




Non-Invasive Chromosome Screening (NICS) Report

Mother's Name	: Mrs. HINAL PATEL	Hospital ID	: NA
Partner/Father's Name	: HENIL PATEL	Patient ID	: 1002419060
Mother's Date of Birth/Age	: 27/11/1991	Sample ID	: 2400096743 +2 more*
Referring Doctor (Dr.)	: Dr. Jayesh Amin	Sample collected on	: 09/05/2024 , 08/05/2024
Embryologist	: Dr. Paresh Makwana	Sample received on	: 14/05/2024 15:19
Centre Name	: Revaba Infertility Clinics Pvt.Ltd-Ahmedabad	Report released on	: 20/05/2024 13:31
Clinical Indication	: Mrs. Hinal Patel has undergone NICS test due to missed abortion and to screen for euploid embryos.		

SureT is an advanced non-invasive pre-implantation genetic screening solution which helps in screening of embryo for chromosomal aneuploidies with higher accuracy and sensitivity.

Result Summary

Embryo ID	Embryo Grade	Results* (Mosaicism range)	Result Summary	Interpretation & Transfer Recommendation*	Transfer Priority** (based on genetic screening results)
2400096742 (HP2)	5AB	46, XA	<ul style="list-style-type: none"> No Aneuploidies detected No SCA 	Euploid 	1
2400096743 (HP3)	4AB	46, XA -Ap, -Aq, -15 (44%-61%)	<ul style="list-style-type: none"> Mosaic abnormality of sex chromosome Mosaic monosomy 15 SCA detected 	High Level Mosaicism 	2
2400096744 (HP5)	4AA	46, XA	<ul style="list-style-type: none"> No Aneuploidies detected No SCA 	Euploid 	1

Note: * Refer below for detailed result, definitions and embryo prioritization PGDIS guidelines.

** Transfer priority suggested here are based on screening results of the embryo using spent culture media. Kindly correlate clinically based on other embryonic parameters.

Patient name : Mrs. HINAL PATEL

Patient ID : 1002419060






Literature on Mosaic Embryo Transfer (MET)

According to a recent position statement by Preimplantation Genetic Diagnosis International Society (PGDIS), mosaic embryos can be transferred without the added risk of abnormal birth outcomes but may be associated with increased implantation failure and miscarriage rates, with higher values of mosaicism appearing to be less favourable for producing good outcomes. Further, a practice guideline by ASRM (2018) has summarized several studies on mosaic embryo transfers and reported a live birth rate ranging from 18% to 45% and a miscarriage rate ranging from 0% to 50%. It should be noted that pregnancy losses after METs were different depending on the type of mosaicism, with segmental mosaicism having better outcomes than whole chromosome mosaicism. Hence couples/ families should be counseled about the uncertainty and variability of outcomes after transferring mosaic embryos.

Abbreviations Used In This Report

A: Undisclosed Sex Chromosome	SCA: Sex Chromosome Aneuploidies	%: Percentage of Mosaicism
N: Normal	W.C.: Whole Chromosome	+: Gain of Chromosome or Segment
NA: No Aneuploidy	0: Absence of Mosaicism	-: Loss of Chromosome or Segment

Terminologies Used In Interpretation Of The Report

Ploidy	Explanation	Transfer Recommendation
Euploid	No aneuploidy or $\leq 30\%$ mosaicism	 • Recommended for Transfer
Low Level Mosaicism	Between 31-50% mosaicism (≤ 3 chromosomal aneuploidies)	 • Recommended for transfer based on clinician's suggestion
High Level Mosaicism	Between 51-70% mosaicism (≤ 3 chromosomal aneuploidies)	 • Transfer decision only post genetic counseling
Complex Mosaicism	Between 31-70% mosaicism (≥ 4 to 6 chromosomal aneuploidies)	 • Transfer decision only post genetic counseling
Aneuploid	Mosaicism greater than 70% (> 6 chromosomal aneuploidies)	 • Not recommended for transfer
Noisy Trace	The ploidy status (euploid/ aneuploid) of this sample cannot be concluded.	

Patient name :

Patient ID :

Transfer recommendation for low-level mosaic embryos

(PGDIS position statement & CoGen recommendations)

1. Prioritization of the mosaic embryos should be done based on:
 - Embryo morphology
 - Chromosomal abnormality (whole/ segmental)
 - Percentage of mosaicism
2. Embryos with lower levels (<50%) of mosaic aneuploidy are preferred to those with higher levels (>50%).
 - This is because, for embryos with higher levels of mosaicism, there exists a higher probability that aneuploidy is present in the inner cell mass (ICM). Such embryos are at an increased risk of implantation failure and miscarriage before 12 weeks.
3. **Low priority Embryos With Chromosomal Abnormality**

Chromosome Involved	Unfavorable Outcome
13, 18, 21	Live-born viability
14, 15	Uniparental disomy
2, 7, 16, 22	Intrauterine Growth Retardation (IUGR)/ Recurrent Pregnancy Loss (RPL)

Post-transfer recommendation

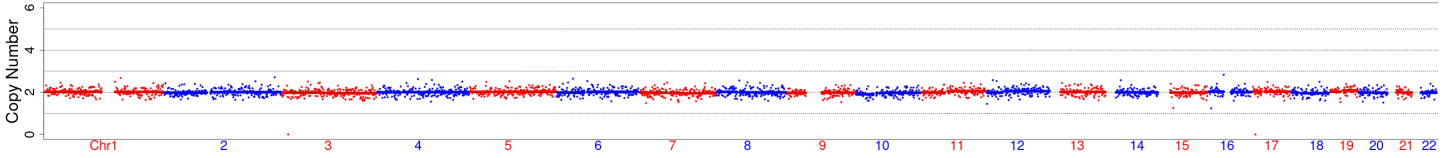
1. **Invasive testing:** Mandatory
 - If a mosaic embryo is transferred.
 - If the pregnancy progresses beyond 12 weeks.
2. **Choice of Invasive Testing :**
 - **Amniocentesis:** Preferred (over CVS), since CVS is known to have CPM (confined placental mosaicism).
3. **Non-invasive Prenatal Screening:**
 - Can be considered, if the abnormality pertains to those of common chromosomes.
 - It can be used to screen the high risk pregnancies, but Amniocentesis should still be offered to the couple/ family.
4. **Reproductive outcomes of Mosaic embryo transfers:**
 - Information of mosaic embryo transfers should be conveyed to the laboratory performing the original diagnosis, this enables refining of the data and also improves practice recommendations.
5. **Pregnancy from Mosaic embryos:**
 - Should be followed up till birth (if possible).

LISTRPT-0523

Patient name : Mrs. HINAL PATEL

Patient ID : 1002419060

CNV Chart for Embryo: 2400096742 (HP2) | Embryo Grade: 5AB



Ch.	1	2	3	4	5	6	7	8	9	10	11	12	13
CNV (+/-)	N	N	N	N	N	N	N	N	N	N	N	N	N
Region & Size	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
% Mosaic	0	0	0	0	0	0	0	0	0	0	0	0	0

Ch.	14	15	16	17	18	19	20	21	22	X	A
CNV (+/-)	N	N	N	N	N	N	N	N	N	N	N
Region & Size	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
% Mosaic	0	0	0	0	0	0	0	0	0	0	0

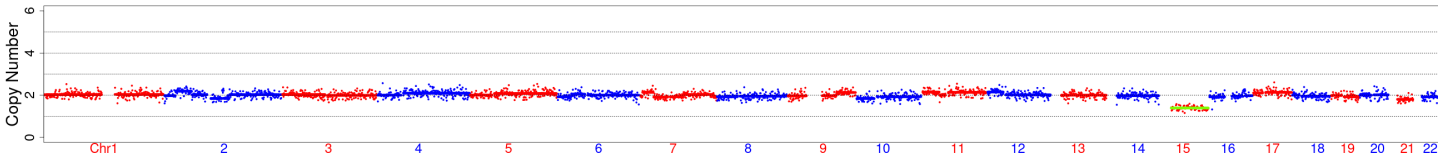
Results	No. of Analyzable reads	Details	Interpretation And Transfer recommendation
46, XA	765641	<ul style="list-style-type: none"> No Aneuploidies detected No SCA 	Euploid <input checked="" type="checkbox"/>

LISTRPT-0523

Patient name : Mrs. HINAL PATEL

Patient ID : 1002419060

CNV Chart for Embryo: 2400096743 (HP3) | Embryo Grade: 4AB



Ch.	1	2	3	4	5	6	7	8	9	10	11	12	13
CNV(+/-)	N	N	N	N	N	N	N	N	N	N	N	N	N
Region & Size	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
% Mosaic	0	0	0	0	0	0	0	0	0	0	0	0	0

Ch.	14	15	16	17	18	19	20	21	22	X	A
CNV(+/-)	N	-	N	N	N	N	N	N	N	N	-/-
Region & Size	NA	W.C.	NA	NA	NA	NA	NA	NA	NA	NA	p arm / q arm
% Mosaic	0	61%	0	0	0	0	0	0	0	0	44% / 48%

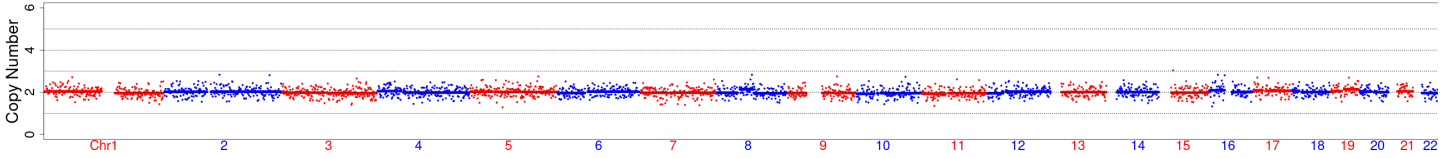
Results	No. of Analyzable reads	Details	Interpretation And Transfer recommendation
46, XA -Ap (44%), -Aq (48%), -15 (61%)	1964489	<ul style="list-style-type: none"> Mosaic abnormality of sex chromosome Mosaic monosomy 15 SCA detected 	High Level Mosaicism

LISTRPT-0523

Patient name : Mrs. HINAL PATEL

Patient ID : 1002419060

CNV Chart for Embryo: 2400096744 (HP5) | Embryo Grade: 4AA



Ch.	1	2	3	4	5	6	7	8	9	10	11	12	13
CNV (+/-)	N	N	N	N	N	N	N	N	N	N	N	N	N
Region & Size	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
% Mosaic	0	0	0	0	0	0	0	0	0	0	0	0	0

Ch.	14	15	16	17	18	19	20	21	22	X	A
CNV (+/-)	N	N	N	N	N	N	N	N	N	N	N
Region & Size	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
% Mosaic	0	0	0	0	0	0	0	0	0	0	0

Results	No. of Analyzable reads	Details	Interpretation And Transfer recommendation
46, XA	897735	<ul style="list-style-type: none"> No Aneuploidies detected No SCA 	Euploid <input checked="" type="checkbox"/>

LISTRPT-0523

Patient name :

Mrs. HINAL PATEL

Patient ID :

1002419060

Test Background

Embryos from the IVF cycle are prone to chromosomal aneuploidies which negatively impacts the outcome of the IVF cycle. These aneuploidies are associated with implantation failures, miscarriages, abnormalities in the fetus and/ or IUGR. In rare cases a fetus may also be born with chromosomal aneuploidies such as Down Syndrome, Patau Syndrome or Edwards Syndrome.

The incidence of such chromosomal aneuploidy is higher in couples with advanced maternal age, history of previous pregnancy losses, primary or secondary infertility, low AMH or previous pregnancy with chromosomal aneuploidy or in couples who are carrier of chromosomal rearrangements

Non-Invasive Chromosomal Screening (NICS)

- NICS, introduced by Lilac Insights, is a novel technique that enables non-invasive pre-implantation genetic testing to be performed in an easier, safer and most efficient way.
- It helps in screening of chromosomal content of the embryos and thus provides insights on suitability of embryo transfer to give you the best chance of implantation and a successful pregnancy.
- This test works by screening of embryos using Next Generation Sequencing technology indicating status of whole chromosomes and/or segments of chromosomes and their ploidy status with extra or missing chromosomes or parts of chromosomes.

Methodology

- Non-Invasive Chromosomal Screening (NICS) is a test method to screen aneuploidies in IVF Embryos using embryonic cell-free DNA (cfDNA) which is a mixture of DNA from Inner Cell Mass (ICM) & Trophectoderm (TE) Cells of the embryos. Spent Culture media of day-5 blastocyst is collected in the sample collection kits and shipped to the lab for analysis as per specifications given.
- cfDNA from the spent culture media is subjected to Pre-PCR and Whole Genome Amplification (WGA) using MALBAC technology. This is followed by Library Preparation and Library Quality Check. The libraries are then sequenced using ThermoFisher Next-Generation Sequencing system. Sequencing is carried out so as to generate over 2 Lakhs raw reads per sample. The data is then analyzed using ChromGo™ Software to determine the analyzable reads, sequencing data QC and aneuploidy calling.

Patient name : Mrs. HINAL PATEL

Patient ID : 1002419060

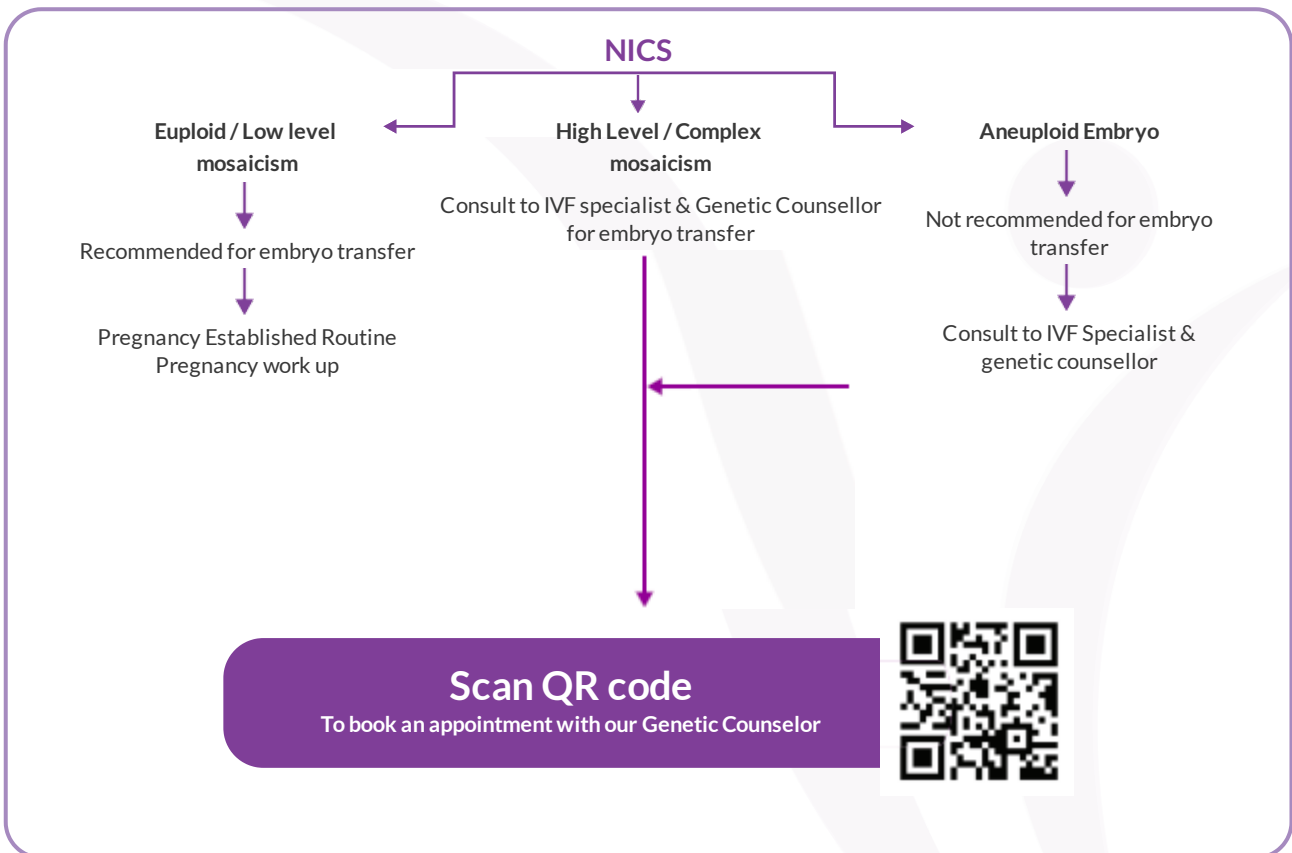
NICS Features

SureT (NICS), pioneered by Lilac Insights, under their comprehensive reproductive health programme offers highly efficient NGS based screening of the embryos.

- **Non-Invasive:** Biopsy free, hence no potential influence on embryo development.
- **Successful Validation:** Comprehensive validation study using large number of samples.
- **AI Auto-Analysis Module:** Established by AI study on over 1000 spent culture medium samples & corresponding embryos. The AI analysis improves the performance of the screening (Sensitivity, Specificity, PPV & NPV).
- **Latest Technology:** Lilac Insights uses Multiple Annealing and Looping-Based Amplification Cycle (MALBAC) technology which provides high-sensitivity, high genome coverage, and high uniformity approach to DNA amplification.
- **Expert Team of Genetic Counselors:** Genetic Counselors at Lilac Insights assists every individual/couple & family to make an informed decision about options available for screening and testing, before and during pregnancy.

What Next After NICS?

NICS aids in prioritization of embryos for transfer based on the results of the test. Thus improving the chances of implantation



Patient name :

Mrs. HINAL PATEL

Patient ID :

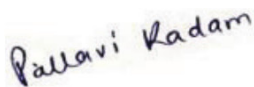
1002419060

Disclaimer

1. As NICS test is a screening test and not a confirmatory diagnostic test, the possibility of false positive or false negative results cannot be denied. The results issued for this test does not eliminate the possibility that this pregnancy may be associated with other chromosomal or sub- chromosomal abnormalities, that cannot be identified within the detection limit of the test.
2. It is assumed that the details provided along with the sample are correct.
3. The manner in which this information is used to guide patient care is the responsibility of the healthcare provide, including advising for the need for genetic counseling or additional/ subsequent diagnostic testing.
4. NICS cannot detect balanced chromosomal rearrangements (i.e inversion, balance translocation etc), Triploidy, Uniparental Disomy, deletion/duplications <10 Mb and other single gene abnormalities.
5. Some samples may not yield interpretable/reportable results due to insufficient analyzable DNA reads or noisy trace.
6. NICS may also result in no embryos being recommended for transfer.
7. Pre and post NICS genetic counseling is strongly recommended.
8. This is a laboratory developed test and the development and the performance characteristics of this test was determined by Lilac Insights Pvt Ltd.
9. According with the Pre-Conception and Pre-Natal Diagnostic Testing (PCPNDT) Act, 2003- Govt. of India; Lab does not disclose the sex of the fetus.

References

1. Leigh, D et al. "PGDIS position statement on the transfer of mosaic embryos 2021." *Reproductive biomedicine online* vol. 45,1 (2022): 19-25.
2. Committee, Practice. "Clinical management of mosaic results from preimplantation genetic testing for aneuploidy (PGT-A) of blastocysts: a committee opinion." *Fertility and Sterility* 114.2 (2020): 246-254.
3. Zhang, Ying Xin et al. "The Pregnancy Outcome of Mosaic Embryo Transfer: A Prospective Multicenter Study and Meta-Analysis." *Genes* vol. 11,9 973. 21 Aug. 2020.
4. García-Pascual, Carmen M., et al. "Optimized NGS Approach for Detection of Aneuploidies and Mosaicism in PGT-A and Imbalances in PGT-SR." *Genes* 11.7 (2020): 724.
5. Huang L, Bogale B, Tang Y, Lu S, Xie XS, Racowsky C. Noninvasive preimplantation genetic testing for aneuploidy in spent medium may be more reliable than trophoctoderm biopsy. *Proc Natl Acad Sci U S A*. 2019 Jul 9;116(28):14105-14112.
6. Fang, R., Yang, W., Zhao, X. et al. Chromosome screening using culture medium of embryos fertilized in vitro: a pilot clinical study. *J Transl Med* 17, 73 (2019).



Pallavi Kadam
Scientific Officer - Genomics



Dr. Madhavi Pusalkar
Technical Head (GM) - Genomics