

Resilience, resistance, and health:

Insights from animal models of social determinants of health

Disclosures: None

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Social Determinants of Health

Poverty / low SES

Social loss / bereavement

Post-traumatic stress

Early life deprivation

Loneliness / isolation

Social instability / violence

Chronic stress

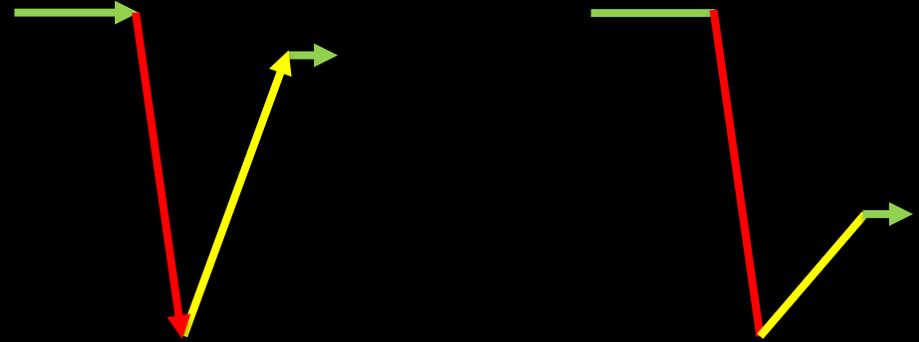
Discrimination

Low social rank

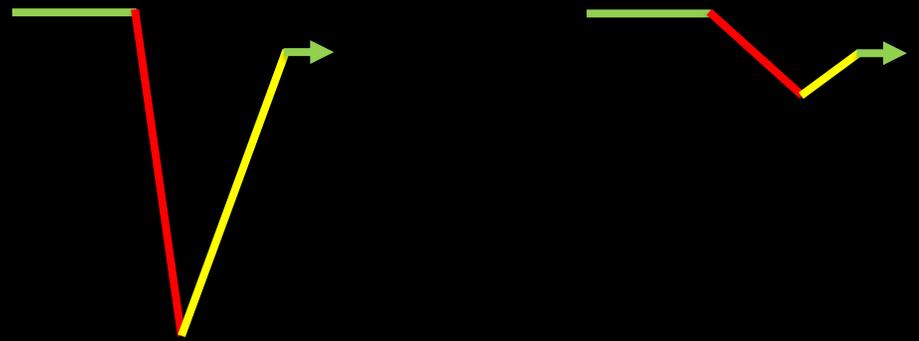
Disease burden

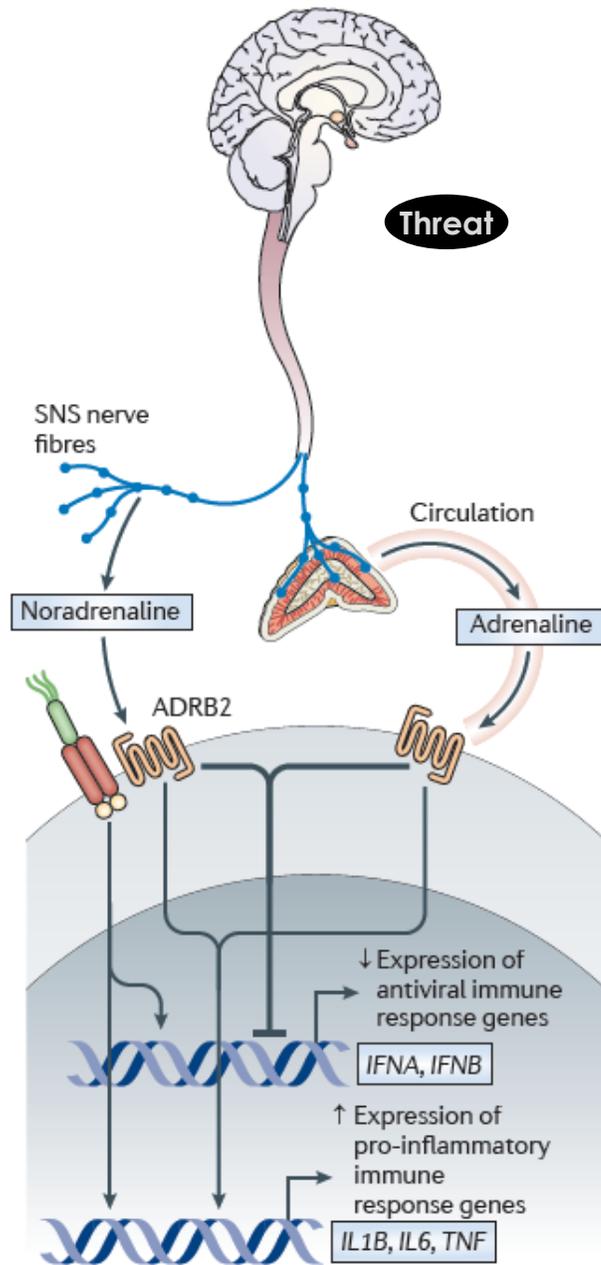
Anxiety

Resilience



Resistance / robustness





Irwin & Cole, Nature Reviews Immunology 2011

Animal modeling value:

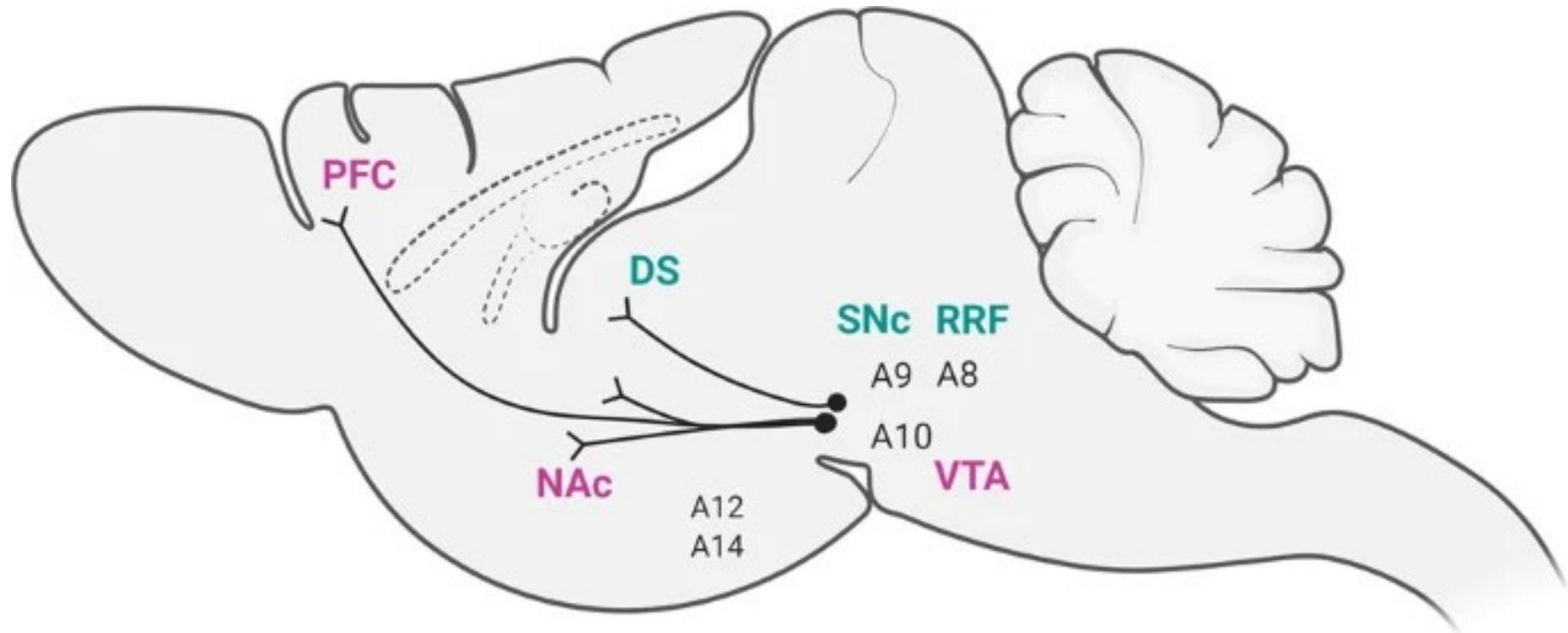
Insult / SDOH adversity

- CNS response
- Peripheral neural response
- End-organ regulation
- Disease pathogenesis
- Cell/molecular mechanisms
- Social resources/interventions
- Pharm/behav. interventions

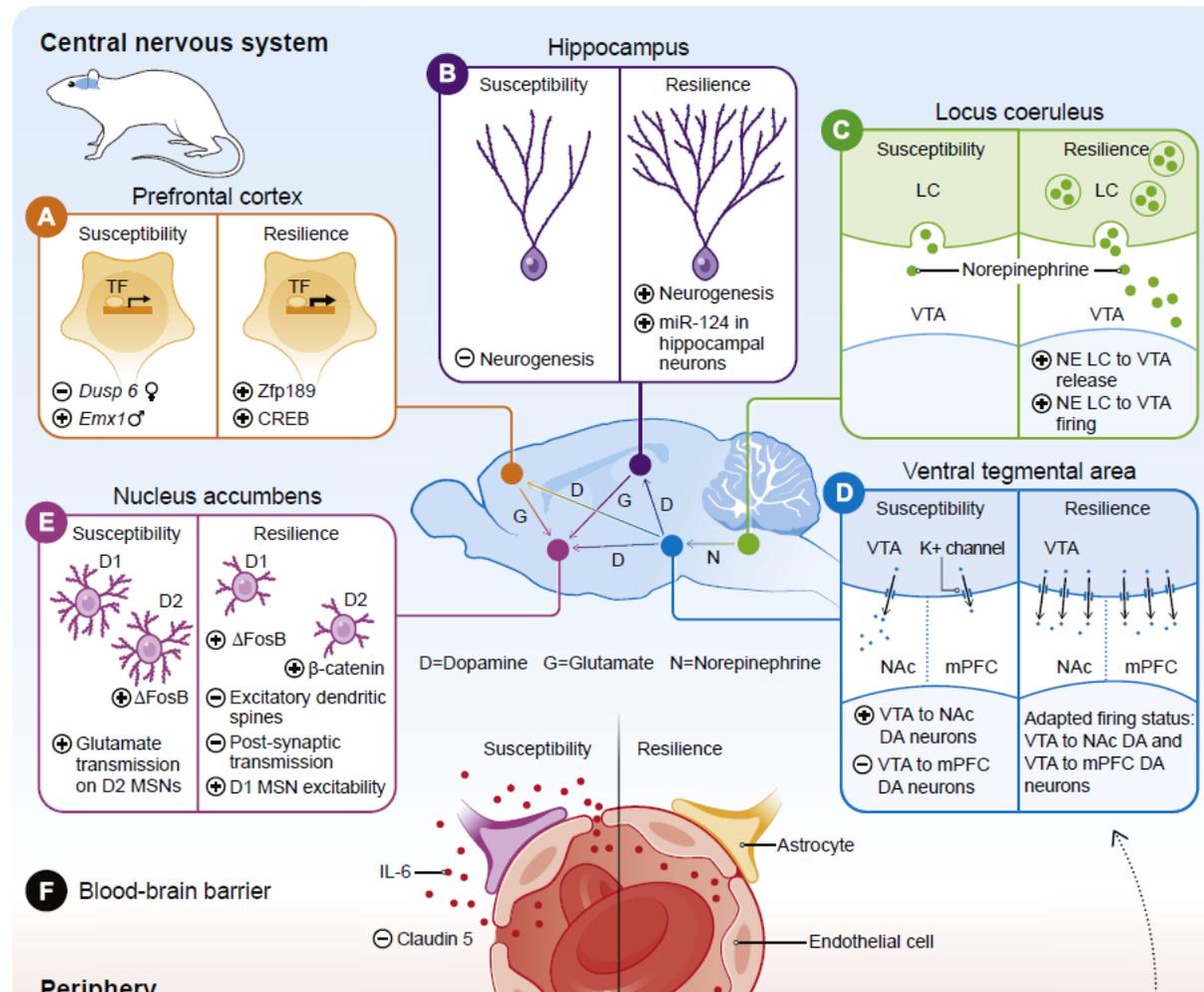
Health / well-being / function

Mouse modeling of CNS stress resilience:

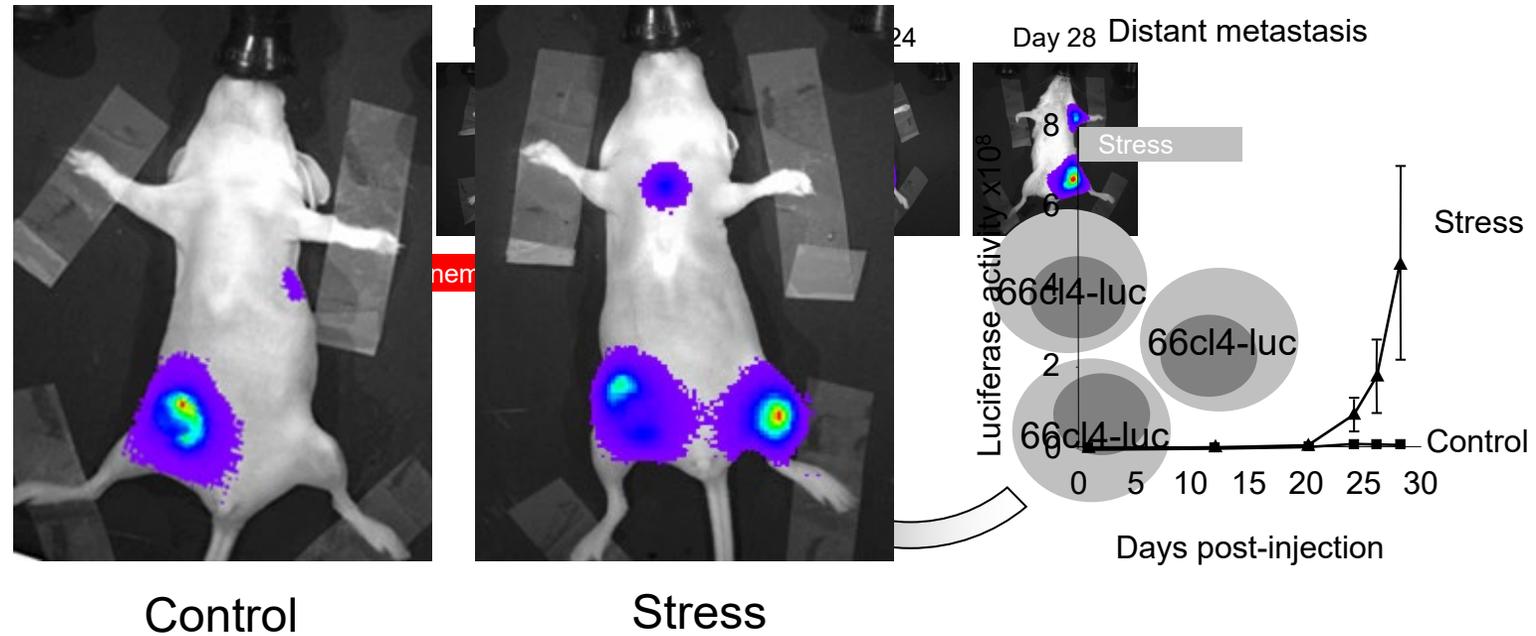
The dopaminergic reward system



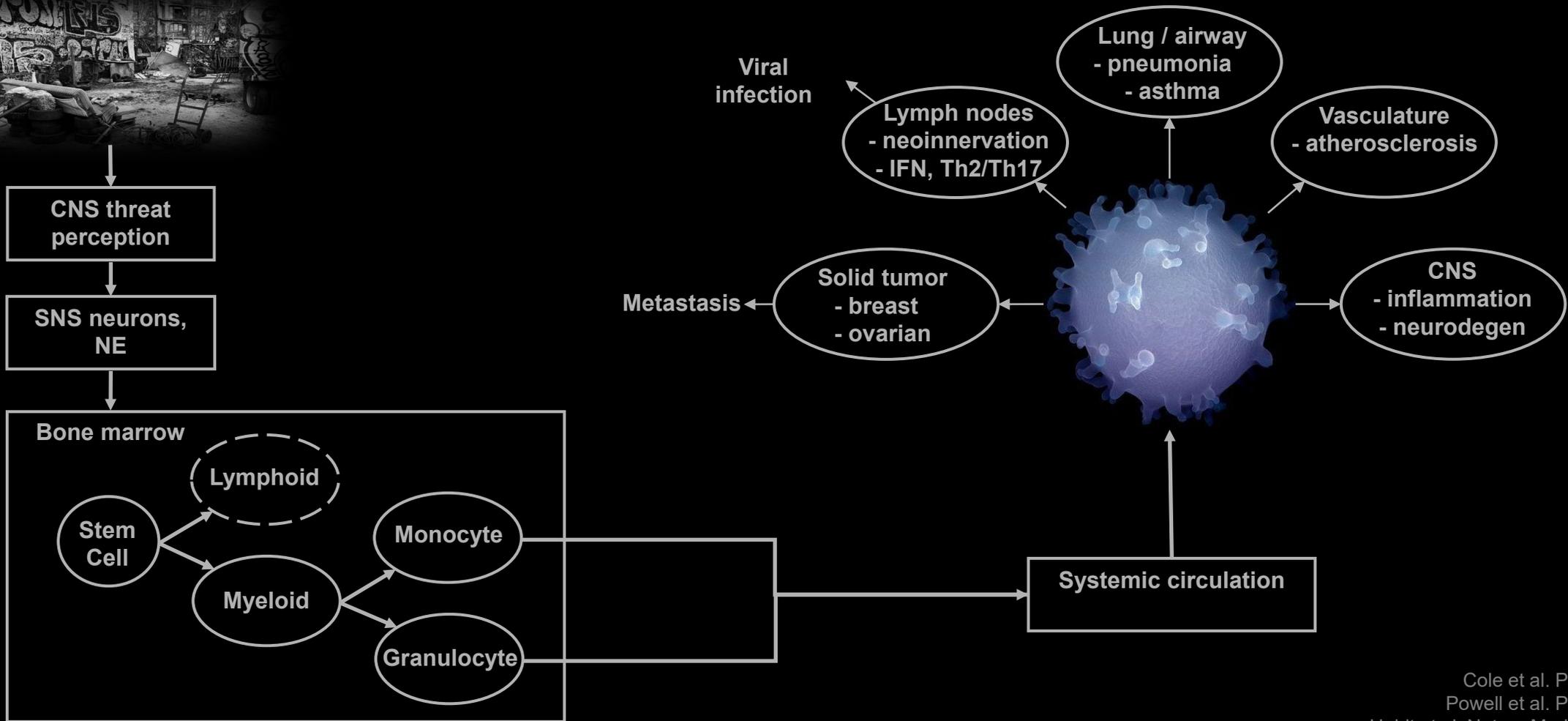
Mouse modeling of CNS stress resistance



Mouse models of disease: Adding “social determinants”



Mouse models of disease: mapping SDOH cell/molecular mechanisms

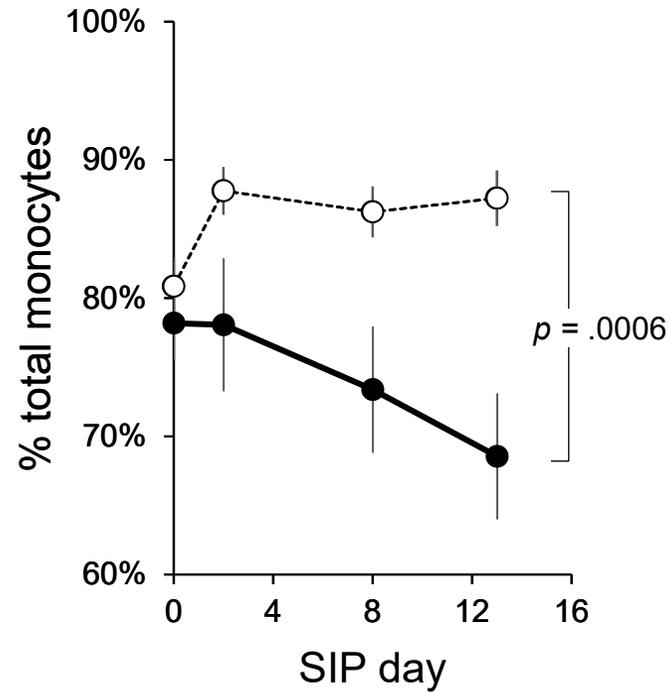


Primate modeling of social processes: resilience

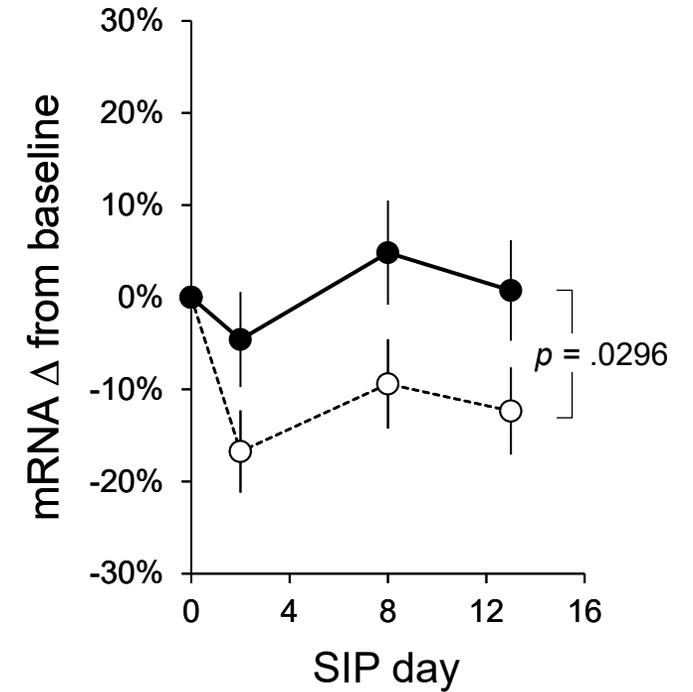
Monkey lockdown



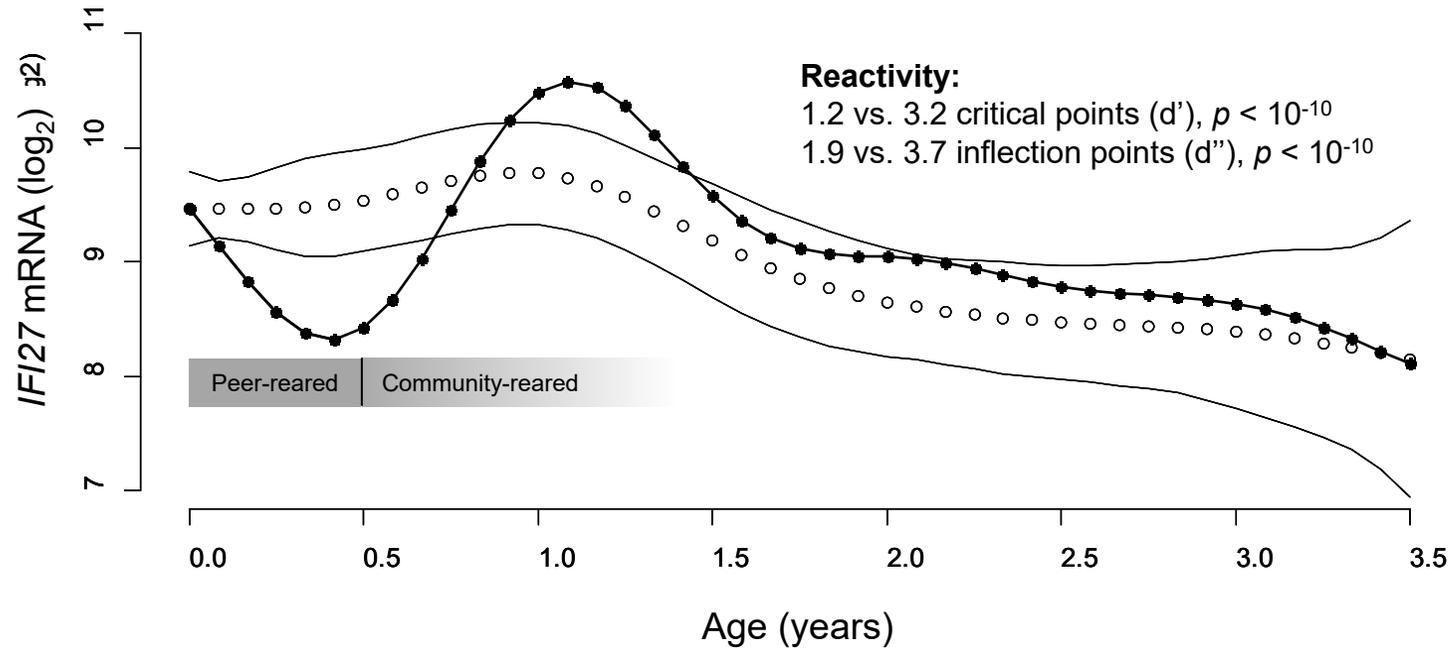
Inflammation:
Classical monocytes



Antiviral:
Type I IFN RNA



Primate modeling of social processes: Resilience to early life adversity



681 Diverged by mo. 6
650 Recovered?— 95%
31 Embedded?— 5%

Take-home points / knowledge gaps / research opportunities

Animal models provide exquisite experimental control and mechanistic analyses of SDOH

- Causal effects of modeled “social determinants” on behavior and health outcomes
- Cellular/molecular/genetic mechanisms *in vivo*
- Genetic/developmental/social resilience factors
- Rapid proof-of-concept testing for resilience remedies/interventions/solutions

CAVEAT: “animal SDOH” differ ethologically from human SDOH (...AND other animals)

e.g., isolation (safety vs threat), loneliness (/social safety signaling), caregiving, neural/endocrine

Implication: NO single animal model will provide a full-cycle, high-fidelity model of human SDOH

Solution: blend different models for different components, with particular attention to ethological validity

- Mice = good for disease modeling and molecular dissection (genetic manipulability, short lifecycle)
- Mice = bad as models of human social behavior (e.g., isolation, caregiving, cognition, etc.)
- Rats = good for “broadly human-similar” social behavior
- Rats = bad as models of human disease (generally not genetically manipulable)
- Non-human primates = great models of human-similar social, cognitive, motor behavior
- Non-human primates = variable fidelity models of disease, expensive & long lifecycle, ethically constrained, generally not genetically manipulable