

# SEQUENOM<sup>®</sup>

Improving Healthcare Through Revolutionary Genetic Analysis Solutions

*From  
Academic  
Research*



*Through  
Translational  
Applications*



*To  
Clinical  
Diagnostics*



## 2011 Webbush Life Sciences: Management Access Conference

Director & EVP R&D, Ronald M. Lindsay, Ph.D.

August 2011

# Forward-Looking Statements



Except for historical information, matters set forth in this presentation, including statements regarding Sequenom's plans, potential, opportunities, financial or other expectations, projections, goals, objectives, milestones, strategies, market growth, timelines, product pipeline, clinical studies, product development, and the potential benefits of its products and products under development, are forward-looking statements within the meaning of the "safe harbor" provisions of the Private Securities Litigation Reform Act of 1995. These forward-looking statements are subject to risks and uncertainties that may cause actual results to differ materially, including the risks and uncertainties associated with Sequenom's operating performance and financial position, the market demand for and acceptance of Sequenom's and Sequenom CMM's products and services, research, development and commercialization of new products, reliance upon the collaborative efforts of others, competition, intellectual property rights, government regulation, obtaining or maintaining regulatory approvals, pending investigations, litigation, and other risks detailed in Sequenom's SEC filings. These forward-looking statements are based on current information that is likely to change, speak only as of the date hereof, and Sequenom undertakes no obligation to revise or update such statements.

# Sequenom, Inc.

*Developing Innovative Technology, Products and Diagnostic Tests to Target and Serve Discovery, Clinical Research and Molecular Diagnostics Markets*

- Two operating segments: Genetic Analysis and Molecular Diagnostics
- Established core business in Genetic Analysis using proprietary MassARRAY<sup>®</sup> instrument platform
- Transitioning from Solutions for Academic Research → Translational Applications → Clinical Diagnostics
- \$47.5M revenue FY2010, \$26.8M revenue 2H11
- 99.1M common shares outstanding
- ~ \$600M market cap
- Founded in 1994
- Headquartered in San Diego, CA



# Sequenom Center for Molecular Medicine (SCMM)



- Wholly owned subsidiary of Sequenom, Inc.
- Laboratory developed test (LDT) in development for proprietary, noninvasive prenatal trisomy 21 (T21)
- LDTs branded under the name MaterniT21™, SensiGene® and RetnaGene™
- Genetic counseling available upon physician request
- Currently perform LDTs for Cystic Fibrosis, RhD and Age-Related Macular Degeneration (AMD)
- Locations in Grand Rapids, MI and San Diego, CA

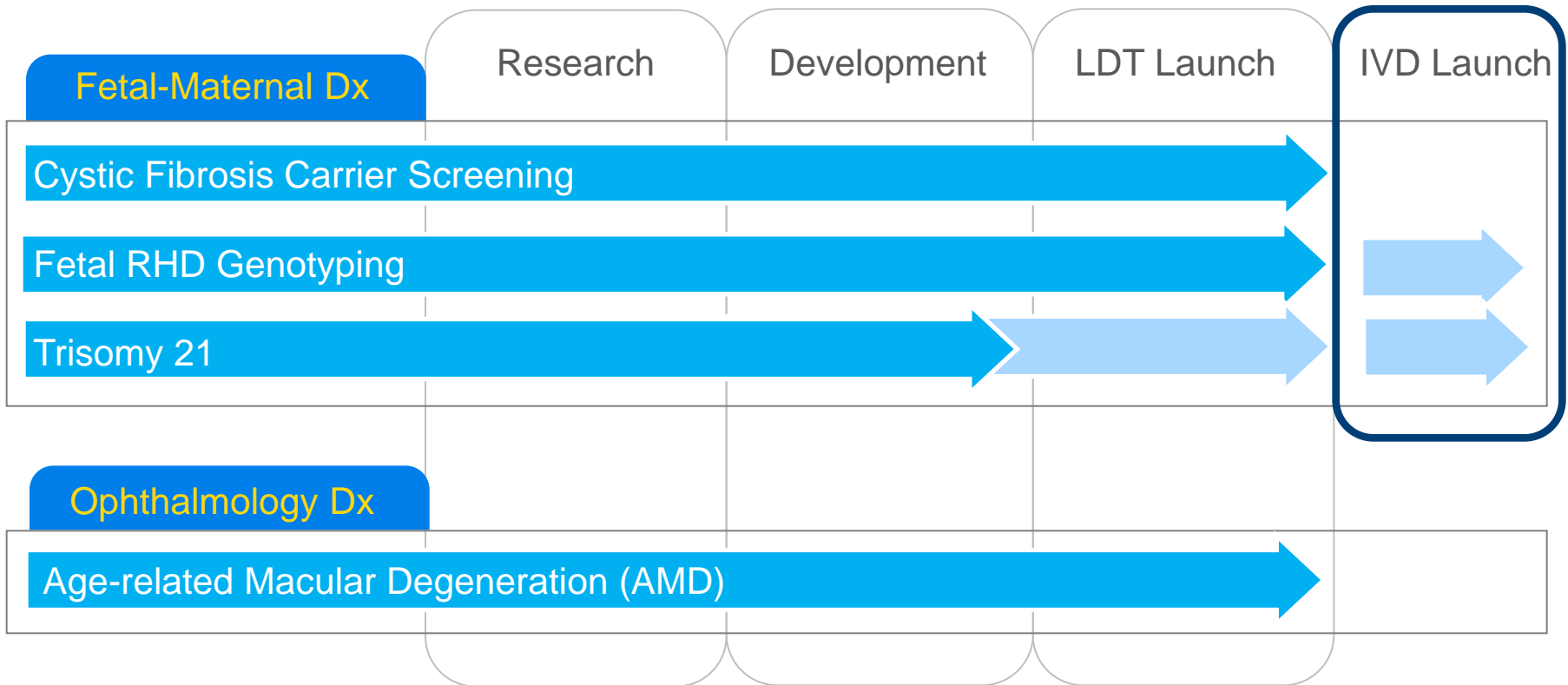
# Genetic Analysis Business

- Good penetration of target markets
  - Translational and Basic Research
  - Agricultural Genomics
  - Pharmaceutical and Biotech
- 19% growth in revenue 2010 vs. 2009 and 10% growth in revenue 1H11 vs. 1H10
- Launched MassARRAY Analyzer 4\* with improved margins
- Operational improvements: reduced working capital investment
- Over 250 published articles in 2010 using Sequenom technology
- Active installed base over 300: an important source of new molecular diagnostic opportunities
- Expanding menu of research use only (RUO) panel content offering



\* The MassARRAY Analyzer 4 is for Research Use Only. Not for use in diagnostic procedures

# Sequenom and Sequenom CMM\* Molecular Diagnostics Product Portfolio

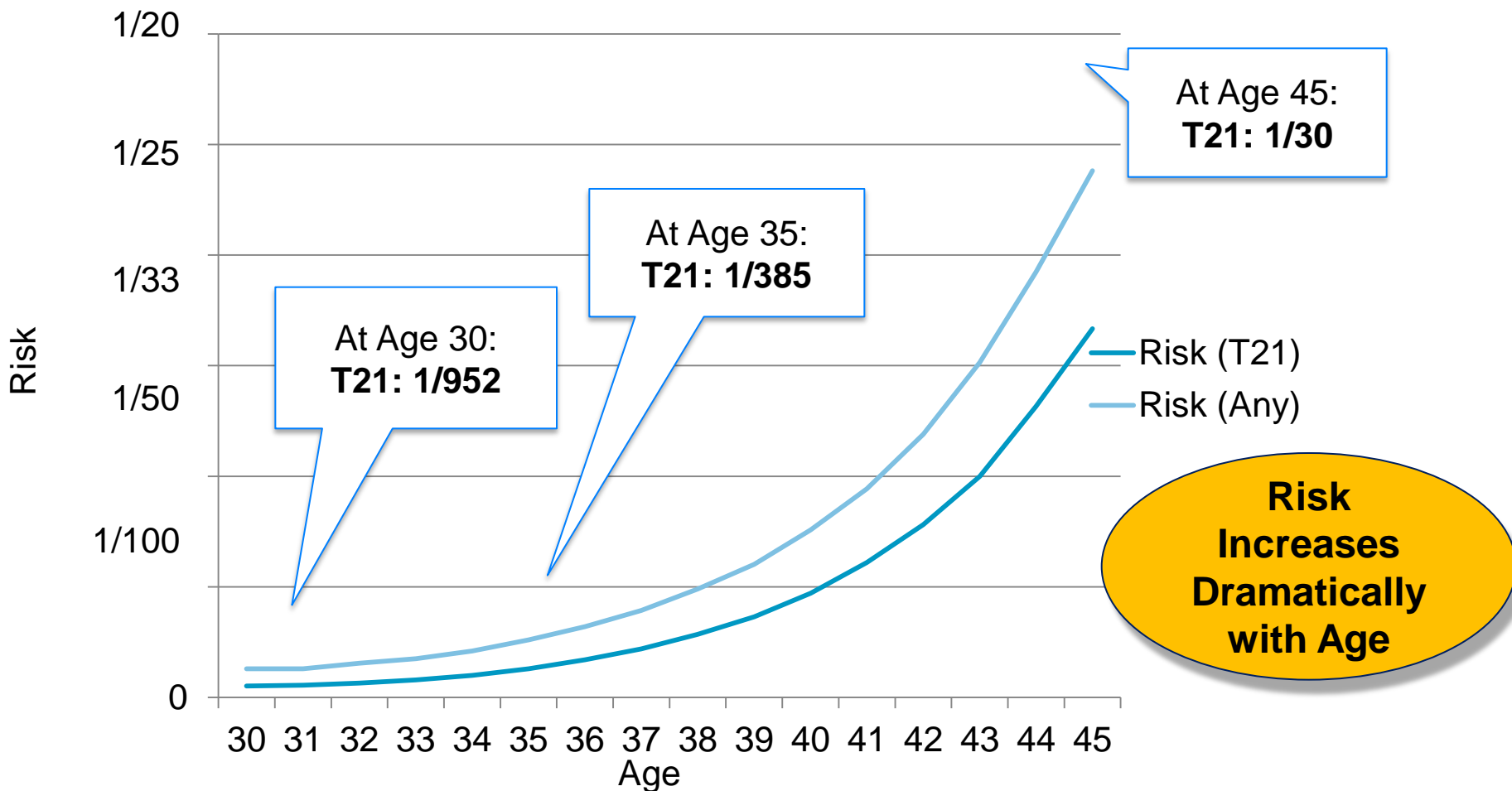


\* Sequenom CMM, a wholly owned subsidiary of Sequenom, Inc. is a CAP accredited, CLIA-certified molecular diagnostics laboratory that develops and validates its laboratory developed tests for use solely by Sequenom CMM

\*\* Light blue arrows denote planned activities

# Trisomy 21 Market Opportunities

## Maternal Age-Specific Risks At Term for Fetal Cytogenetic Abnormalities



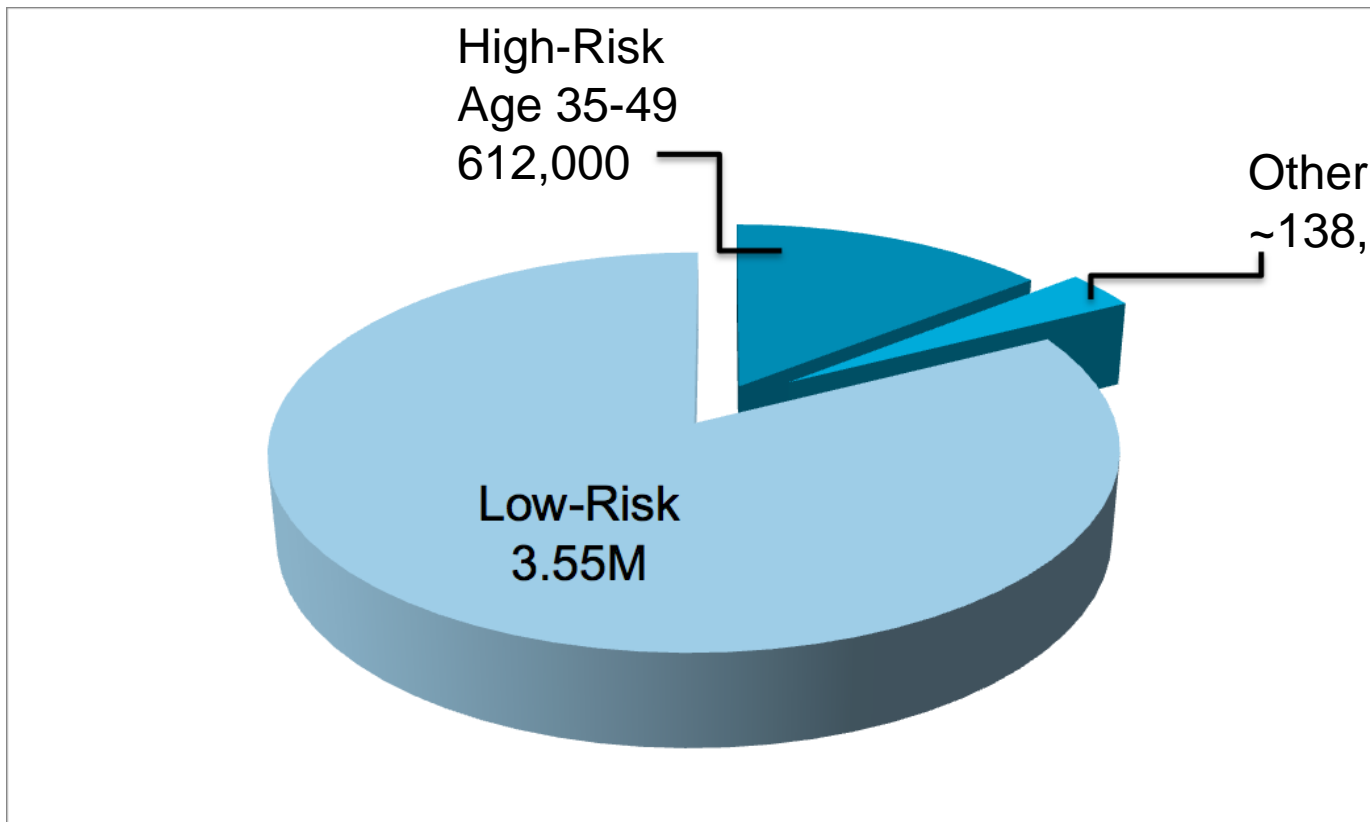
\* Hook EB, Cross PK, Schreinemachers DM. Chromosomal abnormality rates at amniocentesis and in live-born infants. *J Am Med Assoc.* 1983;249:2034

# Trisomy 21 Market Opportunities



## Potential Available Market

**US 2007 Total Births: 4.3M**



\* National Center for Health Statistics, National Vital Statistics Reports; [www.cdc.gov/nchs](http://www.cdc.gov/nchs)

# Product Profile: MaterniT21<sup>TM</sup>

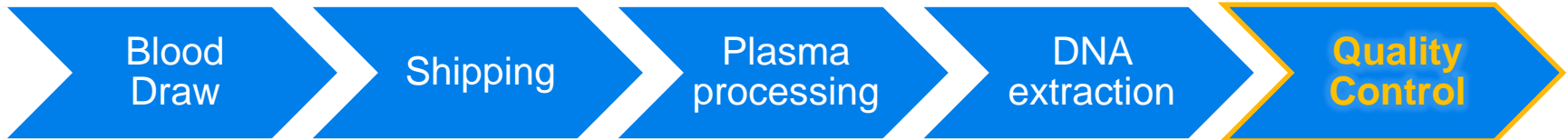


## Trisomy 21 (T21) Test

- Goal:** A noninvasive test to identify pregnancies at risk for fetal trisomy 21
- Use:** First or second trimester
- Initial Market:** Pregnant women at high risk for fetal aneuploidy
- Test Sample:** 2x 10 ml Blood Draw (approx 4 ml Plasma each)
- Test Analyte:** Circulating cell-free fetal DNA in maternal plasma
- Test Method:** Massively parallel “shotgun” DNA sequencing
- Test Platform:** HiSeq 2000 (Illumina, Inc.)
- Turnaround:** 8-10 days
- LDT Launch:** Lab Developed Test (LDT) expected launch late 2011/early 2012
- IVD Submission:** *In Vitro* Diagnostic Device (IVD) planned FDA submission for late 2012/early 2013

# Massively Parallel “Shotgun” Sequencing Process

## Sample Processing



## Library Preparation



## Sequencing



## Data Analysis



# Recent Publications on Non-Invasive Trisomy 21 Test

January 2011: Dennis Lo et al.

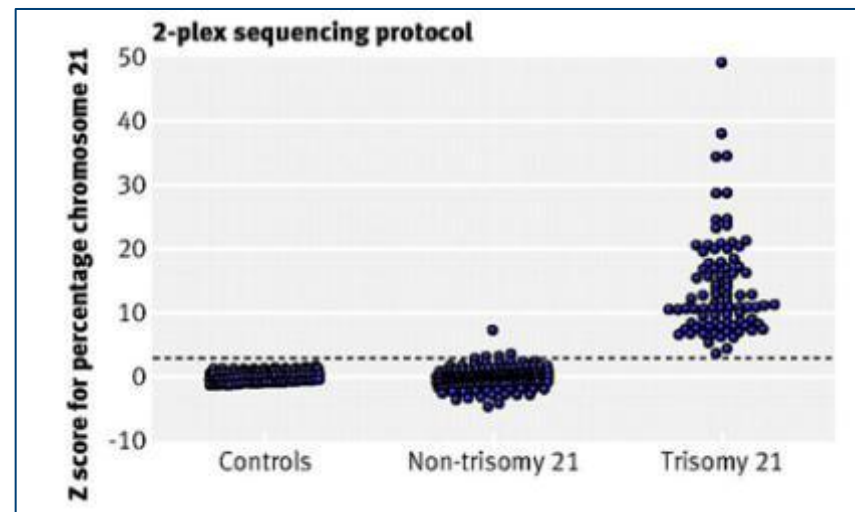
## Non-invasive prenatal assessment of trisomy 21 by multiplexed maternal plasma DNA sequencing: large scale validity study

R.W.K Chiu et al., *Brit Medical J*, on-line first, (Jan 2011)

- Partially blinded study, focused on trisomy 21 detection only
- Results compared to karyotyping (CVS or Amniocentesis)
- Enrolled 824 patient blood samples

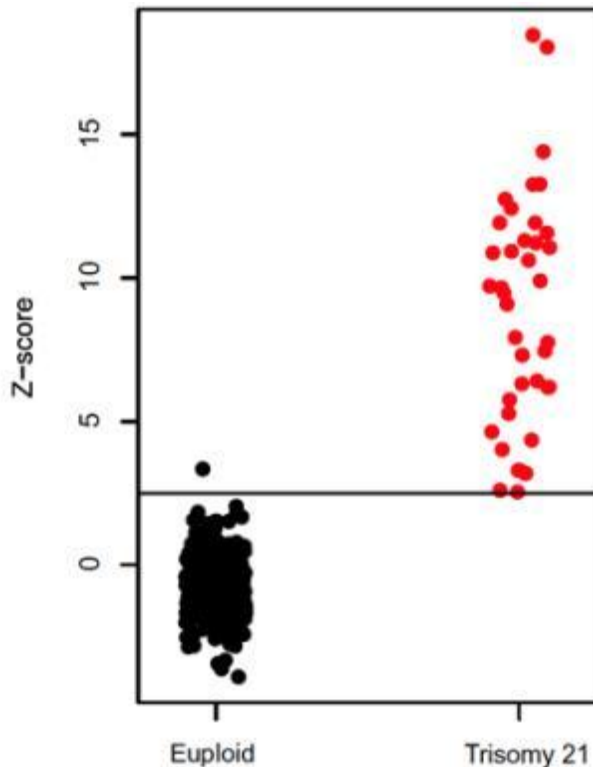
### Top Line Results

- ***In 2 plex protocol, all 86 trisomy 21 positive samples detected***
- ***Sensitivity 100%; Specificity 97.9%***



# Recent Publications on Non-Invasive Trisomy 21 Test

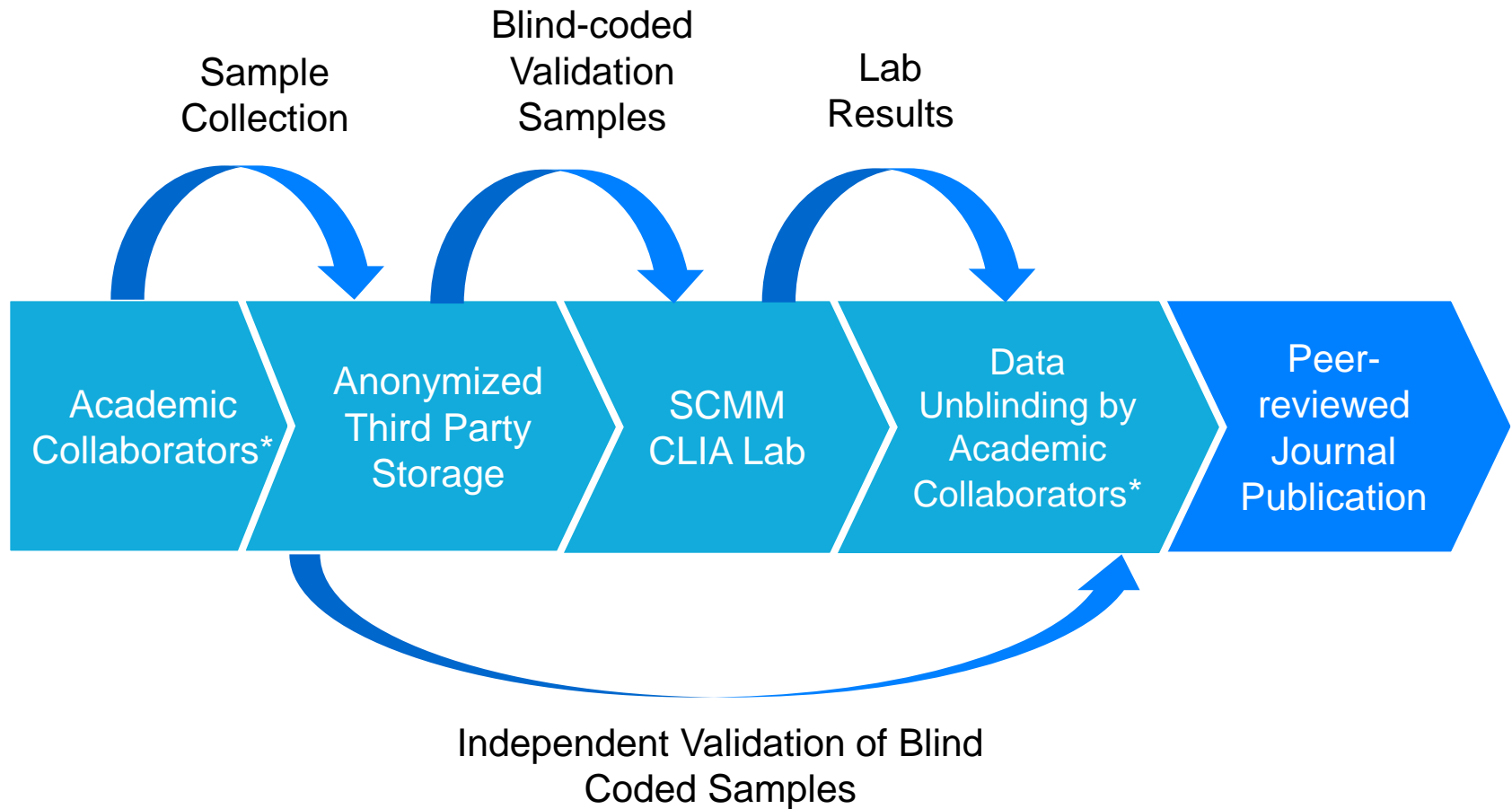
## February 2011: Sequenom CMM “Locked Assay”



- 480 Samples Tested
  - Blinded study focusing on Trisomy 21 detection
  - 449 met entry criteria, 31 failed pre-sequencing QC
  - Results compared to karyotyping
- 39 Trisomy 21 samples correctly classified
  - 100% sensitivity (95% CI; 89-100%)
  - 99.7% specificity (95% CI: 98.5-99.9%)
    - 1 euploid sample misclassified as T21

\* Ehrich M, Deciu C, Zwiefelhofer T, et al. Noninvasive detection of fetal trisomy 21 by sequencing of DNA in maternal blood: a study in a clinical setting. *Am J Obstet Gynecol* 2011;204:205.e1-11.

# MaterniT21™ LDT Clinical Validation Study Process



\* Women & Infants Hospital of Rhode Island (WIHRI)

# Projected MaterniT21™ Timeline and Milestones



Q1-11	Q2-11	Q3-11	Q4-11	Q1-12	Q2-12	Q3-12	Q4-12
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LDT Validation Study\* & Data Analysis (in progress)

Manuscript Submission & Publication

✓ ★ Publication of “Locked Assay”

★ LDT launch upon validation study publication

✓ ★ Meet with FDA

Submit PMA ★

PMA Sample Collection

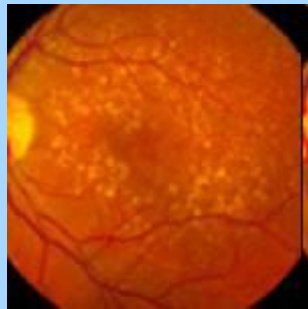
SEQureDx® PMA Clinical Studies

\* Performed by Sequenom CMM

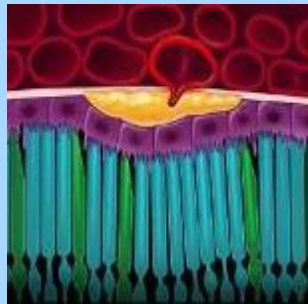
# Age-related Macular Degeneration (AMD)



## Dry AMD (drusen)



15-20%  
Progression

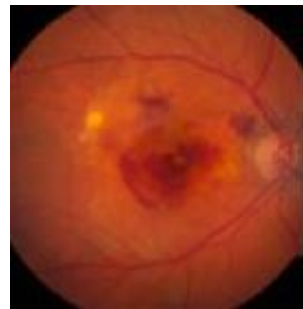


Neovascular  
Leakage



Loss of  
Central  
Vision (Legal  
Blindness)

## Wet AMD (neovascular)



## US prevalence:

- Leading cause of vision loss in people 60+ yrs
- Affects 15-20M people in the US
- Over 10M cases of intermediate and advanced AMD\*

\* [http://www.nei.nih.gov/eyedata/pbd\\_tables.asp](http://www.nei.nih.gov/eyedata/pbd_tables.asp)

# Annual Incidence of AMD



Age	Annual Incidence of any AMD (early + advanced)	Absolute 'any AMD' Incidence Numbers for 2010
50 - 59	0.5%	170,800
60 - 69	1.4%	339,038
70 - 79	3.0%	418,830
≥80	3.8%	385,700
All Ages 50+	1.6%	1,314,368

Friedman DS et al. Prevalence of Age-Related Macular Degeneration in the United States. *Arch Ophthalmol.* 2004;122:564

Rein DB et al. Forecasting Age-Related Macular Degeneration Through the Year 2050. *Arch Ophthalmol.* 2009;127(4):533

\* Census data <http://www.census.gov/popest/national/asrh/NC-EST2006/NC-EST2006-04-WA.xls>

# Opportunities in AMD Testing



## Unmet Medical Need

- Nearly 75% of patients with early/intermediate AMD are unaware of their disease
- Physicians cannot accurately predict the 10-20% of patients who will convert to late stage Choroidal Neovascularization (CNV), or wet AMD
- No test exists to identify the 10% of patients who do not respond to late stage anti-VEGF therapies

## Testing Opportunity

**Test to Predict Risk  
of Developing AMD**

**Test to Predict  
Risk of Wet AMD**

**Test to Predict  
Response to Therapy**

# Product Profile: RetnaGene AMD<sup>TM</sup>



## Age-related Macular Degeneration (AMD) Test\*

- Goal:** A genetic test to assess the risk of developing late stage (wet) AMD
- Use:** To identify high risk patients to optimize their disease management
- Initial Market:** Early stage AMD patients
- Test Sample:** Buccal Swab or Blood Draw
- Test Analyte:** DNA
- Test Method:** Multiplexed SNP analysis
- Test Platform:** MassARRAY Analyzer 4 (Sequenom, Inc.)
- Turnaround:** 8-10 days
- LDT Launch:** Lab Developed Test (LDT) launched May 2011

\* Performed by Sequenom CMM

# Projected AMD Timeline and Milestones



**LDT Analytical Validation Study\***

**In Silico Validation Study Manuscript Submission & Publication**

**LDT launched in May 2011**



*RetnaGene™ AMD Lab Report*

**Interpretation of the Test Result**  
 Age 63 and older  
 Patient Probability of CNV: 76%  
 Patient Risk Score: 1.4  
**High Risk**

**About the Test**  
 RetnaGene™ AMD is a genetic test that allows physicians to assess the risk of a patient developing choroidal neovascularization (CNV), the wet form of age-related macular degeneration (AMD).

**Interpretation of the Test Result**  
 The risk score and probability of developing CNV for this patient were determined based on the risk profiles and associated disease stated in a retrospective validation study of 632 patients with CNV and 322 disease-free subjects. The results were modeled with white patients of European ancestry age 63 and older. The performance of this test has not been established in individuals of different races and age groups. Results should be considered in context with other clinical assessments.

**Patient Genotyping Results**

Gene	SNP ID	Result <sup>1</sup>
CFH	rs1061178	[AA]
CFH	rs2274708	[AA]
CFH	rs403946	[AA]
CFH	rs12144029	[AA]
CFHR4	rs1489153	[AA]
CFHR5	rs1792311	[AA]
CFHR5	rs13622153	[AA]
F13B	rs898989	[AA]
F13B	rs2992818	[AA]
CC	rs8322758	[AA]
CFB	rs641153	[AA]
ARMS2	rs13498924	[AA]
CC	rs2230768	[AA]

**Probability of Developing CNV<sup>2</sup>**

CNV Probability <3%	CNV Probability 28-70%	CNV Probability >75%
Low Risk Risk Score <1.18	Intermediate Risk Risk Score Range: 1.09 to 1.88	High Risk Risk Score >1.18

<sup>1</sup>SNP: single nucleotide polymorphism  
<sup>2</sup>Homozygosity is indicated by matching nucleotides, e.g., AA. Heterozygosity is indicated by different nucleotides, e.g., GT.

**Preparation for ex-US commercialization**

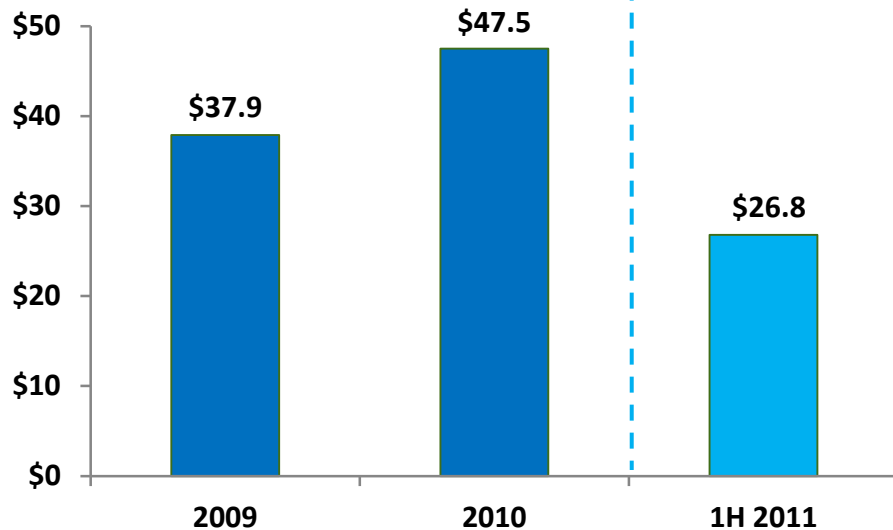
\* Performed by Sequenom CMM

# Financial Highlights

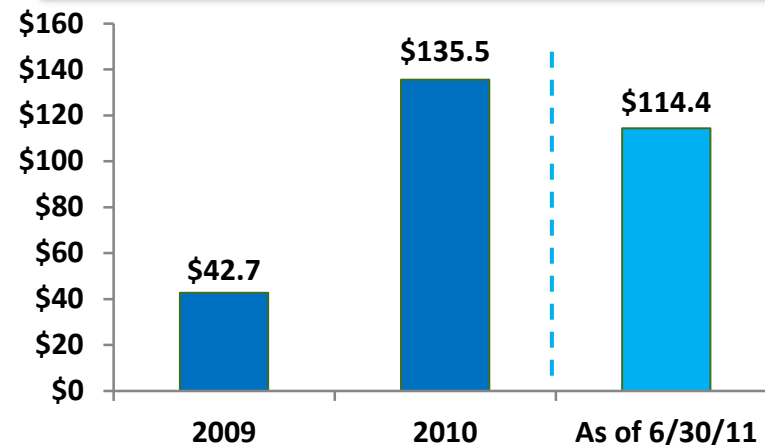
(\$ Millions)



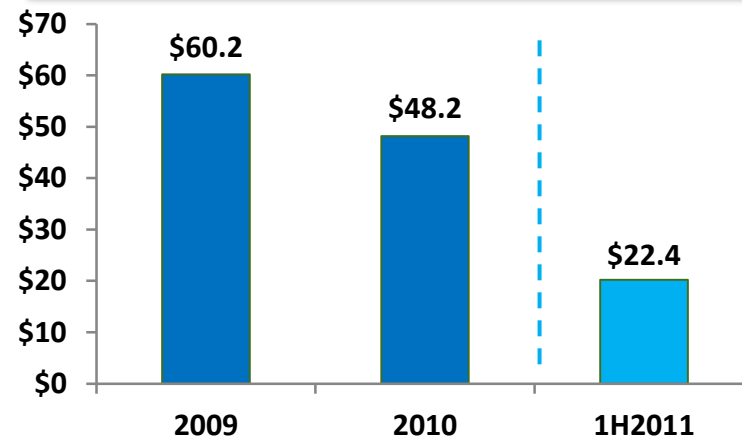
## Revenue



## Available Cash\*



## Cash Burn\*\*



\* Includes cash & marketable securities

\*\* Net cash used in operations of \$48.7M, \$42.6M and \$20.2M for 2009, 2010 and 1H11

# Sequenom 2011 Goals



## Genetic Analysis Business

- Continue to grow Genetic Analysis business with instrument placement and reagent usage
- Launch additional Genetic Analysis Research Use Only (RUO) panels

## Business Development

- Expand product offerings through internal development, in-licensing, partnering and acquisitions
- Expansion of T21 technology and IP into non-US markets (4Q11/1Q12)

## Regulatory

- ✓ Met with FDA to define appropriate Trisomy 21 Test clinical studies for PMA submission
- Continue dialogue with FDA to determine best course of action going forward

# Sequenom CMM 2011 Goals



## Trisomy 21 *Clinical*

- ✓ Publication of “Locked-Assay” study results in AJOG\* (Q1)
- ✓ Complete LDT, W&I clinical validation study (Q2)
- Submission (Q3) and publication (4Q11/1Q12) of LDT clinical validation study results
- LDT launch upon validation study publication (4Q11/1Q12)

## Trisomy 21 *Commercial*

- Establish reimbursement strategy and pricing (Q3/Q4)
- Expand sales force infrastructure build-out for launch (Q3/Q4)
- Install appropriate sequencing capacity prior to launch (Q4)

## AMD

- ✓ Complete clinical validation study (Q1)
- ✓ Submission and announcement of acceptance of study results (Q2)
- ✓ Publication of study results (Q2)
- ✓ LDT launch (Q2 – ahead of scheduled Q3 launch)

\* *American Journal of Obstetrics & Gynecology*

# SEQUENOM®

Improving healthcare through revolutionary genetic analysis solutions

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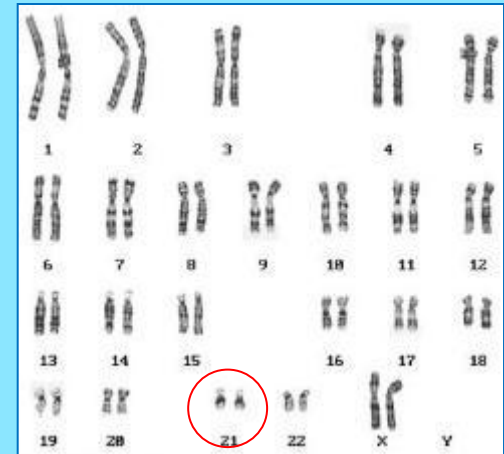
# Trisomy 21 Test Design Goals & Application



- To develop a noninvasive T21 test using circulating cell-free fetal (ccff) nucleic acids as an adjunct to other clinical assessments available to the clinician
- Test must:
  - exceed sensitivity (detection rate) and specificity (false positive rate) of currently available screening tests
  - be applicable in 1<sup>st</sup> and 2<sup>nd</sup> trimesters
  - be a direct genetic test, not a surrogate marker
- Methodology selected in May 2010 uses Massively Parallel Shotgun Sequencing (MPSS)

## Karyotyping: Invasive Gold Standard

Normal



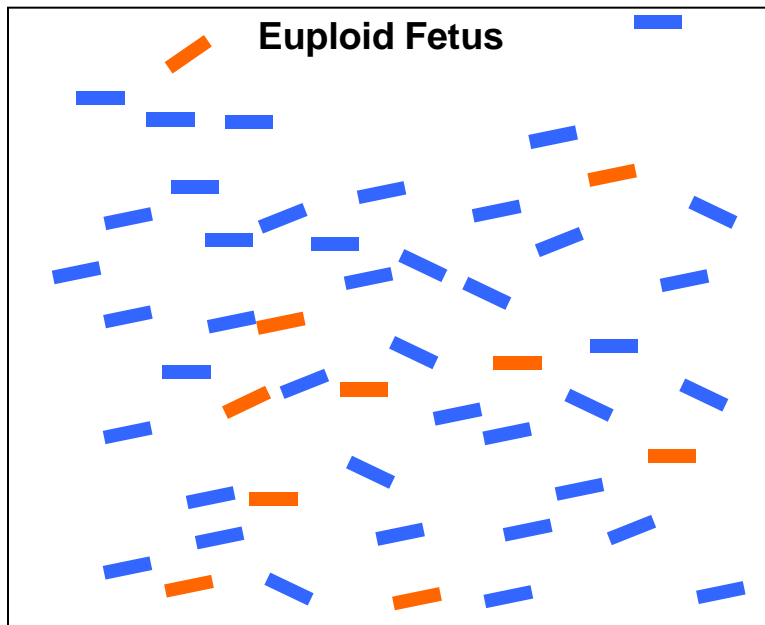
T21



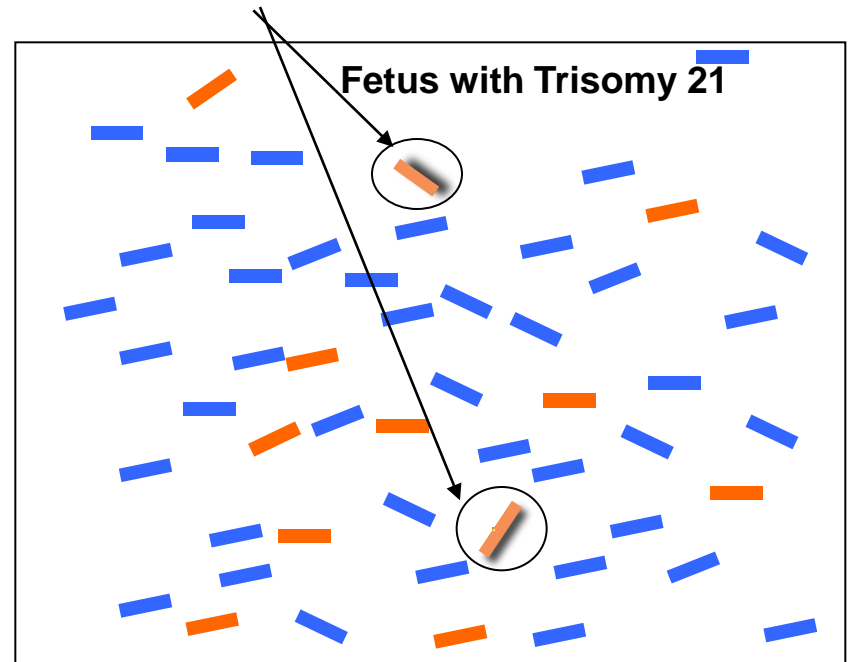
# Principles of Fetal Trisomy 21 Testing From A Maternal Blood Sample Using DNA Sequencing

- ~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

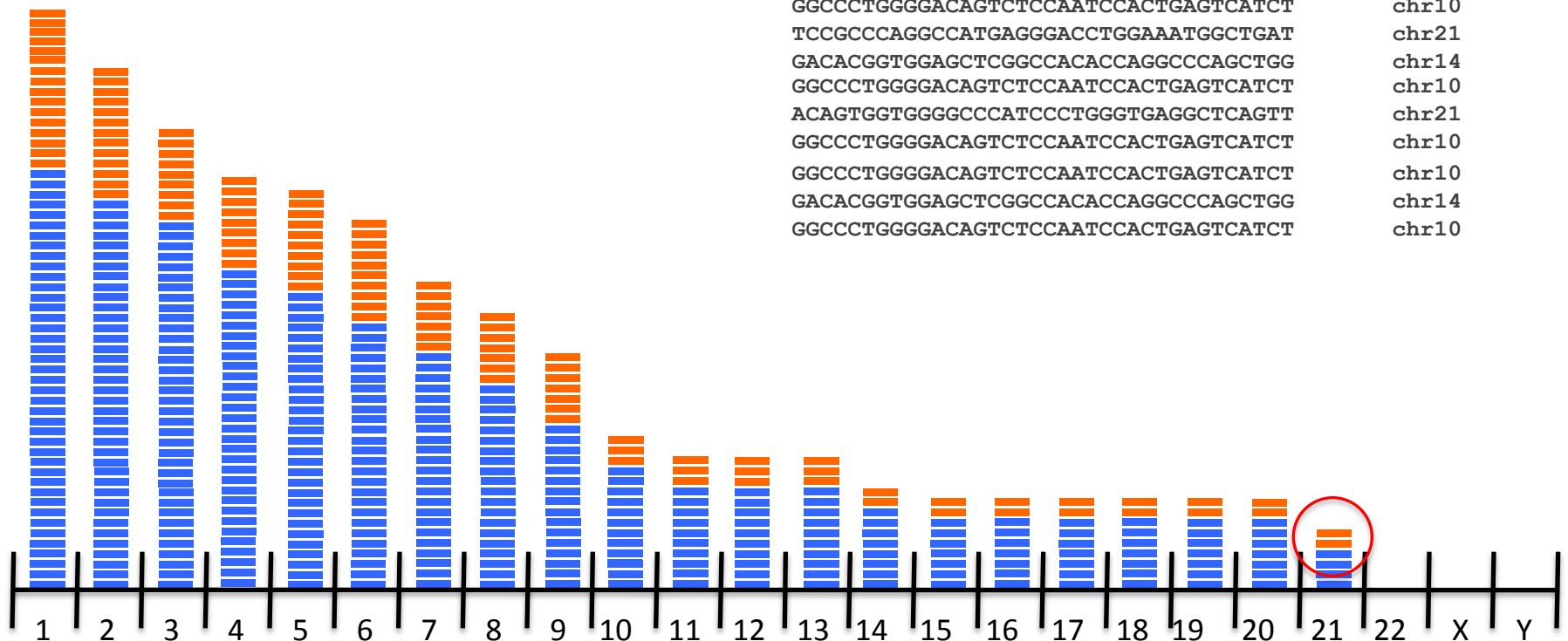


# Principles of Fetal Trisomy 21 Testing Using DNA “Shotgun” Sequencing



Sequencing tells you which chromosome the fragment comes from.

TCCGCCCAGGCCATGAGGGACCTGGAAATGGCTGAT	chr21
GGCCCTGGGGACAGTCTCCAATCCACTGAGTCATCT	chr10
GACACGGTGGAGCTCGGCCACACCAGGCCAGCTGG	chr14
GGCCCTGGGGACAGTCTCCAATCCACTGAGTCATCT	chr10
ACAGTGGTGGGGCCCATCCCTGGGTGAGGCTCAGTT	chr21
GGCCCTGGGGACAGTCTCCAATCCACTGAGTCATCT	chr10
GGCCCTGGGGACAGTCTCCAATCCACTGAGTCATCT	chr10
GGCCCTGGGGACAGTCTCCAATCCACTGAGTCATCT	chr10
TCCGCCCAGGCCATGAGGGACCTGGAAATGGCTGAT	chr21
GACACGGTGGAGCTCGGCCACACCAGGCCAGCTGG	chr14
GGCCCTGGGGACAGTCTCCAATCCACTGAGTCATCT	chr10
ACAGTGGTGGGGCCCATCCCTGGGTGAGGCTCAGTT	chr21
GGCCCTGGGGACAGTCTCCAATCCACTGAGTCATCT	chr10
GGCCCTGGGGACAGTCTCCAATCCACTGAGTCATCT	chr10
GACACGGTGGAGCTCGGCCACACCAGGCCAGCTGG	chr14
GGCCCTGGGGACAGTCTCCAATCCACTGAGTCATCT	chr10



# Fetal Trisomy 21 Detection By DNA Sequencing



Unaffected Chromosome 21 on left (2 fragments)  
Affected Chromosome 21 on right (3 fragments)

