

Emerging Genomic Pathways for Social Risk Exposure and Health Outcomes

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Disclosures

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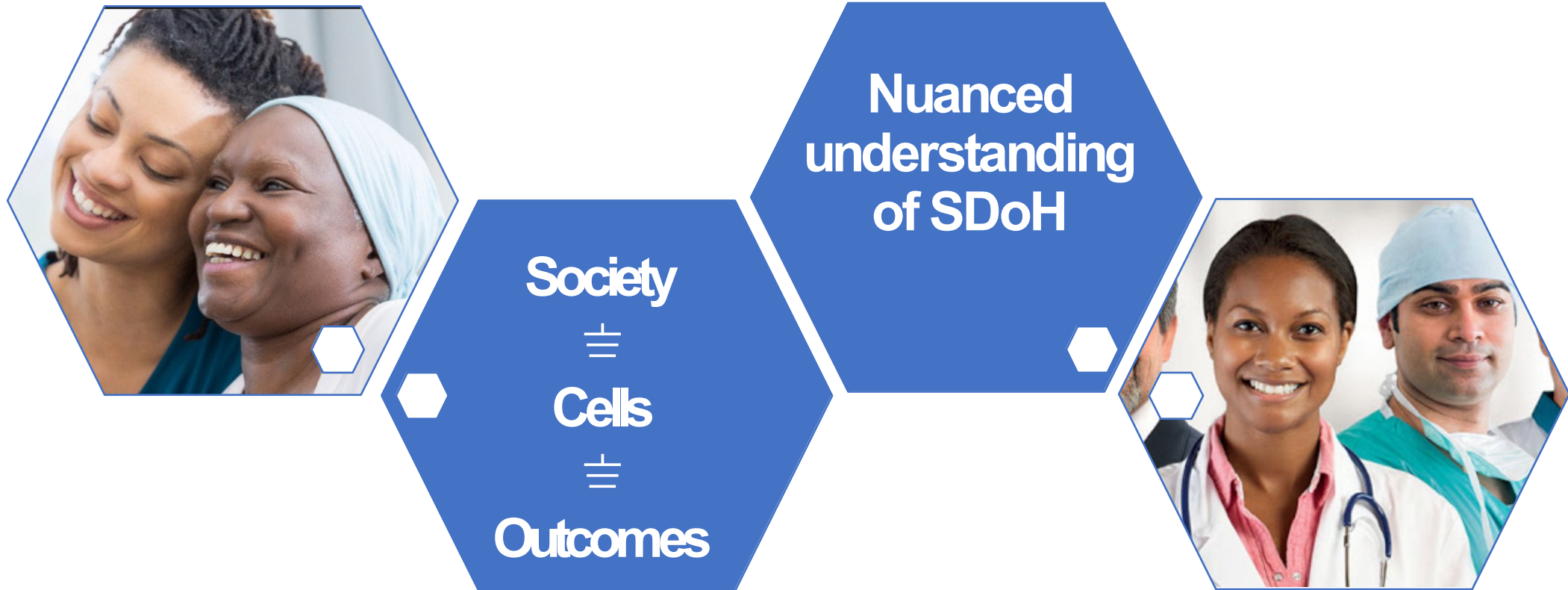
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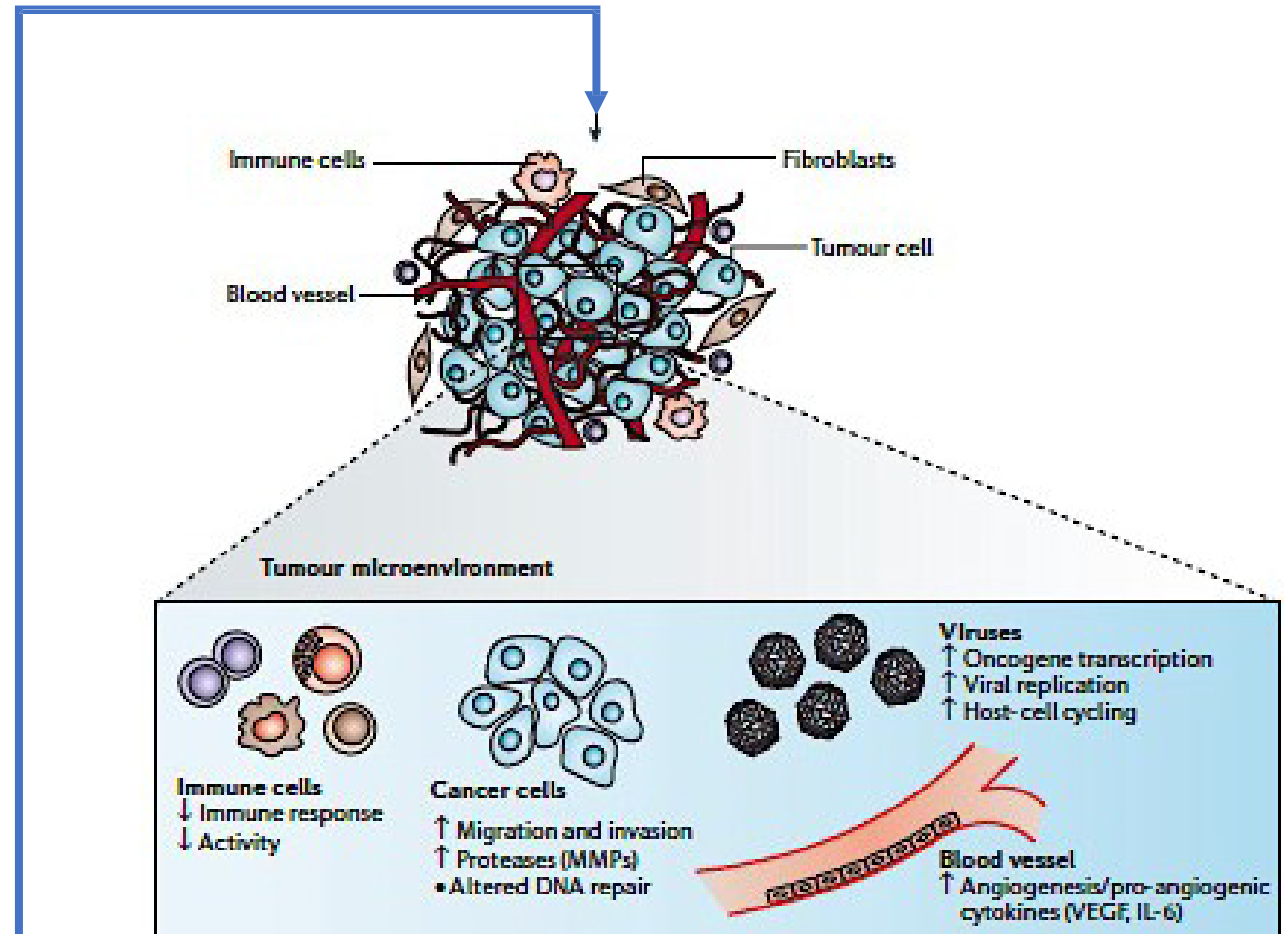
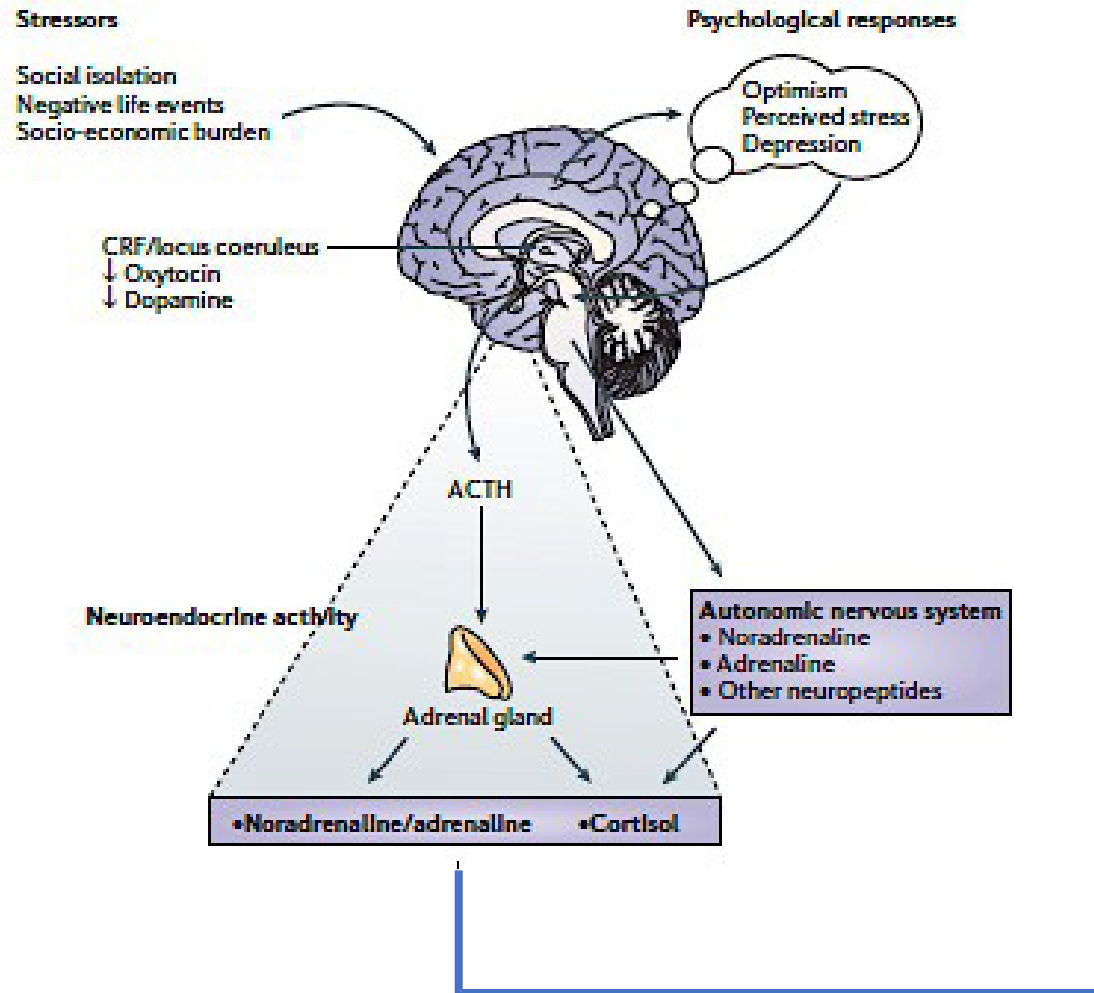
Leadership roles: ECOG-ACRIN, ARBIR



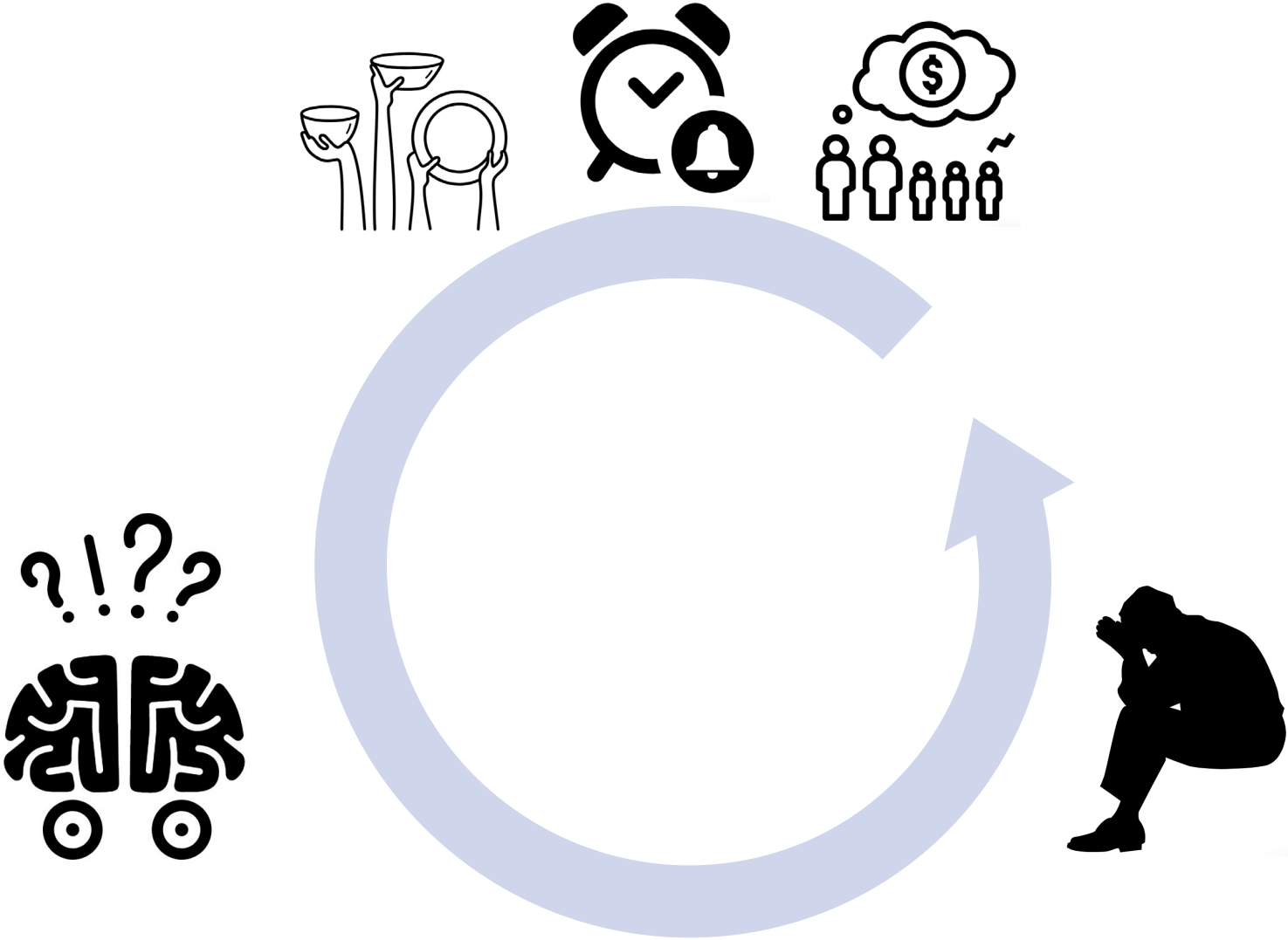
Right patient, right test, right treatment, right time, right price



Stress and cancer



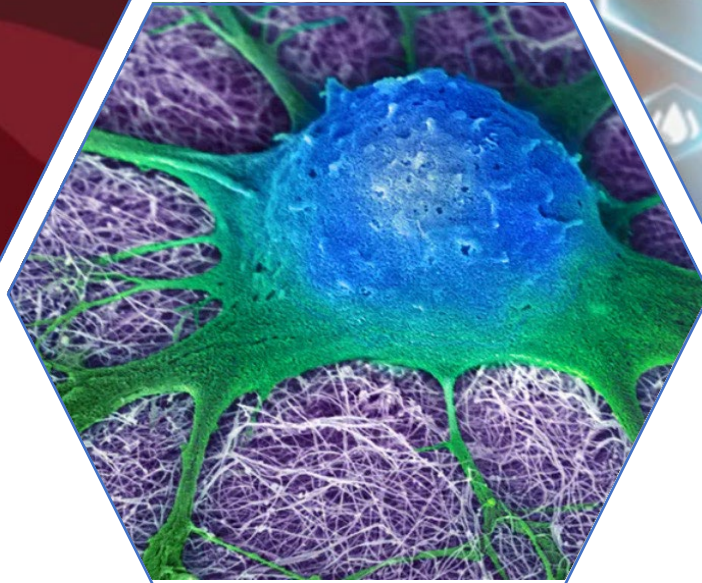
Physiology of scarcity



SOCIETY → CELLS → OUTCOMES: Social Genomics and Health Equity



Social policies & context
Institutions
SDH, HRSN, behavior



Physiologic stress
Genomic/epigenomic
regulation

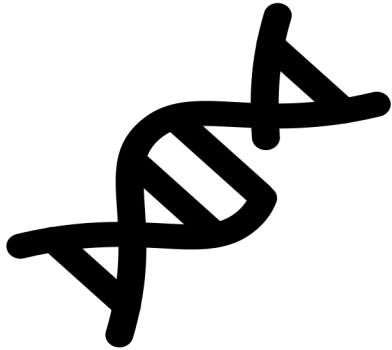


Biological & clinical
outcomes gap

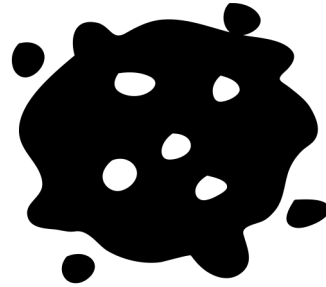
Carbs JCO 2022



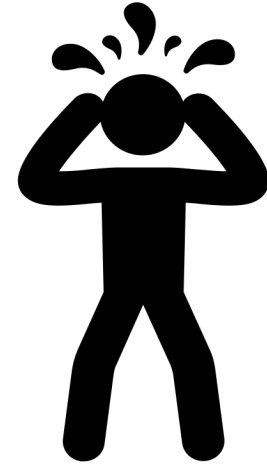
Mechanistic pathways of SDoH effects on health



Genomic/epigenomic changes:
Conserved transcription response to adversity (CTRA), DNA methylation, histone modification, RNA silencing, telomere shortening

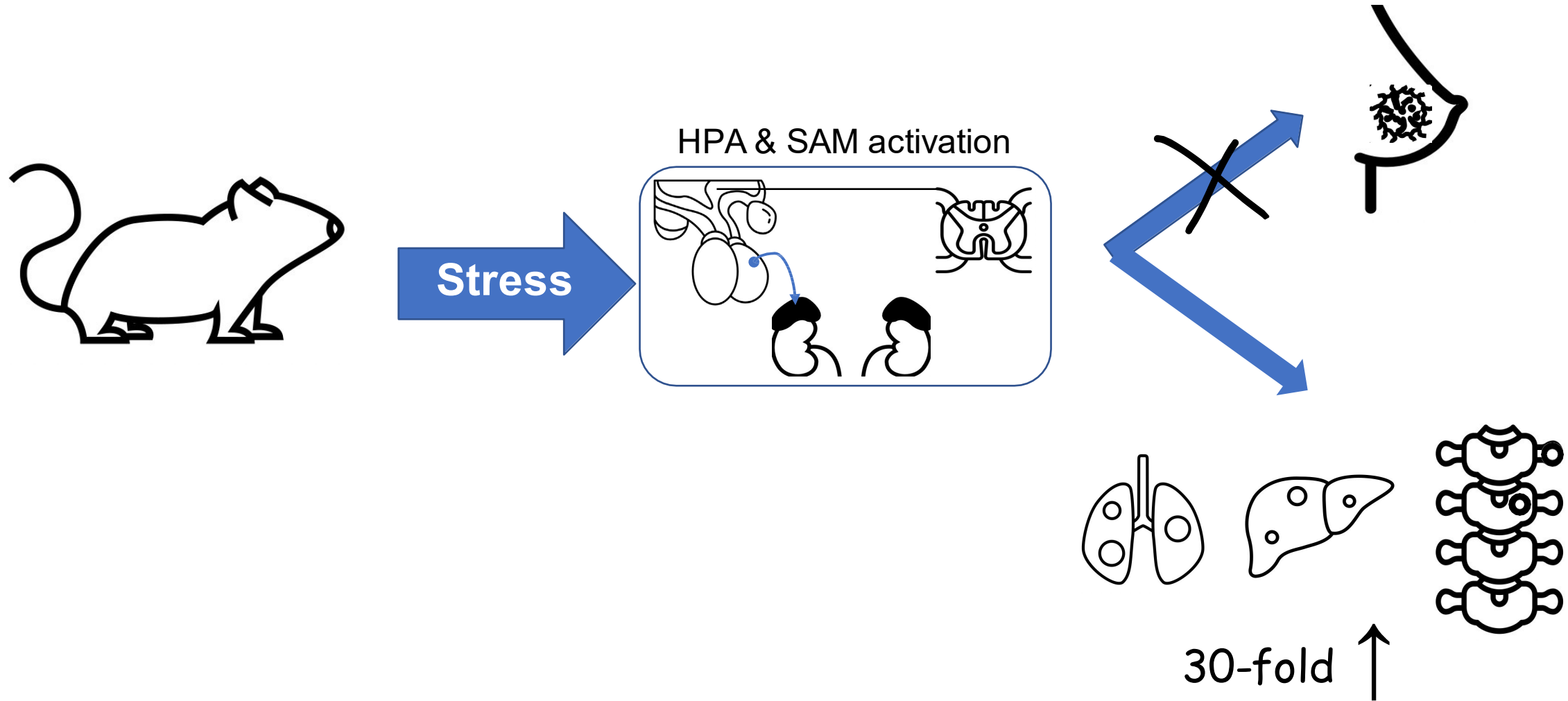


Peri-tumoral environment: racial differences in peri-tumoral immune response, upregulation of genes involved in epithelial mesenchymal transition



Stress response: adversity associated with upregulation of genes involved in inflammation

Stress-induced effects on breast cancer in animal models



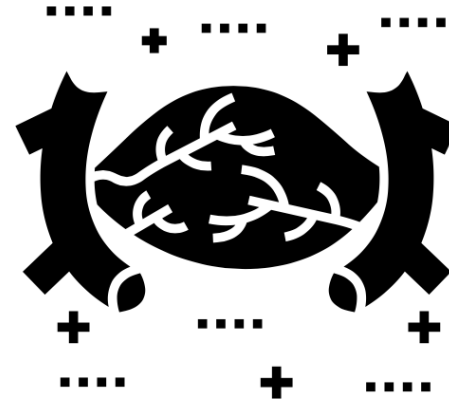
Social conditions and solid tumor gene expression



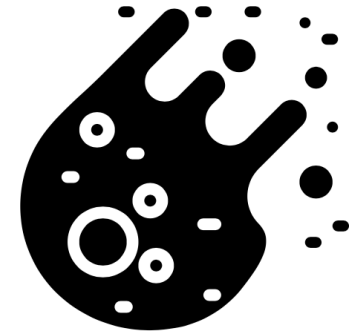
Inflammation



Wound healing



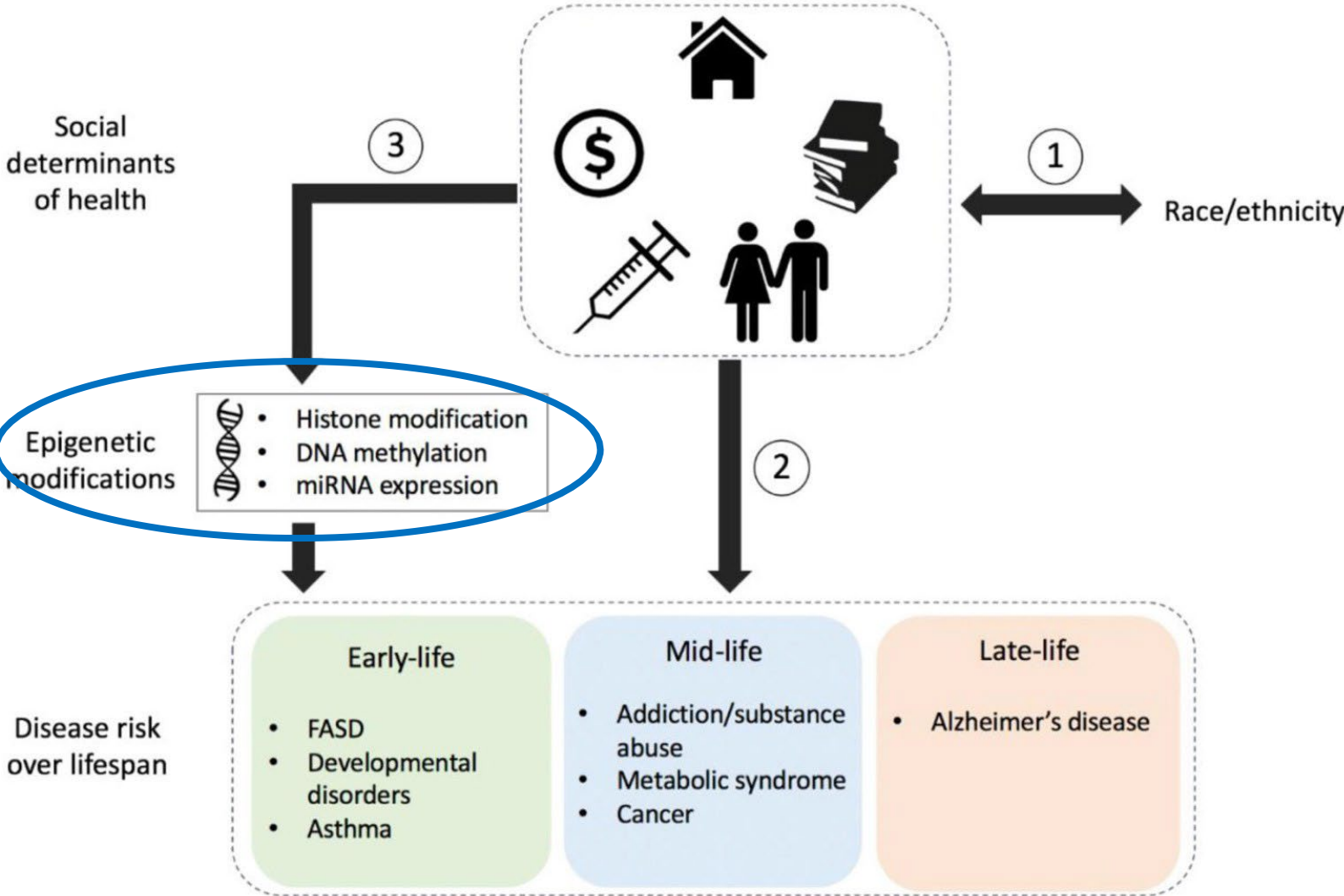
Blood vessel growth



Resistance to apoptosis
Chemotx resistance

Epigenetics and health equity

Potential Heritability of Social Trauma

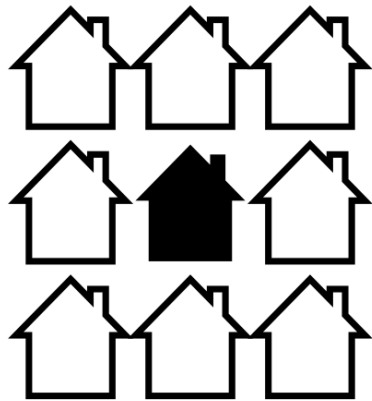


Mancilla 2020

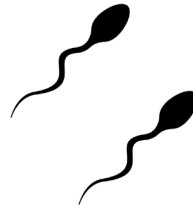


Paternal social determinants and offspring obesity

Exposure



Epigenetic transmission



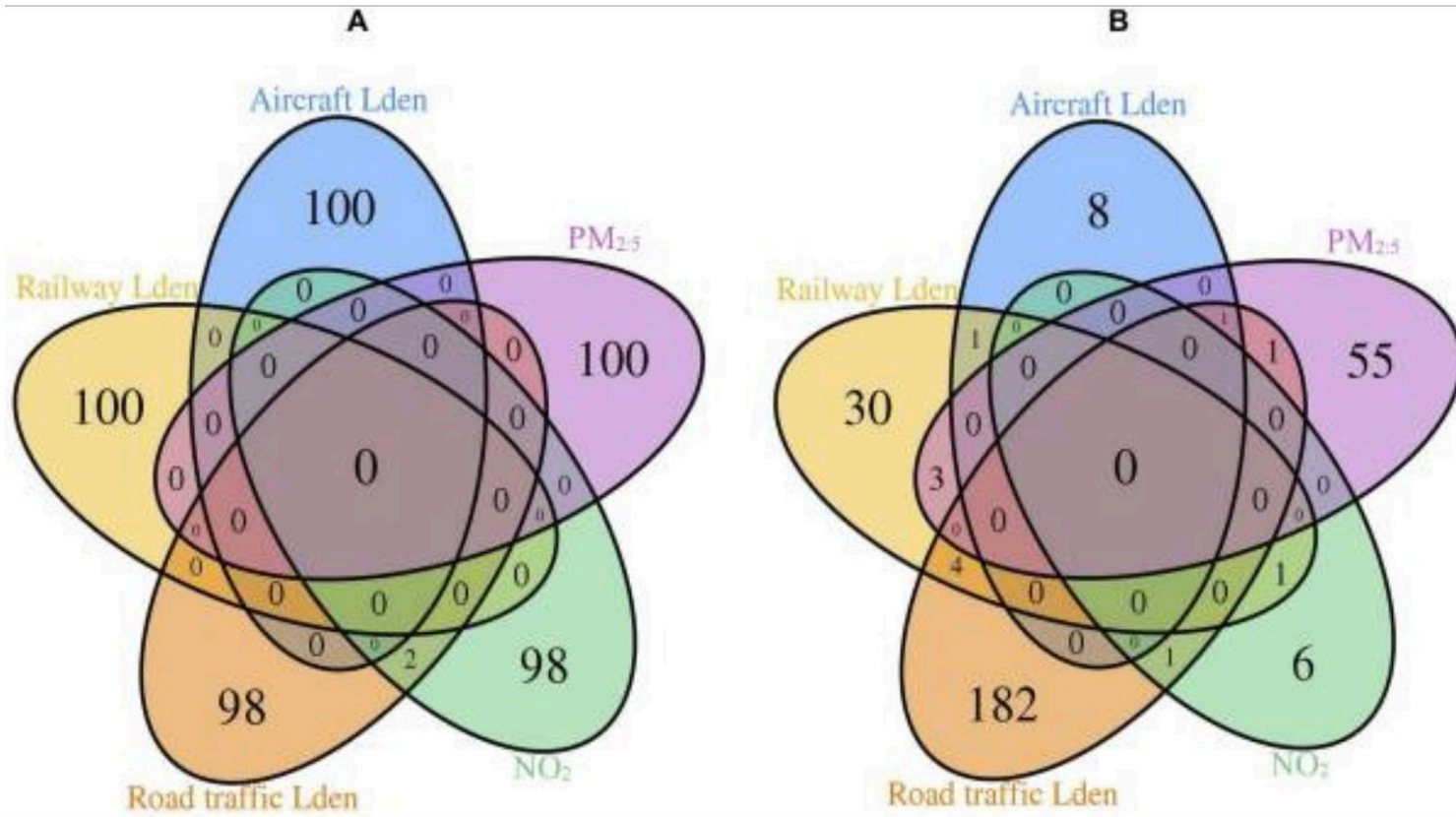
Paternal behavior and developmental programming



Milliken-Smith 2021



Transportation noise/air pollution and epigenetics



SAPALDIA study (Swiss)

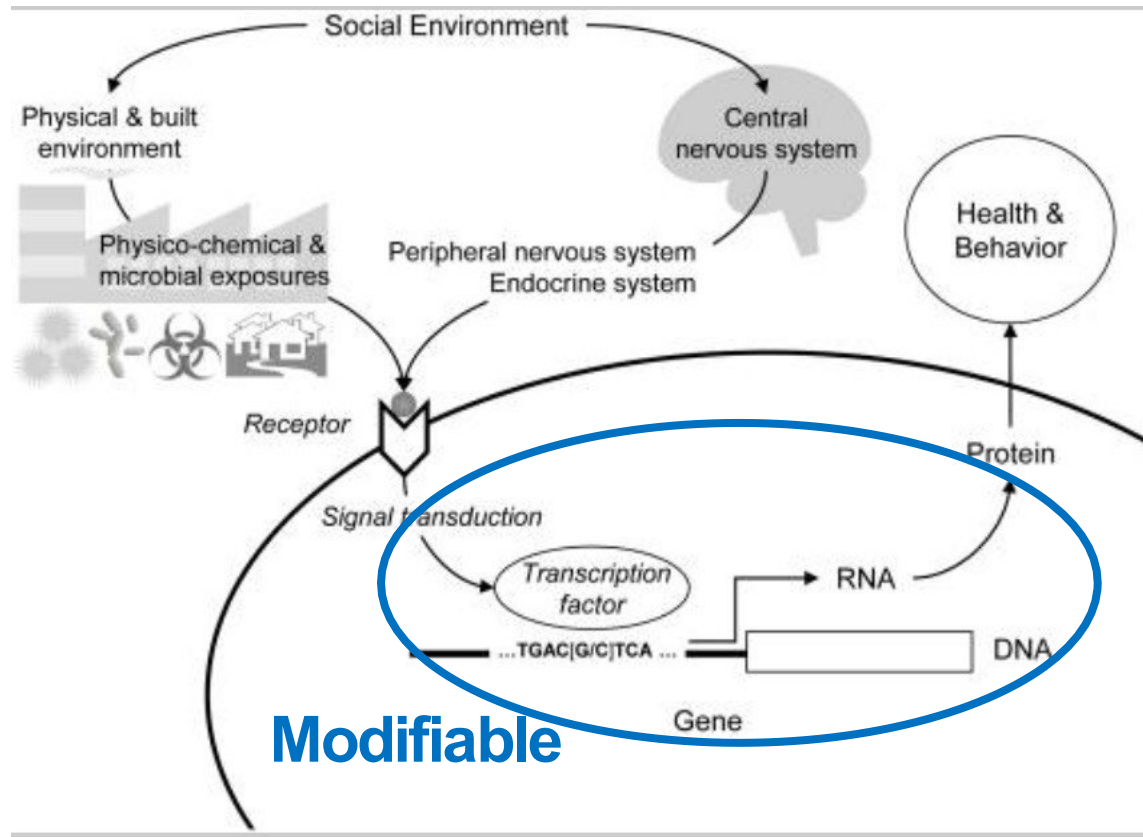
Differentially methylated regions (EWAS)

- inflammatory and immune regulation-related pathways
- mTOR signaling
- Cellular signaling
- apoptotic signaling pathway

Controlled for demographic, nSES, greenness index, smoking exposure, diet and alcohol, asthma and leukocyte composition

Eze 2020

Conserved transcriptional response to adversity (CTRA)

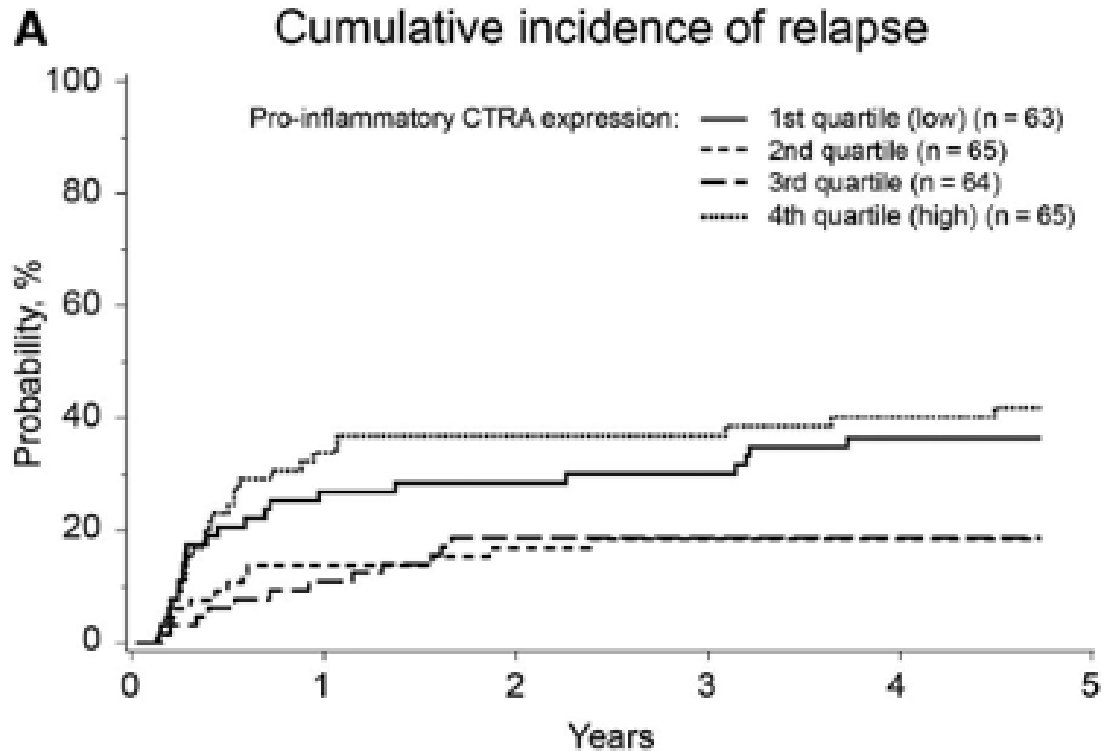


“Loneliness gene signature”
53-gene social stress transcriptome

- Pro-inflammatory genes: e.g., *IL1B*, *IL6*, *IL8/CXCL8*, *TNF*
- Anti-viral genes: e.g., *IFI*-, *MX*-, and *OAS*-family genes

Cole 2014

CTRA and clinical outcomes



Knight 2019, stem cell transplant

Breast cancer survivors, post surgery n=51

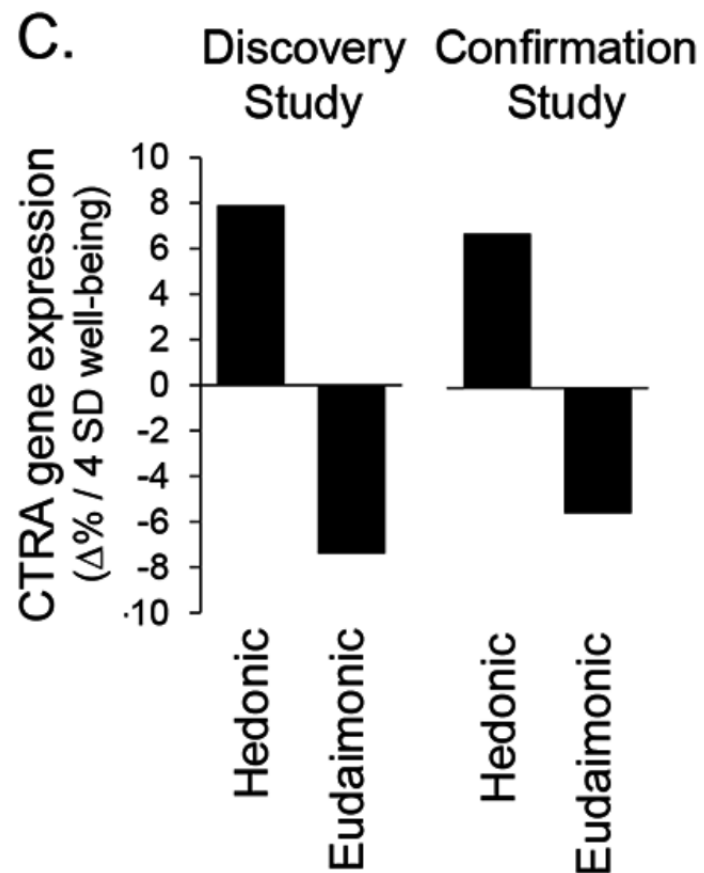
RCT: cognitive behavioral stress management, 1yr

CBSM attenuated CTRA inflammatory gene expression

Greater increases in CTRA → shorter DFS

Antoni, 2019

CTRA and well-being measures

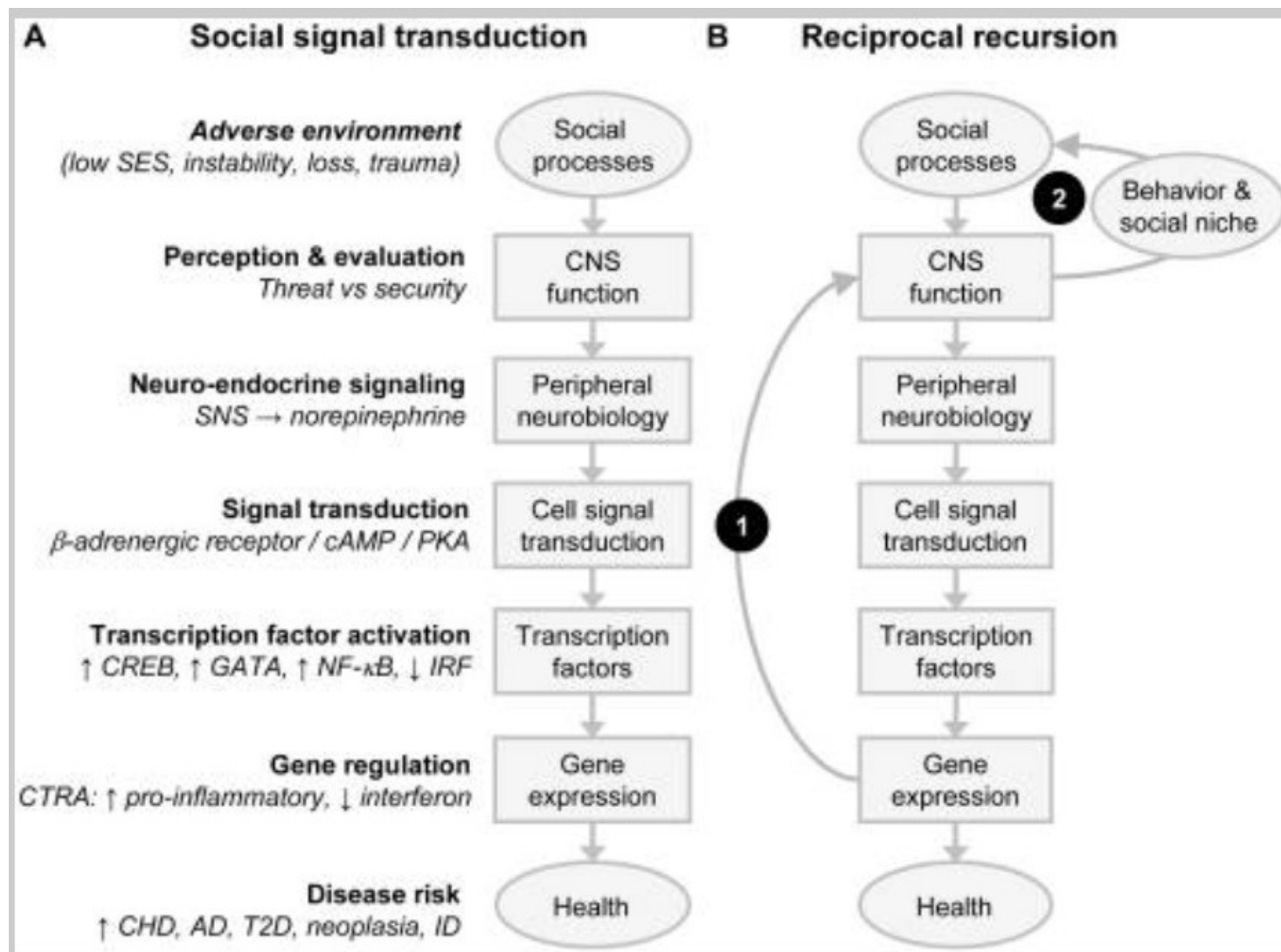


Well-being dimension	
A. 2-dimensional	
	Hedonic well-being
	Eudaimonic well-being
B. 3-dimensional	
	Hedonic well-being
	Psychological well-being
	Social well-being
C. 1-dimensional	
	Total well-being
D. Categorical	
	Flourishing mental health

Fredrickson 2015, Boyle 2019

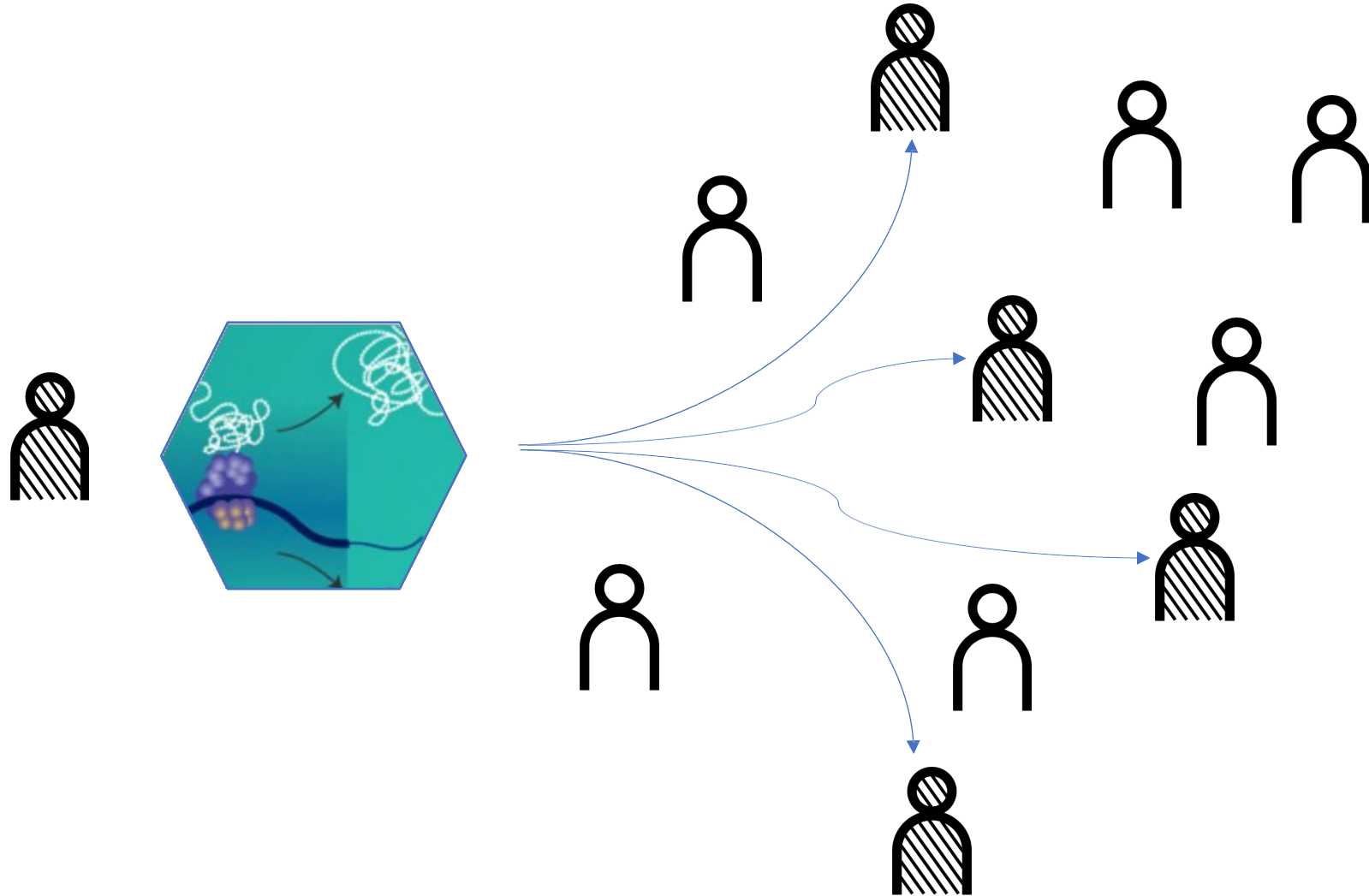


Social signal transduction and recursive network genomics



Cole 2014

Network genomics and “transmissibility”



The ethical dilemma of interventions targeting social genomics



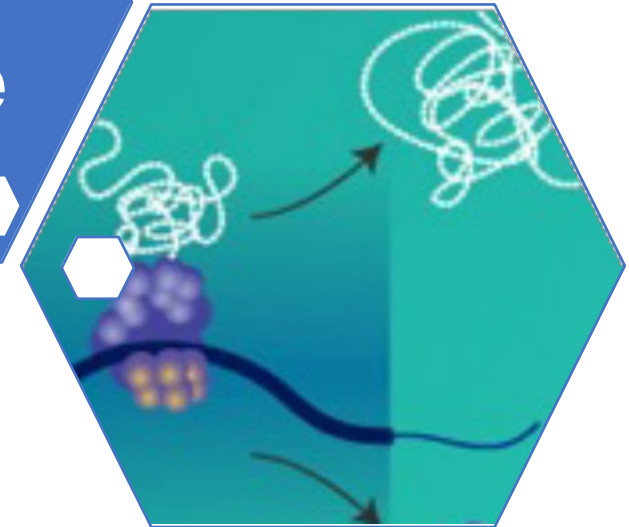
Preventable burden?

Right patient, right test, right treatment, right time, right price



Social
genomics

Equitable
Evidence-
based care



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