Neuberg DIAGNOSTICS

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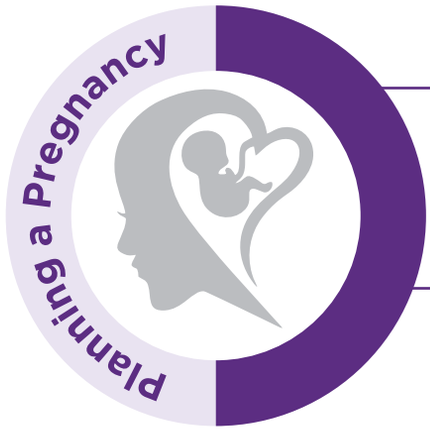
# New INSIGHTS

Neuberg DIAGNOSTICS CENTER FOR GENOMIC MEDICINE

# Reproductive Genomics

## Comprehensive Services

Serial number : 008 Edition : 1. 2022

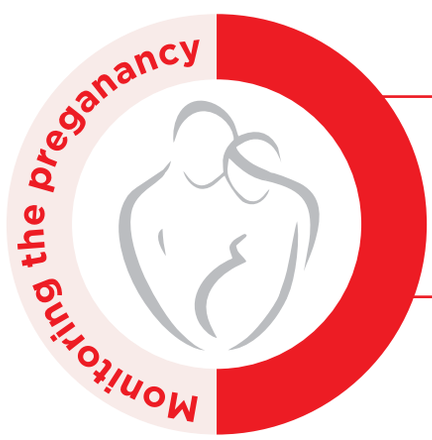



## Preimplantation Genetic Testing (PGT)

- ✓ 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




## Chromosomal Microarray (POC)

- ✓ 315 K
- ✓ 750 K

## NGS based tests (POC)

- ✓ Aneuploidy detection ( >10MB in size )

## Cytogenetic

- ✓ Karyotype of the couple

## Lumos Carrier Screening

- ✓ Focus
- ✓ Comprehensive
- ✓ Plus

## Infertility workup

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


## CHROME (Non Invasive Prenatal Testing)

- ✓ Focus
- ✓ Comprehensive
- ✓ Plus

## Invasive Testing (Amniotic fluid/Chorionic villus sampling)

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


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,

**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]

# and we are glad to be a part of it!

## 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

### PGT (Preimplantation Genetic Testing )

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

### Endometrial Receptivity Assay

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

# having life growing inside of you

## 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]

## 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

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

### 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.

# you covered

## 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)

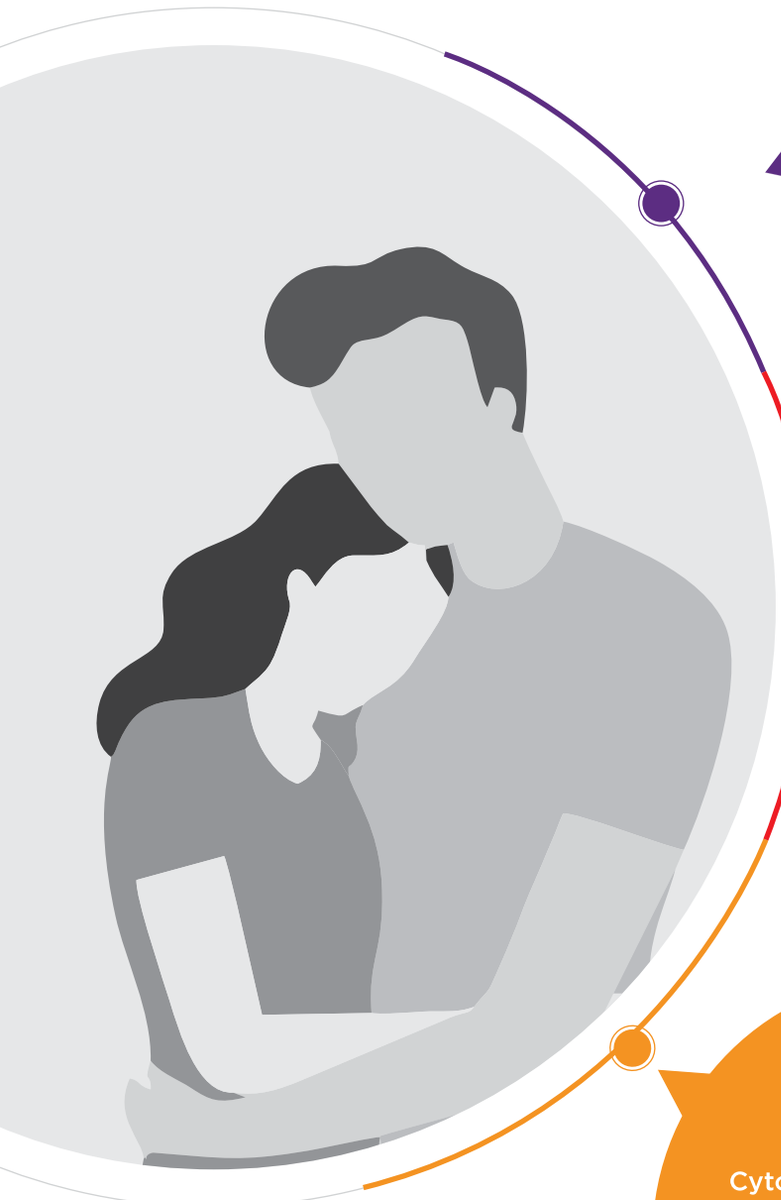
- Karyotype
- Fluorescence in situ hybridization (FISH) for chromosome 13, 18, 21, X, Y
- Quantitative fluorescent PCR (QF-PCR)
- Chromosomal Microarray: Rapidsure (315K) Deepdive (750K)
- NGS based Exome sequencing-ORION

*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



### 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]

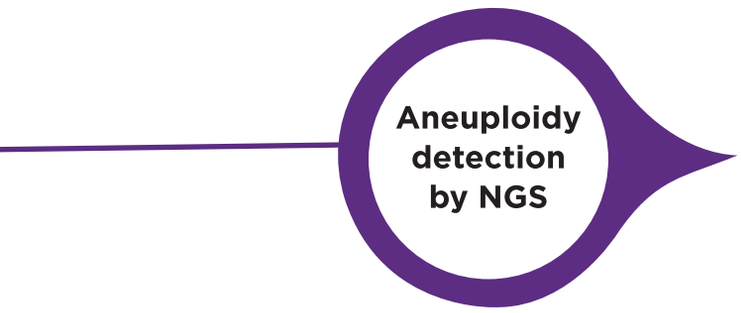
### Chromosomal Microarray

Microarray can be offered to detect chromosomal microdeletion/ microduplications.

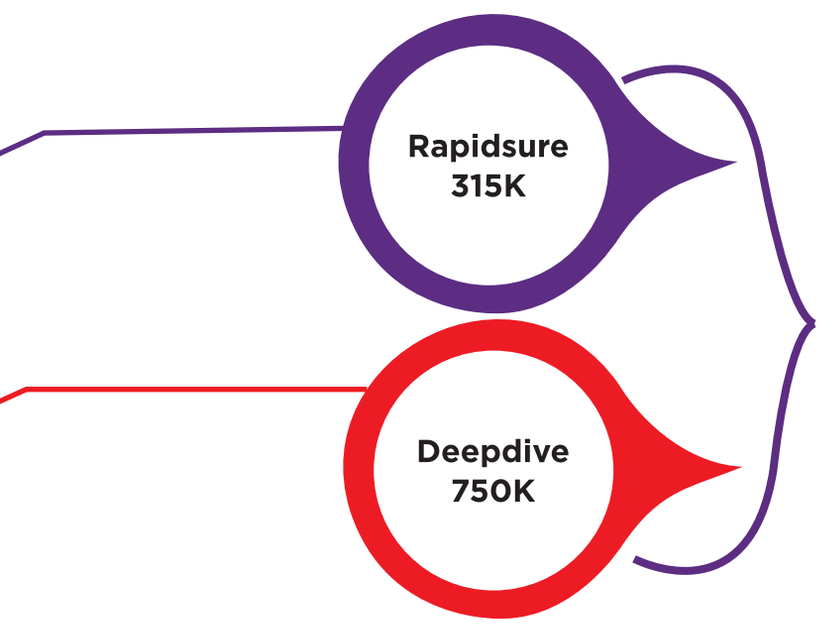
### Cytogenetic Test

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

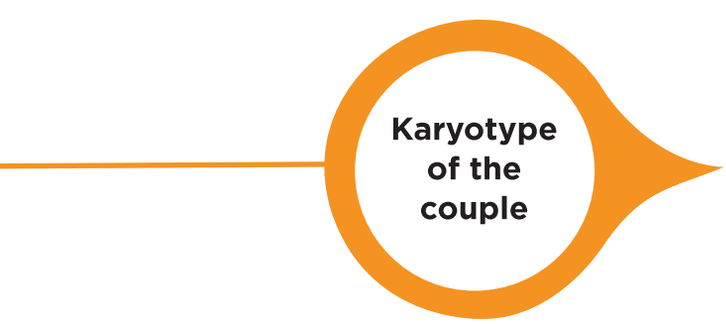
# with Neu-Hope




- 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.




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




- 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.**
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# Our Services

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# Notes :

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