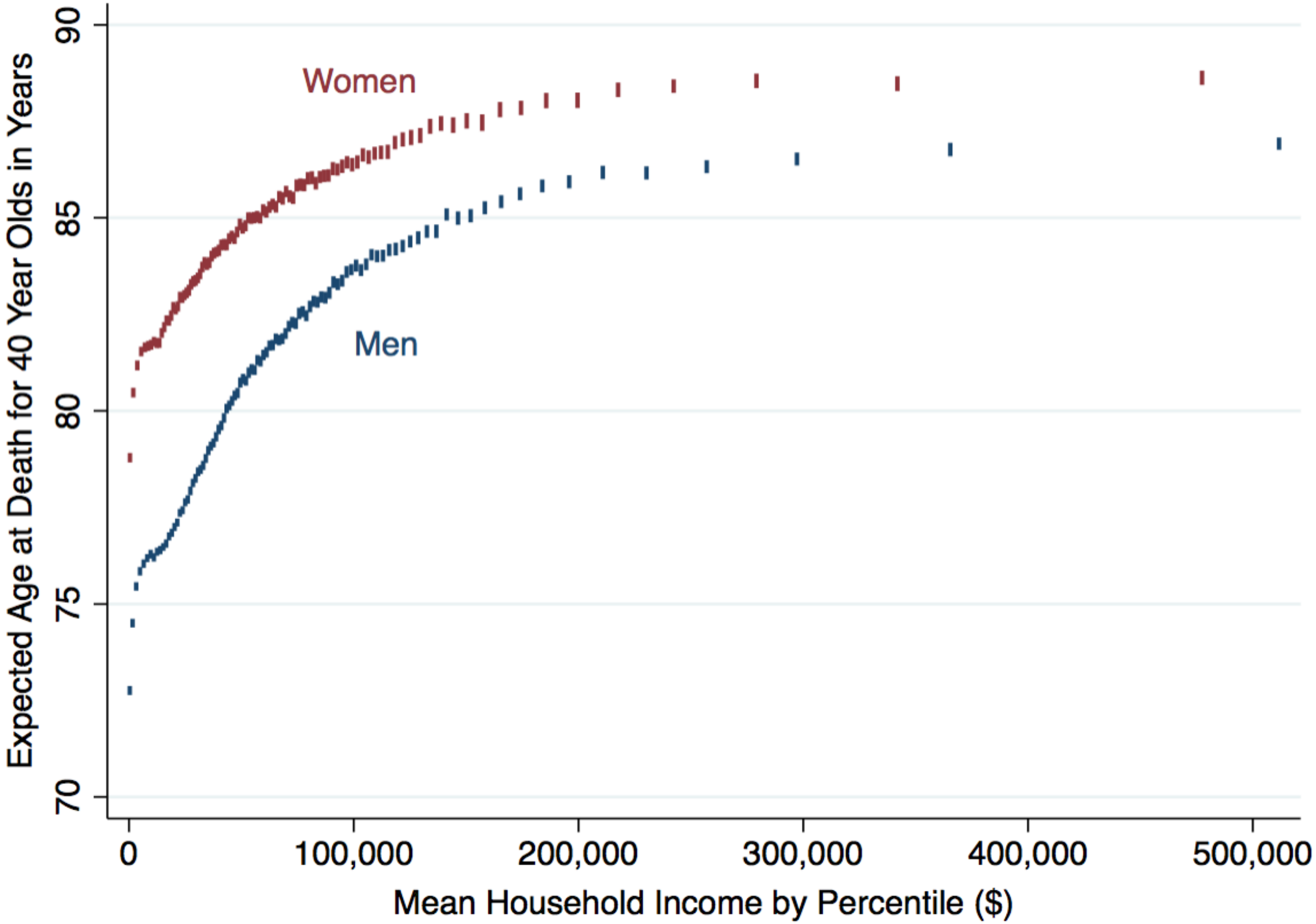
Social gradients, aging, and immunity in social mammals

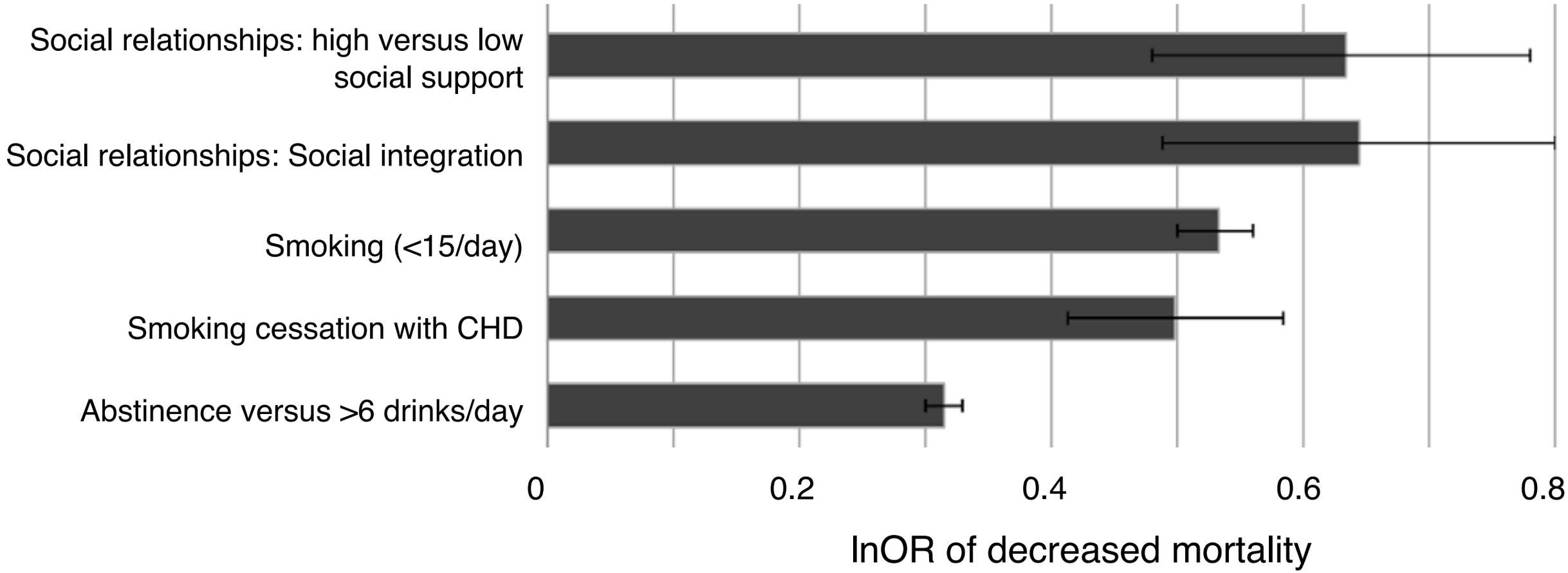
Jenny Tung

Aging and Adaptation in Infectious Diseases: Santa Fe Institute
July 27, 2018

@jtung5
@AmboseliBaboons



from Chetty et al 2016, JAMA



HEALTH

Researchers Confront an Epidemic of Loneliness

By KATIE HAFNER SEPT. 5, 2016

The New York Times

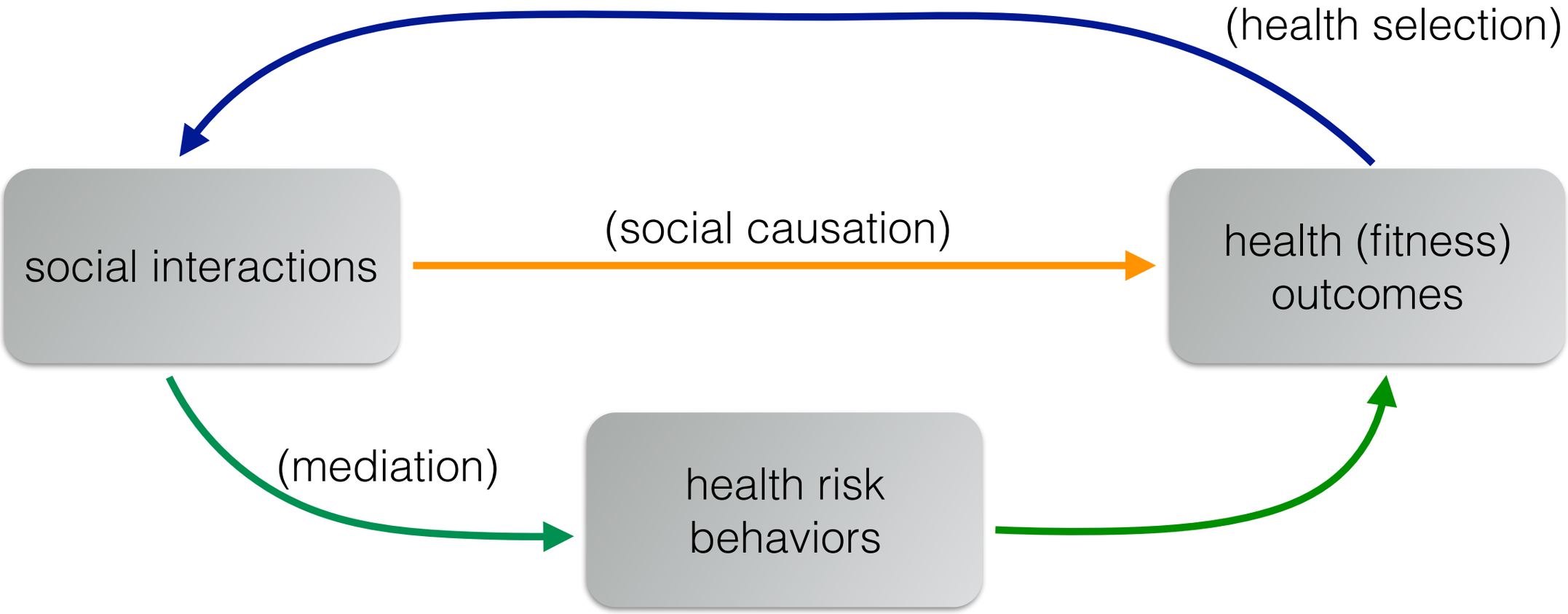
from Holt-Lunstad et al 2010, PLoS Medicine

“we have been accustomed to think…in terms [of] nutritional status, fatigue, overwork or the like. I would suggest…that there is another category of environmental factors capable of producing profound effects on host susceptibility…to disease…and that is the presence of other members of the same species, or more generally, certain aspects of the social environment”

-Cassel (1976)

“…social factors such as socioeconomic status and social support are likely ‘fundamental causes’ of disease that…affect multiple disease outcomes through multiple mechanisms”

-Link and Phelan (1995); Phelan, Link, and Tehranifar (2010)


(health selection)
social interactions
(social causation)
health (fitness) outcomes
(mediation)
health risk behaviors

Beth Archie

Life course studies in natural populations

Alyssa Arre

Experimental studies in captive model systems

Jenny Tung

Jenny Tung

PNAS

Social environment is associated with gene regulatory variation in the rhesus macaque immune system

Jenny Tung[a,1,2], Luis B. Barreiro[a,3], Zachary P. Johnson[b], Kasper D. Hansen[c], Vasiliki Michopoulos[b], Donna Toufexis[b,d], Katelyn Michelini[a], Mark E. Wilson[b], and Yoav Gilad[a,1]

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Edited by Gene E. Robinson, University of Illinois at Urbana–Champaign, Urbana, IL, and approved March 6, 2012 (received for review February 15, 2012)

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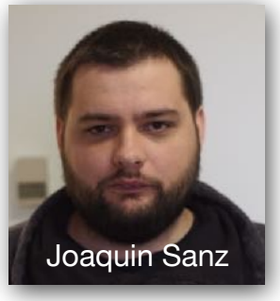
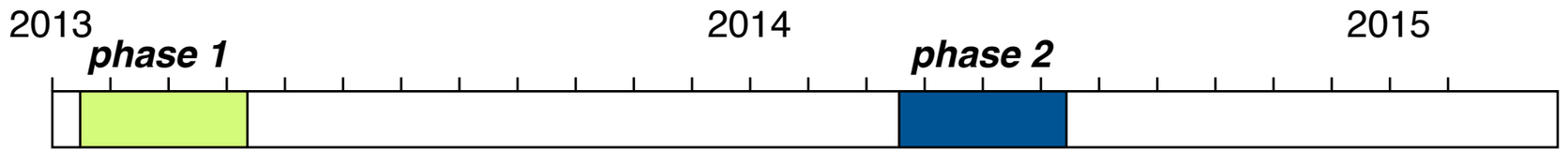
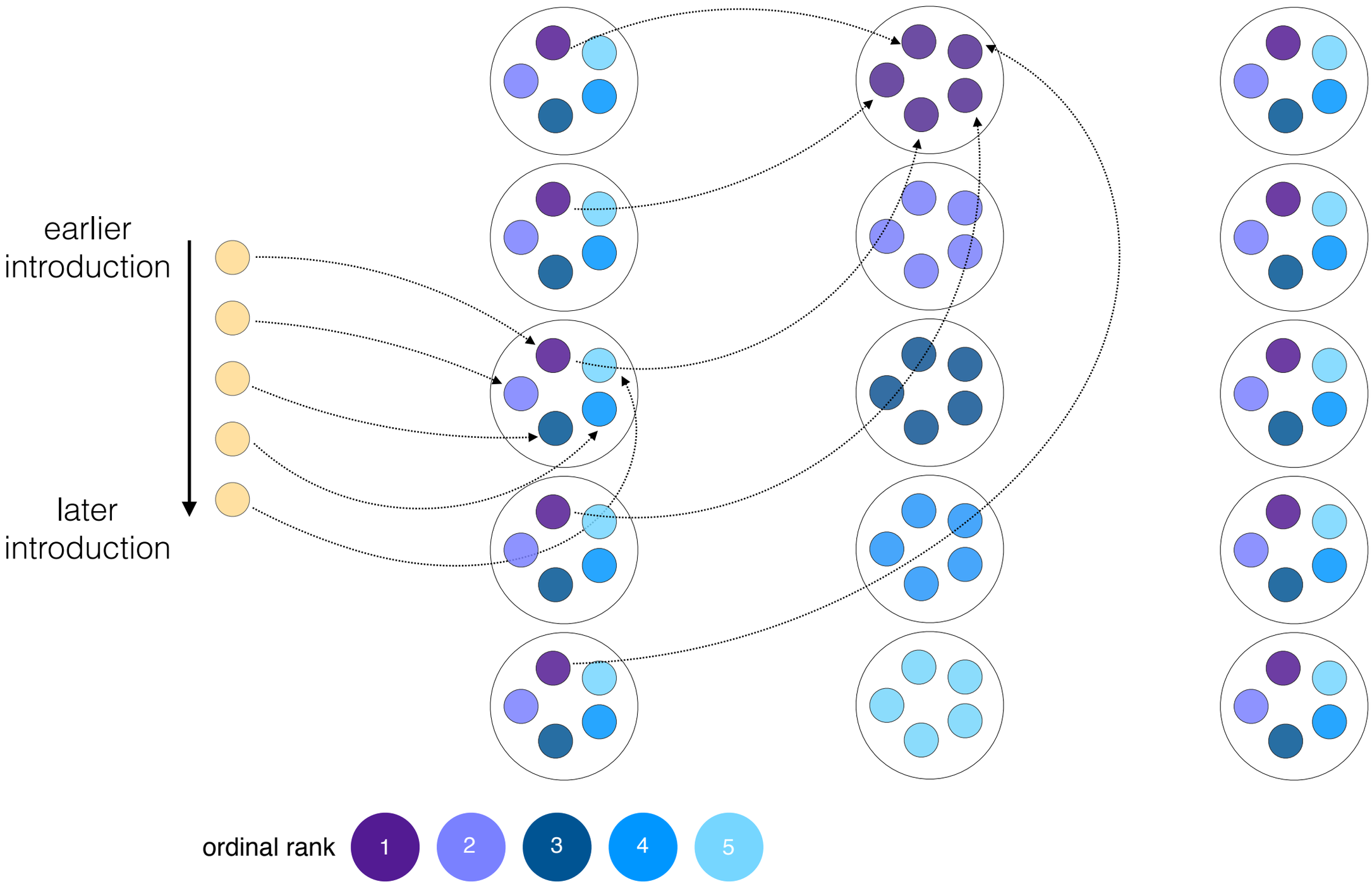
Mark Wilson

Luis Barreiro







Snyder-Mackler, Sanz, et al 2016, Science

order of introduction

1 2 3 4 5

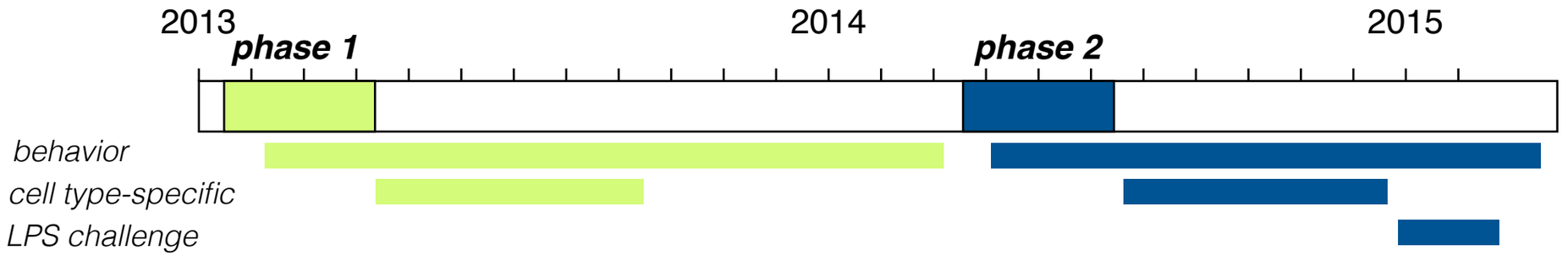
high rank

low rank

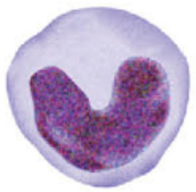
Mar '13

Apr '13

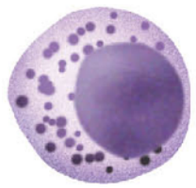
May



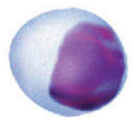
phase 1 + 2



monocyte
CD14+



Natural Killer
CD16+



helper T
CD3+ CD4+

cytotoxic T
CD3+ CD8+

B cell
CD20+

phase 2

media only (control)

4 hour
incubation, 37 C

media + lipopolysaccharide
(LPS)

harvest cells

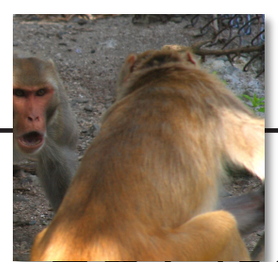
n = 45 females,
matched neg control (NC) and
LPS+ RNA-samples at 4 hrs
(9,047 genes)

$r_{(PC2,Elo)}=0.83$
$p < 10^{-15}$

Elo (NC)
1800
900
0

Elo (LPS)
1800
900
0

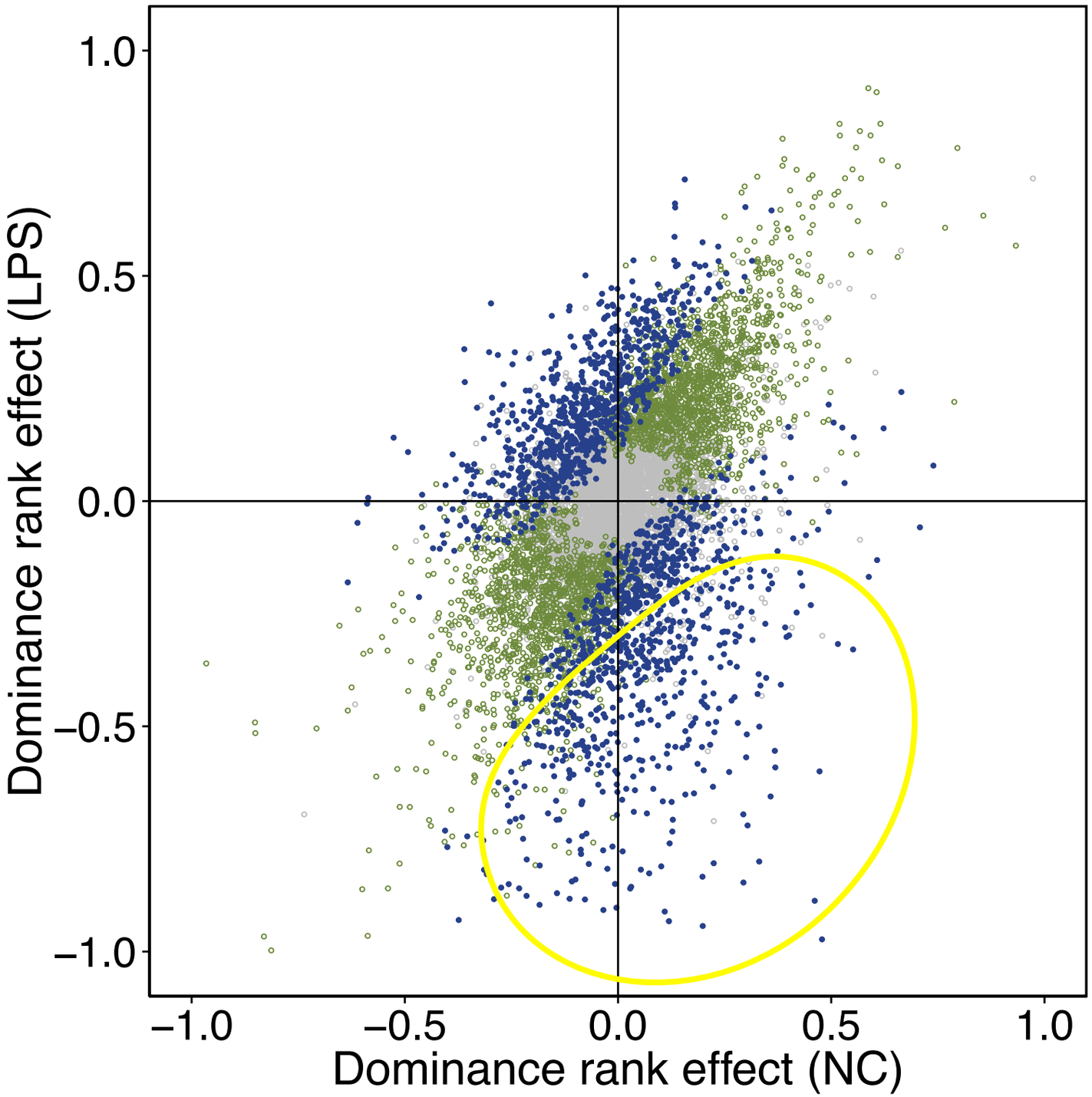
PC2 (22.5% variance)
5
0
−5

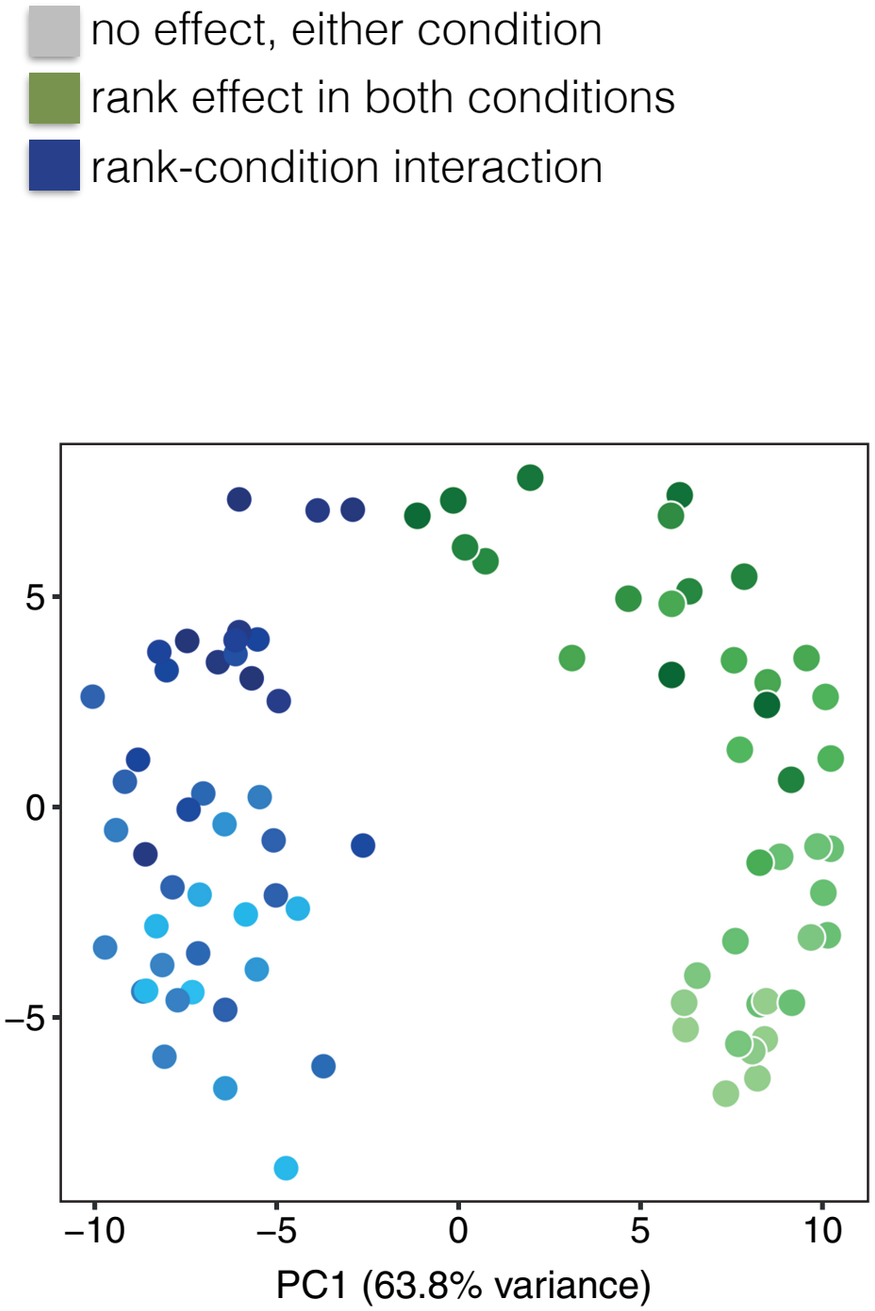


−10
0
5
10

PC1 (63.8% variance)

$r_{(PC1,condition)}=0.942$
$p < 10^{-15}$


1.0
0.5
0.0
−0.5
−1.0
−1.0
−0.5
0.0
0.5
1.0
Dominance rank effect (LPS)
Dominance rank effect (NC)


no effect, either condition
rank effect in both conditions
rank-condition interaction
5
0
−5
−10
−5
0
5
10
PC2 (22.5% variance)
PC1 (63.8% variance)

lower exp in high rank

high exp in high rank

upregulated in LPS

down regulated in LPS

NFKBID

795 genes

IRF9

439 genes

TNFRSF21

742 genes

TNFSF13

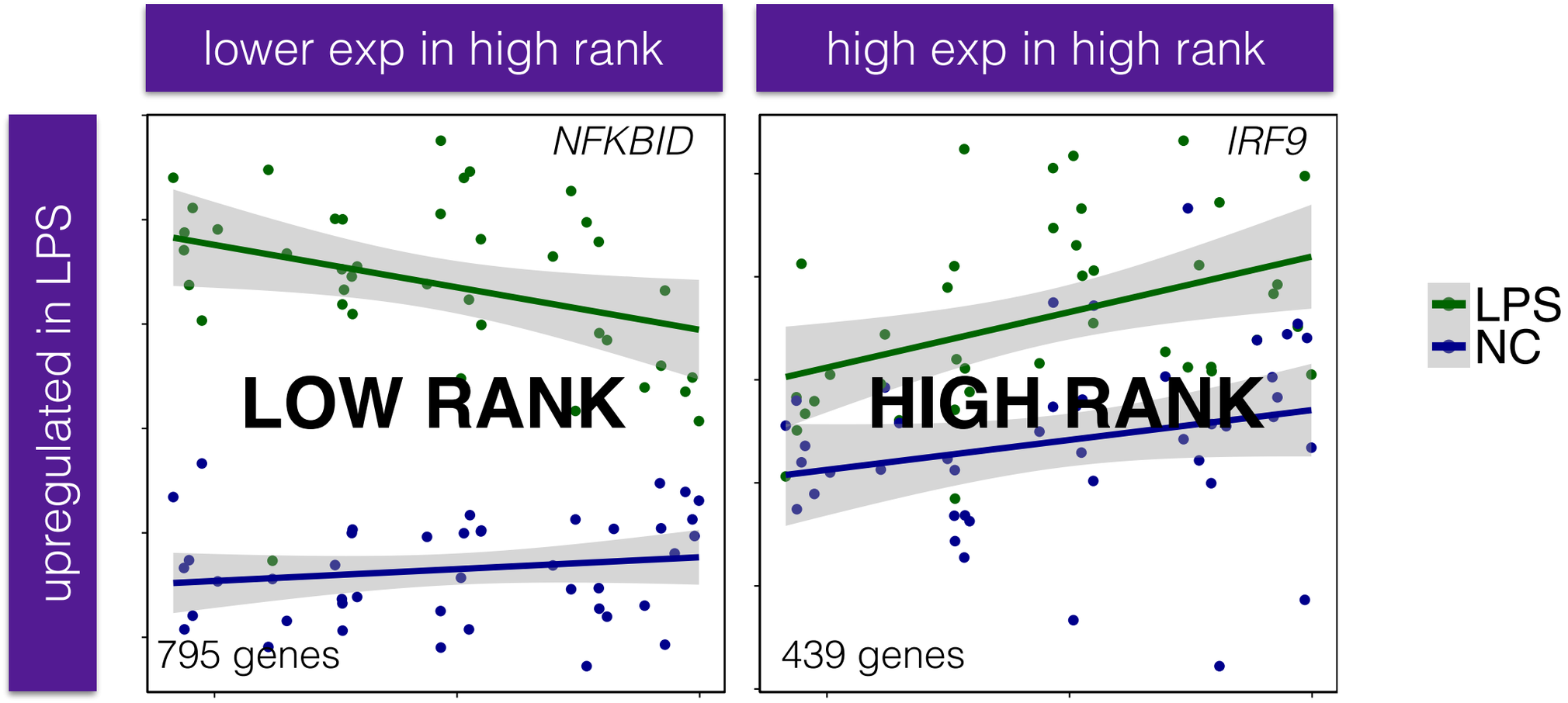
697 genes

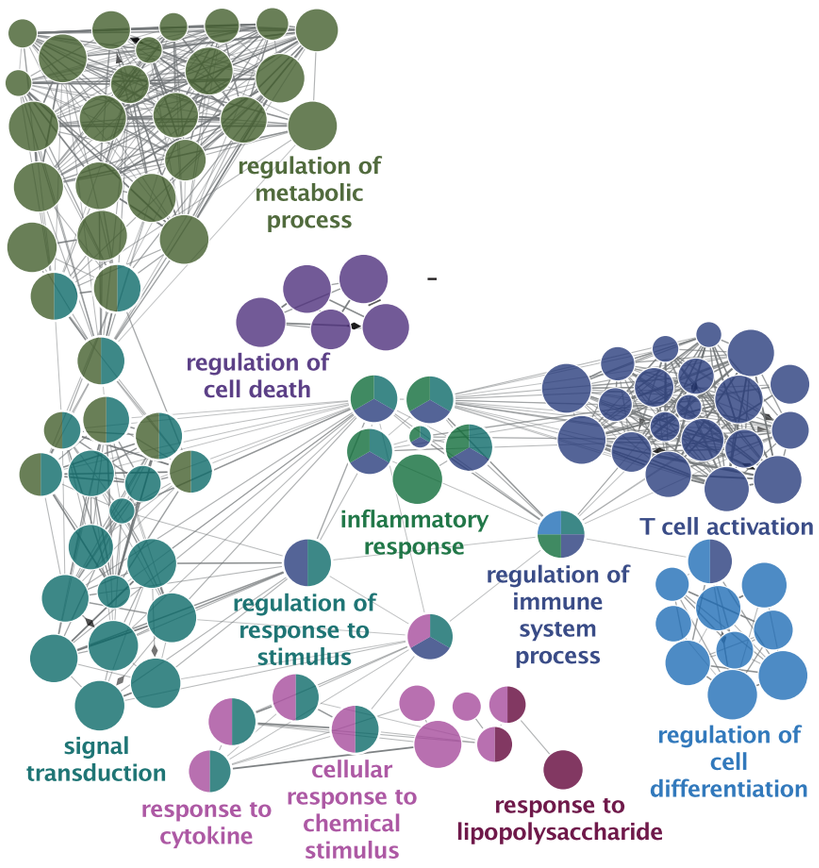
LPS

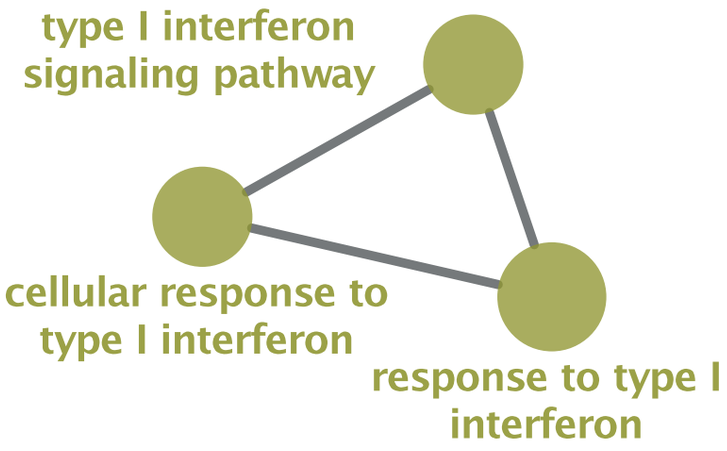
NC

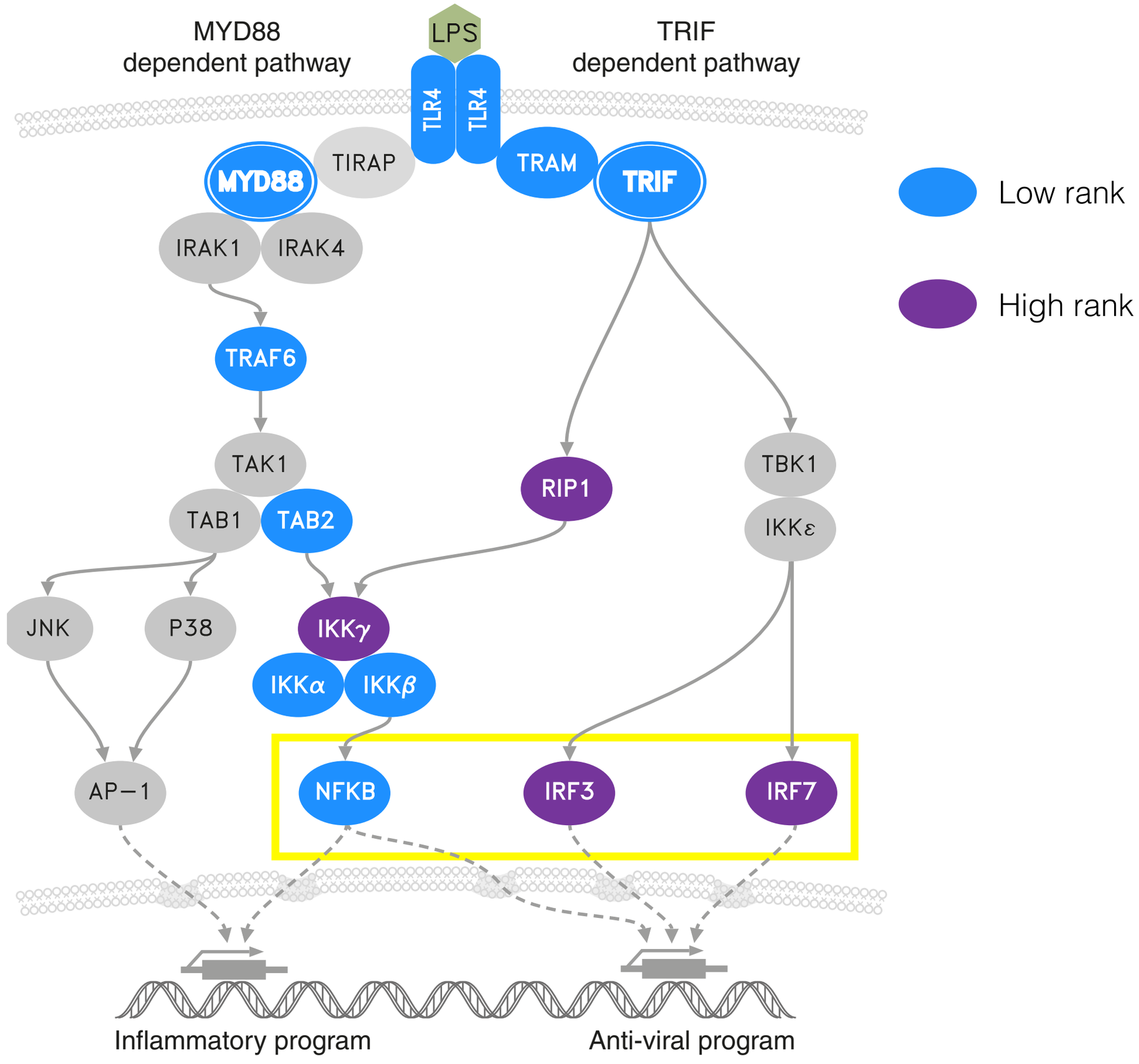
low rank

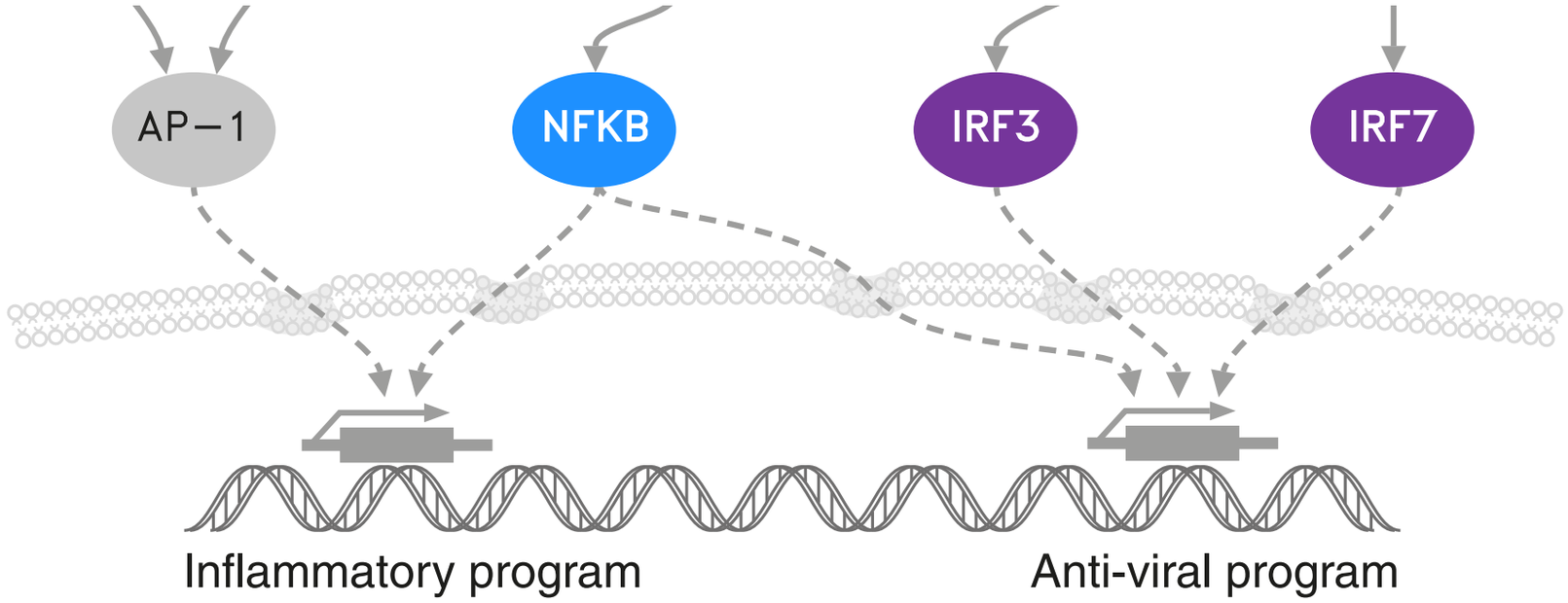
high rank


lower exp in high rank
high exp in high rank
upregulated in LPS
NFKBID
IRF9
LOW RANK
HIGH RANK
795 genes
439 genes
LPS
NC

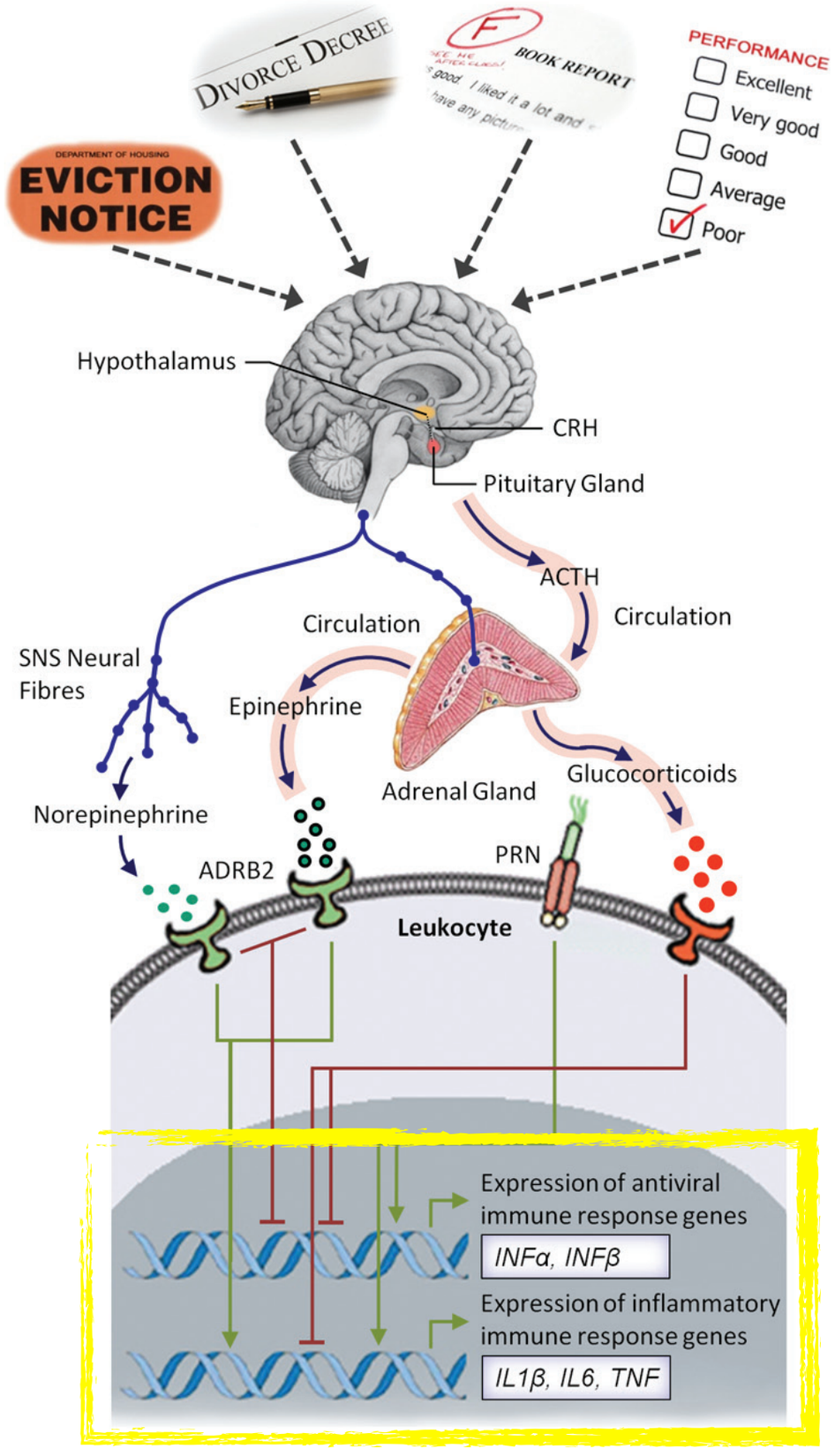

regulation of metabolic process
regulation of cell death
inflammatory response
T cell activation
regulation of response to stimulus
regulation of immune system process
signal transduction
response to cytokine
cellular response to chemical stimulus
response to lipopolysaccharide
regulation of cell differentiation

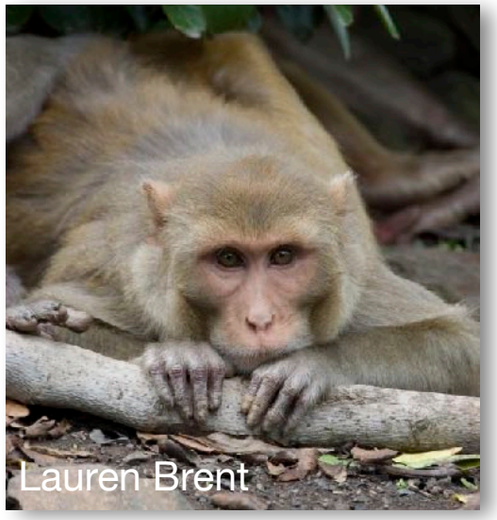

type I interferon signaling pathway
cellular response to type I interferon
response to type I interferon

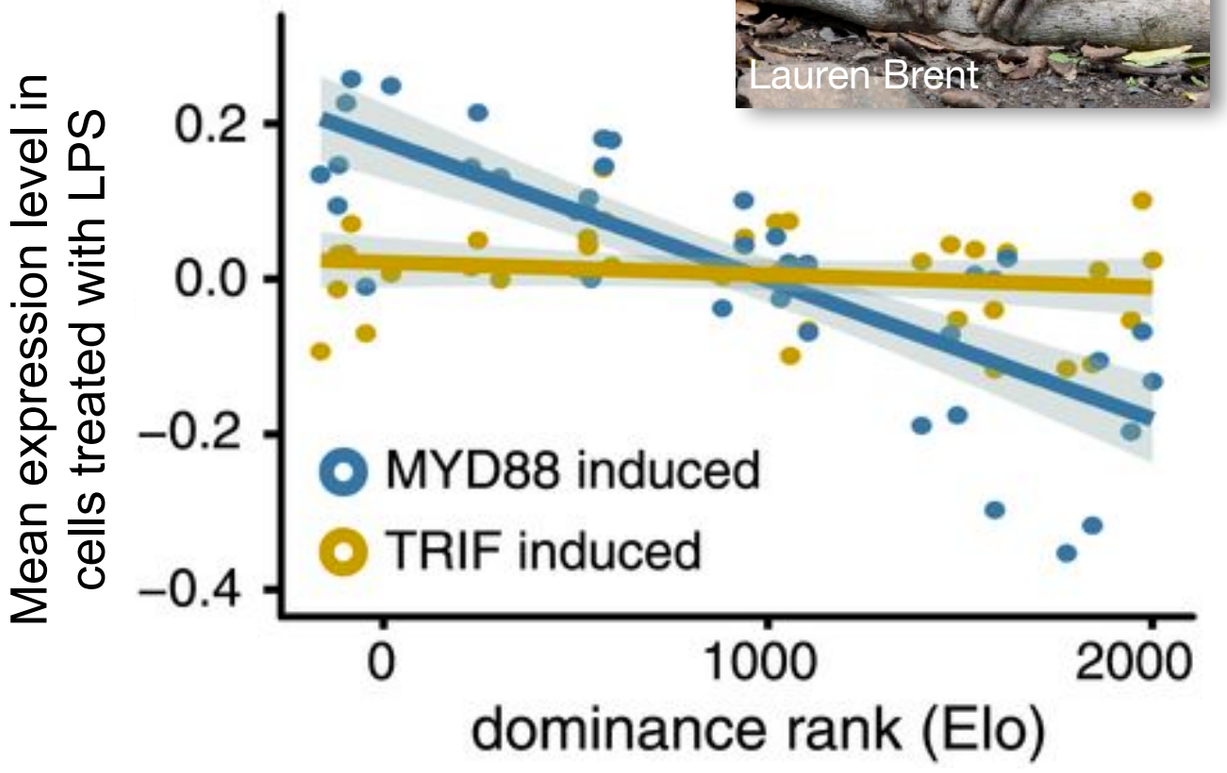

MYD88
dependent pathway
LPS
TRIF
dependent pathway
TLR4
TLR4
TIRAP
TRAM
MYD88
TRIF
IRAK1
IRAK4
TRAF6
TAK1
TAB1
TAB2
RIP1
TBK1
IKKε
JNK
P38
IKKγ
IKKα
IKKβ
AP−1
NFKB
IRF3
IRF7
Low rank
High rank
Inflammatory program
Anti-viral program



(see also Snyder-Mackler et al 2018, bioRxiv)







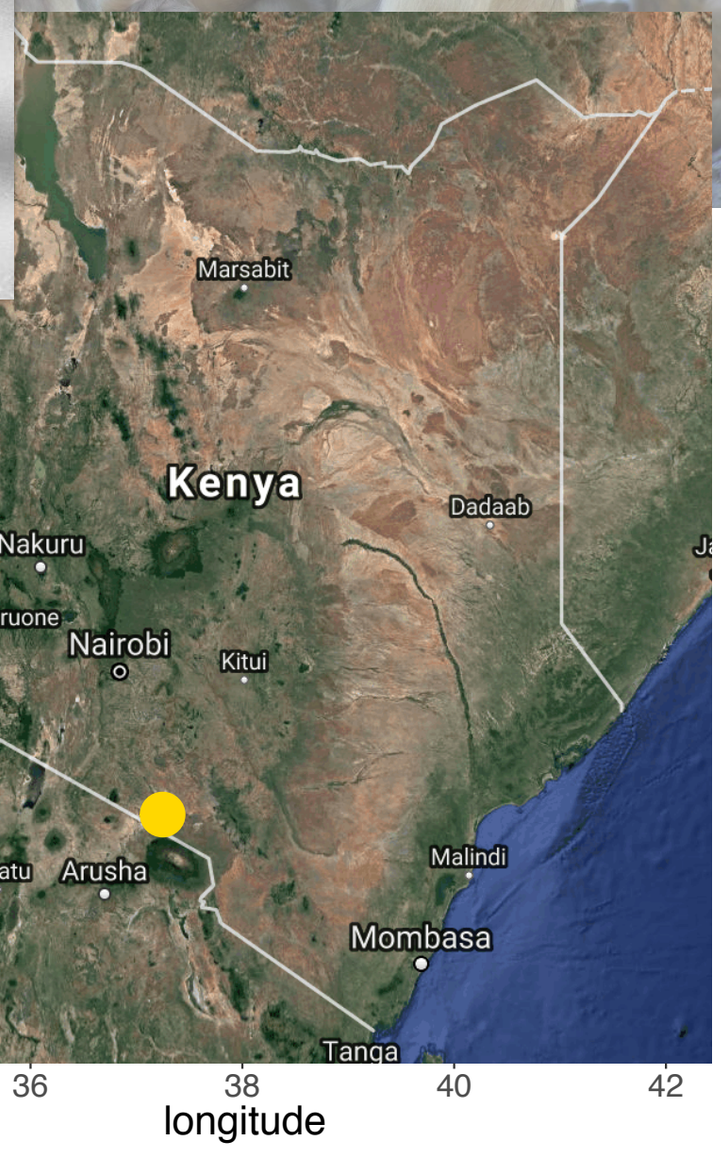
**mouse KO data from Ramsey et al 2008, PLoS Comp Bio*

"conserved transcriptional response to adversity"

from Slavich and Cole 2013, Clin Psych Sci

Beth Archie

Jeanne Altmann



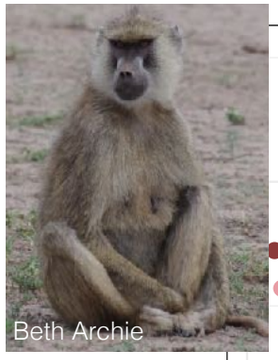
null

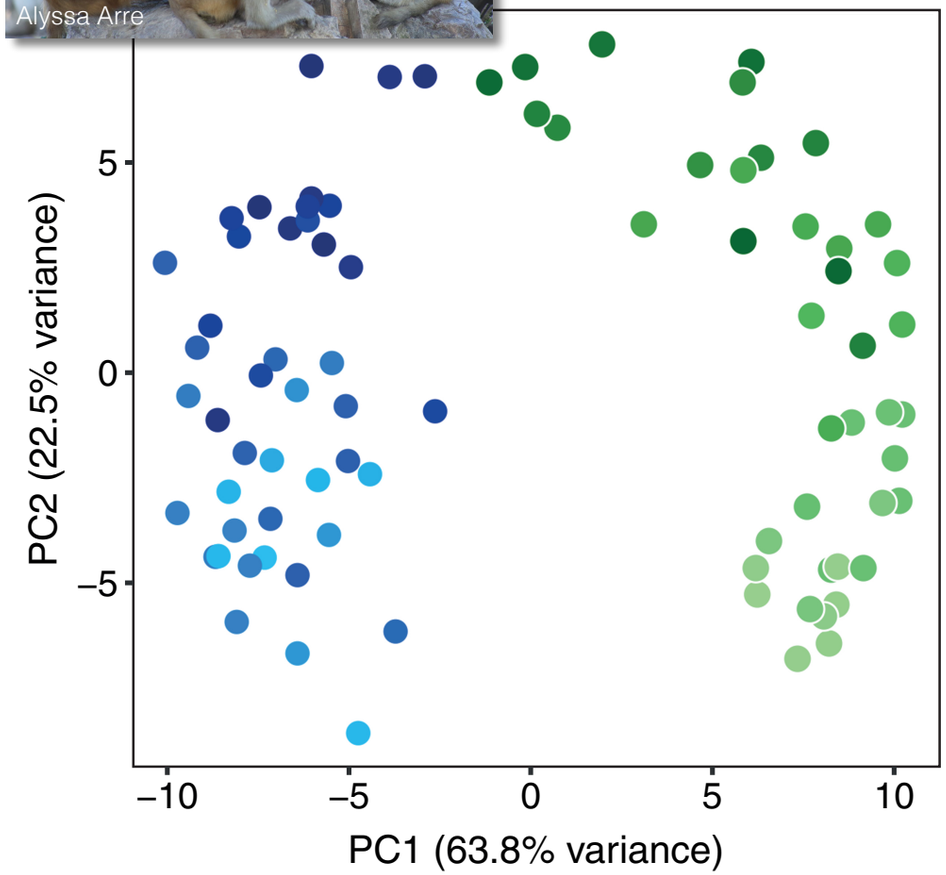
LPS+

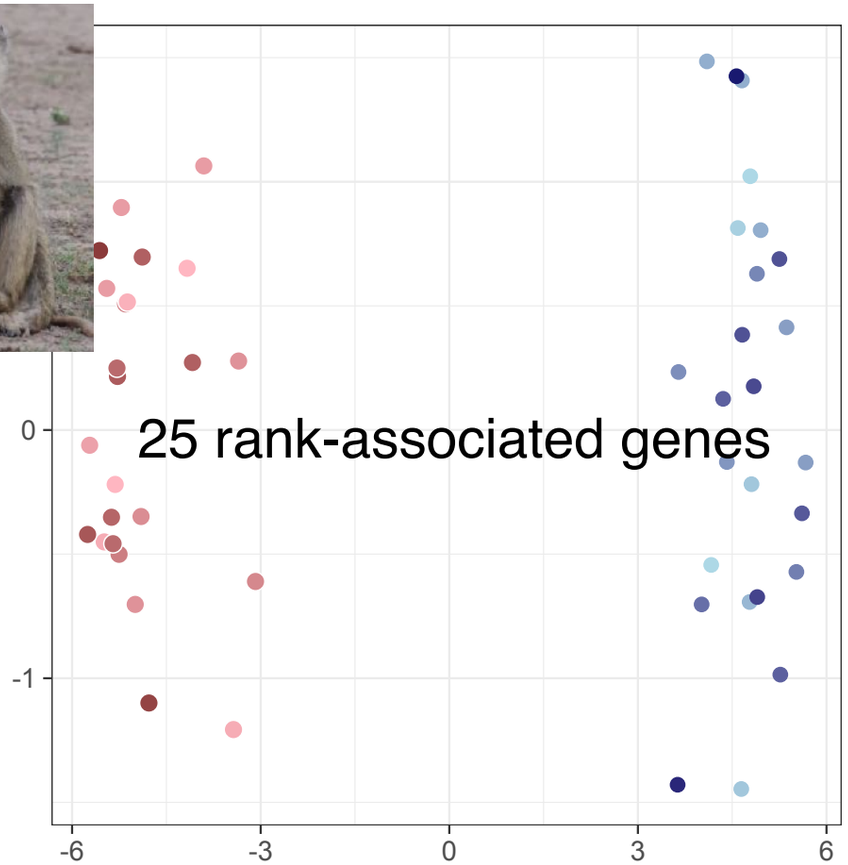
26 adult females, 35 adult males (n=121 post-QC samples)

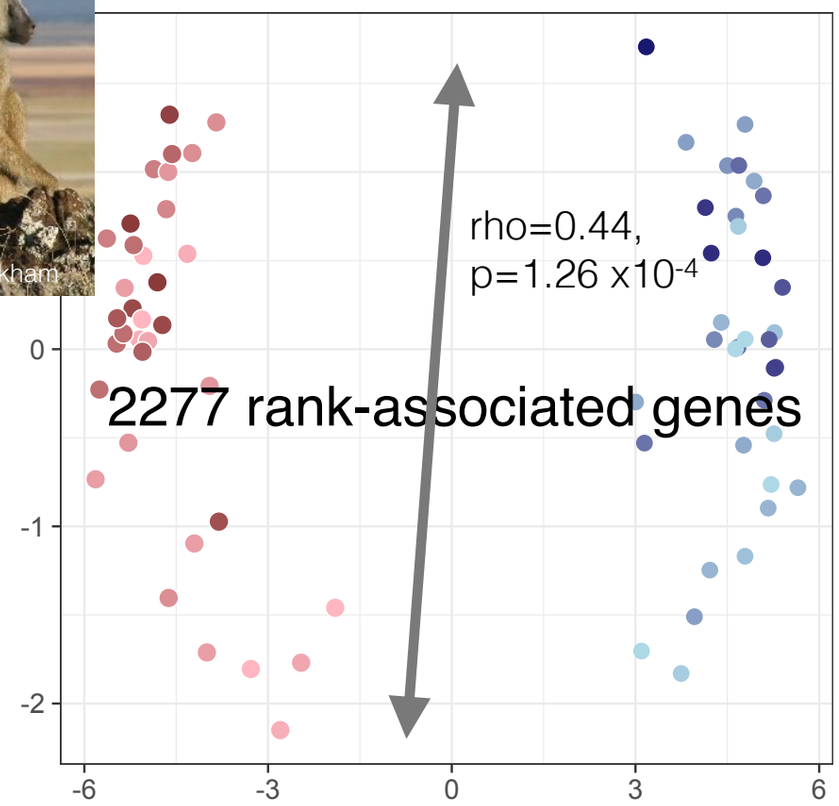
Amanda Lea

Jeanne Altmann



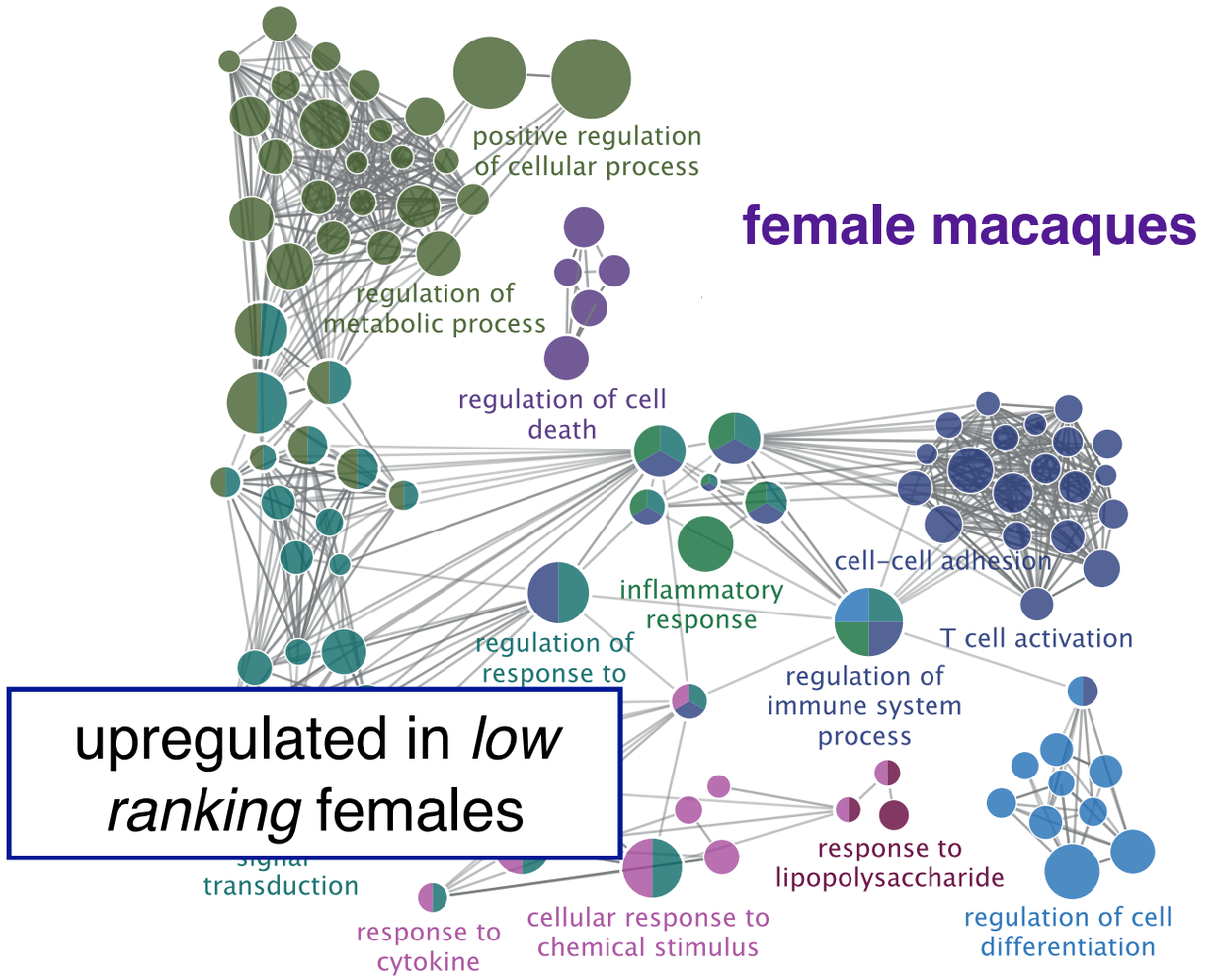




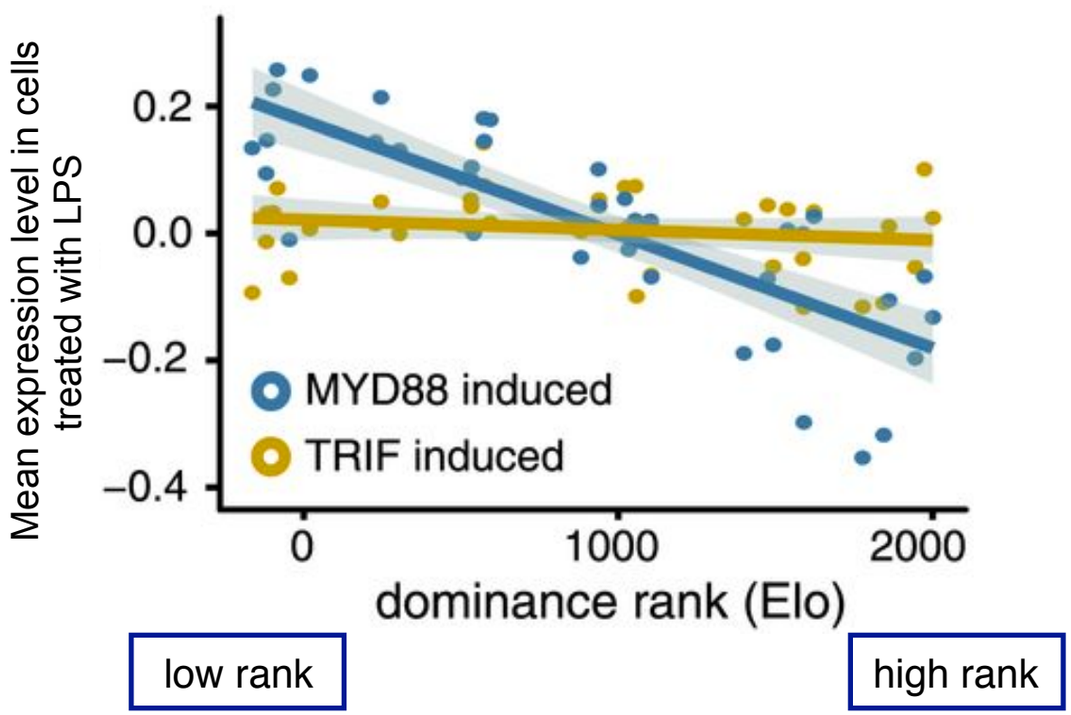


Lea et al 2018, bioRxiv

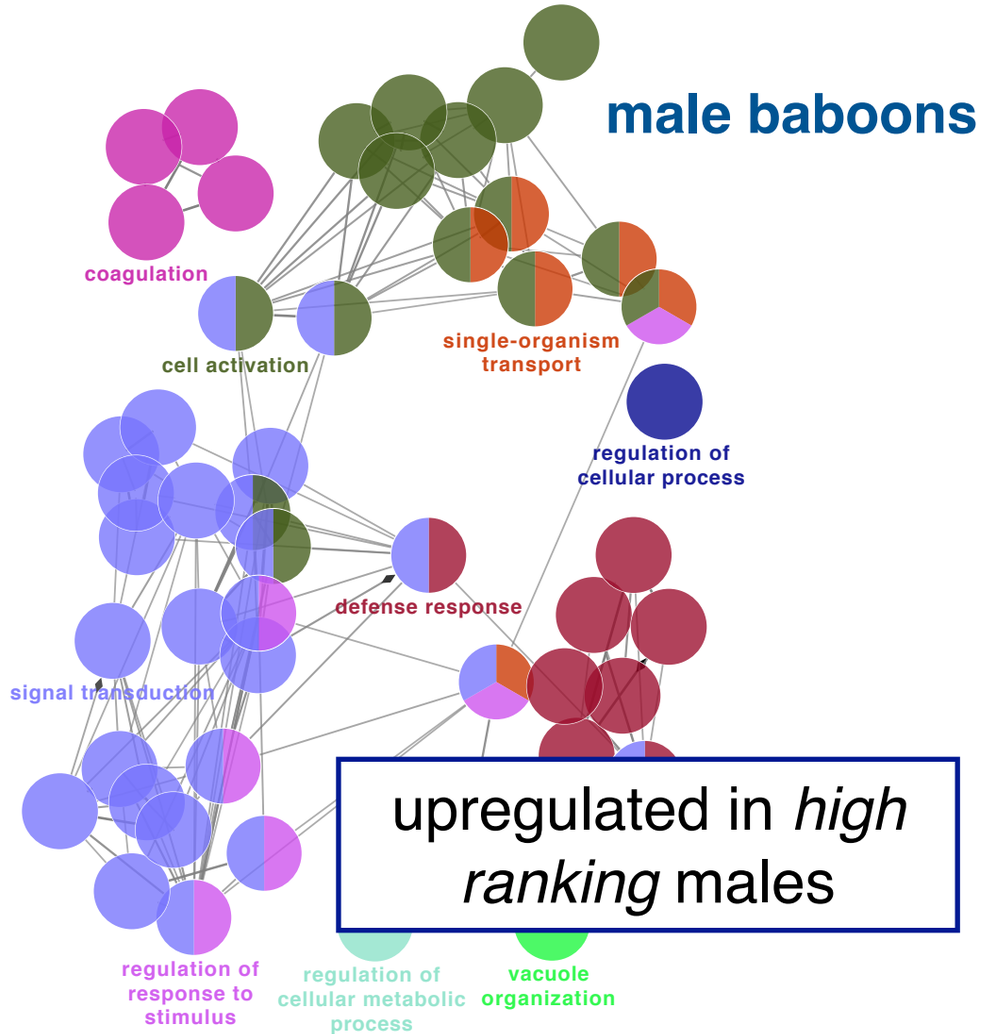
female macaques



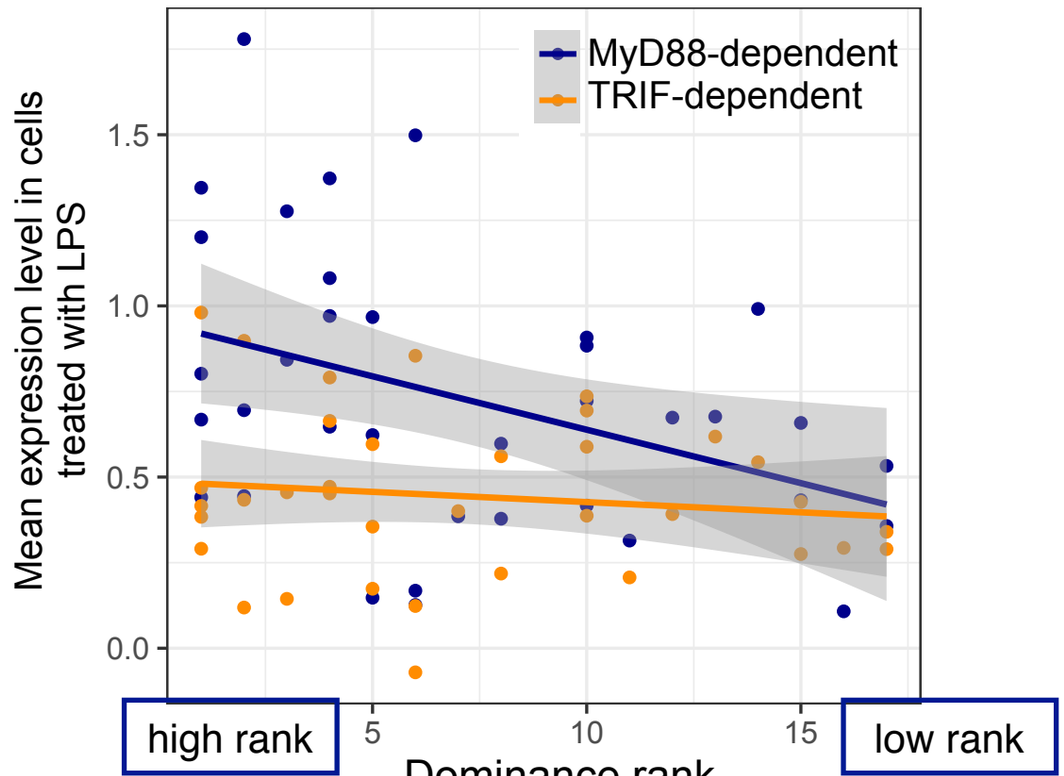
upregulated in *low ranking* females



male baboons

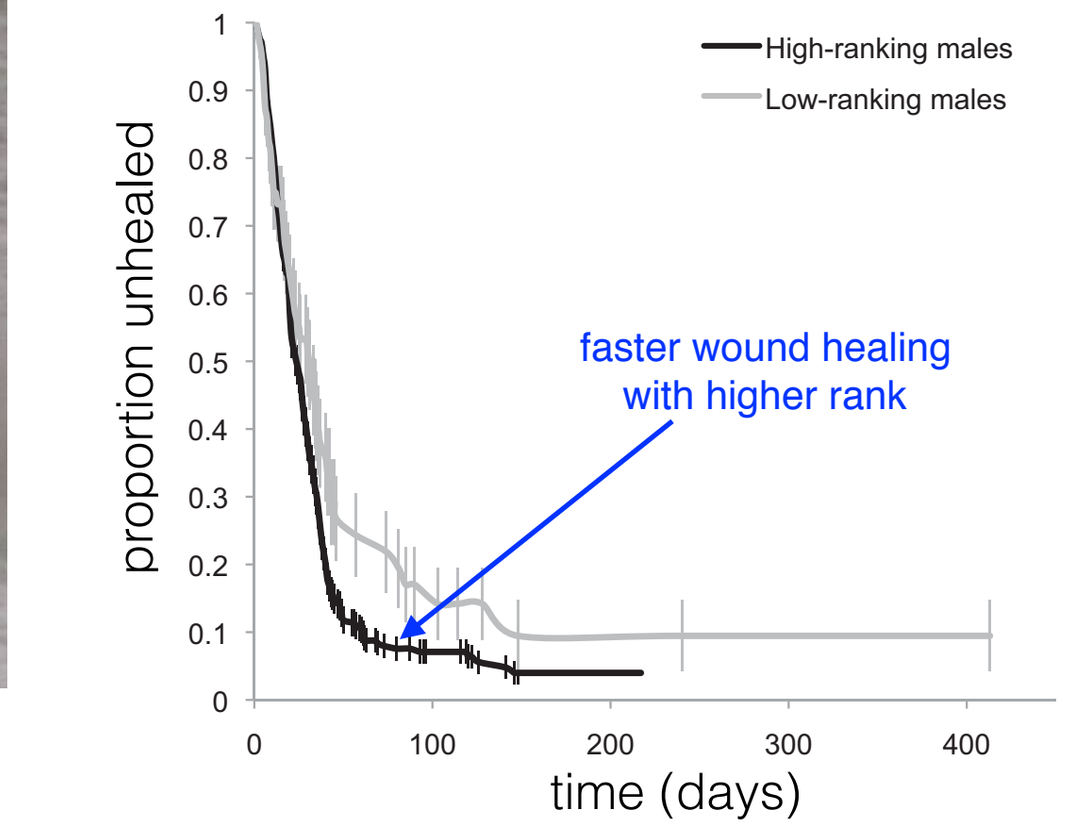


upregulated in *high ranking* males



Beth Archie

from Archie et al 2012



- How does the social environment-immune relationship vary depending on the *nature of hierarchies*, *the local environment, or individual characteristics?*

- How stable are the effects of social interactions over time? How does stability depend on the outcome measure?

- What is the adaptive value (if any) of these responses?

- How does social history interact with exposure history (and age)?

- To what degree do these interactions explain increased variance by chronological age?

Thanks!

BABOONS:
Susan Alberts (Duke)
Jeanne Altmann (Princeton)
Beth Archie (Notre Dame)

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Serah Sayialel
Kinyua Warutere
Tim Wango
Vivian Oudu
Mercy Akinyi
Ruth Nyakundi
Institute of Primate Research
Kenya Wildlife Service

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Vasiliki Michopoulos (Emory)
Jordan Kohn (Emory)
Zach Johnson (now Illumina)
Jessica Brinkworth (now Illinois)
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Robbie Burger
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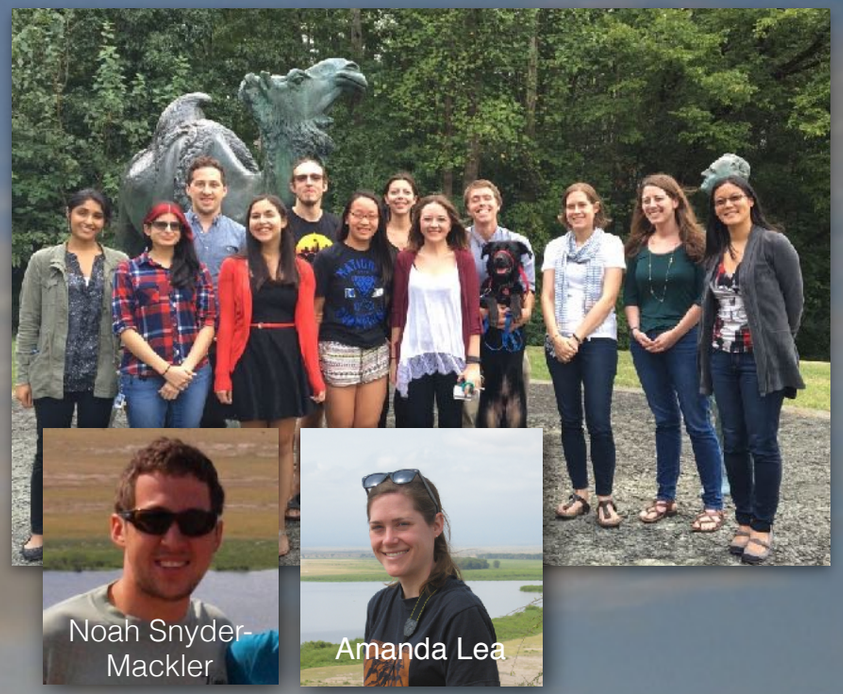

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Yingying Zhang

Jenny Tung