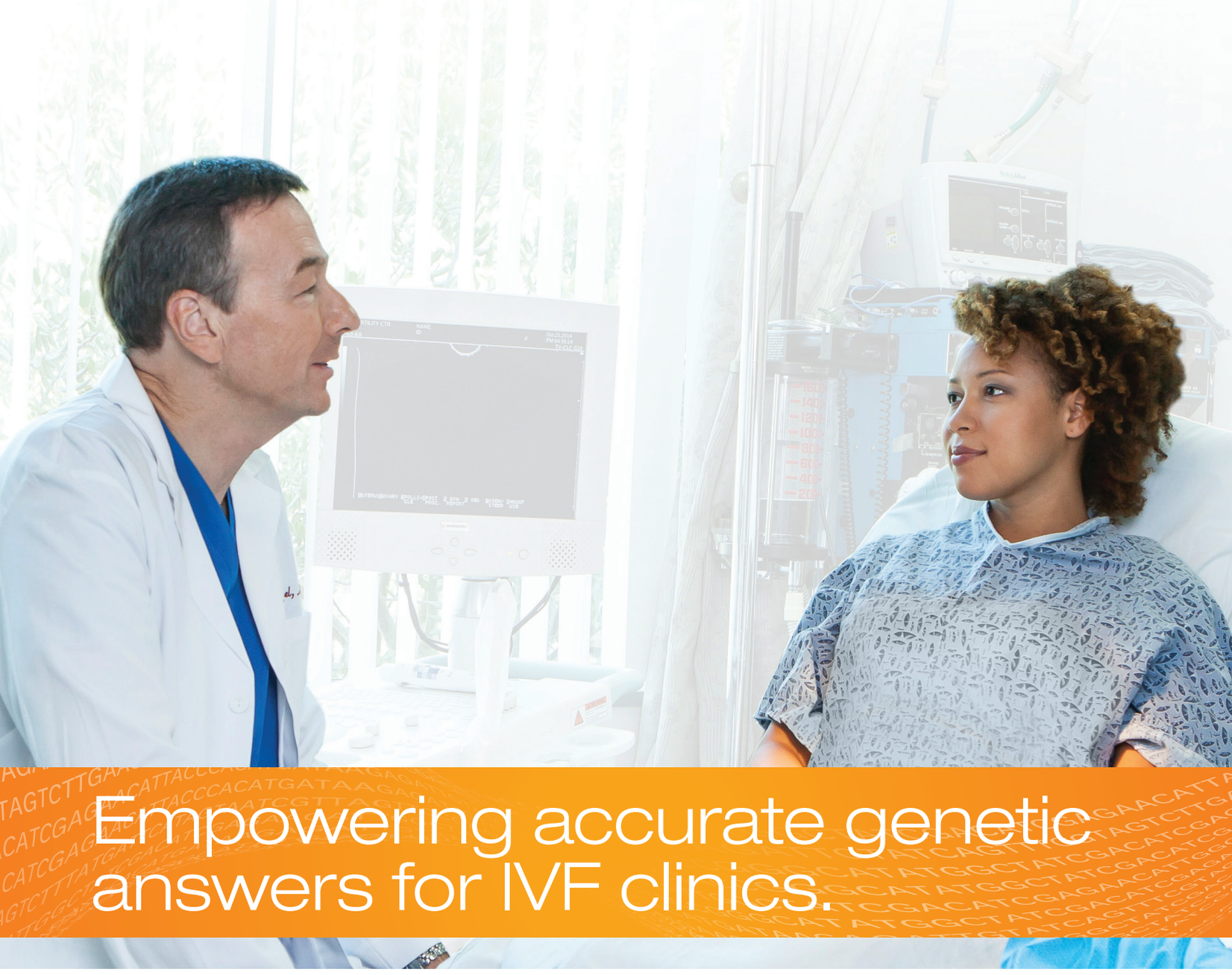


Empowering accurate genetic answers for IVF clinics.

Preimplantation Genetic Screening (PGS) and Preimplantation Genetic Diagnosis (PGD) solutions.

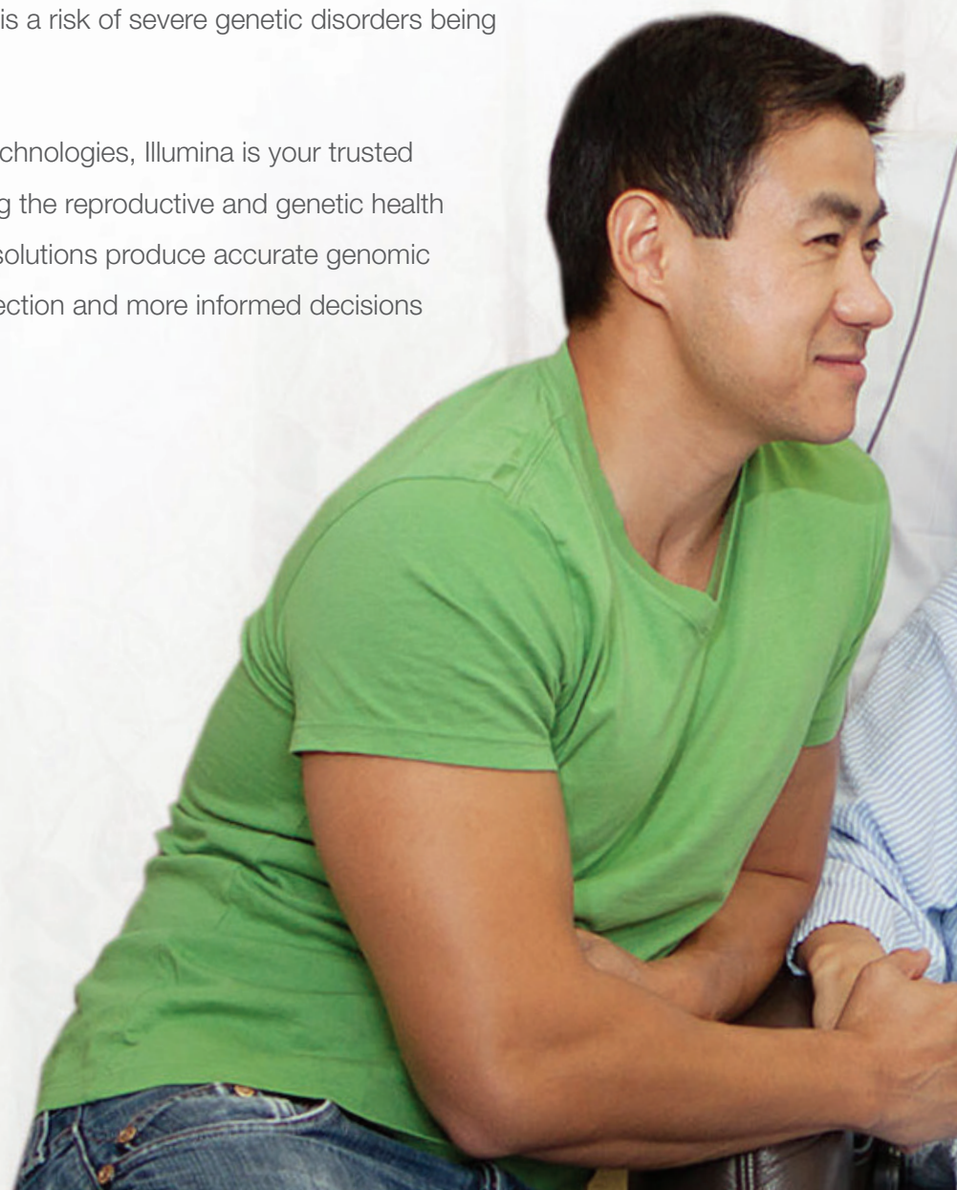
illumina®

Uncovering answers for informed choices.

Illumina is committed to providing solutions that deliver fast, accurate genomic information that can guide choices along the reproductive journey. With this knowledge, clinicians can improve *in vitro* fertilization (IVF) success rates and reduce the risk of severe inherited genetic disorders. Preimplantation genetic screening (PGS) and preimplantation genetic diagnosis (PGD) are 2 of the innovative tools now available to help clinicians assess the genetics of an embryo.

- PGS identifies embryos with a normal number of chromosomes (euploidy), which helps to improve IVF success[1]
- PGD screens embryos when there is a risk of severe genetic disorders being inherited from parents

As a leader in innovative genomics technologies, Illumina is your trusted partner for dependable answers along the reproductive and genetic health care continuum. Our PGS and PGD solutions produce accurate genomic information for optimized embryo selection and more informed decisions about reproductive options.



PGS increases chances for a successful pregnancy.

Vy B.—actual PGS patient and her husband.

While IVF has revolutionized the treatment of infertility, the process remains inefficient and its success rates are low.[2] Implanting embryos with an abnormal number of chromosomes (aneuploidy) is a major cause of IVF failure, as most embryos with aneuploidy will not implant or will miscarry during the first trimester of pregnancy.[3,4]

In natural conception, aneuploid embryos fail to implant or miscarry so early on that they can go unnoticed. However, during IVF, when the embryo is carefully transferred into the uterus of a hopeful patient, these losses can be emotionally devastating.[5] Aneuploid embryo rates increase considerably with increasing maternal age, reaching as high as 85% in women over 42 years of age.[6]

Enabling euploid embryo selection, improving IVF success.

Recent advances in genomic technologies are improving IVF success rates, increasing patient satisfaction and referrals to successful IVF centers in the process. Sustained implantation and delivery rates can significantly increase when PGS is used to identify and transfer embryos with a normal number of chromosomes, with routine IVF care.[1]

PGS—the new standard of success in IVF.

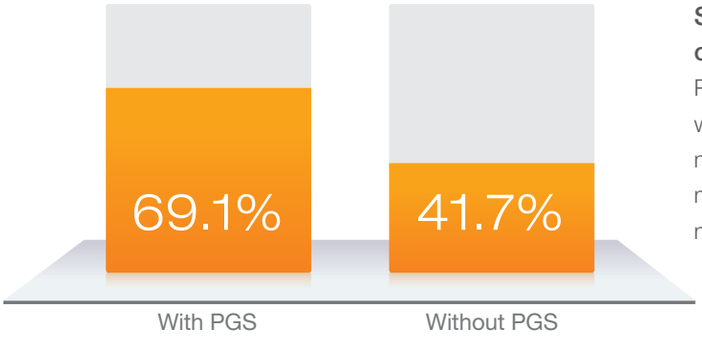
Successful IVF procedures are dependent, in part, on selection of euploid embryos, which can be facilitated using PGS.[7] PGS improves IVF success rates by choosing the most viable embryos for transfer or storage for future use.

The benefits of PGS.

By selectively screening for and implanting euploid embryos, PGS reduces miscarriage rates and improves IVF success.[5,8] Advantages of PGS include:

- Improved implantation rates[1,5]
- Reduced spontaneous abortion and miscarriage[5,9]
- Increased rate of ongoing pregnancy and number of live births[5,8,9]

The accuracy of PGS provides infertility experts with the option to use elective single embryo transfer (eSET), if desired, as a way of reducing the incidence of multiple births.[5,8,9] In fact, PGS patients are nearly 2 times more likely to have a single pregnancy versus those using routine IVF alone.[9]



Significantly Higher Rate of Pregnancy with PGS

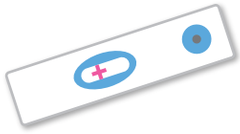
Pregnancy rate shown for IVF implanted with embryos analyzed using PGS and morphology (ie, using a microscope) is 69.1%, much higher than the 41.7% achieved using morphology screening alone.[8]

How PGS Works

Following ovarian stimulation and egg retrieval, a single or few cells are biopsied from the embryo.

DNA from the biopsied samples is screened to identify euploid embryos.

Selected embryos are either transferred to the uterus or frozen for future use.



Improved chance of success for prospective parents undergoing IVF.[5,8,9]

How to access PGS.

Samples are biopsied locally at the IVF clinic and screened in-house or sent to a reference laboratory for testing. All procedures involving patients are performed in the IVF clinic. Patients do not need to travel to the lab performing the screening. For more information about requesting PGS, contact your local reference lab.

PGD can help prevent the inheritance of serious genetic disorders.

PGD is used to screen embryos of couples at risk of passing on severe genetic disorders. PGD can screen for both single-gene mutations linked to serious diseases and unbalanced subchromosomal translocations, which are frequently associated with miscarriage.

The benefits of PGD.

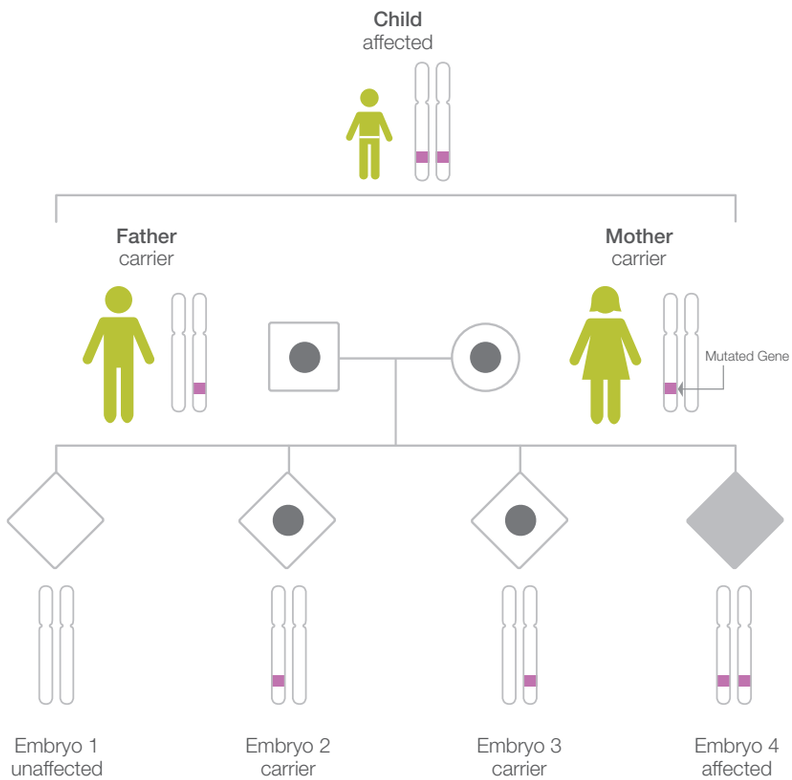
By identifying embryos that do not carry severe genetic disorders, PGD can:

- Enable the transfer of unaffected embryos
- Reduce the risk of having a child with an inherited disorder, such as cystic fibrosis, sickle-cell anemia, and others[10,11]
- Reduce the risk of miscarriage due to structural chromosomal abnormalities[11,12]

PGD for single-gene disorders.

Families concerned with transmitting a known genetic condition to their children can reduce the risk with PGD. Karyomapping is a PGD technique used to assess embryos for single-gene disorders and make sure that only unaffected embryos are transferred during IVF. By screening for unaffected embryos, PGD greatly reduces the chance that a fetus will inherit the genetic condition.[11,12]

Karyomapping Can Identify Embryos Unaffected by a Single-Gene Disorder



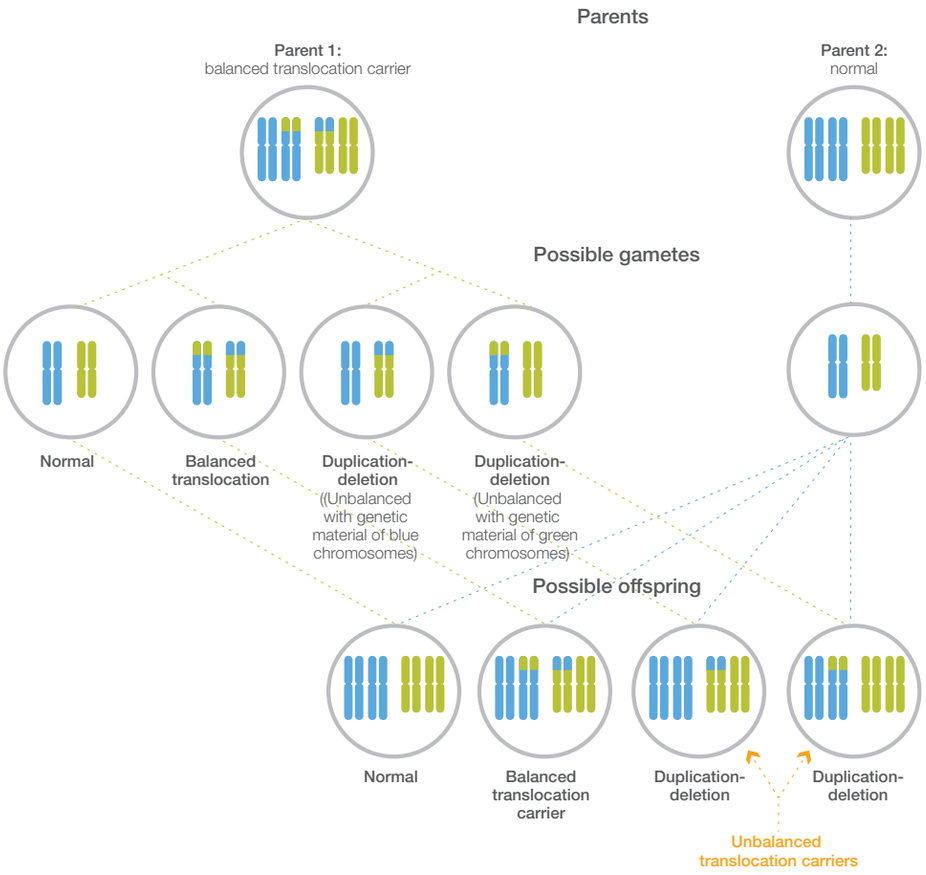
In this illustration, parents of child with a recessive single-gene disorder are assessing the possibility of passing on the single-gene disorder to another child. Using karyomapping, the status of the embryo (affected, carrier, or unaffected) can be established.

PGD—Improving the chance for an unaffected baby.

PGD for chromosomal translocations.

Carriers of balanced translocations are at risk for creating gametes with unbalanced translocations. Unbalanced translocations occur when DNA from one chromosome is unevenly swapped with DNA on another chromosome. This is likely to cause a miscarriage. PGD can screen embryos and identify those with normal chromosome structures for implantation.

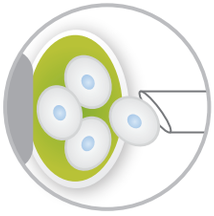
Inheritance of Unbalanced Translocations



Through PGD, it is possible to identify embryos with chromosomal imbalances and make sure that only unaffected embryos are transferred in an IVF cycle.

How PGD Works

IVF begins with ovarian stimulation, egg retrieval, and fertilization.



1 or 2 cells are biopsied from each embryo.

Embryo DNA is screened to identify euploid embryos.

Selected embryos are transferred to the uterus or frozen for future use.

How to access PGD.

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Empowering informed choices

in reproductive and genetic health.

Setting a new standard of IVF success

- Advancing trusted PGS and PGD genomic solutions
- Delivering accurate, timely, and reliable answers
- Offering educational resources and support

Learn more about our reproductive and genetic health solutions.

Visit www.illumina.com/IVFClinicianSolutions

A global genomics leader, Illumina delivers complete next-generation sequencing workflow solutions to the basic and translational research communities. Illumina technology is responsible for generating more than 90% of the world's sequencing data.[13] Through collaborative innovation, Illumina is fueling groundbreaking advancements in the fields of oncology, reproductive health, genetic disease, microbiology, agriculture, and forensic science.

References

1. Scott RT Jr, Upham KM, Forman EJ, et al. Blastocyst biopsy with comprehensive chromosome screening and fresh embryo transfer significantly increases in vitro fertilization implantation and delivery rates: a randomized controlled trial. *Fertil Steril*. 2013;100(3):697-703. 2. MedlinePlus Medical Encyclopedia. In vitro fertilization (IVF). www.nlm.nih.gov/medlineplus/ency/article/007279.htm. Accessed January 31, 2015. 3. SART CORS Clinic Summary Report. www.sartcorsonline.com/rptCSR_PublicMultYear.aspx?ClinicPKID=0. Accessed January 31, 2015. 4. Scott RT Jr, Ferry K, Su J, et al. Comprehensive chromosome screening is highly predictive of the reproductive potential of human embryos: a prospective, blinded, nonselection study. *Fertil Steril.* 2012;97(4):870-875. 5. Grifo JA, Hodes-Wertz B, Lee HL, et al. Single thawed euploid embryo transfer improves IVF pregnancy, miscarriage, and multiple gestation outcomes and has similar implantation rates as egg donation. *J Assist Reprod Genet.* 2013;30(2):259-264. 6. Harton GL, Munné S, Surrey M, et al. Diminished effect of maternal age on implantation after preimplantation genetic diagnosis with array comparative genomic hybridization. *Fertil Steril.* 2013;100(6):1695-1703. 7. Fiorentino F, Bono S, Biricik A, et al. Application of next-generation sequencing technology for comprehensive aneuploidy screening of blastocysts in clinical preimplantation genetic screening cycles. *Hum Reprod*. 2014:29(12):2802-2813. 8. Yang Z, Liu J, Collins GS, et al. Selection of single blastocysts for fresh transfer via standard morphology assessment alone and with array CGH for good prognosis IVF patients: results from a randomized pilot study. *Mol Cytogenet.* 2012;5(1):24. 9. Forman EJ, Hong KH, Ferry KM, et al. In vitro fertilization with single euploid blastocyst transfer: a randomized controlled trial. *Fertil Steril.* 2013;100(1):100-107. 10. American Society for Reproductive Medicine. Frequently asked questions about infertility. ReproductiveFacts.Org Website. http://www.reproductivefacts.org/awards/index.aspx?id=3012. Accessed February 5, 2015. 11. Fiorentino F, Spizzichino L, Bono S, et al. PGD for reciprocal and Robertsonian translocations using array comparative genomic hybridization. *Hum Reprod*. 2011;26(7):1925-1935. 12. Ogilvie CM, Scriven PN. Meiotic outcomes in reciprocal translocation carriers ascertained in 3-day human embryos. *Eur J Hum Genet*. 2002;10(12):801-806. 13. Data on file derived from 2015 study.

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