Host genetic determinants of the microbiome

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Penn State University

https://davenport-lab.github.io

@emo_davenport

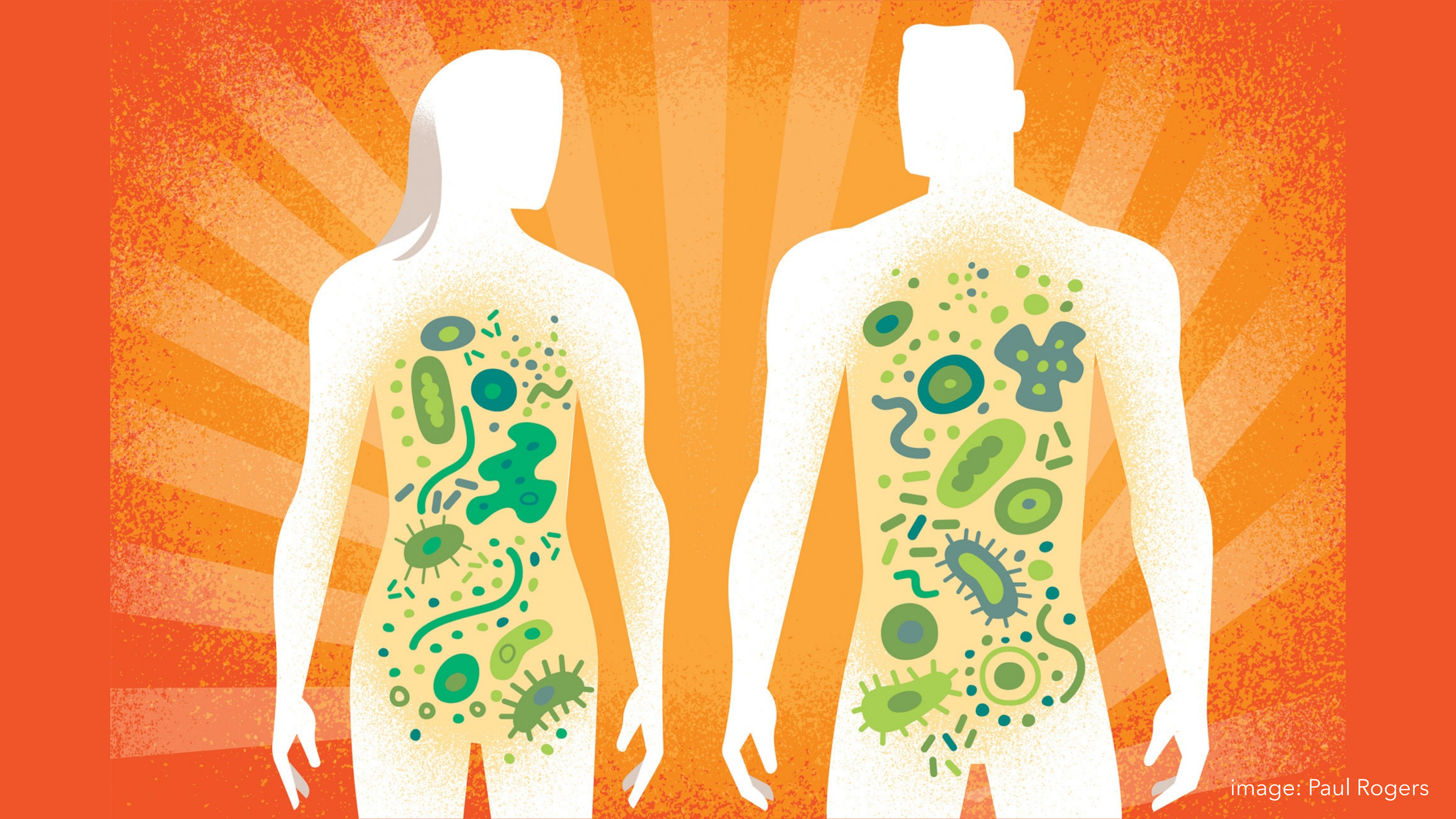
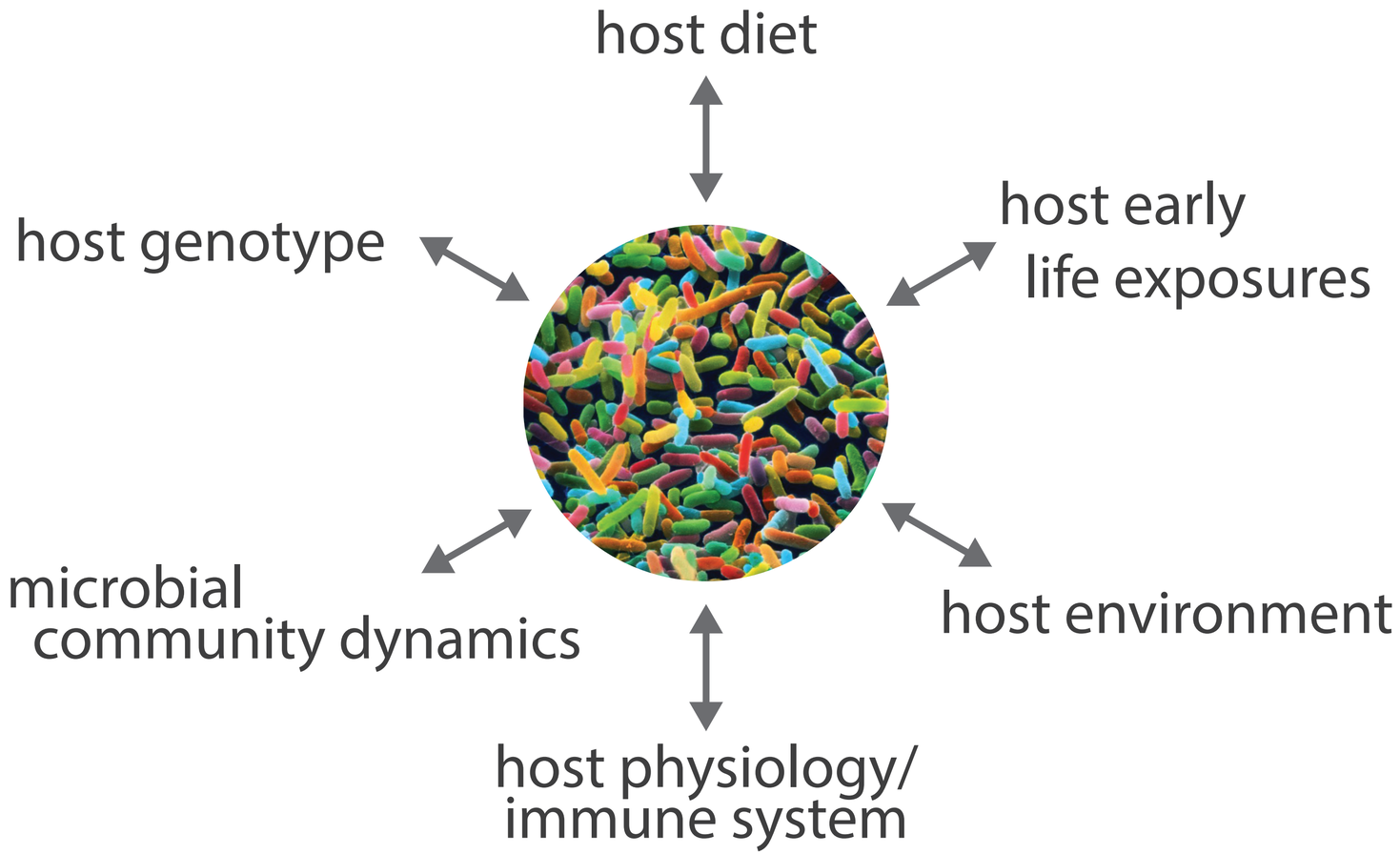


image: Paul Rogers

What determines microbiome *composition*?



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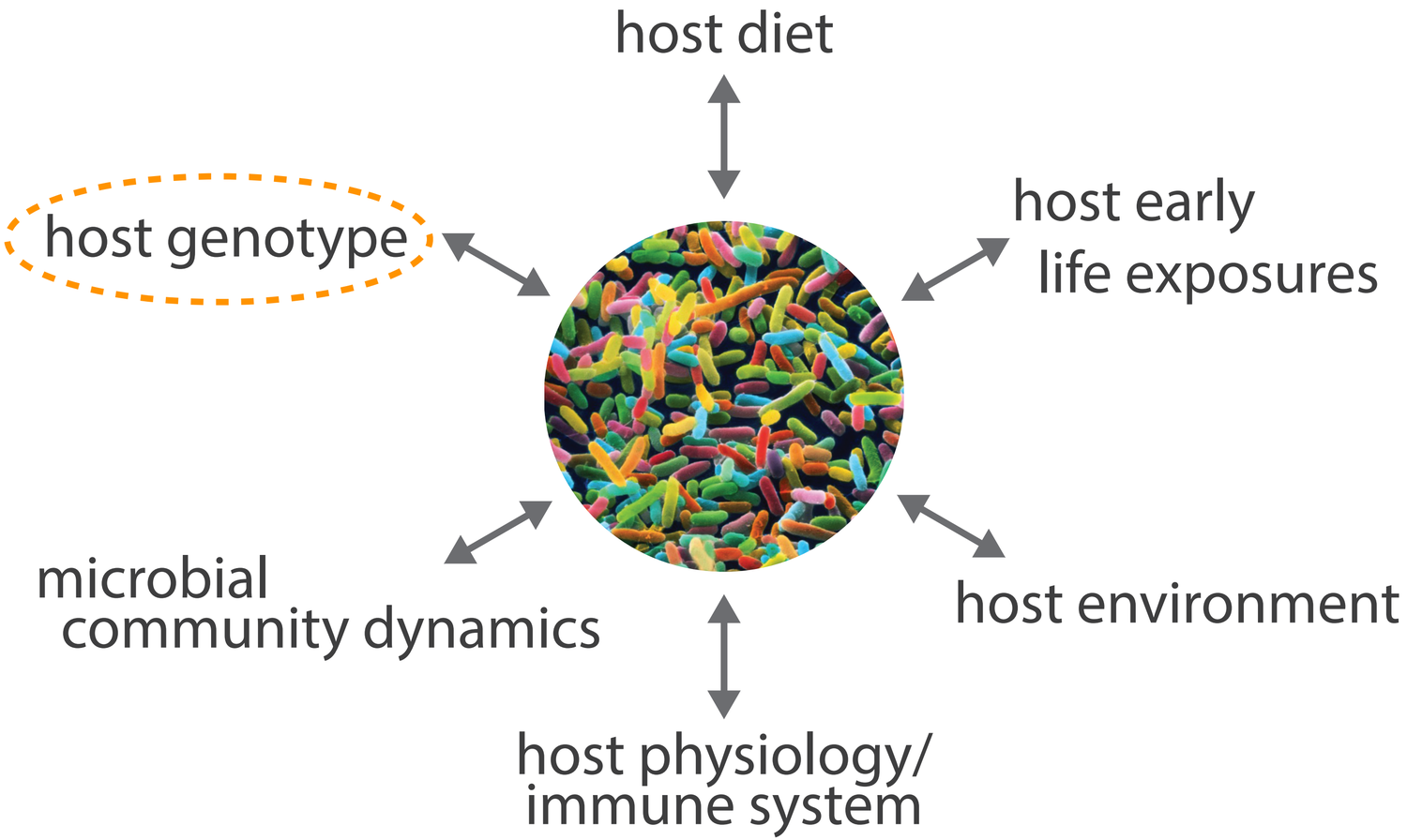

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2. We can identify *variants* in the human genome associated with bacterial abundance.

3. We can identify candidate *host tissues* where this genetic variation acts.

Populations:

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Hutterites

Davenport ER, Cusanovich DA, Michelini K, Barreiro LB, Ober C, and Gilad Y. *Genome-wide association studies of the human gut microbiota*. PLoS ONE. 2015

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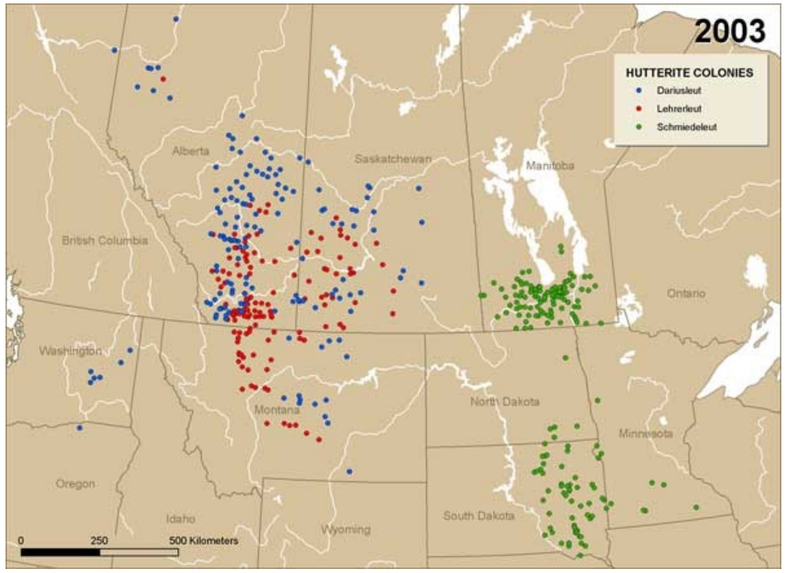
TwinsUK

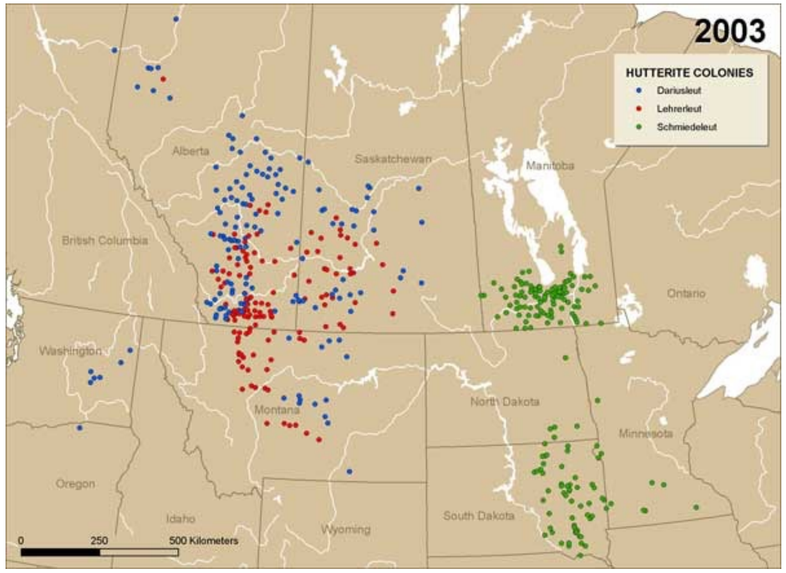
Goodrich JK, **Davenport ER**, Beaumont M, Jackson MA, Knight R, Ober C, Spector T, Bell JT, Clark AC, and Ley RE. *Genetic Determinants of the Gut Microbiome in UK Twins.* Cell Host and Microbe. 2016

Study design: *The Hutterites*



Study design: *The Hutterites*

Hutterites eat *communally.*



Study design: *Sample collection*

127 individuals

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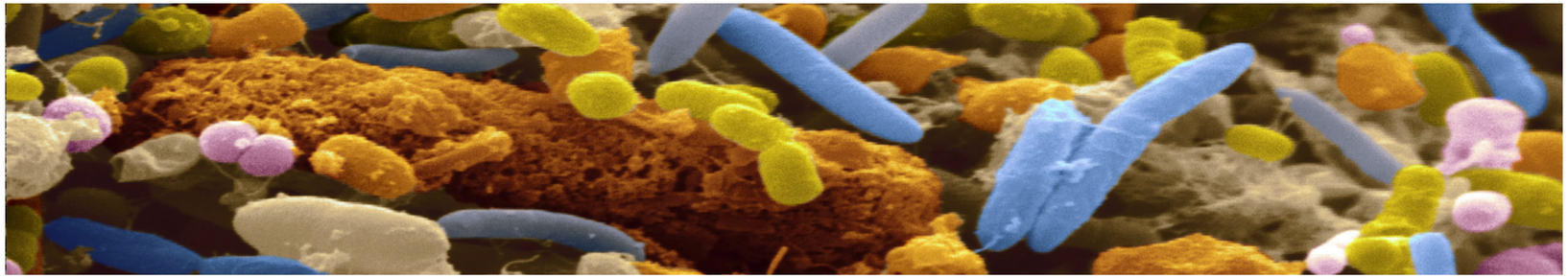
microbiome data

Microbiome data: Deep sequencing of *16S rRNA gene* fragments



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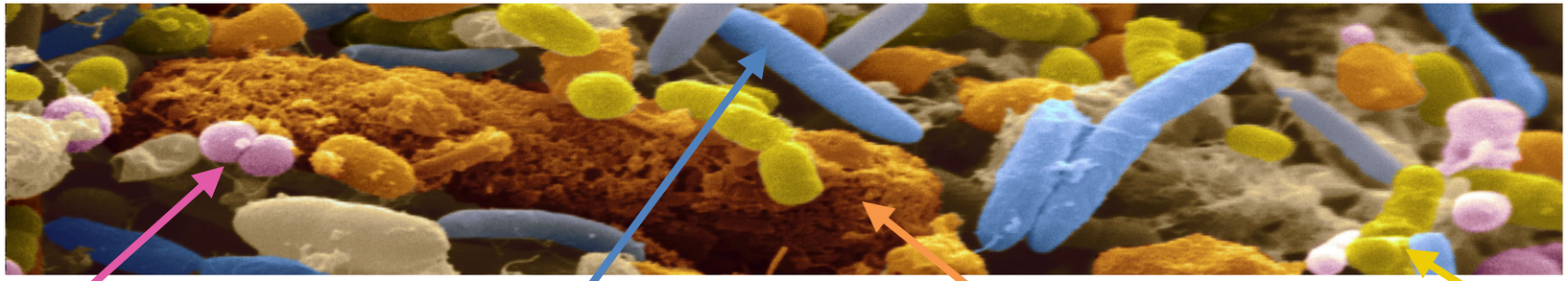

genus: *Bacteroides*

Prevotella

Butyricimonas

Akkermansia

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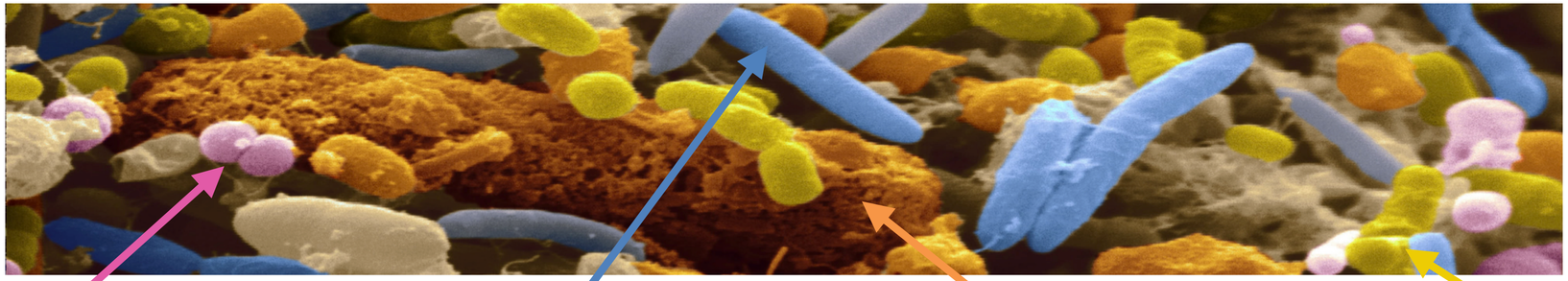

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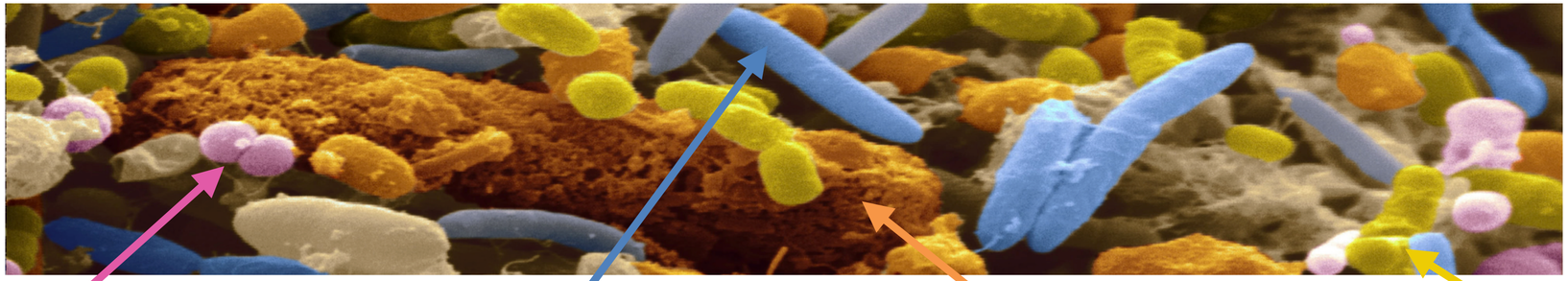

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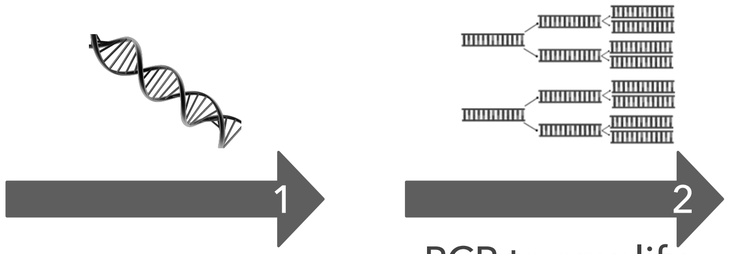

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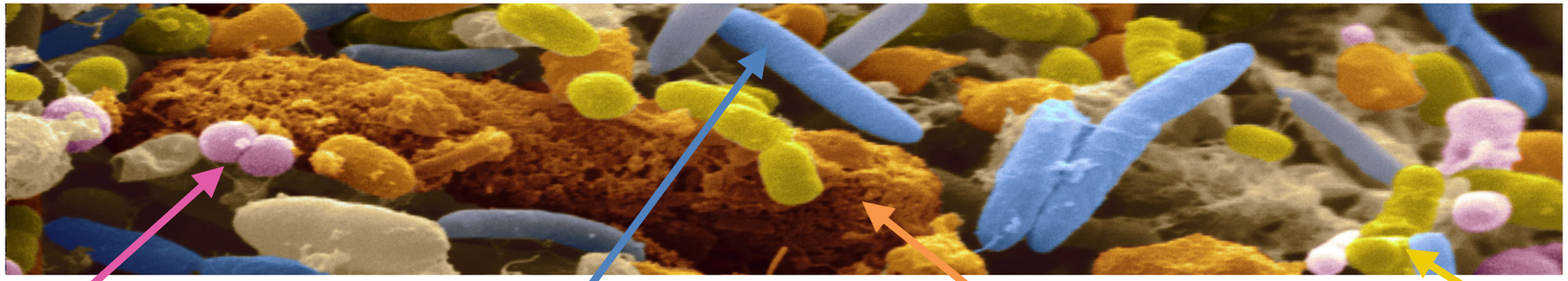

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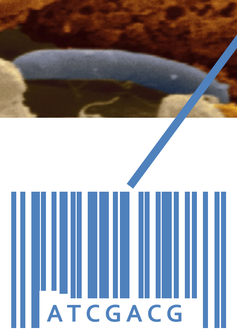

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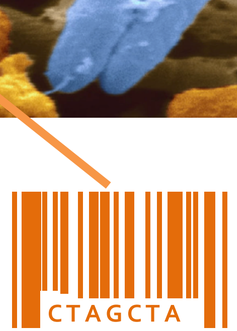

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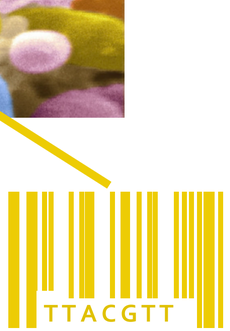

Akkermansia

1

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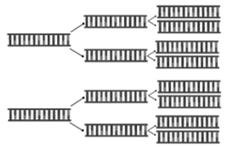

2

PCR to amplify
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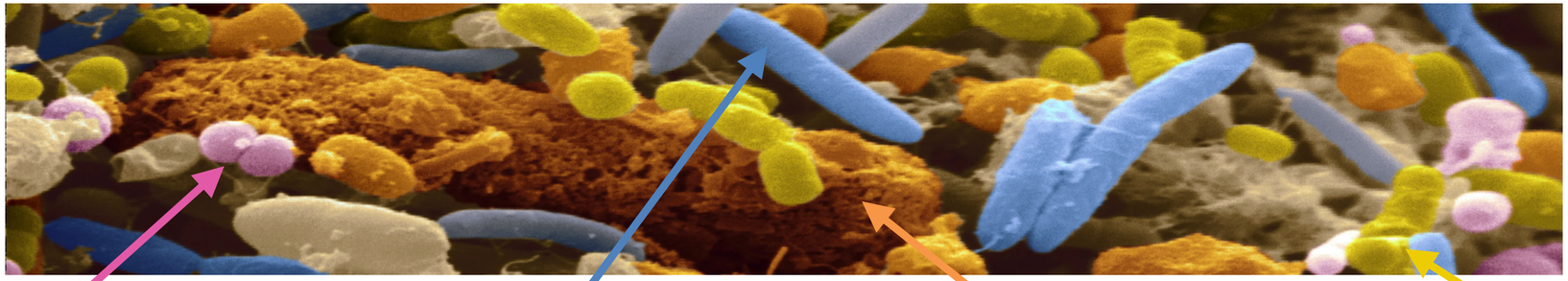
3

Sequence

Microbiome data: Deep sequencing of *16S rRNA gene* fragments



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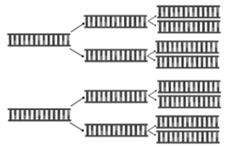

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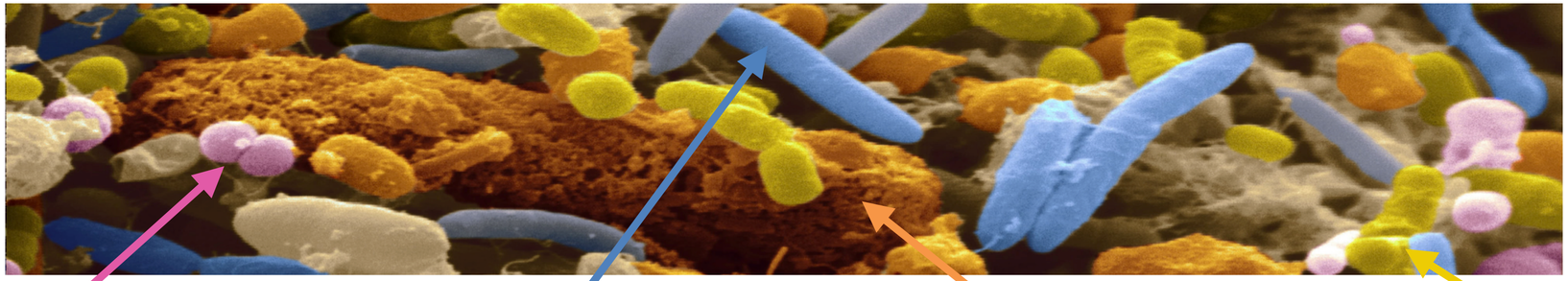

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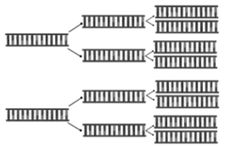

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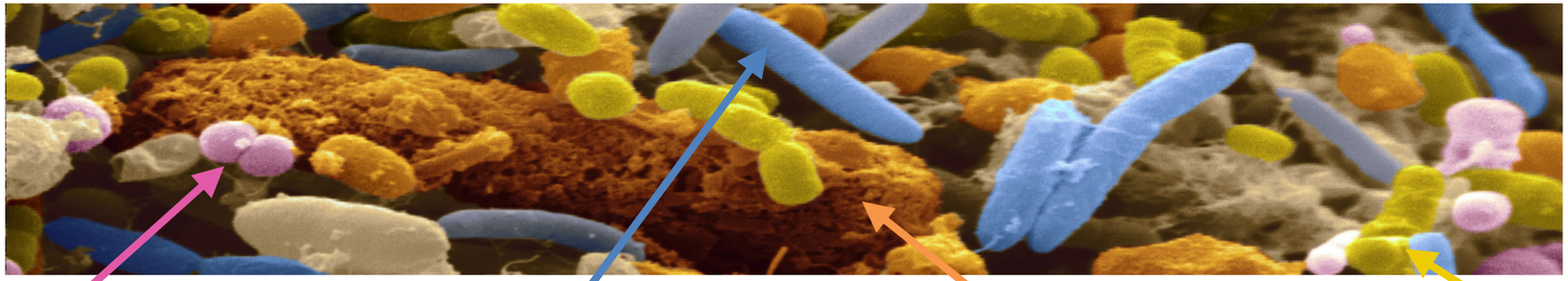

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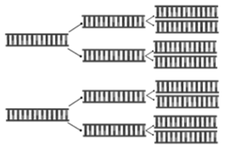

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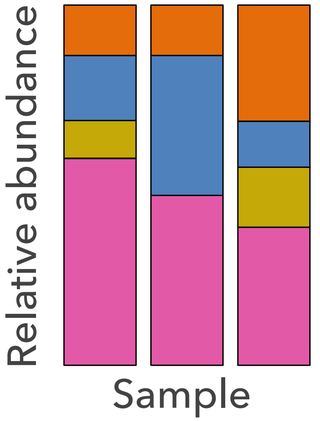

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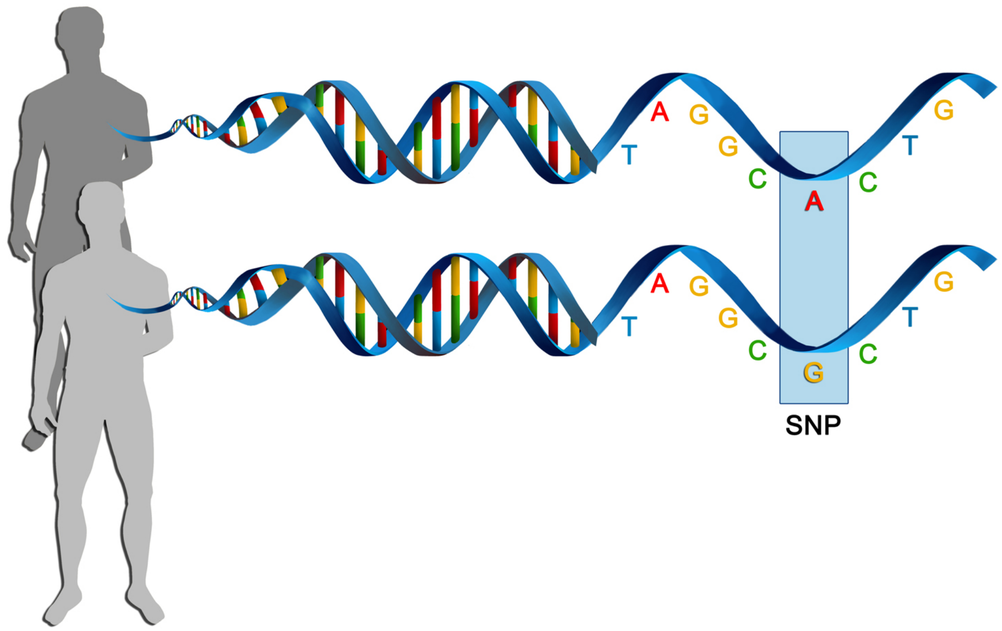
genetic data

Human *genetic* data: single-nucleotide polymorphisms (SNPs)



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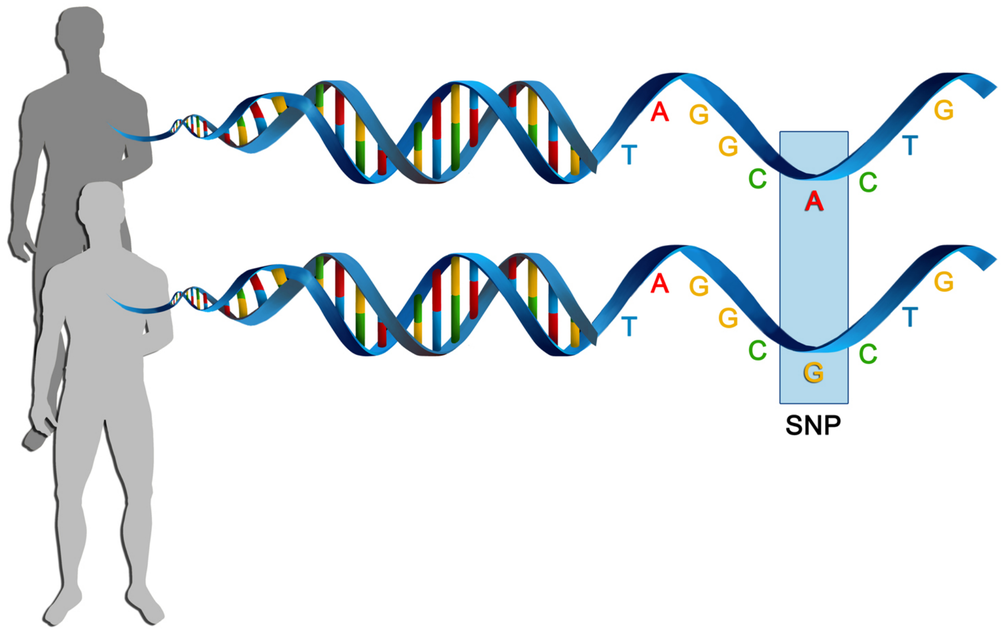

~200,000 genetic variants

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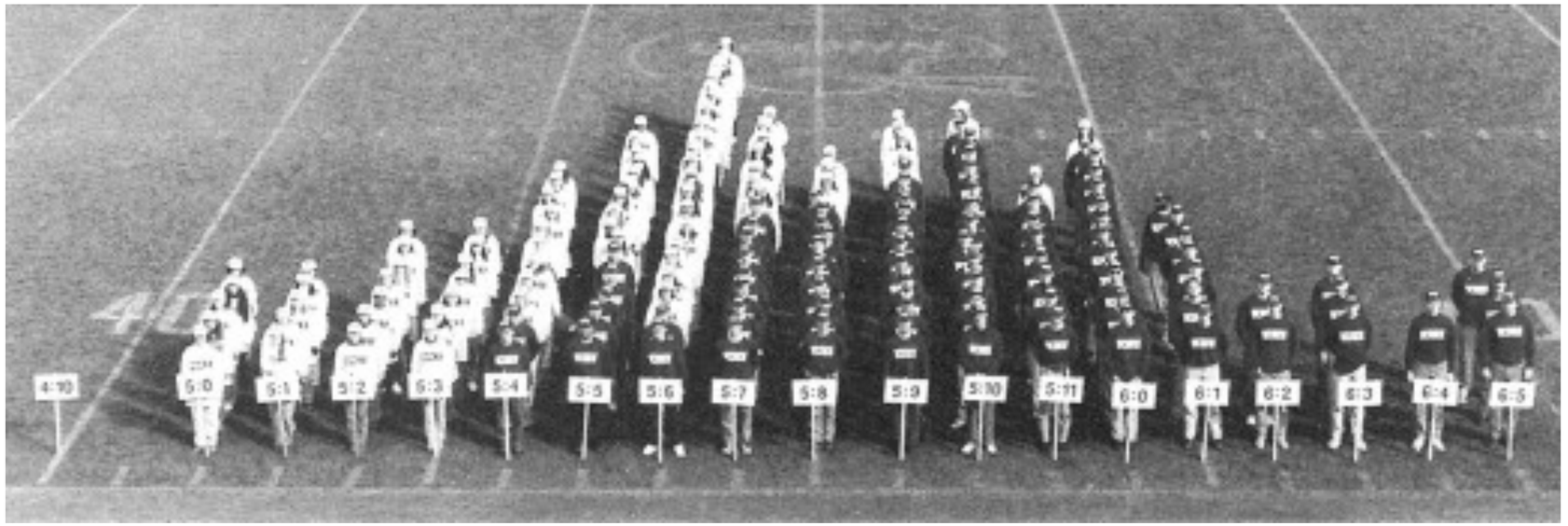
Chip heritability = proportion of variance explained by SNPs



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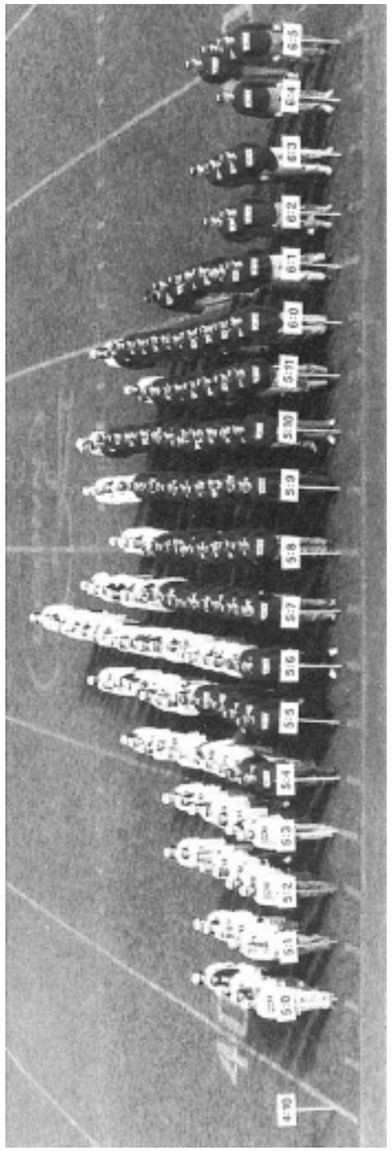

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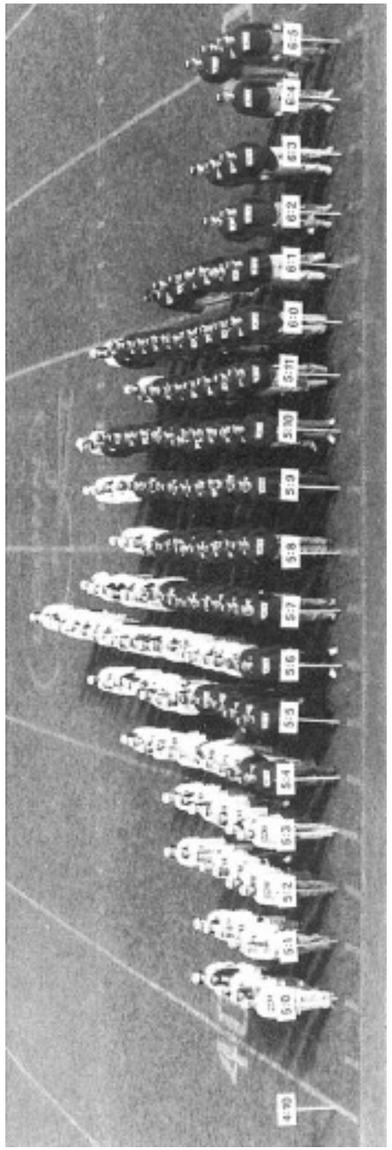

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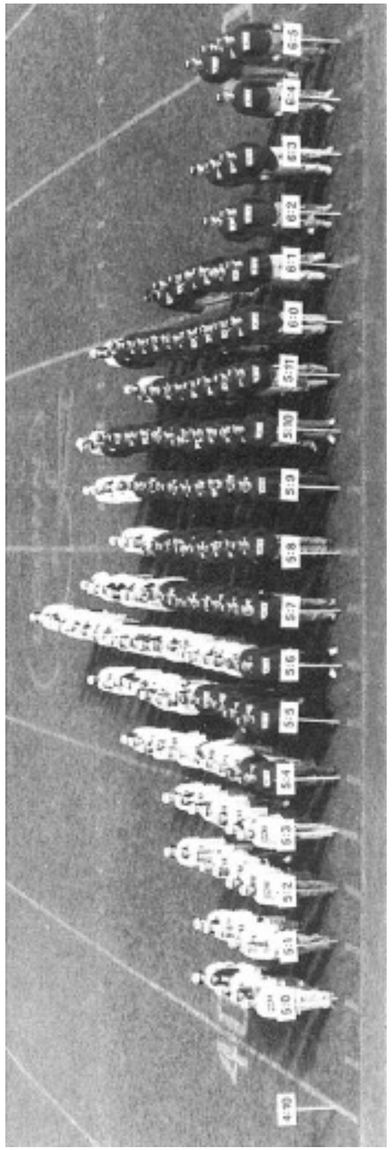

variance in phenotype

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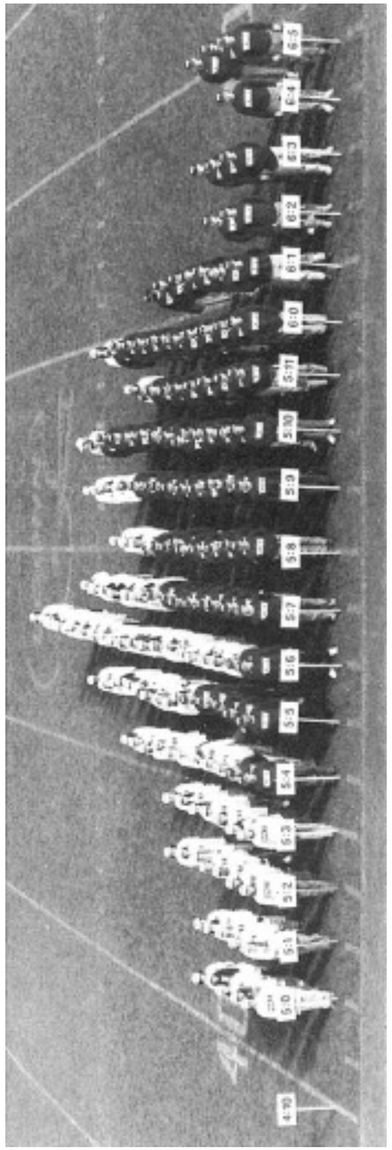

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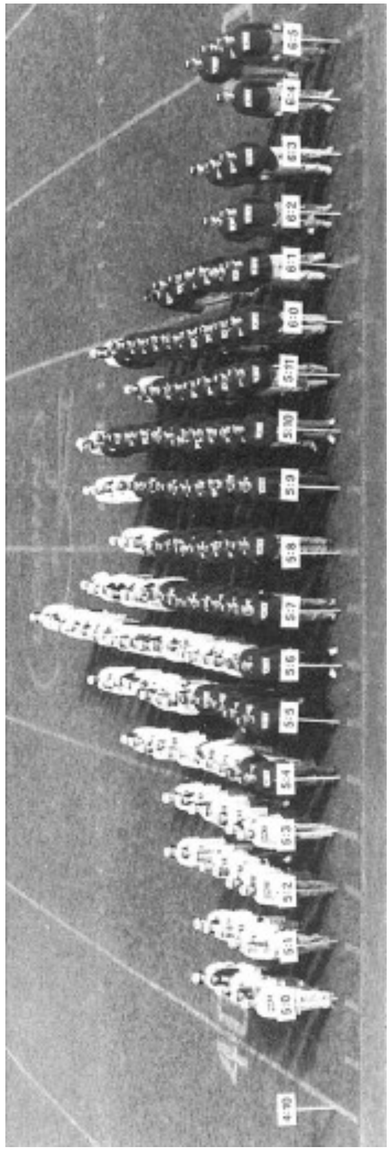

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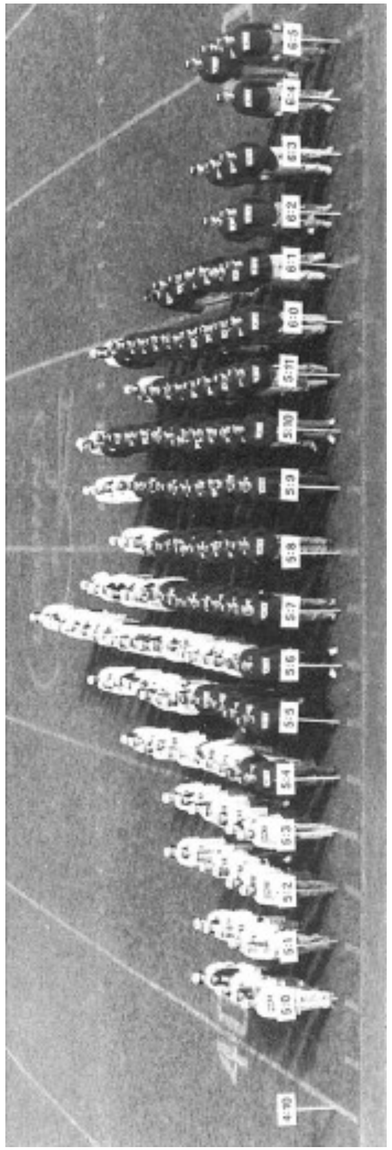

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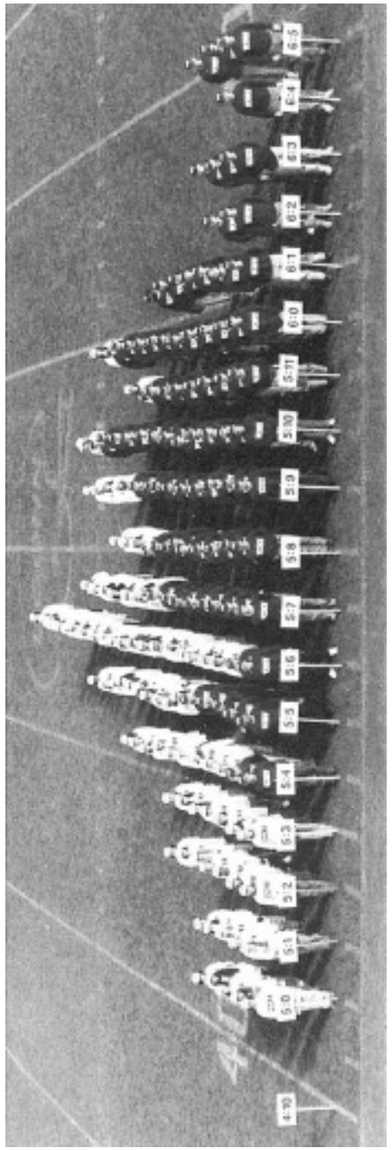

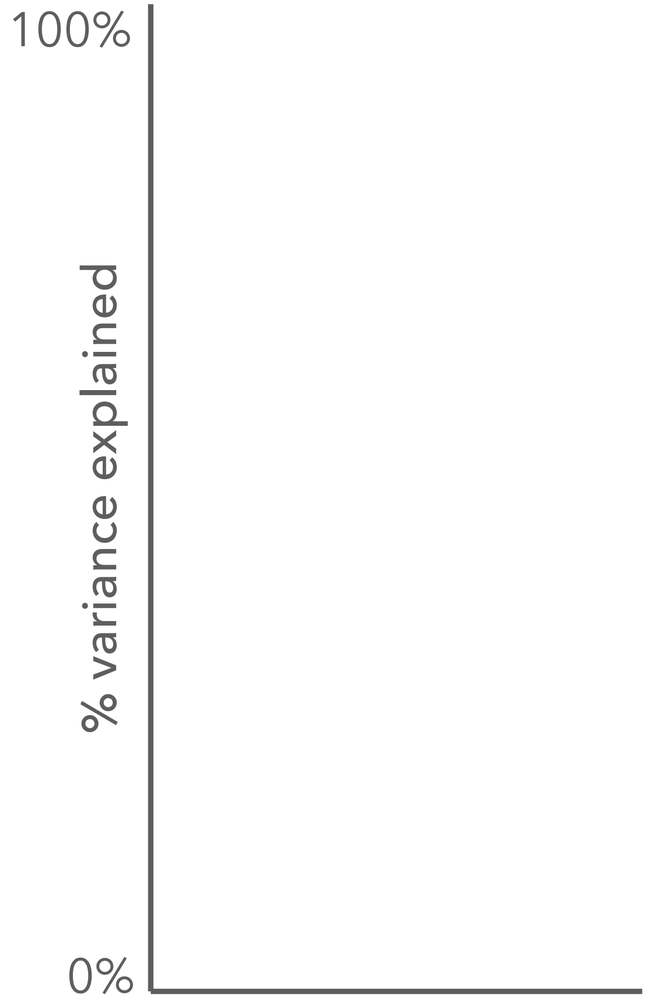

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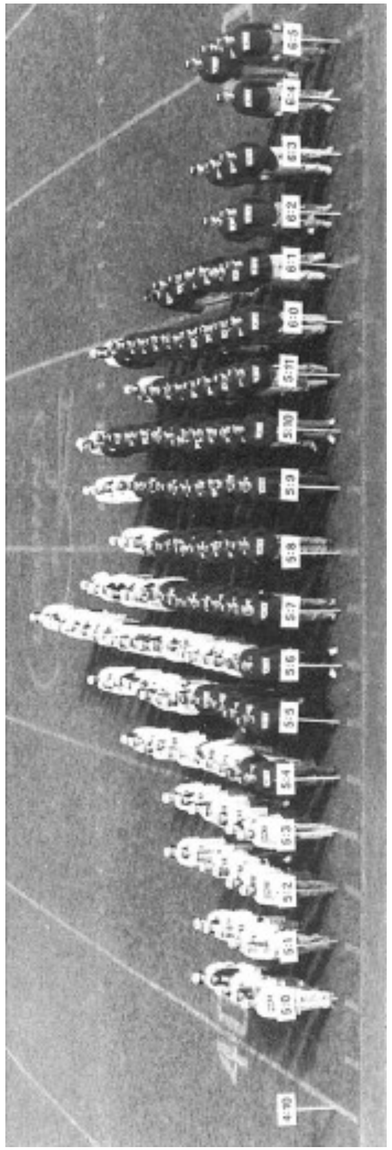

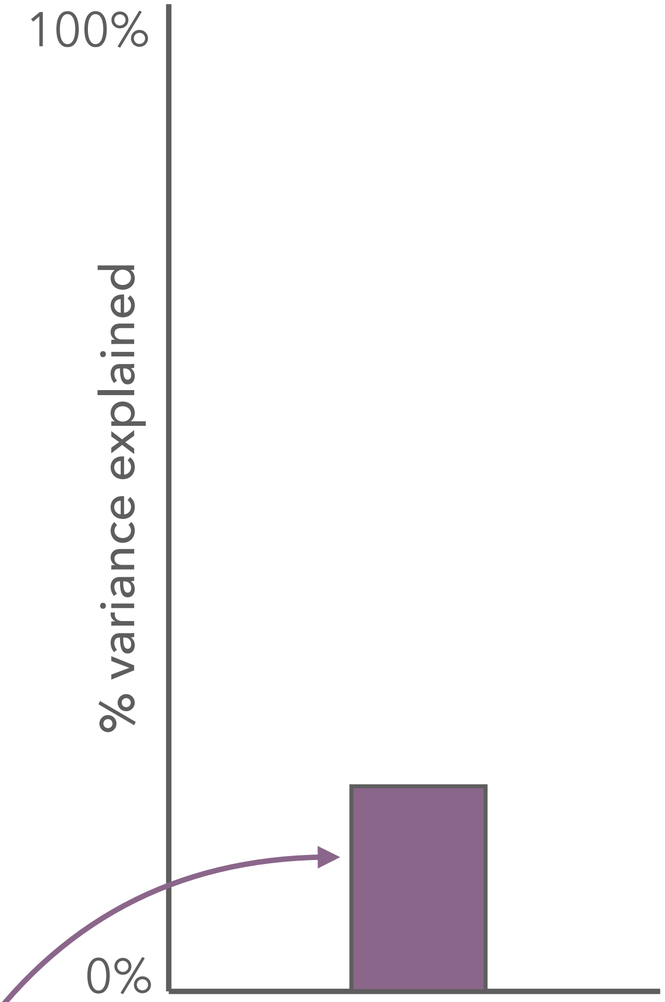

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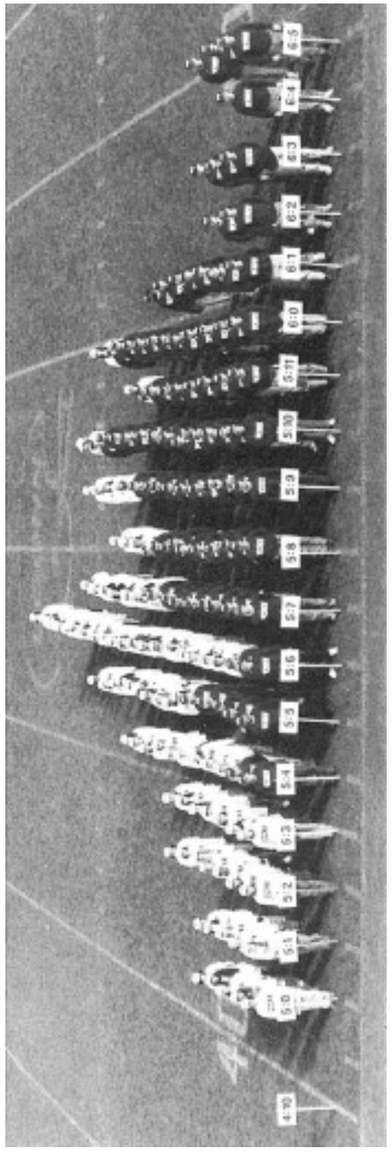

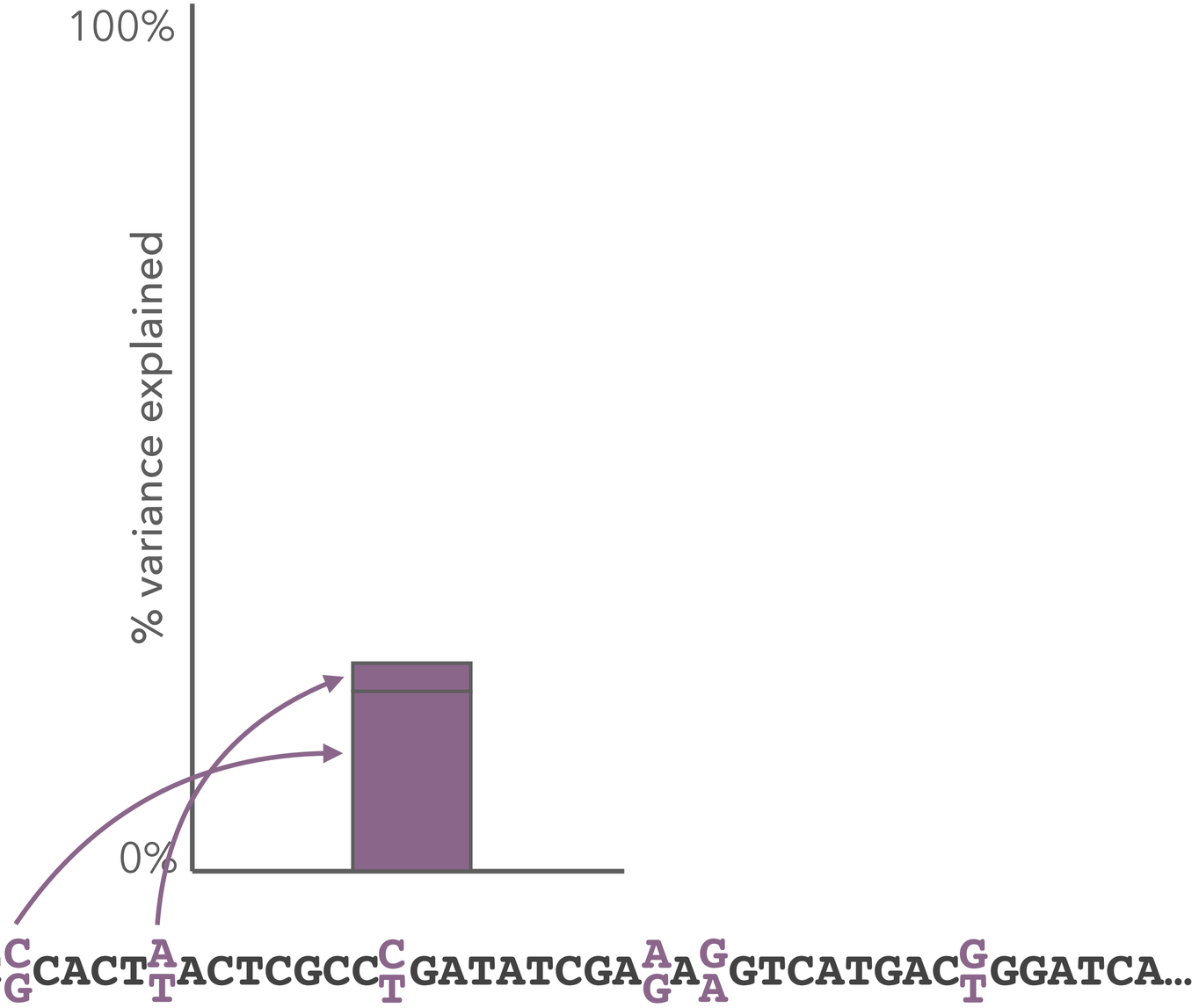

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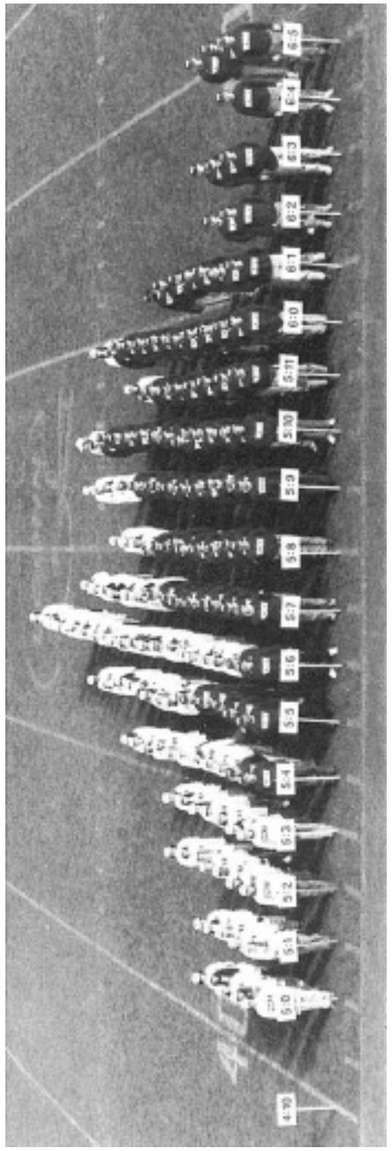

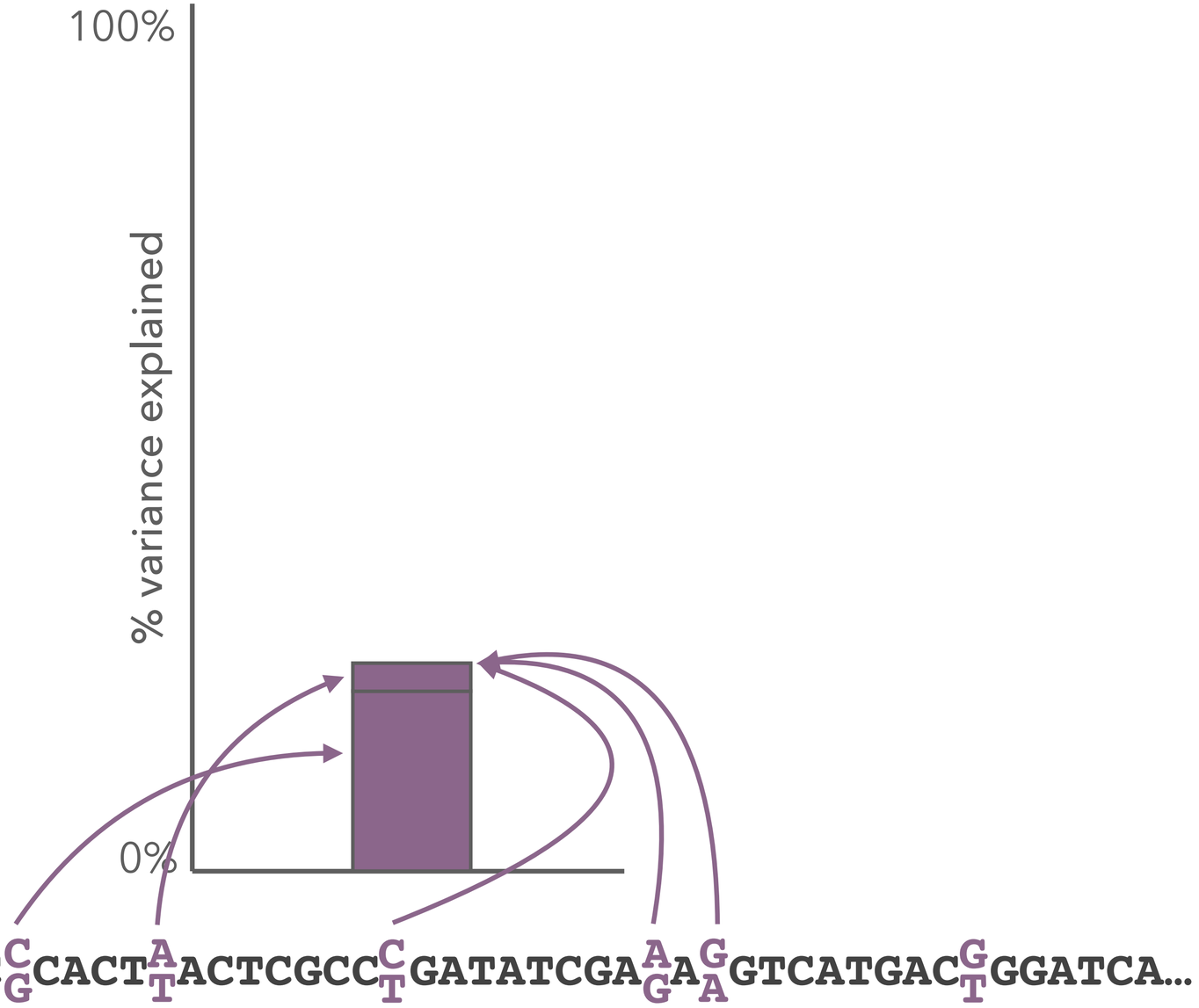

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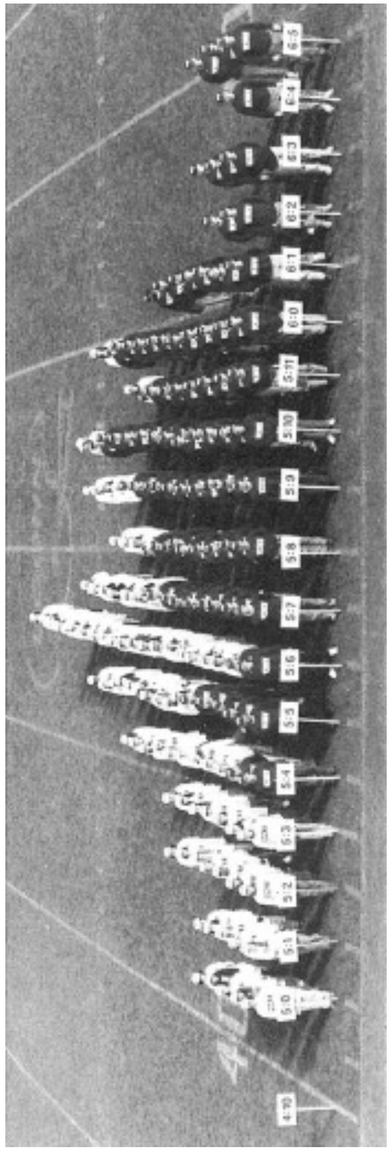

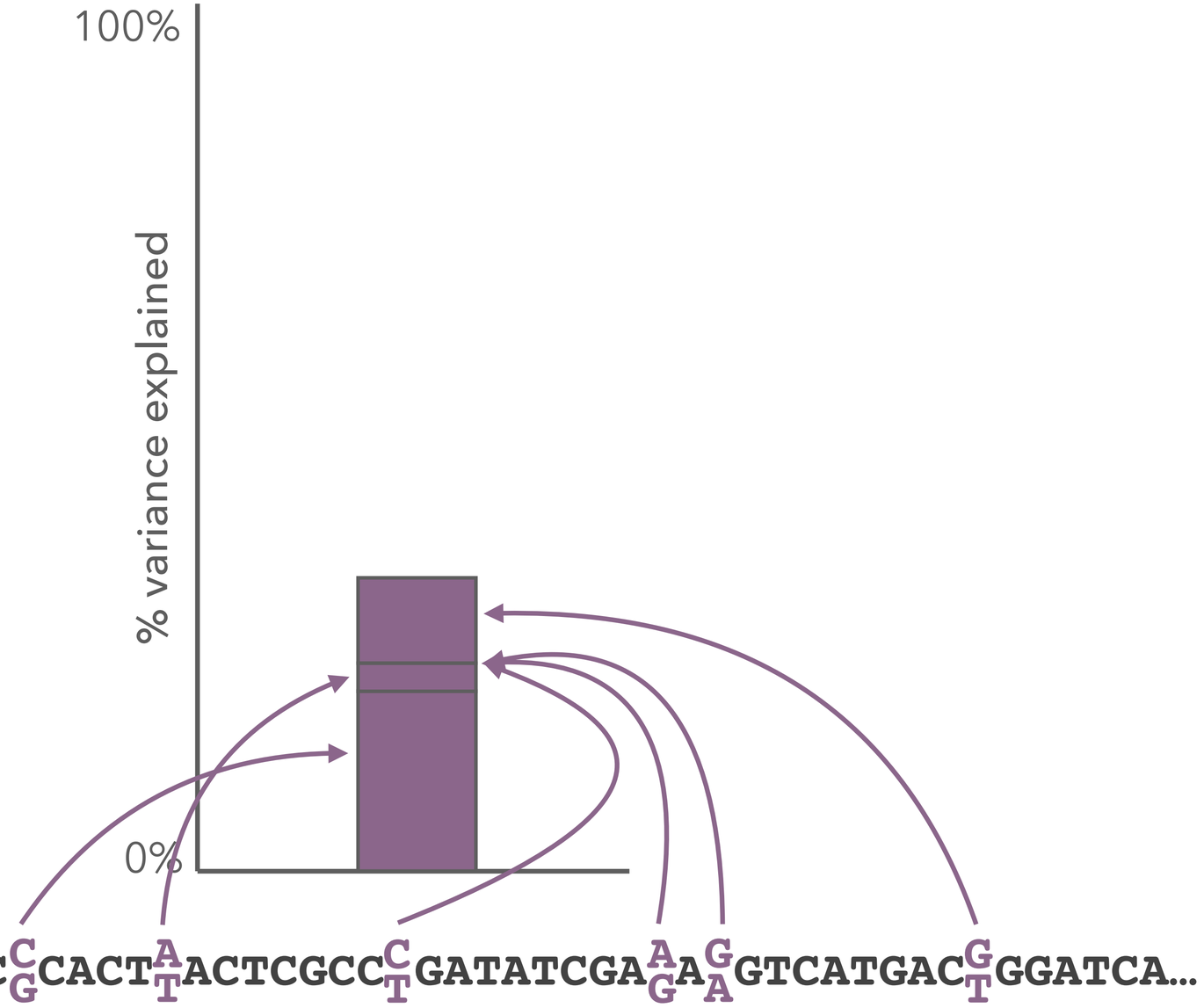

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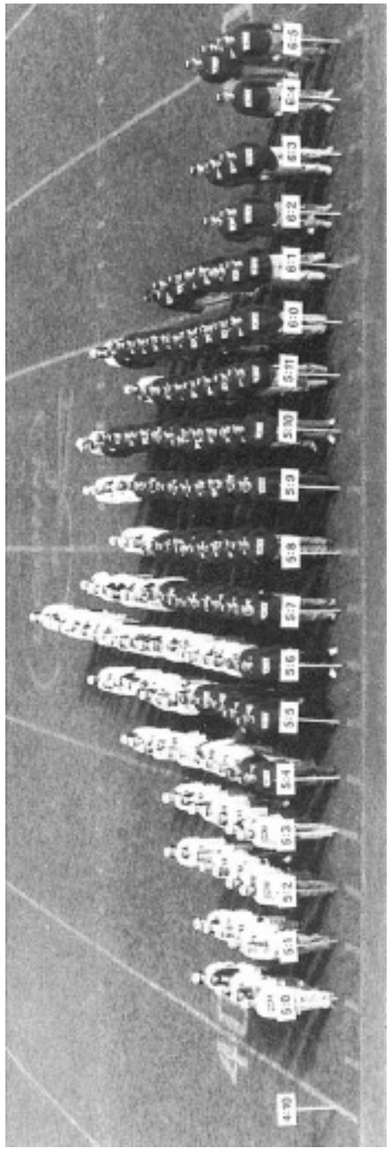

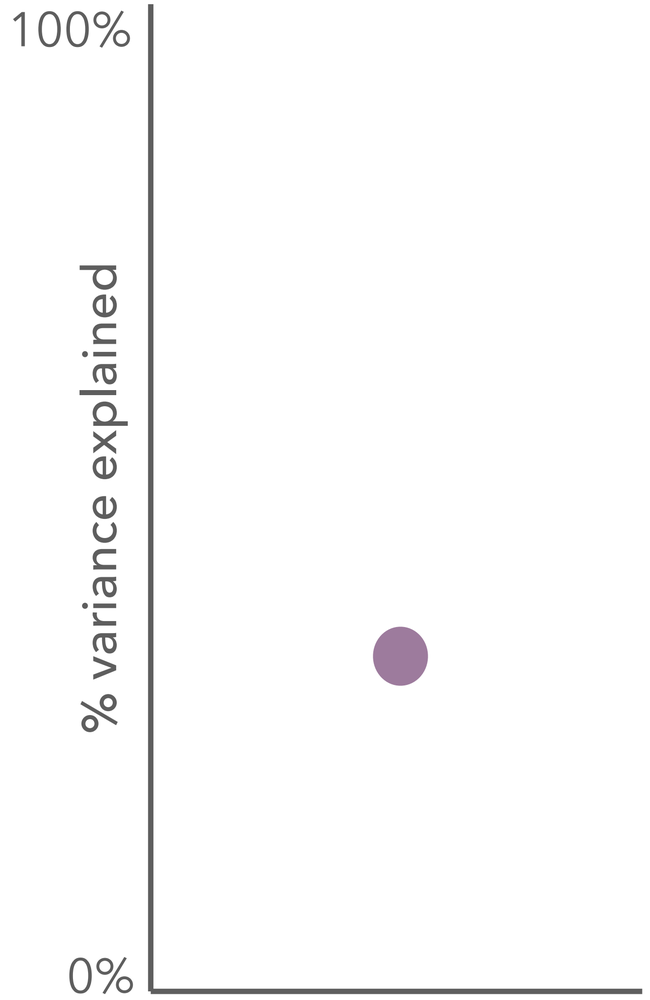

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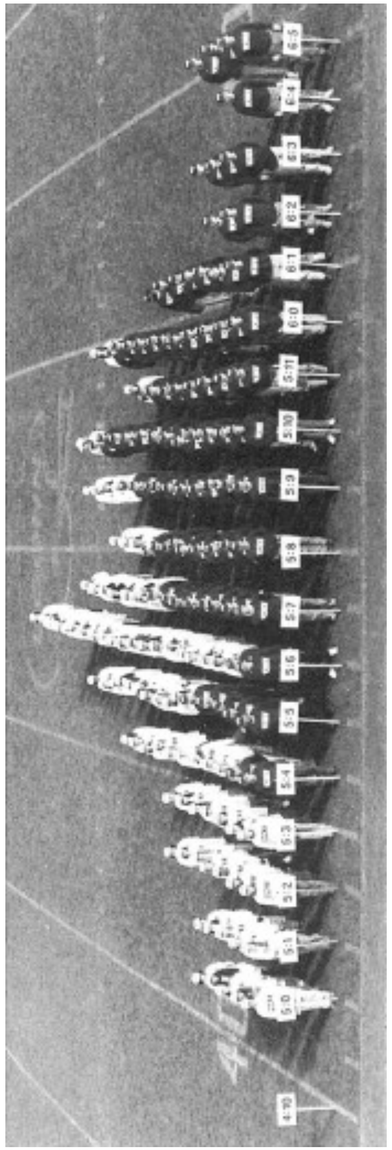
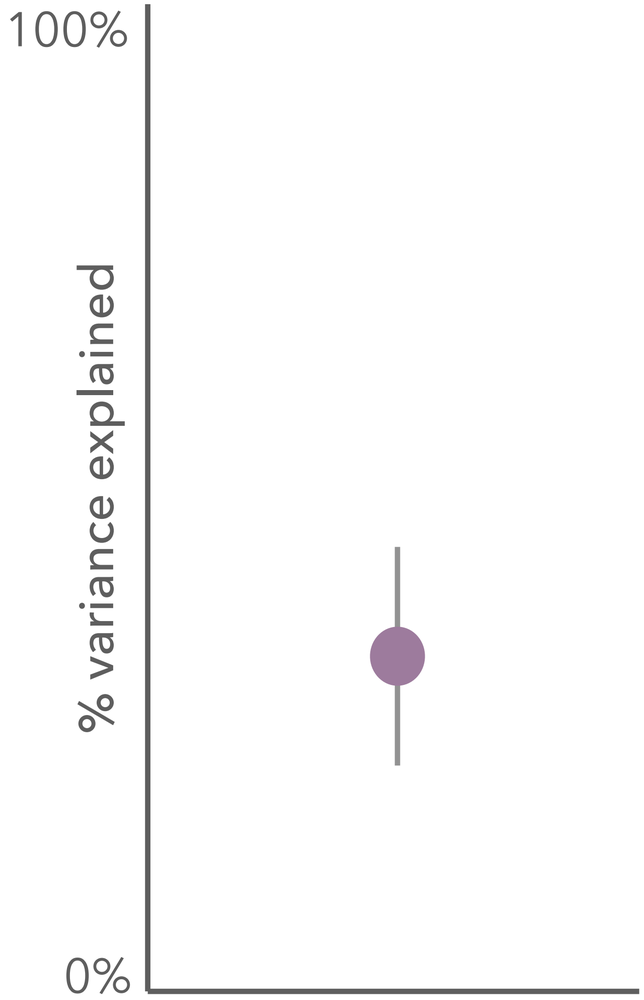
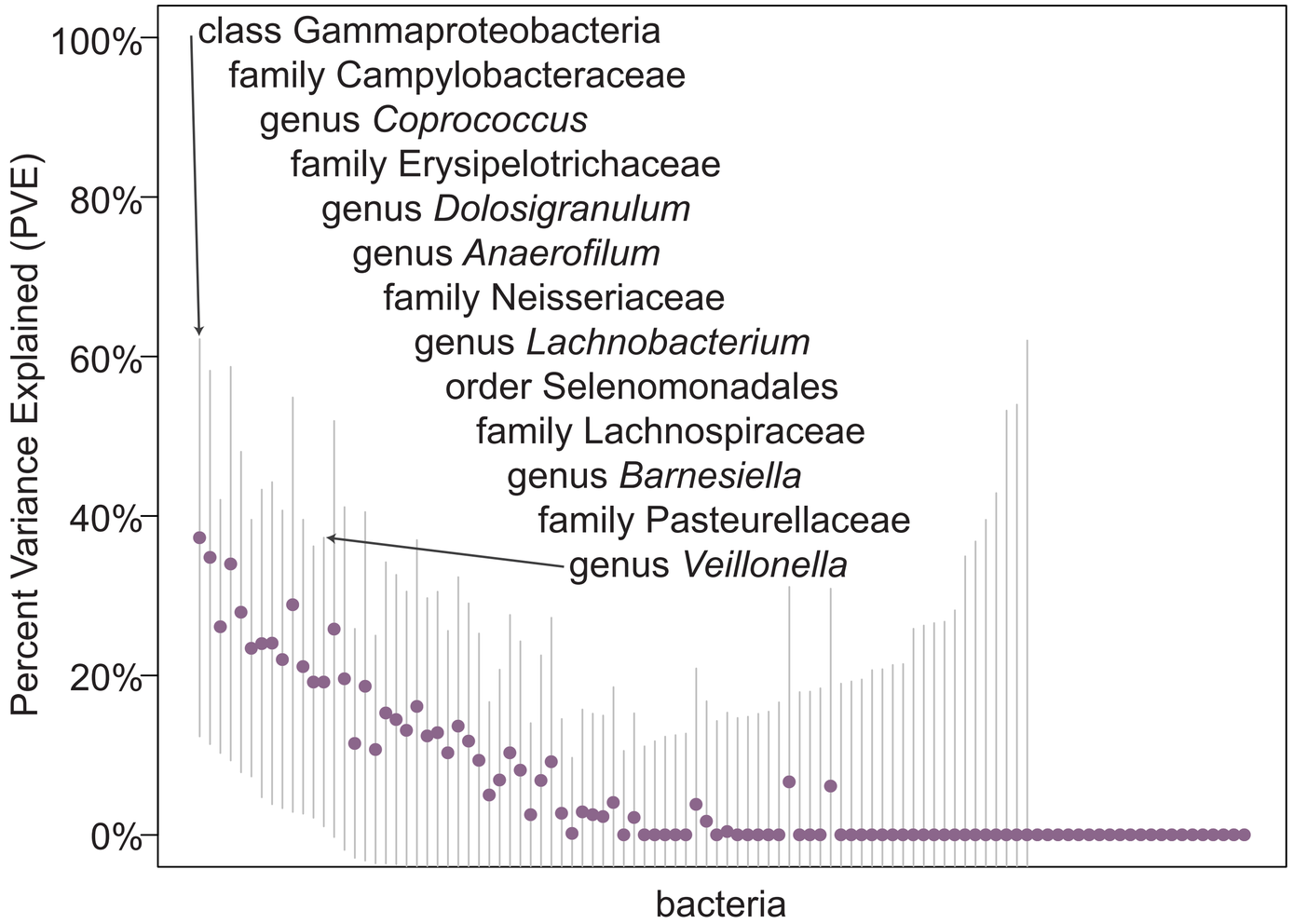




Abundances of select bacteria are *heritable*



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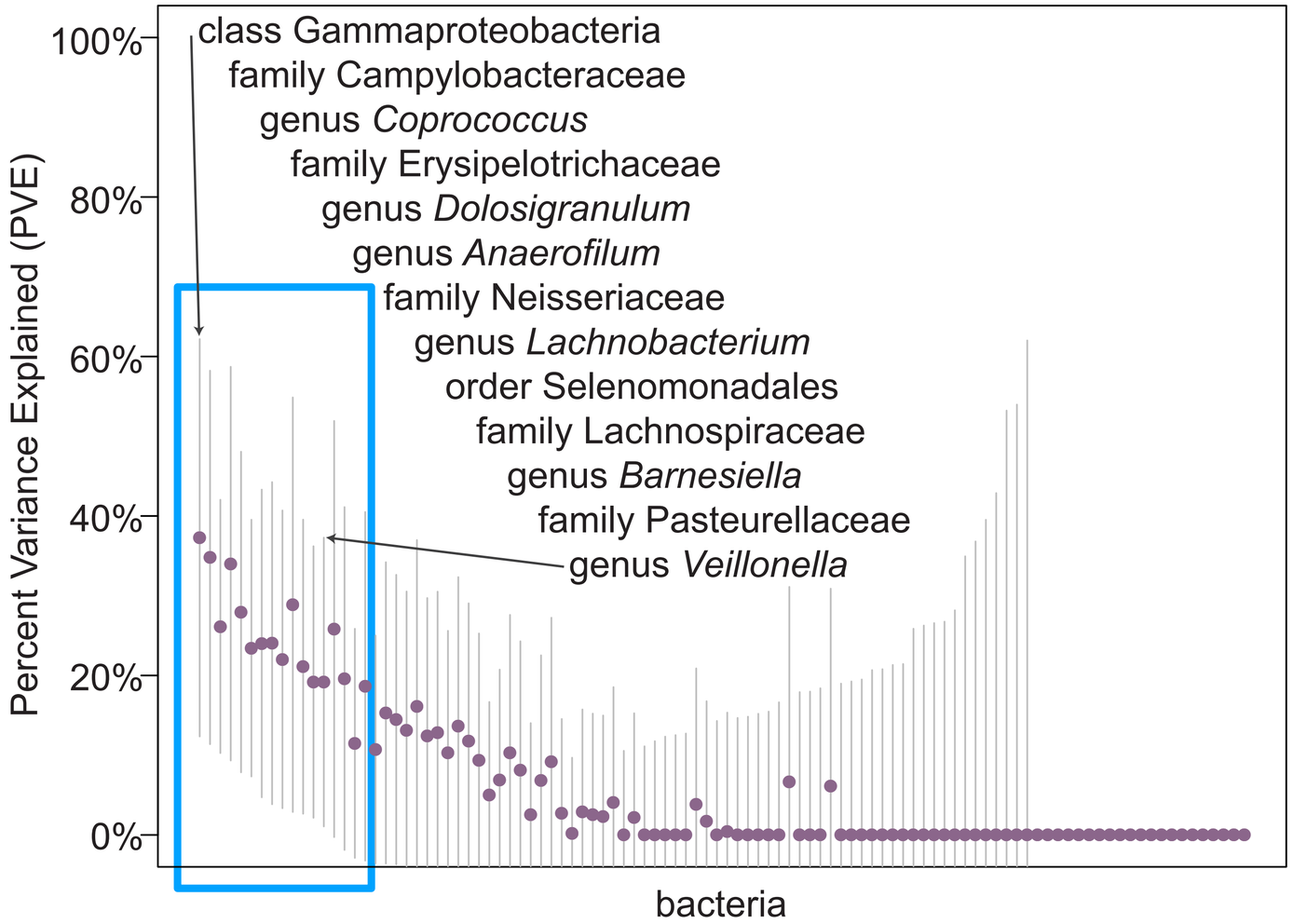

Open *questions*:

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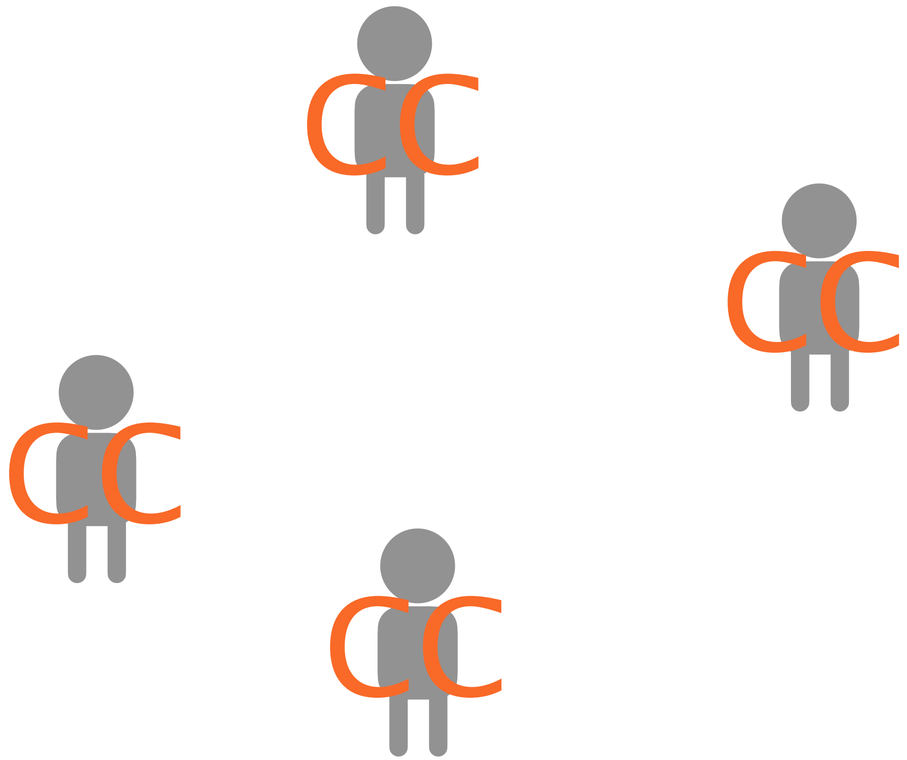
2. Which *variants* in the human genome are associated with bacterial relative abundance?

GWAS identifies *variants* associated with *phenotypes*



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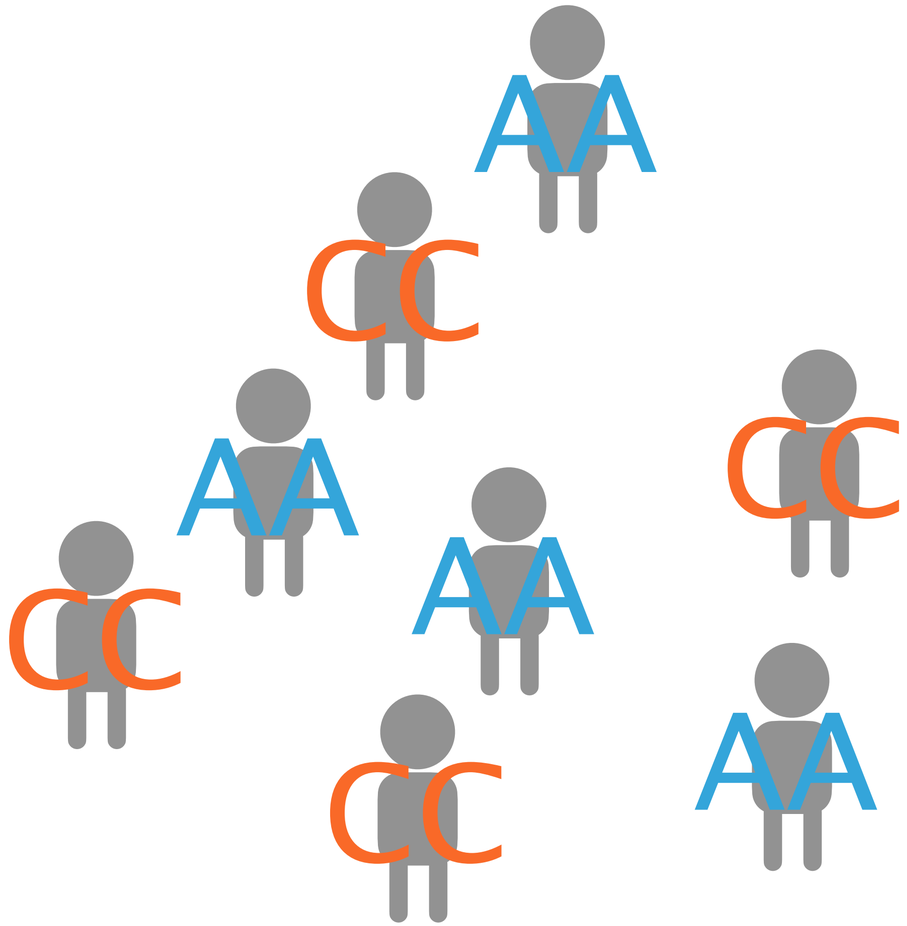

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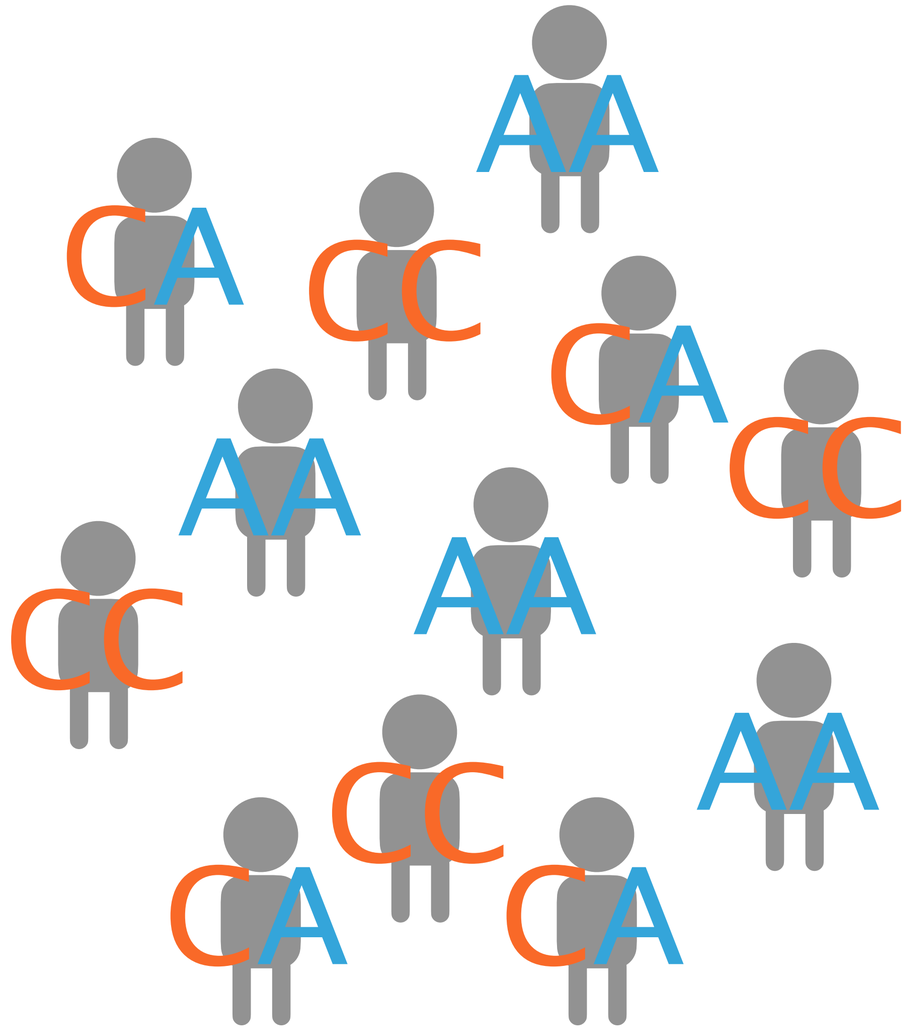

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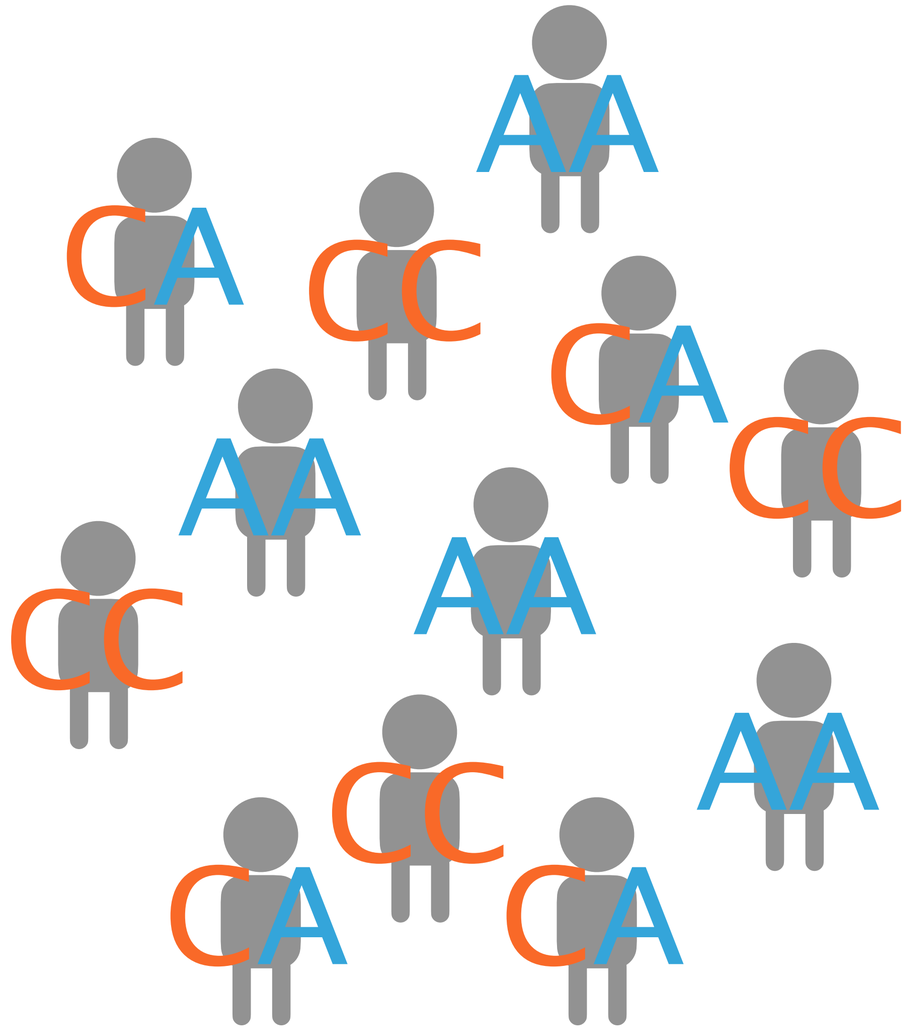

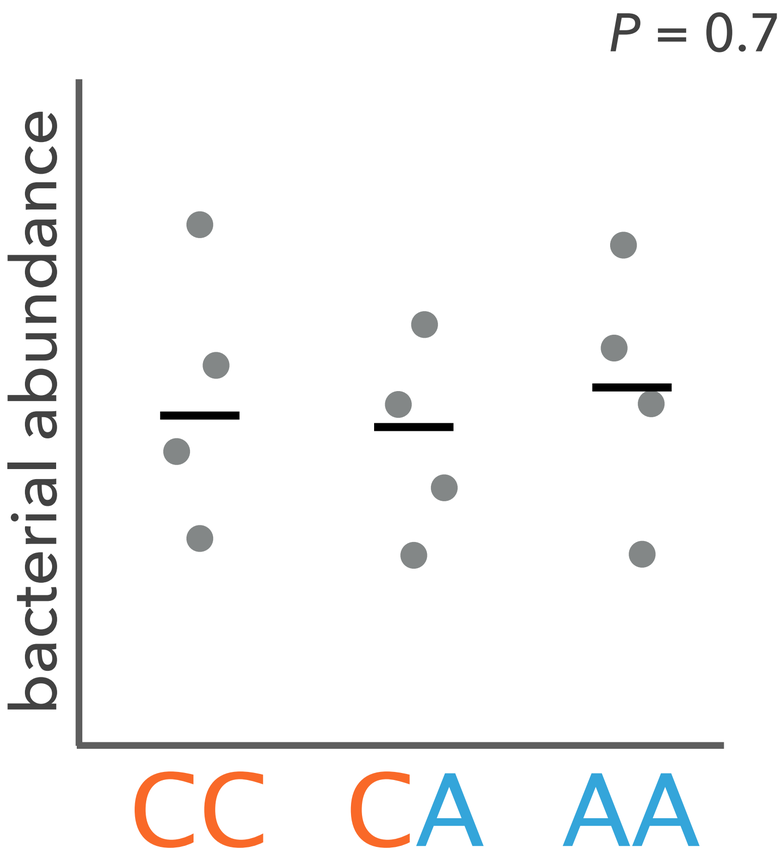

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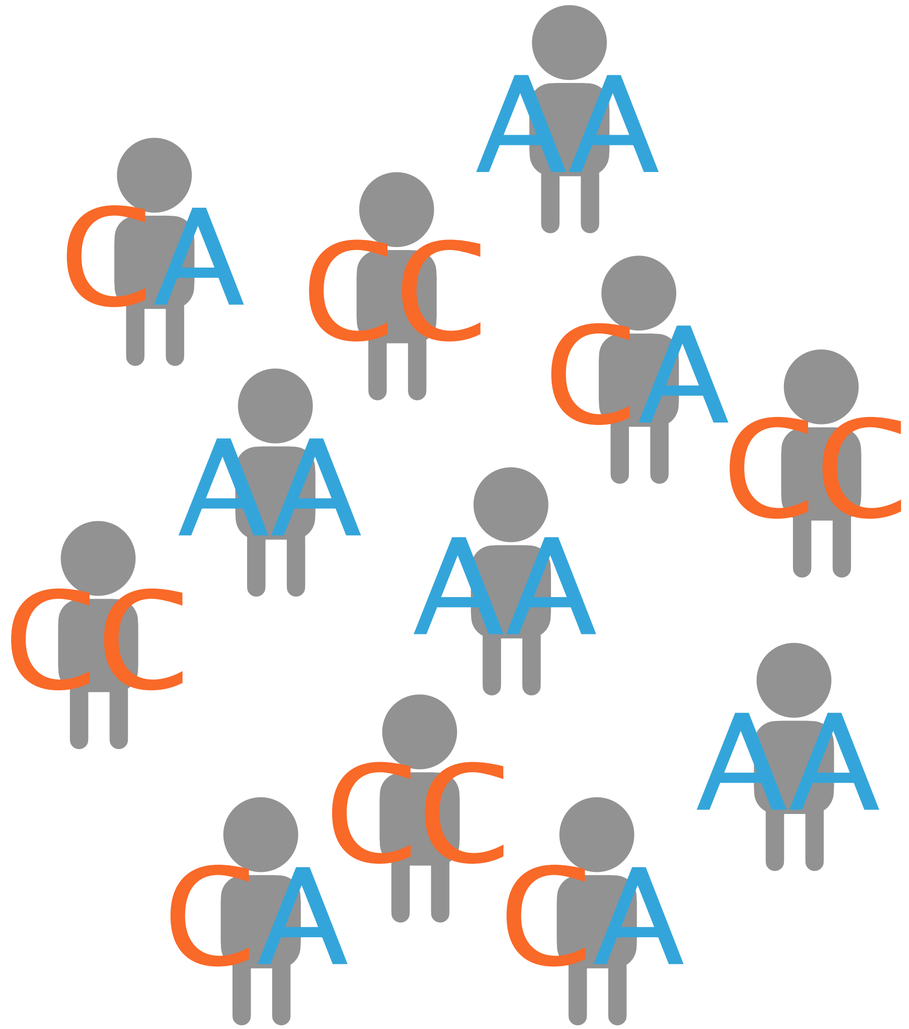

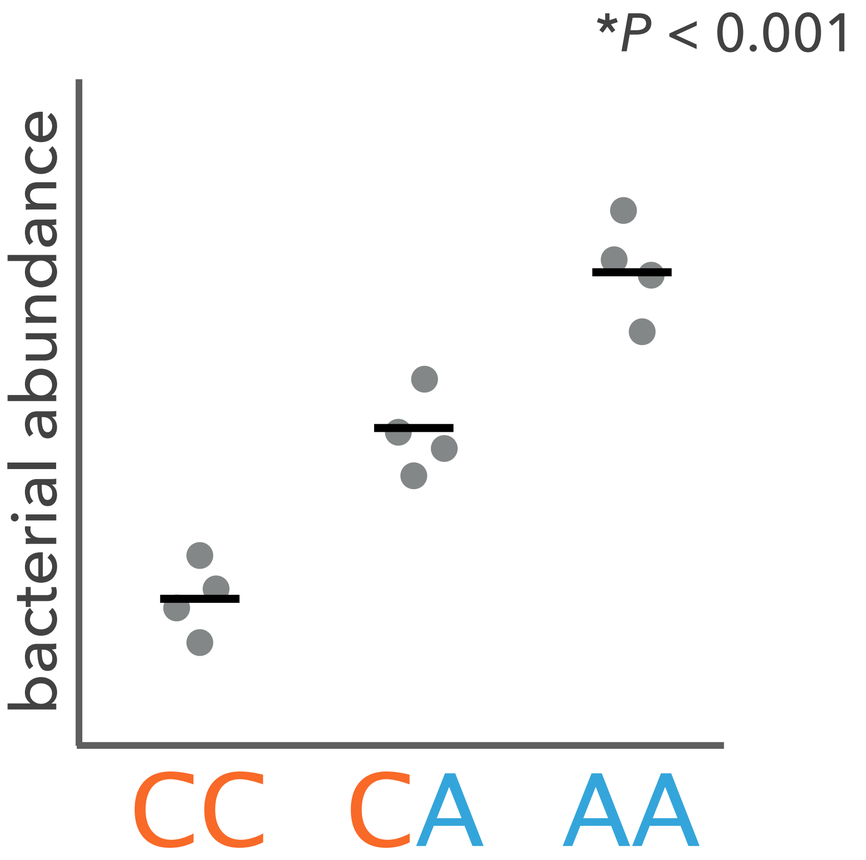

Lactase persistence variant associates with *Bifidobacteria*

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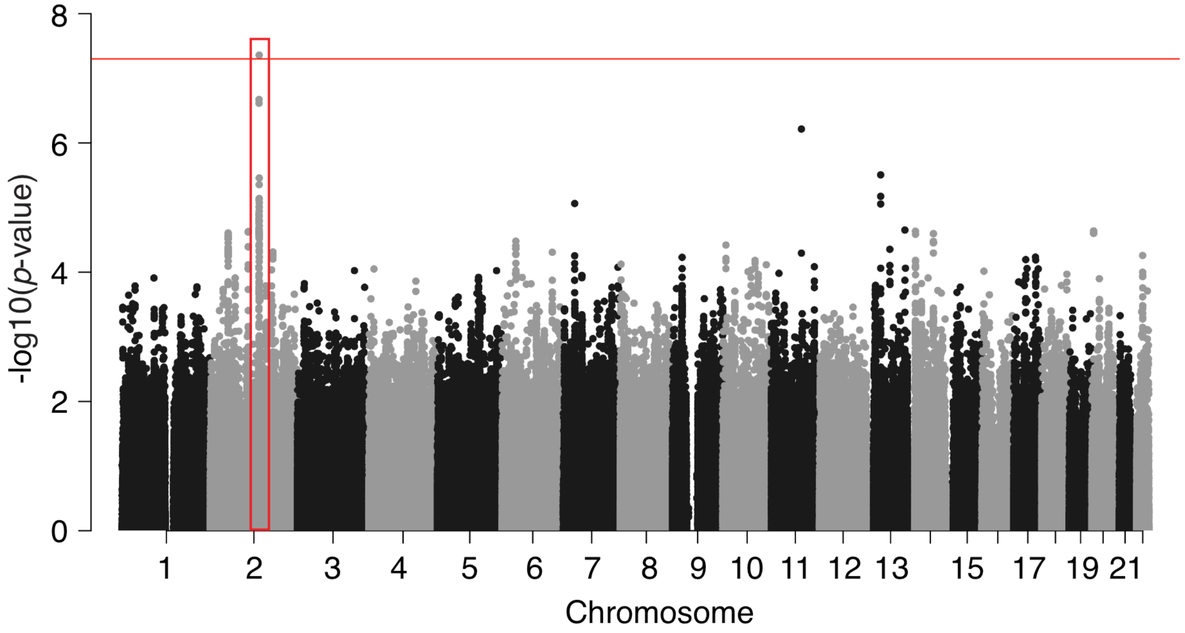

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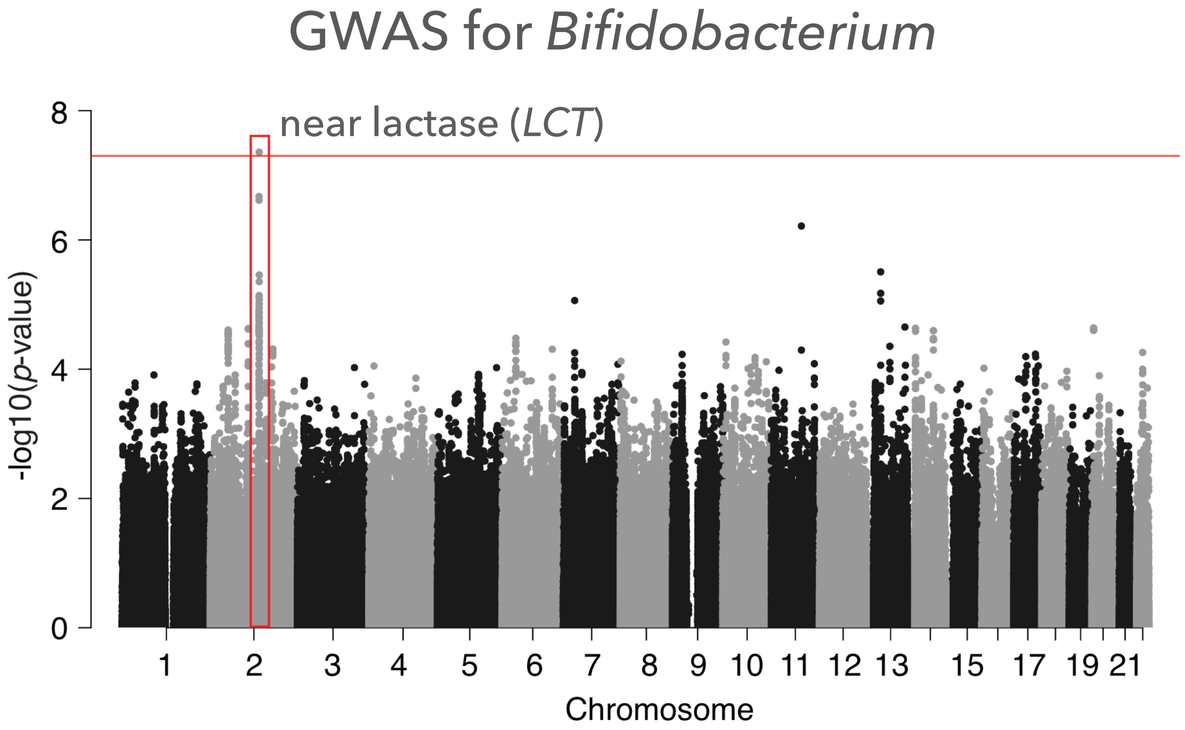

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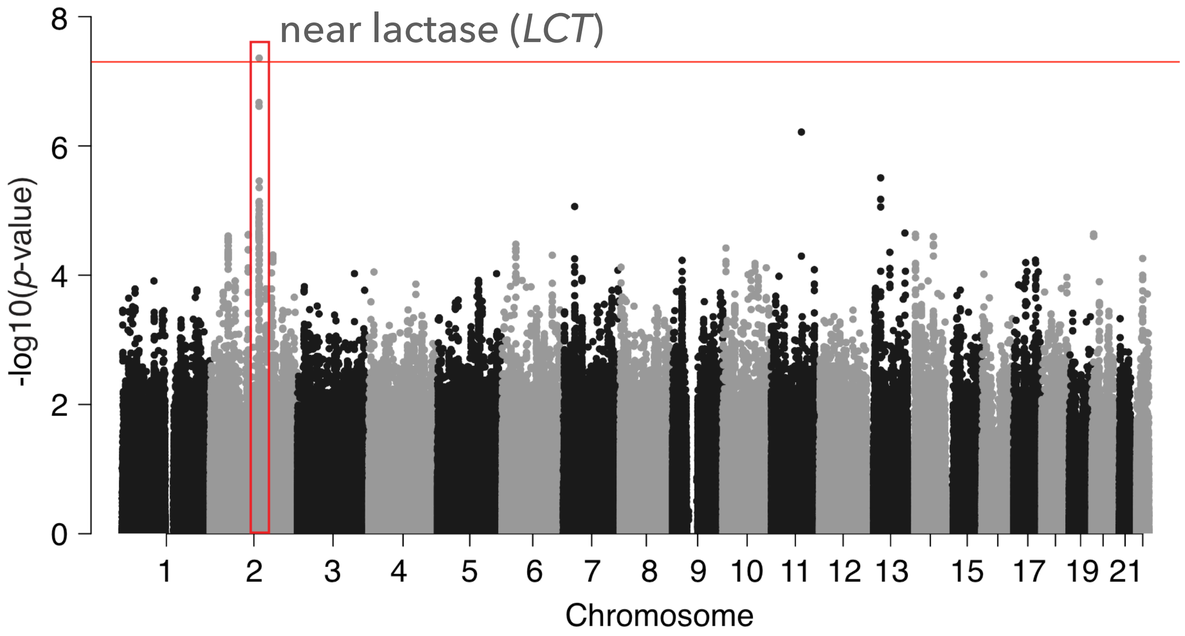

most mammals (including humans)

youth

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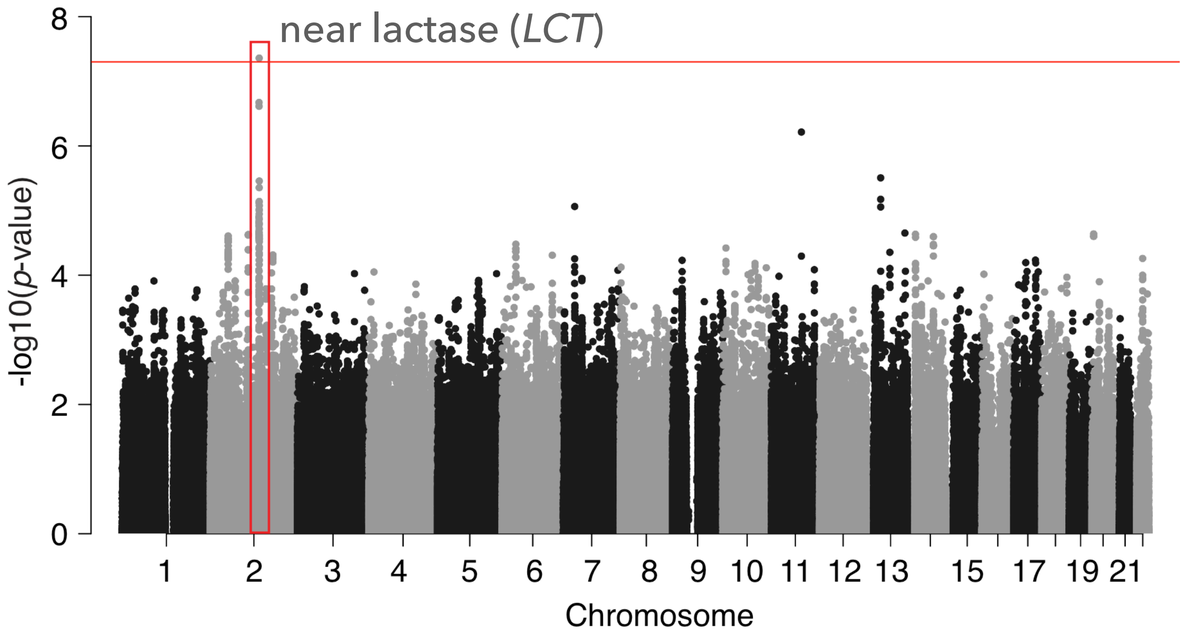

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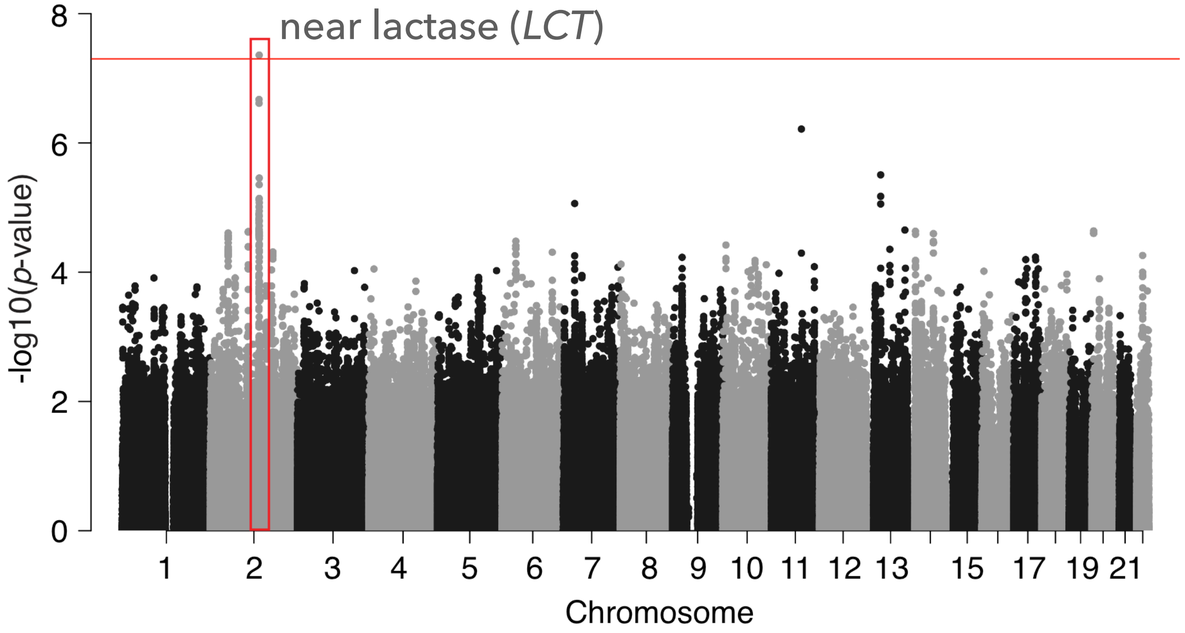

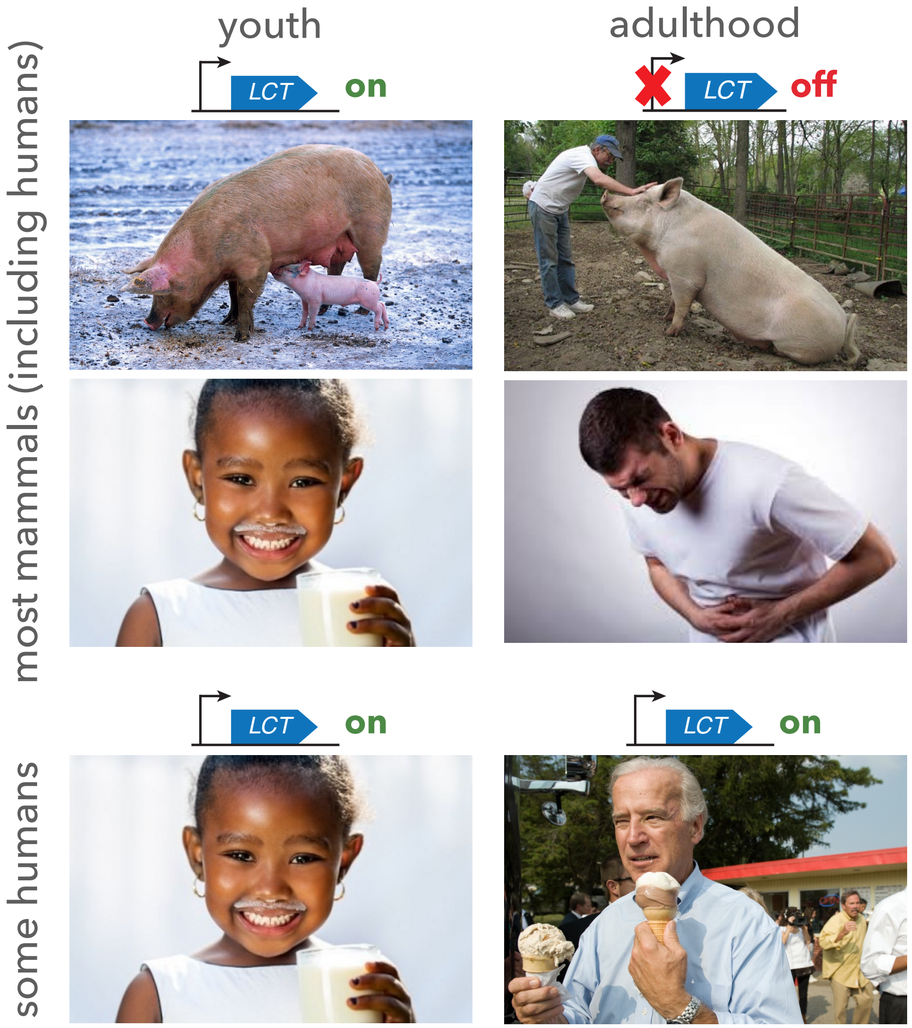

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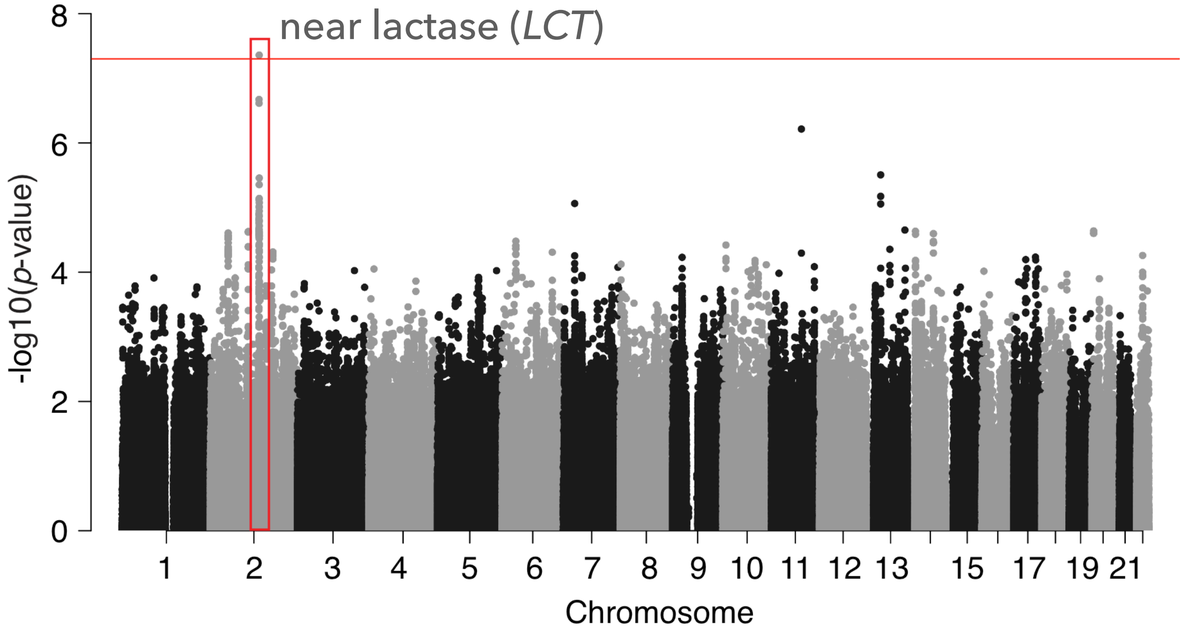

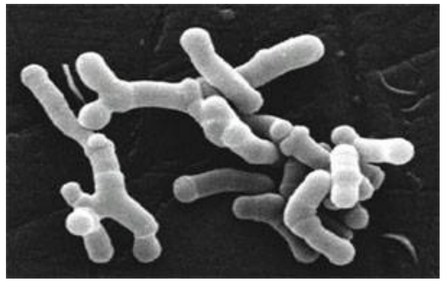

most mammals (including humans)

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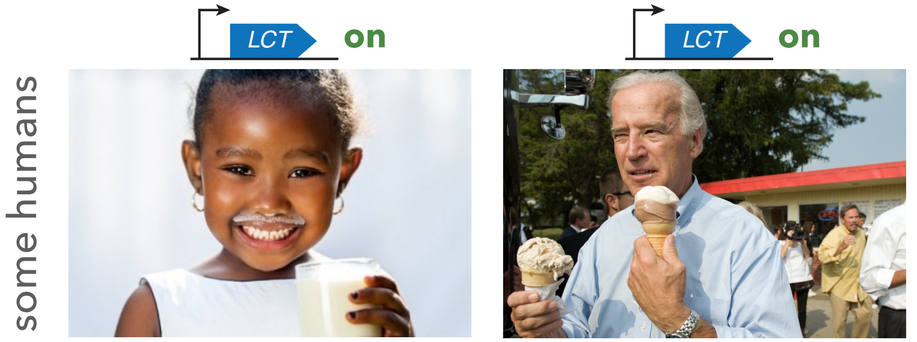

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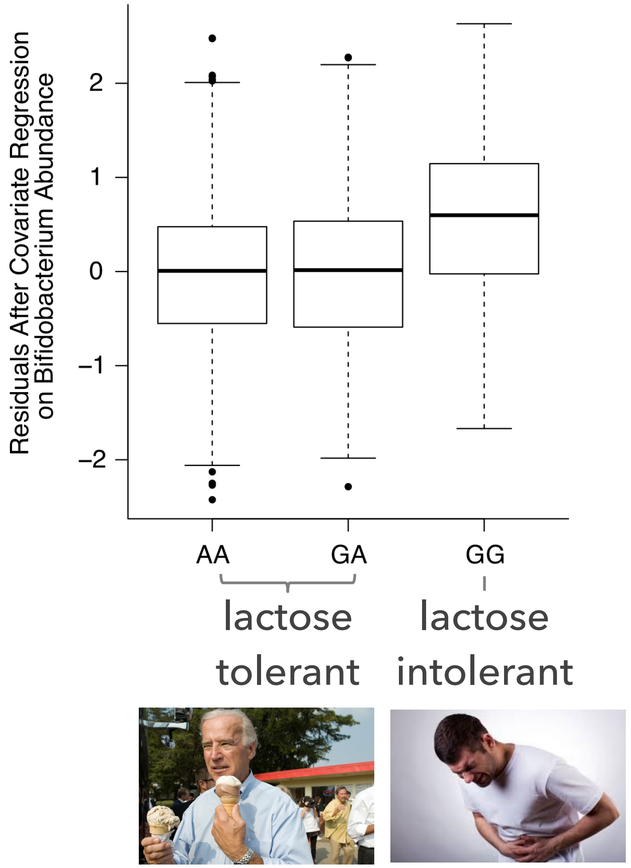

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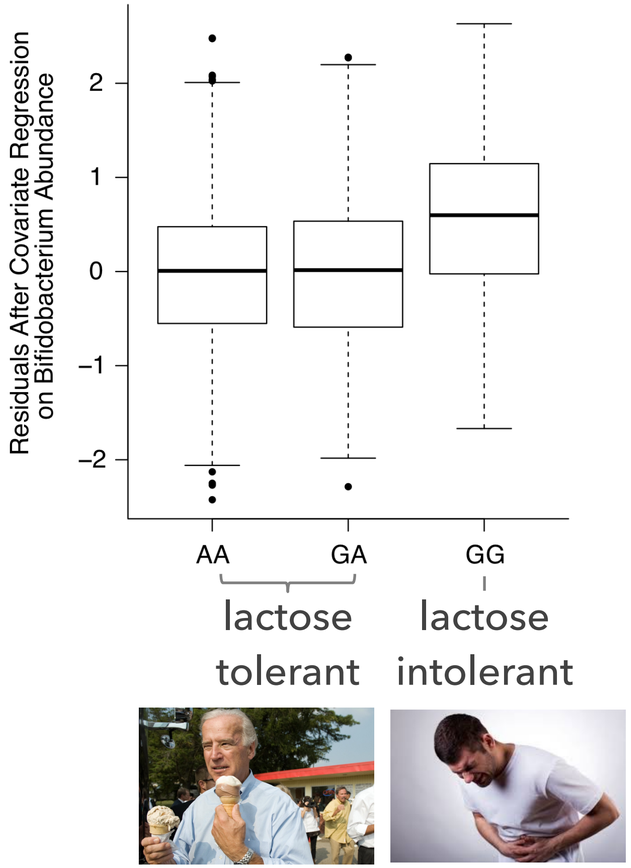

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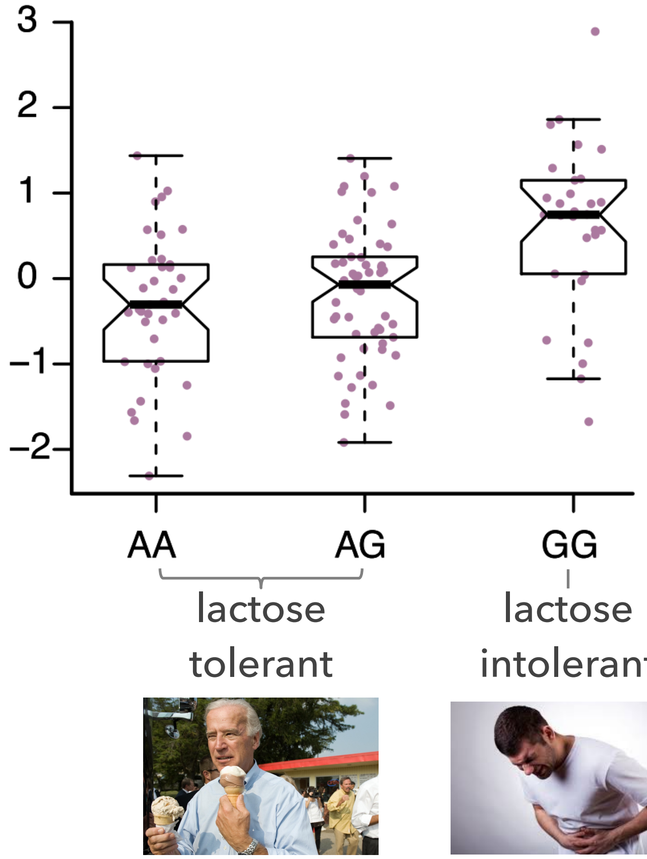
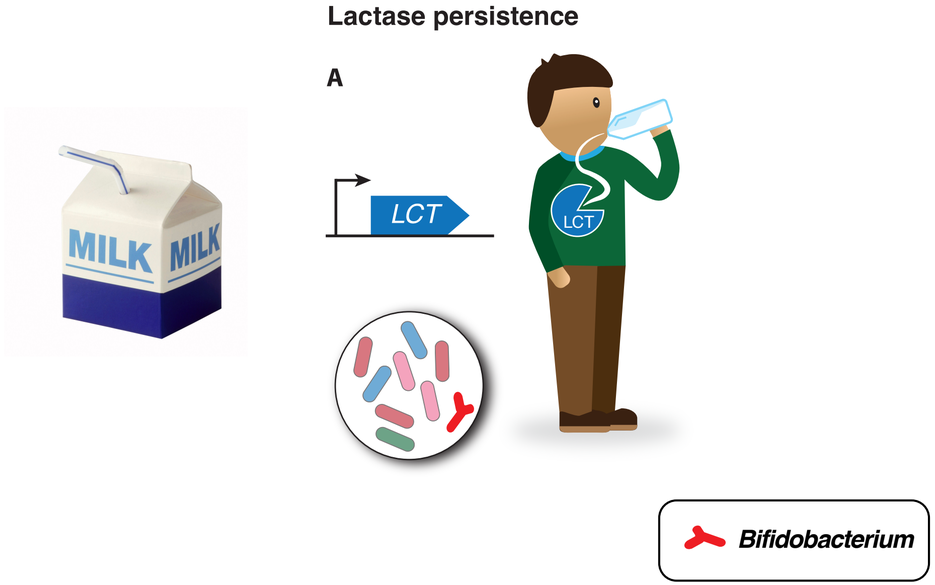


How are *Bifidobacteria*, *lactase persistence*, and *milk* consumption related?



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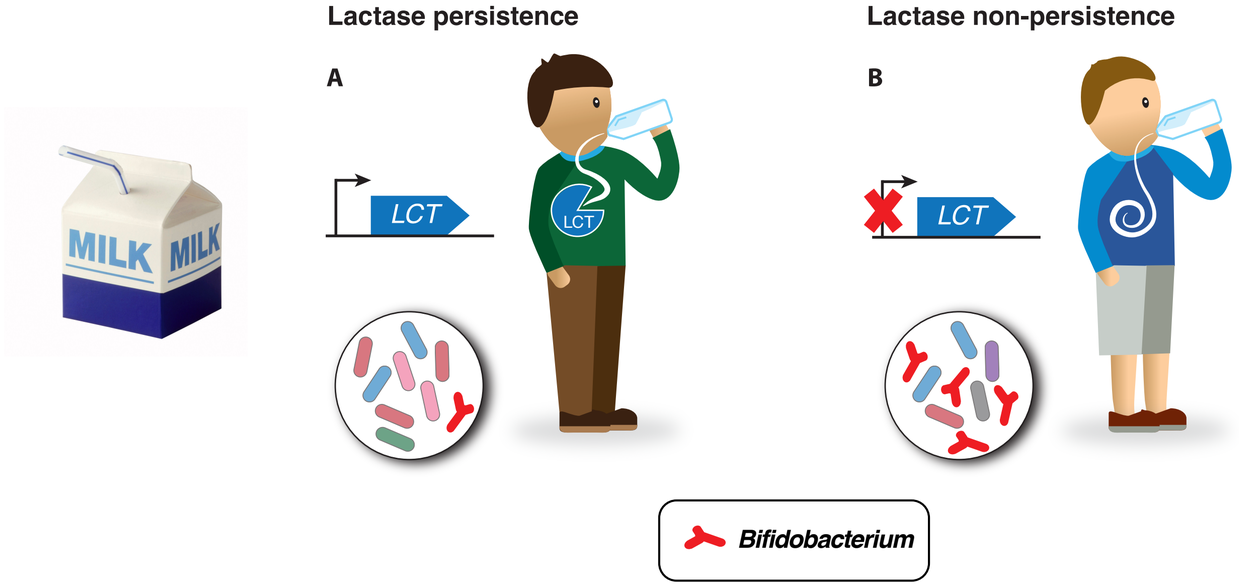

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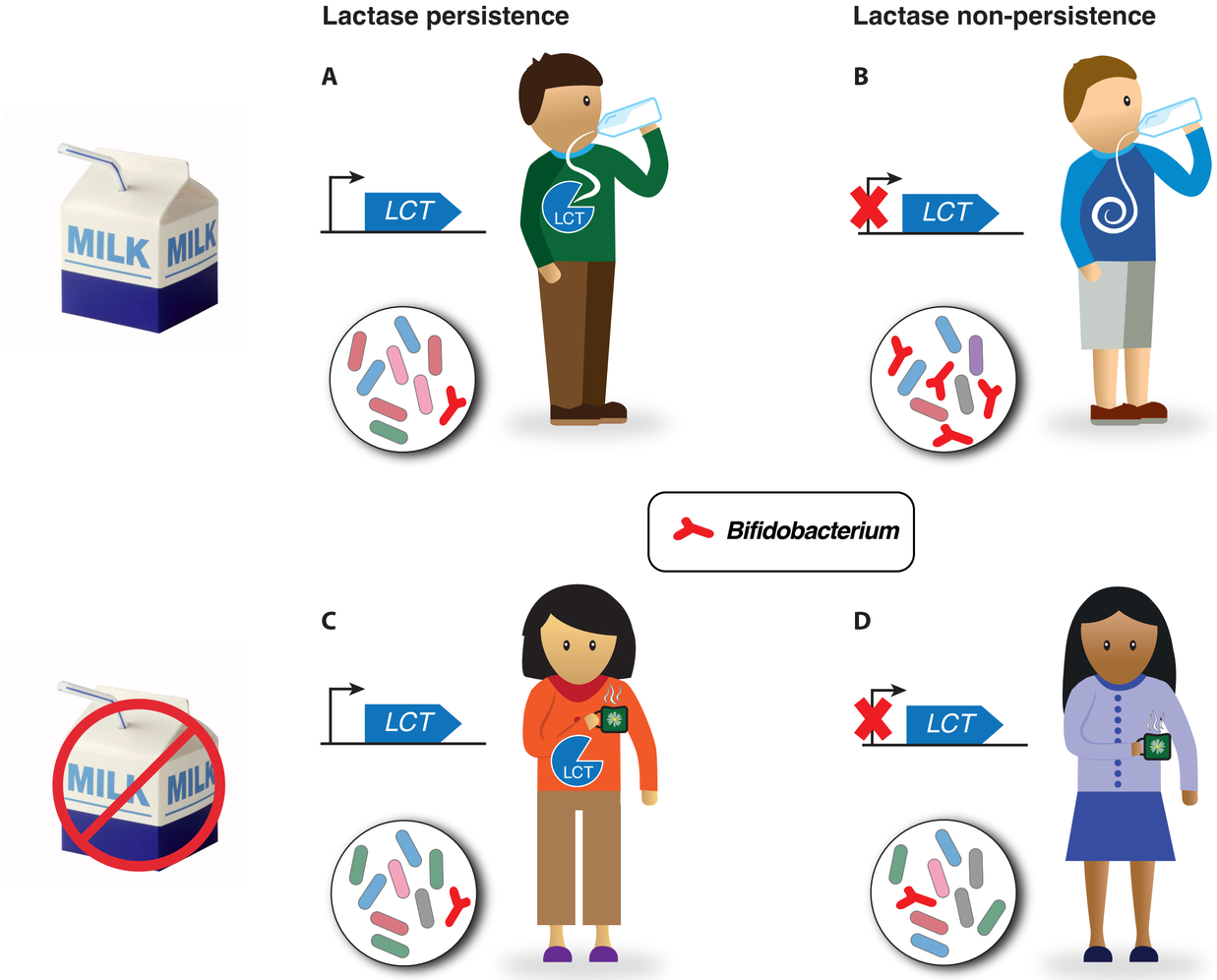

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The *Bifidobacteria - LCT* association replicates across populations

LETTERS

nature genetics

The effect of host genetics on the gut microbiome

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(Dutch)

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(Dutch)

ARTICLE

doi:10.1038/nature25973

Environment dominates over host genetics in shaping human gut microbiota

Daphna Rothschild[1,2]*, Omer Weissbrod[1,2]*, Elad Barkan[1,2]*, Alexander Kurilshikov[3], Tal Korem[1,2], David Zeevi[1,2], Paul I. Costea[1,2], Anastasia Godneva[1,2], Iris N. Kalka[1,2], Noam Bar[1,2], Smadar Shilo[1,2], Dar Lador[1,2], Arnau Vich Vila[3,4], Niv Zmora[5,6,7], Meirav Pevsner-Fischer[5], David Israeli[8], Noa Kosower[1,2], Gal Malka[1,2], Bat Chen Wolf[1,2], Tali Avnit-Sagi[1,2], Maya Lotan-Pompan[1,2], Adina Weinberger[1,2], Zamir Halpern[7,9], Shai Carmi[10], Jingyuan Fu[3,11], Cisca Wijmenga[3,12], Alexandra Zhernakova[3], Eran Elinav[5]§ & Eran Segal[1,2]§

(Israeli)

Blekhman *et al. Genome Biology* (2015) 16:191
DOI 10.1186/s13059-015-0759-1

Genome Biology

RESEARCH Open Access

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Host genetic variation impacts microbiome composition across human body sites

Ran Blekhman[1,2*], Julia K. Goodrich[3,4], Katherine Huang[5], Qi Sun[6], Robert Bukowski[6], Jordana T. Bell[7], Timothy D. Spector[7], Alon Keinan[8], Ruth E. Ley[3,4], Dirk Gevers[5,9] and Andrew G. Clark[3]

(American)

Cell Host & Microbe
Resource

Genetic Determinants of the Gut Microbiome in UK Twins

Julia K. Goodrich,[1] Emily R. Davenport,[1] Michelle Beaumont,[2] Matthew A. Jackson,[2] Rob Knight,[3] Carole Ober,[4] Tim D. Spector,[2] Jordana T. Bell,[2] Andrew G. Clark,[1] and Ruth E. Ley[1,5,*]
[1]Department of Molecular Biology and Genetics, Cornell University, Ithaca, NY 14850, USA
[2]Department of Twin Research & Genetic Epidemiology, King's College London, London SE1 7EH, UK
[3]Departments of Pediatrics and Computer Science and Engineering, University of California San Diego, La Jolla, CA 92093, USA
[4]Department of Human Genetics, University of Chicago, Chicago, IL 60637, USA
[5]Department of Microbiome Science, Max Planck Institute for Developmental Biology, 72076 Tübingen, Germany
*Correspondence: rel222@cornell.edu
http://dx.doi.org/10.1016/j.chom.2016.04.017

(British and Hutterites)

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1. Are relative abundances of specific bacteria *heritable?* ✓

2. Which *variants* in the human genome are associated with bacterial relative abundance?

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3. In which *host tissues* do genetic variants act to influence microbiome composition?

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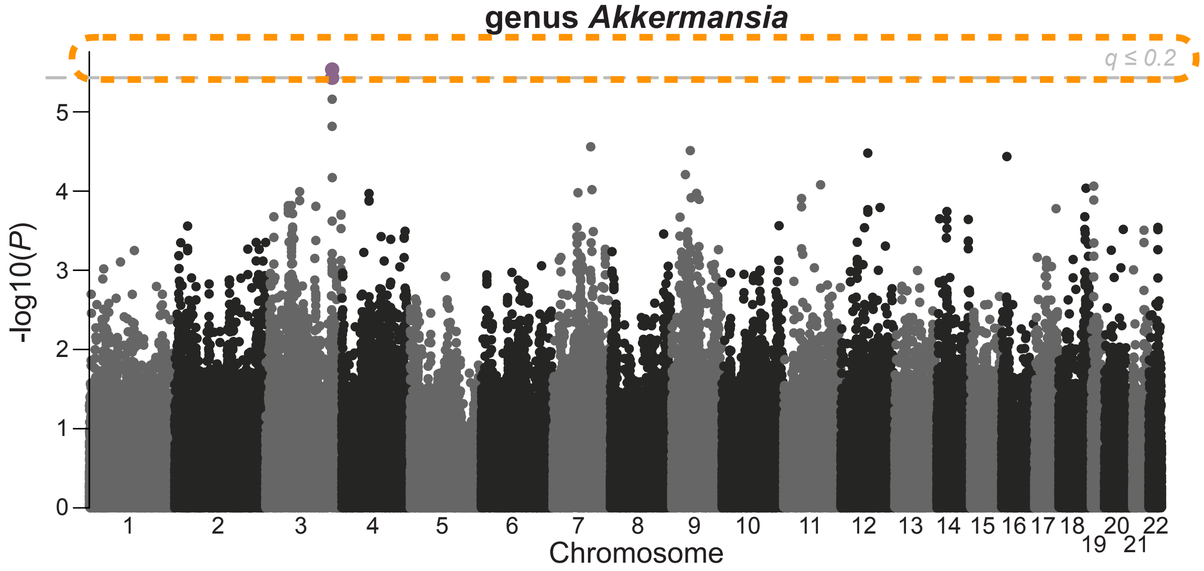

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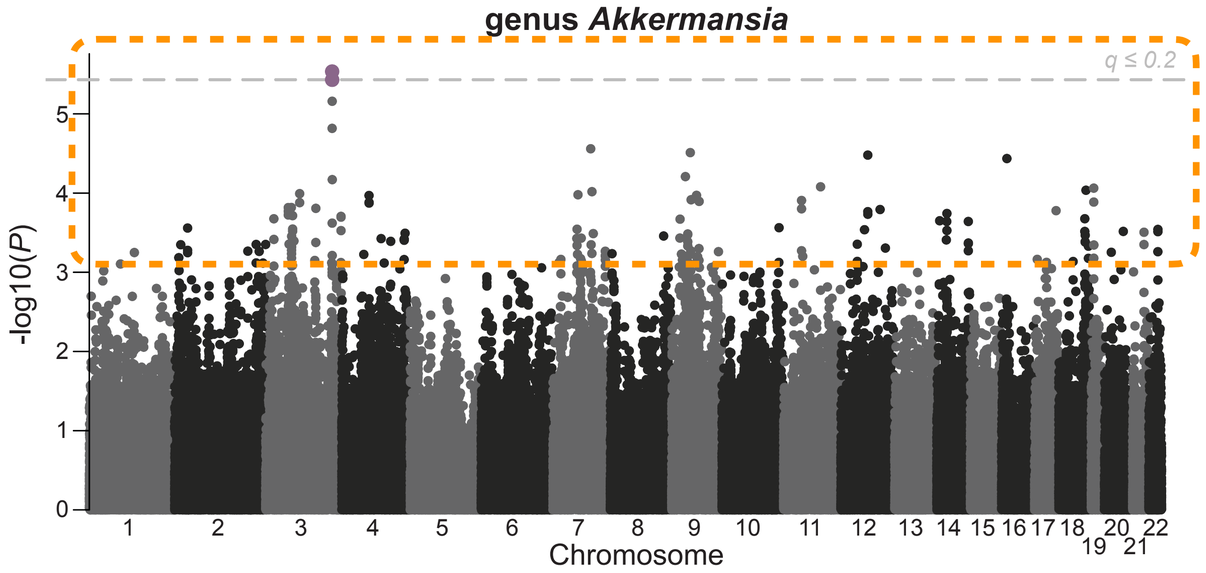

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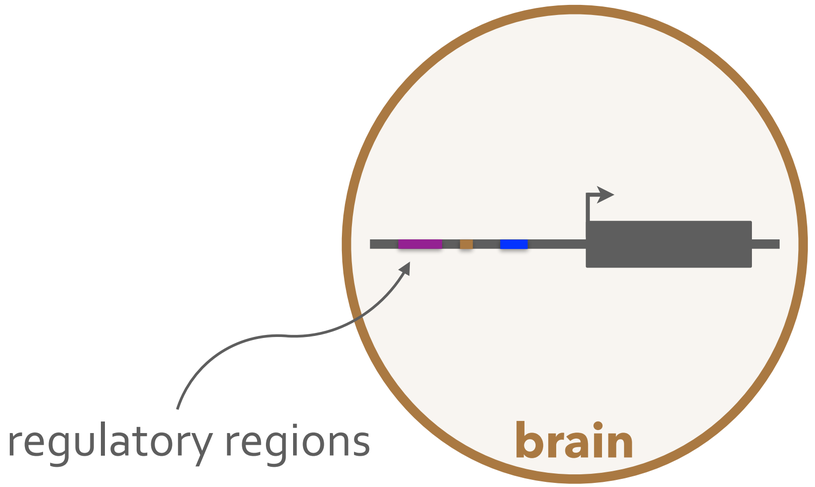

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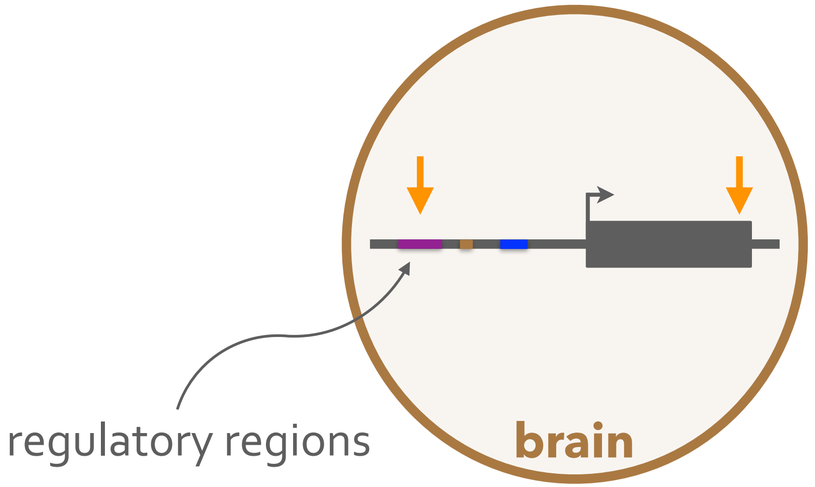

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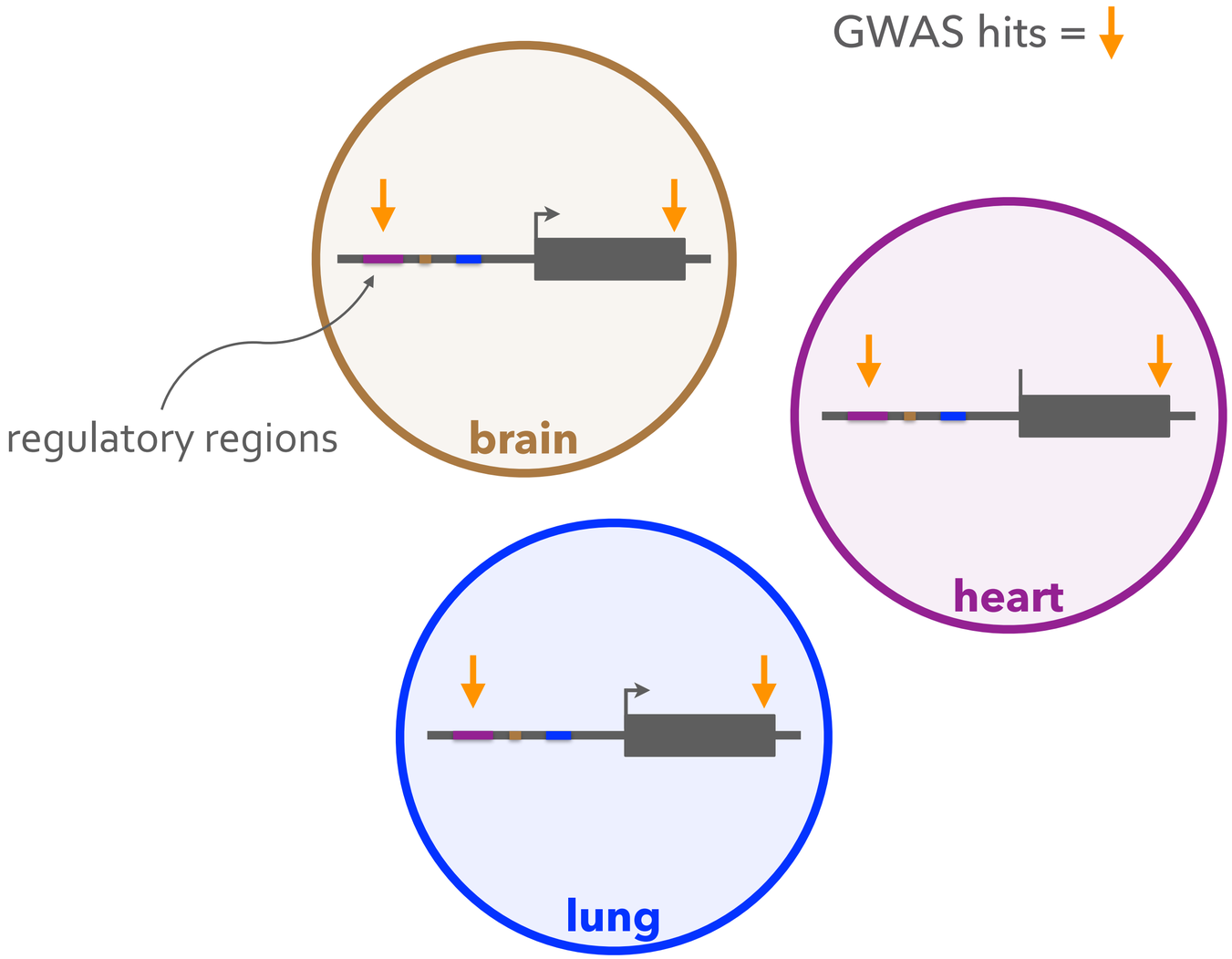

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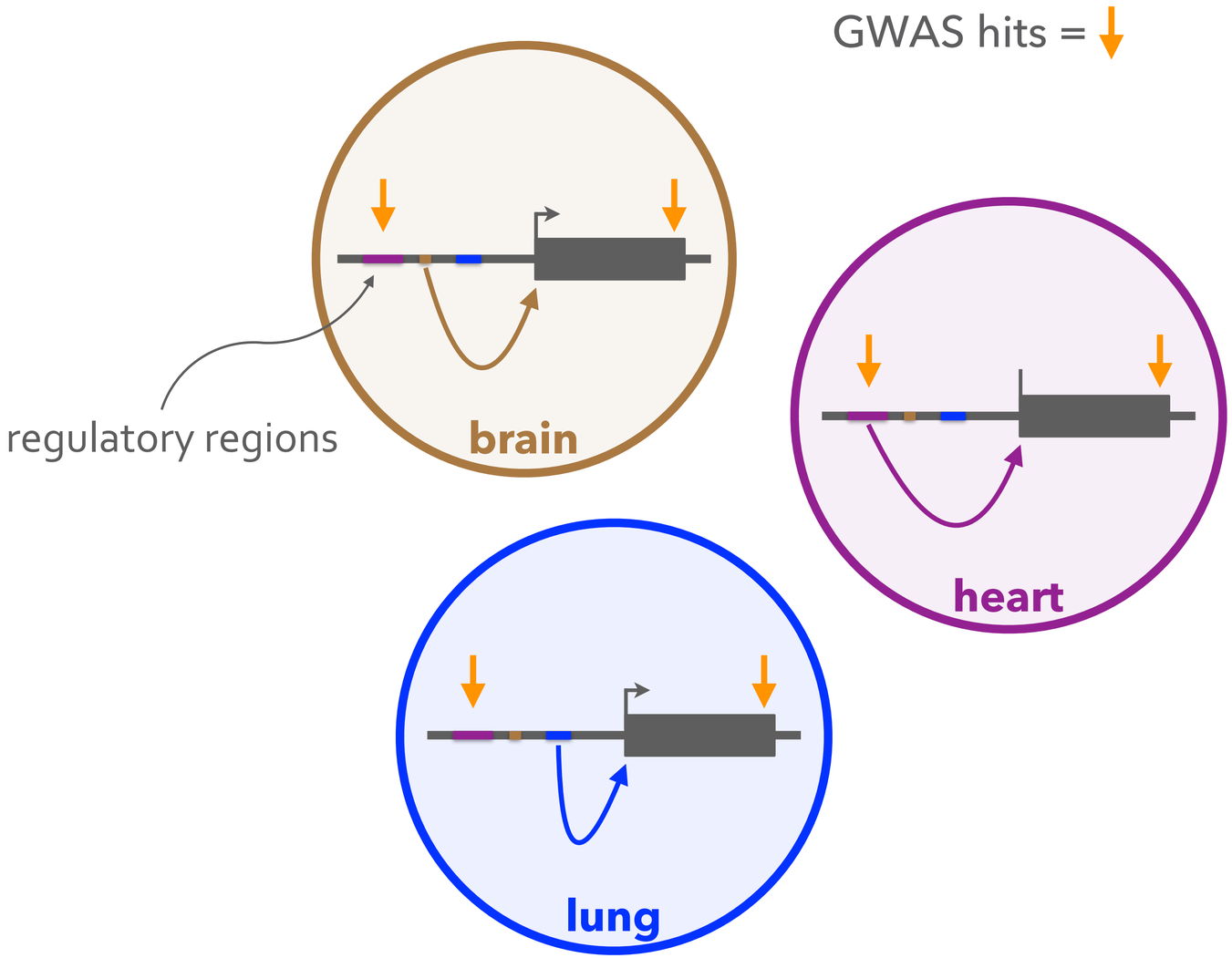

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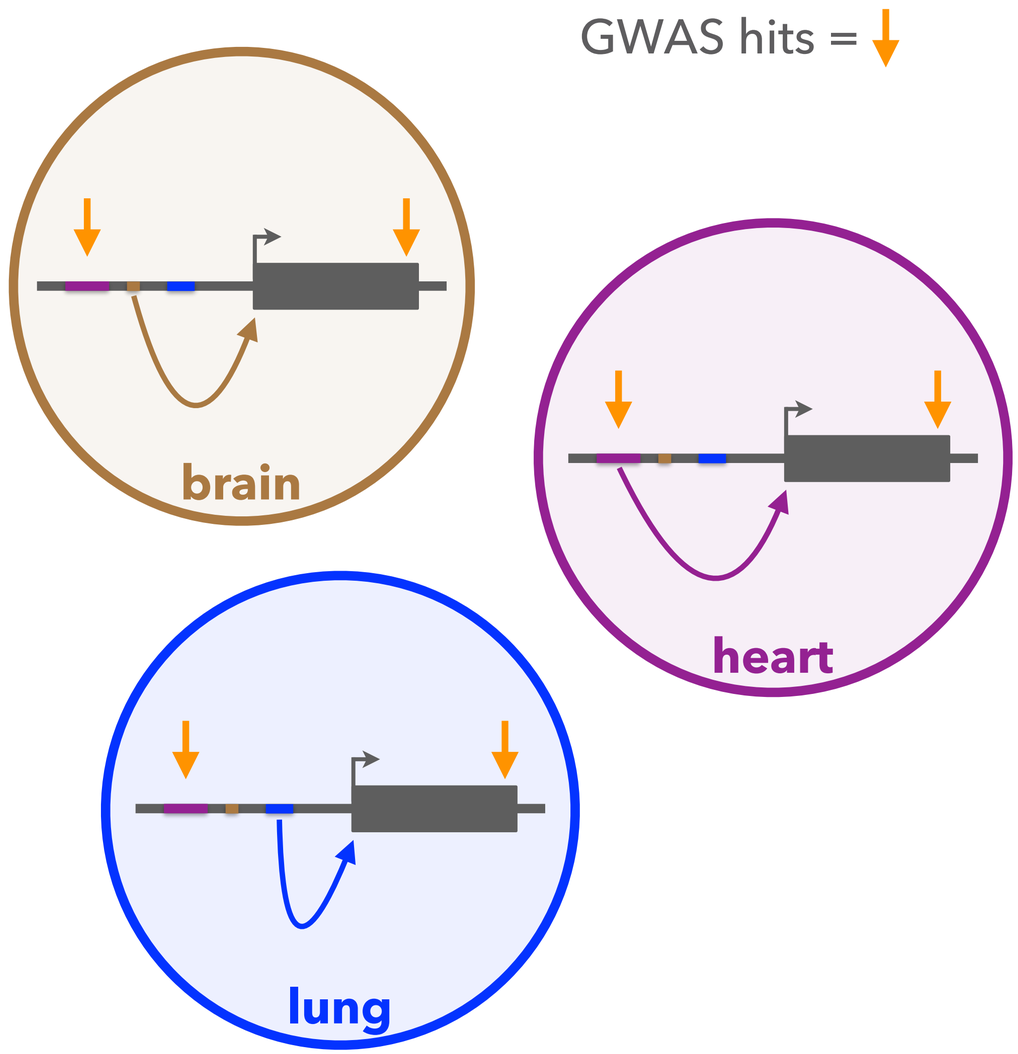

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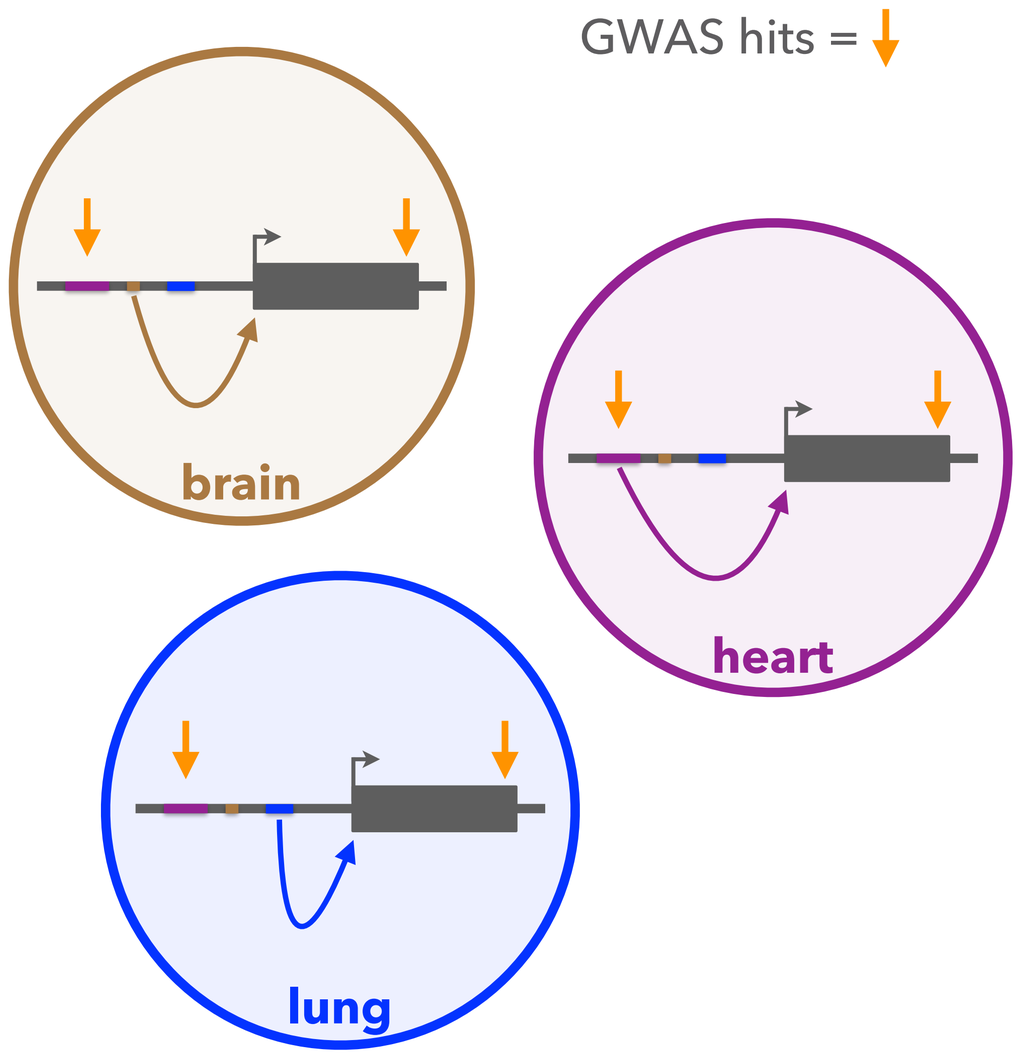

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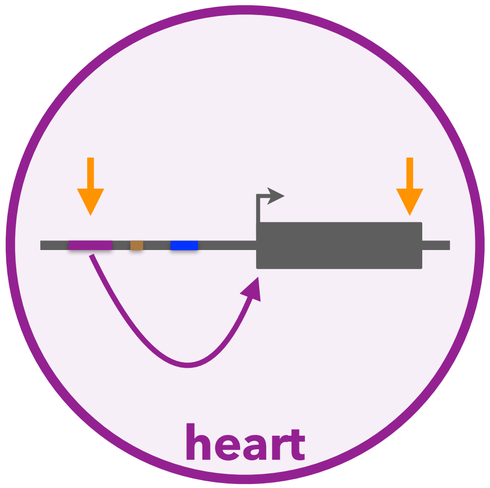
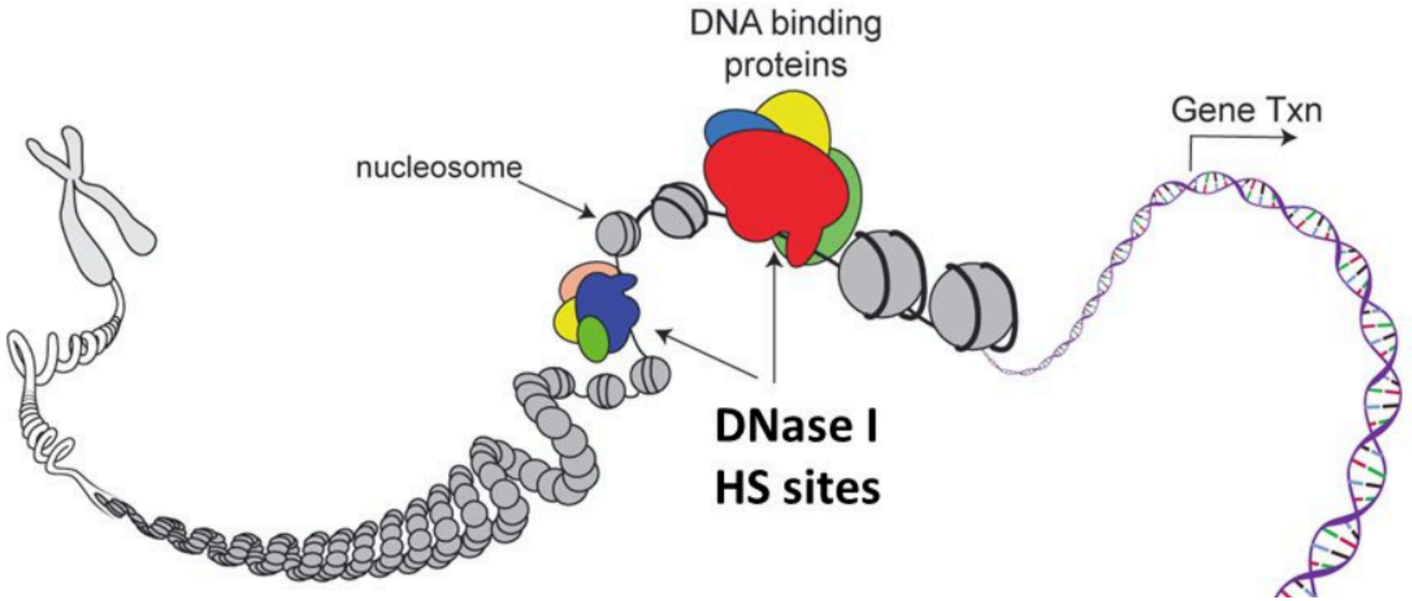
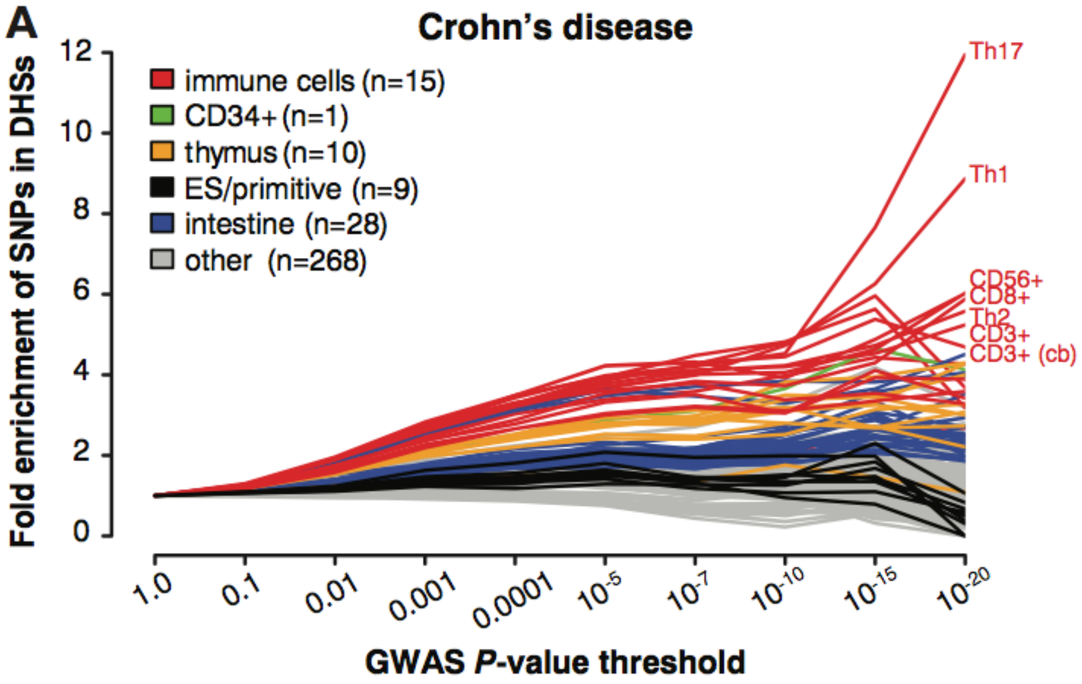


DNase hypersensitivity sites (DHS) identify *active gene regulatory elements*



Crawford *et al*. Nature Methods 2006

Using DNase hypersensitivity sites (DHS) to identify *pathogenic cell types*



Maurano *et al*. Science 2012

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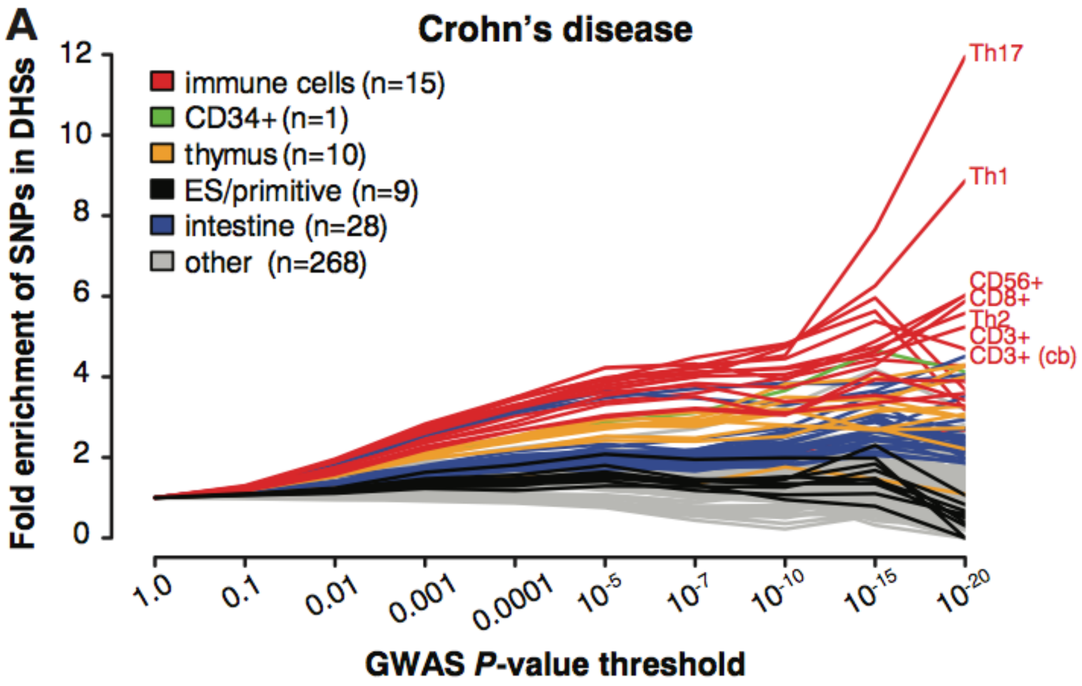

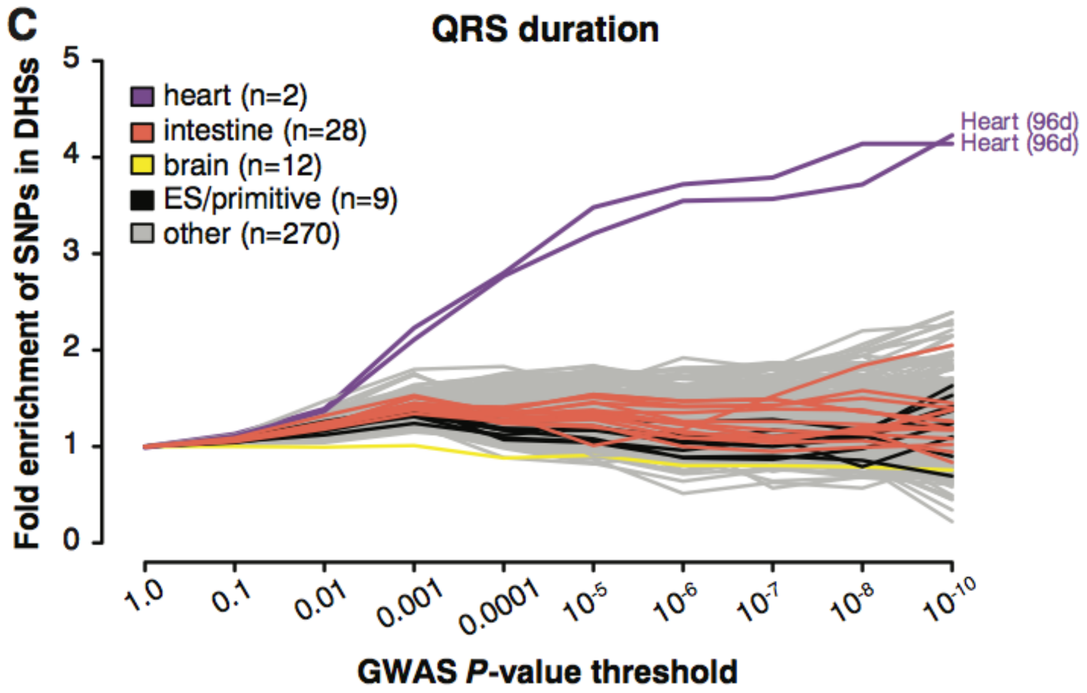

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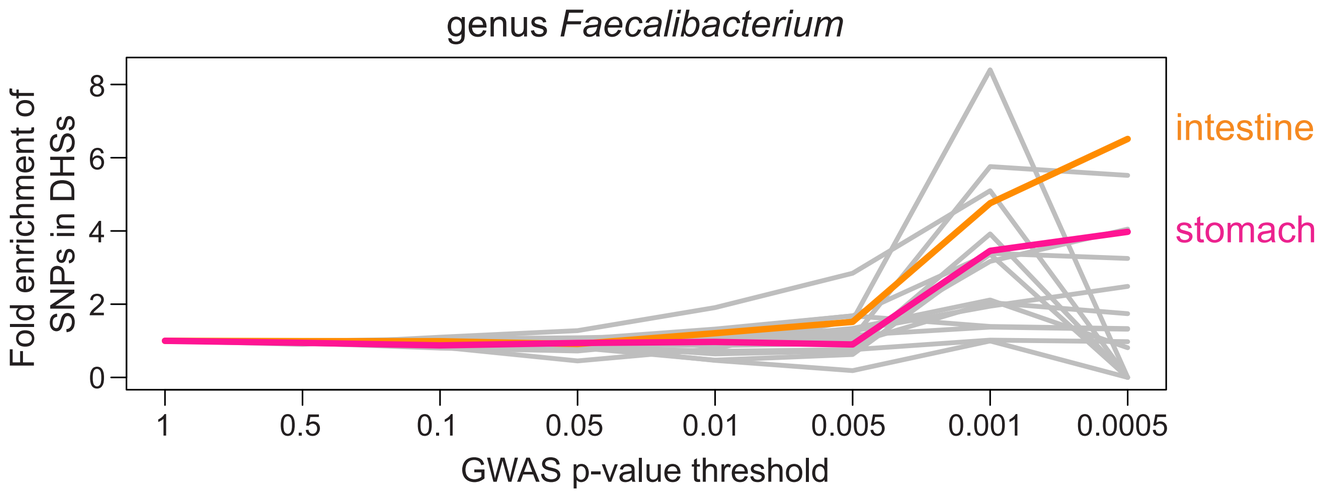

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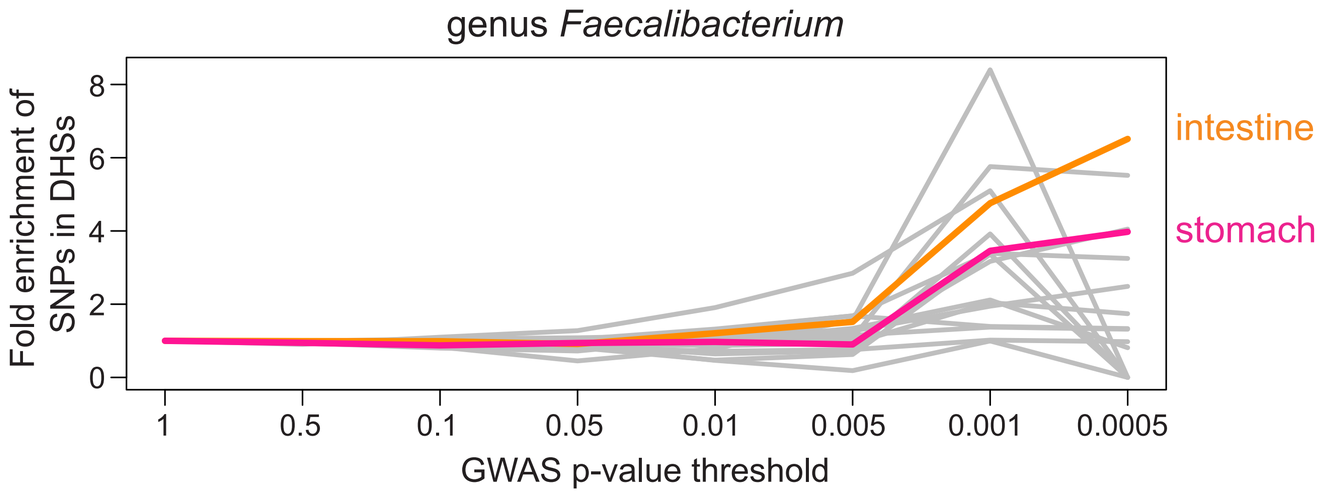

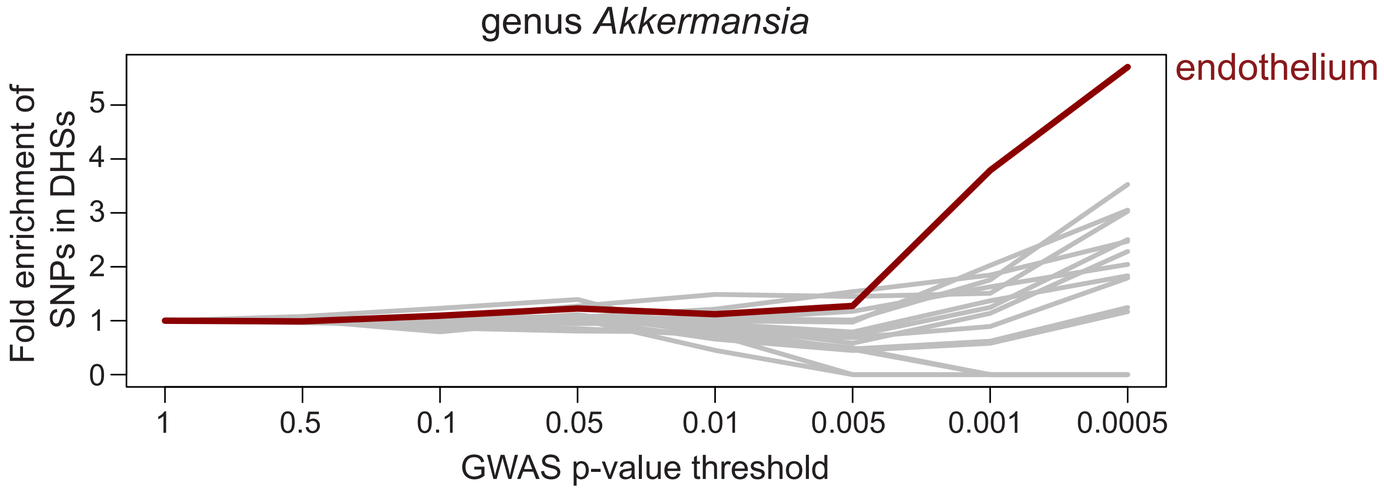

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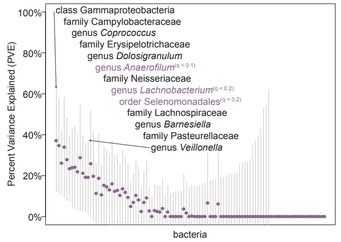

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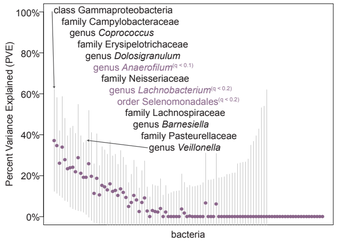

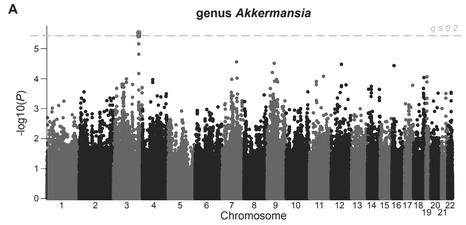

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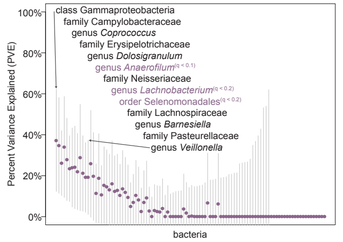
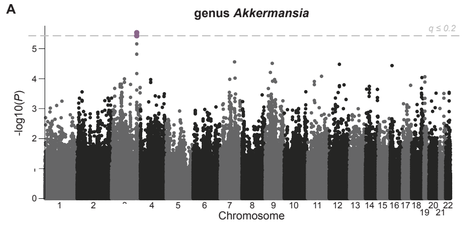
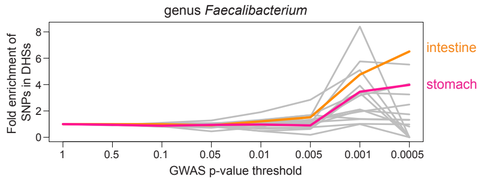


2. We can identify *variants* in the human genome associated with bacterial abundance.



3. We can identify candidate *host tissues* where this genetic variation acts.



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Davenport lab at Penn State is recruiting
grad students, postdocs, and research associates!

see davenport-lab.github.io for more information