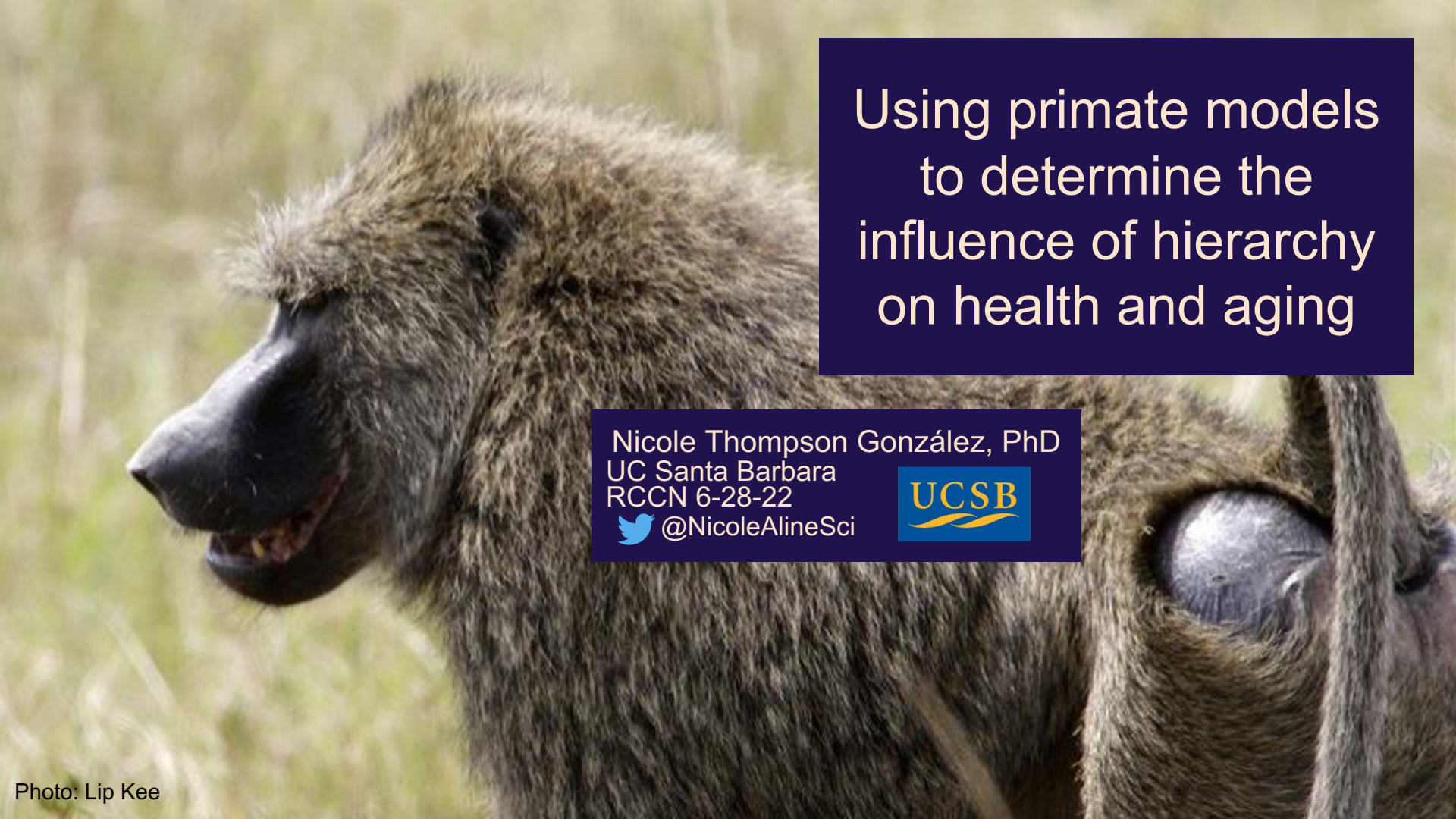

Using primate models to determine the influence of hierarchy on health and aging

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Photo: Lip Kee

Social status structures the experienced environment

Position within hierarchy influences

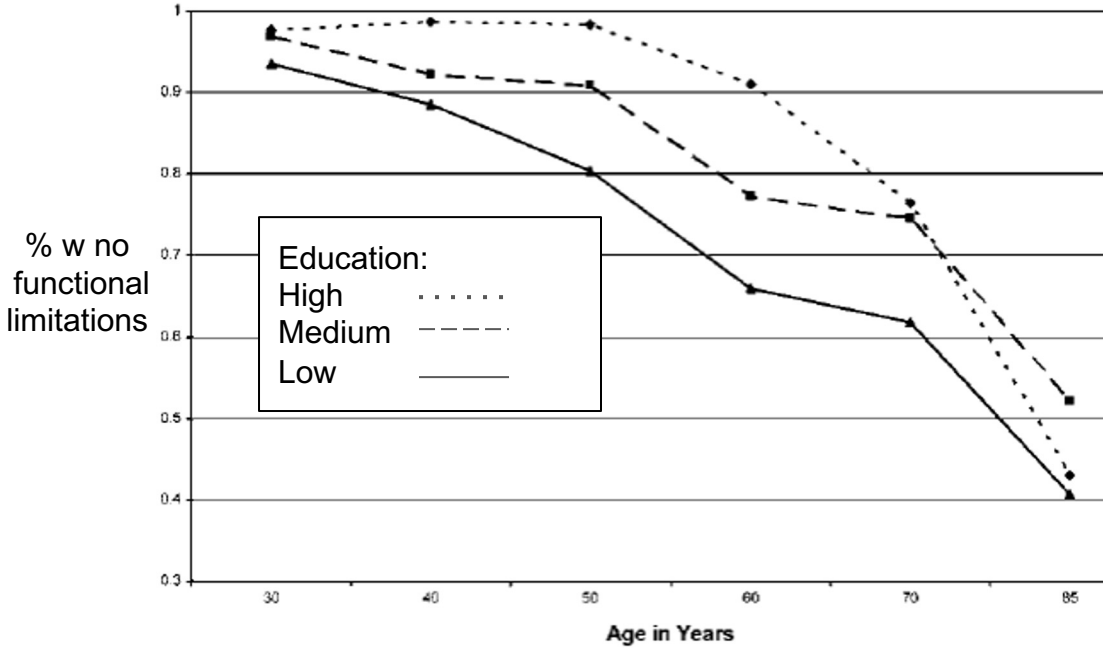
- Access to resources
- Social control:
  - Exposure to aggression & risk
  - Positive social contact

Hierarchies are built relationally…

Not static or chance.

Develop between individuals & groups.

and have salient impacts on health.



House et al. 2005, *Journals of Gerontology Series B*
Americans' Changing Lives Survey 1986-1989

Hierarchies are built relationally…

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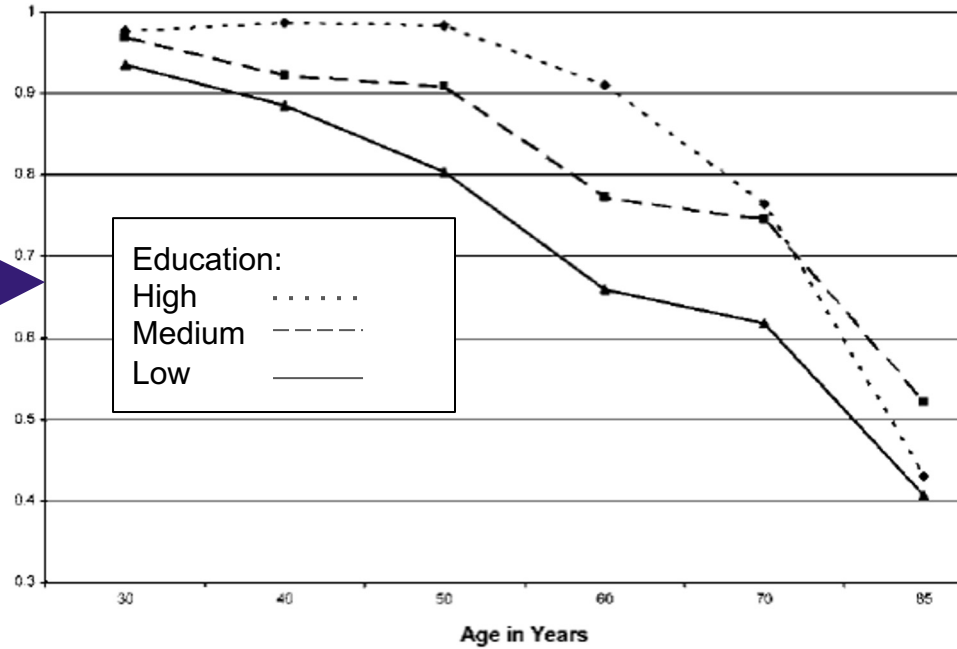
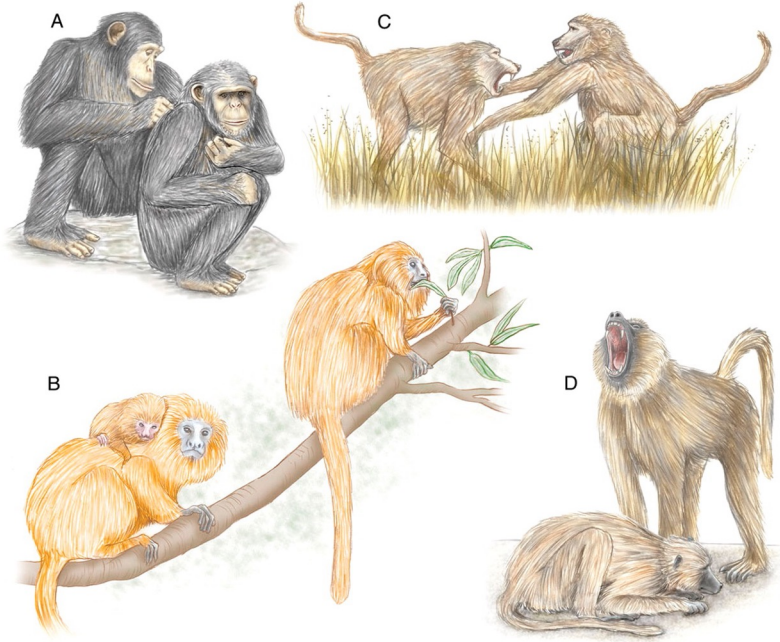
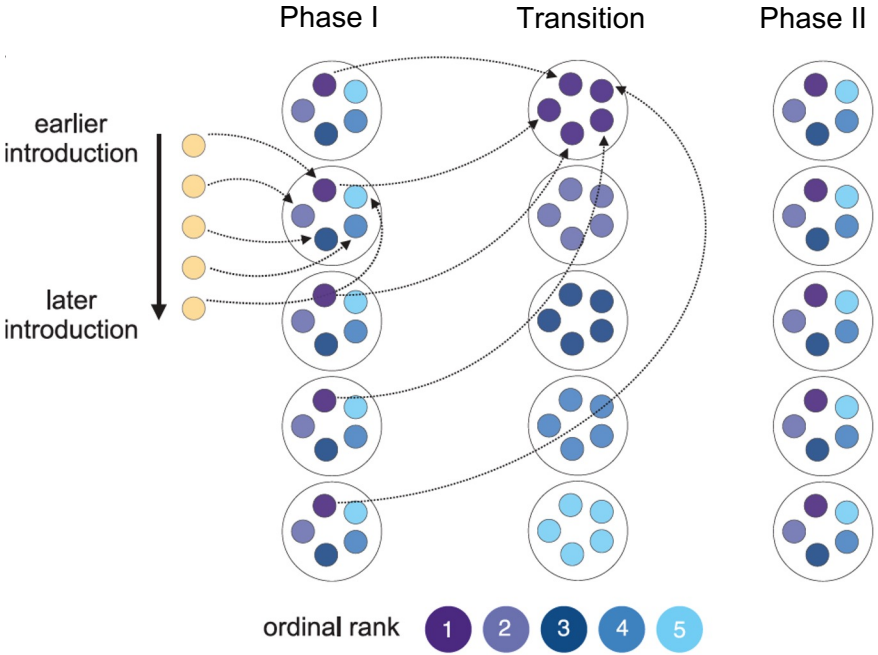


physiologically, how?

NHP provide observational and experimental models of status effects…



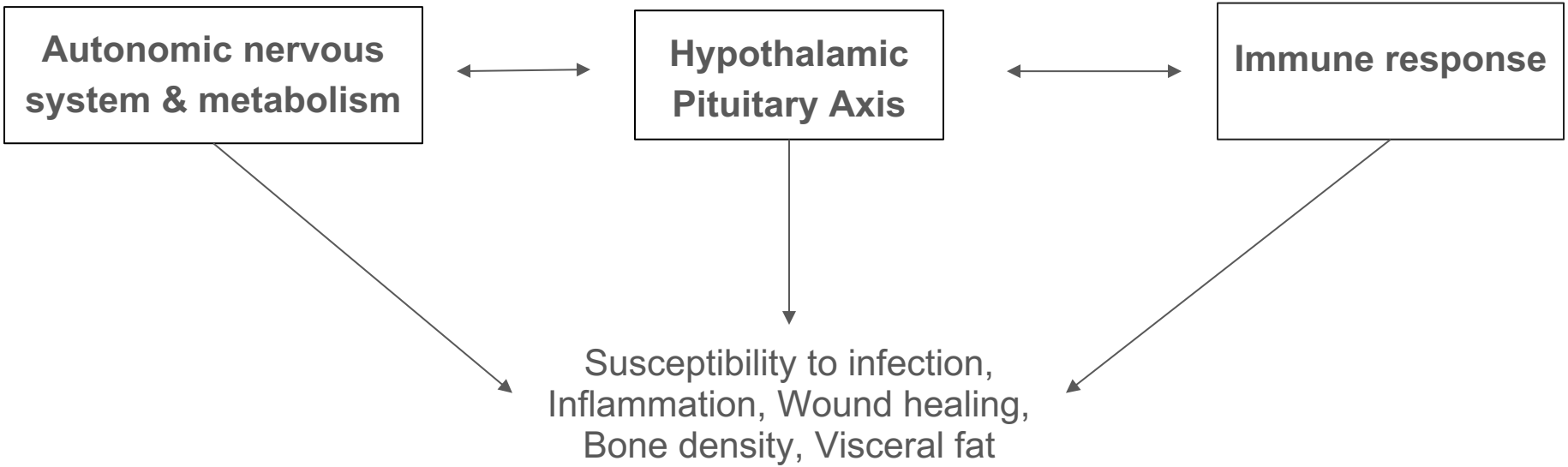
Sapolsky, 2005



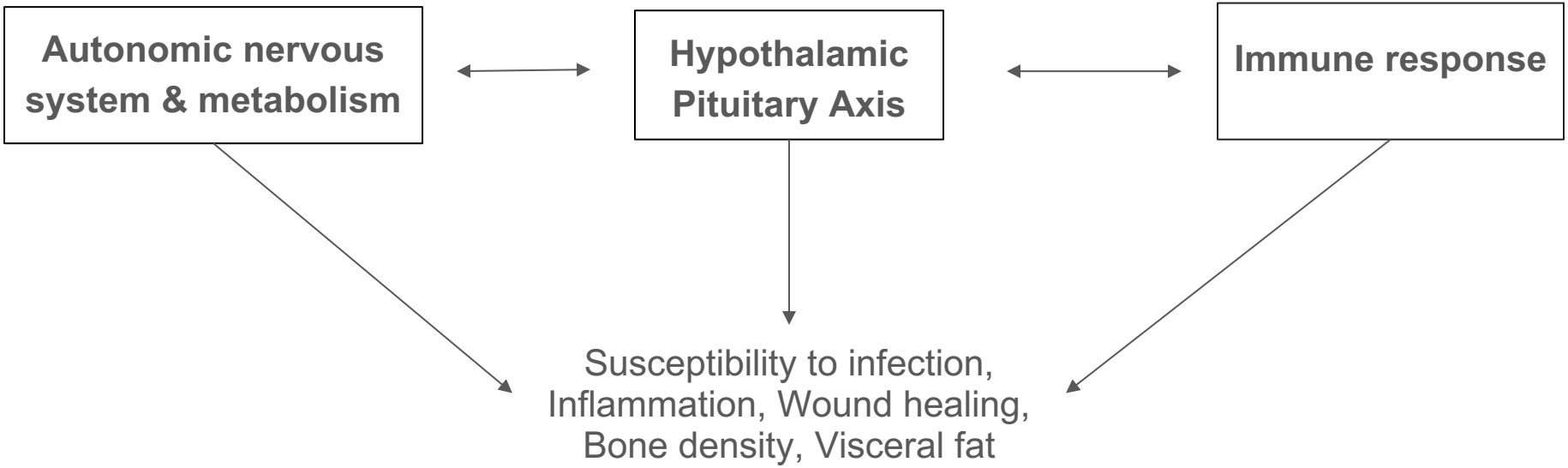
Snyder-Mackler…Tung, 2016

on key physiological pathways.

Physiological pathways responsive* to social status that underlie aging & health disparities

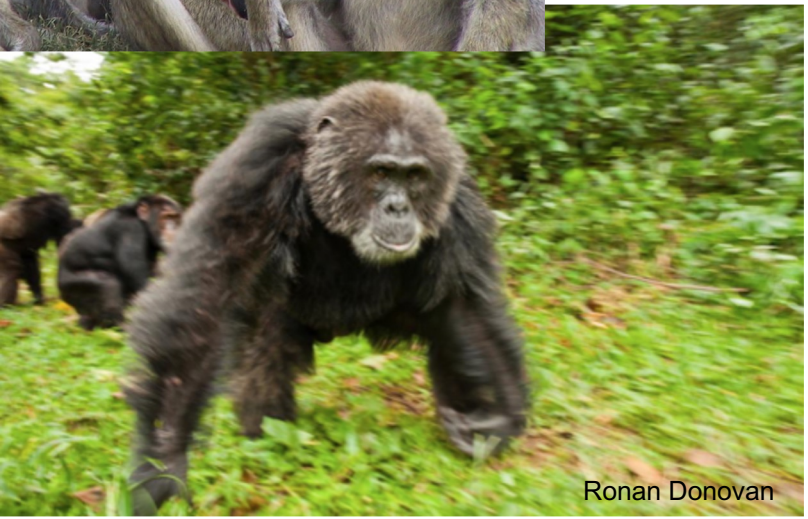


Physiological pathways responsive* to social status that underlie aging & health disparities



*Responsive in some, but not all species…

Status influence on HPA axis



Levy… Alberts, 2020 *Horm & Behav*
Amboseli Baboon Research Project
Muller & Wrangham 2004, *BES*
Kibale Chimpanzee Project
Observational

40+ yrs data on wild primates

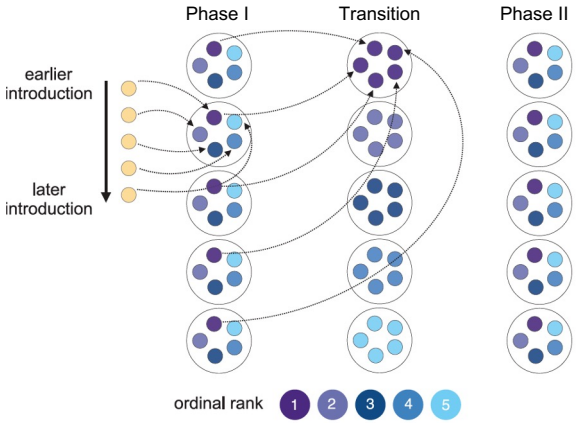
Nature of hierarchy critical:

- Nepotistic
  - Lower rank → higher cortisol
  - Inherited privilege
- Competitive
  - Higher rank → higher cortisol
  - “Executive stress”

Sustained high cortisol → disrupt negative feedback, change gene expression

Status influences immune gene expression

Tung… Gilad, 2012 *PNAS*
Synder-Mackler…Tung, 2016 *Science*
Yerkes National Primate Research Center
Experimental



Immunity strongly differentially expressed by rank

Phenotype: Higher rank ↑ cytotoxic and memory T cell subtypes & NK cells, ↓ granulocytes

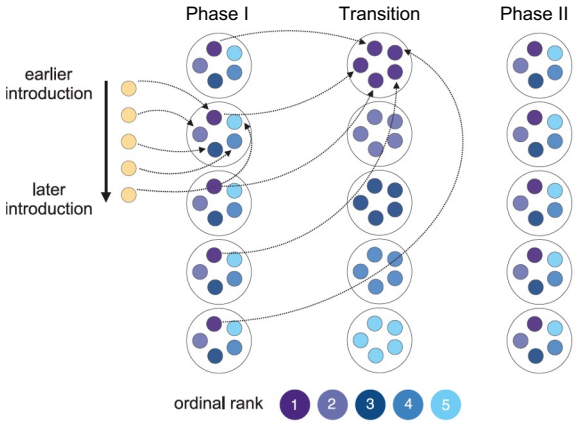
Gene expression: Lower rank ↑ innate & proinflammatory response to bacterial challenge (NFkB, STAT3)

Low status ↑ innate, high ↑ adaptive immunity.

Expression widely mediated by cortisol, grooming, & aggression.

Status influences immune gene expression

Sanz…Barreiro, 2019 PNAS
Yerkes National Primate Research Center
Experimental



Immune response highly plastic to changes in status, but…

Lasting effects:

- **Past** rank determined baseline immune profile
- Past *low* rank moderated current response more strongly than past *high* rank

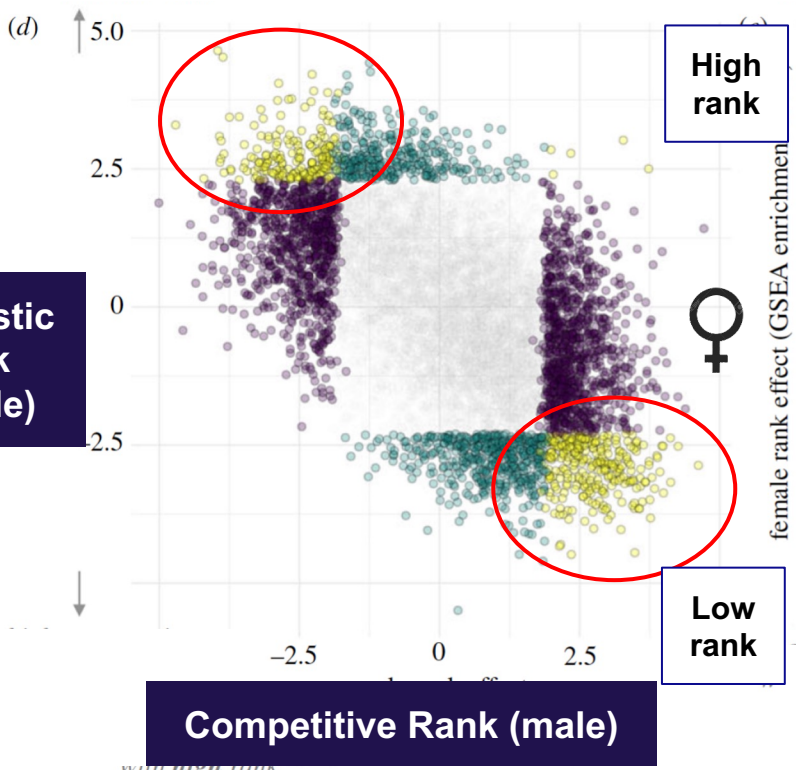
Even adult experiences of subordination influence long-term biology.

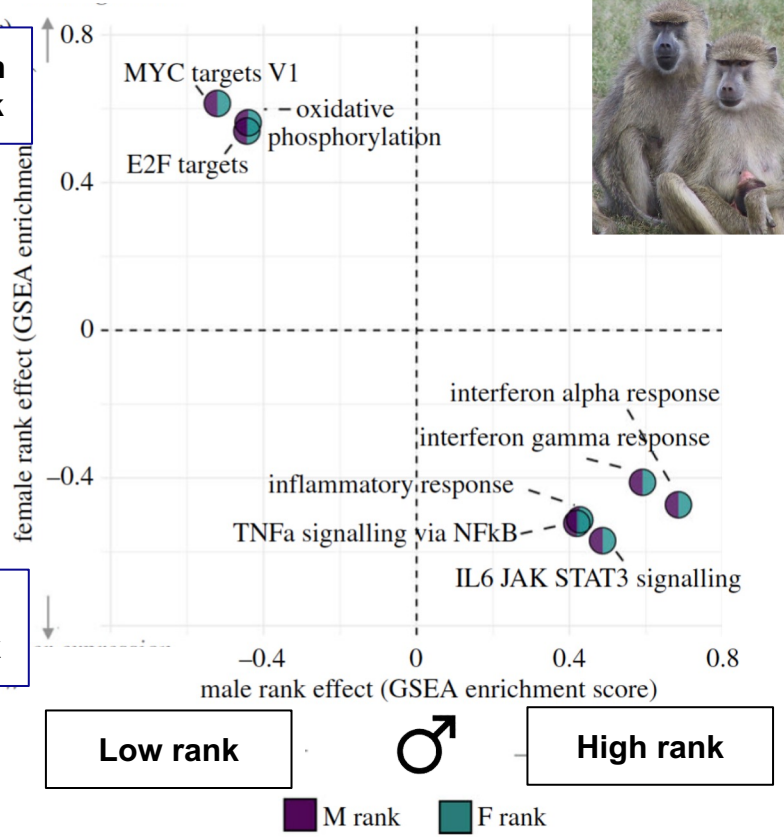
Competitive vs. nepotistic hierarchies yield opposite patterns of gene expression

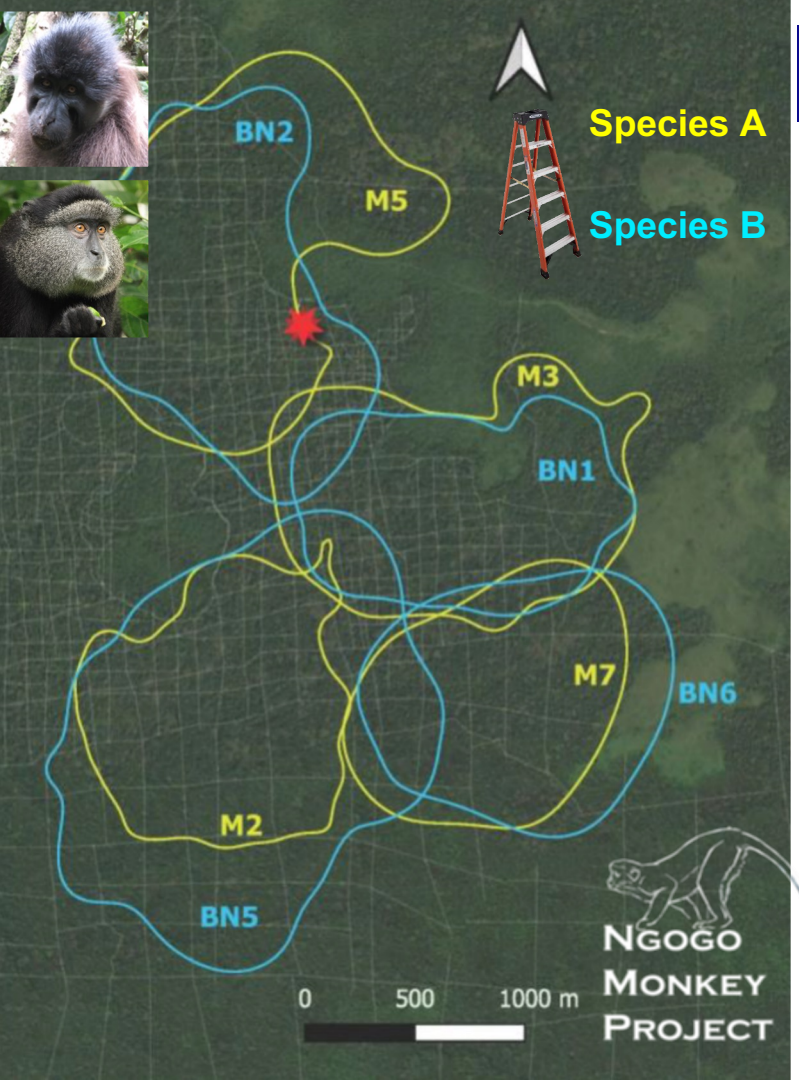
Anderson… Tung, 2022 *Phil Trans*
Amboseli Baboon Research Project
Observational

Nepotistic Rank (female)

Competitive Rank (male)







Primate hierarchies on a larger scale

Thompson González & Brown ***Ngogo Monkey Project***

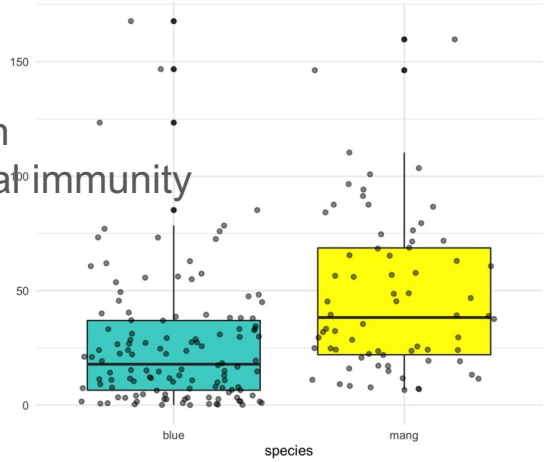
Dominance between naturally co-occurring species common.

Extreme competition → health disparities

Upcoming study:

- Species A dominant to B with high dietary and geographic overlap
- Species B:
  - High parasite load
  - Limited reproduction
  - Suppressed mucosal immunity

sIgA



Primate hierarchies on a larger scale

Thompson González & Brown ***Ngogo Monkey Project***

Study plans:
Subordinate species B at sites 1 vs. 2
with vs. without dominant species A.

Questions:

- Subordination → ↓ adaptive + ↑ innate inflammatory response?
- Cortisol & positive contact mediating?
- Implications for disease susceptibility?

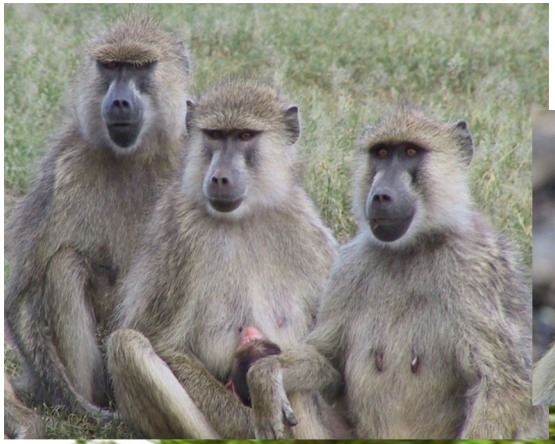
Takeaways

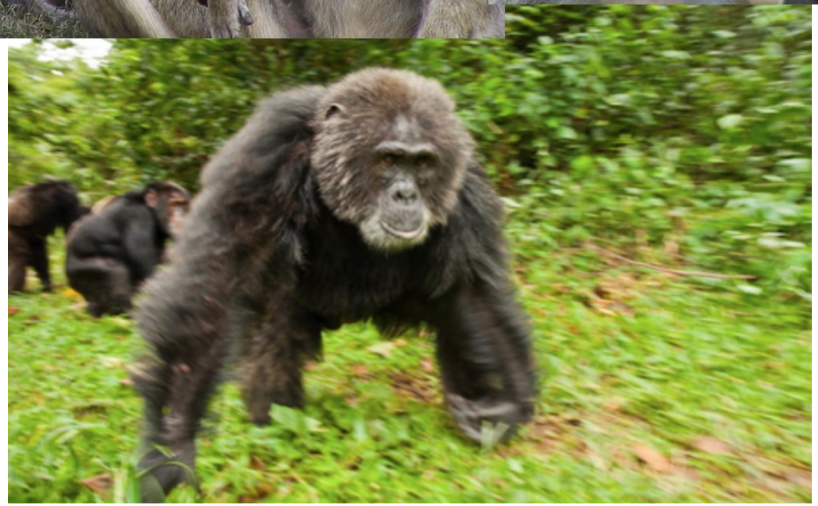
Primates reveal SDOH in tractable models

Low rank in stable, nepotistic hierarchies → higher cortisol, inflammation, & lower adaptive immunity

Past status lingers, especially if low

Links status to healthspan





Takeaways

Primates reveal SDOH in tractable models

Low rank in stable, nepotistic hierarchies → higher cortisol, inflammation, & lower adaptive immunity

Links status to healthspan

Remaining Q's

Mechanism

- Tissue specificity?
- Positive contact & aggression influence different physio pathways?

Environment

- Does subordination at the group level produce disparities?

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