

# **Preterm Birth International Collaborative (PREBIC)**

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**Euro-Peristat Meeting  
London, England  
January 13, 2011**



# PREBIC Community

- Perinatal Obstetricians
- Neonatologists and Pediatricians
- Reproductive Biology Scientists
  - Molecular biologists, immunologists, microbiologists
- Geneticists, Genetic epidemiologists
- Epidemiologists
- Pharmacologists
- Leaders of various research foundations interested in studying preterm birth
  - March of Dimes, Burroughs Wellcome, Johnson & Johnson

# PREBIC

## Initial Goals:

- Generate a forum for
  - international projects
  - future collaborations
  - scientific progress based on fruitful discussions
  - generate research funds
  - exchange of ideas
  - collaboration and friendship
- The final product was to be scientific
- Protocols owned by all participants

# PREBIC History

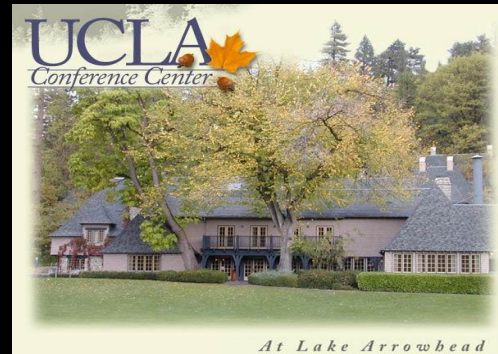
Michigan, March 2003  
Organizer: Dr. Claudia Holzman



Denmark, June 2004  
Organizers: Dr. Poul Thorsen,  
Dr. Ida Vogel



Lake Arrowhead, Los Angeles, CA  
March 2005  
Organizer: Dr. Cal Hobel



# PREBIC

- 4<sup>th</sup> - 9<sup>th</sup> Workshops  
(2006-2011)
- World Health Organization,  
Geneva, April
- Organizers
  - Mario Merialdi
  - Ram Menon
  - Calvin Hobel



Sponsored by March of Dimes and WHO



# PREBIC Annual Meeting at WHO



# PREBIC Goals

Understanding  
Preterm Birth

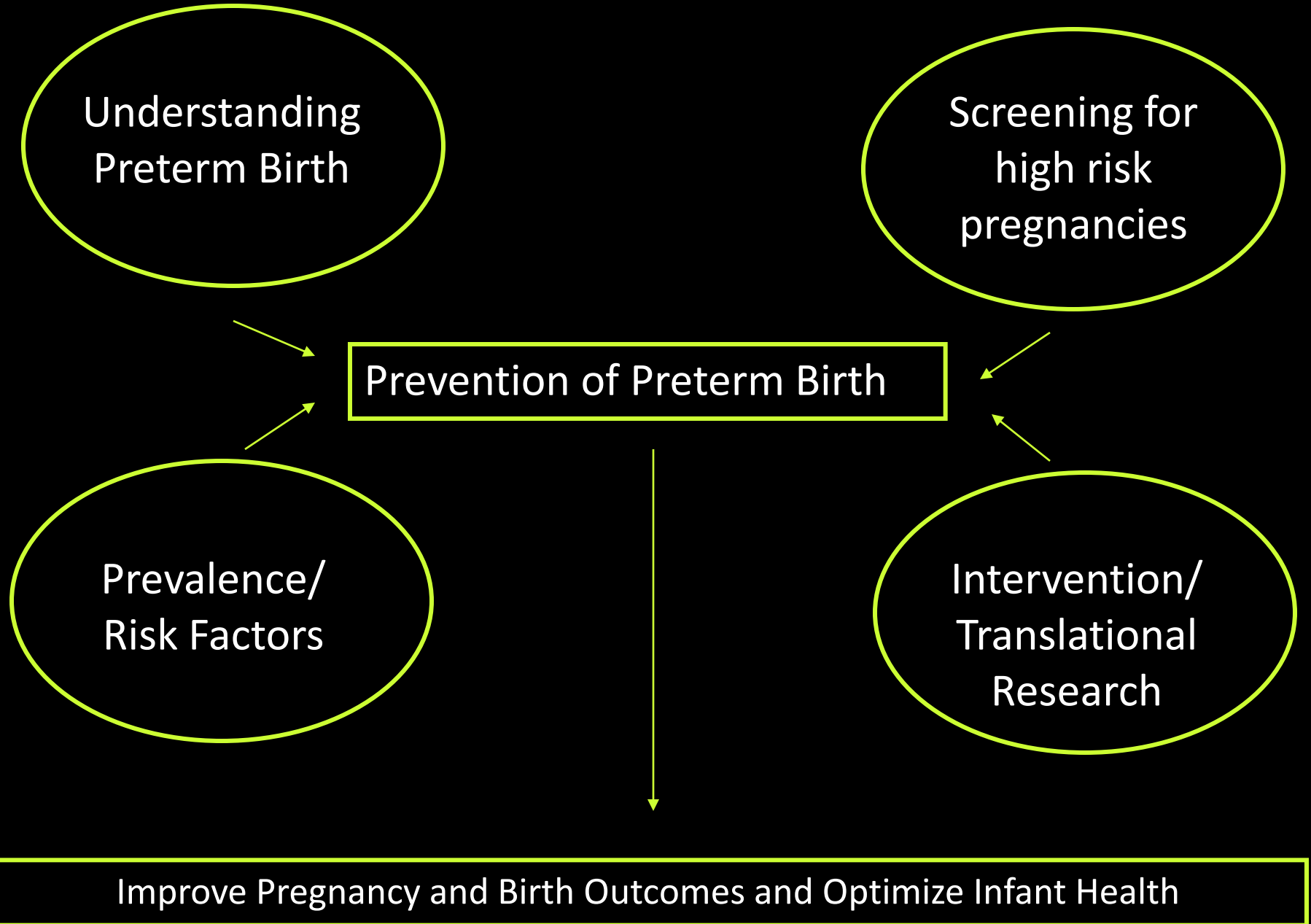
Screening for  
high risk  
pregnancies

Prevention of Preterm Birth

Prevalence/  
Risk Factors

Intervention/  
Translational  
Research

Improve Pregnancy and Birth Outcomes and Optimize Infant Health



# PREBIC Goals

- Describing prevalence and risk factors for preterm birth
- Understanding preterm birth
- Forming consortia to engage in research, especially genetic research
- Educational activities
- Translational Research – Community activities



# PREBIC Achievements So Far

Prevalence/  
Risk Factors



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graph LR; A([Prevalence/  
Risk Factors]) --> B[Epidemiology of preterm birth];
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The diagram consists of a red oval on the left containing the text 'Prevalence/  
Risk Factors'. A horizontal arrow points from this oval to a yellow rectangular box on the right containing the text 'Epidemiology of preterm birth'.

Epidemiology of preterm birth

Publication: Bulletin of the World Health Organization; Type: Research  
Article DOI: 10.2471/BLT.08.062554

**Stacy Beck et al.**

**Worldwide incidence of preterm birth**

## **The worldwide incidence of preterm birth: a WHO systematic review of maternal mortality and morbidity**

Stacy Beck,<sup>a</sup> Daniel Wojdyla,<sup>b</sup> Lale Say,<sup>c</sup> Ana Pilar Betran,<sup>c</sup> Mario Merialdi,<sup>c</sup> Jennifer Harris Requejo,<sup>d</sup> Craig Rubens,<sup>e</sup> Ramkumar Menon<sup>f</sup> & Paul FA Van Look<sup>c</sup>

*(Submitted: 14 January 2009 – Revised version received: 18 April 2009 – Accepted: 18 April 2009 – Published online: 25 September 2009)*

# PREBIC Achievements So Far



Understanding  
Preterm birth

Systematic reviews  
Genetics working group  
Biomarker working group  
Pathways working group

# Systematic Reviews

- BMI as a risk factor for PTB
- Genetic contribution to PTB
- Systematic review of biomarkers of preterm birth
  - In press
- Systematic review of viral infections in preterm birth
  - In preparation
- Other systematic reviews are planned and some of them are underway

# Maternal BMI and preterm birth

*The Journal of Maternal-Fetal and Neonatal Medicine*, November 2009; 22(11): 957–970

**informa**  
healthcare

## **Maternal BMI and preterm birth: A systematic review of the literature with meta-analysis**

MARIA REGINA TORLONI<sup>1</sup>, ANA PILAR BETRÁN<sup>2</sup>, SILVIA DAHER<sup>1</sup>,  
MARIANA WIDMER<sup>2</sup>, SIOBHAN M. DOLAN<sup>3</sup>, RAMKUMAR MENON<sup>4</sup>,  
EDUARDO BERGEL<sup>2</sup>, TOMAS ALLEN<sup>5</sup>, & MARIO MERIALDI<sup>2</sup>

<sup>1</sup>*Department of Obstetrics, São Paulo Federal University, São Paulo, Brazil,* <sup>2</sup>*Department of Reproductive Health and Research, World Health Organization, Geneva, Switzerland,* <sup>3</sup>*Department of Obstetrics and Gynecology and Women's Health, Albert Einstein College of Medicine, New York, USA,* <sup>4</sup>*Department of Epidemiology, Rollins School of Public Health of Emory University, Atlanta, USA,* and <sup>5</sup>*Department of Knowledge Management and Sharing, World Health Organization, Geneva, Switzerland*

*(Received 26 April 2009; revised 10 May 2009; accepted 14 May 2009)*

# Systematic Review and Meta-Analyses of Preterm Birth Genetic Association Studies

## Original Paper

**Public Health  
Genomics**

Public Health Genomics  
DOI: 10.1159/000294202

Received: June 4, 2009  
Accepted after revision: December 1, 2009  
Published online: May 20, 2010

## Synopsis of Preterm Birth Genetic Association Studies: The Preterm Birth Genetics Knowledge Base (PTBGene)

S.M. Dolan<sup>a, o</sup> M.V. Hollegaard<sup>b, o</sup> M. Merialdi<sup>c, o</sup> A.P. Betran<sup>c, o</sup> T. Allen<sup>d</sup>  
C. Abelow<sup>a</sup> J. Nace<sup>e, o</sup> B.K. Lin<sup>f</sup> M.J. Khoury<sup>g</sup> J.P.A. Ioannidis<sup>h, i</sup> S. Bagade<sup>j</sup>  
X. Zheng<sup>k</sup> R.A. Dubin<sup>k</sup> L. Bertram<sup>j, l</sup> D.R. Velez Edwards<sup>m, o</sup> R. Menon<sup>c, e, n, o</sup>

<sup>a</sup>Department of Obstetrics and Gynecology and Women's Health, Albert Einstein College of Medicine/Montefiore Medical Center, Bronx, N.Y., USA; <sup>b</sup>Section of Neonatal Screening and Hormones, Statens Serum Institute, Copenhagen, Denmark; <sup>c</sup>Department of Reproductive Health and Research and <sup>d</sup>Department of Knowledge, Management and Sharing, World Health Organization, Geneva, Switzerland; <sup>e</sup>The Perinatal Research Center, Nashville, Tenn., <sup>f</sup>Office of the Medical Director, March of Dimes, White Plains, N.Y., <sup>g</sup>National Office of Public Health Genomics, Centers for Disease Control and Prevention, Atlanta, Ga., USA; <sup>h</sup>Department of Hygiene and Epidemiology, University of Ioannina School of Medicine, and Biomedical Research Institute, Foundation for Research and Technology – Hellas, Ioannina, Greece; <sup>i</sup>Center for Genetic Epidemiology and Modeling, Tufts Medical Center, and Department of Medicine, Tufts University School of Medicine, Boston, Mass., <sup>j</sup>Genetics and Aqinq Research Unit,

# PTB Gene: Genetics Knowledgebase

<http://bioinformatics.aecom.yu.edu/ptbgene/index.html>

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## PTBGene

### THE PRETERM BIRTH GENETICS KNOWLEDGE BASE



PTBGene provides a comprehensive, unbiased, publicly available and regularly updated collection of published association studies performed on Preterm Birth phenotypes. Eligible publications are identified via systematic searches of MEDLINE and EMBASE. The database can be searched via several mechanisms (see below). For each gene, summary overviews are provided displaying key characteristics for each publication, including links to genotype distributions of the polymorphisms studied, random-effects allelic meta-analyses, and Forest plots. Please contact us to report errors in the presentation of study details or to notify us of publications that should be included.

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
Gene:	<input type="text" value="TNF"/> <input type="button" value="Go"/>
Protein:	<input type="text" value="tumor necrosis factor alpha"/> <input type="button" value="Go"/>
Polymorphism:	<input type="text" value="--Select--"/> <input type="button" value="Go"/>
Study:	<input type="text" value="Menon, 2006 [TNF]"/> <input type="button" value="Go"/>
Significant Findings:	<input type="text" value="--Select--"/> <input type="button" value="Go"/>

Coming Soon: Genome Wide Association Studies



# Preterm Birth Genome Project (PGP)

1. Create a community of researchers to identify PTB susceptibility genes
2. Pool resources from multiple investigators to conduct Genome Wide Association Studies (GWAS) across multiple geographic populations
  - Detailed phenotypic and environmental data
  - Establish a large pool of replication samples
  - Deep re-sequencing of genes with significant/ interesting findings in GWAS

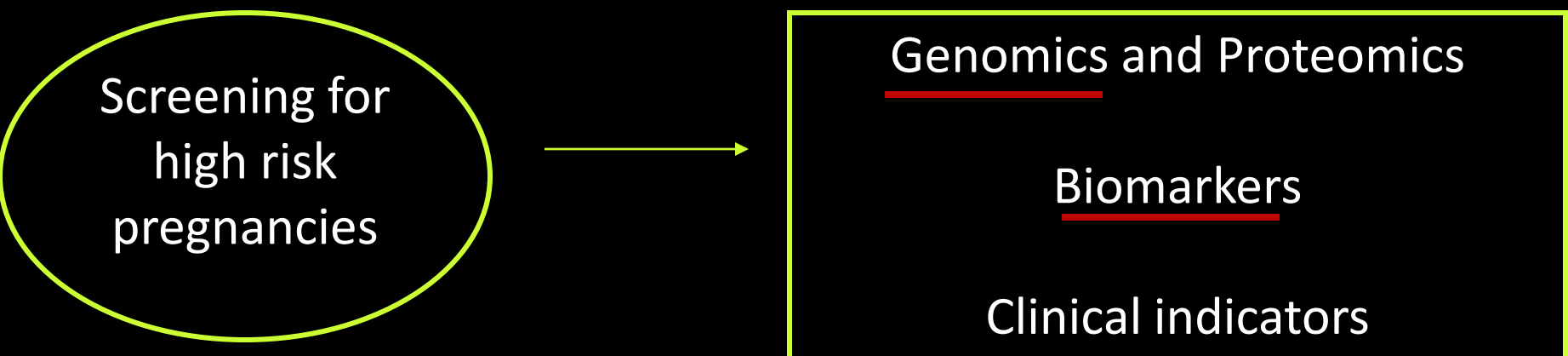


Government  
of  
Mexico



# PREBIC Goals

Screening for  
high risk  
pregnancies



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graph LR; A([Screening for high risk pregnancies]) --> B[Genomics and Proteomics<br/>Biomarkers<br/>Clinical indicators];
```

Genomics and Proteomics

Biomarkers

Clinical indicators

# Epidemiology Working Group

Co-Chairs: Siobhan Dolan and Karla Damus (Northeastern)

- What can we learn about preventable or modifiable risk factors for late preterm birth (34 – 36 6/7 weeks) that may vary by country?
- Variables to be collected:
  - Age at first birth
  - Gravidity and parity
  - Pregnancy history – prior preterm birth
  - Interpregnancy interval
  - Method of conception
  - Smoking
  - Obesity (BMI)
  - Gestational age at delivery
  - Indication for delivery
  - Cesarean section or vaginal delivery
  - Maternal age, race, ethnicity

# Epidemiology Working Group

- Data currently available from Asia, Africa
  - Global Survey on Maternal and Perinatal Health (Jim Zhang)
- Variables from US, Canada and Western Europe will be included
  - *US Data* – Michael Kramer, Josh Garn, Carol Hogue (Emory)
    - US Birth Certificate Data 2003
    - Pregnancy Risk Assessment Monitoring System
  - *Canadian Data* – Suzanne Tough, Amy Metcliffe, Tharsiya Nagulesapillai (Alberta)
    - Maternity Experiences Survey from Statistics Canada
    - Discharge Abstract Database from Canadian Institute for Health Information
  - *Euro Peristats* – Jennifer Zeitlin (Inserm, Paris)
    - Continuing to learn about available data

# Epidemiology Working Group

- Short Term Outcomes:

- Create population-based data globally on late PTB
- Establish base rate of late PTB and cesarean section for epidemiologic surveillance
- Assess incidence of late PTB from elective cesarean section
- Develop country-specific variation in preventable risk factors for late PTB

- Long Term Outcomes

- Reduce Preventable Preterm Births as part of the PREBIC collaborative (Yogesh Shah, Iowa)

## Contact Information:

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[jennifer.zeitlin@inserm.fr](mailto:jennifer.zeitlin@inserm.fr)

Thank you!