6th Annual
Advances in Prenatal Molecular Diagnostics
Tools, Technologies, and Clinical Implementation for Next Generation Prenatal Diagnostics

October 29 - 30, 2018 | Cambridge, MA
Hyatt Regency Cambridge

COVERAGE INCLUDES:
• NIPT in a clinical setting
• Advances in and clinical relevance of cfDNA screening
• The road toward cell-based NIPD
• The future of cfDNA vs. cell-based non-invasive testing
• Sequencing on invasive samples
• Biomarkers for preeclampsia and pre-term birth
• The future of prenatal and reproductive diagnostics, including patient perspective

PANEL DISCUSSIONS:
• Getting to Truly Comprehensive NIPT: What Does Cell-Based NIPT Offer that cfDNA Can’t?
• Predicting the Landscape for Prenatal Molecular Diagnostics: The Next Few Years

PROGRAM ADVISORS
Arthur Beaudet, MD, Chair, Department of Molecular & Human Genetics, Baylor College of Medicine
Cynthia Morton, PhD, Departments of Obstetrics, Gynecology & Reproductive Biology and of Pathology, Harvard Medical School; Director, Cytogenetics, Brigham & Women's Hospital
Joe Leigh Simpson, MD, Senior Vice President for Research and Global Programs, March of Dimes Foundation
Ronald J. Wapner, MD, Director, Reproductive Genetics and Vice Chair, Research, Department of Obstetrics and Gynecology, Columbia University Medical Center

Prenatal-Dx.com
ABOUT THE CONFERENCE

Cell-free DNA screening and the potential for cell-based DNA testing continues to revolutionize the prenatal diagnostics field. While cell-free DNA tests are being used more and more in a clinical setting, with cell-based testing on its heels, there is still a pertinent need for improvements in sensitivity, specificity, and clinician and patient education in order to truly replace invasive testing. Alongside these developments, much research is being done in fetal whole exome sequencing and is beginning to play a large role in miscarriage testing. Furthermore, research into biomarkers for pre-term birth and preeclampsia is playing a large role in prenatal care. With all this research and screening, of course, comes more information than ever before, and test developers, clinicians, and genetic counselors need to keep abreast of these changes, nuances, and guidelines in order to effectively care for patients. This event will not only examine scientific advances, but also clinical implementation and future directions for the field.

MONDAY, OCTOBER 29

NIPT IN THE CLINIC

8:00 am Registration and Morning Coffee

9:00 Chairperson’s Remarks
Louis J. Muglia, MD, PhD, Director, Division of Human Genetics, Department of Pediatrics, Cincinnati Children’s Hospital Medical Center

9:05 Two Years Later: The Implementation of ACMG’s NIPS Practice Guidelines
Brian Skotko, MD, MPP, Co-Director, Down Syndrome Program, Massachusetts General Hospital

It’s been two years since the ACMG published its revised practice guidelines for cfDNA NIPS. Part of those guidelines recommend considerations for laboratories on patient reports and patient education materials. During this talk, Dr. Skotko will take a look at highlights from the field.

9:35 Ethical and Social Issues in Translating cfDNA Screening into Routine Prenatal Care
Marsha Michie, PhD, Assistant Professor, Bioethics, Case Western Reserve University School of Medicine

Since 2011, prenatal cell-free DNA screening has transformed the landscape of options for pregnant women who want genetic information about their developing fetus. This rapid implementation has raised multiple social and ethical issues for families, clinicians, professional organizations, patient groups, laboratories, and many others. With little top-down regulation in this space, stakeholders are working together to guide translation of these technologies into applications that are ethically appropriate and socially beneficial.

10:05 Patient Advocacy Groups and Commercial Companies: An Examination
Stephanie Meredith, MA, Lettercase Program/Medical Outreach Director, Human Development Institute, University of Kentucky

Overview of the increased patient education needs caused by the expansion of prenatal screening and testing and the steps being taken to address those gaps and meet the needs of all the stakeholders: patients, providers, and disability advocacy groups. Further exploration of the role industry in meeting those patient education needs and establishing ethical relationships with patient advocacy groups.

10:35 Networking Coffee Break

CELL-FREE DNA SCREENING

10:55 The VALUE Study: A Novel cfDNA Non-NGS Method to Identify Common Autosomal Trisomies
Geraldyn Lambert-Messerlian, PhD, FAACC, Professor and Laboratory Director, Women & Infants Hospital of Rhode Island

Multiple methods utilizing NGS of cfDNA from maternal circulation are in widespread use as a secondary screening test, but transitioning such testing into a first line screening test for the general pregnancy population has proven difficult. A novel molecular probe technology will be used that enriches for targeted fragments that are counted without the use of PCR. The VALUE study aims to provide both internal and external validation of assay performance as well as document the necessary resources to test 10,000 samples per year. We have enrolled 800 of 2400 low risk pregnancies and will include an additional 100 samples with a common autosomal trisomy.

11:25 Clinical Relevance: Non-Invasive Prenatal Diagnosis of Congenital Adrenal Hyperplasia
Maria New, MD, Director of Adrenal Steroid Disorders Program, Professor of Pediatrics and Genetics, Pediatric Endocrinology, Icahn School of Medicine at Mount Sinai Hospital

Congenital Adrenal Hyperplasia is an autosomal recessive condition that arises from mutations in the CYP21A2 gene that encodes for the steroidogenic enzyme 21-hydroxylase. To prevent genital ambiguity in affected female fetuses, prenatal treatment with dexamethasone must begin on or before gestational week 9. Currently the use of chorionic villus sampling and amniocentesis provides genetic results at approximately 14 weeks of gestation at the earliest. This means that mothers who want to undergo prenatal dexamethasone treatment will be unnecessarily treating seven of eight fetuses, emphasizing the desirability of earlier genetic diagnosis in utero.

11:55 Sponsored Presentation (Opportunity Available)
12:25 pm Luncheon Presentation (Sponsorship Opportunity Available) or Enjoy Lunch on Your Own
12:55 Session Break

1:55 Chairperson’s Remarks
Ronald Wagner, MD, Director, Reproductive Genetics and Vice Chair, Research, Department of Obstetrics & Gynecology, Columbus University Medical Center

What Role Could NIPT Play in Management of Recurrent Pregnancy Losses (RPL)?
Joe Leigh Simpson, MD, President for Research and Global Programs, March of Dimes Foundation

Etiology of miscarriages can be stratified into euploid versus aneuploid causes. Such differentiation points to differing etiology, and, hence, treatments. Professional societies (ACOG, FIGO, RCOG, ESHRE) now recommend determination of chromosomal status of miscarriages as the recommend fetal test. Chromosomal microarrays are preferred over karyotypes because cell culture is not required. However, recovery of tissue is an impediment. Given considerable DNA extruded into the maternal circulation before and during expulsion, NIPT for detection of any aneuploidy should be an ideal method of determining chromosomal status of miscarriage. Such an approach would allow accurate diagnosis of etiology, more robust clinical trials given do, diminished misclassification of miscarriages, and ability to assess whether recurrent miscarriage while on treatment indicates therapeutic failure or occurred for an unrelated reason.
TOWARDS CELL-BASED NON-INVASIVE PRENATAL DIAGNOSIS

2:30 Technical Insights into Next Generation Sequencing Analysis of DNA from Circulating Trophoblastic Cells

Patrizia Paterlini-Brechot, PhD, MD, Cellular & Molecular Biology, University Paris Descartes

Isolation of rare trophoblastic cells from blood is a technical challenge with impact on the number of collected fetal cells and on the quality of their DNA. By using the ISET (Isolation by Size of Tumor/ Trophoblastic cells) system, we have developed protocols for isolation of fixed and live circulating trophoblastic cells, cell free DNA collection allowing scalable NGS analysis of circulating fetal cells and cfDNA. We show the results and technical challenges related to this field and discuss the potential clinical impact of these developments for non-invasive prenatal diagnosis of genetic disorders.

3:00 Imprinted NanoVelcro Microchips for Isolation and Characterization of Circulating Fetal Trophoblasts – Toward Noninvasive Prenatal Diagnostics

Hsian-Rong Tseng, PhD, Professor, Molecular & Medical Pharmacology, University of California, Los Angeles

Circulating fetal nucleated cells (CFNCs) in maternal blood offer an ideal source of fetal genomic DNA for noninvasive prenatal diagnostics (NIPD). We developed a new class of NanoVelcro Microchips to effectively enrich a subcategory of CFNCs, i.e., circulating trophoblasts (cTBs) from maternal blood. Our results support the use of NanoVelcro Microchips for cTB-based noninvasive prenatal genetic testing, which holds potential for further development toward future NIPD solution.

3:30 Refreshment Break in the Exhibit Hall with Poster Viewing

4:10 Fetal Cells in Maternal Blood for Prenatal Diagnosis – From R&D to Clinic

Ripudaman Singh, PhD, MBA, CTO, ARCDI Biotech Aps

Technological advances in enrichment, manipulation and analyses of rare fetal cells from maternal blood have been made in the last 5 years. This has invigorated interest in circulating fetal cells and their application in prenatal testing. The hope is that enriched fetal cells from maternal blood can be used as superior alternatives to conventional NIPD which is based on free fetal DNA in maternal blood. For the last 11 years, we have tried to answer some critical questions pertaining to fetal cells and their use in prenatal diagnosis. After developing a robust technology which is both scalable and cost effective, ARCDI Biotech, in collaboration with Aarhus University Hospital has launched the first ever cell based NIPD in Denmark, covering approximately 17,000 pregnancies per year. Results from that clinical launch will be presented and discussed.

4:40 High Throughput Microchip Systems for Isolation of Fetal Trophoblasts

Cagri Savran, PhD, Professor, Purdue University; Founder & CSO, Savran Technologies, Inc.

We have developed a patented microchip system that has the ability to capture rare trophoblasts with over 90% capture efficiency and near 100% purity, as well as deliver the targeted to the user as single cells, within less than 1.5 hours. We will describe the basic operation of the system as well as results pertaining to the characterization and testing of the system.

5:10 Results of a Validation Study of Cell-Based NIPT Attempting 1 Mb Deletion Detection

Art Beaudet, MD, Department of Molecular & Human Genetics, Baylor College of Medicine

We have completed analysis of over 50 samples in a pre-validation (not CAP and CLIA) study and expect to move to a CAP and CLIA validation study shortly. Results indicate the feasibility of launching a commercial test in the near future.

5:40 Welcome Reception in the Exhibit Hall with Poster Viewing

6:40 Close of Day

TUESDAY, OCTOBER 30

8:00 am Breakfast Breakout Roundtable Discussions

Commercialization Challenges for Fetal Cell-Based NIPT

Patrizia Paterlini-Brechot, PhD, MD, Cellular & Molecular Biology, University Paris Descartes

The Utility of Biomarkers in Pregnancy: What is Beyond NIPT

Thomas F. McElrath, PhD, Attending in Maternal-Fetal Medicine, Obstetrics and Gynecology, Brigham & Women’s Hospital

Patient Education Needs in cfDNA

Stephanie Meredith, MA, Lettercase Program/Medical Outreach Director, Human Development Institute, University of Kentucky

THE FUTURE OF CELL-FREE DNA SCREENING VS. CELL-BASED NIPT

9:00 Chairpersons’ Remarks

Peter Kolchinsky, Managing Director & Portfolio Manager, RA Capital Management

Lee Cooper, JD, MBA, Entrepreneur in Residence, RA Capital Management

9:05 Combining Cell-Free DNA and Circulating Fetal Cell Analysis for Non-Invasive Prenatal Screening and Diagnosis

Haichuan Zhang, PhD, CEO, Celula China Medical Technology Co.

There are both advantages and limitations in utilizing cell free DNA or circulating fetal cell for non-invasive prenatal testing. Cell free DNA analysis is demonstrated for aneuploidy detection with high accuracy, but is limited by its DNA fragmentation and significant amount of maternal background for accurate single gene disorders, especially the recessive genetic diseases detection. Fetal cell in maternal circulation provides a possible solution to such limitations, but has its own challenges in reliable cell isolation and commercially viable single cell analysis. Research and development efforts of combing both cell free DNA and fetal cell approaches have been conducted by Celula, Inc. for more than 10 years. A solution consisting of low cost cell free DNA screening for major trisomies and fetal cell isolation, identification for confirmation of aneuploidy and detection of single gene disorders from the same sample is being developed with support from large clinical collaborations.

9:35 PANEL DISCUSSION: Grand Unified Theory of NIPT – cfDNA [AND or OR] Cell-Based NIPT

Moderator: Peter Kolchinsky, Managing Director & Portfolio Manager, RA Capital Management

Panelists: Paul Billings, PhD, CMO, Natera

Ripudaman Singh, PhD, MBA, CTO, ARCDI Biotech Aps

What is the role of cell-based NIPT once cfDNA achieves its full potential, and what is the role of cfDNA once cell-based NIPT is a reality?

10:35 Coffee Break in the Exhibit Hall with Poster Viewing

ADVANCES IN SEQUENCING

11:15 Transitioning Prenatal Molecular Diagnosis to Neonatal Personalized Medicine

Ronald Wapner, MD, Director, Reproductive Genetics and Vice Chair, Research, Department of Obstetrics & Gynecology, Columbia University Irving Medical Center

Prenatal diagnostic testing now allows us to diagnose fetal disorders in which in utero treatment is available. In addition, diagnosis of the specific genetic cause of fetal structural and metabolic disorders can significantly improve neonatal care.
Exome sequencing has utility in determining an underlying molecular etiology when performed on fetal specimens from pregnancies with structural abnormalities where standard genetic testing (karyotype and microarray) do not provide a diagnosis. Challenges related to genetics literacy and variant interpretation must be addressed by highly tailored pre- and post-test genetic counseling.

**12:15 pm A Time to Sequence in Clinical Cytogenetics: The Need for Nucleotide Resolution**

Cynthia Morton, PhD, William Lambert Richardson Professor, Obstetrics, Gynecology & Reproductive Biology and Pathology, Harvard Medical School; Director, Cytogenetics, Brigham & Women's Hospital

Numerical and structural abnormalities of human chromosomes have been recognized since the late 1950's and have served as a foundation of the understanding of genetic disorders. Despite improved detection of microscopically-cryptic genomic gains and losses by microarrays, balanced chromosome rearrangements such as translocations, inversions and insertions, present in >1 in 500 individuals, remain a challenge in clinical cytogenetics in the setting of de novo rearrangements in prenatal diagnoses. Technological advances such as low-pass, whole-genome sequencing to define most chromosomal rearrangements, combined with knowledge of the 3D structure of the genome to predict gene expression, underscore the importance of nucleotide resolution of chromosomal structural rearrangements for clinical interpretation.

**12:45 Sponsored Presentation (Opportunity Available)**

**1:15 Luncheon Presentation (Sponsorship Opportunity Available) or Enjoy Lunch on Your Own**

**1:45 Session Break**

**2:15 Refreshment Break in the Exhibit Hall with Poster Viewing**

**BIOMARKERS FOR PREECLAMPSIA AND PRE-TERM BIRTH**

**2:45 Chairperson's Remarks**

Thomas F. McElrath, PhD, Attending in Maternal-Fetal Medicine, Obstetrics and Gynecology, Brigham & Women's Hospital

**3:00**

Neeta Vora, MD, Associate Professor, Department of OB GYN, Division of Maternal-Fetal Medicine, University of North Carolina Chapel Hill

Exome sequencing has utility in determining an underlying molecular etiology when performed on fetal specimens from pregnancies with structural abnormalities where standard genetic testing (karyotype and microarray) do not provide a diagnosis. Challenges related to genetics literacy and variant interpretation must be addressed by highly tailored pre- and post-test genetic counseling.

**3:20 Risk Stratification in Pregnancy: The Potential of Extracellular Vesicle Protein Biomarkers in Prenatal Care**

Thomas F. McElrath, PhD, Attending in Maternal-Fetal Medicine, Obstetrics and Gynecology, Brigham & Women's Hospital

The major third trimester complications of pregnancy (preeclampsia, spontaneous preterm birth) have their origins in aberrant vascular development at the end of the first trimester. Our group has identified differences in extracellular vesicular proteins sampled at the end of the first trimester that predict increased third trimester risk. This work represents a means to stratify pregnancy associated risk during early prenatal care and constitutes a "liquid" biopsy of the maternal-placental microenvironment.

**THE FUTURE OF PRENATAL AND REPRODUCTIVE DIAGNOSTICS**

**3:50 Preventing Genetic Disease: From Innovator to Patient, and Back Again**

Lee Cooper, JD, MBA, Entrepreneur in Residence, RA Capital

Framed around the inherent market challenges of prevention versus treatment, I will discuss a first-hand experience of going from drug development to a personal odyssey in genetic disease and reproductive genetics. I will leave the audience with a view toward the ways that consumer-driven demand is going to shape the future of reproductive genetics, and where I see the field going in terms of both market and non-market actors.

**4:20 CLOSING PANEL: Predicting the Landscape for Prenatal Molecular Diagnostics: The Next Few Years**

Joe Leigh Simpson, MD, President for Research and Global Programs, March of Dimes Foundation

Patrizia Pasternici-Brechet, PhD, MD, Cellular & Molecular Biology, University Paris Descartes

Ronald Wapner, MD, Director, Reproductive Genetics and Vice Chair, Research, Department of Obstetrics & Gynecology, Columbia University Medical Center

Art Beaudet, MD, Department of Molecular & Human Genetics, Baylor College of Medicine

Cynthia Morton, PhD, William Lambert Richardson Professor, Obstetrics, Gynecology & Reproductive Biology and Pathology, Harvard Medical School; Director, Cytogenetics, Brigham & Women's Hospital

There are a number of advancements that the prenatal field will pursue: cell-based NIPT, NIPT for microdeletions, biomarkers for preeclampsia and preterm birth, and ultimately patient and physician education. This panel will discuss future directions for the field and potential directions for these areas.

**4:50 Close of Conference**
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HOTEL & TRAVEL INFORMATION

Conference Hotel:
Hyatt Regency Cambridge
575 Memorial Drive
Cambridge, MA 02139
(617) 492-1234

Discounted Room Rate: $179 s/d
Discounted Room Rate Cut-off Date: October 1st, 2018

Reservations and Additional Travel Information:
Go to the travel page of Prenatal-Dx.com