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Neu INSIGHTS

Neuberg DIAGNOSTICS CENTER FOR GENOMIC MEDICINE

Reproductive Genomics

Comprehensive Services

Serial number : 008 Edition : 1. 2022

Lumos Carrier Screening

- ✓ Focus
- ✓ Comprehensive
- ✓ Plus

Infertility workup

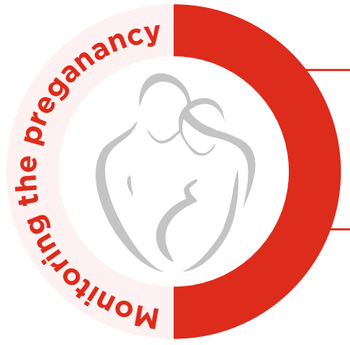
- ✓ Karyotype
- ✓ Y Chromosome microdeletion
- ✓ Sperm DNA Fragmentation
- ✓ ORION - Exome sequencing

Preimplantation Genetic Testing (PGT)

- ✓ PGT-A (Aneuploidies)
- ✓ PGT-SR (Structural rearrangements)
- ✓ PGT-M (Single gene disorder)
- ✓ niPGT (Non invasive preimplantation genetic testing)

Endometrial assay

- ✓ Opera (Optimal time for Endometrial Receptivity Assay)
- ✓ EndoBiome



CHROME (Non Invasive Prenatal Testing)

- ✓ Focus
- ✓ Comprehensive
- ✓ Plus

Invasive Testing(Amniotic fluid/Chorionic villus sampling)

- ✓ Karyotype
- ✓ FISH
- ✓ QF-PCR
- ✓ Chromosomal Microarray
- ✓ ORION - Exome sequencing

Chromosomal Microarray (POC)

- ✓ 315 K
- ✓ 750 K

NGS based tests (POC)

- ✓ Aneuploidy detection (>10MB in size)

Cytogenetic

- ✓ Karyotype of the couple

In accordance with the PCPNDT act, fetal gender will not be disclosed in preimplantation and prenatal genetic testing.

Planning a pregnancy!

Your best adventure is about to begin, and we are glad to be a part of it!

Carrier screening-
(Couple testing for AR and XLR conditions)
Applicable in presence of :
- Positive family history
- Consanguinity
- Any couple planning a pregnancy

Infertility
- Primary or secondary infertility
- 15-30% of infertility cases are associated with a genetic cause [1]

Karyotype
- 10-15% of couples are affected with Recurrent Pregnancy Loss (RPL)[2]
- In 2-5% of couples, one of the partner is identified as a carrier of balanced translocation [3]

Y chromosome microdeletion
- Microdeletion of the azoospermia factor (AZF) region on Y chromosome is considered the most common genetic cause of male infertility [4]

Sperm DNA fragmentation
- 15% of men struggle with infertility in spite of a normal semen analysis
- This test assesses the level of DNA damage in sperms and helps evaluate the utility of assisted reproductive technology [5]

NGS based ORION
- Single gene disorders account for ~20% of infant mortality and ~10% of pediatric hospitalizations[6]
- Incase of deceased proband, the couple can be screened for suspected disorder

LUMOS- Carrier Screening

Tests	Lumos Focus	Lumos Comprehen-sive	Lumos Plus
Gene involved in AR and XLR disorders	✓	✓	✓
SMA by MLPA	✓	✓	✓
DMD by MLPA*	✓	✓	✓
Fragile X by TP-PCR*	✓	✓	✓
CAH by MLPA and sequencing		✓	✓
Alpha Thalassemia by MLPA			✓
Hemophilia A (Including F8*Intron 1/22 Inversion)*			✓

Autosomal recessive (AR) and X-linked recessive (XLR) disorders, Spinal Muscular Atrophy (SMA), triplet repeat primed polymerase chain reaction(TP- PCR) Duchenne Muscular Dystrophy (DMD), Congneital Adrenal Hyperplasia (CAH)

In the absence of a family history or specific phenotype, only pathogenic/ likely pathogenic variants based on current evidence will be reported.

*** These tests will only be performed in female partner**

Optimization of ART

Life's biggest miracle is the gift of having life growing inside of you

PGT (Preimplantation Genetic Testing)

- Evaluates embryos before transfer to the uterus
- Performed on the trophectodermal cells of day-5 embryo

PGT-A
Pre-Implantation Genetic Testing for Aneuploidy

Tests What ?
Numerical chromosomal abnormalities across all 24 chromosomes (22 autosomes and 2 sex chromosomes)

For Whom ?
- Advanced maternal age (> 35 yrs)
  Bad obstetric history
- Implantation failure
- Severe male factor infertility

PGT-SR
Pre-Implantation Genetic Testing for Structural Rearrangements

Tests What ?
Specific imbalances arising from parental chromosomal rearrangements as well as other numerical or structural abnormalities across all 24 chromosomes

For Whom ?
Couples carrier for chromosomal rearrangement like
- Inversion
- Reciprocal translocation
- Robertsonian translocation

PGT-M
Pre-Implantation Genetic Testing for Monogenic Disorders

Tests What ?
Specific monogenic disorders (autosomal recessive/ autosomal dominant/ X linked)

For Whom ?
- Previous child with a genetic disorder
- Carrier for a specific genetic pathogenic variant associated with a known diagnosis or known predisposition within a family

niPGT
Non Invasive Pre-Implantation Genetic Testing

Tests what?
Chromosomal aneuploidies in all 23 pairs of chromosomes.

For whom?
To minimise the invasive nature of embryo biopsy, niPGT is performed from the spent cuture media of the embryo.

Prior discussion with technical team mandatory before undergoing PGT-SR and PGT-M. PGT-M is not recommended in cases of variants of uncertain significance.[7]

Endometrial Receptivity Assay

- Optimization of window of implantation by understanding transcriptomic and microbiotic makeup of endometrium

OPERA (Optimal time for Endometrial Receptivity Assay)

- Next Generation Sequencing (NGS) Technology
- Analyses transcriptomic signature of the window of receptivity (P+5 in HRT/ LH+7 in natural cycle)
- Successful pregnancy in 69.2% of patients after endometrial receptivity testing guided personalised ET [8]

Endobiome

- Increase in non-Lactobacillus-dominated microbiota in a receptive endometrium has been reported to be associated with significant decreases in implantation.
- EndoBiome analyses the microbial population of endometrium for a better reproductive prognosis.

HRT- Hormone replacement therapy; ET- embryo transfer

Monitoring the pregnancy!

We have got you covered

As early as 9 weeks

2% Fetal Fraction as low as 2%

Validated for twin pregnancy and donor egg

CHROME- Non Invasive Prenatal Testing (NIPT)

- No risk for the baby as the test screens for fetal chromosomal abnormalities from the cell-free (cf) fetal DNA from maternal blood

CHROME-Focus:

- Screens for chromosomal aneuploidies in :
- chromosome 13 (Patau syndrome)
- chromosome 18 (Edward's syndrome)
- chromosome 21 (Down syndrome)
- XXY (Klinefelter syndrome)
- XYY (Jacobs Syndrome)
- X0 (Turner syndrome)

CHROME-Comprehensive:

- Screens for chromosomal aneuploidies in all 23 pairs of chromosomes.

CHROME-Plus:

- Screens for chromosomal aneuploidies in all the 23 Chromosomes
- Microdeletions
  1. DiGeorge(22q11.2)
  2. Angelman(15q11.2)
  3. Prader-willi(15q11.2)
  4. Cri-du-chat(5p),
  5. Wolf-Hirschhorn syndrome(4p)
  6. 1p36 deletion

Invasive prenatal testing (from Amniotic fluid or Chorionic villus sample)

- Reproductive decisions cannot be based on screening test alone.
- Following tests help confirm the risk in ongoing pregnancy with great accuracy.

Invasive Prenatal Testing (from Amniotic fluid or Chorionic villus sample)

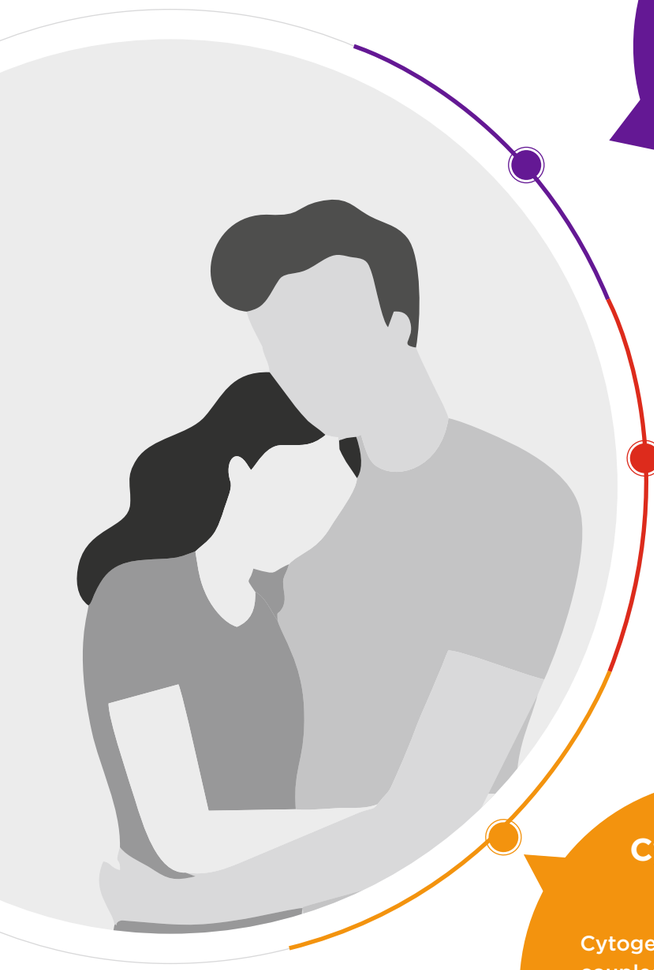
- Karyotype
- Fluorescence in situ hybridization (FISH) for chromosome 13, 18, 21, X, Y
- Quantitative fluorescent PCR (QF-PCR)
- Chromosomal Microarray: Rapidsure (315K) Deepdive (750K)
- NGS based Exome sequencing- ORION

*It is essential to rule out maternal cell contamination (MCC) in prenatal samples (AF/CVS) by a separate test.

Prenatal testing is not recommended in case of variants of uncertain significance [9]

Recurrent pregnancy Loss

Let there be a Neu-beginning with Neu-Hope



POC aneuploidy testing by NGS

Genetic assessment of tissue from products of conception (POC) can elucidate the reason for miscarriage in approximately 50-70% of first trimester miscarriages. [10]

Aneuploidy detection by NGS

- 48% of pregnancy loss tissue contains chromosomal abnormalities
- NGS based testing detects chromosomal aneuploidies of >10MB in size.
- The detection rate is >95% [11].
- No requirement of cell culture.

Chromosomal Microarray

Microarray can be offered to detect chromosomal microdeletion/ microduplications.

Rapidsure 315K

Deepdive 750K

The detection rate of CMA for chromosomal aneuploidies in POC sample is ~10-13% higher than conventional karyotype[11].

Cytogenetic Test

Cytogenetic abnormalities in couples with RPL include reciprocal translocation (~60%), Robertsonian (~40%) or rarely paracentric and pericentric inversions

Karyotype of the couple

- 2-4% of couples are affected with RPL
- In ~4-12% of couples, one of the partner is identified as a carrier of balanced translocation [4]
- Conventional karyotype can detect all balanced translocation in couples.

Sample	Specification	Comments
Whole Blood	4 ml in lavender top (EDTA)	CMA, NGS based tests, Y chromosome microdeletion
Whole Blood	4 ml in green top (Sodium heparin)	Karyotype
Amiotic fluid	10-20 ml in falcon tubes	Prenatal tests (MCC required)
Chorionic villus sampling	50 mg cleaned villi in 15 ml falcon tubes with 3 ml Amniomax media	Prenatal tests (MCC required)
Products of conception	50 mg of villus material of fetal origin / fetal tissue sample (toe-thumb) in sterile container with culture media/ normal saline with 0.25 ml gentamycin/amikacin	Chromosomal microarray, NGS based aneuploidy detection on POC, FISH
Maternal blood	10 ml in cell-free DNA tubes	Non Invasive Prenatal Testing
Semen	Sterile container	Sperm DNA fragmentation
Tropho - ectodermal cells	Trophoectodermal biopsy in -20°C Mini Cooler provided by NCGM (please follow "PGT protocol" provided with the kit).	Preimplantation Genetic Tests
Endometrial biopsy	Endometrial biopsy in RNA stabilizing solution provided by NCGM. (please follow "PGT protocol" provided with the kit).	OpERA, EndoBiome

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Pre-test and post -test genetic counseling is recommended for any genetic test.
Kindly contact :
+91-6357244307/ customer.support@ncgmglobal.com
+916357244305/ GC.Team@ncgmglobal.com

PARTNERS IN HEALTH

DR. SHIVA MURARKA

Senior Scientist (Molecular Genetics)
PhD Reproductive Sciences
shiva.murarka@ncgmglobal.com

DR. UDHAYA KOTECHA

Clinical Geneticist (M.D. Pediatrics)
Fellowship in Medical Genetics
udhaya.kotecha@ncgmglobal.com

DR. SHEETAL SHARDA

Director - Clinical Genomics
Development & Implementation
sheetal.sharda@ncgmglobal.com

DR. PARTH SHAH

Senior Advisor
MD (Hematology and Medical Oncology)
parth.shah@neubergdiagnostics.com

DR. SANDIP SHAH

Consultant Pathologist
M.D (Pathology & Bacteriology)
Laboratory Director
drsandip@neubergdiagnostics.com

FOR MORE DETAILS, CONTACT US AT

079 4040 8181

ncgmglobal.com

Neuberg DIAGNOSTICS

● India ● UAE ● South Africa ● USA