Cincinnati Children's

Perinatal Institute

march of dimes prematurity research center

Ohio Collaborative

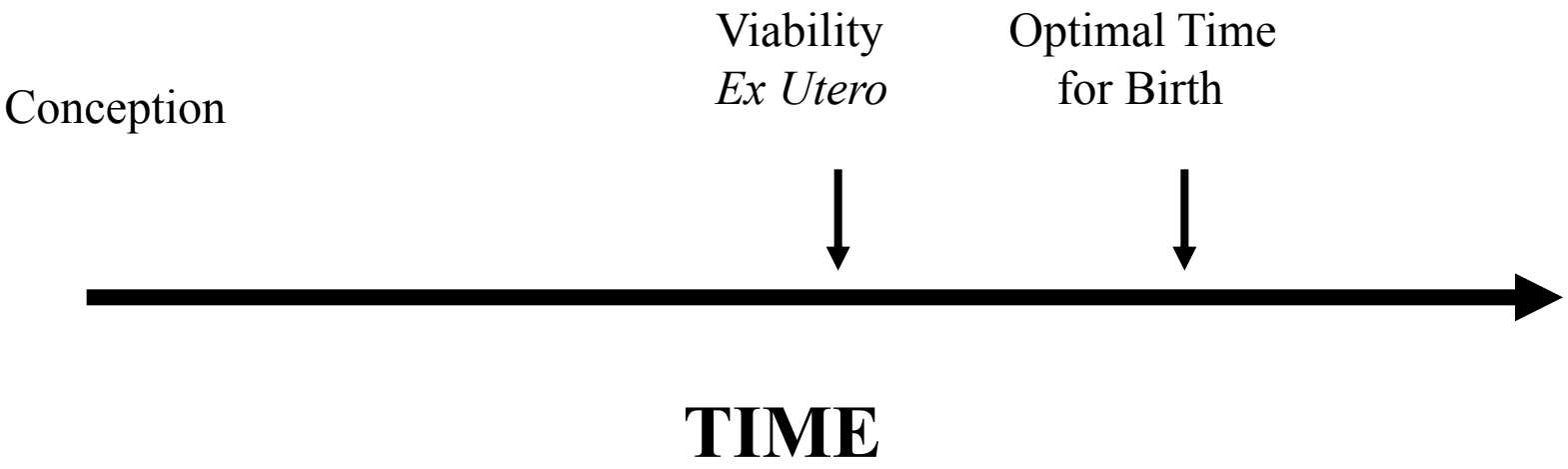
Louis J. Muglia, MD PhD, Coordinating Principal Investigator, Cincinnati Children's

Charles Lockwood, MD, Principal Investigator, Ohio State University Wexner Med Ctr

Sam Mesiano, PhD, Principal Investigator, Case Western Reserve University

Case Western Reserve University · University of Cincinnati · march of dimes · The Ohio State University · Cincinnati Children's change the outcome · MetroHealth · Nationwide Children's · University Hospitals MacDonald Women's Hospital · Rainbow Babies & Children's Hospital

What determines the timing of birth?



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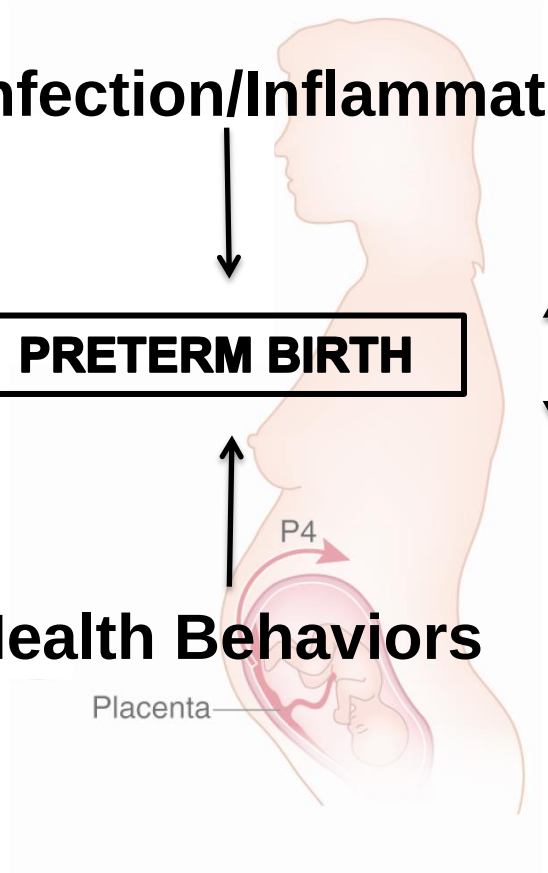
Many Factors Lead to Preterm Birth



Genetics

Infection/Inflammation

Stress

PRETERM BIRTH

Nutrition

Health Behaviors

Socioeconomic Influences

Cross Ohio Collaboration

Case Western Reserve University EST. 1826

University Hospitals Case Medical Center

MetroHealth

University of Cincinnati

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The Ohio State University Wexner Medical Center

Nationwide Children's When your child needs a hospital, everything matters.

Transdisciplinary and Trans-Institutional Collaboration

Primary Institutions

- Cincinnati Children's
- University of Cincinnati College of Medicine
- University of Cincinnati McMicken College of Arts and Sciences
- The Ohio State University
- Nationwide Children's Hospital
- Case Western Reserve University
- University Hospitals Case Medical Center
- MetroHealth

Collaborating Investigators

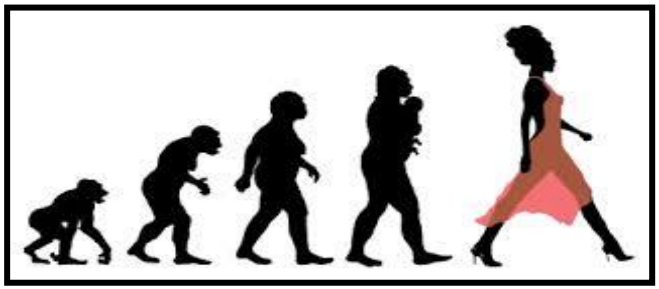
- Vanderbilt University
- University of Iowa
- Washington University in St. Louis
- Dartmouth

Disciplines

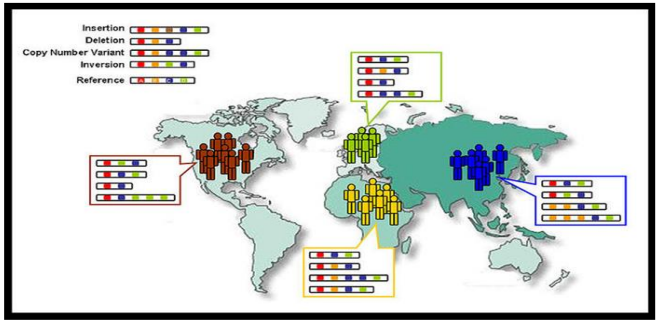
- Anthropology
- Biological Sciences/Evolutionary Biology
- Biomedical Informatics
- Biostatistics/Epidemiology
- Cell Biology
- Developmental Biology
- Geography
- Health Policy
- Human Genetics
- Immunobiology
- Infectious Diseases
- Neonatology
- Neurology
- Obstetrics & Gynecology
- Nursing
- Pediatrics
- Psychology
- Reproductive Sciences
- Rheumatology
- Sociology

Building Connections Across Centers and the Country

Thematic Areas of Discovery and Innovation

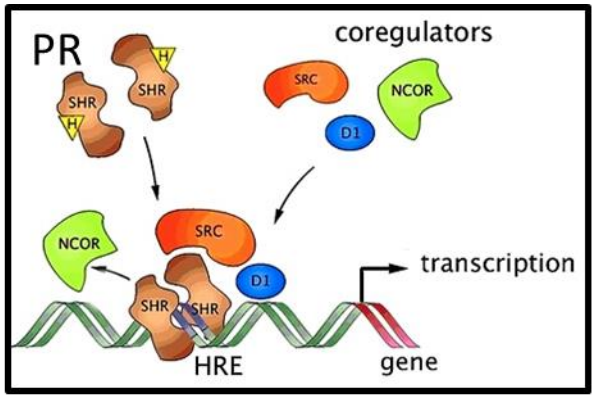


Theme 1: Evolutionary Synthesis of Human Pregnancy



Theme 2: Genetics of Unique Human Populations

Theme 3: Molecular Developmental Biology of Pregnancy



Theme 4: Progesterone Signaling in Pregnancy Maintenance and Preterm Birth

Theme 5: Sociobiology of Racial Disparities in Preterm Birth

Theme 1 – Evolutionary Synthesis of Human Pregnancy

- **Human pregnancy must accommodate specific adaptations**
  - Large head and relatively small birth canal
  - Bipedalism

- **Prediction: delivering the human fetus at a relatively earlier gestational age still mature enough for survival will be beneficial**
  - Humans will be relatively immature at birth compared to other primates
    - Dentition
    - Vision

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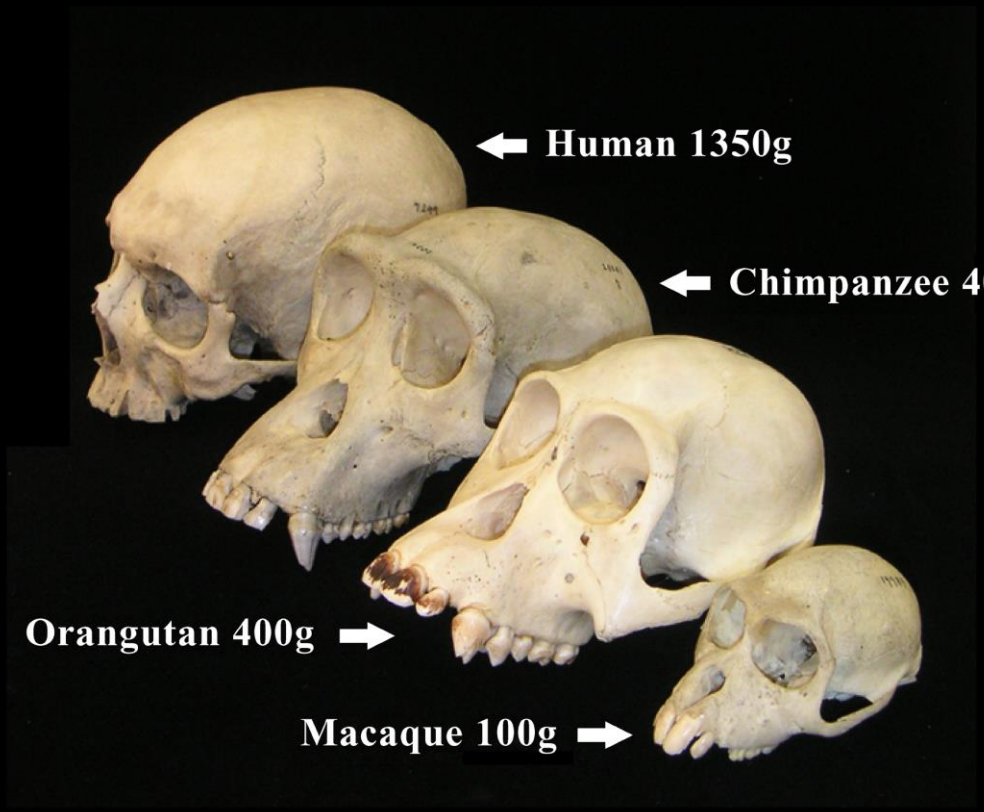
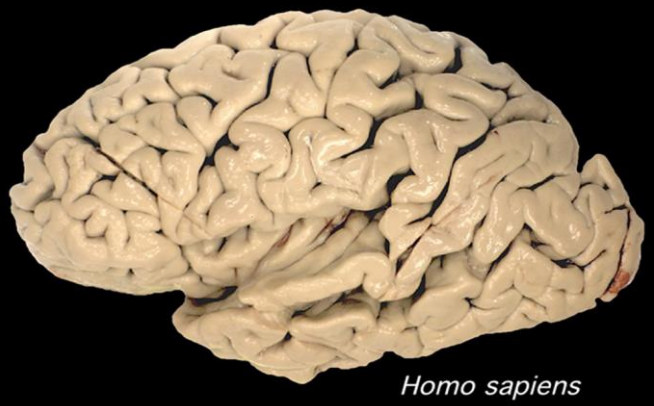
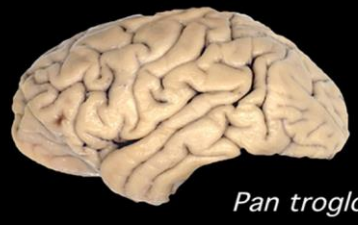
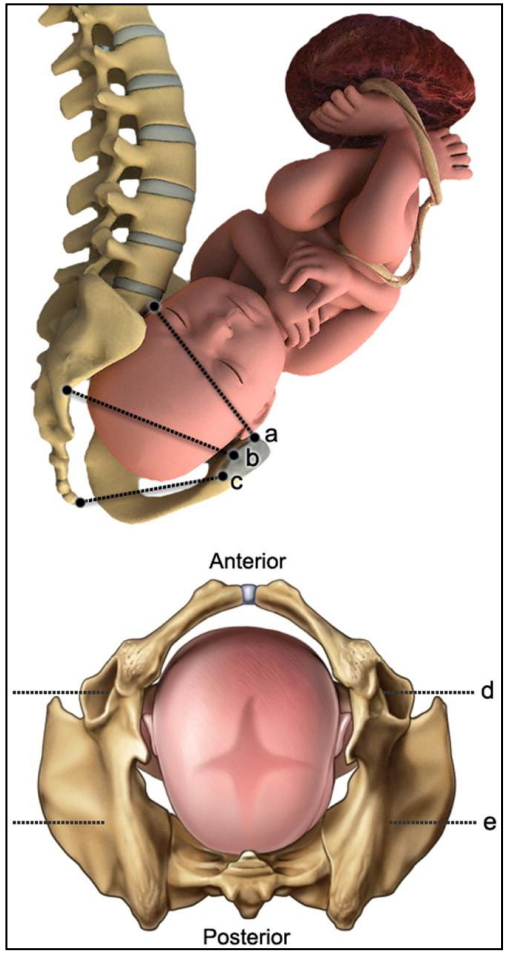
Theme 1 - Becoming Human and Birth Timing



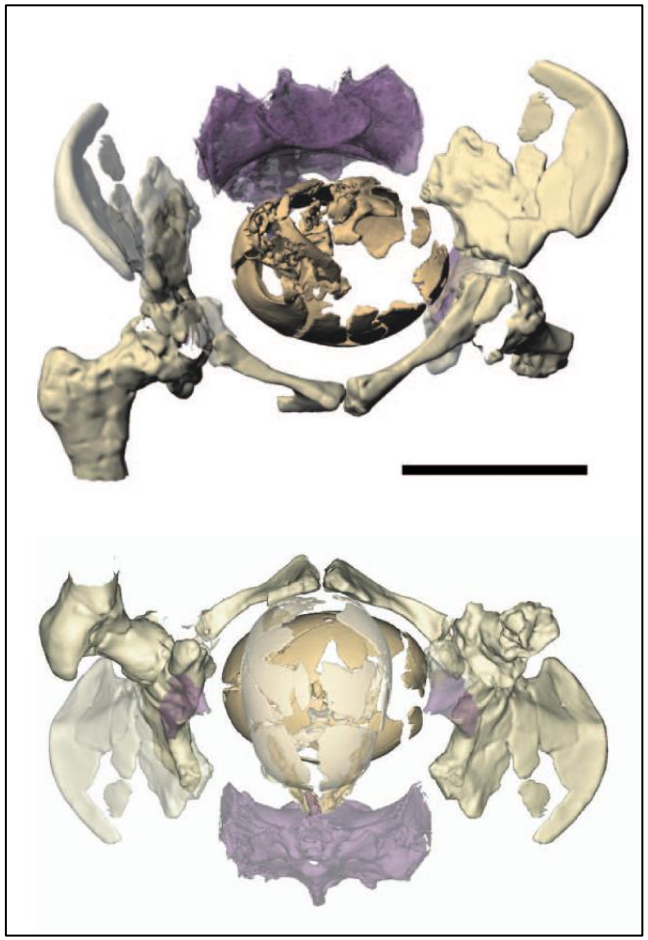




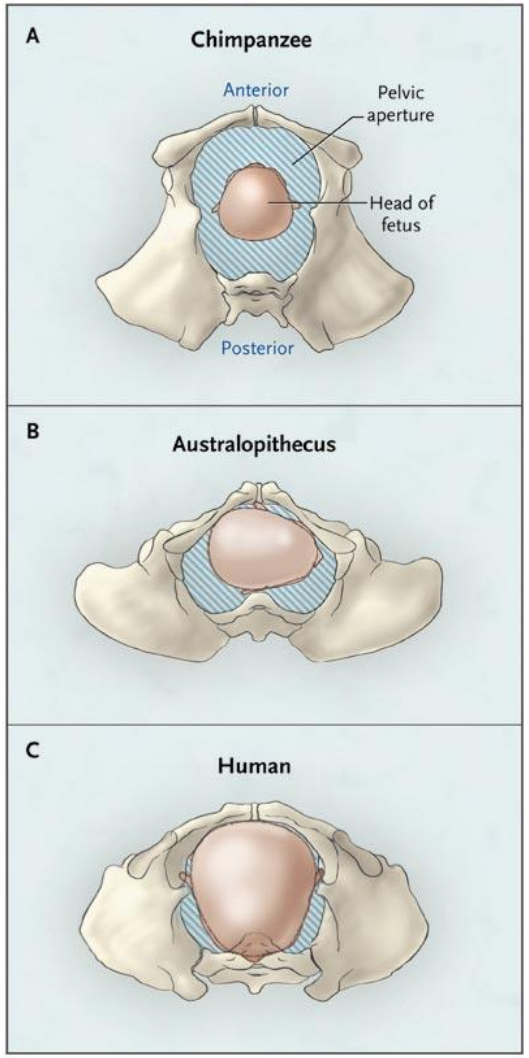
Human Birth - What makes us different?



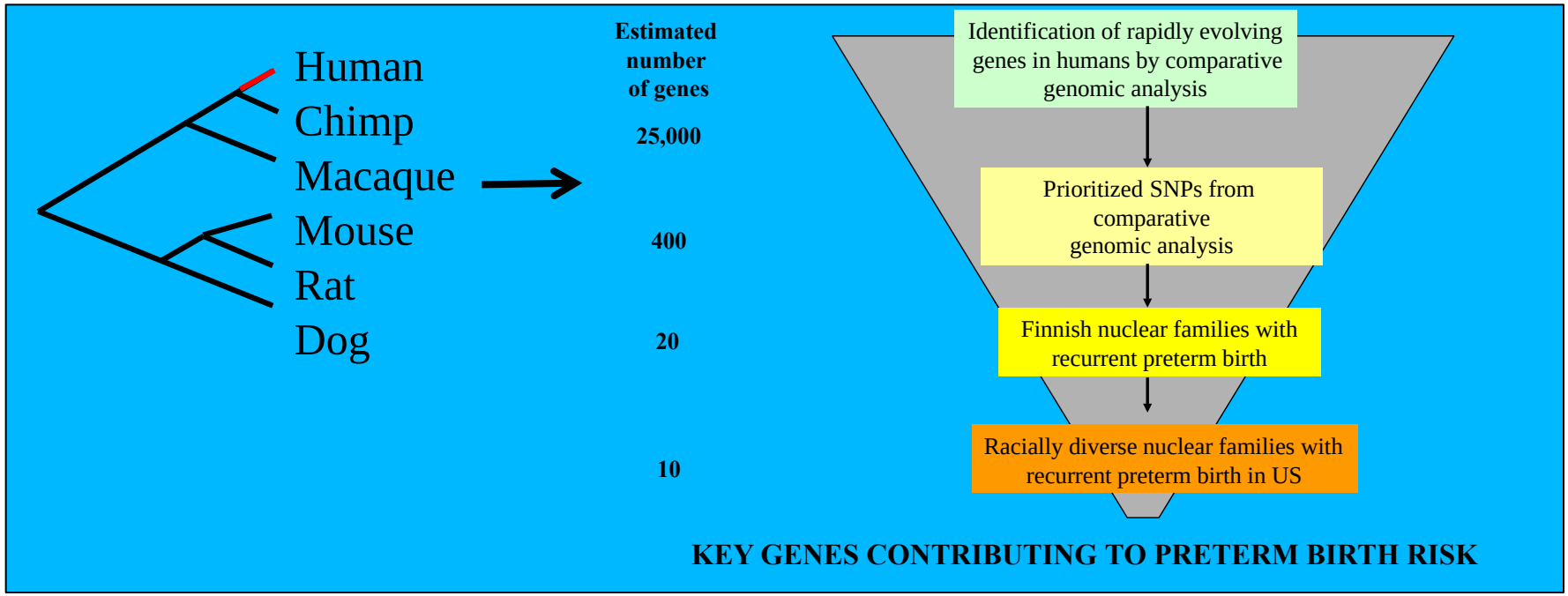
Modern Humans



Neanderthals



Comparative Genomics
Identifying key genes contributing to preterm birth

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Chimp                   TTAGAGGTAGAGATGGTCTAGTAAAGATGTAGTA-GTAATGTTTTATCCATTTAGCATGTGTTTATTTTTTCATATGTACTC
Macaque                 TTAGAG--------------GTAAAGATGTAGTA-GCAATGTTTAATCCATTTAACATGTGTTTATTTTT-CATATGTACTA
Mouse                   TTAGAGGTAGAAATGGTCTAGTAAAG-TGTAATG-------TTTTATTCATTTAGCATGTGTTTA-TTTTCCTTATGTTCTC
Rat                     TTAGAGGTAGAAATGGTCTAGTAAAGATGTAATG--------TTTATCCATTTAGCATGTGTTTATTTTTCCTTATGTACTC
Dog                     TTAGAGGTATAGATGGTTTAGTAAAGATGTAGTTTGTAATGTTTTATCCATTTAGCATGTGTTTATTTTTCCTTATGTACTC
Cow                     TTAGAGGTAGAGATGGTCTAGCAAAGATGTAGTTTGTAATGTTTTATCCATTTAGCATGTGTTTATTTTTTGTTATGTACTA
                        ******              * * ** ***             * ** * **** ****** *** ****   ***** **
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ARTEMIS – An Evolutionary Encyclopedia of Preterm Birth

Existing knowledge and thematic contributions

- Genetic
- Functional Data
- Phenotype
- Environment

Analysis, research and prediction

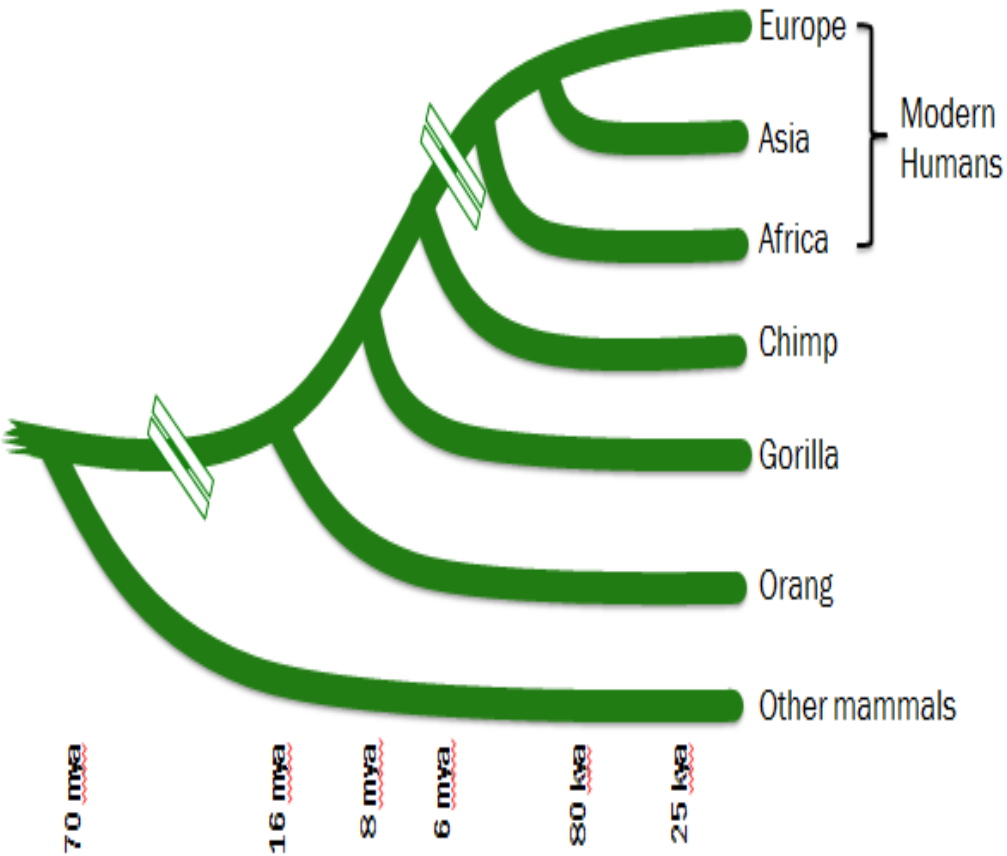
- Evolutionary History
- Pathways & Function
- Phenotype Correlations
- Environment Effects

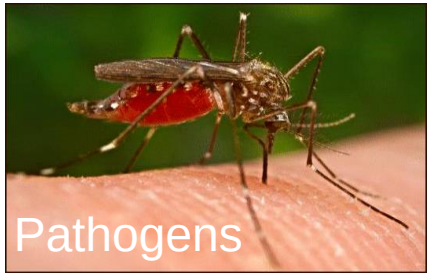
ARTEMIS

The Evolutionary Encyclopedia of Pre-term Birth

march of dimes

Theme 2: The Genetics of Unique Human Populations





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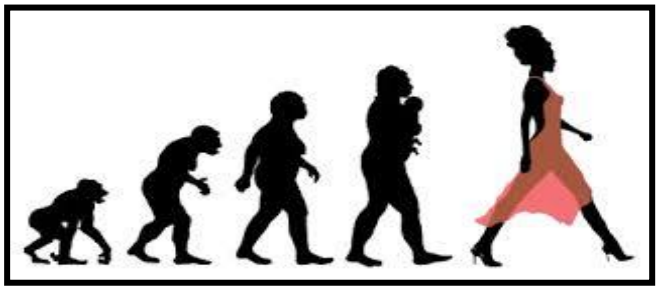
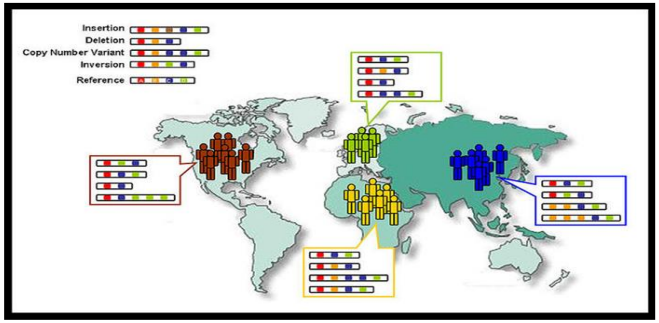
Hypothesis

- Genetic variations that differ between different populations will be highly enriched for genes that affect the normal timing for birth and risk of preterm birth.

Thematic Areas of Discovery and Innovation

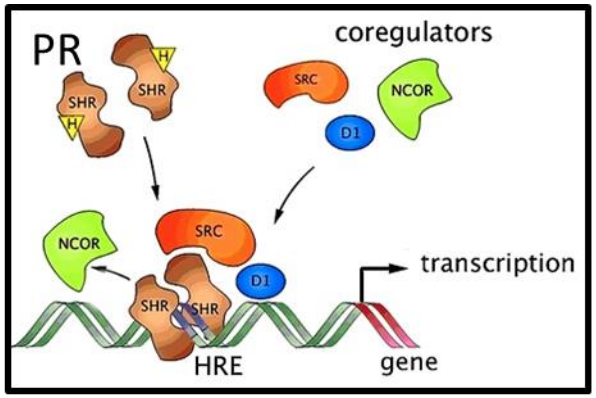


Theme 1: Evolutionary Synthesis of Human Pregnancy



Theme 2: Genetics of Unique Human Populations

Theme 3: Molecular Developmental Biology of Pregnancy



Theme 4: Progesterone Signaling in Pregnancy Maintenance and Preterm Birth

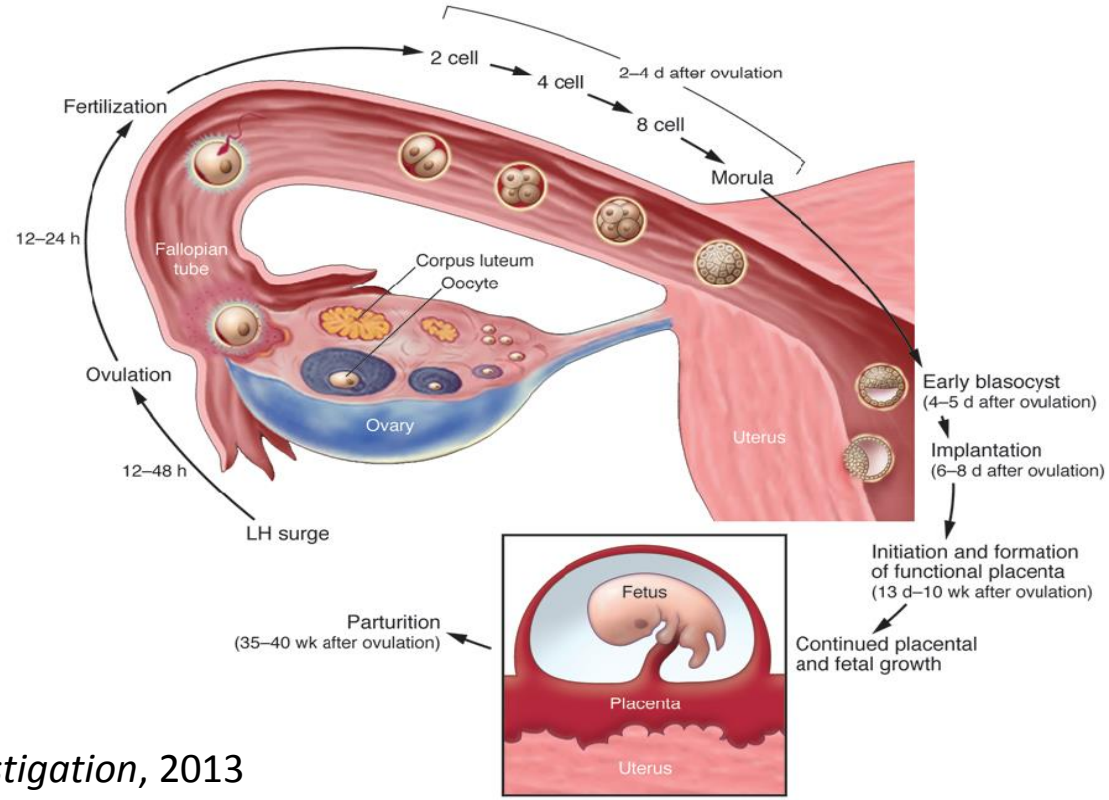
Theme 5: Sociobiology of Racial Disparities in Preterm Birth

Research article

Combinatory approaches prevent preterm birth profoundly exacerbated by gene-environment interactions

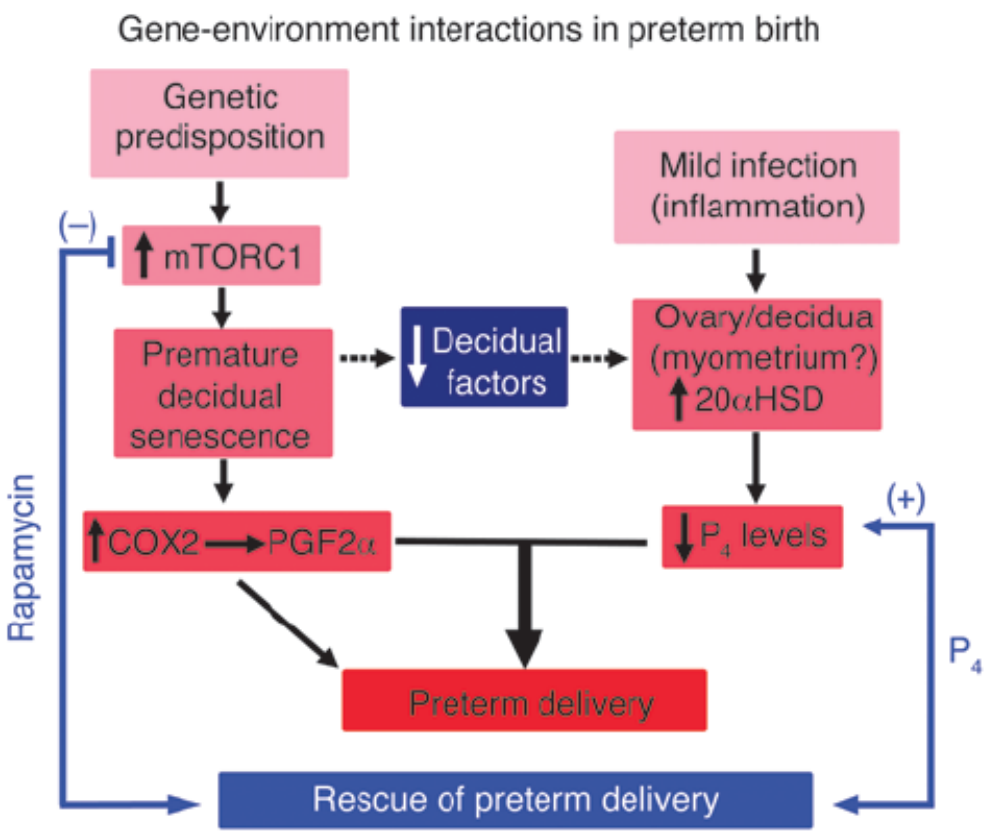
Jeeyeon Cha,[1] Amanda Bartos,[1] Mahiro Egashira,[2] Hirofumi Haraguchi,[2] Tomoko Saito-Fujita,[2] Emma Leishman,[3] Heather Bradshaw,[3] Sudhansu K. Dey,[1] and Yasushi Hirota[1,2,4]

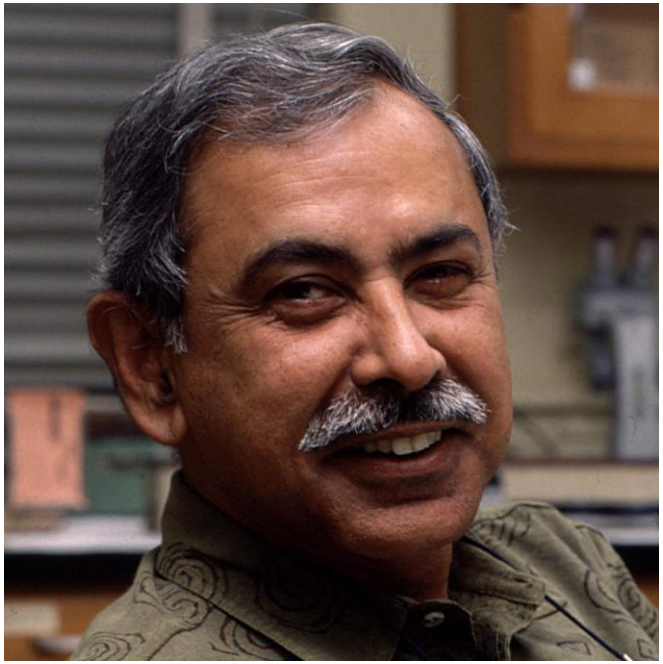
[1]Division of Reproductive Sciences, Perinatal Institute, Cincinnati Children's Research Foundation, Cincinnati, Ohio, USA. [2]Department of Obstetrics and Gynecology, Graduate School of Medicine, University of Tokyo, Tokyo, Japan. [3]Department of Psychological and Brain Sciences, Kinsey Institute for Research in Sex, Gender, and Reproduction, Indiana University, Bloomington, Indiana, USA. [4]Precursory Research for Embryonic Science and Technology (PRESTO), Japan Science and Technology Agency, Saitama, Japan.



Journal of Clinical Investigation, 2013

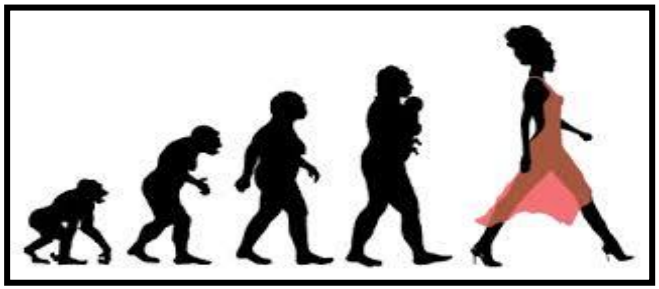
Identification of Progesterone and Rapamycin as Potential Prevention Strategies





SK Dey, PhD
Cincinnati Children's, Univ. Cincinnati
Theme 3 Leader

Thematic Areas of Discovery and Innovation



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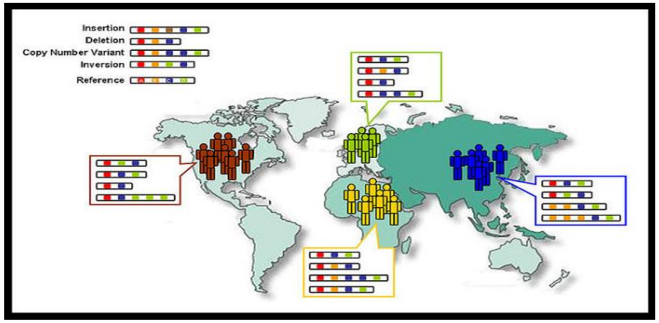

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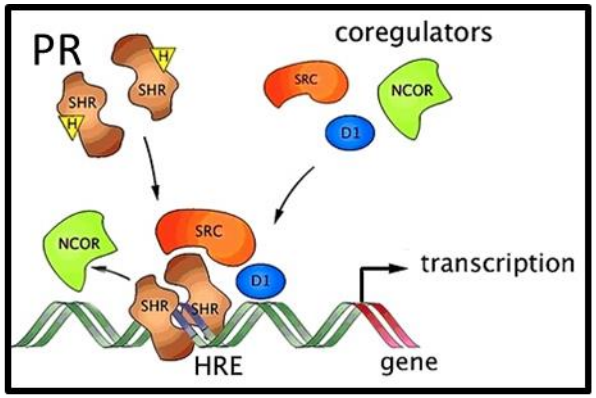

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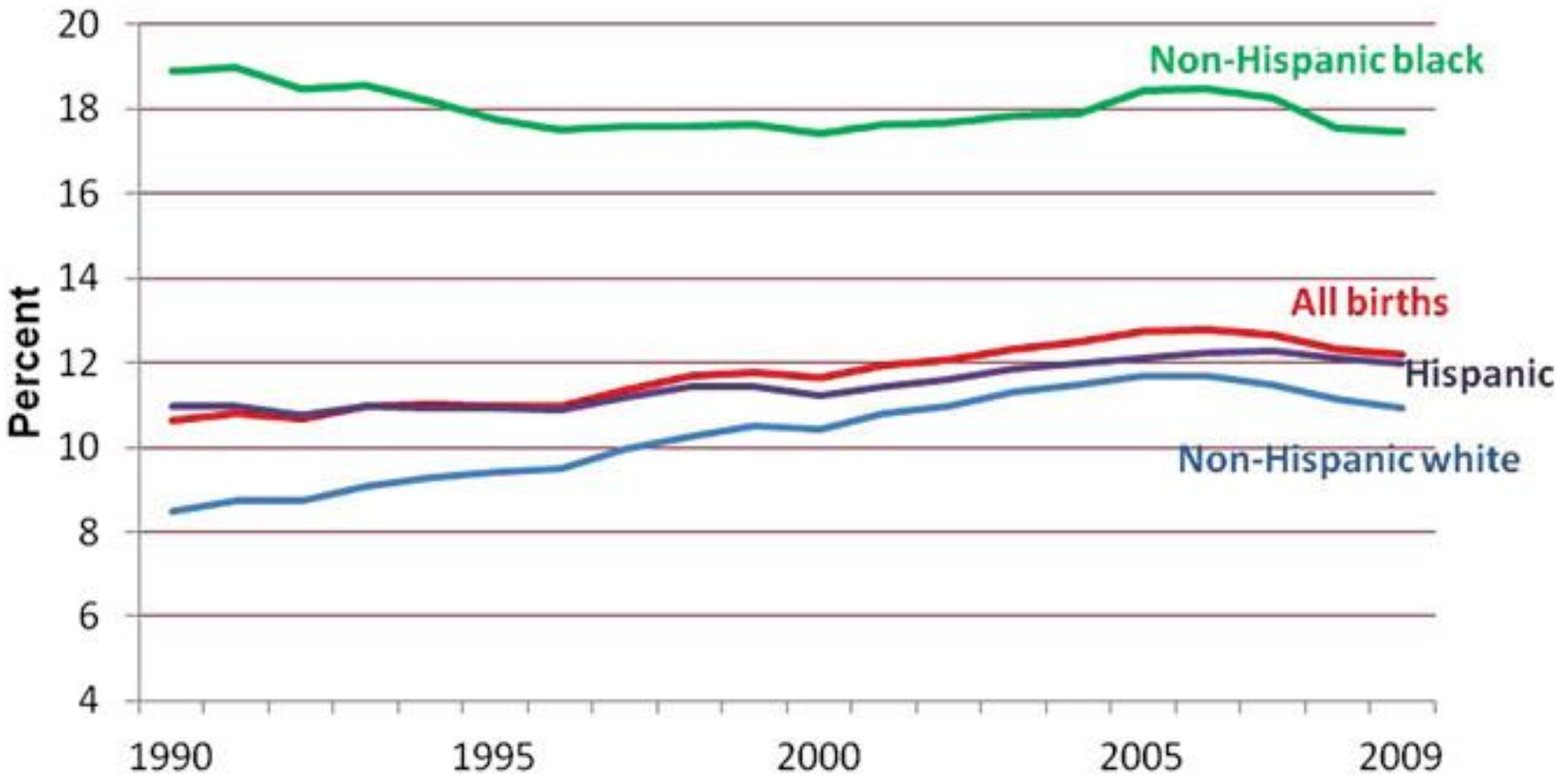
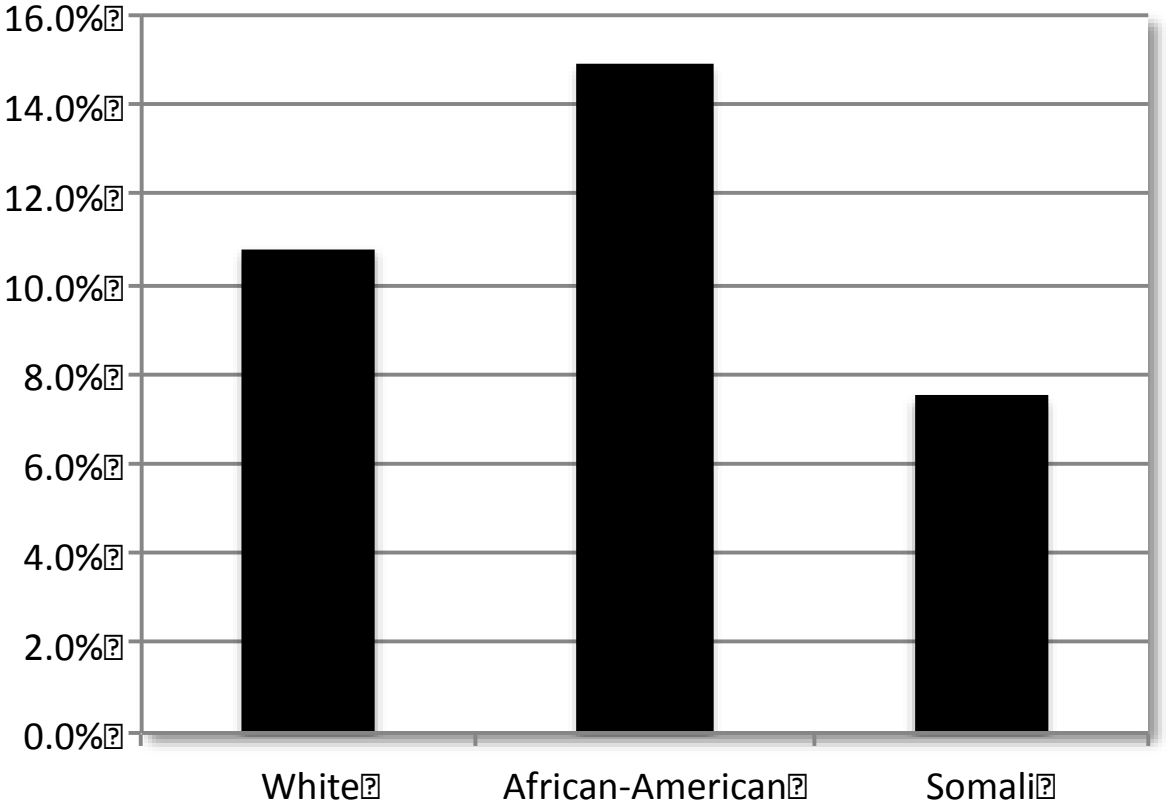


African Americans have about twice the rate of preterm birth of other racial and ethnic groups even after adjusting for other risk factors.

Theme 5 – Sociobiology of Racial Disparities in Preterm Birth

The Paradox of Somali Pregnancy



Irina Buhimschi, MD
Nationwide Children's, Ohio State Univ.
Theme 5 Leader

Theme 5 – Sociobiology of Racial Disparities in Preterm Birth

The Paradox of Somali Pregnancy

Learning from Unique Populations
The Paradox of Somali Pregnancy

- Protective social environment?
- Distinct health behaviors?
- Nutritional differences?
- Differences in overall genetic make-up?

What do we see as the time line for real change in outcomes and prevention of prematurity?

- Important new insights from laboratory and population studies over the next 1-2 years
- Preclinical testing to determine if safe and effective strategies have emerged over next 2-4 years
- Implementation of measures to reduce preterm birth over next 3-5 years

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