Epigenetic Processes Over Time Among Children With Early Adversity: Implications for Home Visiting Research

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"They were identical twins until Jim joined the army and John joined the Peace Corps."
Kids Markers Study
NIMH R01MH083704

- Impoverished, mixed race families, children aged 3-5
- Families studied at home
- Maltreated, N=134
  Episode of moderate-severe abuse and/or neglect in last 6 months
- Non-maltreated, N=126
  Recruited from low income clinic and childcare centers, no RI child protective service record of maltreatment.

- Interviews and Questionnaires
  - Psychiatric symptoms and diagnoses
  - Social support, parenting, environmental enrichment/poverty
- Additional Adverse Exposures:
  - Parental loss, parental arrest
  - Food insecurity, clothing, paying bills
  - Moves, homelessness, violence
- Cortisol and inflammatory proteins
  - During normal daily routine
  - During challenging/stressful play tasks
- Saliva DNA
  - Candidate genes and exome array
  - Gene methylation (NR3C1, FKBP5, 5HTR2A)
  - Telomere length
  - Mitochondrial DNA
- 6 Month Follow Up
DNA Methylation: NR3C1
DNA Methylation: \textit{NR3C1}
DNA Methylation: *NR3C1*

Parade et al. 2016, *Child Development*
DNA Methylation: NR3C1

Parade et al. 2016, Child Development
DNA Methylation: *NR3C1*

Parade et al. 2016, *Child Development*
NR3C1 Methylation: 340 Healthy Adults

Mean CpG 1-13% Methylation

Disorder - Adversity - N=96
Disorder - Adversity + N=60
Disorder + Adversity - N=51
Disorder + Adversity + N=133

Tyrka, Parade et al. 2016, Translational Psychiatry
Longitudinal Change NR3C1 Methylation

Parent, Parade et al. 2017, Development and Psychopathology
DNA Methylation: $FKBP5$
DNA Methylation: \textit{FKBP5}

Tyrka et al. 2015, \textit{Development and Psychopathology}
How do we promote resilience???
DNA Methylation: FKB5

Parade et al. 2017, Development and Psychopathology

% Mean Methylation

Baseline Follow-Up

No Services (n = 66)
1 Service (n = 48)
2+ Services (n = 117)
DNA Methylation: *FKBP5*

![Graph showing DNA methylation percentages for baseline and follow-up for different service groups.](image)

- **No Services (n = 66)**
- **1 Service (n = 48)**
- **2+ Services (n = 117)**

Parade et al. 2017, *Development and Psychopathology*
DNA Methylation: *FKBP5*

Parade et al. 2017, *Development and Psychopathology*
Utilization of Epigenetics Research to Support Interventions and Policy

Are there sensitive periods for epigenetic processes?
• Inform the developmental timing of preventive interventions

How quickly does methylation occur in response to stress?
• Identification of appropriate time to provide services following acute stressor or life event

How does methylation change in response to intervention?
• Methylation as a biomarker of treatment efficacy

Methylation as a marker of toxic stress
• Demonstrate effects of stress on biology and the brain to compliment behavioral health outcomes
Maternal ACES and Home Visiting Study

• **Impoverished families** who have been referred to RI Home Visiting

• **Prenatal period through 1 year postpartum**

• **Maternal reports** of childhood and perinatal stress

• **Observations** of mother-infant interaction and infant behavior

• **Interviews** to assess service utilization

• **Home visiting record review**

• **Saliva DNA** from mothers and infants
  – Gene methylation
  – Telomere length
  – Mitochondrial DNA

• **Pediatrician Reports** of Infant Health Outcomes

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Community Partners

DCYF
Rhode Island Department of Children, Youth & Families

HEAD START

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Women, Infants, & Children

Hasbro Children’s Hospital
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