

# First pregnancy after preimplantation genetic screening (PGS) in a balanced translocation carrier with 46,XX,t(4;14)(q25;q32.1) karyotype



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## Introduction

Array based preimplantation genetic screening (PGS) was recently introduced to assisted reproductive treatment in Germany. To the standard of knowledge today PGS promises the highest benefit for carriers of balanced chromosomal translocations. We report on our initial experience in the establishment of a PGS diagnostic procedure in our preimplantation genetic diagnostic center and the first successful outcome after PGS for a couple with a healthy daughter and the desire for a second child. The 33 year old consuler was diagnosed as balanced translocation carrier of a t(4;14)(q25;q32.1) (see Fig. 1).

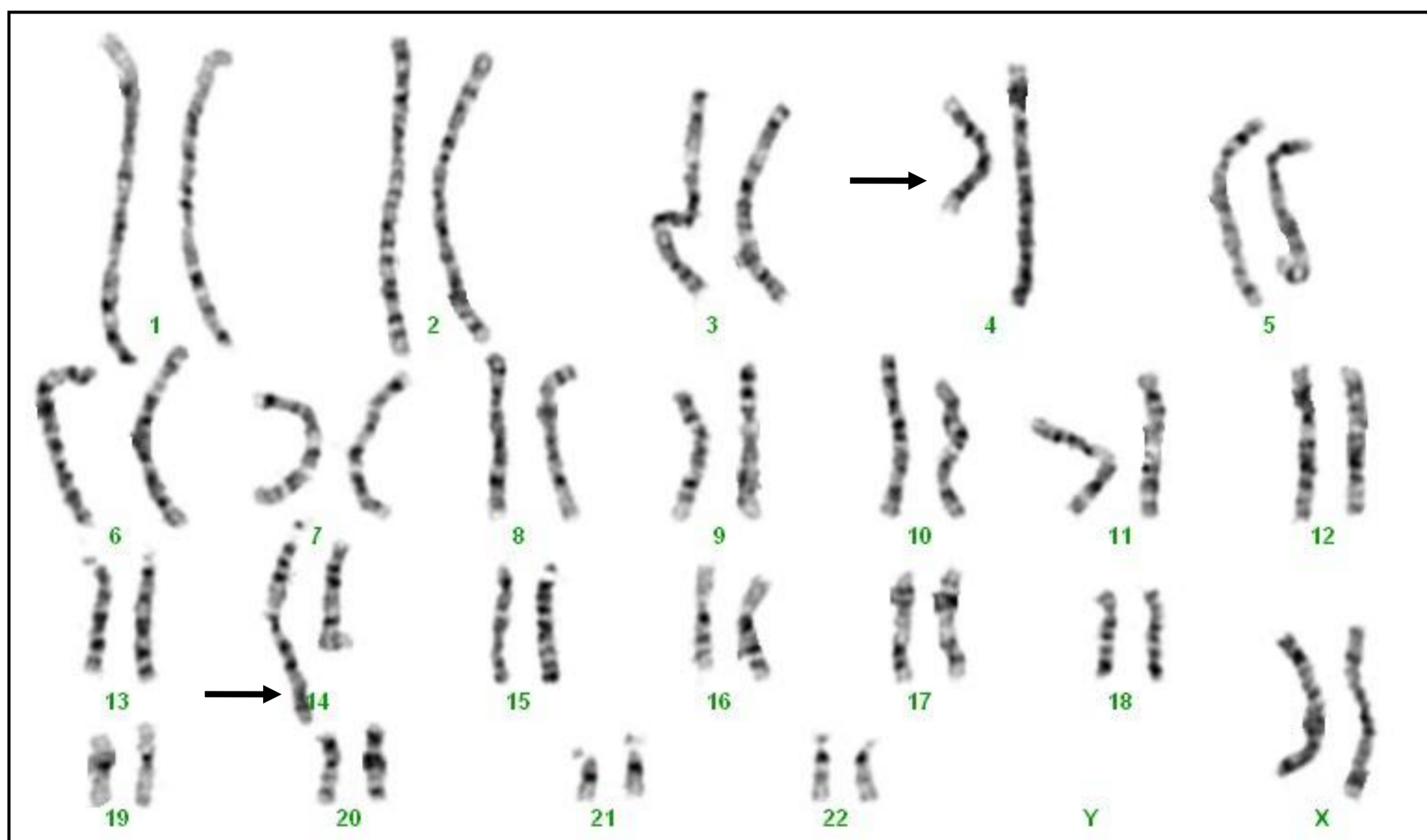


Fig. 1: Maternal karyotype: 46,XX,t(4;14)(q25;q32.1)

Her non-consanguineous partner displayed a normal karyotype. They reported a history of seven pregnancy losses. Cytogenetic analysis on the most recent product of conception revealed an unbalanced translocation due to the presence of a maternally inherited derivative chromosome 14 (see Fig. 2).

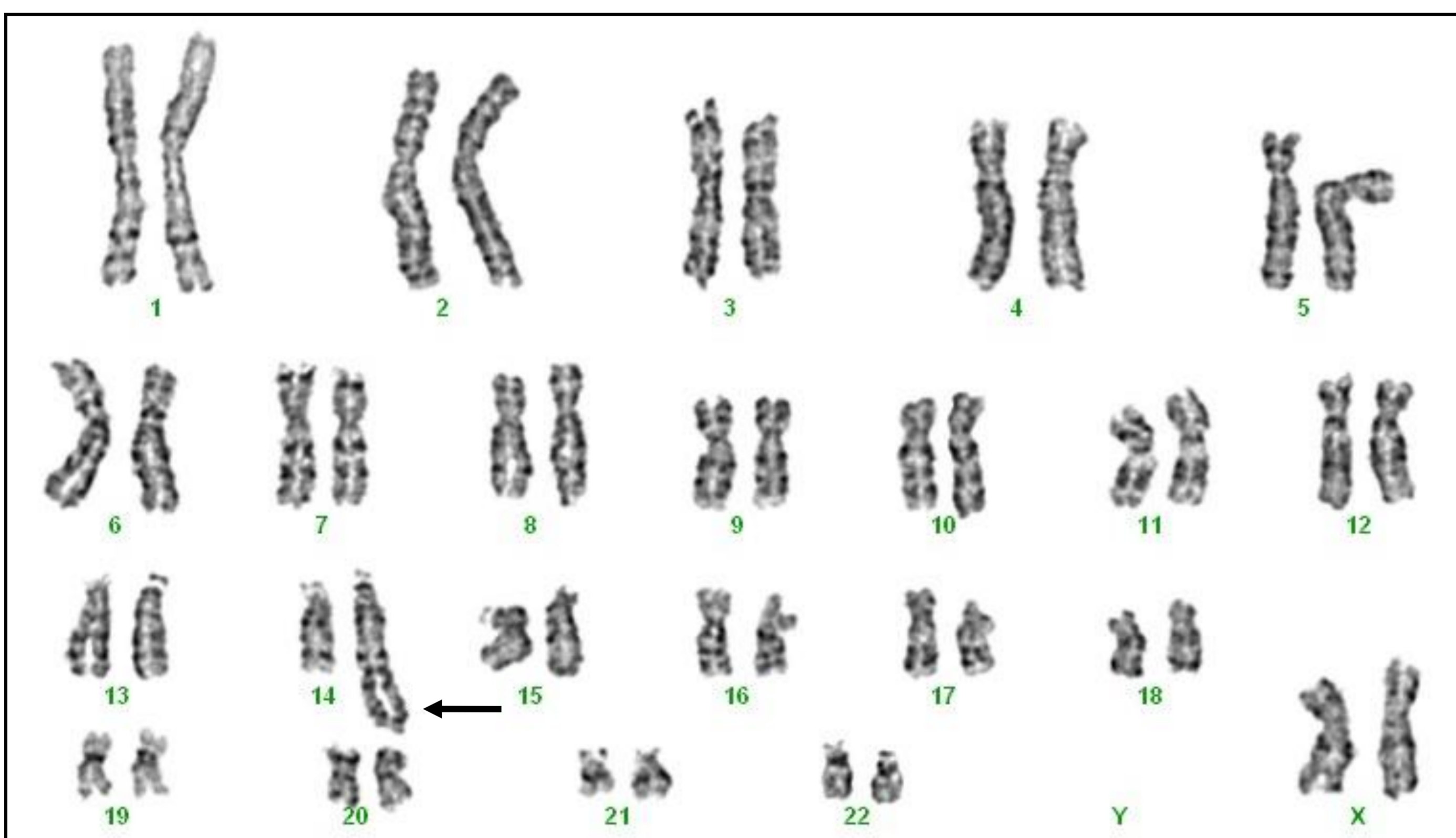


Fig. 2: Unbalanced karyotype in the most recent product of conception: 46,XX,der(14)t(4;14)(q25;q32.1)mat

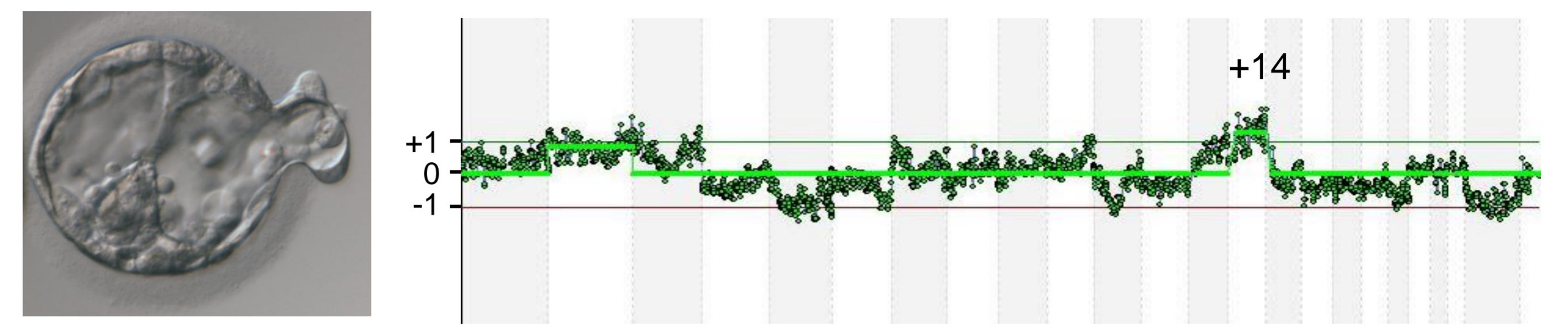
## Diagnostic process

After genetic counselling the couple started with IVF treatment according to routine protocols. From trophoctoderm of day 5-blastocysts laser dissected biopsies of two to six cells each were obtained. Embryos were vitrified using RapidVit BlastTM (Vitrolife, Sweden) for transfer in a natural cycle. Biopsies were subjected to whole genome amplification and hybridized to 24sure+ v1.0 BAC-microarrays utilizing the SurePlex DNA amplification system and the 24sure protocol (BlueGnome, Cambridge, UK).

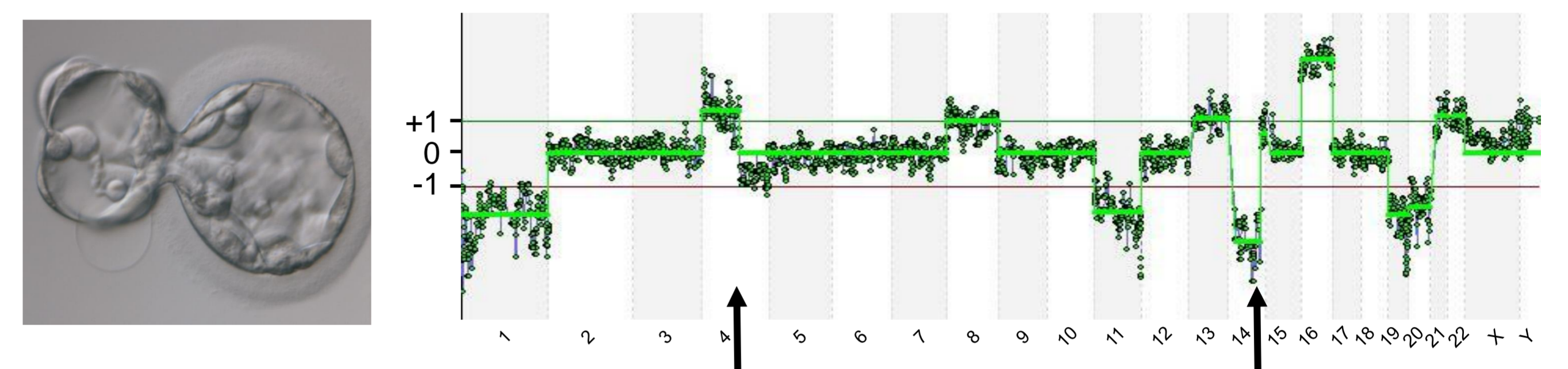
## Results

Stimulation resulted in 19 oocytes, all 15 mature oocytes were fertilized by intracytoplasmic sperm injection. Five embryos developed until blastocyst stage and were biopsied. Although all of them presented with normal morphology, four of five blastocysts were assigned a minimal potential for nidation and normal development due to the presence of aneuploidies (see Fig. 3). Three profiles displayed partial and whole chromosome abnormalities due to the maternal translocation. Interestingly, at least one of them harboured a plethora of imbalances affecting additional chromosomes as well. The fourth showed a trisomy 9q as sole abnormality. One biopsy appeared euploid and the respective embryo was transferred. Ongoing pregnancy was confirmed biochemically and by ultrasound.

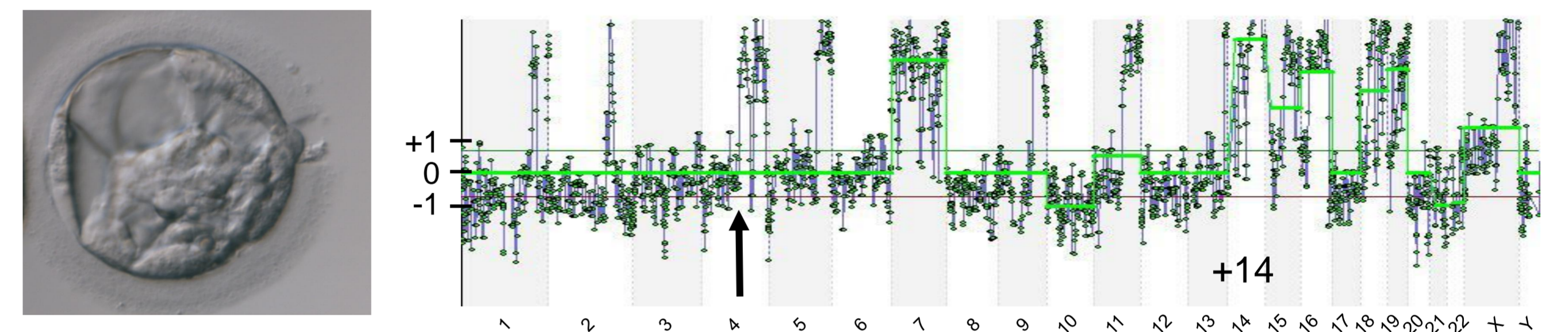
### Trophoctoderm biopsy profile 1 (embryo 1): not recommended for transfer



### Trophoctoderm biopsy profile 2 (embryo 2): not recommended for transfer

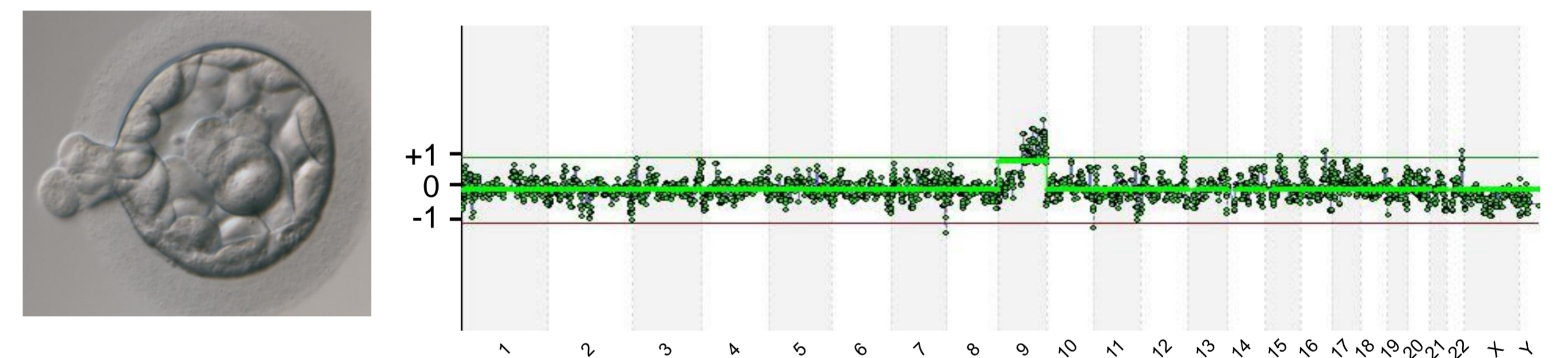


### Trophoctoderm biopsy profile 3 (embryo 3): not recommended for transfer



Although this profile was of minor quality, the copy number change in 4q clearly indicated the presence of a derivative chromosome der(14)t(4;14)(q25;q32.1). Due to low quality the associated loss in 14q32.1qtel was too small to detect.

### Trophoctoderm biopsy profile 4 (embryo 4): not recommended for transfer



Follow-up analysis on this high quality profile by rebiopsy of the embryo rejected for transfer hinted at a mosaic constellation of aneuploid and euploid cells.

### Trophoctoderm biopsy profile 5 (embryo 5): recommended for transfer

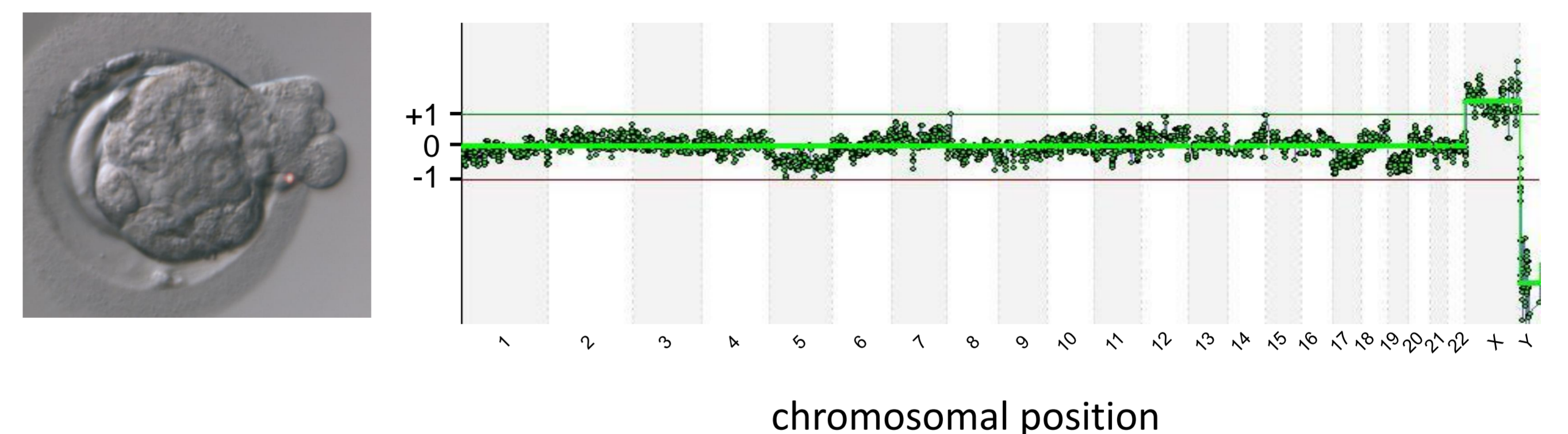


Fig. 3: Blastocyst morphology and imbalance profiles of PGS-analyses, log<sub>2</sub>-ratios are stated on the respective y-axes, arrows highlight translocation associated copy number changes

## Conclusion

This case exemplifies the insights we gained from PGS diagnostic cases so far:

- Most translocation carrier cases comprise some profiles with aneuploidies affecting other chromosomes than the ones involved in the translocation.
- These aneuploidies occur either additional to aneuploidies due to parental derivatives or as sole abnormalities.  
→ It is important to not restrict PGS to translocation chromosomes only.
- Mosaicism is an issue in PGS for translocation carriers as it is in PGS for other indications (e. g. advanced maternal age).
- There are no hard and fast quality criteria for profile evaluation.  
→ We are suggesting to gather experience in the judgment of PGS imbalance profiles and to follow up this learning process by confirmation of diagnostic results (e. g. via analysis of embryos rejected for transfer)