# *Biological Mechanisms of Socially Determined Pain - Implications for Pain Management*

Edwin N. Aroke, PhD, CRNA
Associate Professor
Assistant Dean for Research and Scholarship (Interim)

# Disclosure Statement

- I have no financial relationships with any commercial interest related to the content of this activity.
- I will not discuss off-label use during my presentation.

# Disclosure Statement

National Institute of Arthritis and Musculoskeletal and Skin Diseases

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Center for Addiction and Pain Prevention and Intervention

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MINORITY HEALTH & HEALTH DISPARITIES RESEARCH CENTER

The University of Alabama at Birmingham

National Institute on Minority Health and Health Disparities

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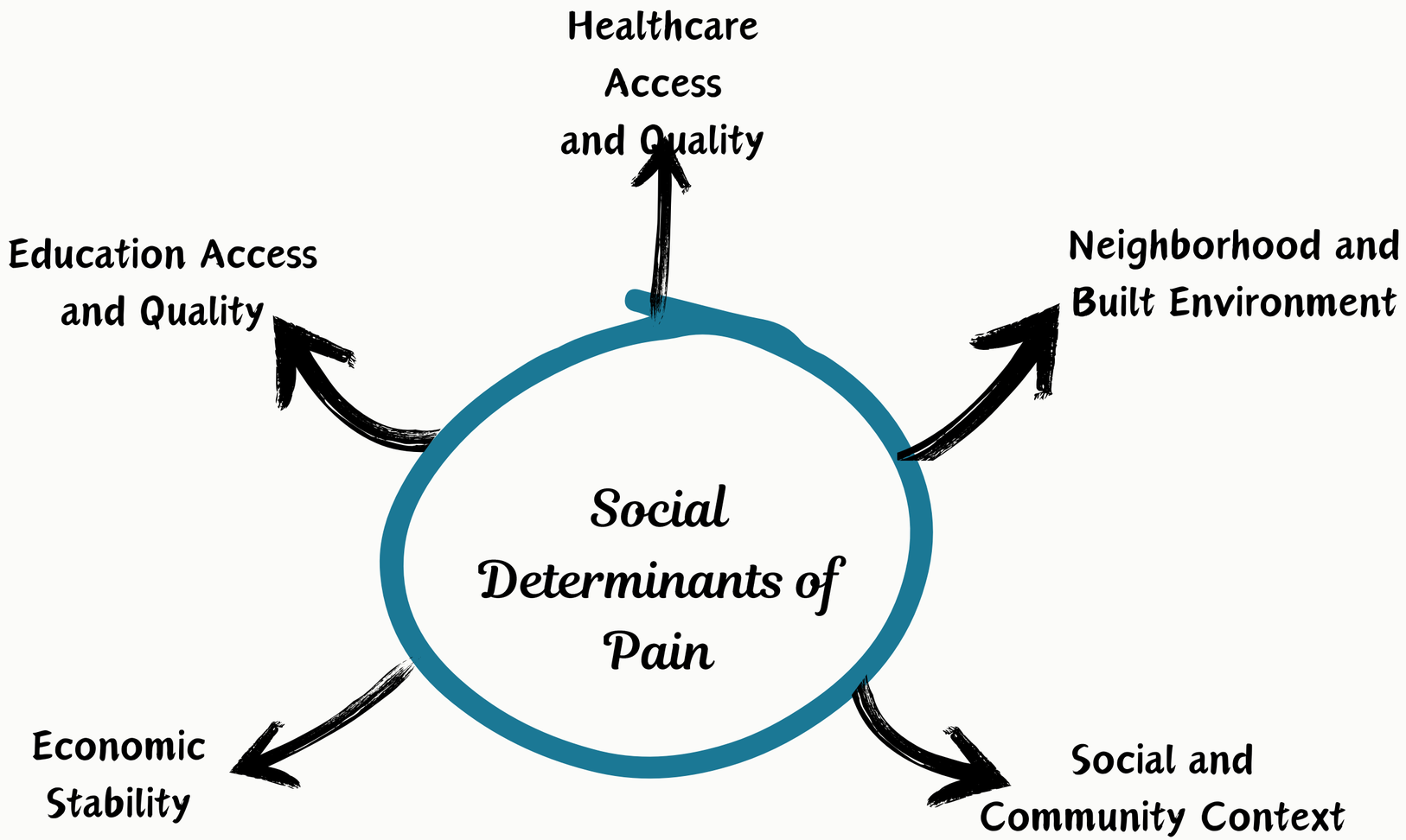
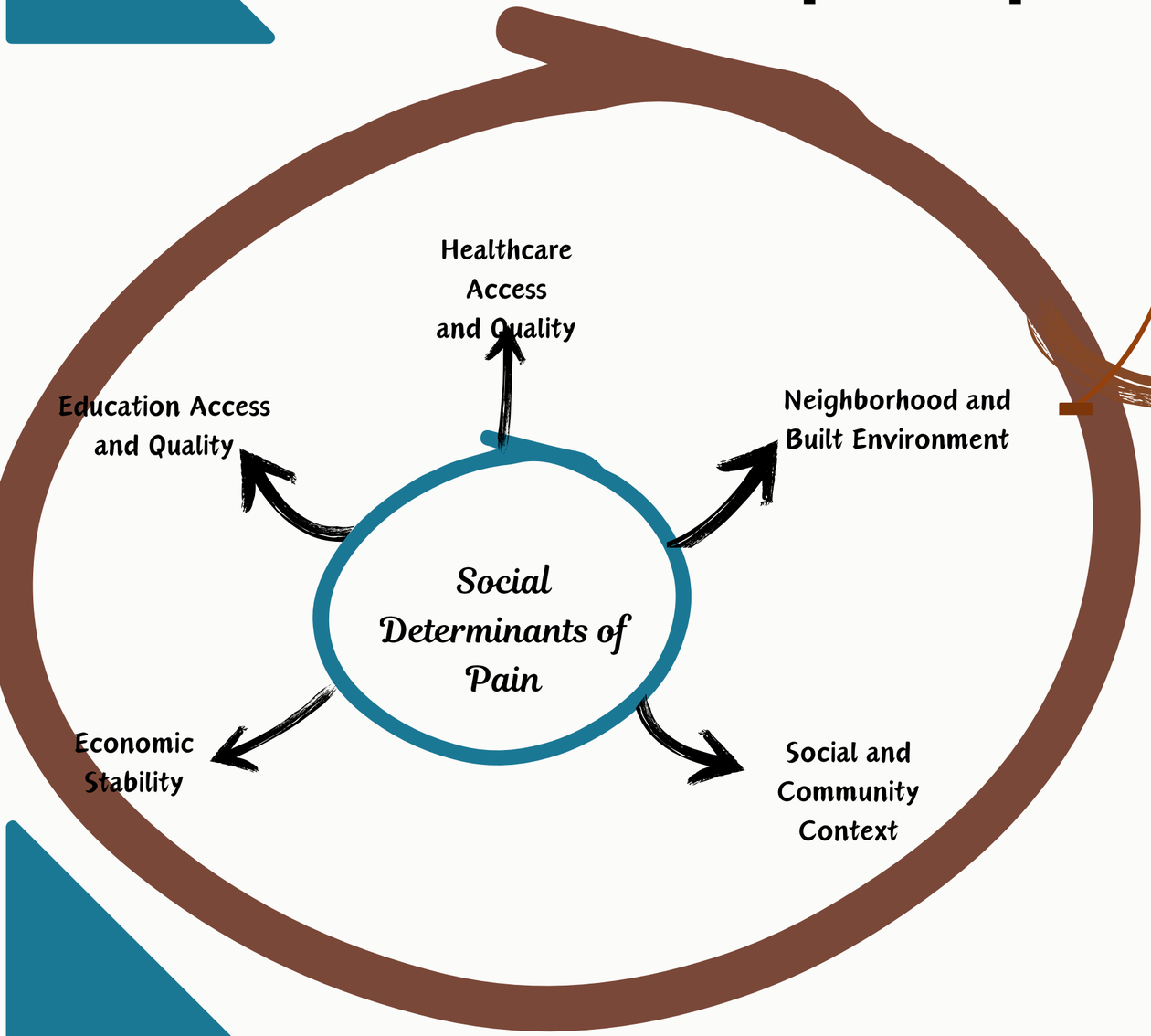
**A wide set of non-medical forces and systems, such as economic policies and systems, development agendas, social norms, social policies, and political systems, shape daily life and influence pain outcomes**

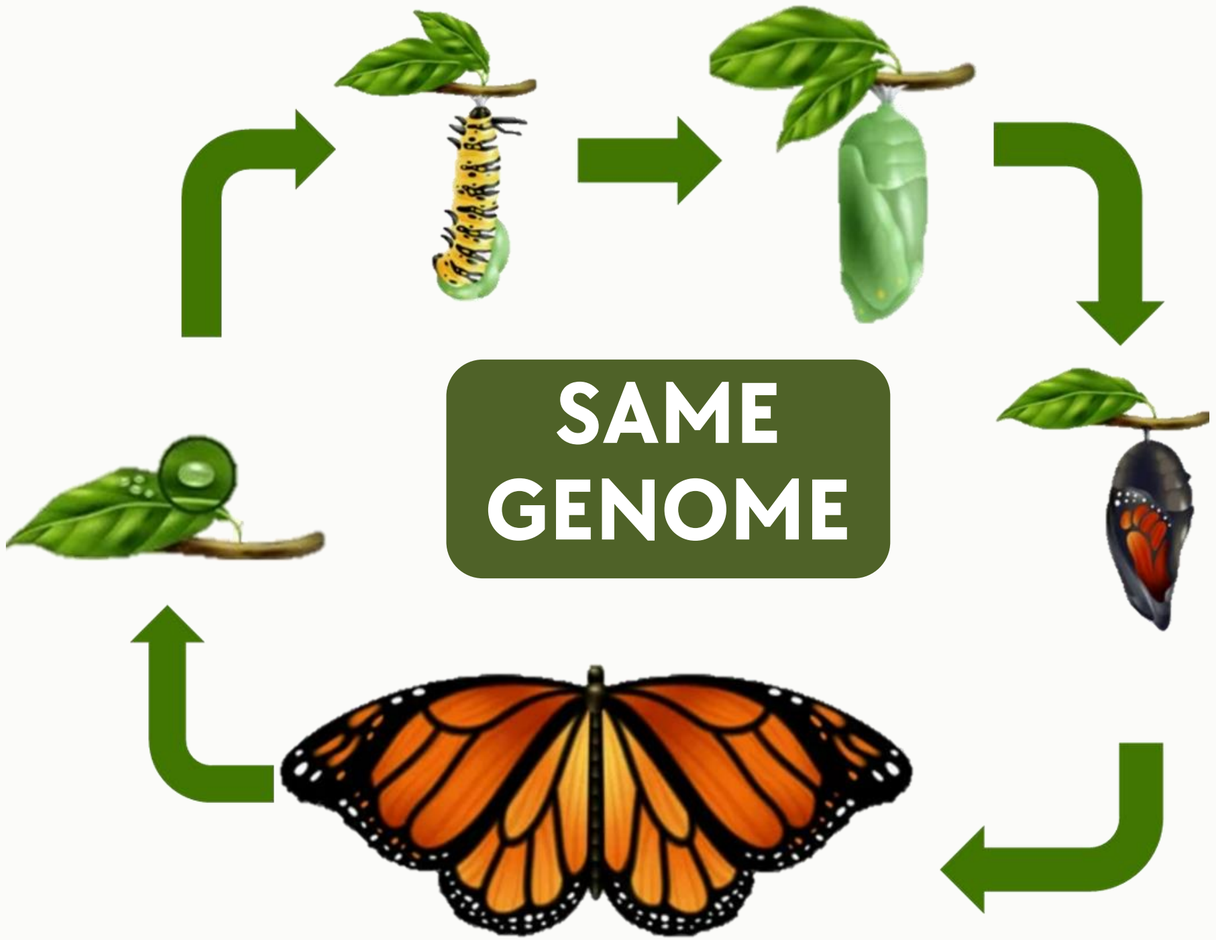


# How do social factors “get under the skin” to impact pain outcomes?




Epigenetics

# Why the Epigenome?




- Epigenetics explains how early experiences and environmental exposures can have lifelong and transgenerational impacts

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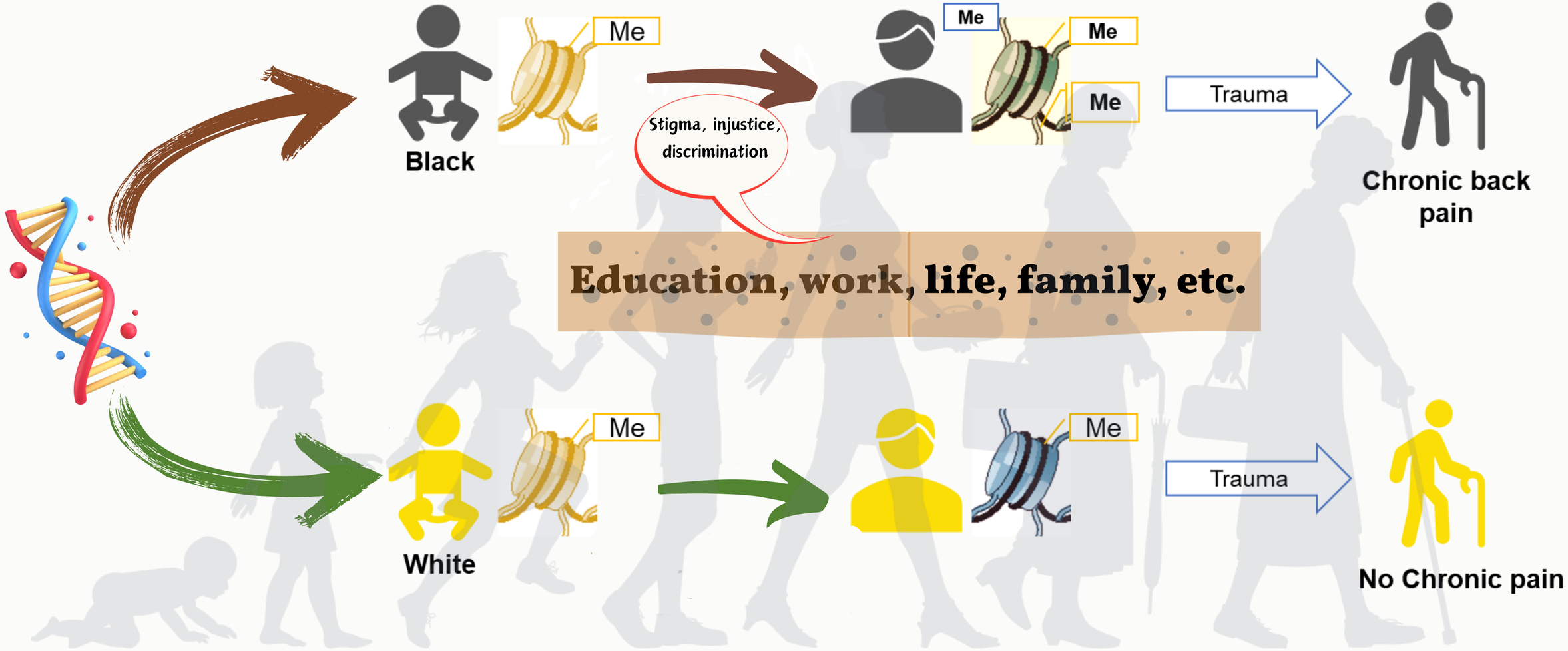
REVIEW

# Could epigenetics help explain racial disparities in chronic pain?



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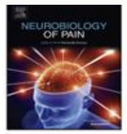
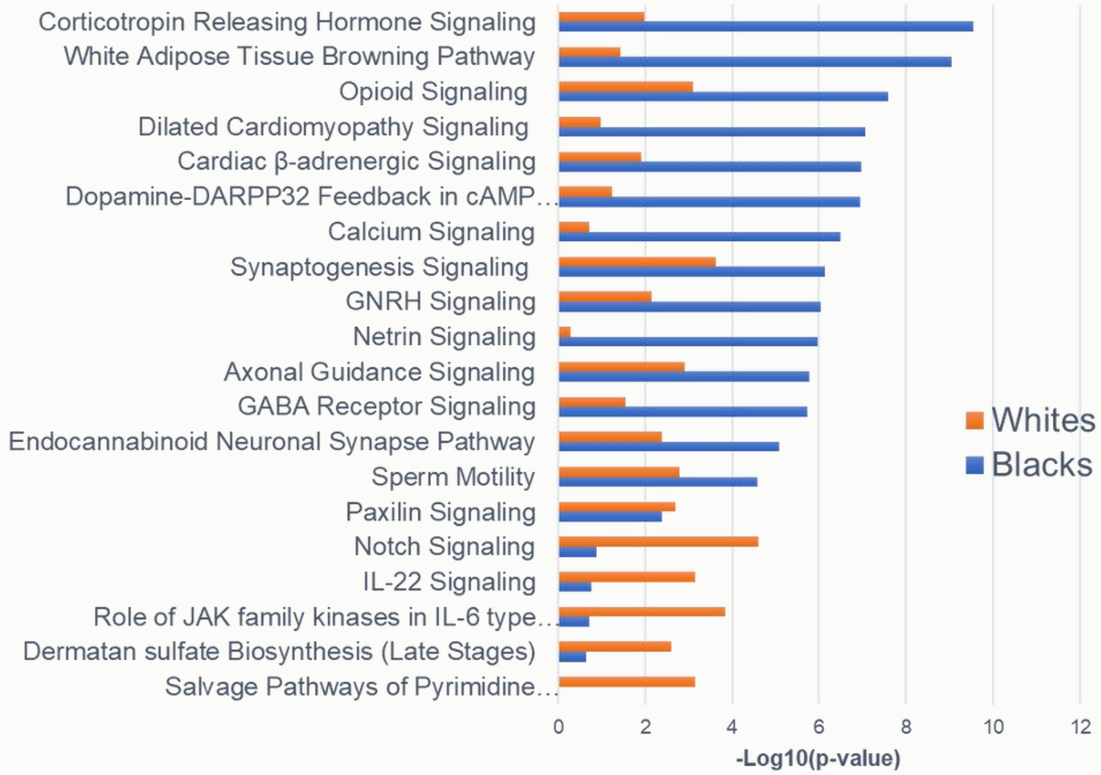


# Pain and stress-related genomic pathways are more significant in Blacks than Whites with chronic low back pain

Differential DNA methylation in Black and White individuals with chronic low back pain enrich different genomic pathways

Edwin N. Aroke [a,*], Pamela Jackson [a], Lingsong Meng [c], Zhiguang Huo [c], Demario S. Overstreet [b], Terence M. Penn [b], Tammie L. Quinn [b], Yenisel Cruz-Almeida [d,e], Burel R. Goodin [b]

[a] School of Nursing, University of Alabama at Birmingham, Birmingham, AL, USA
[b] Department of Psychology, University of Alabama at Birmingham, Birmingham, AL, USA
[c] Department of Biostatistics, University of Florida, Gainesville, FL, USA
[d] College of Dentistry, University of Florida, Gainesville, FL, USA
[e] Pain Research & Intervention Center of Excellence, University of Florida, Gainesville, FL, USA




- **Chronic pain and chronic stress**
  - Chronic pain and chronic stress are two sides of the same coin.
  - Chronic stress can modify the expression of genes related to the stress response, such as the NR3C1 gene
  - These modifications can influence pain sensitivity and threshold

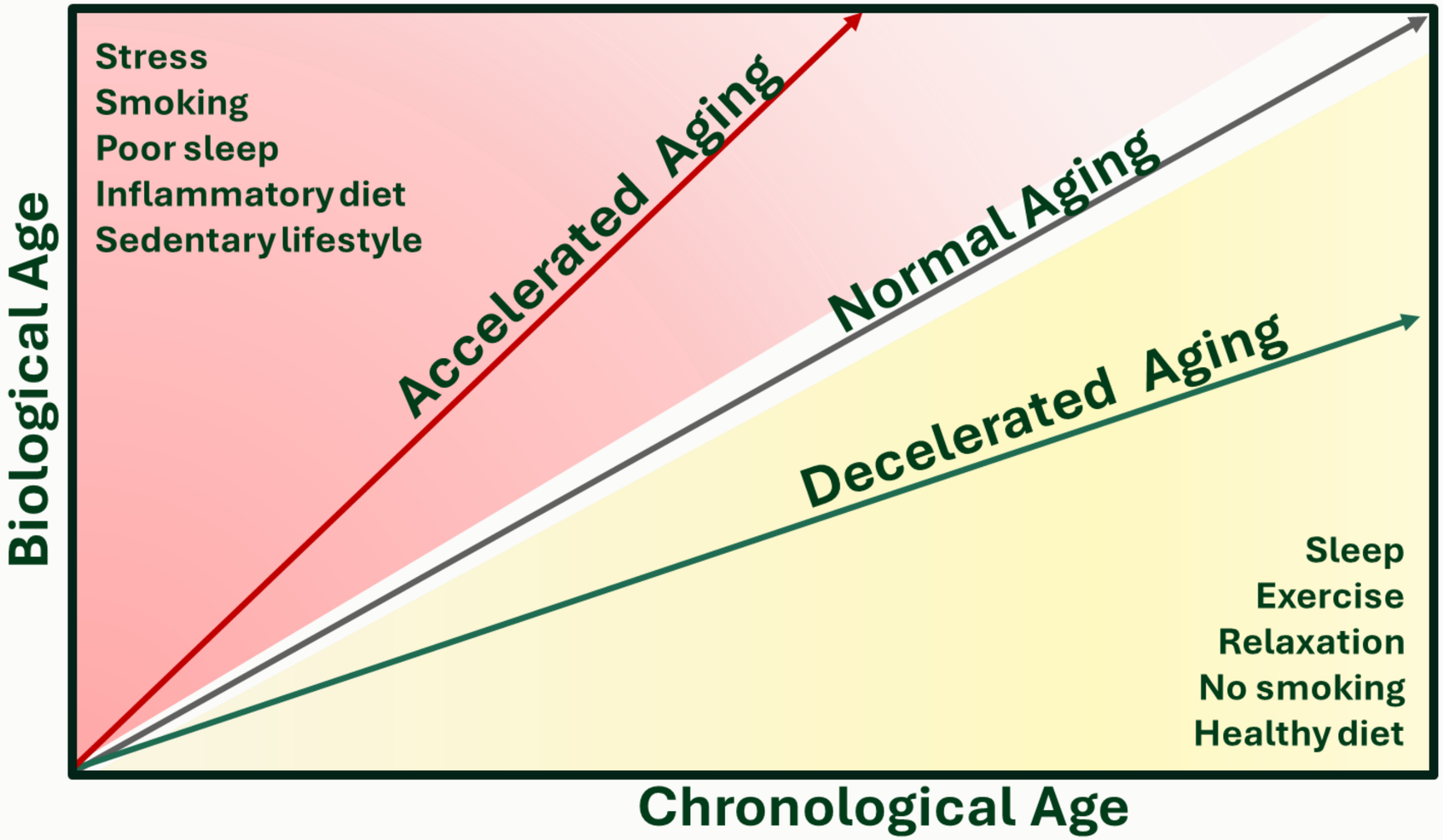
- **Neuroinflammation and chronic pain**
  - Epigenetic alteration of genes involved in neuroinflammatory processes can affect the development and maintenance of chronic pain
  - Stress can exacerbate inflammation and pain sensitivity

# Internalized stigma of chronic pain is associated with worse pain outcomes and differential methylation of genes in the Hippo signaling pathway

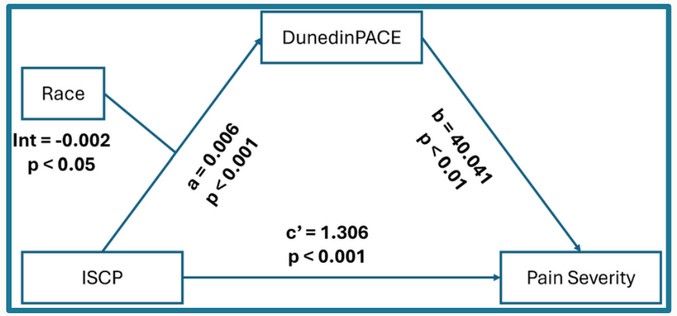
- Hippo signaling plays a prominent role in stress regulation
- Mechanical and oxidative stress (Mao et al. 2015)
- Epigenetically-induced upregulation of genes in the Hippo Signaling pathway has been linked to
  - learning and memory
  - increased risk of stress-related psychiatric disorders e.g., depression and PTSD (Stepan et al. 2018)
- Hippo and downstream Wnt signaling are involved in chronic pain
- Cancer pain, diabetic neuralgia, endometriosis, and low back pain (Tang et al. (2022)

*Aroke et al. 2022, doi.org/10.3389/fpain.2022.1021963*

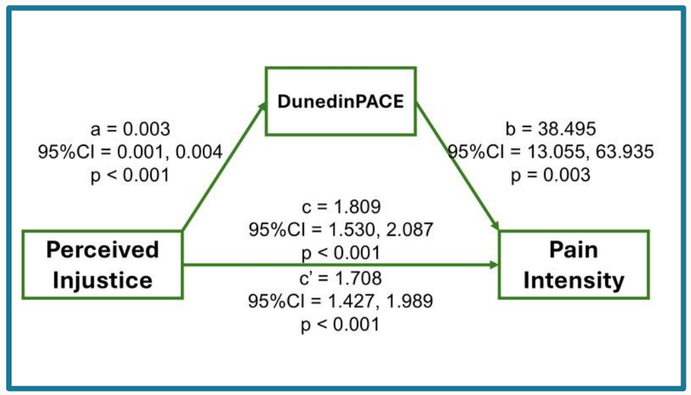
# Biological aging is a stronger predictor of chronic pain than chronological pain



# Internalized stigma and perceived injustice in the experience of chronic pain is associated with a faster pace biological aging and worse pain outcomes



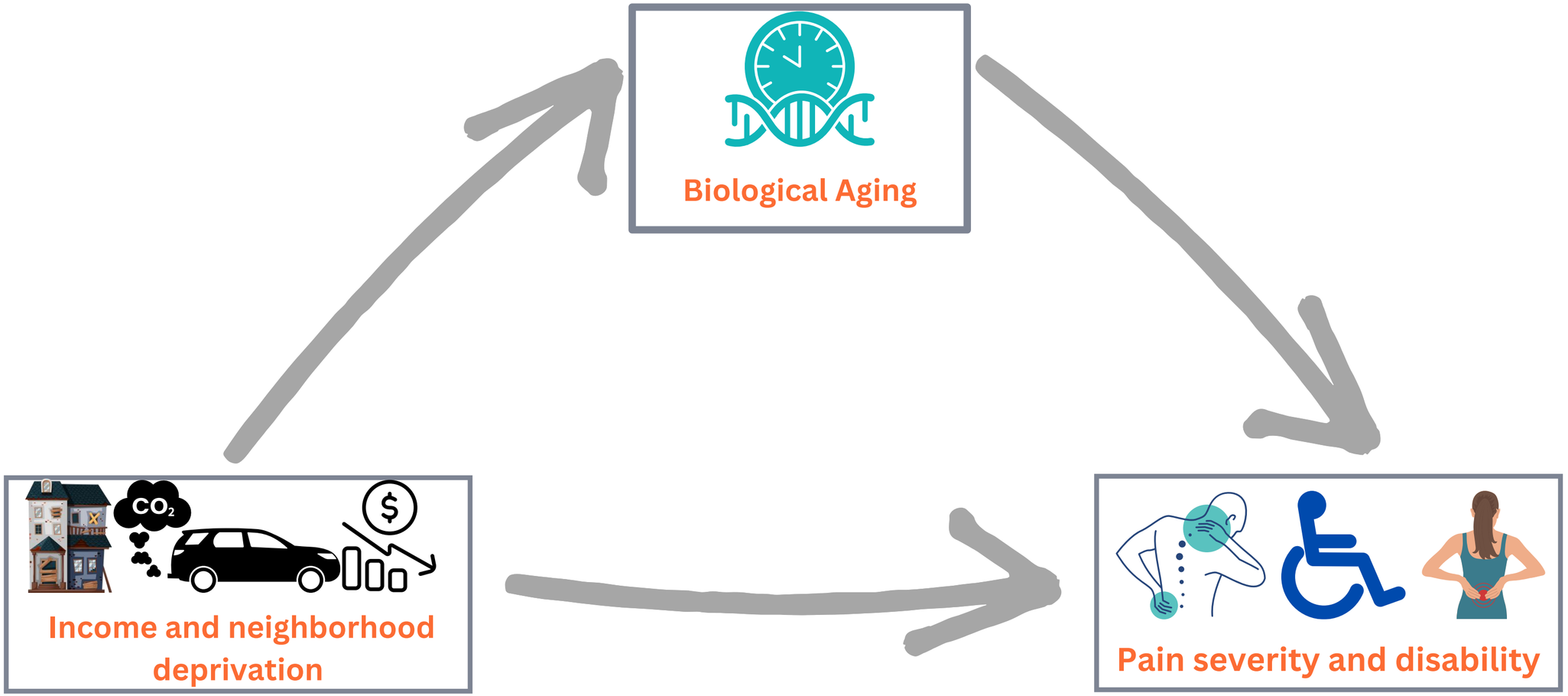

- There is a significant positive relationship between DunedinPACE and internalized stigma of chronic pain (ISCP) ($r = 0.34$, $p < 0.001$)
- DunedinPACE mediates the relationship between ISCP and pain severity
  - Mediation was significant for non-Hispanic Blacks but not for non-Hispanic Whites




- There is a significant positive relationship between DunedinPACE and perceived injustice in the experience of chronic pain ($r = 0.33$, $p < 0.001$)
- DunedinPACE mediates the relationship between perceived injustice and pain severity
  - Mediation significant for both non-Hispanic Blacks and non-Hispanic Whites adults

*Freij et al. 2024 doi.org/10.1016/j.ynpai.2024.100170; Aroke et al. Unpublished work*

## Lower socioeconomic status is associated with a faster pace of biological aging and worse pain outcomes. Epigenetic age acceleration mediates the relationship between SES and pain outcomes




*Jackson et al. 2023. doi.org/10.1016/j.socscimed.2023.116088 & Aroke et al. Unpublished work*

# Implications and Conclusion

- Shared environmental exposures to policies and sociocultural norms that marginalize particular segments of the population are the root causes of pain disparities
    - Social and structural forces not only impact treatment outcomes but also mediate epigenetic and nervous system changes that sustain pain disparities across lifetimes, generations, and cultural histories

- Achieving health equity in pain management will require addressing these root causes
    - critical understanding of the lived experiences of marginalized groups
    - address bias, stigma, and all forms of injustice in health care
    - multi-level interventions that adopt  whole person approach

# CONTACT

Edwin N. Aroke earoke@uab.edu