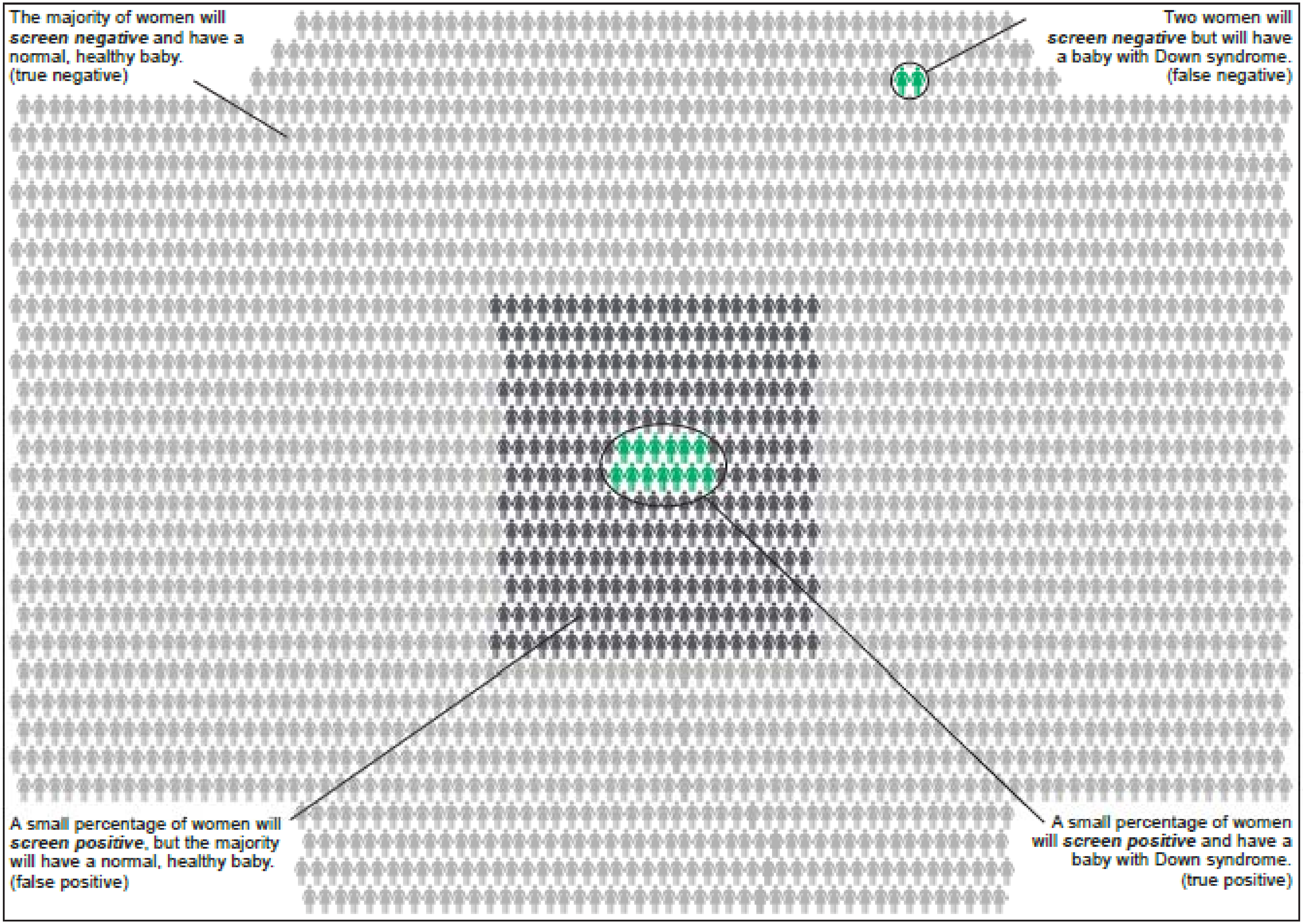
Understanding Prenatal Screening: A Visual Aid for Patients

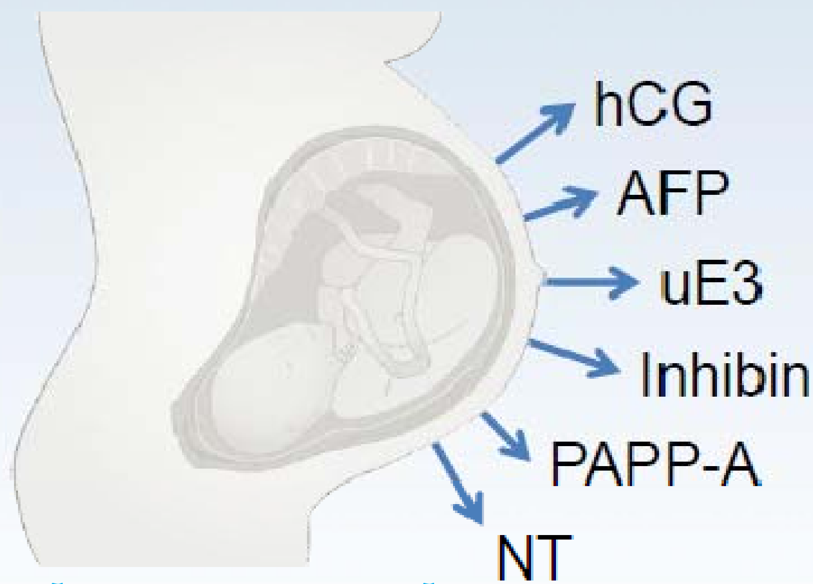
This visual aid illustrates 5,000 pregnant women who chose Down Syndrome screening.



Statistics based on singleton pregnancies choosing screening in BC.

BC Prenatal Genetic Screening Program - Revised July 2015

Pregnancy Risk Screens Estimate Risks Based Largely on Phenotypic Factors



Commonly Utilized Screens

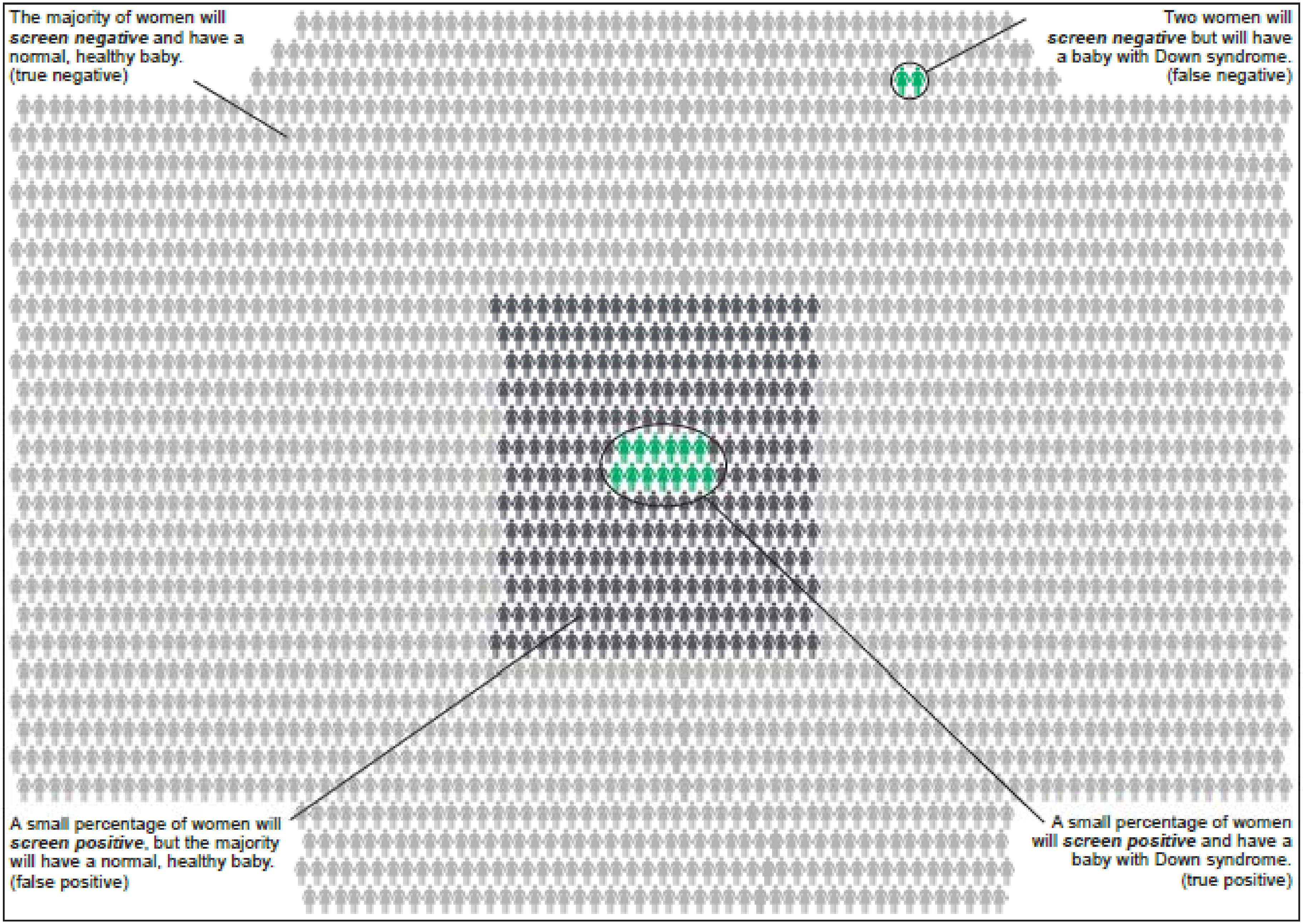
Test	1st Trimester				2nd Trimester						
	10	11	12	13	14	15	16	17	18	19	20
Sequential Screen	NT, PAPP-A, hCG					AFP, hCG, uE3, DIA					
Serum Integrated Screen	PAPP-A					AFP, hCG, uE3, DIA					
Quad Screen						AFP, hCG, uE3, DIA					

بروز ناهنجاری های کروموزومی در نوزادان

ناهنجاری	بروز به ازای هر ۱۰۰۰۰ تولد
اتوزومی	
تریزومی ۱۳	**۲**
تریزومی ۱۸	**۳**
تریزومی ۲۱	**۱۵**
کروموزم های جنسی تولد های دختر	
45,X	**۱–۲**
47,XXX	**۱۰**
تولدهای پسر	
47,XXY	**۱۰**
47,XYY	**۱۰**
سایر حالت های نوآرایی	
نامتعادل	**۱۰**
نوآرایی متعادل	**۳۰**
مجموع	**۹۰**

Understanding Prenatal Screening: A Visual Aid for Patients

This visual aid illustrates 5,000 pregnant women who chose Down Syndrome screening.



Statistics based on singleton pregnancies choosing screening in BC.

BC Prenatal Genetic Screening Program - Revised July 2015

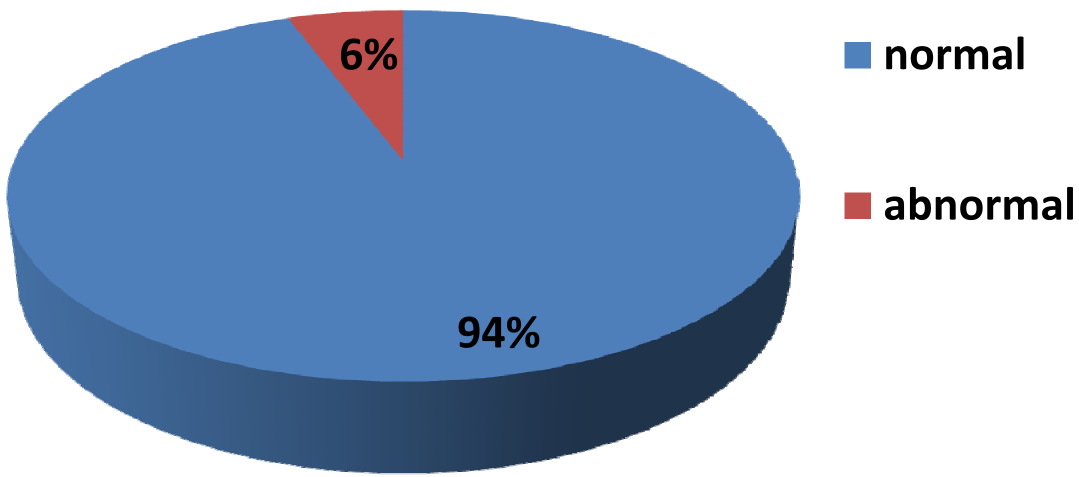
بررسی ۳۰۰۰ کاریوتیپ جنینی

- مطالعه حاضر نتیجه بررسی ۳۰۰۰ کاریوتیپ روی نمونه های جنینی است که عمدتا آمینیو سنتز و تعداد کمتری هم CVS (ویلوزیته های جفتی) شده وبه آزمایشگاه ژنتیک تهران طی دو سال ۱۳۹۰-۱۳۹۱ مراجعه کرده بودند.

- البته ما سالهای بیشتری است که تشخیص پیش از تولد را برای اختلالات کروموزومی در آزمایشگاه ژنتیک تهران انجام میدهیم ولی این ۳۰۰۰ مورد خاص با علت مراجعه شان تطبیق داده شده اند.

Number of normal and abnormal diagnosis in the study population

No. of pregnancies studied	3000
Normal diagnosis	2830 (94%)
Abnormalities diagnosed	170 (6%)

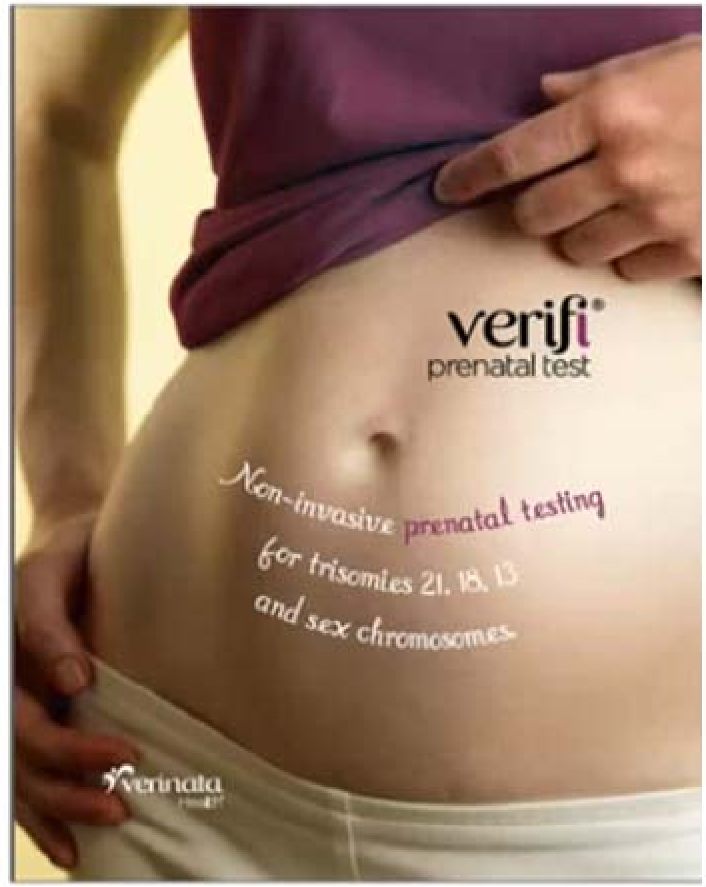


What are the Goals of NIPT?

*Future goal

illumina verinata Health®

Introduction to NIPT and the Serenity (verifi®) prenatal test



آزمایشگاه ژنتیک پزشکی تهران
۱۳۷۱ 1992
Tehran Medical Genetics Laboratory

Presenter: **Mohammad Taghi AKBARI**

verinata
Health®

آزمایشگاه ژنتیک پزشکی تهران
۱۳۷۱ 1992
Tehran Medical Genetics Laboratory

- **Dedicated to maternal and fetal health**
  - Founded in 2002
- **State-of-the-art facility**
  - Redwood City, CA
  - 40,000 ft^2
  - CLIA, CAP accredited
  - Board certified medical directors, counselors

genesis serenity®

Non Invasive Prenatal Test

This genetic screening test is run in the London laboratory of Genesis Genetics, the UK's only private lab to use Illumina verifi® NIPT technology.

With the Genesis Serenity® test, private clinics and ultrasound centres can now offer a high quality, professional NIPT service to expectant parents

- Tests chromosomes 13, 18 & 21 plus sex aneuploidies
- Exceptional accuracy: > 99.7%
- As early as 10 weeks pregnant
- Speedy reporting: fewer than 5 working days
- Low blood sample redraw rate: < 0.1%
- Licensed test and genetic counselling

Contact us today to find a clinic near you.

آزمایشگاه ژنتیک پزشکی تهران
۱۳۷۱ 1992
Tehran Medical Genetics Laboratory

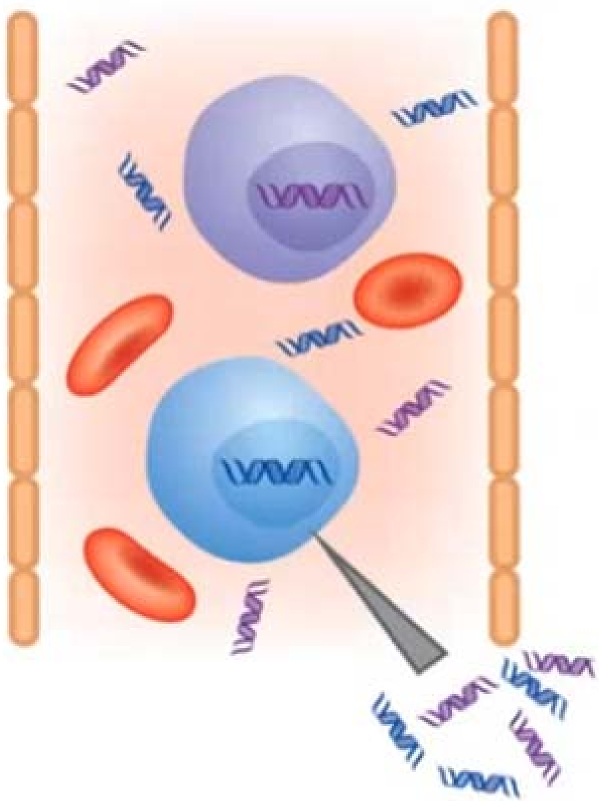
Proudly working with private clinics including:

this is my
because you have a choice
www.thisismy.co.uk

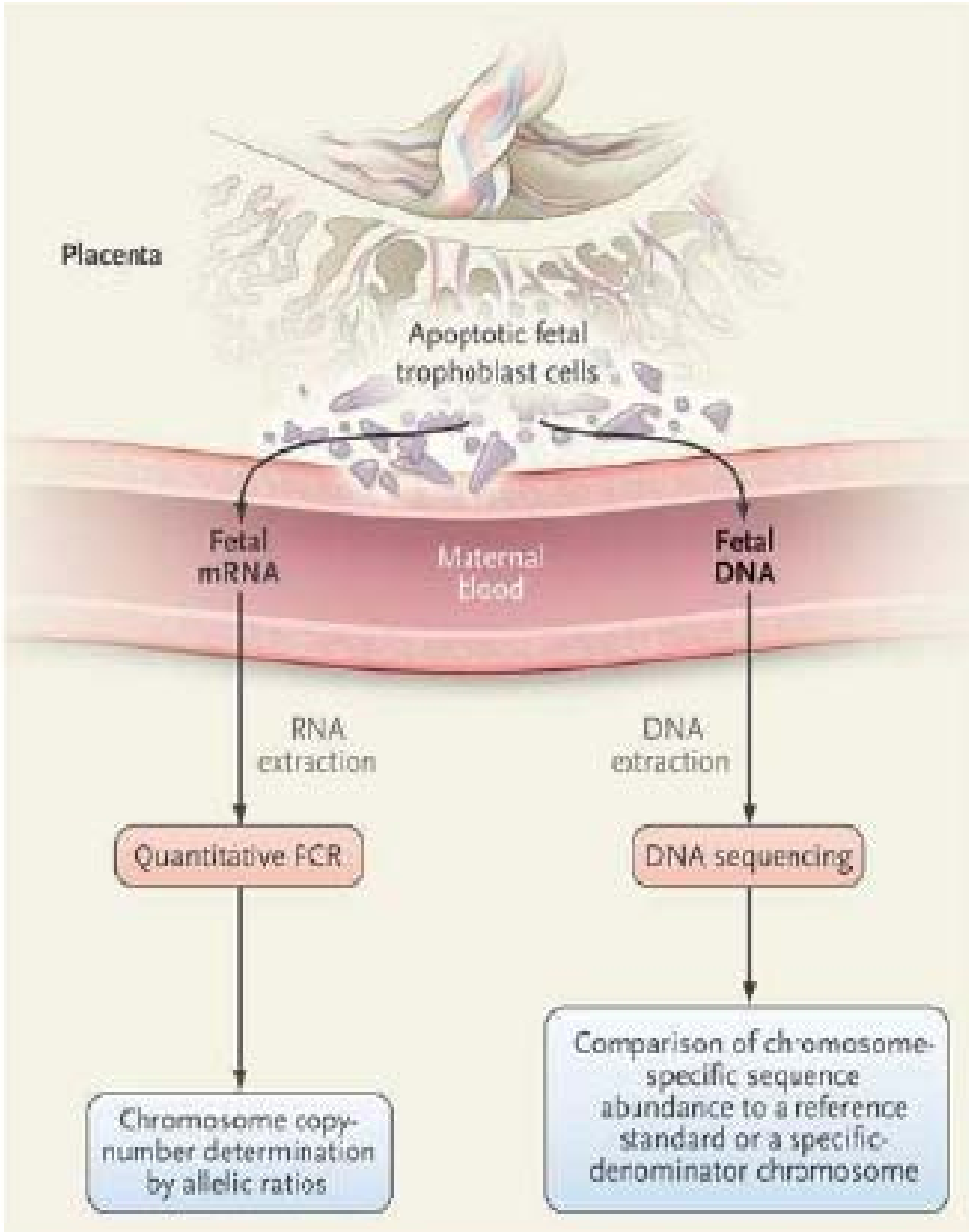
Antenatal Babyscan Clinic
ABC 4D
www.abc4d.co.uk/serenity-clinic

Genesis Genetics UK serenity@genesisgenetics.org www.genesis-serenity.com @genesisserenity

Two Sources of Fetal DNA in Maternal Blood



- **Fetal cells**
  - 1 in billion total cell population
  - Require isolation via mechanical and/or biochemical means
- **Cell-free DNA (cfDNA)**
  - 2–20% of total cfDNA is fetal
  - Requires DNA isolation and counting
  - Counting method developed by Dr. Stephen Quake, Stanford University

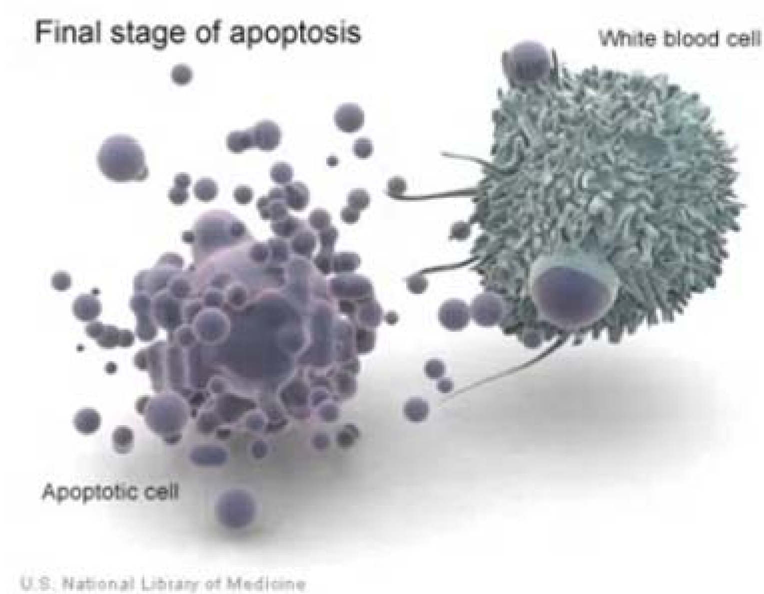


Placenta
Apoptotic fetal trophoblast cells
Fetal mRNA
Maternal blood
Fetal DNA
RNA extraction
DNA extraction
Quantitative PCR
DNA sequencing
Chromosome copy-number determination by allelic ratios
Comparison of chromosome-specific sequence abundance to a reference standard or a specific-denominator chromosome

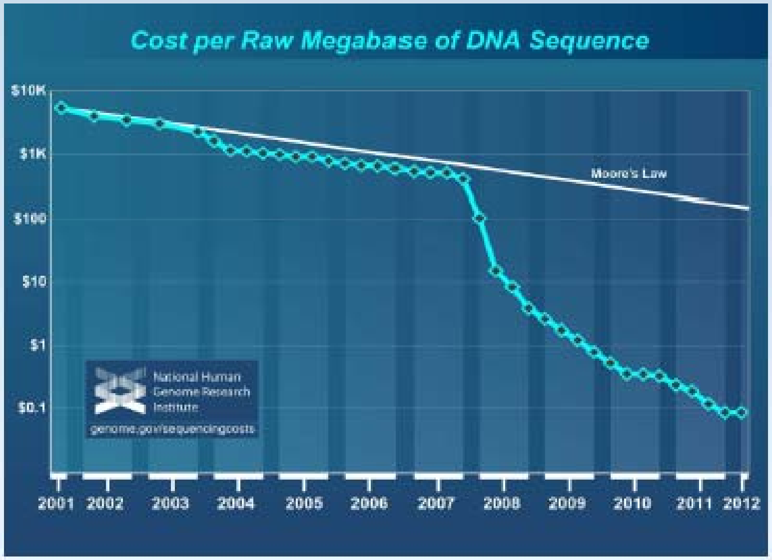
Cell Free DNA (cfDNA)

A Reliable Analyte During Pregnancy

- Released through apoptosis (programmed cell death)
  - Released into bloodstream as small DNA fragments (150-200bp)
  - Maternal blood contains both fetal, maternal cfDNA
  - Detected after 7 weeks gestation
  - Undetectable after 2 hours postpartum



Sequencing Technology Explodes



< 10¢ per
1 million base pairs
by January 2012

Method	Base pairs sequenced per run	Time
Sanger	Tens of thousands	< 1 day
“Next Generation”	Hundreds of billions (our genome is 3 billion bp in length)	days

آزمایشگاه ژنتیک پزشکی تهران نخستین آزمایشگاه قبل از تولد در ایران

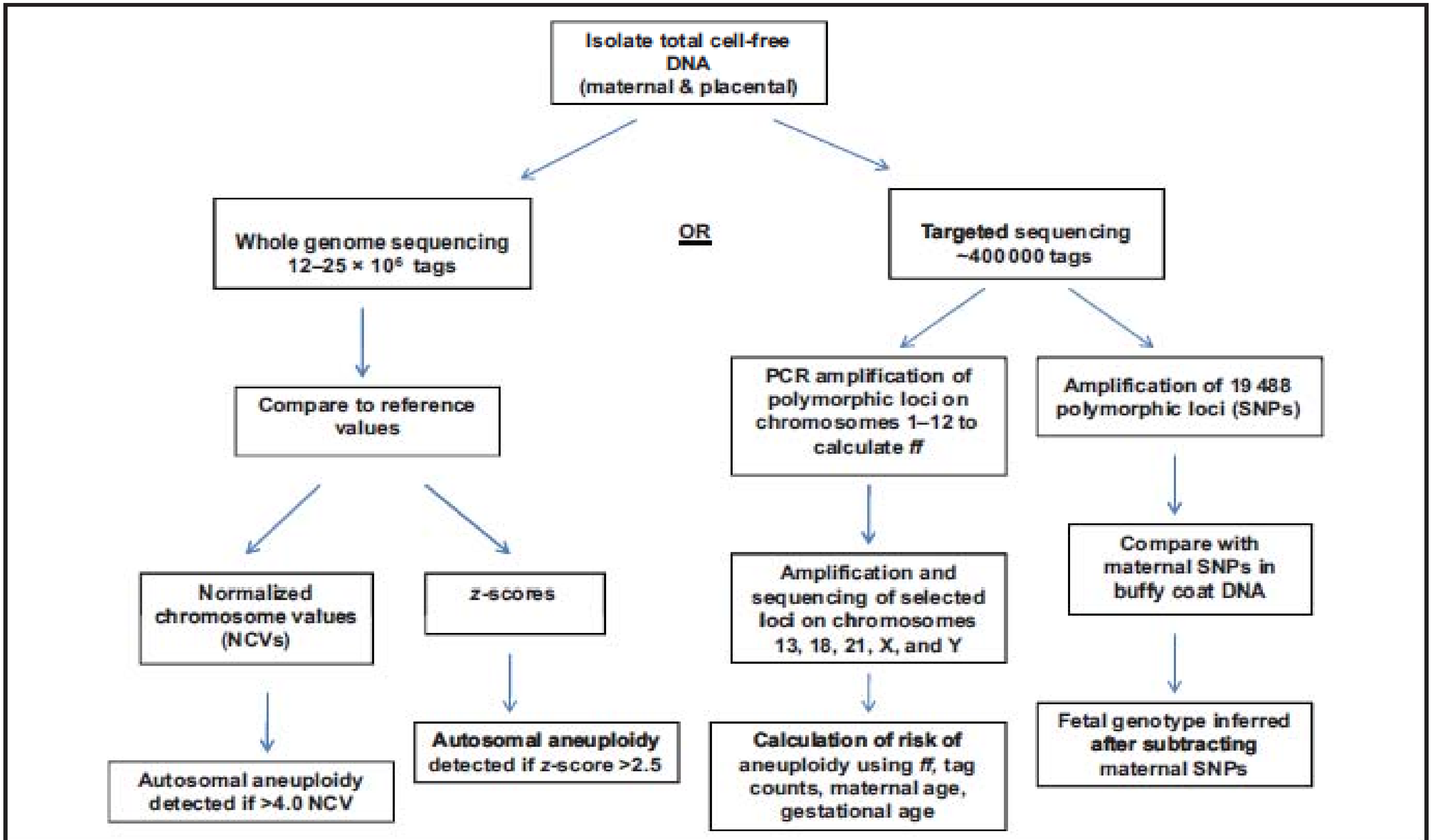


Fig. 1. Major differences in the technical approaches to sequencing of circulating cell-free DNA in the plasma of pregnant women.

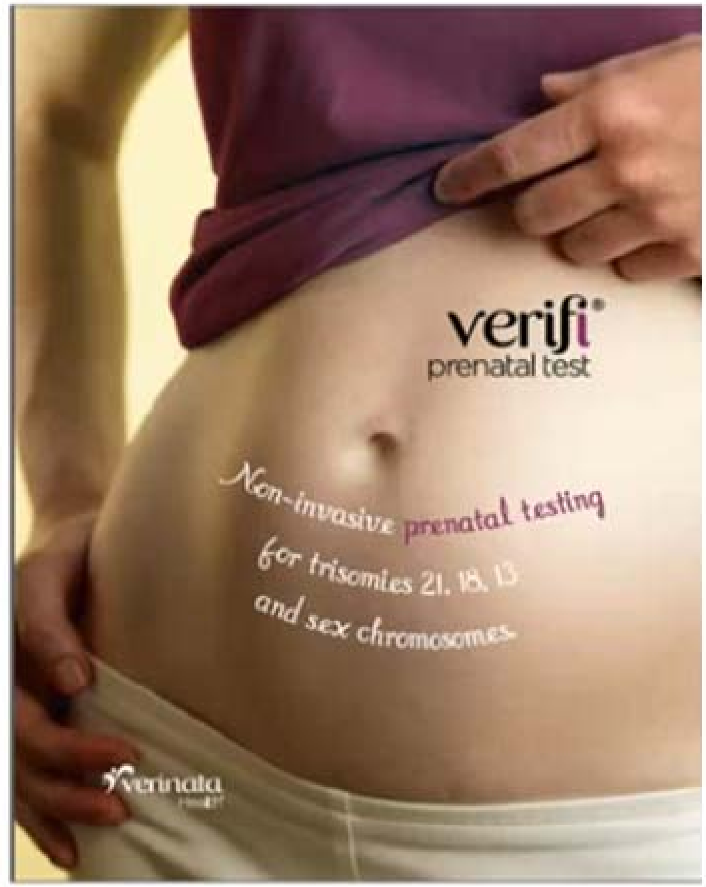
Companies Offering NIPT

SEQUENOM®	MaterniT21™ PLUS
verinata Health®	verifi® prenatal test
Integrated GENETICS LabCorp Specialty Testing Group / Ariosa DIAGNOSTICS	Harmony™ PRENATAL TEST
natera™	**Launching early 2013**

illumina verinata Health®

Introduction to NIPT and the

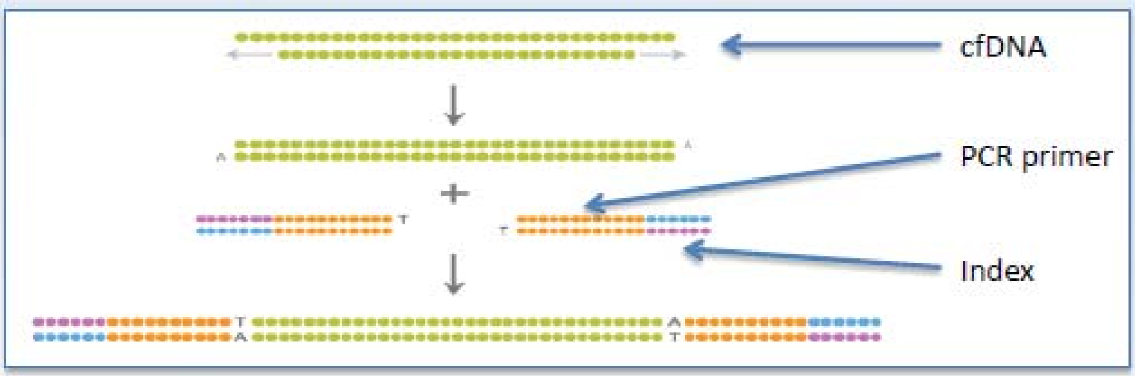
Serenity (verifi®) prenatal test



Presenter: **Mohammad Taghi AKBARI**

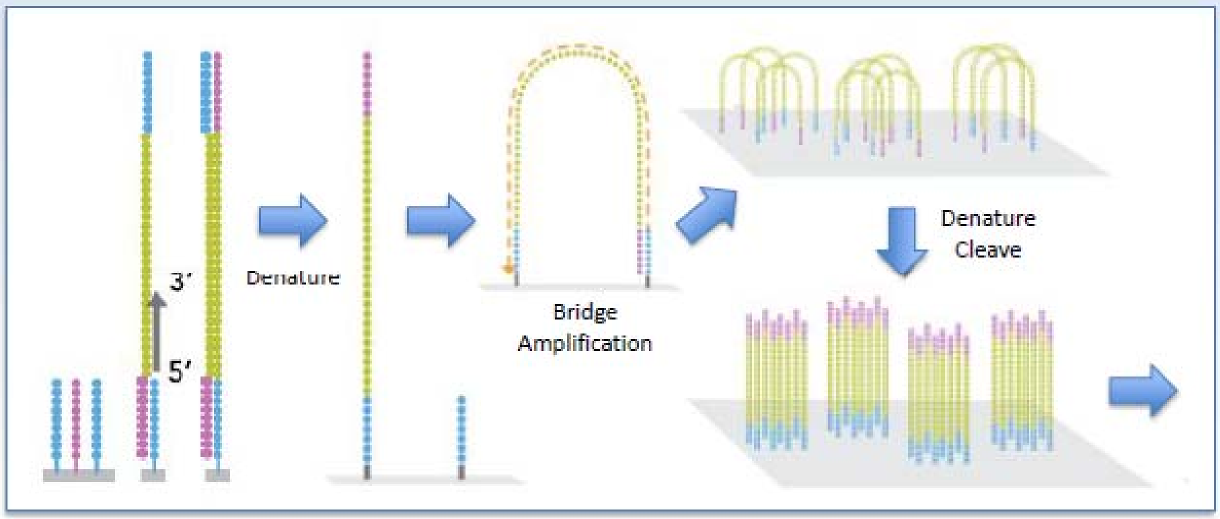
Library Preparation

- PCR primers and indexes added to DNA sample
  - Several libraries will be pooled (run in parallel), so each given unique index
- Pooled libraries loaded into flow cell



Cluster Generation

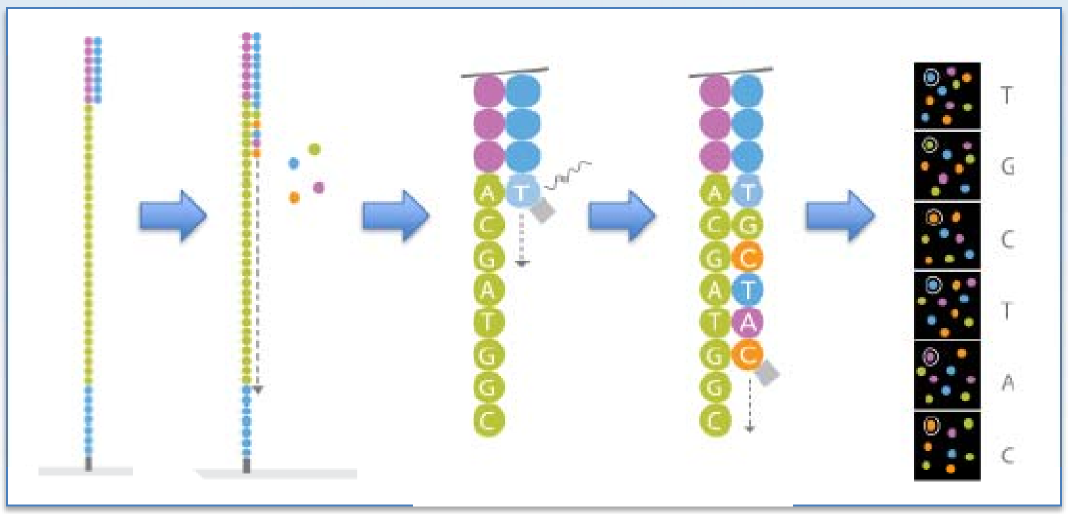
- Single strand library DNA hybridizes to complementary oligonucleotides anchored to the flow cell's surface
- PCR bridge amplification results in clusters of DNA
- Reverse strands are cleaved and washed away
- Sequencing primer is hybridized to the DNA



Illumina

Massively Parallel Sequencing

- Clusters are sequenced simultaneously
- One by one, fluorescently-labeled reversible terminator nucleotides are incorporated and fluoresced by laser
  - Each base (A, T, C, G) has its own color
- Each cycle is captured digitally

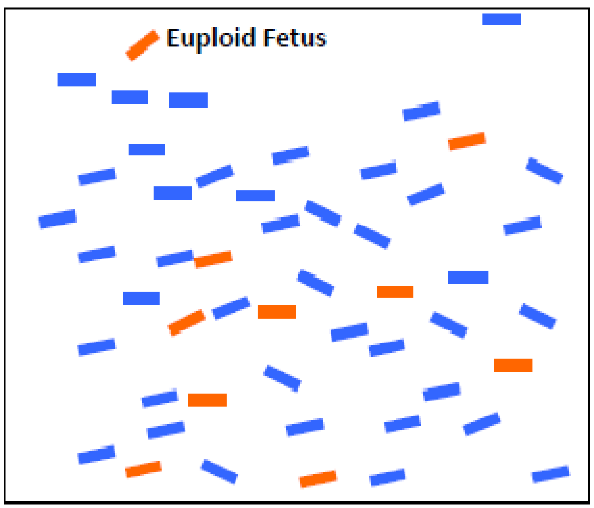


آزمایشگاه ژنتیک پزشکی تهران نخستین آزمایشگاه قبل از تولد در ایران

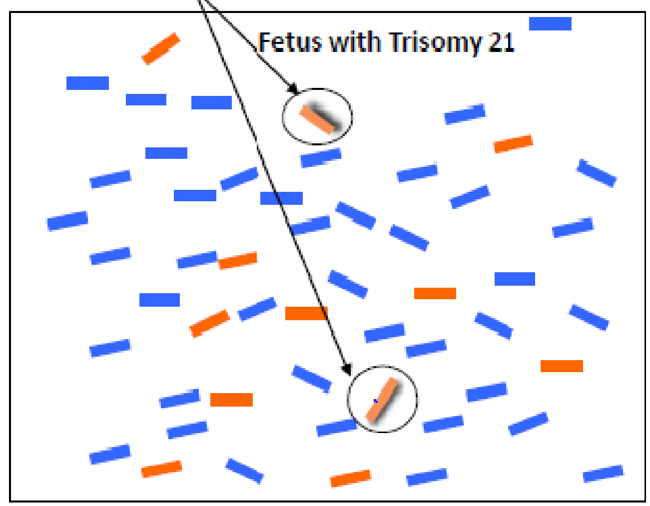
Principles of Fetal Trisomy 21 Testing From Maternal Blood Sample Using DNA Sequencing

- ~10% of the DNA fragments in a pregnant woman's blood are from the fetus ( )
- ~90% are from the mother ( )

Schematic of DNA Fragments Isolated From Maternal Plasma Containing Maternal DNA and Euploid Fetal DNA

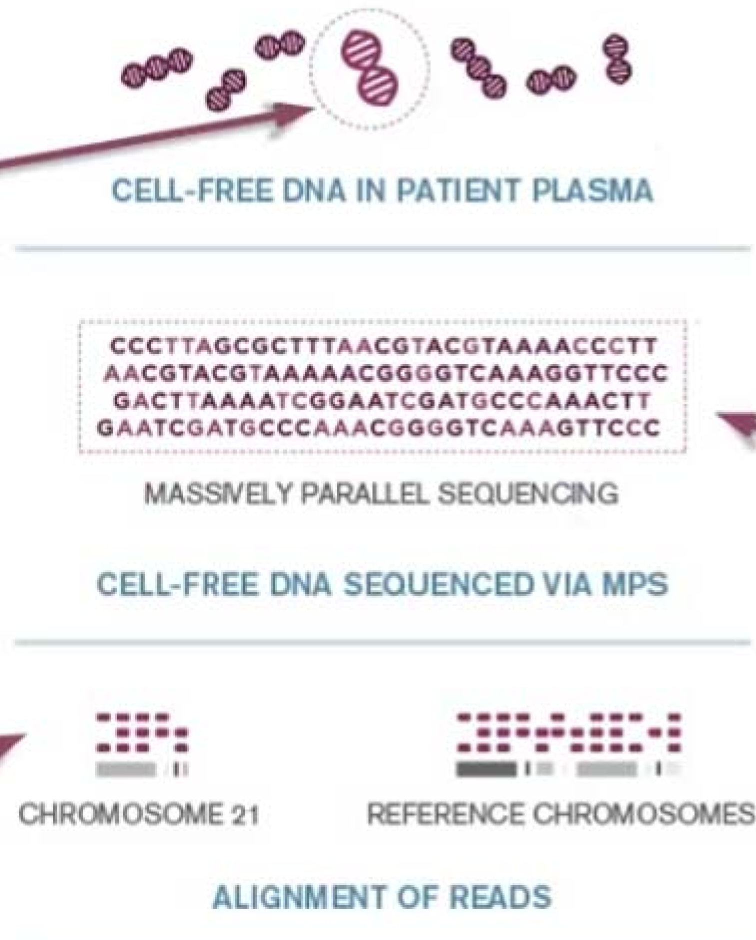


Schematic of DNA Fragments Isolated From Maternal Plasma Containing Maternal DNA, Fetal DNA and Extra Fragments of Chromosome 21 Contributed by a Fetal Trisomy 21



DNA Sequencing using cell free DNA

Fetal DNA fragments in maternal blood.

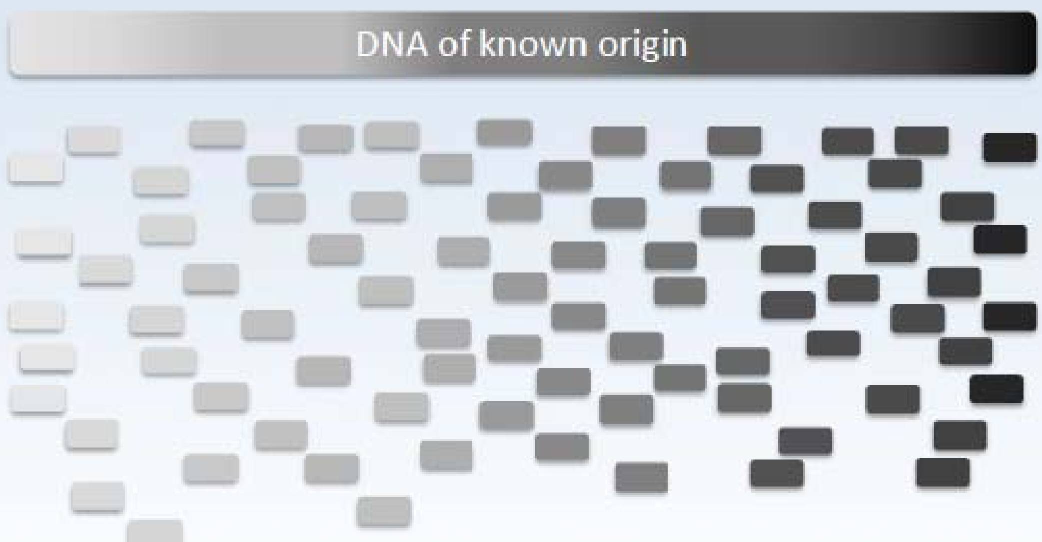


Cell free DNA fragments are then sequenced.

Compare the individual sequenced chromosomes against a reference for analysis.

Mapping Reads

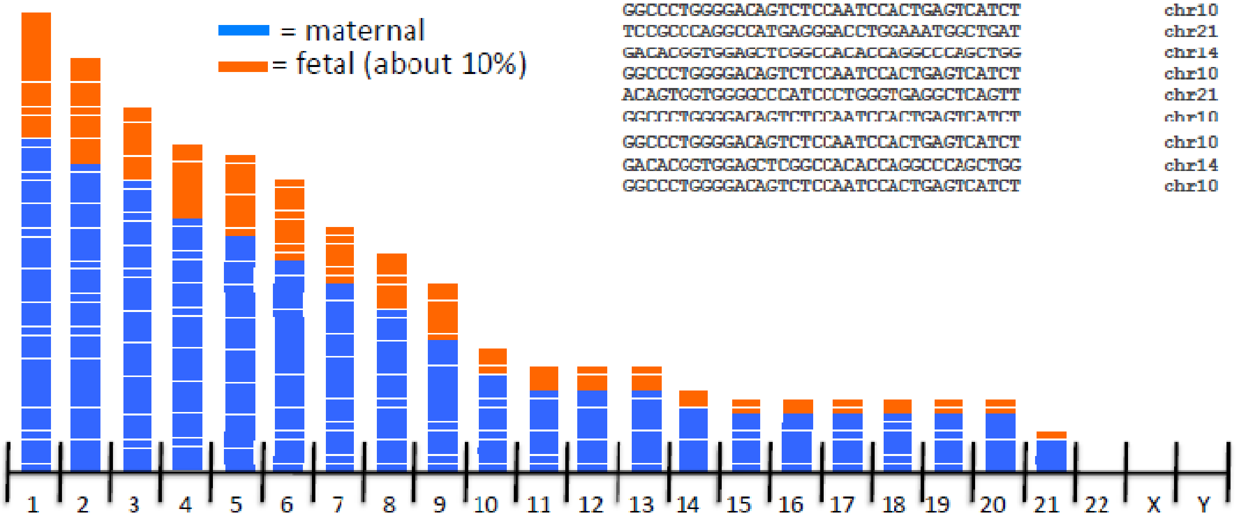
- 1 read = 1 fragment of contiguous nucleotide sequence
- Chromosomal origin of each fragment is determined by comparison to genome map



Massively Parallel (“Shotgun”) Sequencing tabulates chromosomal source of DNA fragment

Sequencing tells you which chromosome the ccf fragment comes from (but not who produced it)

TCCGCCCAGGCCATGAGGGACCTGGAAATGGCTGAT	chr21
GGCCCTGGGGACAGTCTCCAATCCACTGAGTCATCT	chr10
GACACGGTGGAGCTCGGCCACACCAGGCCCAGCTGG	chr14
GGCCCTGGGGACAGTCTCCAATCCACTGAGTCATCT	chr10
ACAGTGGTGGGGCCCATCCCTGGGTGAGGCTCAGTT	chr21
GGCCCTGGGGACAGTCTCCAATCCACTGAGTCATCT	chr10
GGCCCTGGGGACAGTCTCCAATCCACTGAGTCATCT	chr10
GGCCCTGGGGACAGTCTCCAATCCACTGAGTCATCT	chr10
TCCGCCCAGGCCATGAGGGACCTGGAAATGGCTGAT	chr21
GACACGGTGGAGCTCGGCCACACCAGGCCCAGCTGG	chr14
GGCCCTGGGGACAGTCTCCAATCCACTGAGTCATCT	chr10
ACAGTGGTGGGGCCCATCCCTGGGTGAGGCTCAGTT	chr21
GGCCCTGGGGACAGTCTCCAATCCACTGAGTCATCT	chr10
GGCCCTGGGGACAGTCTCCAATCCACTGAGTCATCT	chr10
GACACGGTGGAGCTCGGCCACACCAGGCCCAGCTGG	chr14
GGCCCTGGGGACAGTCTCCAATCCACTGAGTCATCT	chr10



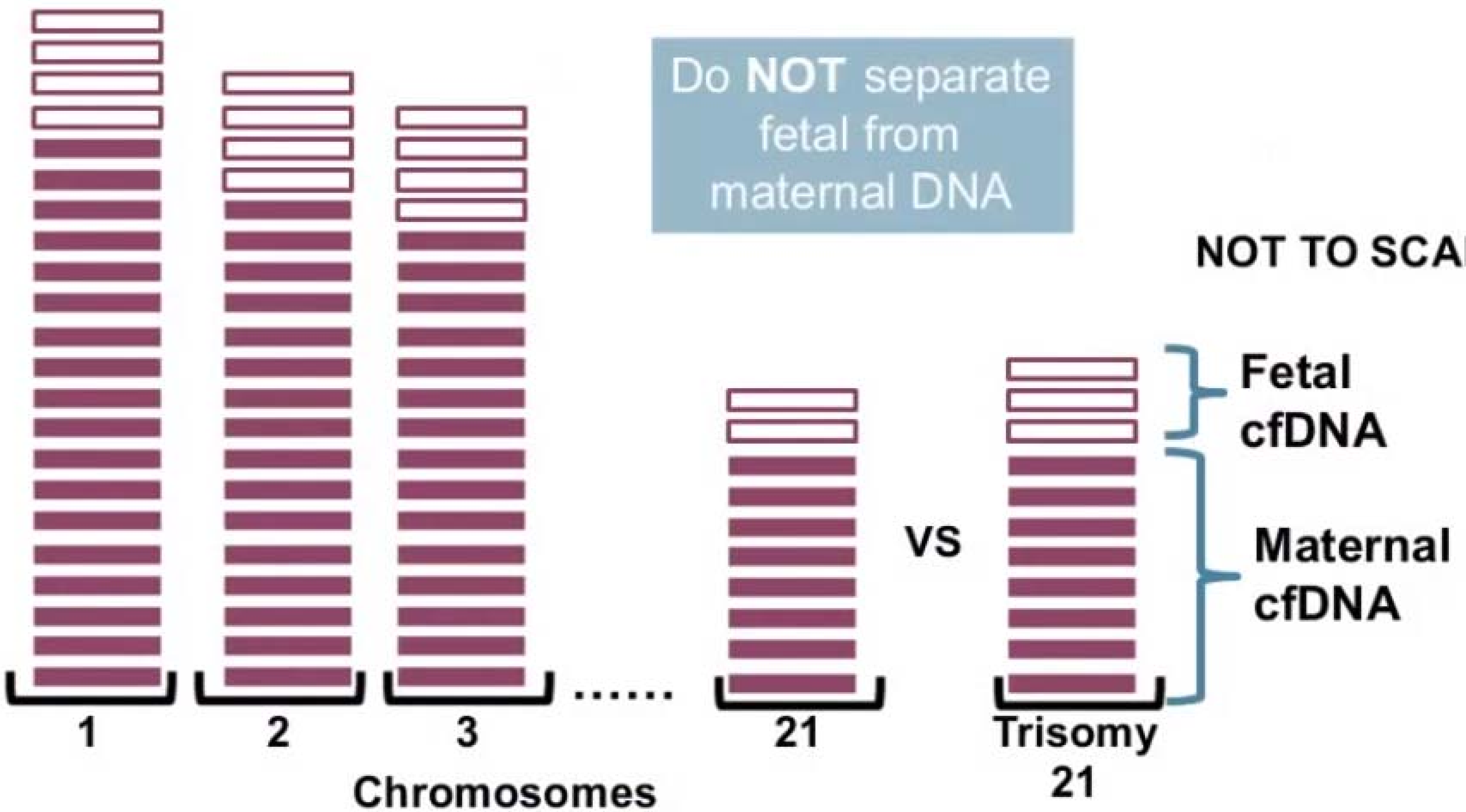
In euploid genome, chrom 21 accounts for ~1.35%

Detection of Fetal Aneuploidy

MPS Enables Precise Molecular Counting

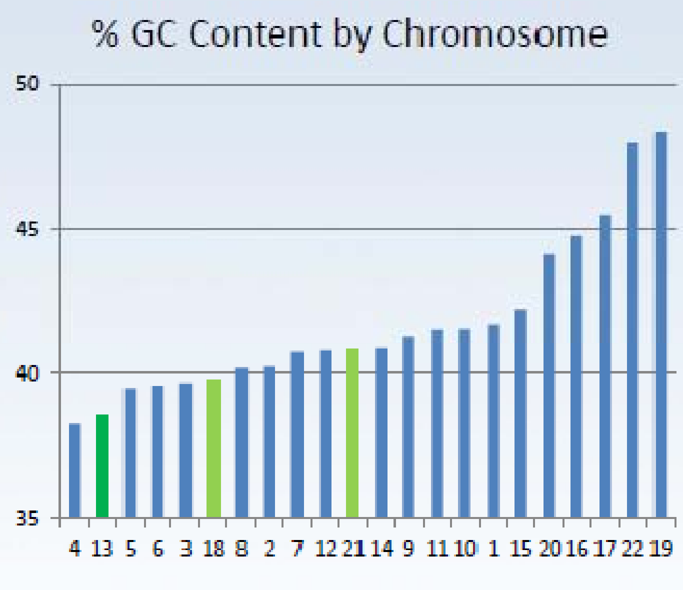
Do **NOT** separate fetal from maternal DNA

NOT TO SCALE

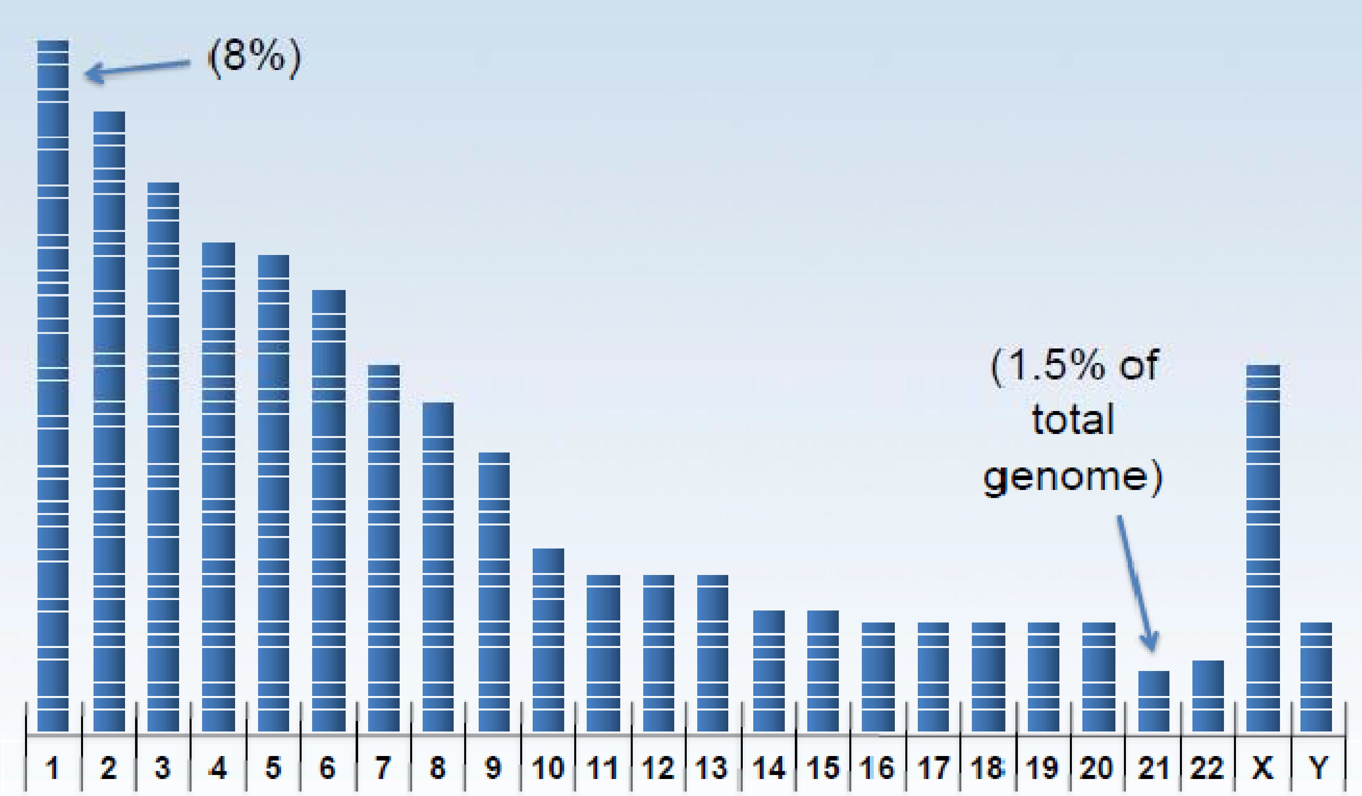


Factors Influencing Sequencing

- Depth of sequencing coverage
  - Average number of times each base pair is sequenced
- GC content
  - G-C nucleotide pairs held together by 3 hydrogen bonds and A-T pairs by two
  - When GC content high or low, DNA forms hairpins and polymerase does not bind well
  - In some types of data analysis a correction factor is needed



Quantifying Fragments



- Trisomy increases total DNA by only a small amount
  - Accurate analysis requires ≥ 4% (currently)

Fetal fraction	Fetal Karyotype	Chromosome 21 DNA as % of total DNA
Any (0-100%)	euploid	1.5
0%	trisomy 21	1.5
4%	trisomy 21	1.53
10% (typical)	trisomy 21	1.58

- 1.5% of our genome is chromosome 21 DNA
- When a pregnancy has trisomy 21 and the fetal fraction is 10%, the amount of chromosome 21 DNA increases to 1.6% of the total DNA:

= (%maternal)(%chr21)(#chr21 to #expected) + (%fetal)(%chr21)(#chr21 to #expected)

= (90%)(1.5%)(2/2) + (10%)(1.5%)(3/2)

= 0.0135 + 0.00225

= 0.01575 = 1.6%

Normalizing Quantified Fragments

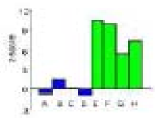
- Intra- & inter-run variation in the chromosomal distribution of reads can obscure aneuploidy
- Therefore, # reads mapping to chromosome of interest is normalized to # reads mapping to reference chromosomes
  - # of standard deviations from the mean is calculated
    - If reference chromosomes = all chromosomes:
      - Called Z-score
      - Correction factor for GC content needed
    - If reference chromosomes = chromosomes with biochemical behaviors similar to chromosome of interest:
      - Called Normalized Chromosome Value (NCV)
      - If GC content similar, correction factor not needed

Massively parallel sequencing

Statistical approaches

Chiu et al:

$\boxed{\text{Disease status determination}}$ $\quad \text{chrN z-score for test sample} = \dfrac{\%\,\text{chrN}_{\text{sample}} - \text{mean}\ \%\,\text{chrN}_{\text{reference}}}{\text{S.D.}\ \%\,\text{chrN}_{\text{reference}}}$ ← Z-score of 3.0 or above = abnormal



A statistical Z-score is determined to differentiate excess chromosomal material relative to the amounts of other chromosomes (why triploidy, balanced rearrangements not detected)

Sehnert et al:

$$\mathrm{NCV}_j = \frac{x_j - \hat{\mu}_j}{\hat{\sigma}_j},$$

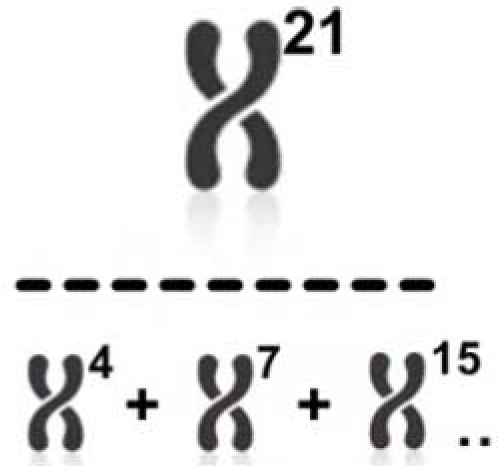
NCV > 4.0 = abnormal

NCV >1.5 but <4.0 = “suspect” (formerly known as indeterminate)

Normalized Chromosome Value (NCV)

NCV method effectively reduces data variation

- NCV is ratio of counts on test and reference chromosomes
- Optimal reference chromosomes selected through empirical analysis
  - Optimal = least variation from test chromosome under sequencing
  - Over **6 quadrillion** possible combinations!
- NCV is # standard deviations difference from average diploid ratio

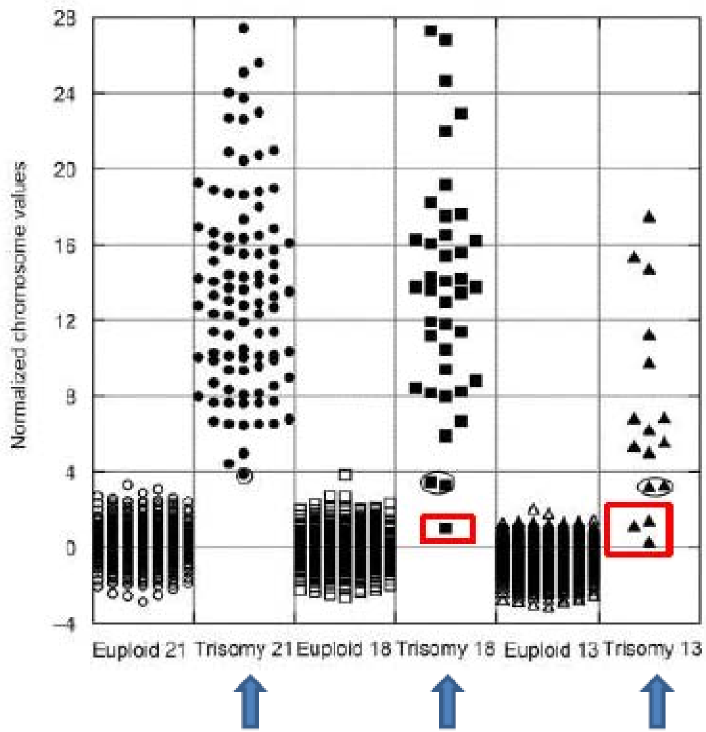


(Example)

MPS – alternative approach

(Verinata)

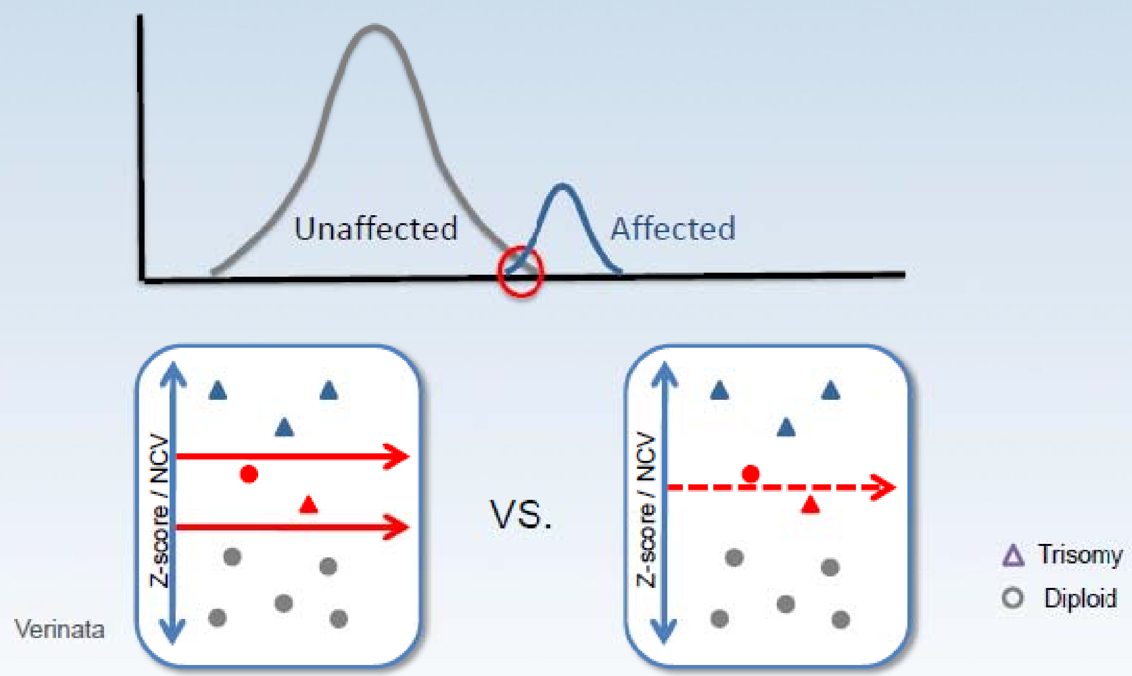
- 516/532 samples with result
- Reported 100% DR (89/89) but 1 unclassified (89/90=98.8%)
- Reported 97.2% (15/16)DR for T18, but 2 unclassified (15/18=83.3%)
- Reported 78.6% (11/14) for T13, but 2 unclassified (11/16=68.8%)
- Unclassified (NCV between 2.5 – 4.0 std dev.) ~1.5%



Bianchi et al, Obstet Gynecol, 2012

آزمایشگاه ژنتیک پزشکی تهران نخستین آزمایشگاه قبل از تولد در ایران

Challenge of Threshold Results



Dual Threshold Method (Verinata)

Single Threshold Method (Sequenom)

- Care must be taken not to generate unrealistic risks
- Risks only relevant in area of overlap
  - May be reasonable to generate likelihood ratios in this area
- Not clear at this time whether post-test risk calculation is appropriate
  - e.g. not yet determined whether NIPT behaves similarly in high-risk and general-risk populations

Some Limitations

- ≠ Diagnostic testing, = Advanced screening
  - **Diagnostic testing is recommended following all positive results**
    - **Chance pregnancy affected ≥ 50%**
  - **Negative result does not ensure unaffected pregnancy**
- Placental mosaicism (such as seen with CVS)
- Maternal mosaicism
- Unrecognized or vanishing twin
- Some screens not appropriate if egg donated
- Generating post-screen risks (continued …)

Ethical Considerations

- Informed consent for a complex test without fetal risk
  - "Just a tube of blood"
  - Will NIPT be lumped into other blood draws?
  - Will ramifications be adequately presented by providers?
  - Will ramifications be adequately considered by patients?

ACOG Committee Opinion on NIPT

The American College of Obstetricians and Gynecologists
WOMEN'S HEALTH CARE PHYSICIANS

The Society for Maternal-Fetal Medicine

COMMITTEE OPINION

Number 545 • December 2012

- *"Cell free fetal DNA appears to be the most effective screening test for aneuploidy in high risk women… is one option that can be used as a primary screening test in women at **increased risk** of aneuploidy"*
- *"[NIPT] should be an **informed patient choice** after pretest counseling"*
- *"[NIPT] should **not** be offered to low-risk women or women with multiple gestations"*
- *"A patient with a positive test result should be referred for genetic counseling and should be offered invasive prenatal diagnosis for confirmation of test results."*

Also supporting NIPT for high risk pregnancies:

ispd

Society for Maternal-Fetal Medicine

National Society of Genetic Counselors

The American College of Obstetricians and Gynecologists
WOMEN'S HEALTH CARE PHYSICIANS

The Society for Maternal-Fetal Medicine

COMMITTEE OPINION

Number 545 • December 2012

- Patients at increased risk of aneuploidy can be offered testing
  (AMA, associated u/s anomaly, prior affected pregnancy, positive risk screen, parent carries robertsonian translocation involving chromosome 13 or 21)
- Should not be part of routine prenatal laboratory assessment, but an informed patient choice after appropriate pretest counseling.
- Should not be offered to low-risk women or women with multiple gestations.
- If a fetal structural anomaly is identified on ultrasound, invasive prenatal diagnosis should be offered.
- A patient with a positive test result should be referred for genetic counseling and offered invasive prenatal diagnosis for confirmation of test results.
- Does not replace the accuracy and diagnostic precision of CVS or amniocentesis, which remain an option for women.

Published Guidelines

ISPD RAPID RESPONSE STATEMENT

International Society for Prenatal Diagnosis (2011)

- With suitable genetic counseling MPS can be helpful for women who may have been determined to be high risk.
- Before routine MPS-based population screening for fetal Down syndrome is introduced additional trials are needed.
- This test is not fully diagnostic and therefore constitutes an advanced screening test. Accordingly, confirmation of MPS positive results through invasive testing would still be required.

NSGC currently supports NIPT "as an option for patients whose pregnancies are considered to be at an increased risk for certain chromosome abnormalities. NSGC urges that NIPT/NIPD only be offered in the context of informed consent, education, and counseling by a qualified provider, such as a certified genetic counselor. Patients whose NIPT results are abnormal, or who have other factors suggestive of a chromosome abnormality, should receive genetic counseling and be given the option of standard confirmatory diagnostic testing." (2012)

REVIEW Genetics inMedicine

Noninvasive prenatal testing: limitations and unanswered questions

Monica A. Lutgendorf, MD[1,*], Katie A. Stoll, MS[1], Dana M. Knutzen, MS[1] and Lisa M. Foglia, MD[1,*]

The clinical use of noninvasive prenatal testing to screen high-risk patients for fetal aneuploidy is becoming increasingly common. Initial studies have demonstrated high sensitivity and specificity, and there is hope that these tests will result in a reduction of invasive diagnostic procedures as well as their associated risks. Guidelines on the use of this testing in clinical practice have been published; however, data on actual test performance in a clinical setting are lacking, and there are no guidelines on quality control and assurance. The different noninvasive prenatal tests employ complex methodologies, which may be challenging for health-care providers to understand and utilize in counseling patients, particularly as the field continues to evolve. How these new tests should be integrated into current screening programs and their effect on health-care costs remain uncertain.

Genet Med advance online publication 5 September 2013

Key Words: aneuploidy; cell-free DNA; genetic counseling; noninvasive prenatal screening; noninvasive prenatal testing

Verinata Health MELISSA Study

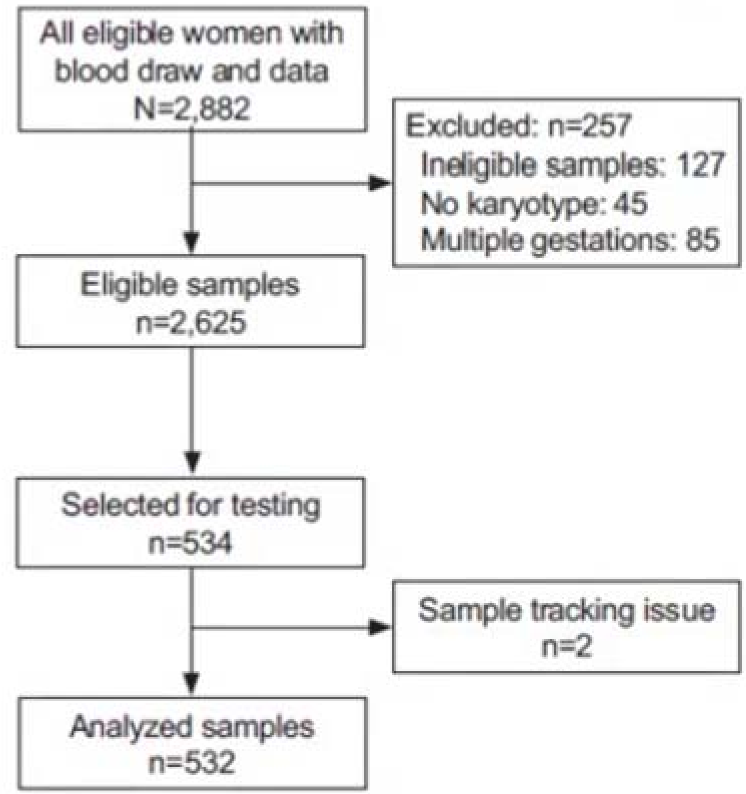
MatErnal BLood IS Source to Accurately Diagnose Fetal Aneuploidy

- Large-scale, **prospective** and **blinded** clinical validation
  - High-risk patient population
  - Singleton gestations analyzed
  - Over 60 U.S. centers enrolled
- **All** samples with **any abnormal karyotype** analyzed
  - Emulates real-world testing, fetal karyotype not known beforehand
- Samples analyzed for aneuploidy **across the genome**
  - Demonstrates the true potential of verifi® test MPS technology

MELISSA Study

Study Design, Demographics

- 2,882 samples collected
- 532 samples analyzed
  - Including ***all*** abnormal karyotypes (N=221)
  - Gestational age: 10 – 23 weeks
  - BMI (kg/m2): 17 – 59
  - **Includes 38 ART** pregnancies
  - Diverse (27.3% non-white)



verifi® prenatal test – Updated Performance

"Detected" and "Aneuploidy Suspected" results considered positive for performance calculations

Chr	N	Sensitivity	95% CI	Specificity	95% CI
21	500	>99.9% (90/90)	96.0-100.0	99.8% (409/410)	98.7-100.0
18	501	97.4% (37/38)	86.2-99.9	99.6% (461/463)	98.5-100.0
13	501	87.5% (14/16)	61.7-98.5	>99.9% (485.485)	99.2-100.0

Data on file.

Rate of aneuploidy suspected

T21 = 0.6%

T18 = 0.4%

T13 = 0.2%

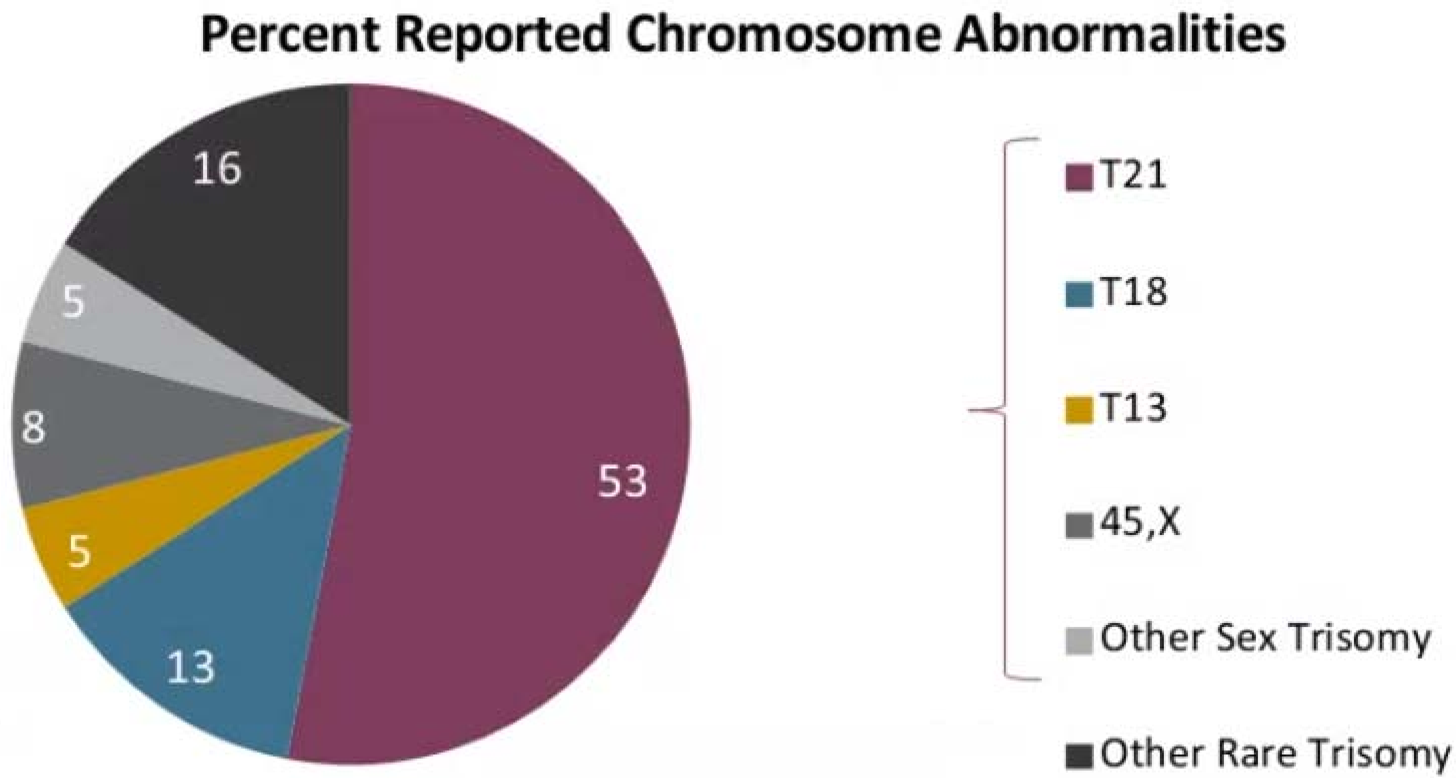
False positives

T21 = 0.2%

T18 = 0.4%

T13 = <0.1%

Why Sex Chromosomes?



Data adapted from Wellesley, D, et al., Rare chromosome abnormalities, prevalence and prenatal diagnosis rates from population-based congenital anomaly registers in Europe. *Eur J of Hum Gen*, 11 January 2012.

verifi® prenatal test Sex Chromosomes Option

- Physician and patient can choose this option at their discretion
- Monosomy X now available as part of sex chromosomes option, cystic hygroma indication accepted, but not required.
- Sex chromosome aneuploidies:
  - XXX – Triple X
  - XXY – Klinefelter syndrome
  - XYY – Jacob's syndrome
- Fetal sex reported
  - If no aneuploidy detected, fetal sex reported
  - Aids in risk assessment for X-linked disorders

Sex Chromosome Aneuploidy Performance

Chromosome	N	Sensitivity	95% CI	Specificity	95% CI
Monosomy X	508	95% (19/20)	75.1-99.9	99.0% (483/488)	97.6-99.7

Chr	N	Sensitivity	95% CI	Specificity	95% CI	Accuracy	95% CI
XX	508	97.6% (243-249)	94.8-99.1	99.2% (257/259)	97.2-99.9	98.4%	96.9-99.3
XY	508	99.1% (227-229)	94.8-99.1	98.9% (276/279)	96.9-99.8	99.0%	97.7-99.7

Chromosome	
XXX, XXY, XYY	Other sex aneuploidies will be reported if detected. (Limited prevalence precludes performance calculations.)

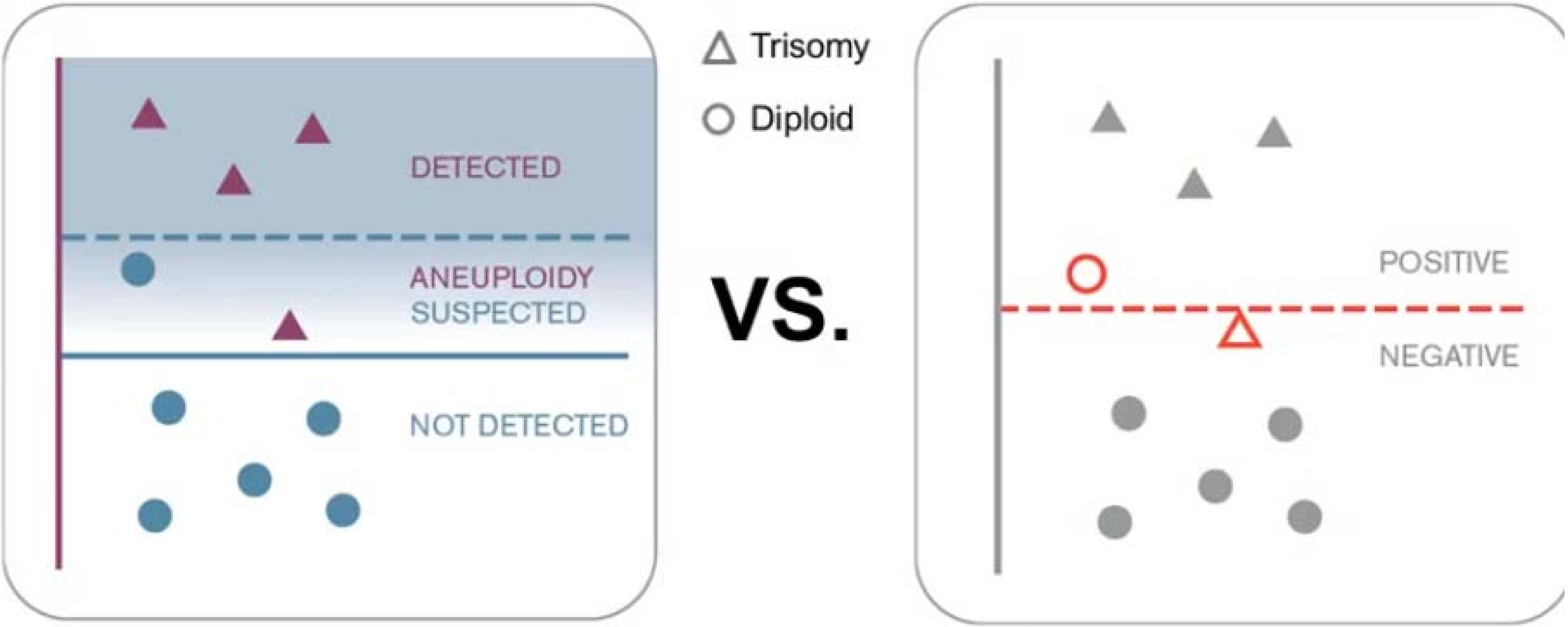
Data on file.

Table 2. Potential explanations for NIPT fetal karyotype discordance.

NIDT	Fetal karyotype	Explanation	Reference
Autosomal aneuploidy			
Trisomy 13	46,XX (amniocentesis)	CPM: 46,XX,+13,der(13;13)(q10;q10)[5] in direct preparation	Mennuti et al. *(42)*
Trisomy 13	46,XY (fetal tissue)	CPM: trisomy 13 in direct preparation	Mennuti et al. *(42)*
Trisomy 13	46,XY (amniotic fluid and cord blood)	CPM: 47,XY,+13[10]/46,XY[12]	Hall et al. *(53)*
Trisomy 21	46,XX,upd(21)mat	CPM: trisomy 21 in placenta	Pan et al. *(54)*
Trisomy 22	Umbilical cord blood normal	CPM: trisomy 22 in placenta	Choi et al. *(56)*
Trisomy 18	46,XX	Maternal mosaicism 46,XX[47]/47,XX+18[13]	Song et al. *(49)*
Trisomy 13 (2 cases)	Unknown	Cotwin demise	Futch et al. *(43)*
Trisomy 13 (2 cases)	Unknown	CPM: trisomy 13	Futch et al. *(43)*
Trisomy 21 and monosomy X	Unknown	Cotwin demise	Futch et al. *(43)*
Trisomy 21	Euploid	Laboratory error	Futch et al. *(43)*
Trisomy 13, monosomy 18	46,XY	Maternal tumor with increased chromosome 13 relative to chromosome 18	Osborne et al. *(58)*
SCA			
47,XXY	49,XXX,+7,+21	CPM	Lau et al. *(55)*
47,XXX	46,XX	Maternal nonmosaic SCA 47,XXX	Yao et al. *(57)*
45,X	46,XX	Maternal SCA mosaicism 45,X[3]/46,XX[27]	Lau et al. *(55)*

Aneuploidy Suspected Result

Indicates borderline result, warrants further evaluation



verifi® prenatal test Dual Threshold

Single Threshold Method

verifi® prenatal test

A Revolutionary Advance in Prenatal Testing

verifi®
prenatal test

- **Safe** - Routine maternal blood draw, **just one tube** (7-10 mL)
- **Accurate** - Directly analyzes cell-free DNA
- **Easy** - Test early as 10 weeks, no limitations for patient ethnicity, BMI, egg-donor status
- **Comprehensive** - Optional analysis of most common sex chromosome aneuploidies

verifi® prenatal test Ordering Options

Test Requisition Form (TRF)

Test Requested – Choose only one option!

☐ verifi prenatal test

- The verifi prenatal test will report on fetal aneuploidy of chromosomes 21, 18, and 13

☐ verifi prenatal test including option for **sex chromosomes analysis**

- Fetal aneuploidy detection of chromosomes 21, 18 and 13 as above
- This option will also report the presence of Monosomy X, XXX, XXY, or XYY.
- If no sex chromosome aneuploidy is detected, fetal sex (XX or XY) will be reported.

verifi® prenatal test - Specifics

- Cost
  - No additional charge for sex chromosome analysis
- Blood draw requirement
  - Only 1 tube (7 -10 ml)
  - Has a “built in” 2nd aliquot if testing needs to be repeated
- TAT
  - 8-10 days
- Test failure result rate
  - <1%

Test Report – Autosomes Only
No Aneuploidy

verifi® prenatal test

Prenatal Aneuploidy Test Report

REPORT DATE AND TIME	
12/15/2012	10:45 AM

PROVIDER INFORMATION	PATIENT INFORMATION
....	....

PRENATAL ANEUPLOIDY TEST RESULTS

TEST	RESULT	INTERPRETATION
Chromosome 21	No aneuploidy detected	Results consistent with diploid chromosomes 21, 18, and 13
Chromosome 18	No aneuploidy detected	
Chromosome 13	No aneuploidy detected	

Comments:
Clinical correlation with ultrasound findings and other screening tests is indicated. If definitive diagnosis is desired, chorionic villus sampling or amniocentesis is necessary.

Test Report – with Sex Chromosomes No Aneuploidy

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Prenatal Aneuploidy Test Report

REPORT DATE AND TIME	
12/15/2012	10:45 AM

PROVIDER INFORMATION

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PATIENT INFORMATION

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PRENATAL ANEUPLOIDY TEST RESULTS

TEST	RESULT	INTERPRETATION
Chromosome 21	No aneuploidy detected	Results consistent with diploid chromosomes 21, 18, 13, and with two sex chromosomes (XX)
Chromosome 18	No aneuploidy detected	
Chromosome 13	No aneuploidy detected	
Sex Chromosomes	No aneuploidy detected	

Comments:
Clinical correlation with ultrasound findings and other screening tests is indicated. If definitive diagnosis is desired, chorionic villus sampling or amniocentesis is necessary.

Test Report – with Sex Chromosomes Aneuploidy Detected

آزمایشگاه ژنتیک پزشکی تهران
Tehran Medical Genetics Laboratory
۱۳۷۱ 19

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Prenatal Aneuploidy Test Report

ANEUPLOIDY DETECTED
See Below

REPORT DATE AND TIME	
12/15/2012	10:45 AM

PROVIDER INFORMATION	PATIENT INFORMATION
....	....

PRENATAL ANEUPLOIDY TEST RESULTS

TEST	RESULT	INTERPRETATION
Chromosome 21	ANEUPLOIDY DETECTED	Result consistent with trisomy for chromosome 21
Chromosome 18	No aneuploidy detected	Result consistent with diploid chromosome 18
Chromosome 13	No aneuploidy detected	Result consistent with diploid chromosome 13
Sex Chromosomes	No aneuploidy detected	Result consistent with two sex chromosomes (XY)

Comments:
Genetic counseling is recommended. Clinical correlation with ultrasound findings and other screening tests is indicated. If definitive diagnosis is desired, chorionic villus sampling or amniocentesis is necessary.

Test Report – with Sex Chromosomes Aneuploidy Suspected

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Prenatal Aneuploidy Test Report

ANEUPLOIDY SUSPECTED
See Below

REPORT DATE AND TIME	
12/15/2012	10:45 AM

PROVIDER INFORMATION	PATIENT INFORMATION
....	....

PRENATAL ANEUPLOIDY TEST RESULTS		
TEST	**RESULT**	**INTERPRETATION**
Chromosome 21	No aneuploidy detected	Result consistent with diploid chromosome 21
Chromosome 18	ANEUPLOIDY SUSPECTED (Borderline Value)	Result suggestive of trisomy for chromosome 18
Chromosome 13	No aneuploidy detected	Result consistent with diploid chromosome 13
Sex Chromosomes	No aneuploidy detected	Result consistent with two sex chromosomes (XY)

Comments:
Genetic counseling is recommended. Clinical correlation with ultrasound findings and other screening tests is indicated. If definitive diagnosis is desired, chorionic villus sampling or amniocentesis is necessary.

Test Report – Sex Chromosome Aneuploidy

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Prenatal Aneuploidy Test Report

ANEUPLOIDY DETECTED
See Below

REPORT DATE AND TIME	
12/15/2012	10:45 AM

PROVIDER INFORMATION	PATIENT INFORMATION
....	....

PRENATAL ANEUPLOIDY TEST RESULTS

TEST	RESULT	INTERPRETATION
Chromosome 21	No aneuploidy detected	Result consistent with diploid chromosome 21
Chromosome 18	No aneuploidy detected	Result consistent with diploid chromosome 18
Chromosome 13	No aneuploidy detected	Result consistent with diploid chromosome 13
Sex Chromosomes	ANEUPLOIDY DETECTED	Result consistent with presence of a single X chromosome and no detectable Y chromosome (Monosomy X)

Comments:
Genetic counseling is recommended. Clinical correlation with ultrasound findings and other screening tests is indicated. If definitive diagnosis is desired, chorionic villus sampling or amniocentesis is necessary.

What's next?

- Detection of microdeletion/duplication syndromes
- Detection of single gene disorders
- Application in whole genome/exome sequencing

Search continues for fetal/trophoblast cells in maternal circulation

Reproductive BioMedicine Online (2012) 25, 508–520

ARTICLE

Circulating trophoblastic cells provide genetic diagnosis in 63 fetuses at risk for cystic fibrosis or spinal muscular atrophy

Hussein Mouawia [a,d], Ali Saker [a,e], Jean-Philippe Jais [b], Alexandra Benachi [c], Laurence Bussières [f], Bernard Lacour [g], Jean-Paul Bonnefont [h], René Frydman [c], Joe Leigh Simpson [i], Patrizia Paterlini-Brechot [a,g,*]

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Clarity™ Prenatal Genetic Test


Thank you ...