PGD X-Linked™
PGD for X-linked diseases

Ready-to-use universal
INVICTA PGD BIOPSY KIT™

Innovators in Reproductive Genetics!
Experience matters

January 2005 – April 2015

1,813 cycles, average patient’s age: 36.5 ± 4.6 years
2,045 embryos without genetic load
7,139 embryos underwent diagnosis
6,628 diagnostic embryos tested
49.4% pregnancy success rate

World’s 6th PGD Lab According to the ESHRE PGD Consortium*

* concerning number of PGD/PGS procedures conducted
Sex-linked diseases

Inheritance of some genetic diseases is linked to a sex chromosome. These disorders are also called sex-linked diseases. Approximately 800 various genes were identified on the X chromosome. The Y chromosome contains only 45 genes, which are predominantly connected with the determination of male sex and with spermatogenesis. For this reason, sex-linked diseases are primarily determined by the presence of abnormal variations of genes located on the X chromosome. It has become customary to refer to sex-linked diseases as X-linked diseases.
What is PGD X-Linked™?

The PGD X-linked™ test consists of determination with QF-PCR technique, which sex chromosome (normal or abnormal) has been inherited by the embryo. In some cases, it is enough to determine the chromosomal sex of the embryo in order to establish whether it contains an altered chromosome.

The test can be carried out on material collected by biopsy on the 5th/6th day of the embryo culture. Because of the risk of misdiagnosis caused by possible presence of any extra sperm near the egg when using standard in vitro fertilization, the ICSI procedure is recommended. In each case performance of PGD X-Linked™ is treated individually and preceded by examination of the material from the prospective parents. Following the tests embryos are transferred in a frozen cycle.
Case 1

X-Linked Dominant Inheritance
Mother has the Condition

DAD DOES NOT HAVE THE CONDITION
MOM HAS THE CONDITION

50% OF BOYS DON'T HAVE THE CONDITION
50% OF BOYS HAVE THE CONDITION
50% OF GIRLS DON'T HAVE THE CONDITION
50% OF GIRLS HAVE THE CONDITION

X CHROMOSOME WITH WORKING GENE
X CHROMOSOME WITH NON-WORKING GENE
Case 2

**X-Linked Recessive Inheritance**

*Mother is a Carrier of the Condition*

- **Dad does not have the condition**
- **Mom is a carrier (no condition)**

- **Boy does not have condition**
  - 50% of sons don’t have the condition

- **Boy has condition**
  - 50% of sons have the condition

- **Girl does not have condition**
  - (No carrier)
  - All daughters don’t have the condition

- **Girl is carrier**
  - (No condition)

- **X chromosome with working gene**
- **X chromosome with non-working gene**
Case 3

**X-Linked Dominant Inheritance**
Father has the Condition

DAD HAS THE CONDITION
MOM DOES NOT HAVE THE CONDITION

ALL SONS DO NOT HAVE THE CONDITION
ALL DAUGHTERS HAVE THE CONDITION

X CHROMOSOME WITH WORKING GENE
X CHROMOSOME WITH NON-WORKING GENE
Case 4

X-Linked Recessive Inheritance
Father has the Condition

DAD HAS THE CONDITION
MOM DOES NOT HAVE THE CONDITION

ALL SONS DO NOT HAVE THE CONDITION
ALL DAUGHTERS ARE CARRIERS BUT DO NOT HAVE THE CONDITION

X CHROMOSOME WITH WORKING GENE
X CHROMOSOME WITH NON-WORKING GENE
Case 5

Y-Linked Inheritance
Father has the Condition

DAD HAS THE CONDITION

MOM DOES NOT HAVE THE CONDITION

ALL SONS HAVE THE CONDITION

ALL DAUGHTERS DO NOT HAVE THE CONDITION

X CHROMOSOME WITH WORKING GENE

Y CHROMOSOME WITH NON-WORKING GENE
What we can diagnose?

We can perform **PGD X-Linked™** for all known X-linked diseases based on the current ClinVar database

The list of all disorders is available at:


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Why is it worth to perform PGD X-Linked™?

- It allows to indirectly find embryo’s genetic status by determining which sex chromosome (normal or abnormal) has been inherited by the embryo.
- It optimizes diagnostic and treatment costs – thus being the alternative for PGD ONE™ or PGD ONE FM™ for single-gene diseases.
- It can be combined with PGS-NGS 360°™ – at an attractive price
- It allows all (female and male) embryos testing – the alternative for selection based on sex differentiation. Thus, all healthy embryos (without an abnormal chromosome) can be available for transfer, thereby increasing the chances of pregnancy (higher effectiveness of a single cycle).
Indications for PGD X-Linked™

Couples carrying a sex-linked single-gene disease
(where partners carry a mutation in genes located on either X or Y chromosome)

The test allows reduction of single-gene disease risk in children of the couple carrying this disease. The genetic material of both female and male embryos is verified. This is the alternative for selection based on sex differentiation aimed at avoiding an X-linked disease (in most cases, female embryos will only be the carriers of the disease, and the disease will not manifest). Thanks to the test, its optimized costs, the couple will also get the chance of having a male child.
INVICTA Genetic Laboratory offers:

- Free PGD BIOPSY KIT™
- Free shipment
- Online access to results
Cooperation step by step

1. Diagnosis of parents

2. Biopsy

| Development of the diagnosis | • Development of an individual preimplantation genetic diagnosis, based on the material collected from the patients and the subsequent genetic laboratory results.

   • Upon request, INVICTA sends a SALIVA KIT for collection of biological material from the parents and relatives (if required).

| Embryo biopsy | • A sample is collected via biopsy of an embryo on the 5/6th day of the culture.

| Completion of the biopsy report | • Blastomere or trophectoderm cells are used for testing. |
Cooperation step by step cont.

- Transport
  - Preparation of material for transport
  - Preparation of shipping document
  - Shipment to the INVICTA Genetic Laboratory

- Result
  - Results available within 2 weeks

- Until dispatch, the material sample is stored at -20°C.
- For transportation, 3 cooling cartridges are used that are also frozen to -20°C. The cartridges are placed around the test-tube rack inside the box.
- During transport, the biopsy material is kept cool, or preferably frozen.
- Transport duration depends on the time and place of shipment.
Limitations

In PGD X-Linked™, the presence and number of sex chromosomes is determined. The test allows to determinate the proper chromosomal sex: female (XX) or male (XY), and the presence of the following syndromes: Turner (X0), Klinefelter (XXY), Jacobs (XYY), X Trisomy (XXX) and X Tetrasomy (XXXX). The test does not determine the genetic status of autosomal chromosomes. The test does not detect segmental aneuploidies, germinal mosaicism concerning aneuploidies, structural chromosome disorders (e.g. chromosome fragment deletions, inversions, duplications). The test does not include targeted, direct diagnosis of the abnormal gene. The test allows only for indirect verification of whether the embryo has inherited an abnormal gene/disease linked to a sex chromosome. The test allows to differentiate which of maternal X chromosomes has been inherited. To this aim, not less than 8 molecular markers will be subjected to the analysis. The test may also be used in the case of diseases caused by a mutation located on the X chromosome.
Next Generation Sequencing

The world’s first use of Next Generation Sequencing (NGS) in the preimplantation genetic diagnosis (PGD) for X-linked diseases.

INVICTA Genetic Laboratory: May 2015
Innovators in Reproductive Genetics!

Literature

Our Team
Comprehensive approach to ART

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About INVICTA GENETICS
INVICTA is an experienced genetics laboratory (since 2000) offering wide range PGD / PGS tests using state of art Next Generation Sequencing (NGS) techniques.