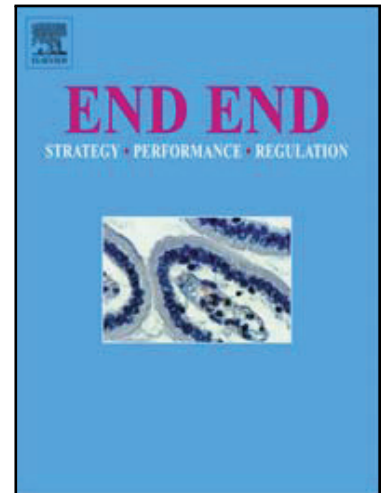


## Accepted Manuscript

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## Short title: PGT for complex chromosomal rearrangement carriers by NGS

Preimplantation genetic testing for complex chromosomal rearrangement carriers by next-generation sequencing

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### Key message

Six complex chromosome rearrangement (CCR) carriers underwent seven preimplantation genetic testing cycles using next-generation sequencing, among which four cycles had euploid embryos. The study results show that CCR carriers have more euploid embryos than expected and, following genetic counselling, achieved a normal/balanced euploid pregnancy.

### Abstract

**Research question:** Can preimplantation genetic testing (PGT) with next-generation sequencing (NGS) increase the chance of achieving a balanced euploid pregnancy in complex chromosome rearrangement (CCR) carriers?

**Design:** Six couples underwent PGT at the Clinical Centre of Reproductive Medicine, First Affiliated Hospital, Nanjing Medical University. The CCR carriers in the six couples were: Case A: 46,XY,t(1;4;11)(p31;p16;q22); Case B: 46,XY,t(3;13;5)(p14;q21;p14); Case C: 46,XX,t(6;11;21)(q21;q21;q13); Case D: 46,XX,inv(9)(p12;q13),t(13;15)(q14;q24); Case E: 46,XX,inv(9)(p12;q13),t(7;9)(q22;p22); and Case F: 46,XX,t(2;7)(q21;q36),t(2;4)(p10;q10),t(2;4)(q15;q10). After ovarian stimulation followed by oocyte retrieval and embryo culture, PGT was performed on day 5 or 6 blastocyst biopsies using NGS to identify normal/balanced euploid embryos. Vitrified-warmed single embryo transfers were performed using normal/balanced euploid embryos.

**Results:** After seven cycles, 84 oocytes were retrieved. Whole genome sequencing by NGS was performed on 25 trophoctoderm biopsies. Six (24%) embryos were identified as normal/balanced euploid, four were transferred resulting in four live births. Case A gave birth to a healthy baby with the same karyotype as Case A. Case C, D and E achieved live births after their first cycle. There was no transferable embryo after two cycles for Case B and one cycle for Case F. The implantation rate per transfer was 4/4 and the live birth rate was 4/4.

**Conclusion:** These results strongly support the use of NGS for CCR carriers.

*Keywords:* complex chromosome rearrangement, genetic counselling, next-generation sequencing, preimplantation genetic testing

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