EDGC NICE service

Non-Invasive Prenatal Testing

AMG

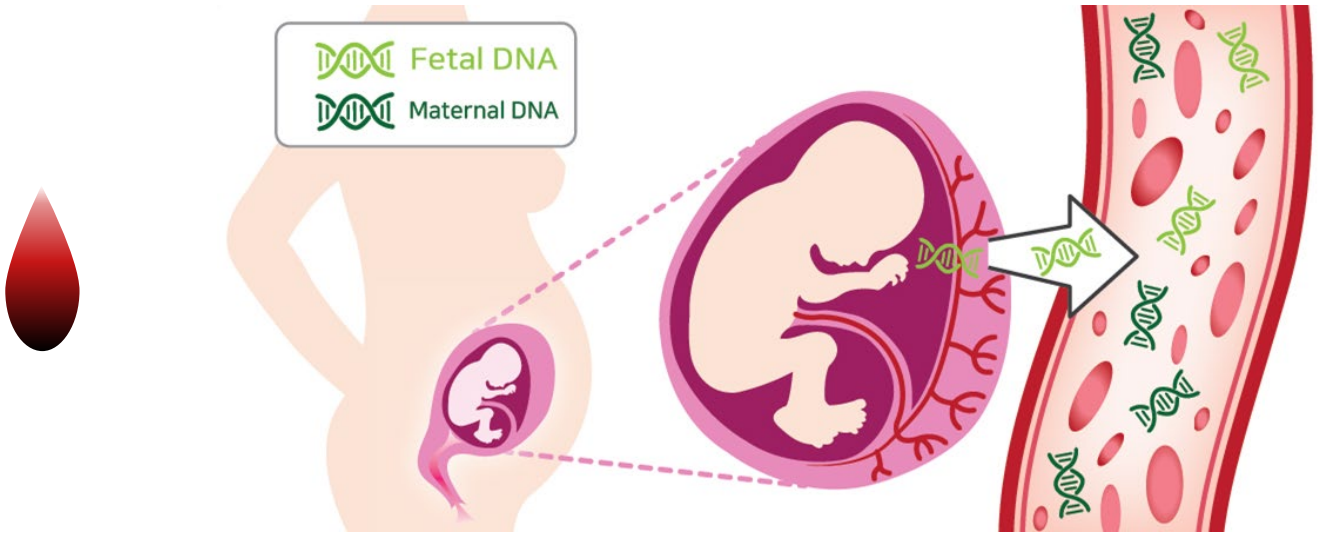
EDGC
EONE-DIAGNOMICS
Genome Center

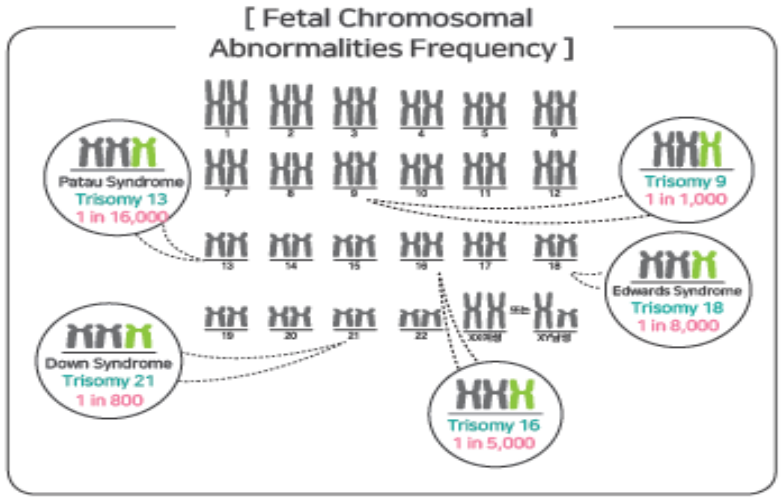
Objectives:

- What is NIPT or NIPS?
- History of NIPT
- Recommendations of NIPT
- EDGC methodology
- Case examples
- Argument for all chromosome testing

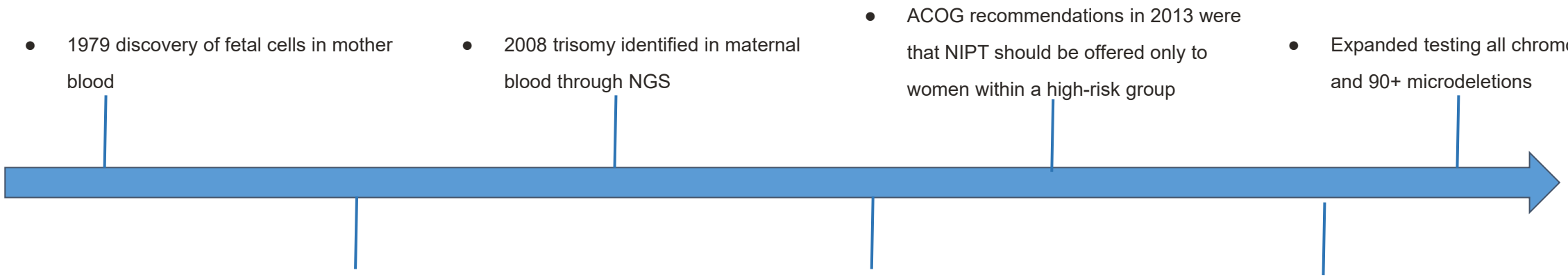
Maternal Age Related Risk for Chromosome Abnormalities

	First Trimester		Second Trimester		Live-birth	
Maternal Age	Down Syndrome	All	Down Syndrome	All	Down Syndrome	All
20	1 in 1152		1 in 1211		1 in 1477	
21	1 in 1125		1 in 1184		1 in 1461	
22	1 in 1110		1 in 1168		1 in 1441	
23	1 in 1090		1 in 1147		1 in 1415	
24	1 in 1064		1 in 1120		1 in 1382	
25	1 in 1032		1 in 1085		1 in 1340	1 in 476
26	1 in 978		1 in 1029		1 in 1287	1 in 476
27	1 in 928		1 in 997		1 in 1221	1 in 455
28	1 in 856		1 in 901		1 in 1141	1 in 435
29	1 in 775		1 in 827		1 in 1047	1 in 417
30	1 in 868		1 in 733		1 in 939	1 in 385
31	1 in 591		1 in 632		1 in 821	1 in 385
32	1 in 494		1 in 536		1 in 696	1 in 323
33	1 in 401		1 in 435		1 in 572	1 in 286
34	1 in 315		1 in 346		1 in 456	1 in 244
35	1 in 240	1 in 114	1 in 265	1 in 141	1 in 353	1 in 179
36	1 in 179	1 in 87	1 in 197	1 in 111	1 in 267	1 in 149
37	1 in 131	1 in 66	1 in 147	1 in 88	1 in 199	1 in 123
38	1 in 96	1 in 51	1 in 108	1 in 70	1 in 148	1 in 105
39	1 in 71	1 in 38	1 in 80	1 in 56	1 in 111	1 in 81
40	1 in 53	1 in 28	1 in 60	1 in 44	1 in 85	1 in 63
41	1 in 41	1 in 22	1 in 47	1 in 35	1 in 67	1 in 49
42	1 in 32	1 in 17	1 in 38	1 in 28	1 in 54	1 in 39
43	1 in 27	1 in 13	1 in 31	1 in 22	1 in 45	1 in 39
44	1 in 22	1 in 10	1 in 26	1 in 18	1 in 39	1 in 31
45	1 in 19	1 in 8	1 in 23	1 in 14	1 in 35	1 in 24


Fetal DNA
Maternal DNA


[Fetal Chromosomal Abnormalities Frequency]
Patau Syndrome
Trisomy 13
1 in 16,000
Trisomy 9
1 in 1,000
Edwards Syndrome
Trisomy 18
1 in 8,000
Down Syndrome
Trisomy 21
1 in 800
Trisomy 16
1 in 5,000

History of NIPT



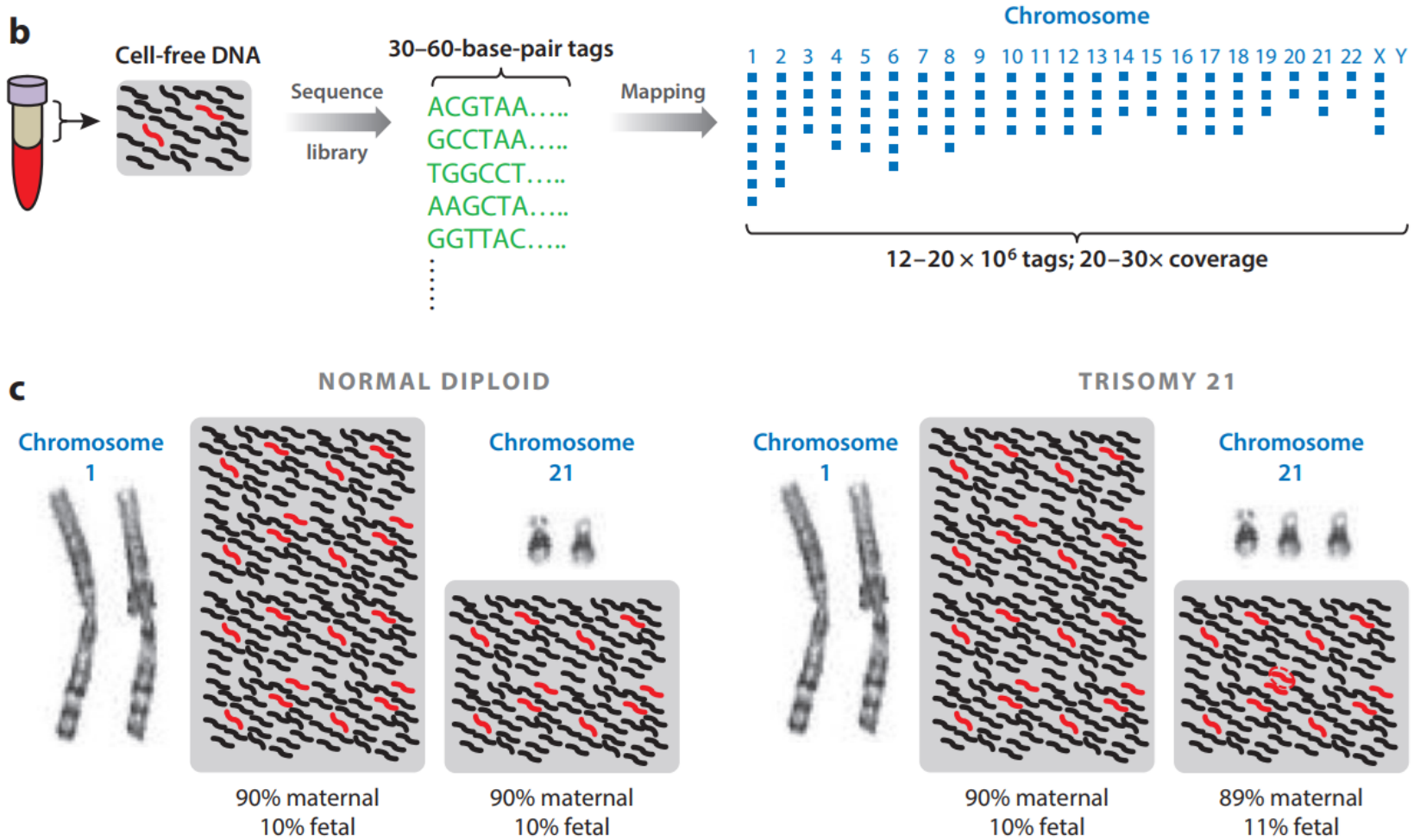
- 1979 discovery of fetal cells in mother blood
- Dr. Dennis Lo 1997 discovered fetal DNA in maternal plasma
- 2008 trisomy identified in maternal blood through NGS
- 2011 commercial NIPT available
- trisomy 13, 18 and 21
- ACOG recommendations in 2013 were that NIPT should be offered only to women within a high-risk group
- 2016 ACOG issued new recommendations stating that NIPT should now be offered to all pregnant women
- Expanded testing all chromosome and 90+ microdeletions

ACMG recommends:

- “Laboratories should provide readily visible and clearly stated detection rate (DR), clinical specificity (SPEC), positive predictive value (PPV), and negative predictive value (NPV) for conditions being screened, in pretest marketing materials, and when reporting laboratory results to assist patients and providers in making decisions and interpreting results.
- Laboratories should not offer to screen for Patau, Edwards, and Down syndromes if they cannot report DR, SPEC, and PPV for these conditions
- All laboratories should include a clearly visible fetal fraction on NIPS reports.
- All laboratories should establish and monitor analytical and clinical validity for the fetal fraction.
- All laboratories should specify the reason for a no-call when reporting NIPS results

NICE vs traditional prenatal screening

	Screening	How to	Since when	How long	Detection Rate(%)
NIPT	NICE	Non-Invasive	From 10 weeks	7~10 days	>99%
Conventional Blood Test	Triple Screen	Non-Invasive	From 11-13 weeks	2 days	67~71%
	Quadruple Screen		From 11-13 weeks		79~81%
Integrated Screening Test	Integrated Screen	Non-Invasive	From 11-13 weeks From 11-13 weeks	4~5 weeks	94~96%
Cell Culture Test	Chorionic Screen	Invasive	From 11-13 weeks	1~2 weeks	>99%
	Amniocentesis		From 11-13 weeks		


b
Cell-free DNA
Sequence
library
30–60-base-pair tags
ACGTAA…..
GCCTAA…..
TGGCCT…..
AAGCTA…..
GGTTAC…..
Mapping
Chromosome
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 X Y
12–20 × 10⁶ tags; 20–30× coverage
c
NORMAL DIPLOID
Chromosome 1
Chromosome 21
90% maternal
10% fetal
90% maternal
10% fetal
TRISOMY 21
Chromosome 1
Chromosome 21
90% maternal
10% fetal
89% maternal
11% fetal

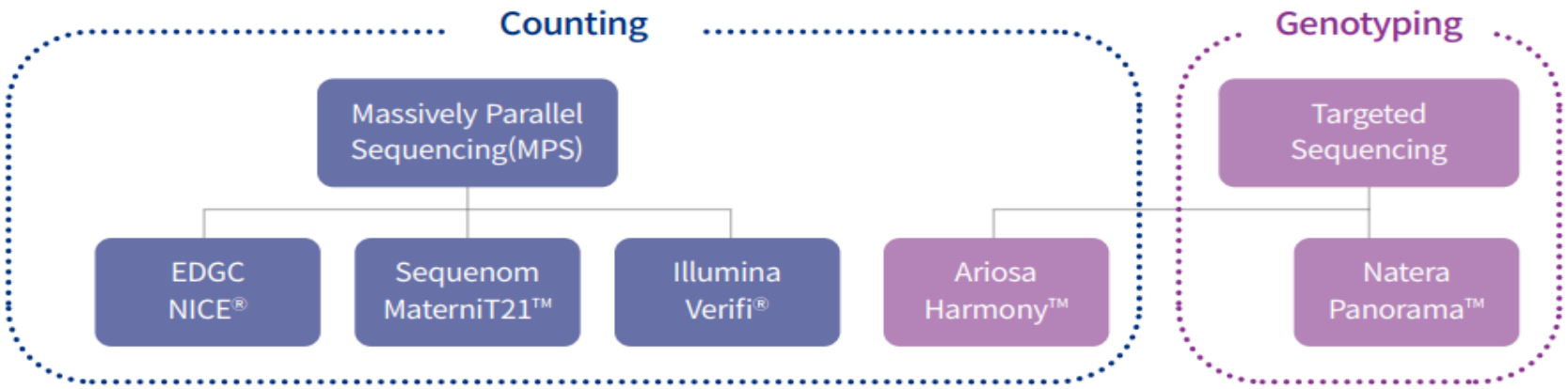


Table1. Differences between NICE® and targeted sequencing methods

NICE® - Massively Parallel Sequencing	Targeted Sequencing
All chromosomal abnormalities can be detected	Only major chromosomal abnormalities can be detected
Unlike other MPS-based NIPT tests, it reports using 21 z-score thresholds	Reported as a risk score similar to serum screening
There is also no effect due to differences between ethnicities	Depending on the SNP, it may be affected by differences between ethnicities
Amplification of fetal-derived cfDNA/maternalderived cfDNA by size selection method using paired-end sequencing	Inability to isolate fetal-derived cfDNA and maternal-derived cfDNA

Sensitivity (False-positive rates)	EDGC NICE®	Sequenom MaterniT21	Illumina Verifi®	Ariosa Harmony	Natera Panorama
Trisomy 21 Down syndrome	>99% (<0.01%)	99.1% (0.2%)	>99.9% (0.3%)	>99% (<0.1%)	99% (0%)
Trisomy 18 Edwards syndrome	96.5% (<0.01%)	96.9% (<0.01%)	97.3% (0.4%)	96.7% (<0.1%)	94.1% (<0.1%)
Trisomy 13 Patau syndrome	92.31% (<0.01%)	89.3% (0.3%)	87.5% (0.1%)	80% (0.05%)	>99% (0%)
Monosomy X Turner syndrome	>99.99% (<0.01%)	94.7% (0.5%)	95% (1.0%)	96.7% (unreported)	94.7% (<0.1%)
Sex chromosome Trisomies	>99.99% (0%)	>99.9%	67-100%	67-100%	73.1%
Female	>99% (0%)	97.9% (0.5%)	97.6% (0.8%)	>99% (unreported)	>99.9% (0%)
Male	>99% (0%)	99.4% (2.1%)	99.1% (1.1%)	>99% (<0.01%)	>99.9% (0%)

NICE® Publication

EDEGC EONE-DIAGNOMICS Genome Center

Scientific Research Publishing

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Multiple z-Score Based Method for Noninvasive Prenatal Test Using Cell-Free DNA in Maternal Plasma

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Abstract

Objective: To improve the detecting accuracy of chromosomal aneuploidy of fetus by non-invasive prenatal testing (NIPT) using next generation sequencing data of pregnant women's cell-free DNA. **Methods:** We proposed the multi-Z method which uses 21 z-scores for each autosomal chromosome to detect aneuploidy of the chromosome, while the conventional NIPT method uses only one z-score. To do this, mapped read numbers of a certain chromosome were normalized by those of the other 21 chromosomes. Average and standard deviation (SD), which are used for calculating z-score of each sample, were obtained with normalized values between all autosomal chromosomes of control samples. In this way, multiple z-scores can be calculated for 21 autosomal chromosomes except oneself. **Results:** Multi-Z method showed 100% sensitivity and specificity for 187 samples sequenced to 3 M reads while the conventional NIPT method showed 95.1% specificity. Similarly, for 216 samples sequenced to 1 M reads, Multi-Z method showed 100% sensitivity and 95.6% specificity and the conventional NIPT method showed a result of 75.1% specificity. **Conclusion:** Multi-Z method showed higher accuracy and robust results than the conventional method even at low coverage reads.

Keywords

Cell-Free DNA, z-Score, Multiple Thresholds, Coefficient of Variance, Noninvasive Prenatal Testing, NIPT

1. Introduction

The most common chromosomal aneuploidy for a new born infant is Trisomy 21. The overall occurrence of trisomy 21 is around 0.001%, but the risk increases

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Noninvasive Prenatal Testing for Fetal Chromosomal Abnormalities Using Massively Parallel Sequencing: Clinical Experience from 7910 Korean Pregnancies

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https://doi.org/10.4236/ojgen.2018.83005

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Abstract

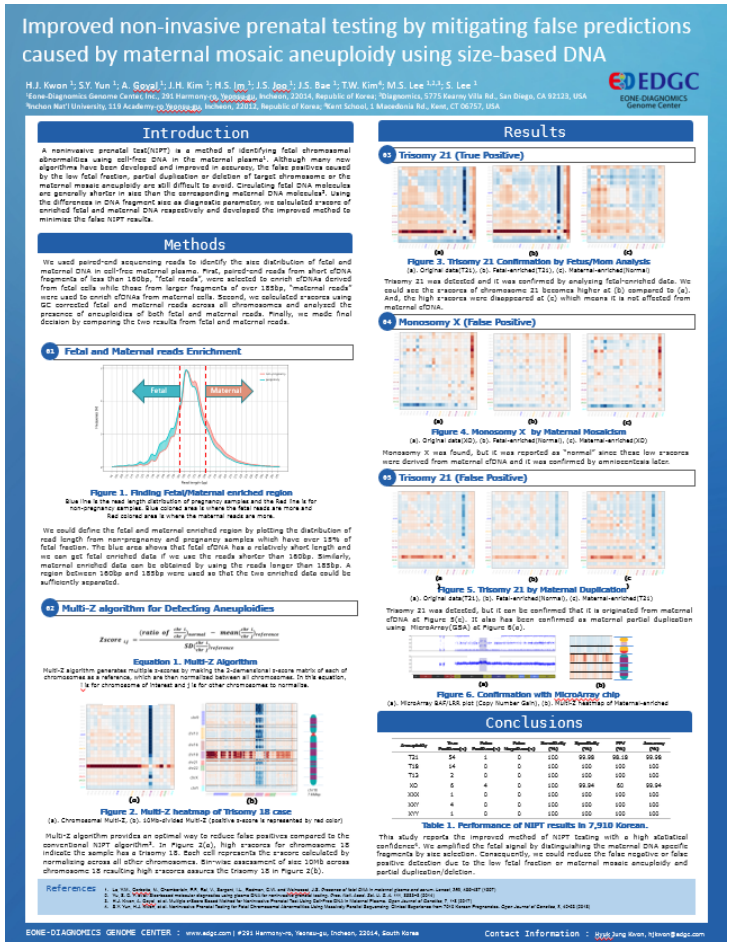
Objective: The purpose of this study is to review the clinical experience and performance of noninvasive prenatal testing (NIPT) method, using cell-free DNAto detect chromosomes 21, 18, 13, X, and Y abnormalities in over 7910 clinical samples from South Korean population. ***Method:*** Pregnant women between 1st of November 2015 to 18th of February 2018, with obstetric clinical findings participated in the study. NIPT was performed based on masively parallel sequencing with 0.3x low coverage paired-end sequencing using cell-free DNA in maternal plasma. Further invasive prenatal testing was recommended for pregnant women with positive NIPT results. ***Results:*** Of the total 7910 participants, 7890 (99.75%) were tested for NIPT and the remaining 20 (0.25%) were below the Quality Control (QC) standards. T13, T18, XXX, XXY and XYY had 100% of sensitivity, specificity, positive predictive values (PPV) and accuracy. The overall sensitivity was 100% and specificity, PPV and accuracy of all chromosomal abnormalities with further validation were 99.92%, 94.25%, and, 99.92% respectively. ***Conclusion:*** Our NIPT results showed high positive predictive value for the detection of autosomal trisomies and sex chromosome aneuploidies in our sample cohort.

Keywords

Cell-Free DNA, Trisomy, Clinical Performance, Mosaicism, CPM, Fetal Abnormality, Noninvasive Prenatal Testing, NIPT

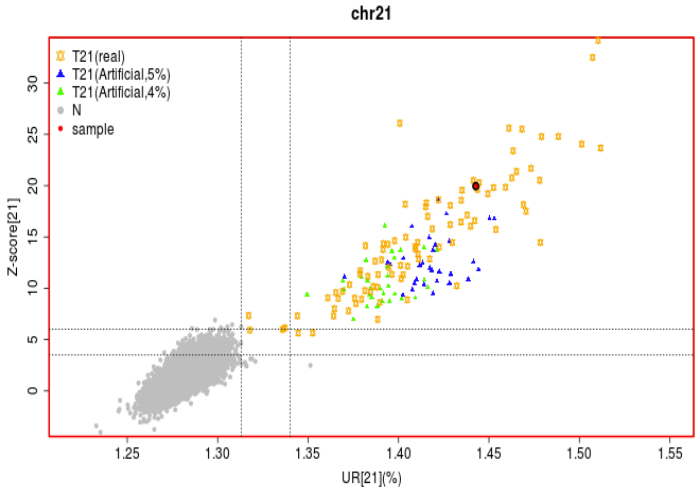
1. Introduction

In 2017, there were about 360,000 newborn babies in South Korea. Although the



Algorithm : Double-Z, Multi-Z and Size selection method

Double Z-score



Multi-Z

Is the core technology to detect fetus chromosomal abnormalities

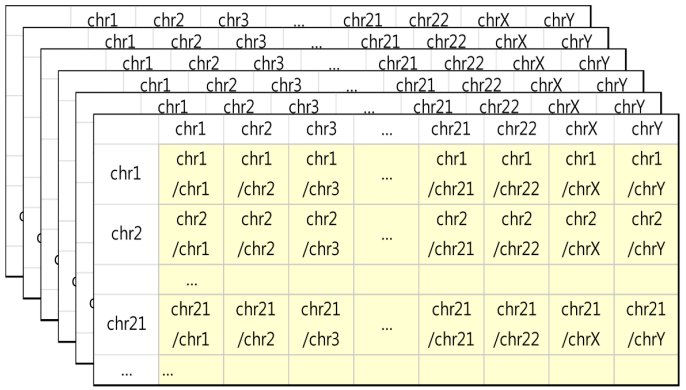
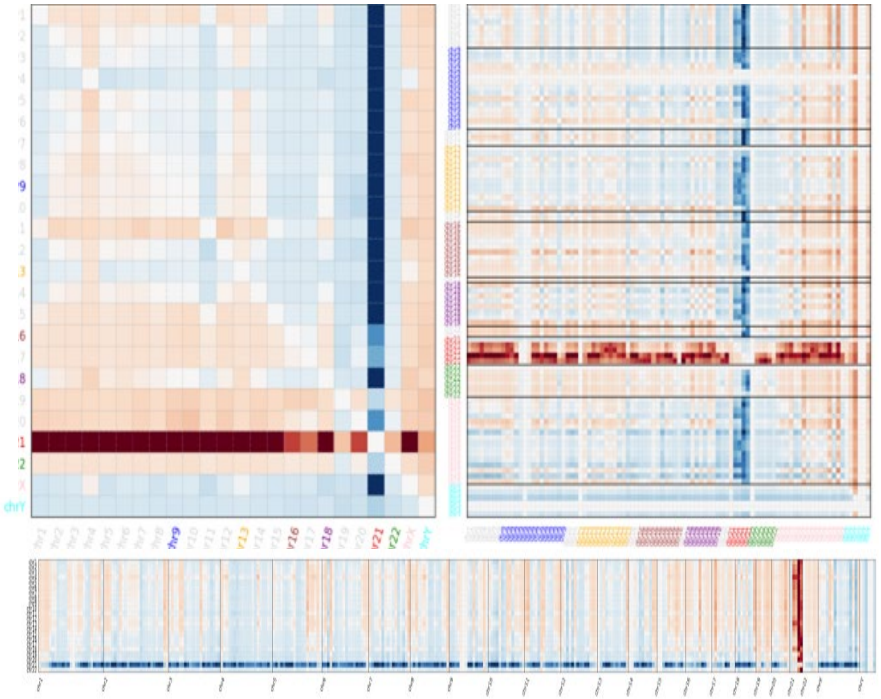
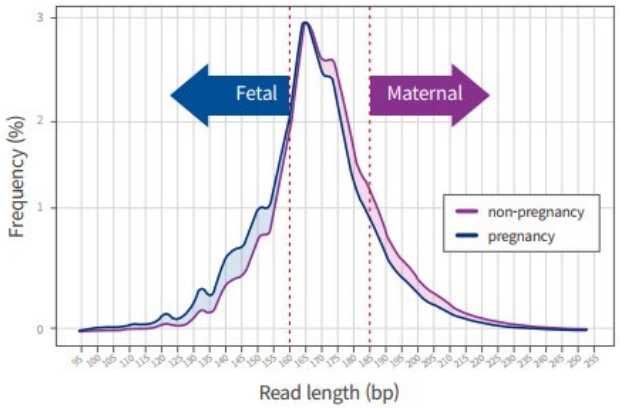
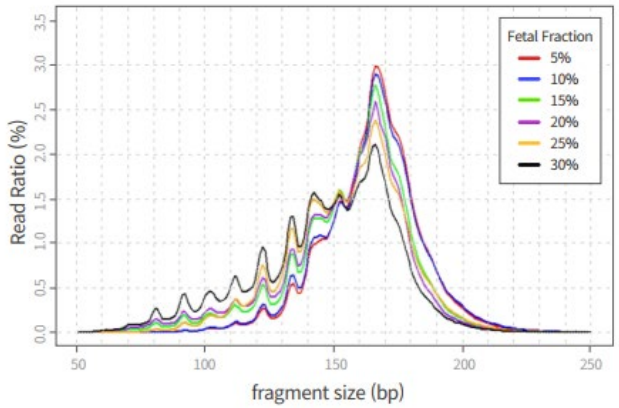


Figure 1. Normalization between chromosomes. Normalized value between two chromosomes is calculated by dividing the value of interested chromosome by that of each chromosome.

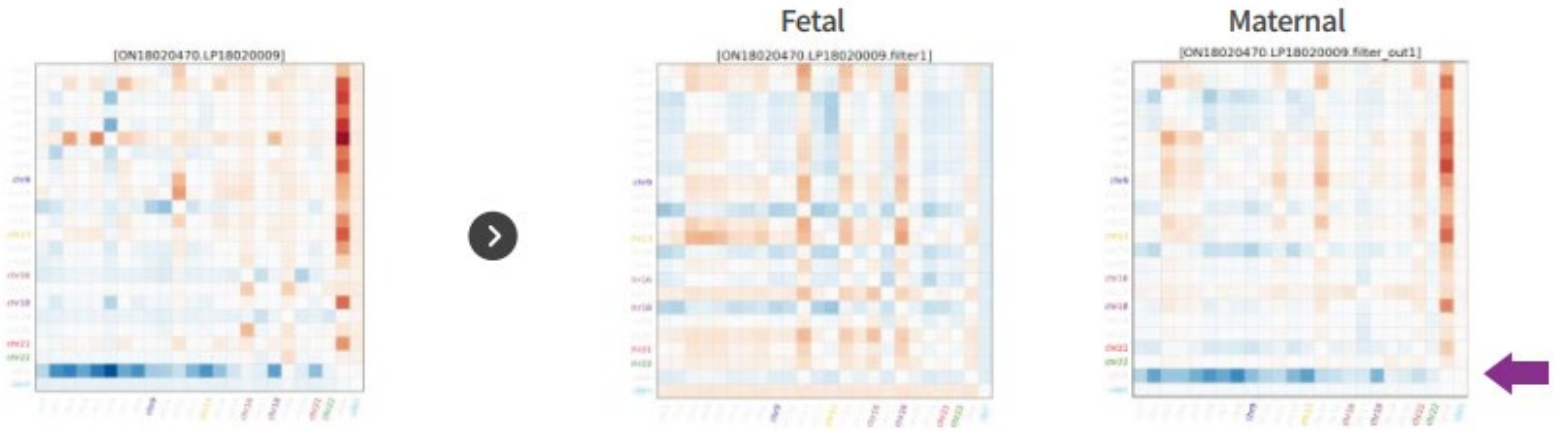


Size Selection

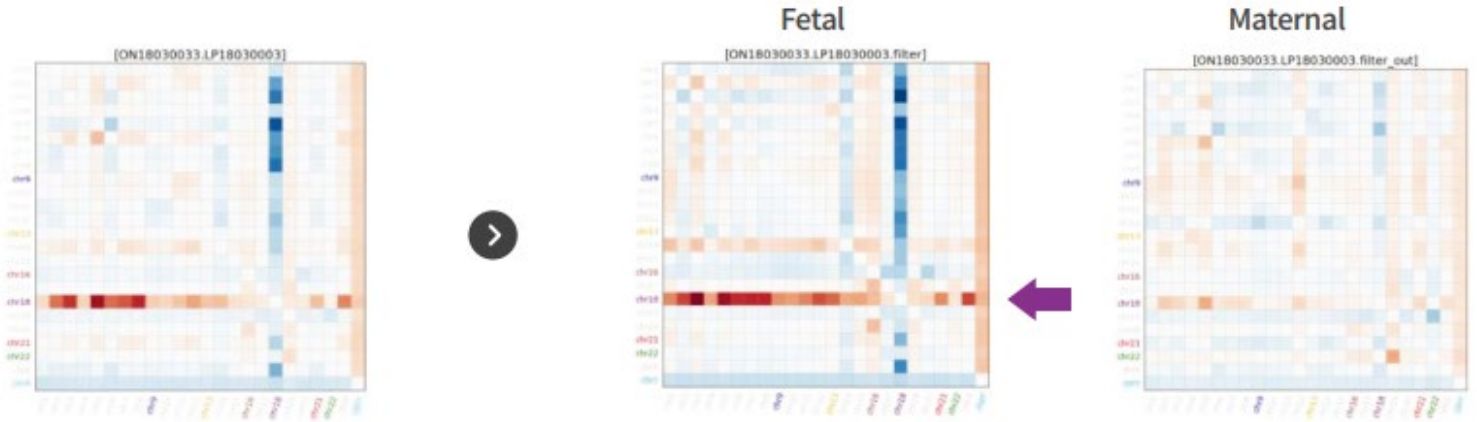


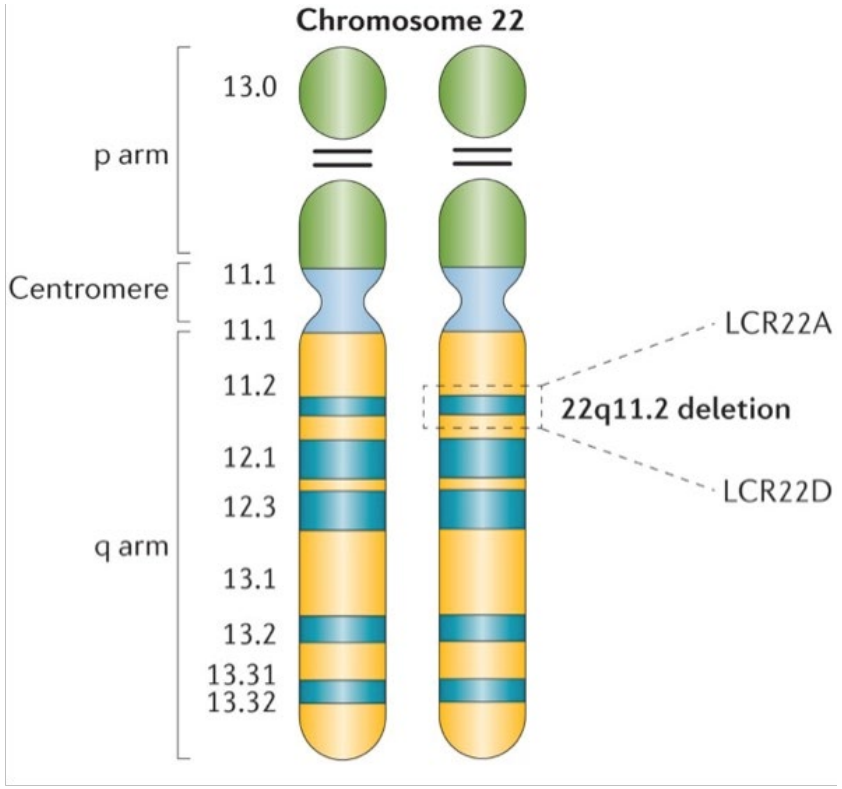


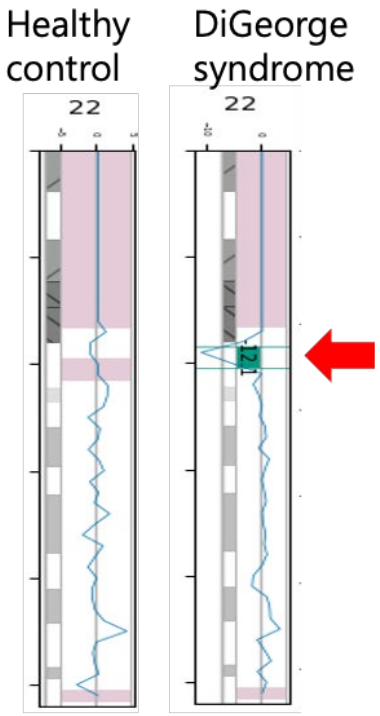
XO Case : Not detected (Maternal Mosaicism)

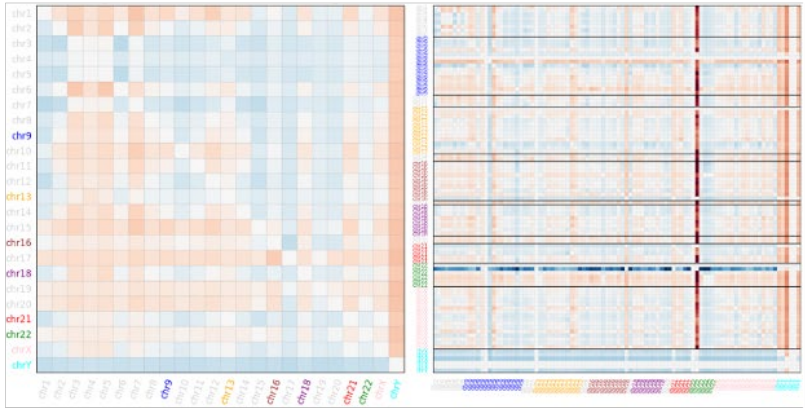


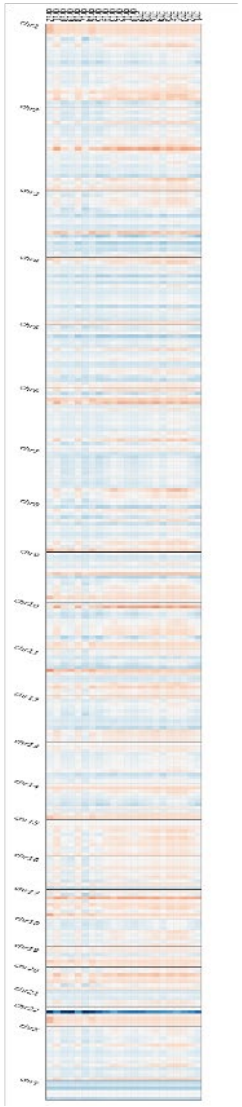
Trisomy 18 : 2-step confirmation




Chromosome 22
13.0
p arm
Centromere
11.1
11.1
11.2
12.1
12.3
q arm
13.1
13.2
13.31
13.32
LCR22A
22q11.2 deletion
LCR22D


Healthy control
DiGeorge syndrome
22
22





NICE® Microdeletions

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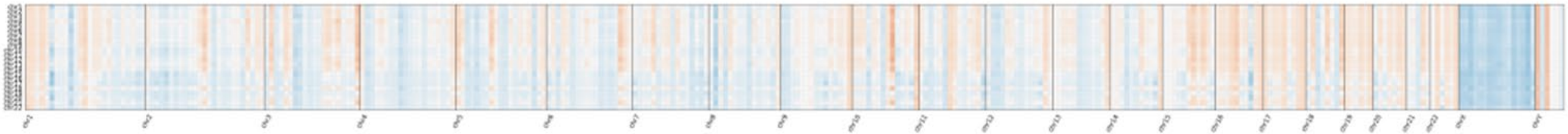
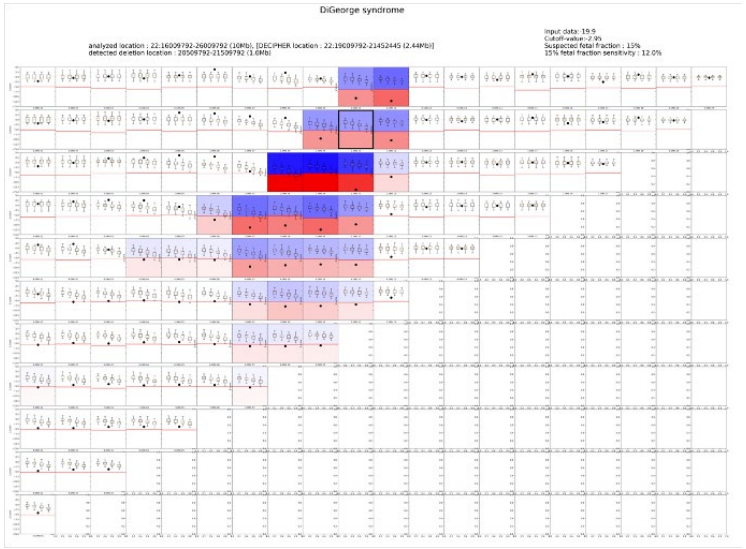
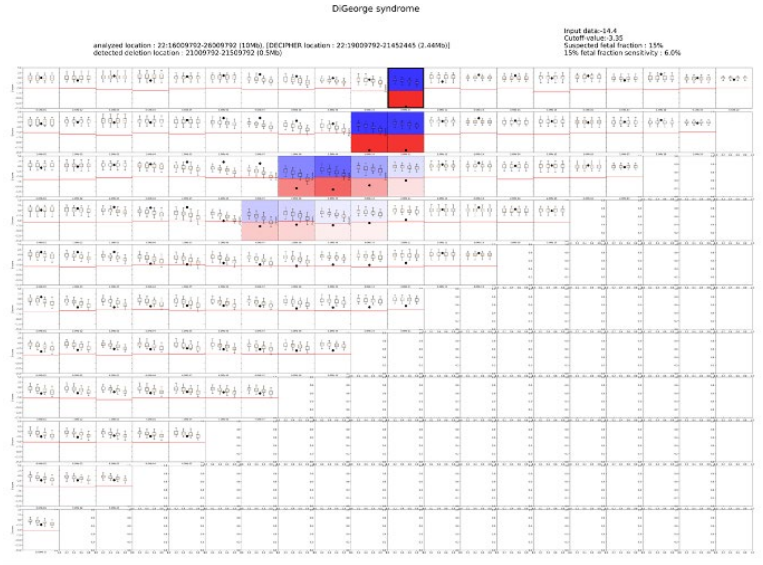
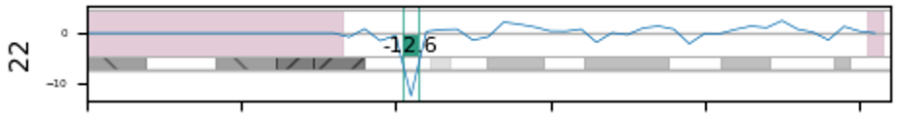
Multi-Z 10mb heatmap



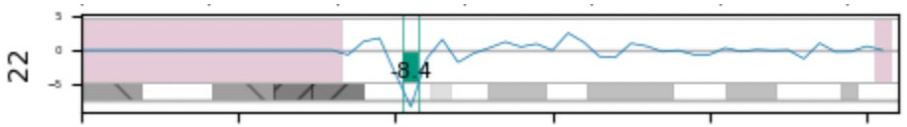


Stair-Matrix
(in-house algorithm)





WiseCondor



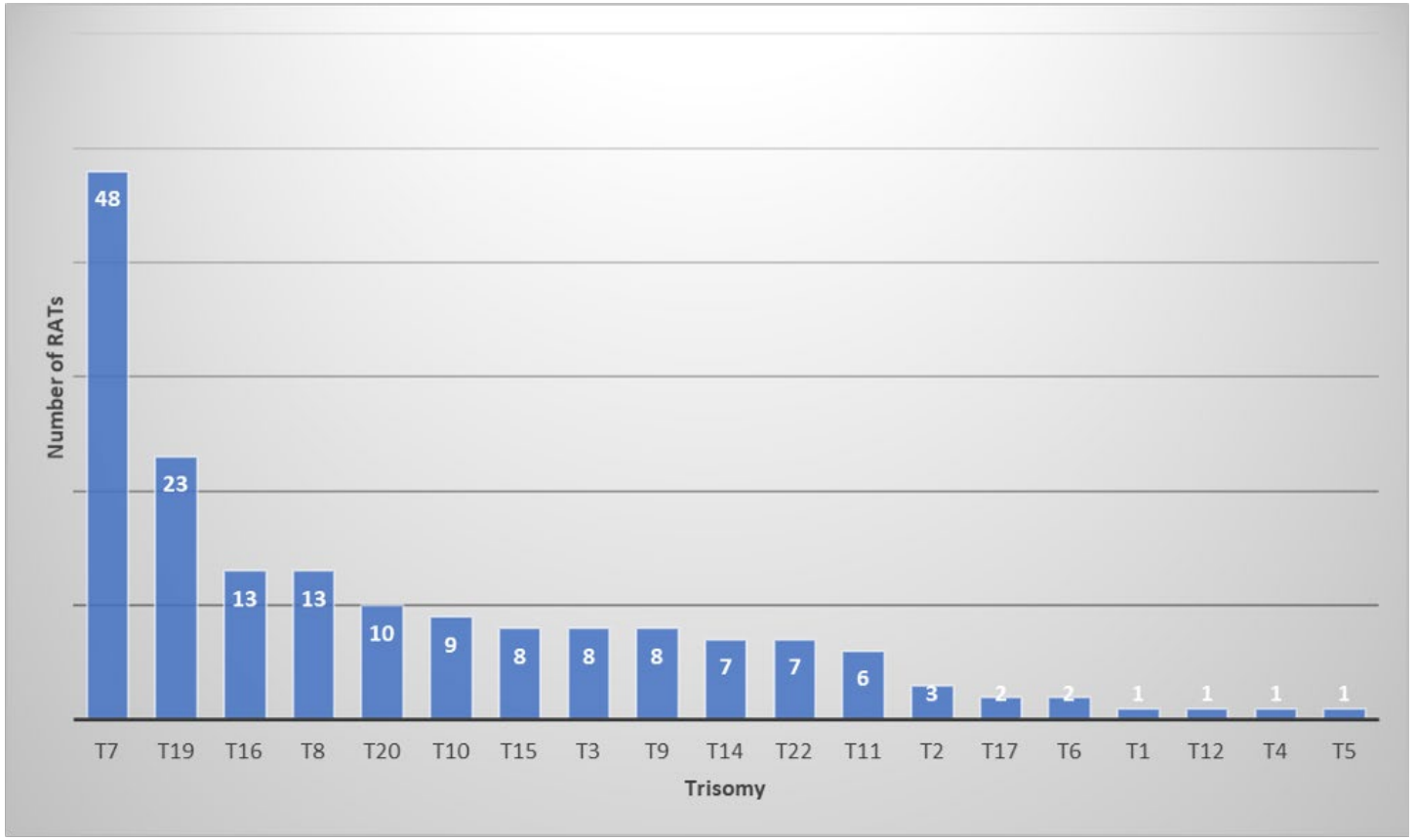
EDEGC

22:20509792-21509792 (1Mb)

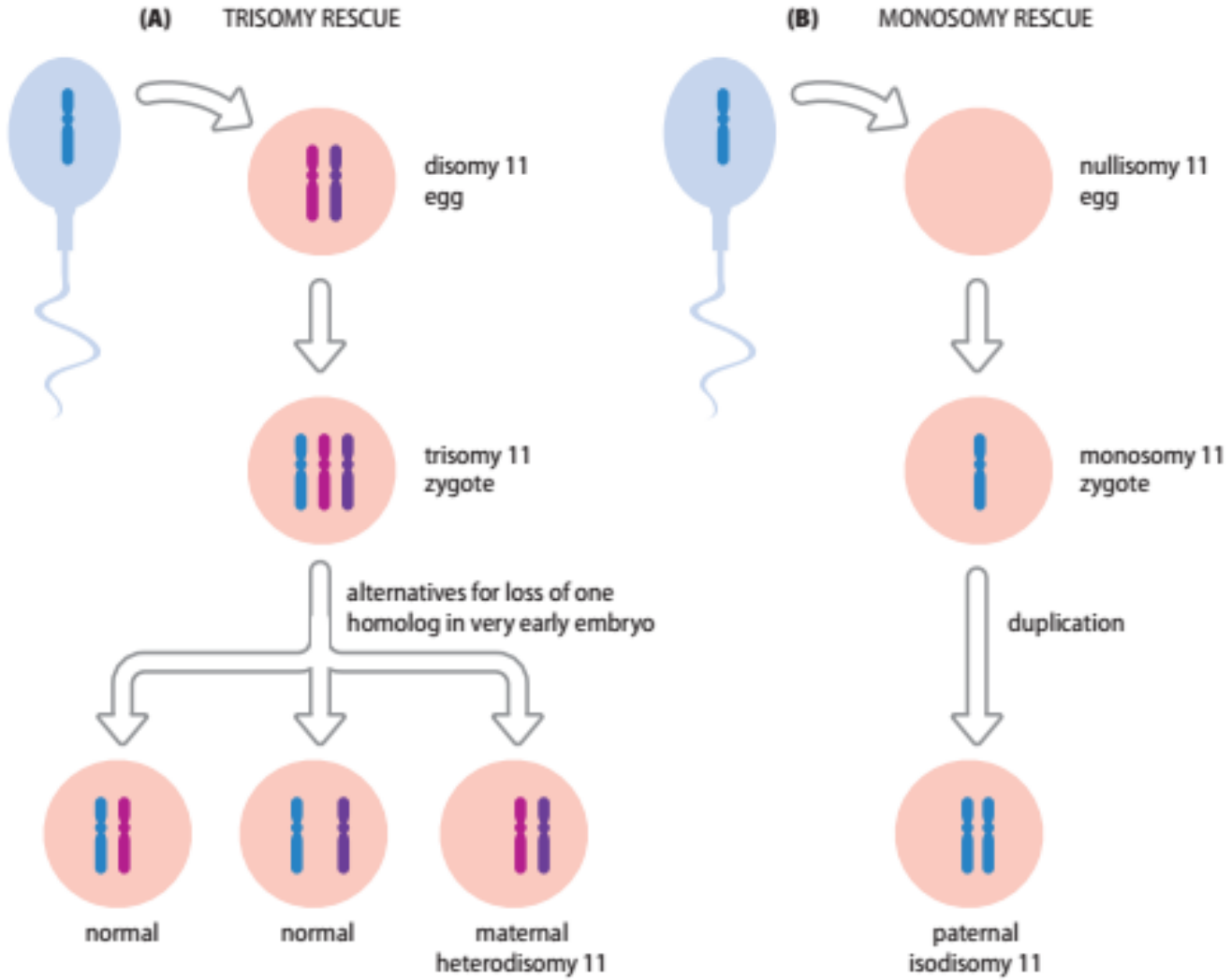
22:21009792-21509792 (0.5Mb)

Validation All Chromosomes

	Full	Partial	SUM
T7	47	1	48
T19	23	0	23
T16	12	1	13
T8	10	3	13
T20	9	1	10
T10	7	2	9
T15	7	1	8
T3	8	0	8
T9	8	0	8
T14	5	2	7
T22	7	0	7
T11	5	1	6
T2	3	0	3
T17	2	0	2
T6	2	0	2
T1	0	1	1
T12	1	0	1
T4	1	0	1
T5	1	0	1
SUM	158	13	171

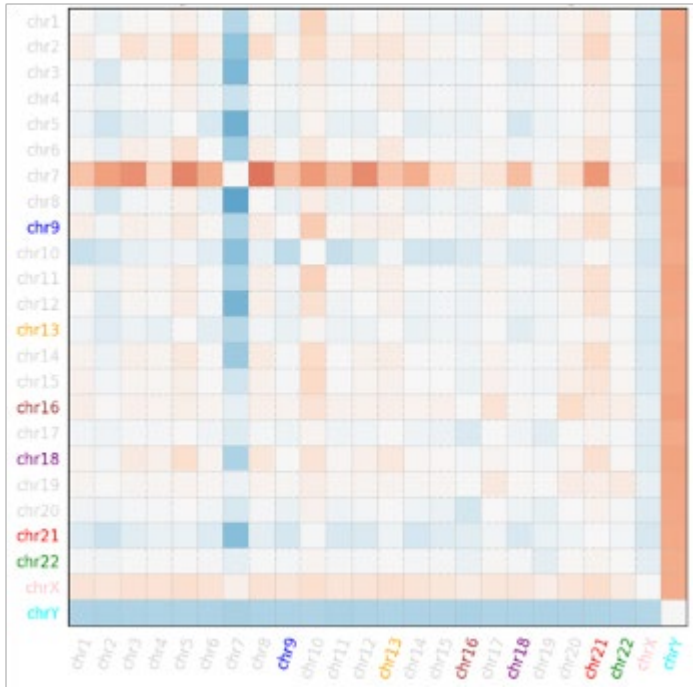


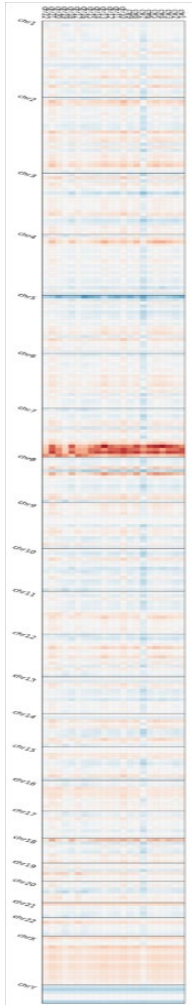
21,644 samples


(A) TRISOMY RESCUE
disomy 11
egg
trisomy 11
zygote
alternatives for loss of one
homolog in very early embryo
normal
normal
maternal
heterodisomy 11
(B) MONOSOMY RESCUE
nullisomy 11
egg
monosomy 11
zygote
duplication
paternal
isodisomy 11

UPD	Parent	Syndrome/Disorder	Phenotype
6	Paternal	Transient neonatal diabetes mellitus	IUGR, neonatal diabetes
7	Maternal	Russell-Silver	IUGR/FTT, dysmorphic
11	Paternal	Beckwith-Wiedemann	Omphalocele, organomegaly, neonatal hypoglycemia, Wilms tumor
11	Maternal	Russell-Silver	IUGR/FTT, dysmorphic
14	Paternal	Temple syndrome	IUGR, dysmorphic
14	Maternal	Kagami-Ogata syndrome	Bell-shaped thorax, developmental retardation, dwarfisms, dysmorphic
15	Maternal	Prader-Willi	Obesity, dysmorphic, ID
15	Paternal	Angelman	ID, dysmorphic
20	Maternal	Growth failure, hyperactivity	IUGR/FTT
20	Paternal	Pseudohypoparathyroidism 1b	Pseudohypoparathyroidism

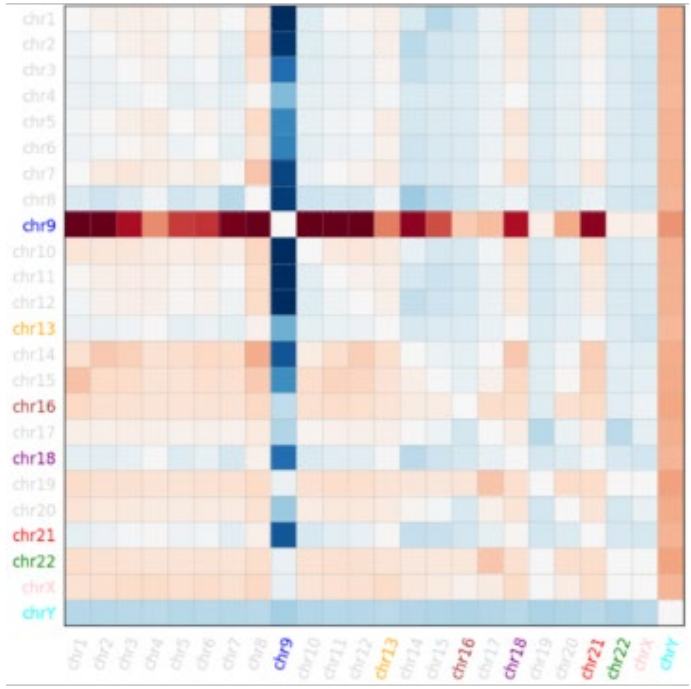
T7 partial, FF: 9.75 10w 4d

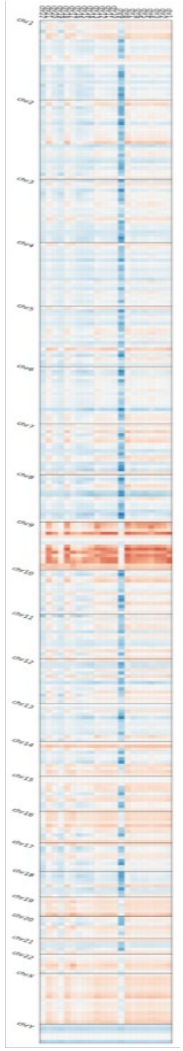




T9, FF: 5.5 17w 6d

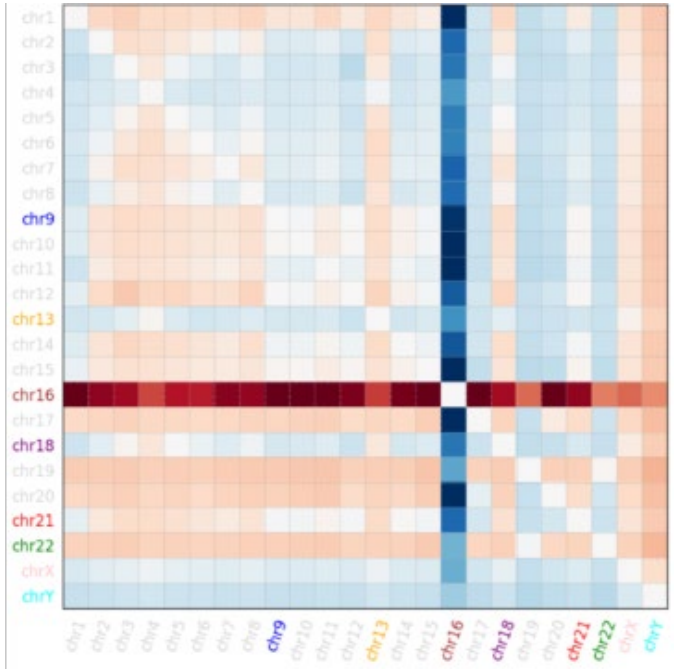
47,X(),+9[14]/46,X()[16]

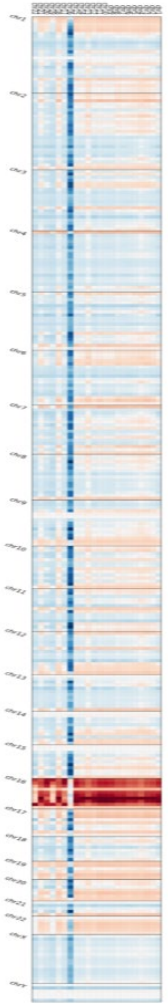




T16 FF: 14.98 17w 3d

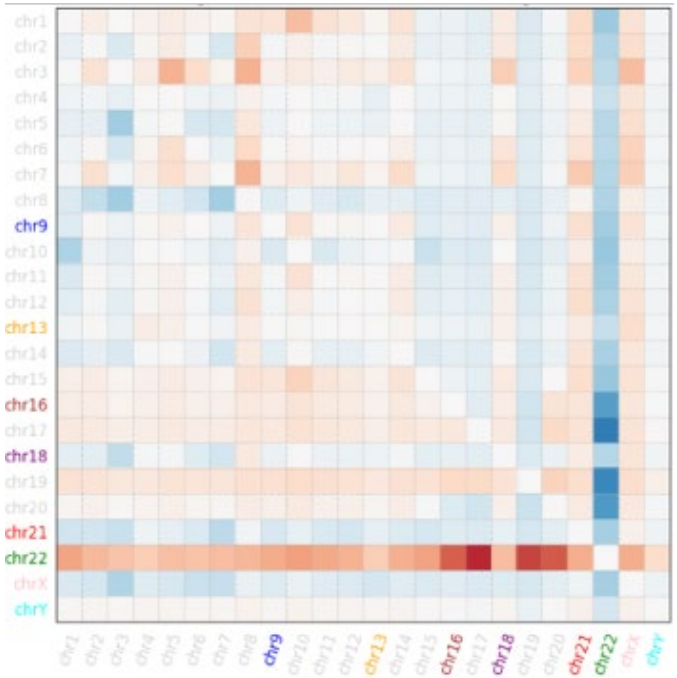
47,X(),+16[3]/46.X()[37]

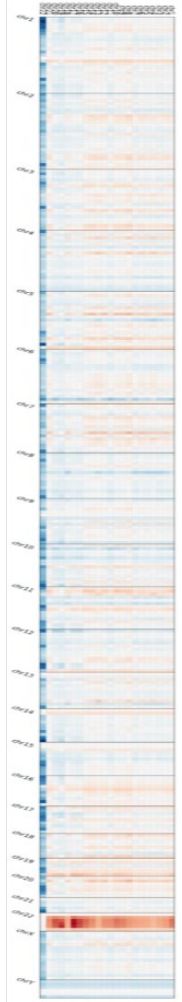




T22, FF: 10.92 17w 0d

47,X(),+22

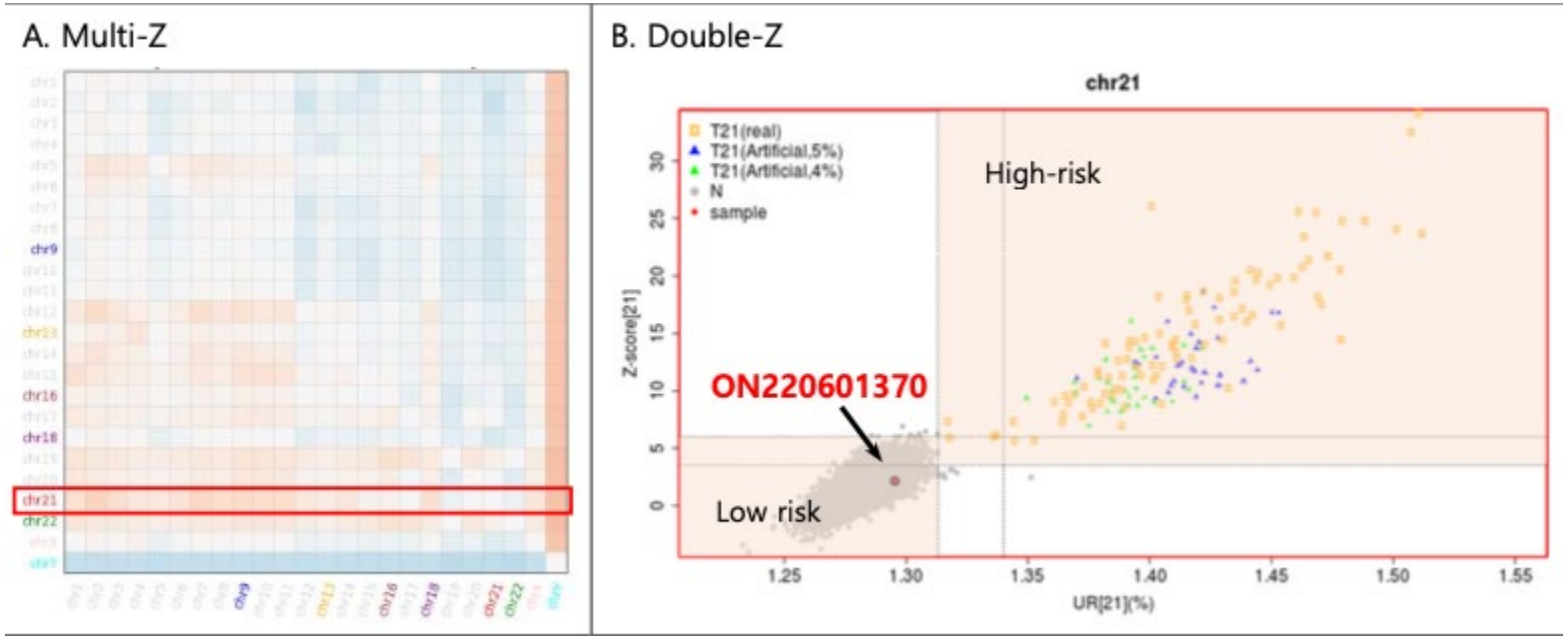


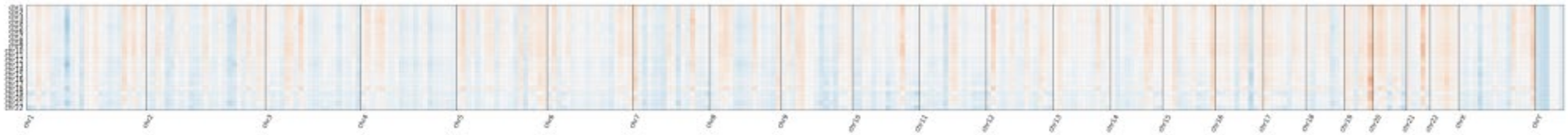


NICE® Cases

EDGC EONE-DIAGNOMICS Genome Center

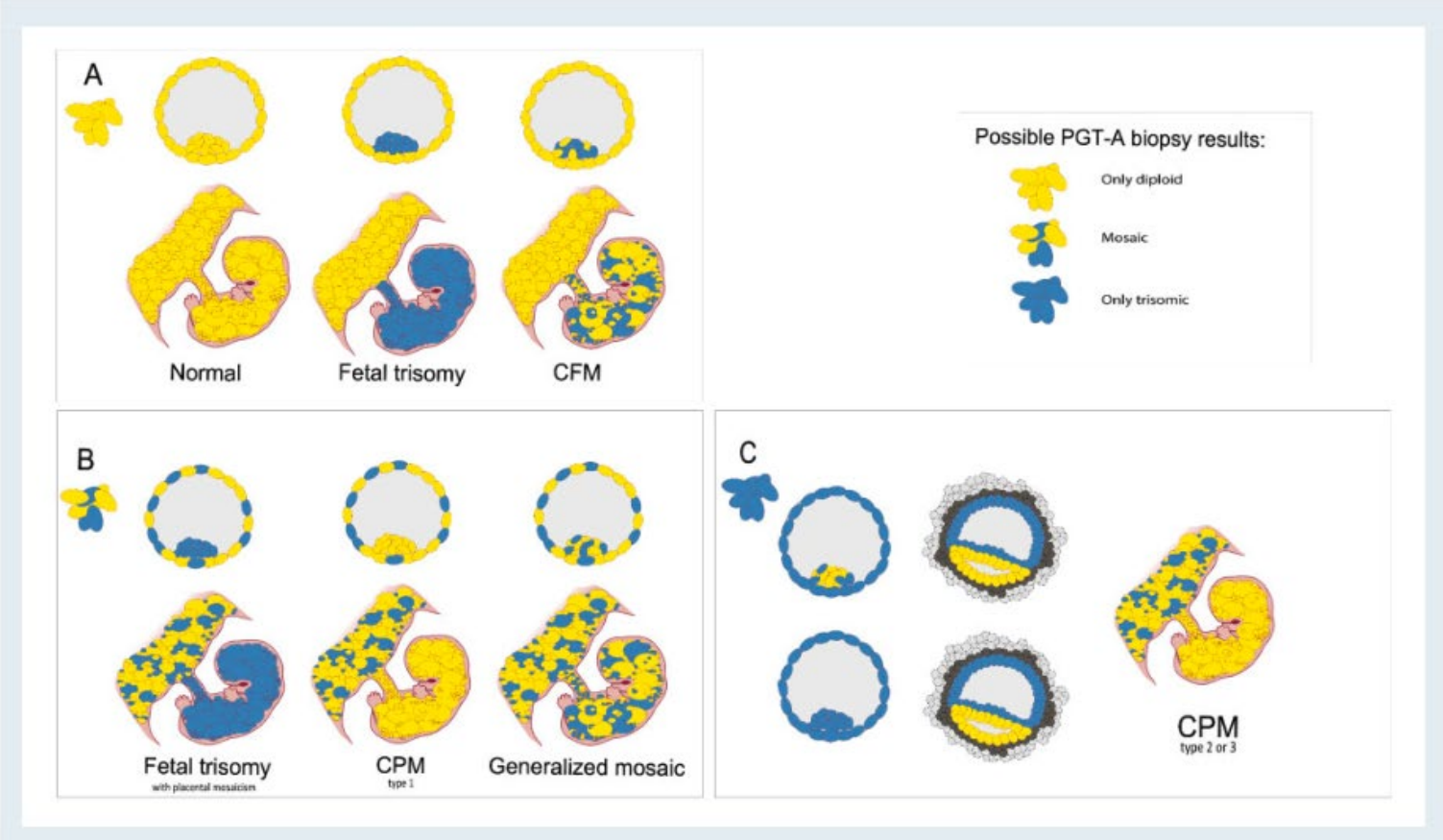
- 31 yo female
- NICE at 11w5d - negative, FF 10.3%
- Repeated NICE at 24w1d- negative, FF 21.2% (no nasal bone)





EDGC

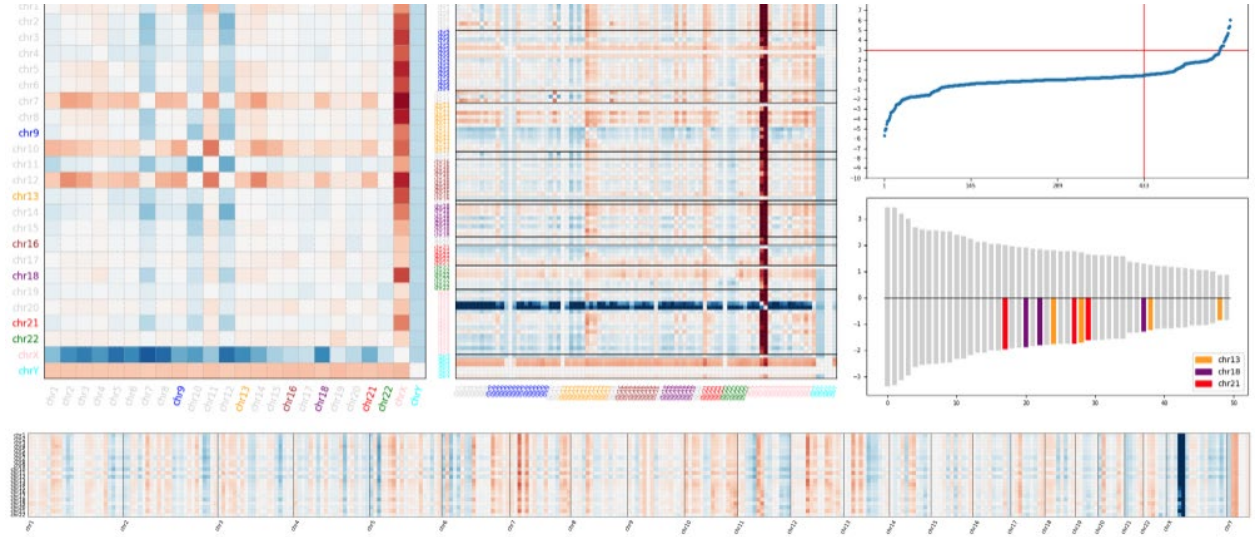
- No amnio- baby born 47, XY +21
- No Nasal Bone ultrasound
- Repeat NICE should not have been performed
- CPM cause

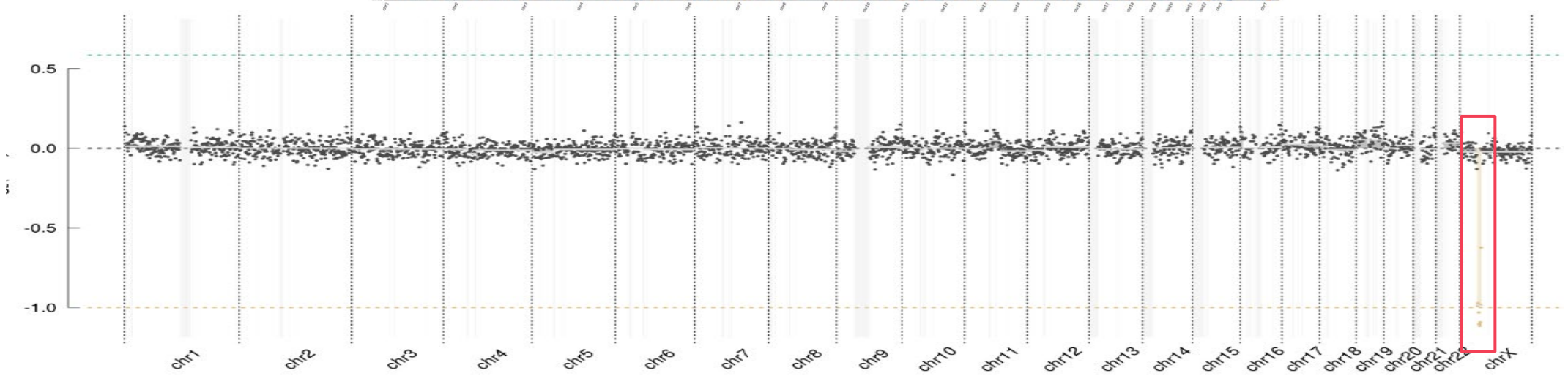


NICE® Cases

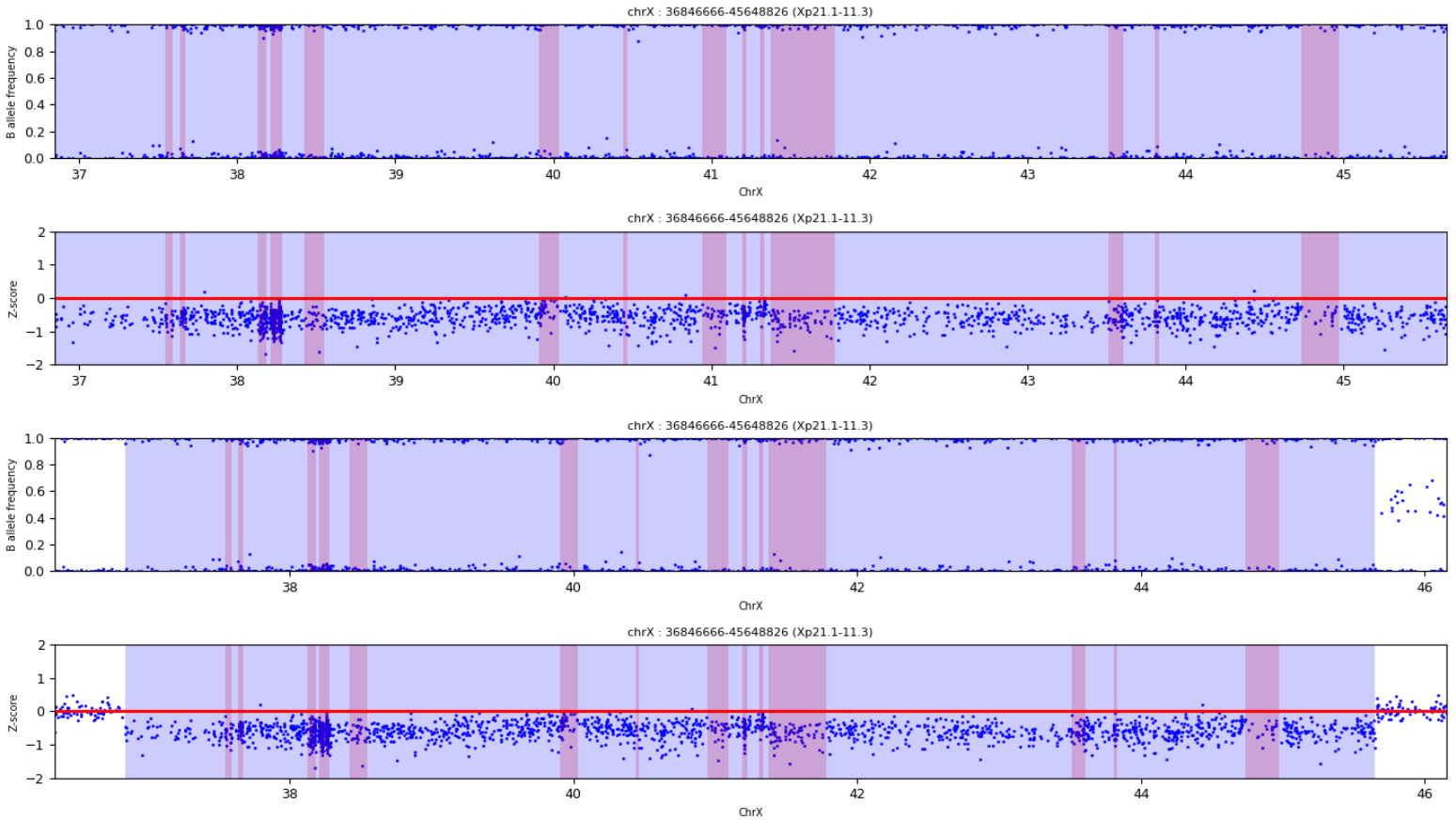
EDEGC EONE-DIAGNOMICS Genome Center

Sample	Original	Fetus	Mom	Final Sex	Fetal Fraction	FFGap	Sample Bias QC	Size QC	Final result	MD results	Pregnancy type
ON221102255.LP22120005	Not Detected	XO Suspected	Not Detected	XX	8.29	NA	PASS	PASS	XO Detected	Not Detected	Singleton





- Mom and fetus Xp21.1 - 11.3



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EONE-DIAGNOMICS
Genome Center

Test Option

	NICE® LITE	NICE® BASIC	NICE® PREMIUM
T13, T18, T21	✓	✓	✓
T9, T16, T22		✓	✓
All Chromosome			✓
*8 Microdeletions			
*116 Microdeletions			
*Sex Chromosome Disorder			

* Any or all can be added to LITE, BASIC, or PREMIUM service

NICE®
Nice Test Report

EDGC
EONE-DIAGNOMICS
Genome Center

NICE® Test Report

NICE
Non Invasive Chromosome Examination

Sample Information	Patient Information	Provider Information
Sample Type :	Name :	Hospital :
Client Sample ID :	Date of Birth :	Physician :
Date of Draw :	Gest. Age at Draw :	Phone :
Date Received :	Pregnancy type :	Fax :
Reporting Date :	Indication :	
Resample :	Medical Record/Patient ID :	

Quality Test

Sample suitability	Pass	NGS data quality	Pass
DNA quality	Pass	Reference material test	Pass
Library quality	Pass	Fetal fraction	9.8%

Results

V4.2k.1a.2a

Chromosome	Result	PPV or NPV	Risk score (before)	Risk score (after)
Trisomy 21	Low Risk	>99(NPV)	1/307	<2/10,000
Trisomy 18	Low Risk	>99(NPV)	1/1,047	<2/10,000
Trisomy 13	Low Risk	>99(NPV)	1/3,222	<2/10,000
Trisomy 9	Low Risk	NA	NA	<2/10,000
Trisomy 16	Low Risk	NA	NA	<2/10,000
Trisomy 22	Low Risk	NA	NA	<2/10,000
XO	Low Risk	>99(NPV)	NA	<3/10,000
XXX	Low Risk	>99(NPV)	NA	<3/10,000
XXY	Low Risk	>99(NPV)	NA	<3/10,000
XYY	Low Risk	>99(NPV)	NA	<1/10,000
All other autosomal trisomies	Low Risk	NA	NA	<2/10,000

Fetal Sex	female

1. All probabilities and PPVs and NPVs are calculated on the site [https://www.perinatalquality.org/Vendors/NSGC/NIPT/] based on maternal age and NICE sensitivity/specificity data.
   - NPV : Negative Predictive Values (In case of Low Risk)
   - PPV : Positive Predictive Values (In case of High Risk)
2. The risk score (before) for aneuploidy was reported in a published study of 17,885 women [Dar et al. Am J Obstet Gynecol. 2014 Nov;211(5):527.e1-527.e17] based on maternal age, gestational age and/or general population.
3. The risk score (after) value is calculated as a probability value obtained through the Gaussian distribution of the normal group and the abnormal group using the fetal DNA percentage (fetal fraction), chromosome read% (Unique Read%) value, and Z-score value. The risk score (after) may not reflect the actual PPV of this patient, and other test results, ultrasound findings, and personal/family history are not included in the risk assessment.

Interpretation

Sample Report

NICE® Microdeletion/duplication Report

NICE
Non Invasive Chromosome Examination

Sample Information	Patient Information	Provider Information
Sample Type :	Name :	Hospital :
Client Sample ID :	Date of Birth :	Physician :
Date of Draw :	Gest. Age at Draw :	Phone :
Date Received :	Pregnancy type :	Fax :
Reporting Date :	Indication :	
Resample :	Medical Record/Patient ID :	

Quality Test

Sample suitability	Pass	NGS data quality	Pass
DNA quality	Pass	Reference material test	Pass
Library quality	Pass		

Results

V4.2k.1a.2a

Location	Disease	Result	Location	Disease	Result
1p36	1p36 deletion syndrome	Low Risk	11q23	Jacobsen syndrome	Low Risk
2q33.1	2q33.1 deletion syndrome	Low Risk	15q11.2-q13	Prader-willi / Angelman syndrome	Low Risk
4p16.3	Wolf-Hirschhorn syndrome	Low Risk	22q11.2	DiGeorge syndrome	Low Risk
5p-	Cri Du Chat syndrome	Low Risk	Etc	108 syndrome sites	High Risk
7q11.23	Williams-Beuren syndrome	Low Risk			

Interpretation

Sample Report

Limitations of Test

1. This test is designed to screen for subchromosomal deletions in chromosomal regions- 1p36, 2q33.1, 4p16.3, 5p-, 7q11.23, 11q23, 15q11.2-q13, 22q11.2, 108 syndromes and is available for singleton pregnancies with gestational age of at least 10 weeks 0 days, as estimated by last menstrual period, crown rump length, or other appropriate method.
2. These results do not eliminate the possibility that this pregnancy may be associated with other chromosomal or subchromosomal abnormalities, birth defects, and other conditions. This test is not intended to identify pregnancies at risk for open neural tube
3. In addition, there is a small possibility that the test results might not reflect the chromosome status of the fetus, but may reflects subchromosomal changes of the placenta (confined placental mosaicism), or of the mother.
4. This is a screening test and this can result in false positive or false negative. Therefore negative results do not eliminate the possibility of 1p36 deletion, 2q33.1 deletion, 4p16.3 deletion, 5p- deletion, 7q11.23 deletion, 11q23 deletion, 15q11.2-q13 deletion, 22q11.2 deletion and 108 microdeletions/duplication syndromes. If definitive diagnosis is desired, chorionic villus sampling or amniocentesis would be necessary, with consideration of prenatal microarray or region specific DNA probes.
5. In addition to the above-mentioned abnormalities, chromosomal and sub-chromosomal findings greater than 3 Mb may be reported. The advanced chromosomal and sub-chromosomal findings are rare and complex, insufficient validation may result in lower specificity. For microdeletion detection, Low fetal fraction or short CNV size is a technical limitation. Consultation on the advice of a physician(s) will be necessary for such findings.

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List of 108 microdeletion/duplication syndromes

No.	Disease
1	1p32-p31 deletion syndrome
2	1q41-q42 deletion syndrome
3	1q43-q44 deletion syndrome
4	2p12-p11.2 deletion syndrome
5	2p15-p16.1 deletion syndrome
6	2q13 deletion syndrome
7	2q13 duplication syndrome
8	2q31.1 microdeletion syndrome
9	2q31.1 duplication syndrome
10	2q35 duplication syndrome
11	3p25.3 deletion syndrome
12	3pter-p25 deletion syndrome
13	3q13.31 deletion syndrome
14	Dandy-Walker syndrome (DWS)
15	3q26 microduplication syndrome
16	3q29 deletion syndrome
17	4q21 deletion syndrome
18	Axenfeld-Rieger syndrome, type 1 (RIEG1)
19	5p13 duplication syndrome
20	5q12 deletion syndrome
21	5q14.3 deletion (proximal) syndrome
22	Sotos syndrome
23	6p22 microdeletion syndrome
24	6q11-q14 deletion syndrome
25	6q24-q25 deletion syndrome
26	Coffin-Siris syndrome 1 (CSS1)
27	Chordoma
28	Greig cephalopolysyndactyly syndrome (GCPS)
29	7p22.1 microduplication syndrome
30	7q11.23 deletion (distal) syndrome
31	Williams-Beuren syndrome (WBS)
32	Currarino syndrome
33	7q36.3 duplication syndrome
34	8p11.2 deletion syndrome
35	8p23.1 deletion syndrome
36	8q12 microduplication syndrome
37	Nablus mask-like facial syndrome (NMLFS)
38	Trichorhinophalangeal syndrome type 2 (TRPS2)
39	9p deletion syndrome
40	9p13 microdeletion syndrome
41	9p24.3 deletion syndrome
42	9q33.3q34.11 microdeletion syndrome
43	Early infantile epileptic encephalopathy 4 (EIEE4)
44	Kleefstra syndrome 1 (KLEFS1)
45	10p11.21-p12.31 microdeletion syndrome
46	DiGeorge syndrome/velocardiofacial syndrome complex 2 (DSG2)
47	10q22.3-q23.2 deletion syndrome
48	Split-hand/foot malformation 3 (SHFM3)
49	10q26 deletion syndrome
50	Potocki-Shaffer syndrome
51	WAGR syndrome
52	WAGRO syndrome
53	11q13.2-q13.4 deletion syndrome
54	11q22.2-q22.3 microdeletion syndrome
55	11q23 deletion syndrome
56	12p12.1 microdeletion syndrome
57	12q14 microdeletion syndrome
58	12q15q21.1 microdeletion syndrome
59	13q14 deletion syndrome
60	14q11-q22 deletion syndrome
61	Frias syndrome
62	14q24.1-q24.3 microdeletion syndrome
63	15q13.3 deletion syndrome (BP4 to BP5) (loss)
64	15q13.3 deletion syndrome (BP4 to BP5) (gain)
65	15q14 microdeletion syndrome
66	15q25.2 deletion (proximal) syndrome
67	15q26-qter deletion syndrome
68	16p11.2-p12.2 microduplication syndrome
69	16p12.2 deletion (proximal) syndrome
70	16p13.11 duplication syndrome
71	16p13.11 deletion syndrome
72	Polycystic kidney disease, infantile severe, with tuberous sclerosis (PKDTS)
73	Rubinstein-Taybi syndrome
74	Alpha-thalassemia/intellectual disability syndrome, chromosome 16-related (ATR-16 syndrome)
75	16q22 deletion syndrome
76	Smith-Magenis syndrome
77	Yuan-Harel-Lupski syndrome (YUHAL)
78	17p12 deletion syndrome
79	17p12 duplication syndrome
80	17p13.1 deletion syndrome
81	Miller-Dieker lissencephaly syndrome (MDLS) (loss)
82	Miller-Dieker lissencephaly syndrome (MDLS) (gain)
83	17p13.3 telomeric duplication syndrome
84	17q12 deletion syndrome
85	17q21.31 deletion syndrome
86	17q23.1-q23.2 deletion syndrome
87	Tetrasomy 18p syndrome
88	18p deletion syndrome
89	18q deletion syndrome
90	19p13 duplication syndrome
91	19q13.11 microdeletion syndrome
92	20p13 microdeletion syndrome
93	21q22.11-q22.12 microdeletion syndrome
94	22q11.2 deletion syndrome (distal, D-E/F)
95	22q11.2 deletion syndrome (LCR22 B/C-D)
96	22q13 deletion syndrome
97	22q13 duplication syndrome
98	Xp11.22 duplication syndrome
99	Xp11.22-p11.23 duplication syndrome
100	Xp11.23 microdeletion syndrome
101	Xp11.3 deletion syndrome
102	Xp21 microdeletion syndrome
103	Xp21.2 microduplication syndrome
104	Xp22.31 microdeletion syndrome
105	Xq21 microdeletion syndrome
106	Xq22.3 telomeric deletion syndrome
107	Xq27.3-q28 duplication syndrome
108	Xq28 deletion syndrome

EDGC

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EDGC
EONE-DIAGNOMICS
Genome Center

Available after 10 weeks pregnant

More than 99% test success rate

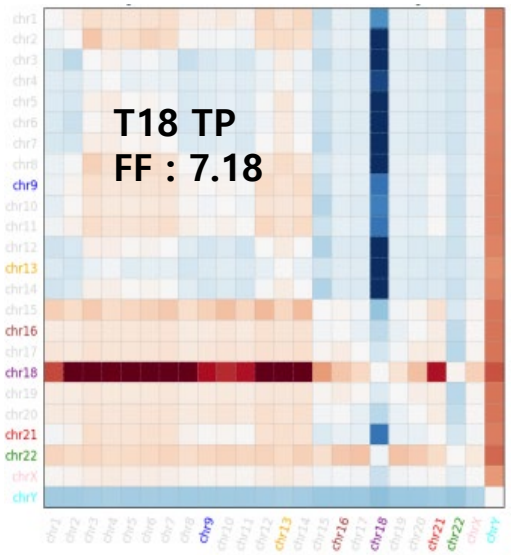
Safe and easy test with maternal blood

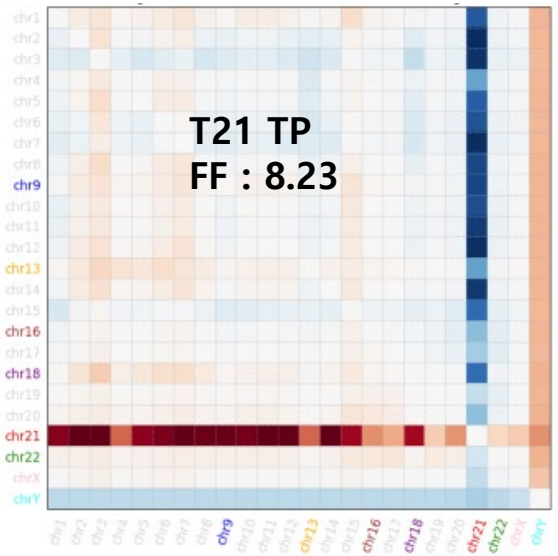
Bioinformatics pipeline accuracy

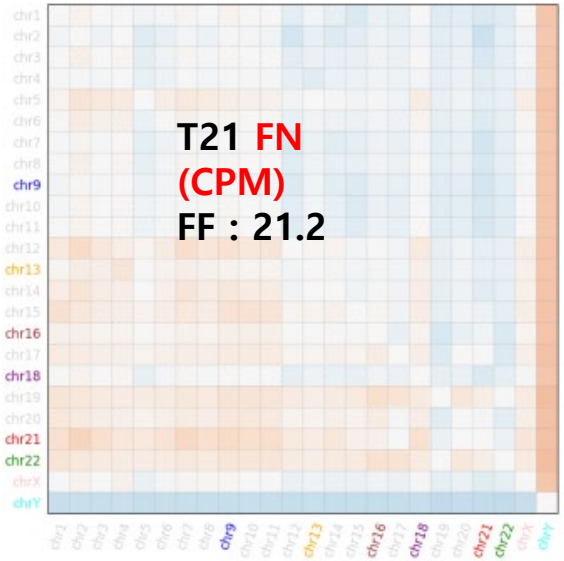
NICE® Cases

EDGC EONE-DIAGNOMICS Genome Center

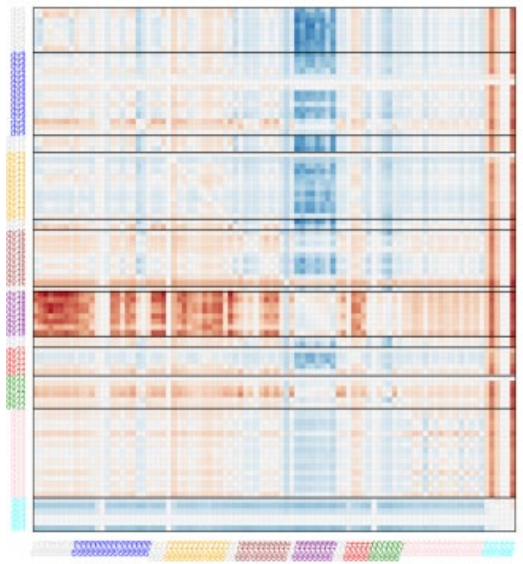
Chromosomal heatmap

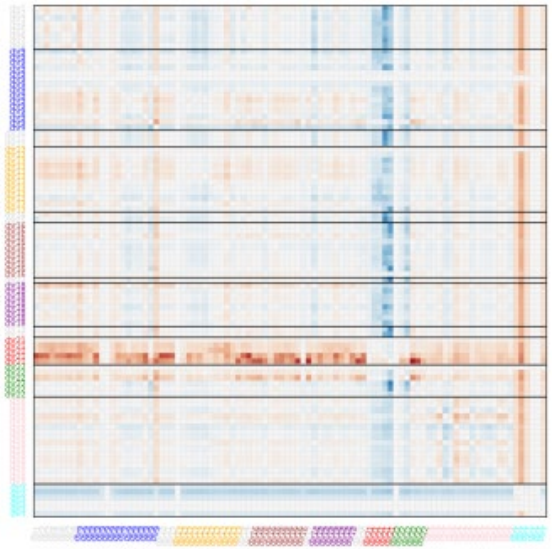


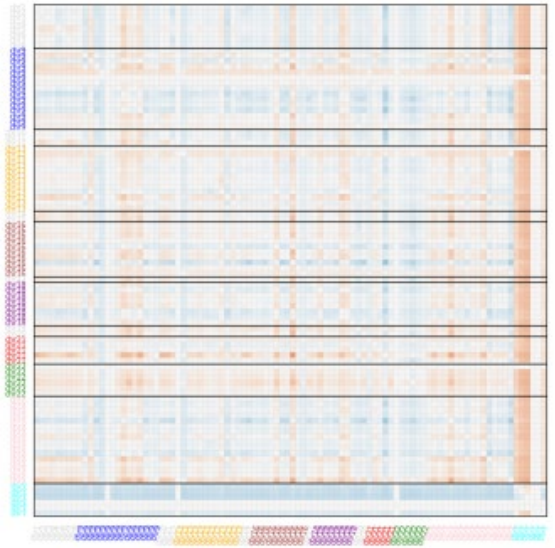




10mb bin heatmap







NICE® Cases

EDEGC EONE-DIAGNOMICS Genome Center

T9 **17W 6D**
FF : 5.5

47,X(),+9[14]/46,X()[16]

T16 **17W 3D**
FF : 14.98

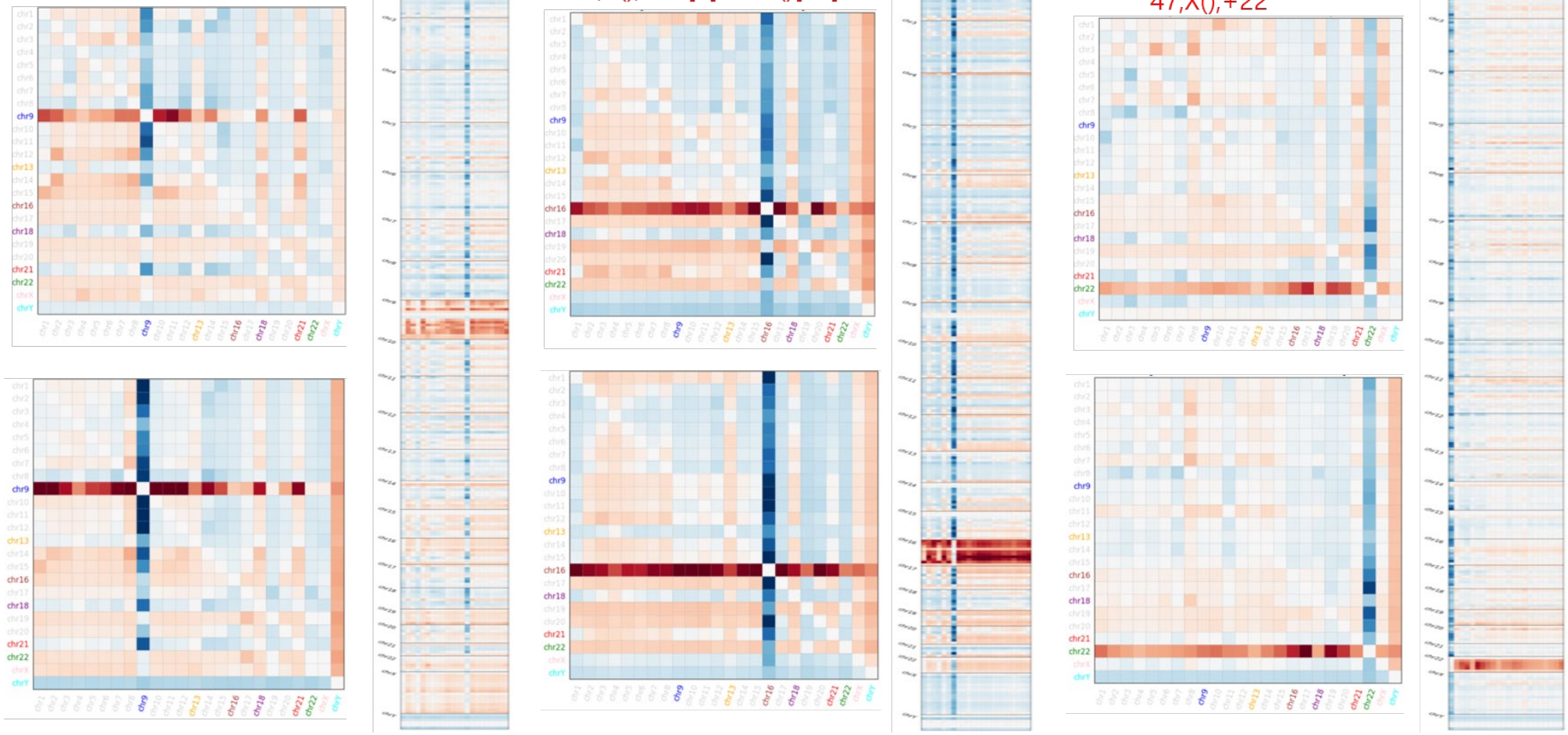
47,X(),+16[3]/46.X()[37]

T22 **17W 0D**
FF : 10.92

47,X(),+22

Original

Fetus



NICE®
Microdeletions

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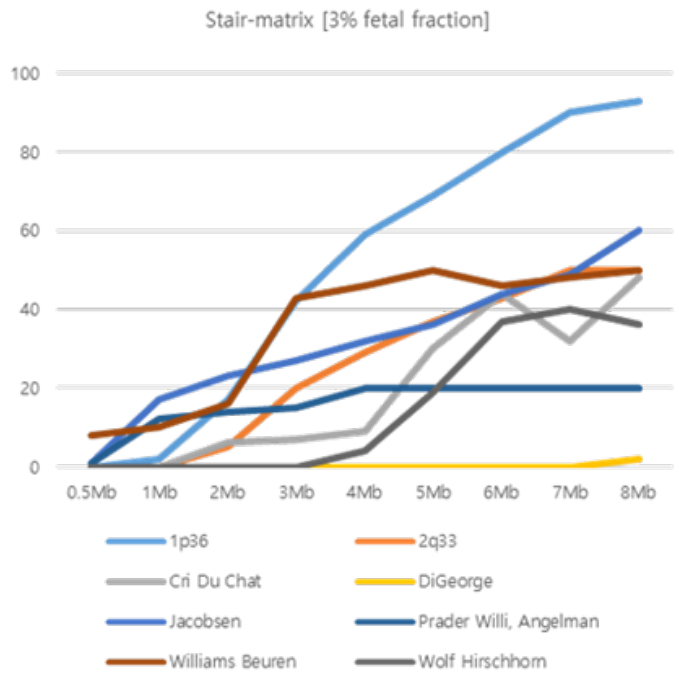
* Total : **28,800** samples (Artificial samples due to lack of clinical samples)
* Create a known region for DECIPHER and OMIM

Disease	deletion location and length (DECIPHER)	Detected Range (Mb)	LOD length (Mb)	LOD Fetal Fraction	sensitivity	specificity
1p36 deletion syndrome	1:10001-12840259 (12.83Mb)	0.5~12.83	≥3	≥3%	42~100%	100%
2q33.1 deletion syndrome	2:196925121-205206939 (8.23Mb)	0.5~10	≥3	≥3%	20~97%	100%
Wolf-Hirschhorn syndrome (4p16.3 deletion)	4:1569197-2110236 (0.54Mb)	1~10	≥3	≥5%	19~87%	100%
Cri du chat syndrome (5p15.3 deletion)	5:10001-12533304 (12.52Mb)	0.5~12.52	≥4	≥5%	44~95%	100%
Williams beuren syndrome (7q11.23 deletion)	7:72744455-74142672 (1.39Mb)	0.5~10	≥4	≥3%	46~92%	100%
Jacobsen syndrome (11q23 deletion)	11:110470724-121170709 (10.69Mb)	0.5~10.69	≥3	≥3%	27~96%	100%
Prader-Willi / Angelman syndrome (15q11.2 deletion)	15:22749354-28438266 (5.68Mb)	0.5~10	≥4	≥3%	20~87%	100%
DiGeorge syndrome (22q11.2 deletion)	22:19009792-21452445 (2.44Mb)	2~10	≥5	≥5%	34~97%	100%



- Technical limitation : Low Fetal Fraction, Short CNV size
- In the shallow-depth NGS sequencing method, there are chromosomal regions that are difficult to read mapping to the reference sequence depending on the chromosomal characteristics.