

Breast Cancer and Social Interactions: Identifying Multiple Environments that Regulate Gene Expression

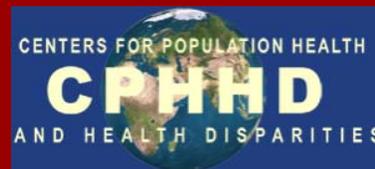


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Supported by P50-ES012382





Cancer Risk Clinic

**Institute for
Mind and Biology**



University of Ibadan

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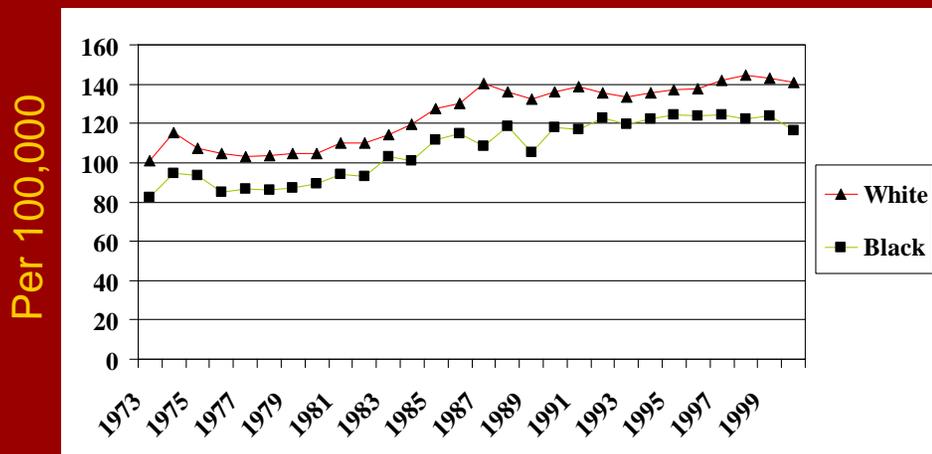
School of Soc. Serv. Admin.
Department of Psychology
Department of Medicine
Department of Medicine
Department of Pathology

CIHDR Central Research Question

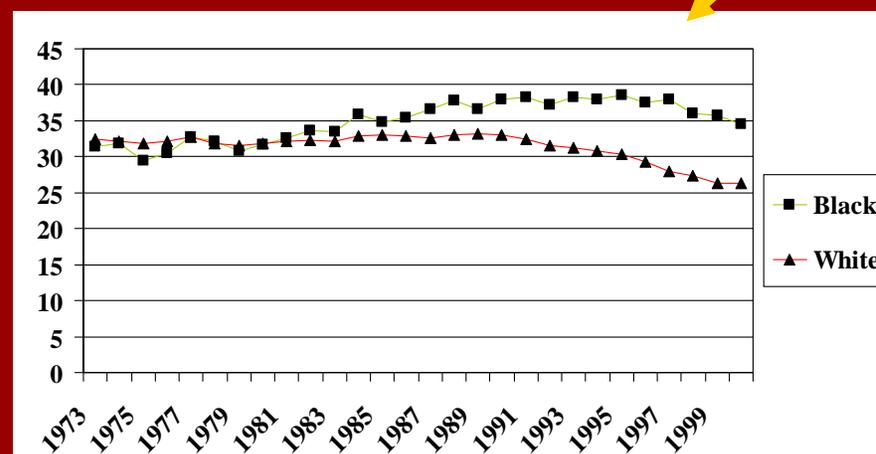
How do factors in women's social environments contribute to the African American and white disparity in breast cancer mortality in the U.S.?

Black and White Age-Adjusted Breast Cancer Statistics, 1975-2000

Incidence



Mortality



SEER Cancer Statistics Review, 1975-2000

Mutually Informative Multi-Level and Multi-Modal Approach

Projects 1 and 4

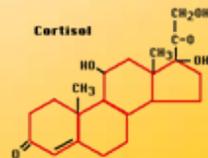
McClintock
Conzen



genes



hormones



psychological
state

behavior
patterns

Projects 2 and 3

Olopade
Gehlert



social
circum-
stances

(social
isolation,
social
support)

housing

environ-
mental
exposure

community/
neighbor-
hood

(crime,
collective
efficacy,
social
ecology)

Total Tumor Burden: 17 Months

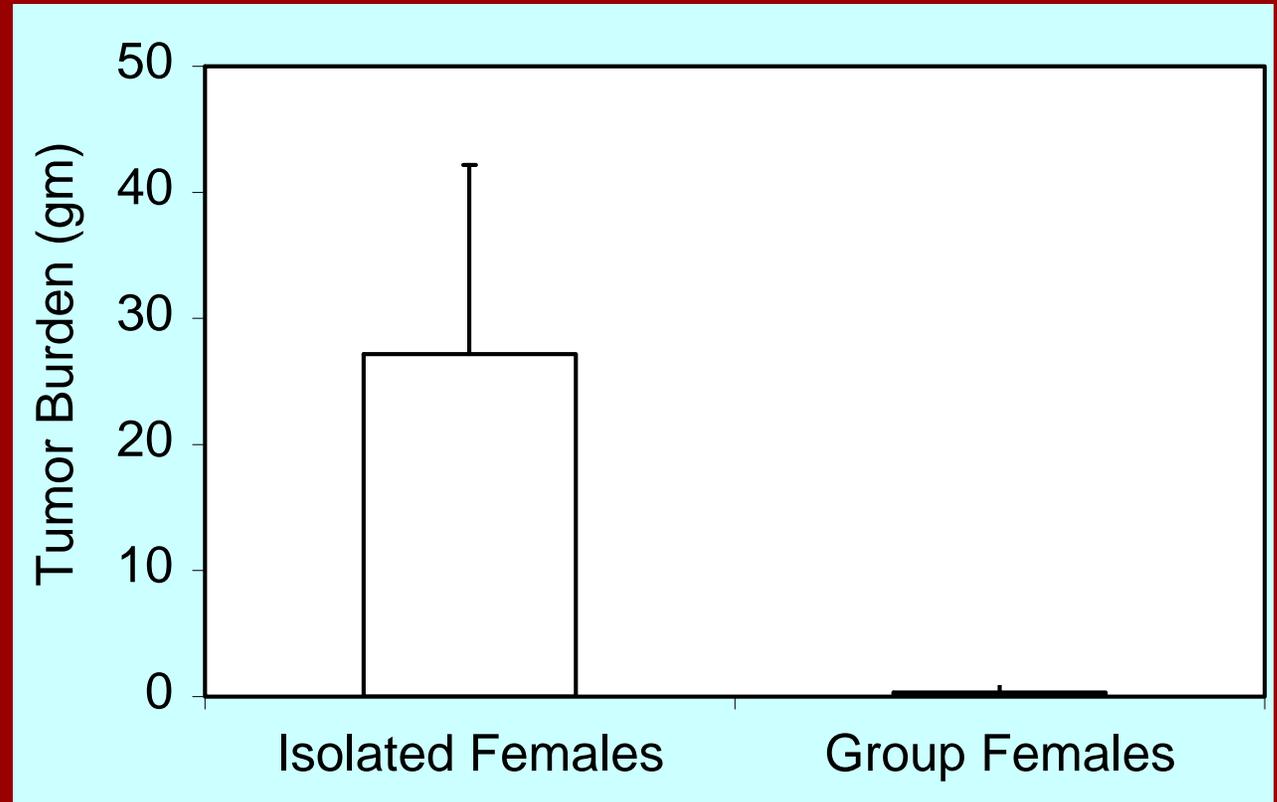


Grouped



Isolated

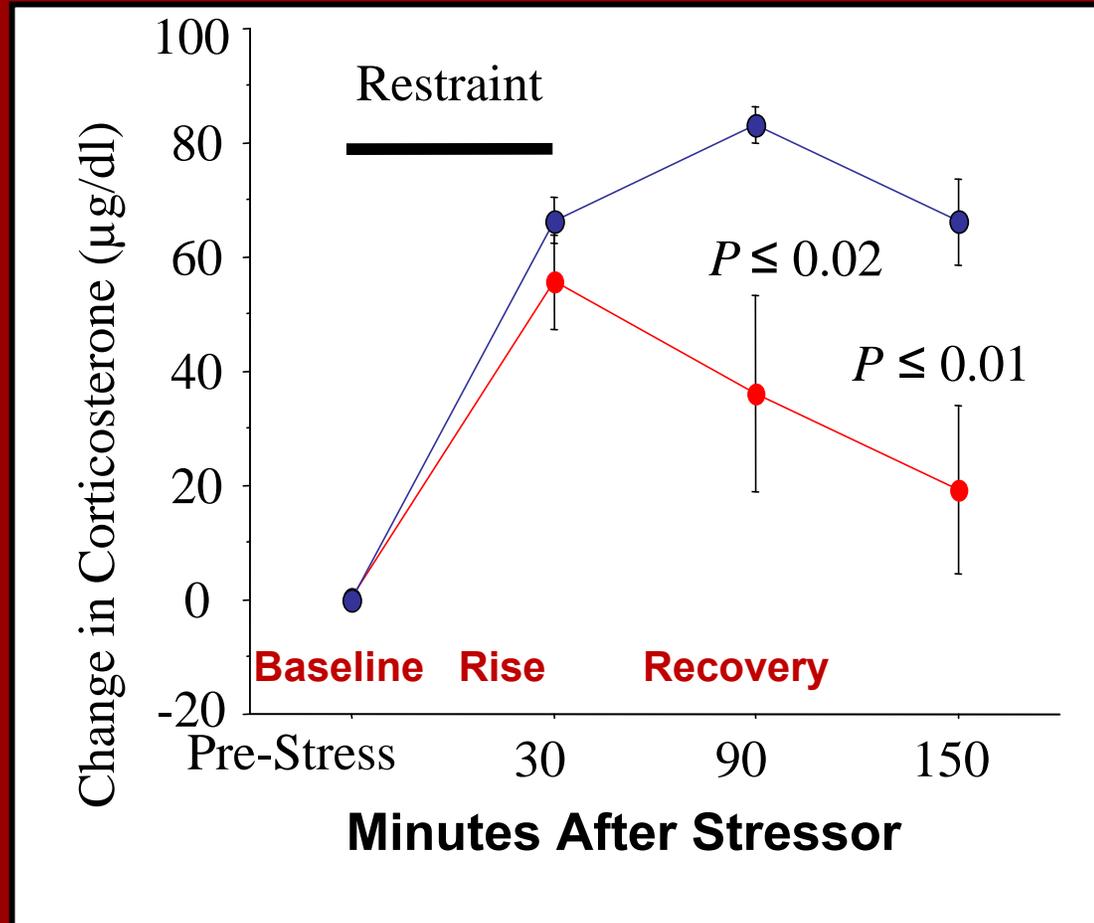
Litter mates at 26 months



$p \leq 0.0001$

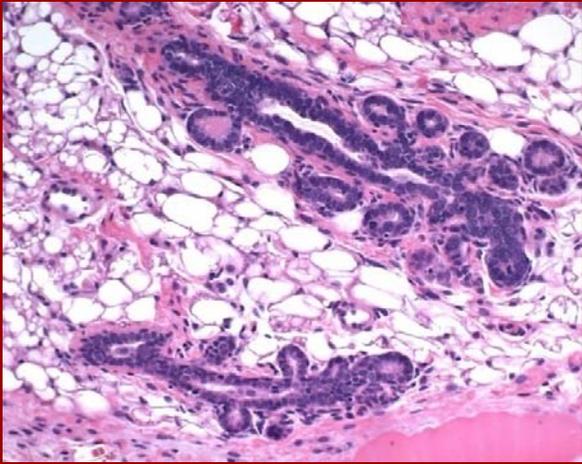
Corticosterone Dynamics at 15 Months

Endocrine Stress Response at Age 15 Months

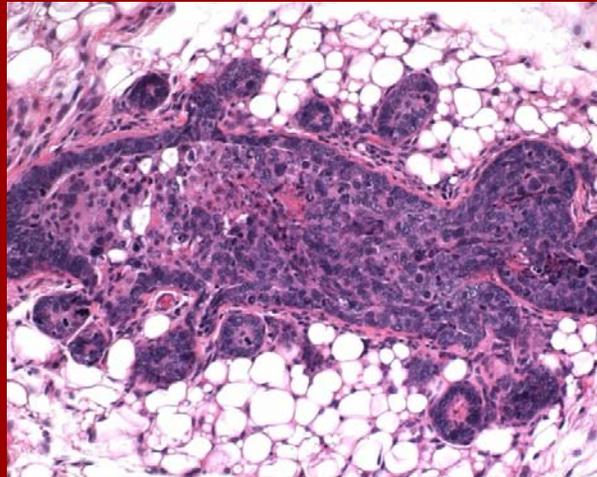


● Group ● Isolated

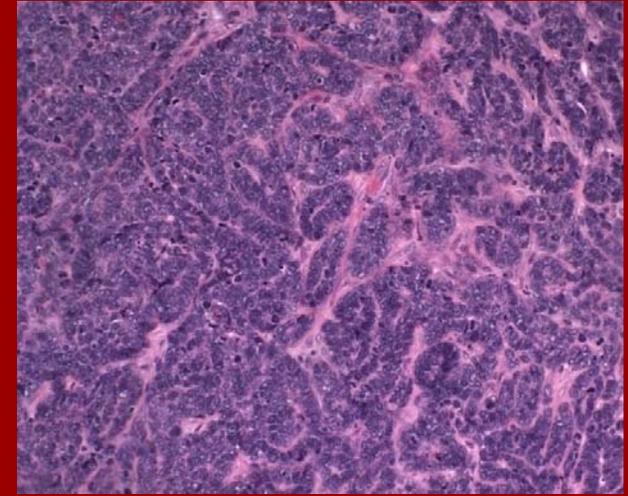
GR Expression in Normal, CIS, and Invasive Carcinoma (SV40 mice)



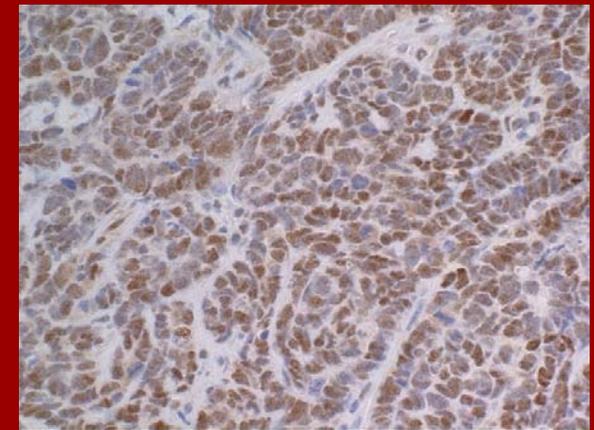
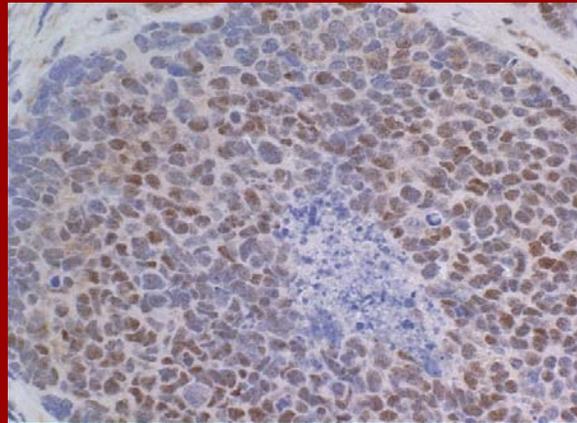
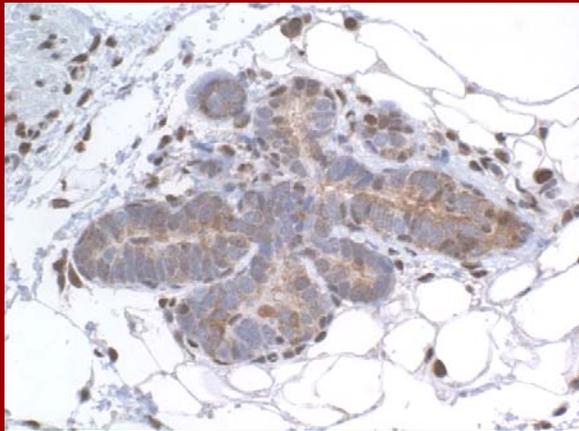
normal



in situ



invasive



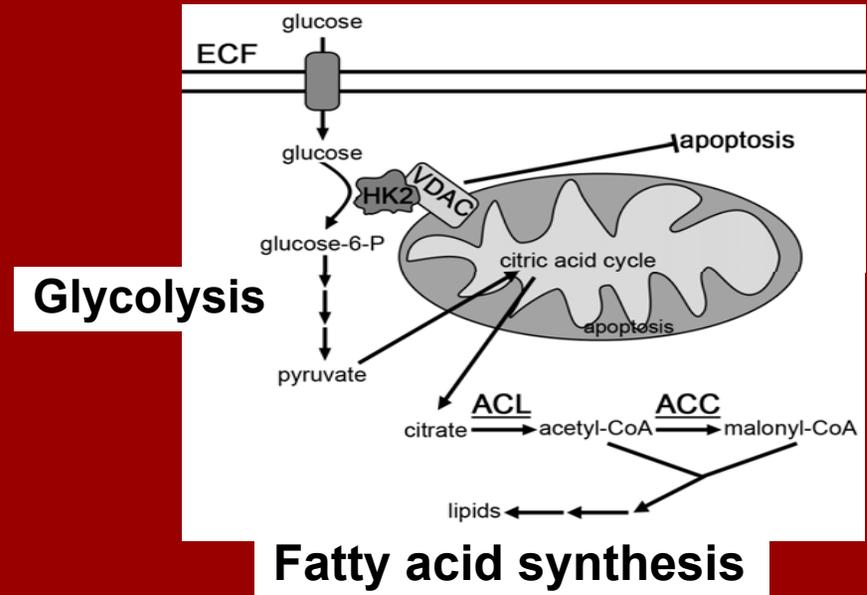
In this model of breast cancer, as tumors become more invasive, ER and PR ↓

Metabolic Genes are Upregulated in Isolated versus Group Housed Premalignant Mammary Glands (MG)

Isolation → upregulated MG fatty acid synthesis & glycolytic pathway gene expression, both of which can contribute to breast cancer growth

Isolated mice also developed a heightened corticosterone stress response compared to group-housed mice

Suggests potential interventions, molecular biomarkers and/or targets (e.g., fatty acid synthesis) for prevention

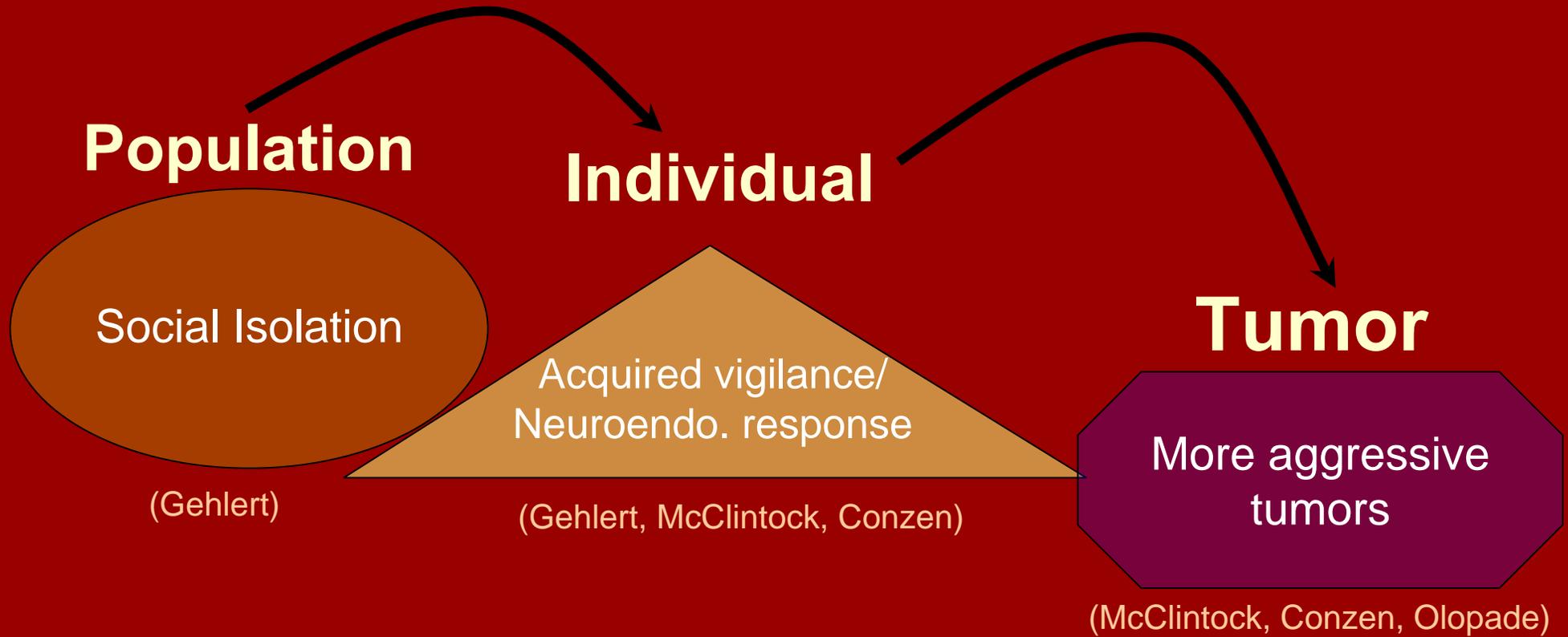


Williams et al., *Cancer Prevention Research*, in press

Lessons Learned From Animal Work

Endocrine stress response should be considered in understanding the biology of health disparities (hormone response is a conduit from social environmental stressors to gene expression)

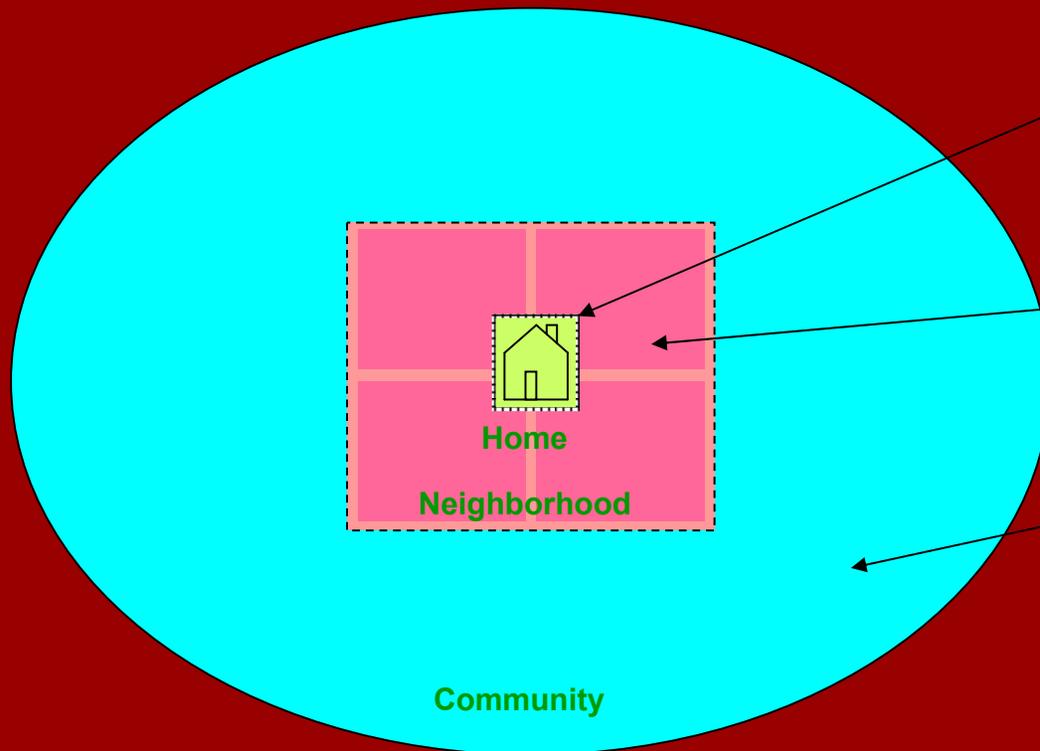
How Does Social Environment Affect Tumor Growth?



← Transdisciplinary Research →

Multi-Level Sources of Psychosocial and Hormonal Data from the Same Newly Diagnosed Women

Two-day visits every 6 months for 1.5 years (10 visits/woman with >18 hours of face-to-face contact).



Home: (interview in home) psychosocial functioning, social network, health behaviors, perceived discrimination, daily (4X) salivary cortisol.

Neighborhood: (four block radius around home; Built Environment Team) opportunities for social interaction (vacant lots, traffic in neighborhood, vacant buildings).

Community: (geocoded data) violent crime, collective efficacy, dilapidation of housing, SES, trust, health indicators.

Olopade lab collects and analyses tumors from same women

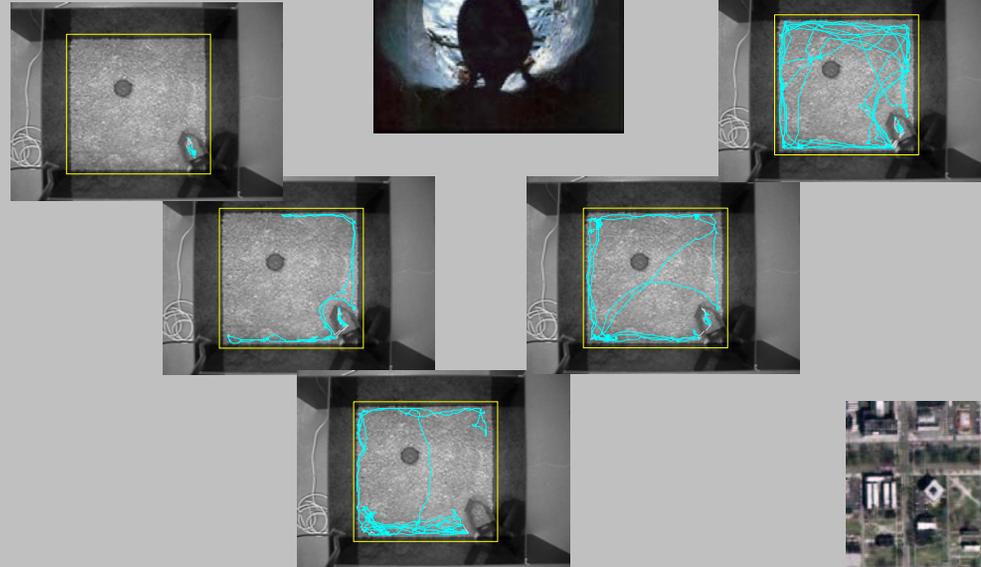
Acquired Vigilance in Environment



Isolated



Grouped



Neighborhood's Built Environment



Diurnal Salivary Cortisol Patterns Based on Cluster Analysis

Legend:
Blue = Flat
Green = Endocrine burnout

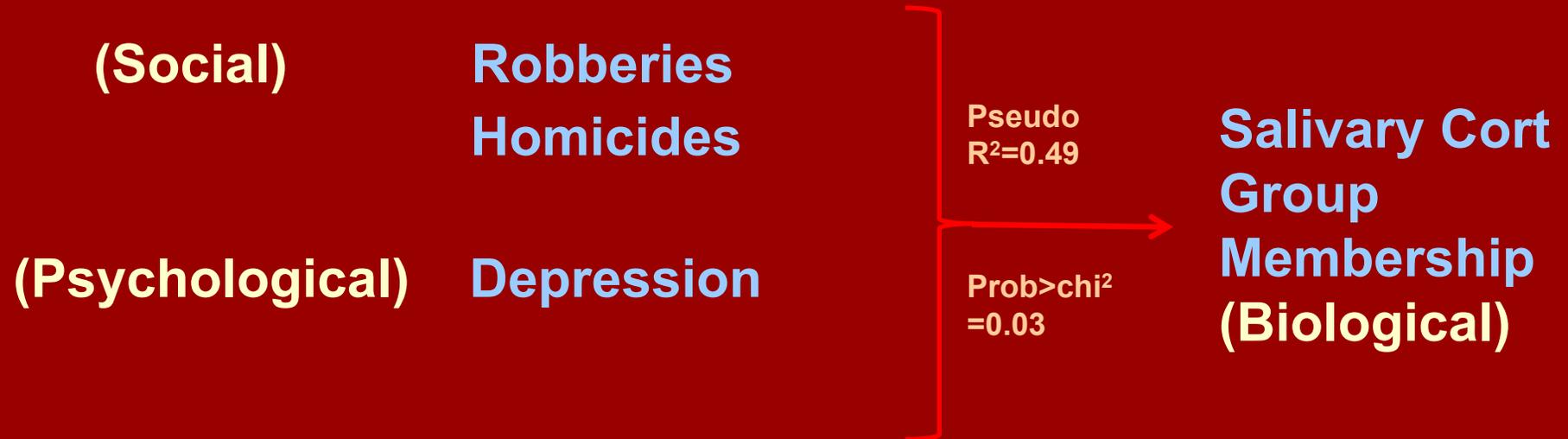


Measurement Time

Lessons Learned

Cortisol rhythms are affected by neighborhood factors & psychological responses. Within-group variability in cortisol response must be considered in designing interventions.

Logistic Regression Predicting Diurnal Salivary Cortisol Group



Lessons Learned from Combined Animal and Human Work

Biological factors with clinical implications can be predicted from neighborhood factors. Targeting neighborhood factors with interventions conserves resources.

Center for Interdisciplinary Health Disparities Research



Degraded
Infrastructure

Crime

Unsafe
Housing

**African-American
women with mixed-SES
(Chicago)**

Sexual Assault

+
 $p = 0.00$



2-factor psychosocial suite:
1. depression and loneliness
2. anomie

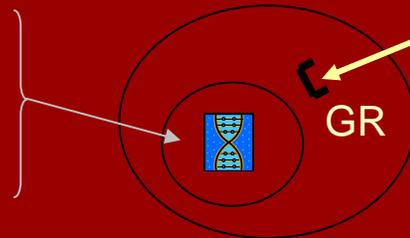
+
 $p = 0.01$

Inflammatory
Process

Cortisol
Dynamics

Nighttime Rise in
Cortisol

? Alteration of Metabolic
& Inflammatory Genes



GR Glucocorticoid Receptors

Strategically Selecting Targets of Intervention

