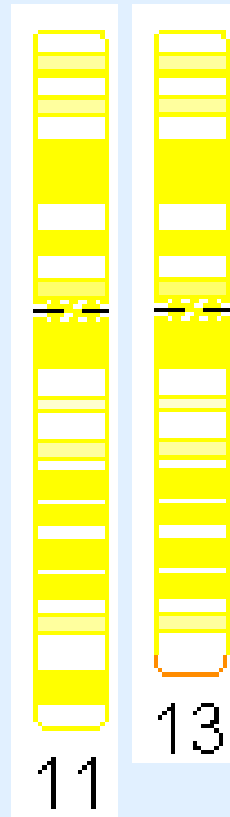
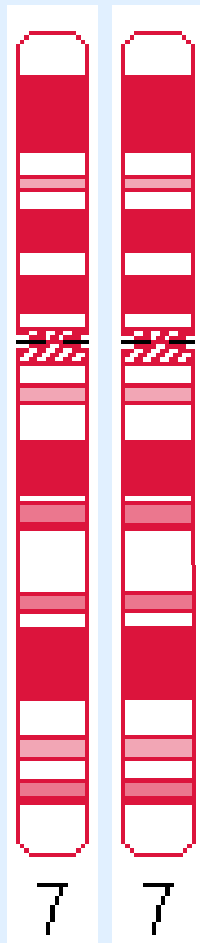
Double two-way exchange “a”



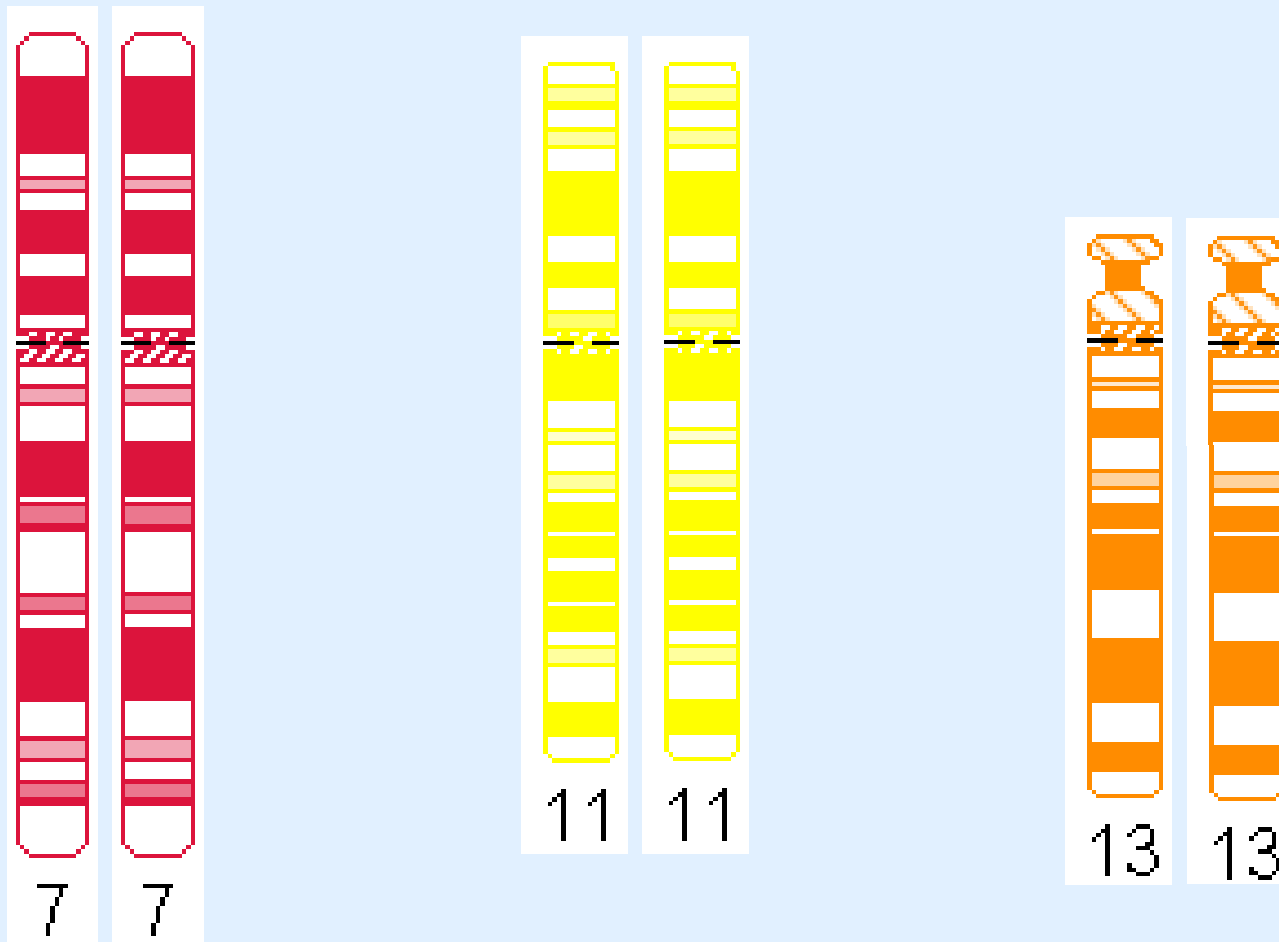
Double two-way exchange “b”



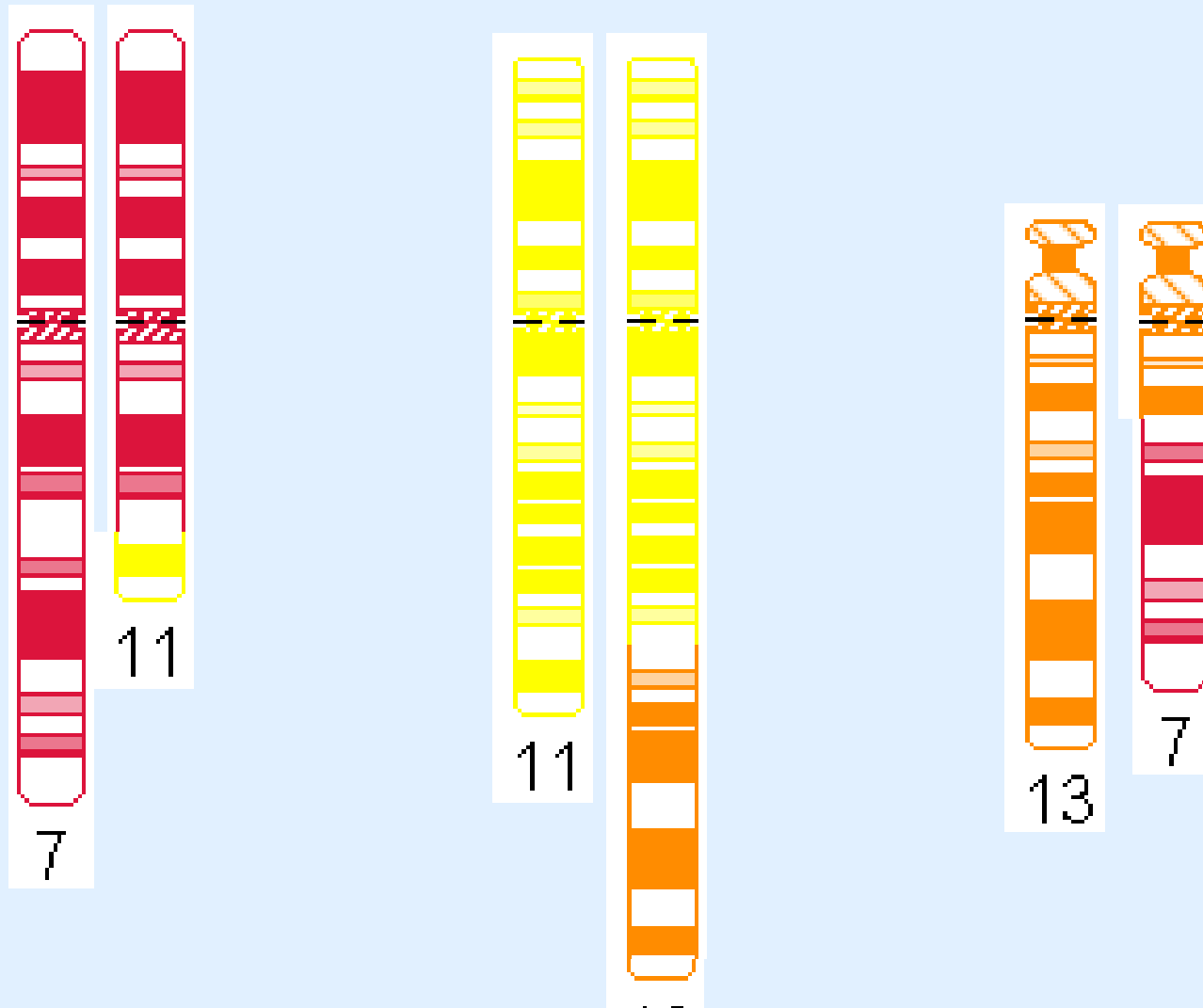
Double two-way exchange “b”



Three-way translocation with insertion



Three-way translocation with insertion



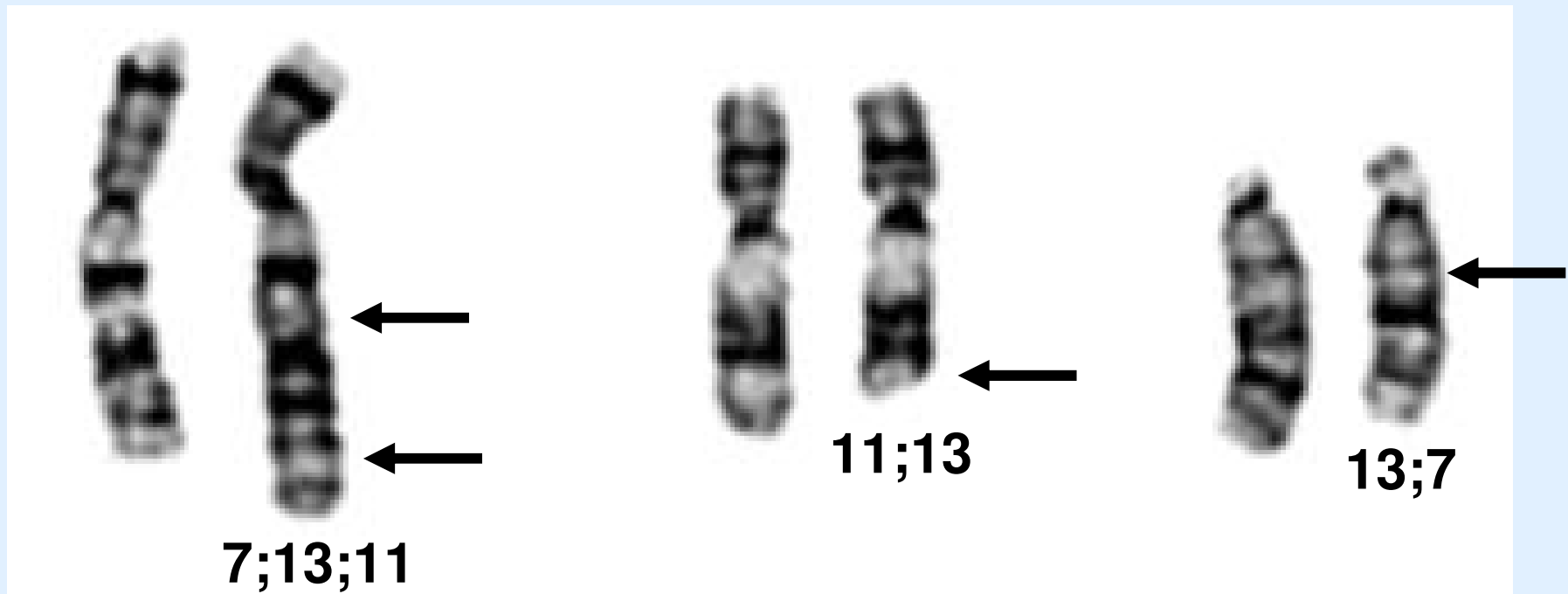
Patient AB

- 46,XX,der(7)t(7;13)(q22.1;q14.1)t(11;13)(q23.3;q34), der(11)t(11;13)(q23.3;q34), der(13)t(7;13)(q22.1;q14.1)
- Referred in 1998 with recurrent miscarriages (x7) but no other medical history of note
- Further miscarriage at 11-12 weeks in April 2000
- CVS in September 2000 (46,XX), baby delivered at 39 weeks

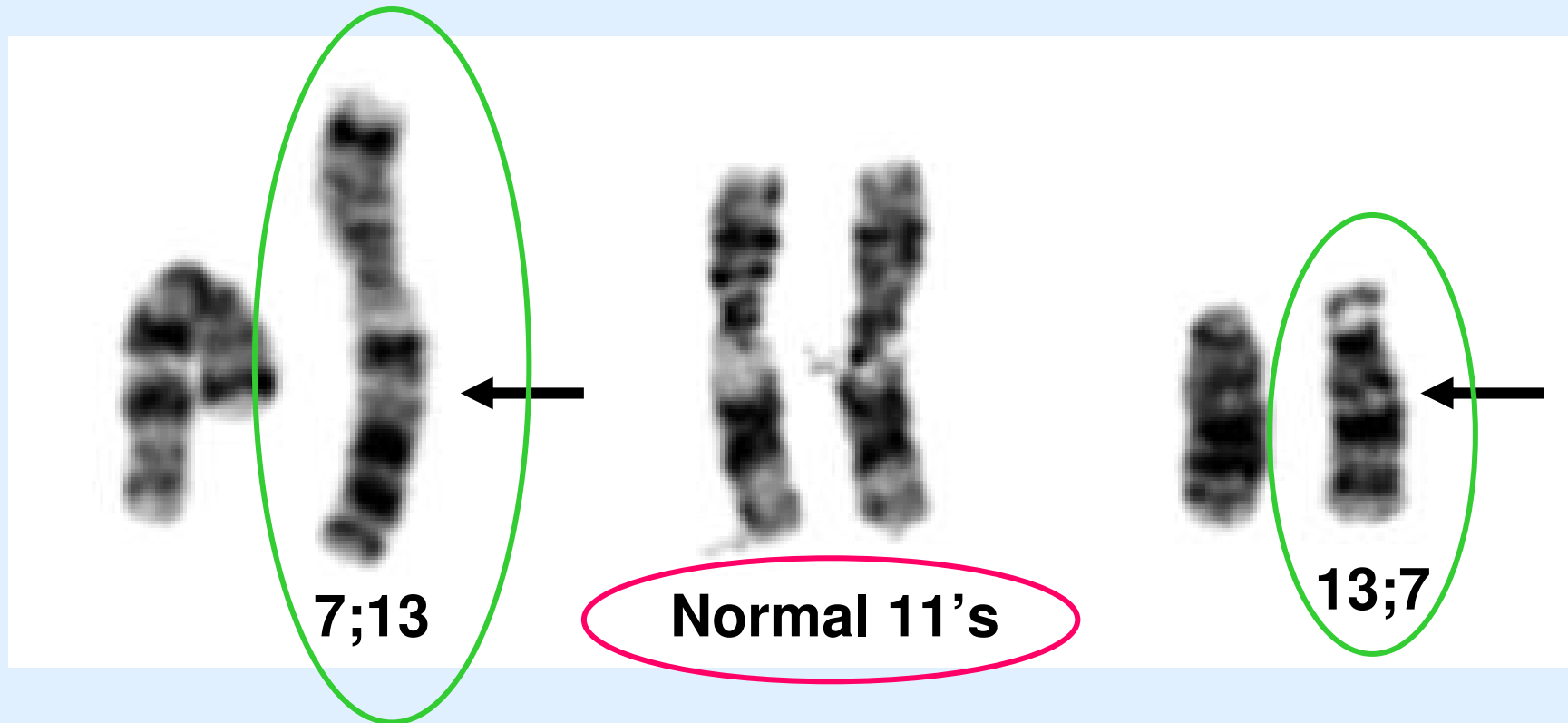
Recent pregnancy

- CVS received in May 2010 (12+1 weeks gestation) – mother now 36 years old
- Apparently balanced karyotype but not the same as the mother!

Mother

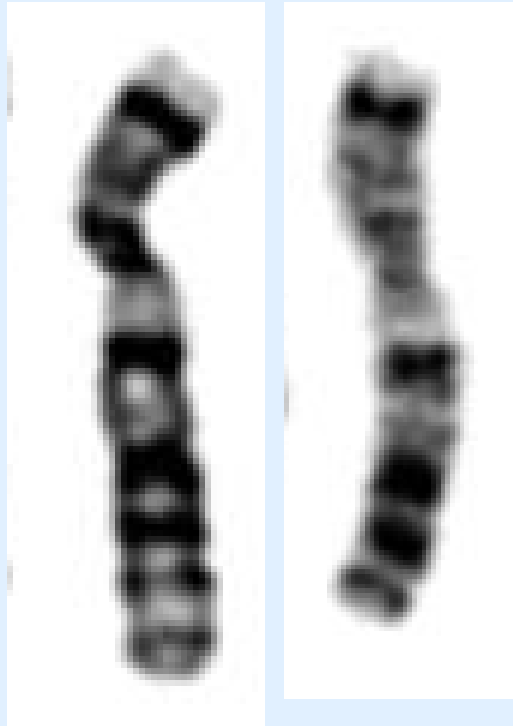


CVS



Different derivative 7's!

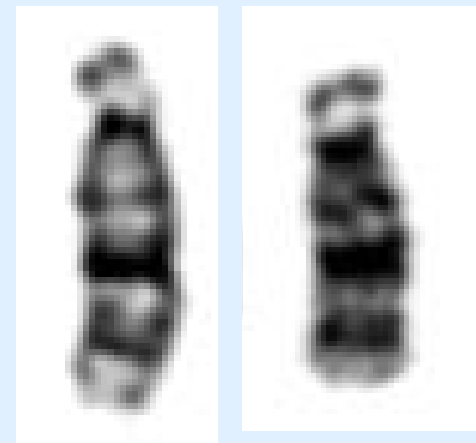
Different der(7)'s



Mother

CVS

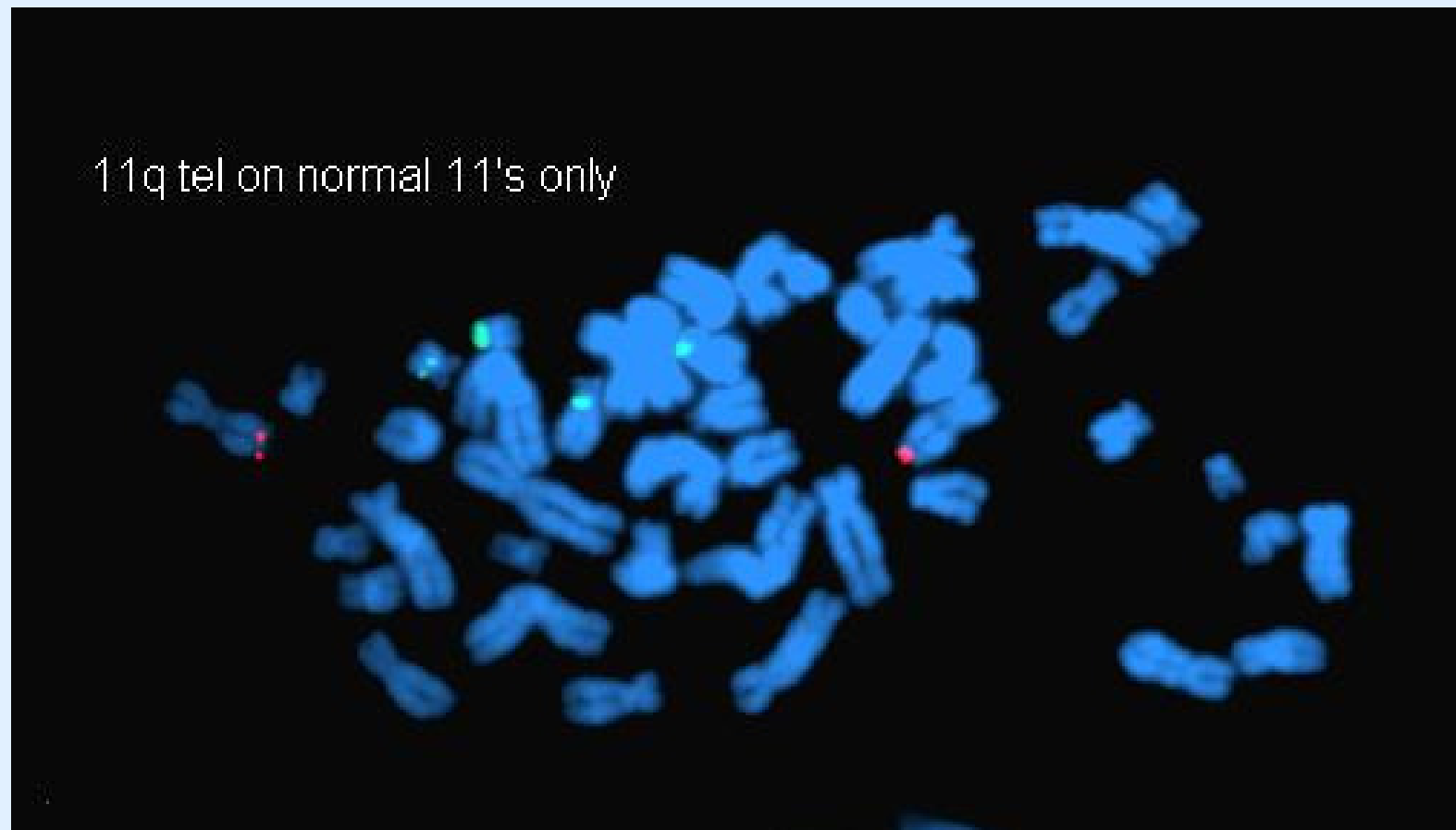
Same der(13)'s



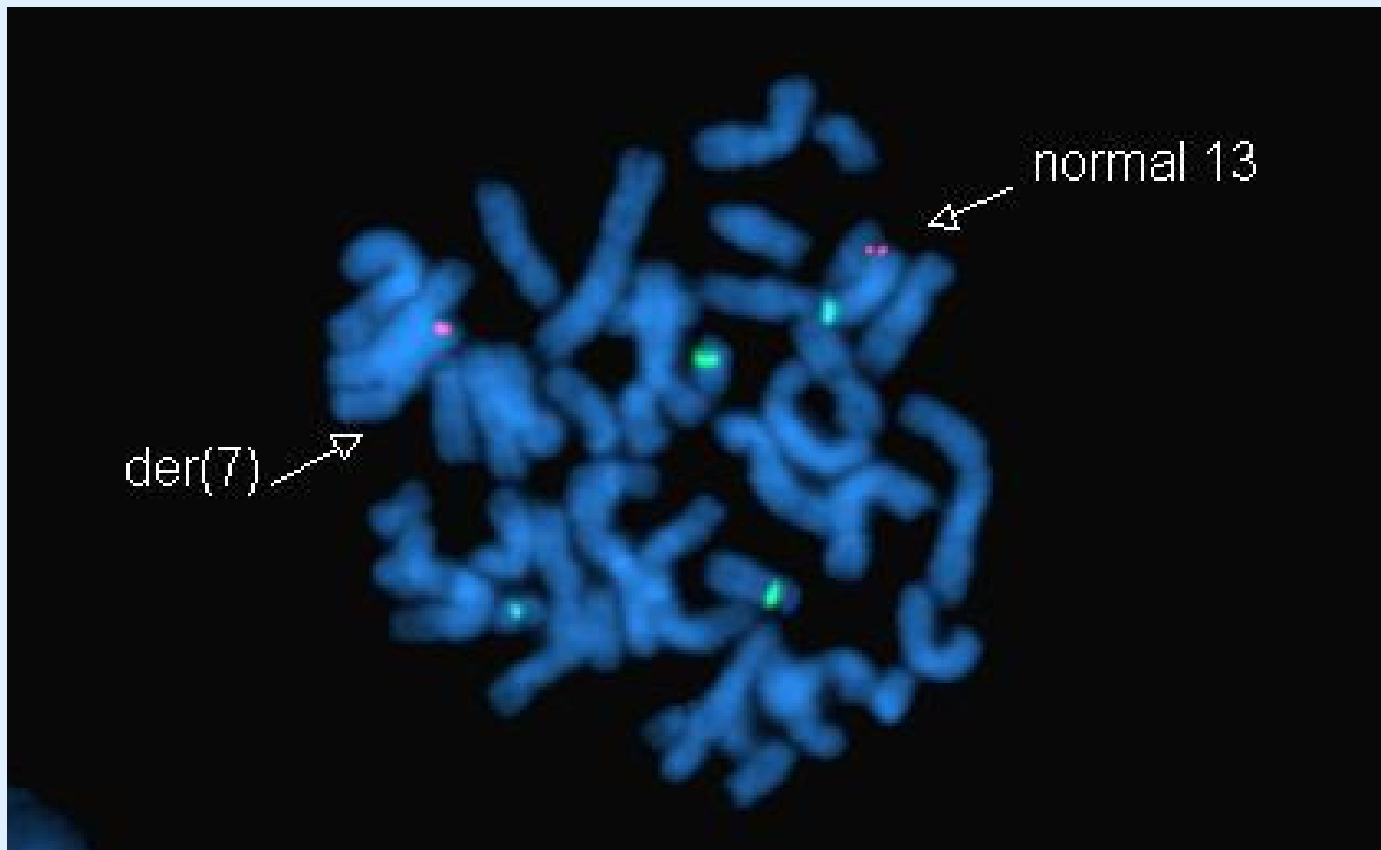
Mother

CVS

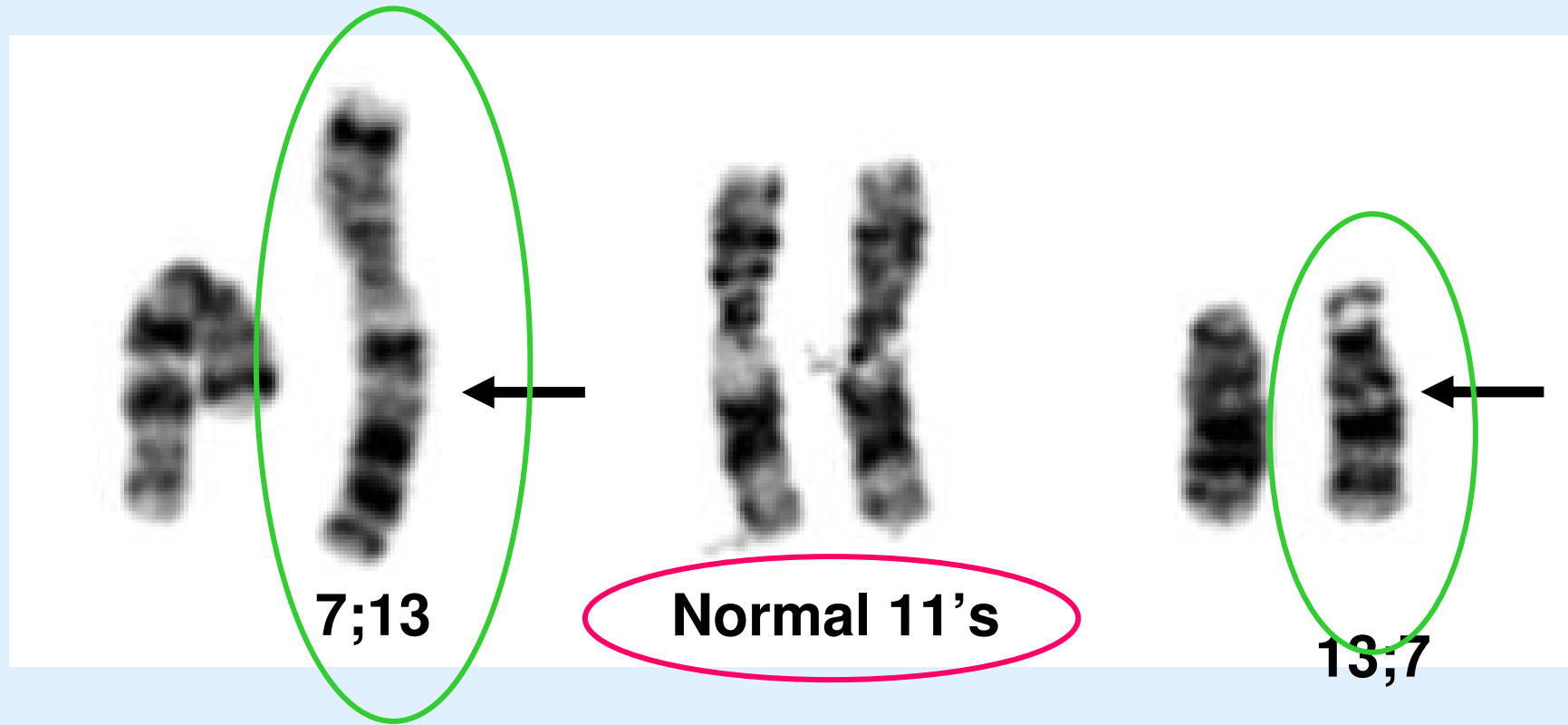
11q tel FISH



13q tel FISH



CVS



t(7;13)(q22.1;q14.1)

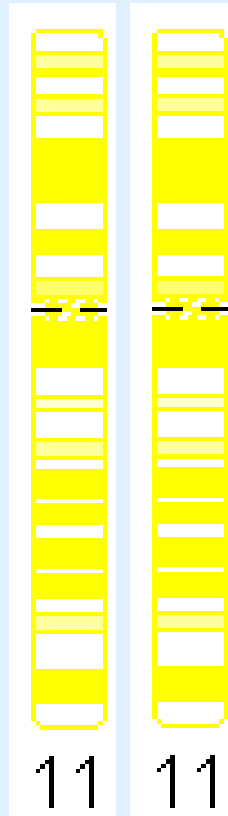
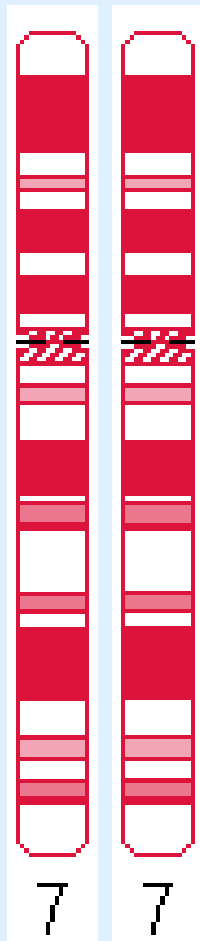
How could this happen?

- Two possible mechanisms:
 - a) Gonadal mosaicism
 - b) Meiotic recombination

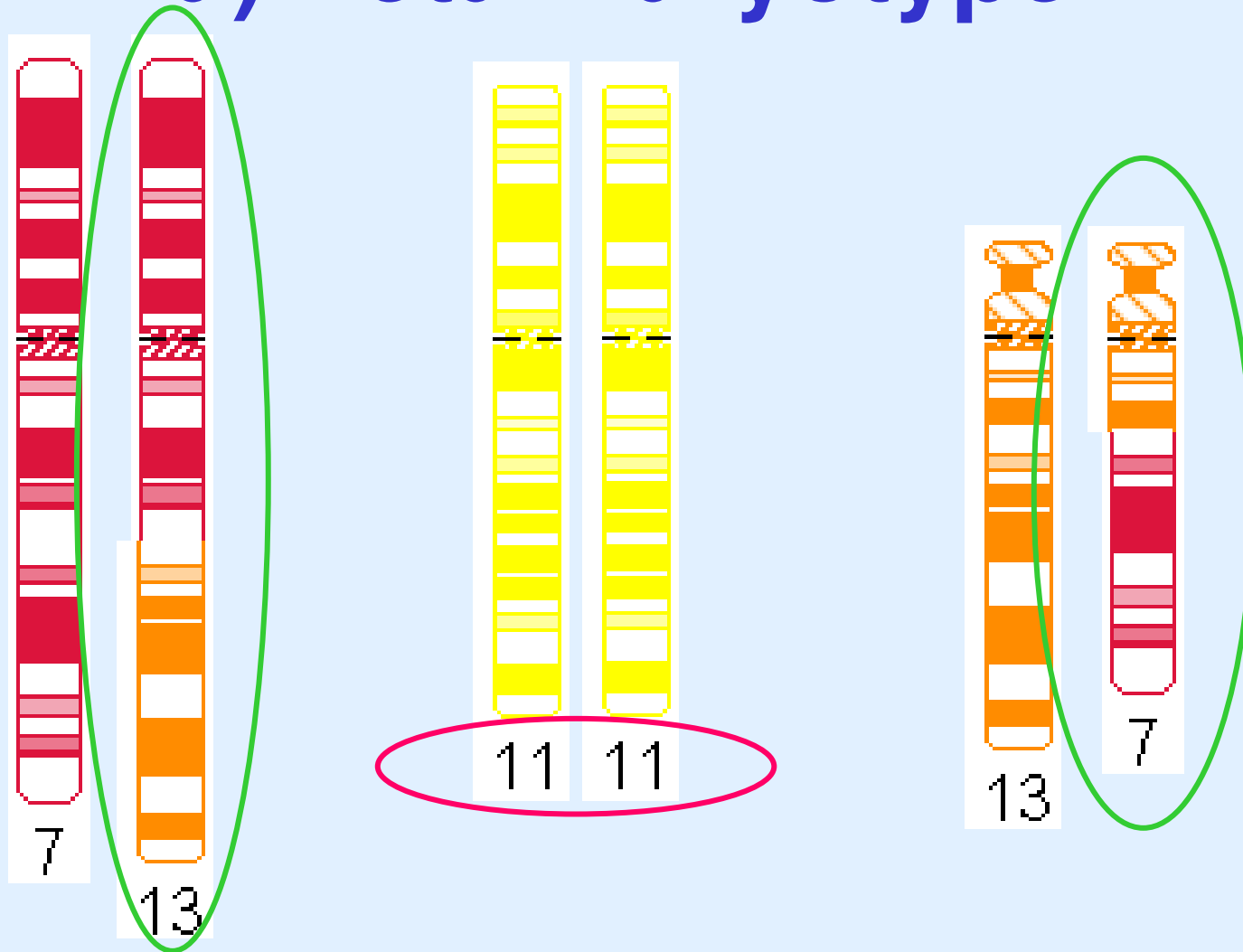
a) Gonadal mosaicism

- ?Mother is a gonadal mosaic carrying both the 7;13 translocation cells and 7;11;13 translocation cells
- Two separate simple reciprocal translocations coinciding

a) Gonadal mosaicism



a) Fetal karyotype

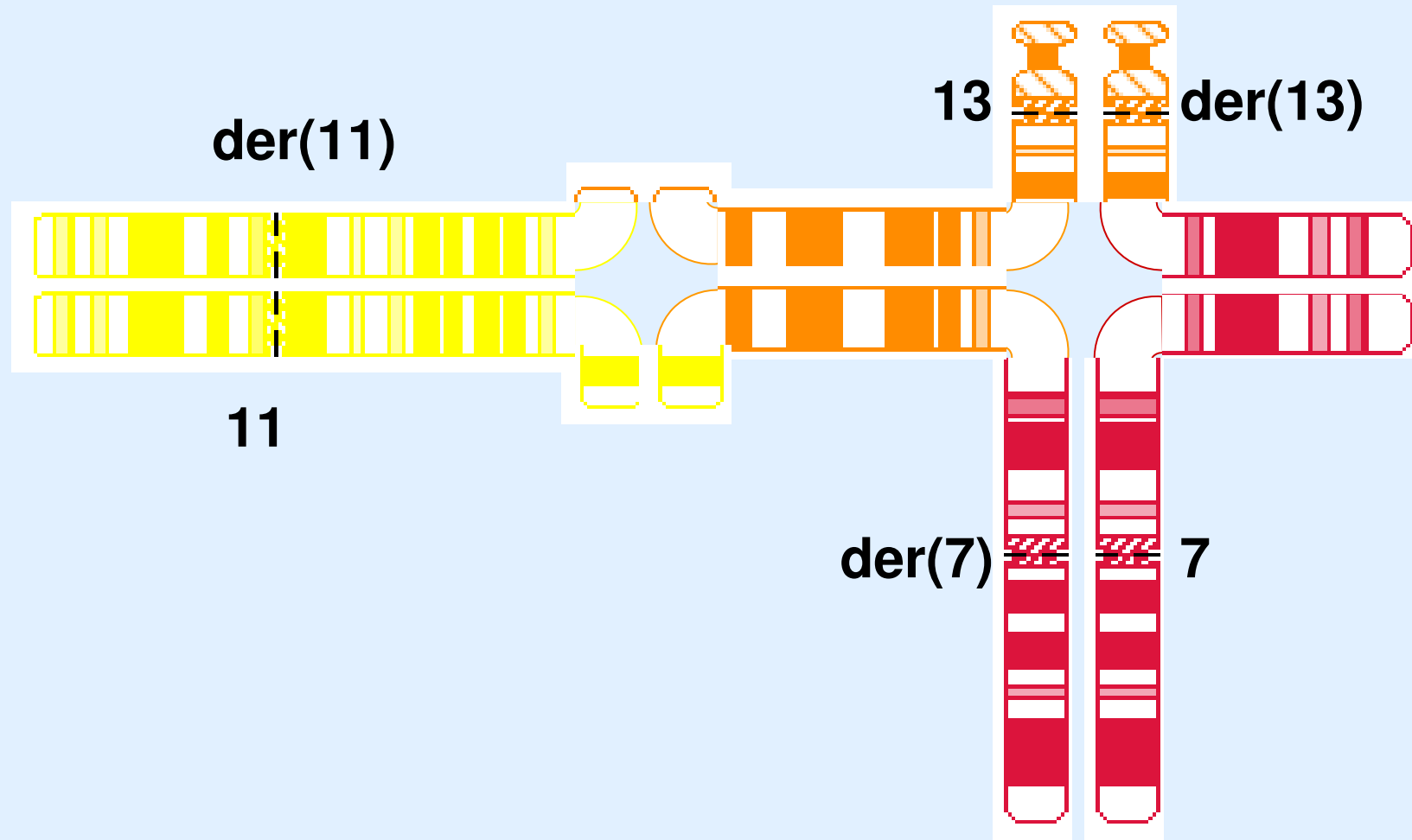


- No evidence of mosaicism in blood sample
- Parental samples not available
- ?test other tissues
- Buccal sample not helpful as metaphases are required to identify the balanced rearrangement

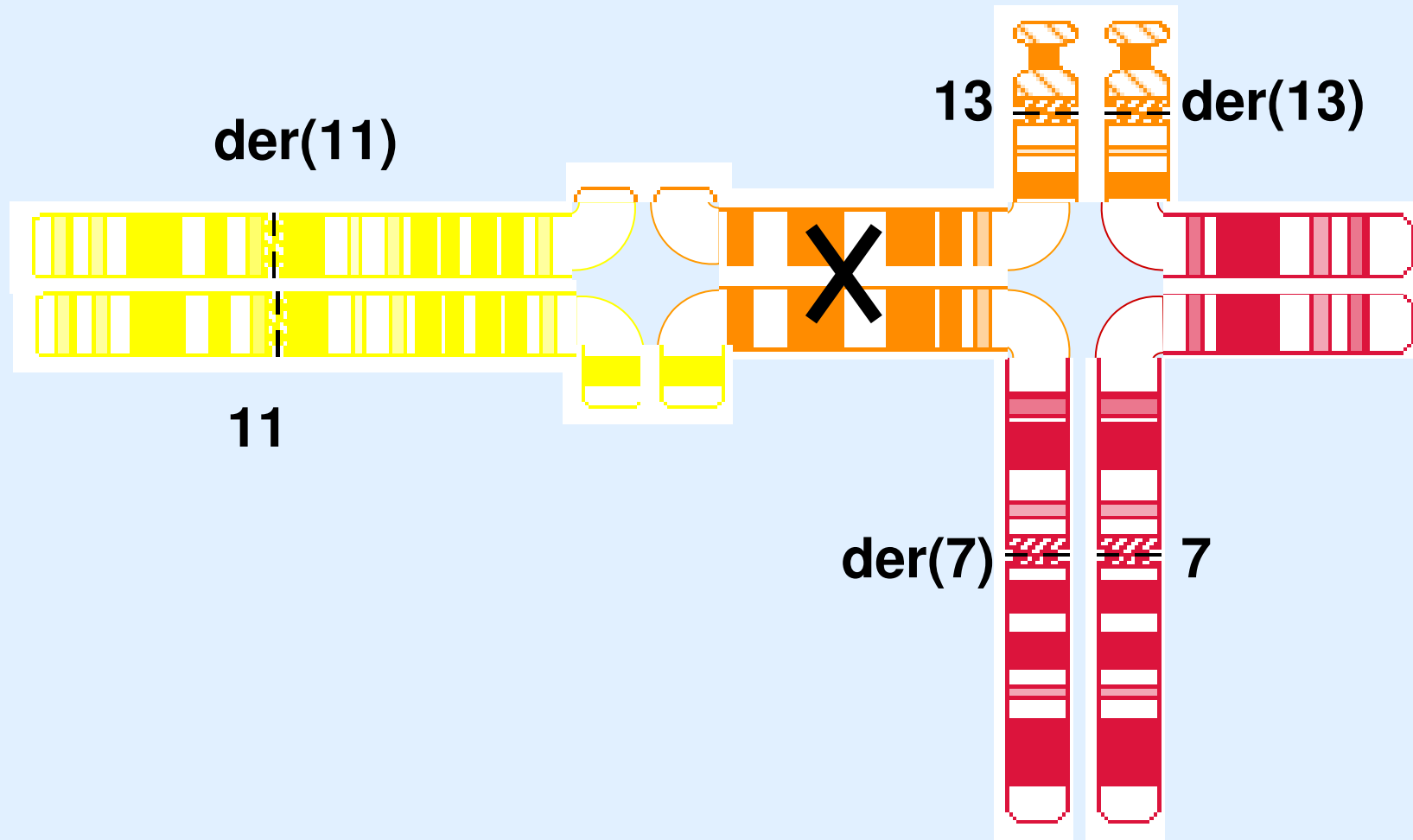
b) Meiotic recombination

- A normal process in gamete formation
- Cross-overs between homologous chromosomes hold bivalents together and create genetic variation
- Rearranged chromosomes pair with each other to create quadrivalents or in this case, a hexavalent

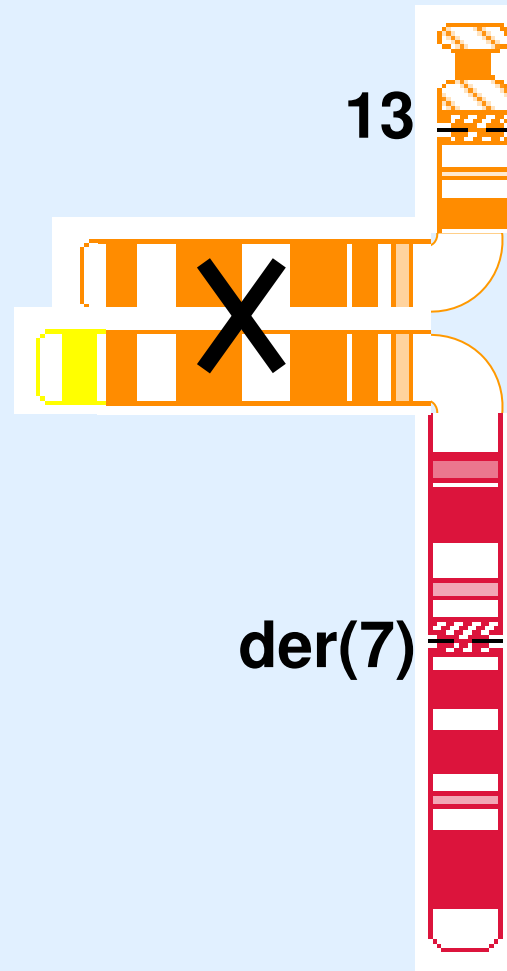
b) Meiotic recombination



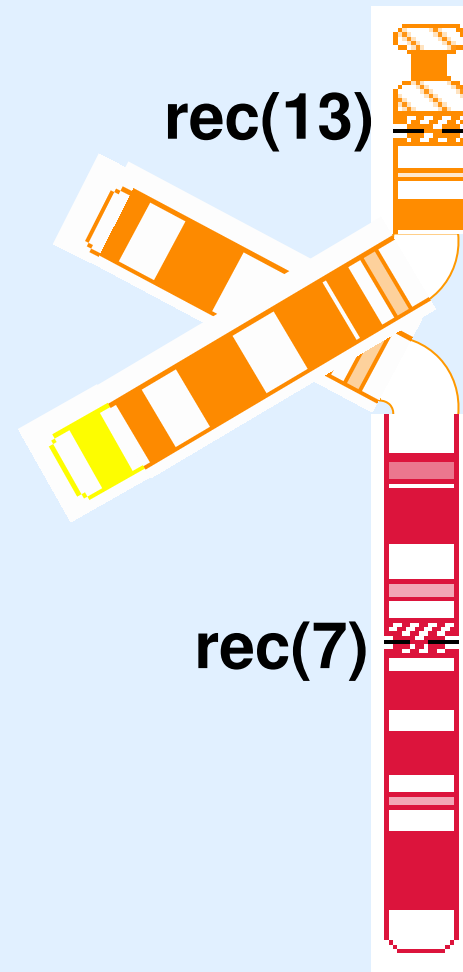
b) Meiotic recombination



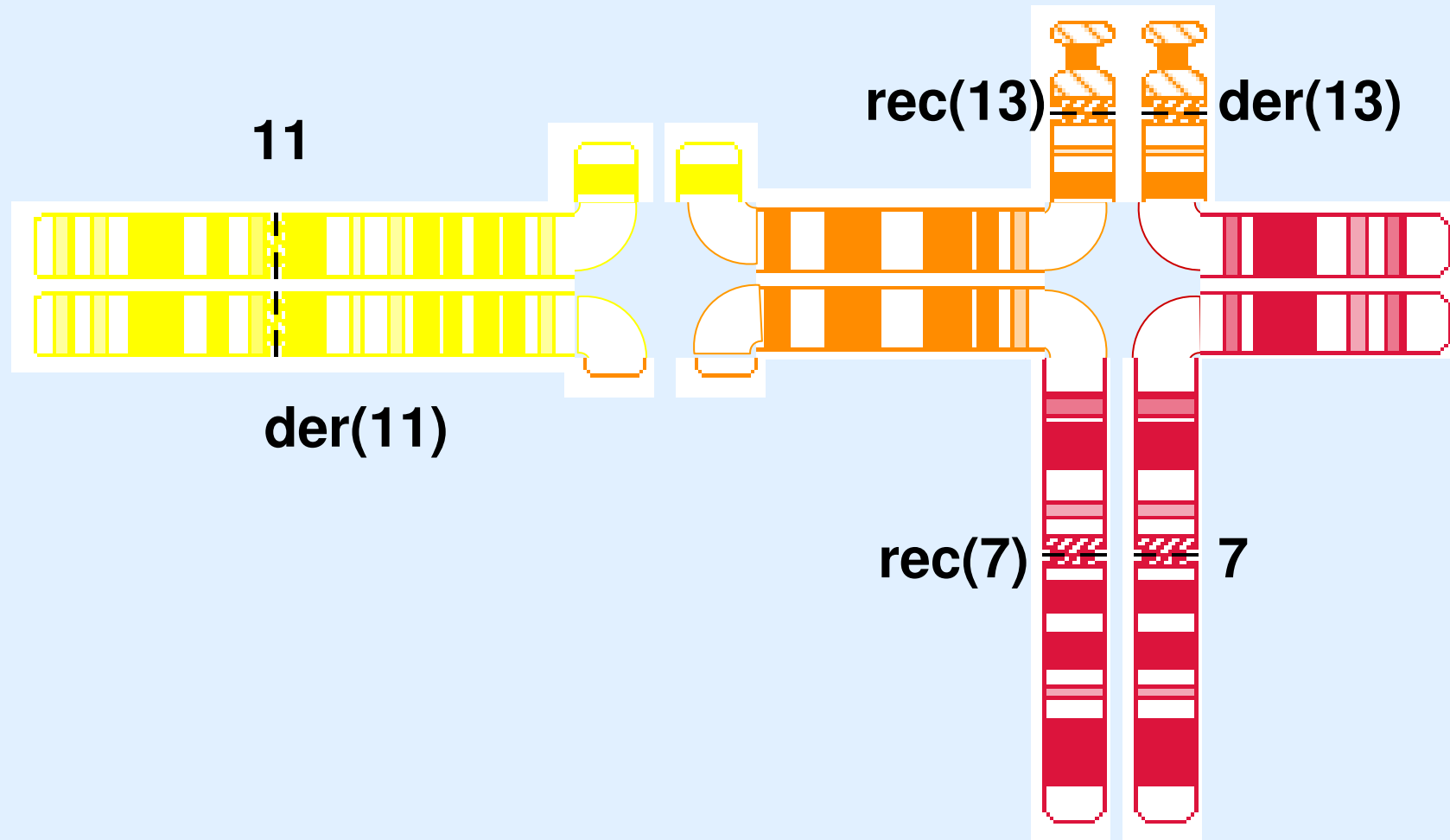
b) Meiotic recombination



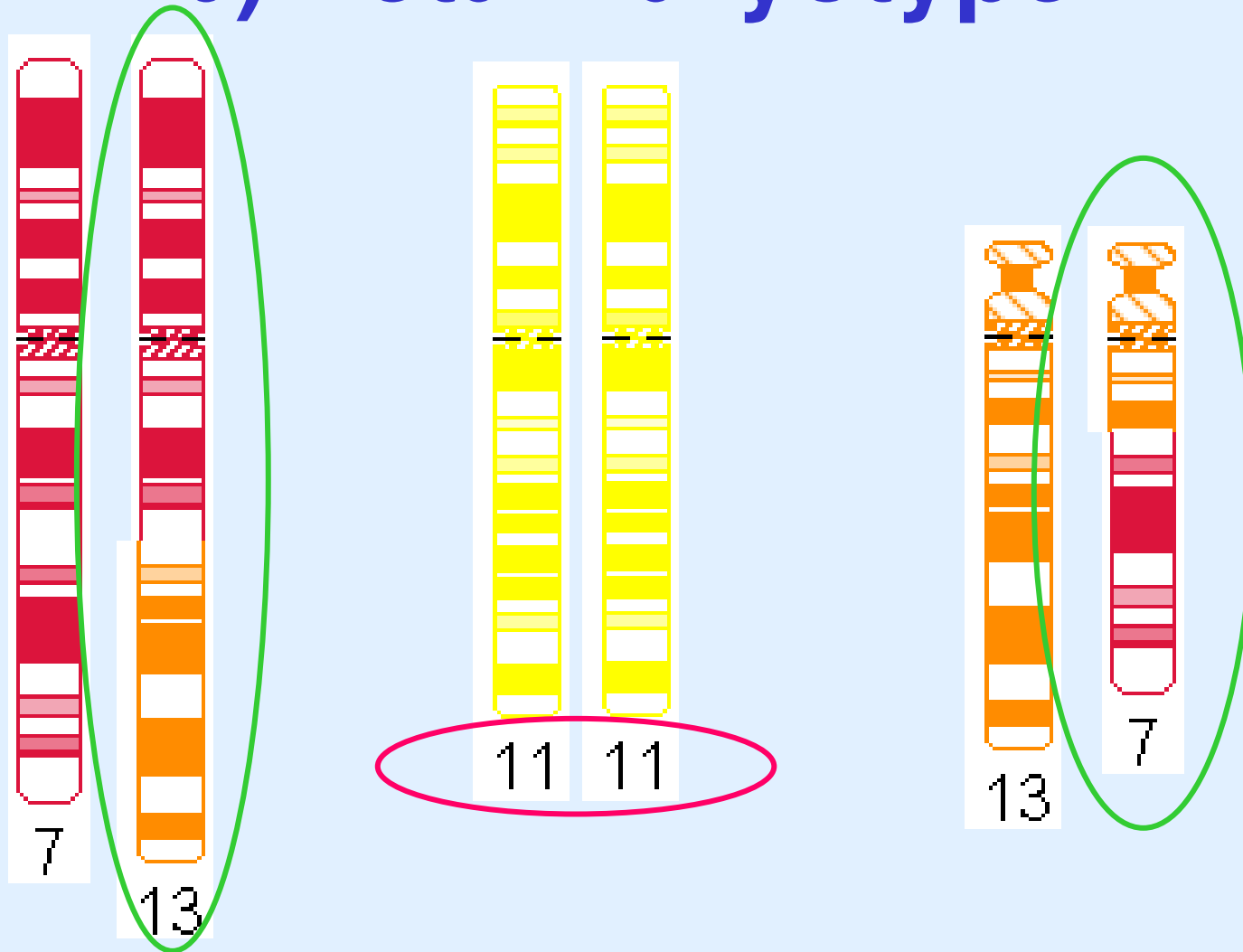
b) Meiotic recombination



b) Meiotic recombination



b) Fetal karyotype



Outcome

- Fetal karyotype appears balanced and contains part of the complex rearrangement carried by mother, therefore unlikely to be associated with any adverse phenotypic effect
- No morphological abnormalities detected in fetal ultrasonography examinations
- Healthy baby delivered at term in December 2010

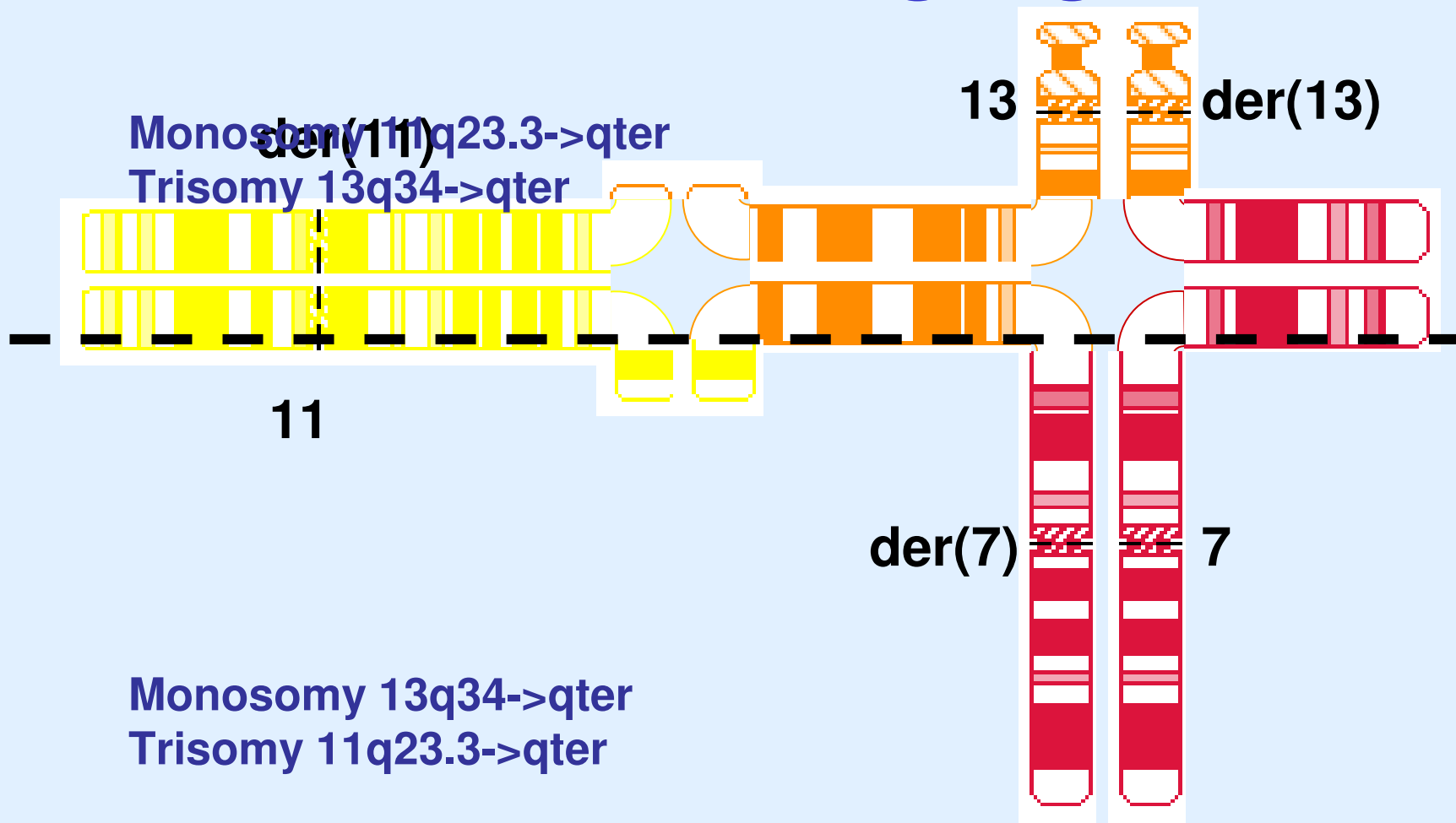
Future

- Baby: Effectively simple reciprocal translocation
- Risk of producing unbalanced gametes

Future

- Mother: risk is difficult to estimate but likely that she will continue to have problems conceiving
- Risk of producing unbalanced gametes

Unbalanced segregation



Future

- Mother: risk is difficult to estimate but likely that she will continue to have problems conceiving
- Risk of producing unbalanced gametes
- Offer prenatal diagnosis in any future pregnancies

Acknowledgements

Mark Selinger

Mark Crocker

Kim Smith

Staff at Oxford Cytogenetics Lab, particularly Beth Beesley and Charlotte Noakes

Patient AB has consented for this information to be presented

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