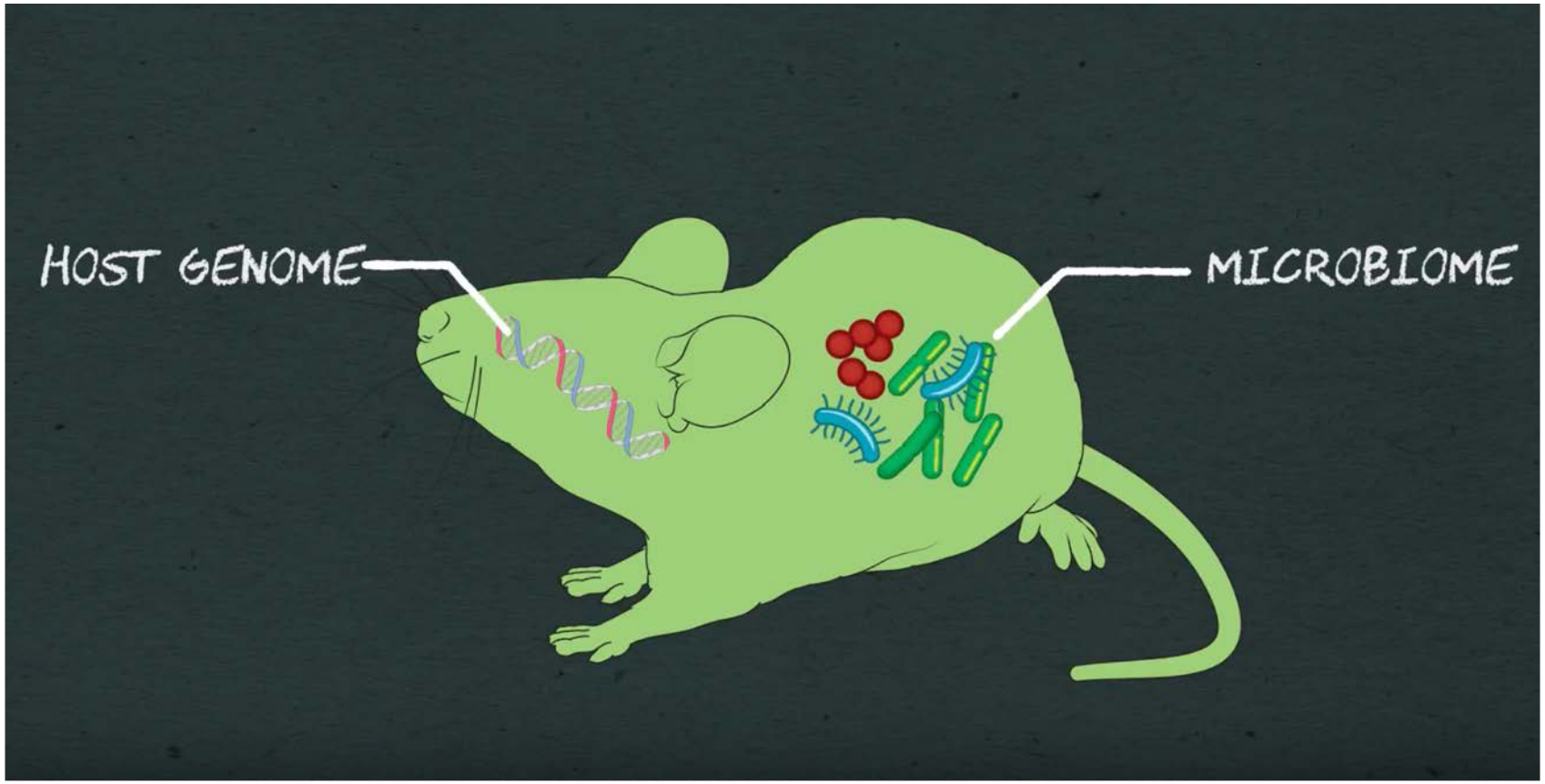
Men, Mice and Natural Microbiota

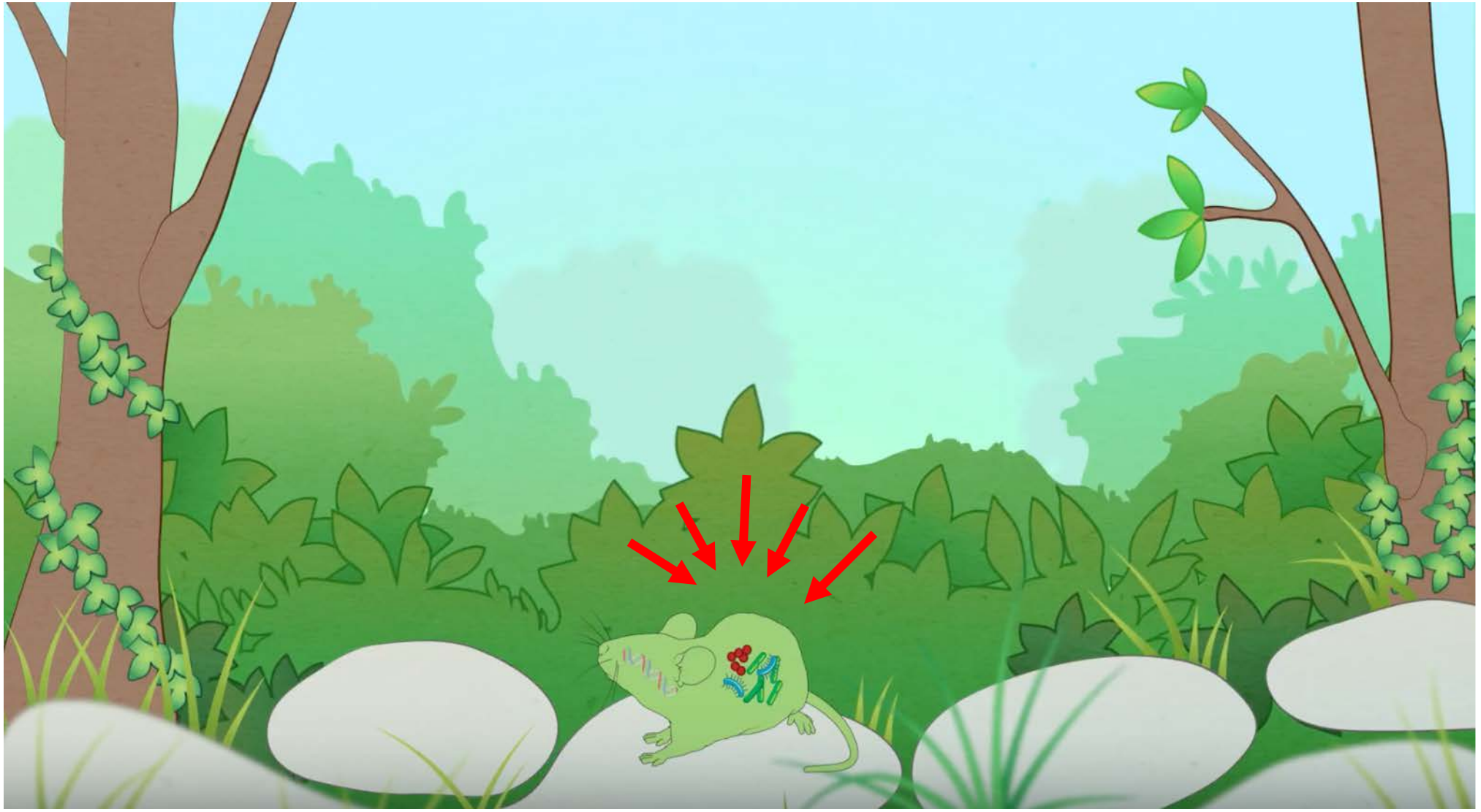
Barbara Rehermann, MD

Liver Diseases Branch, NIDDK,
National Institutes of Health
Bethesda, Maryland, USA

Meta-genome and Meta-organism

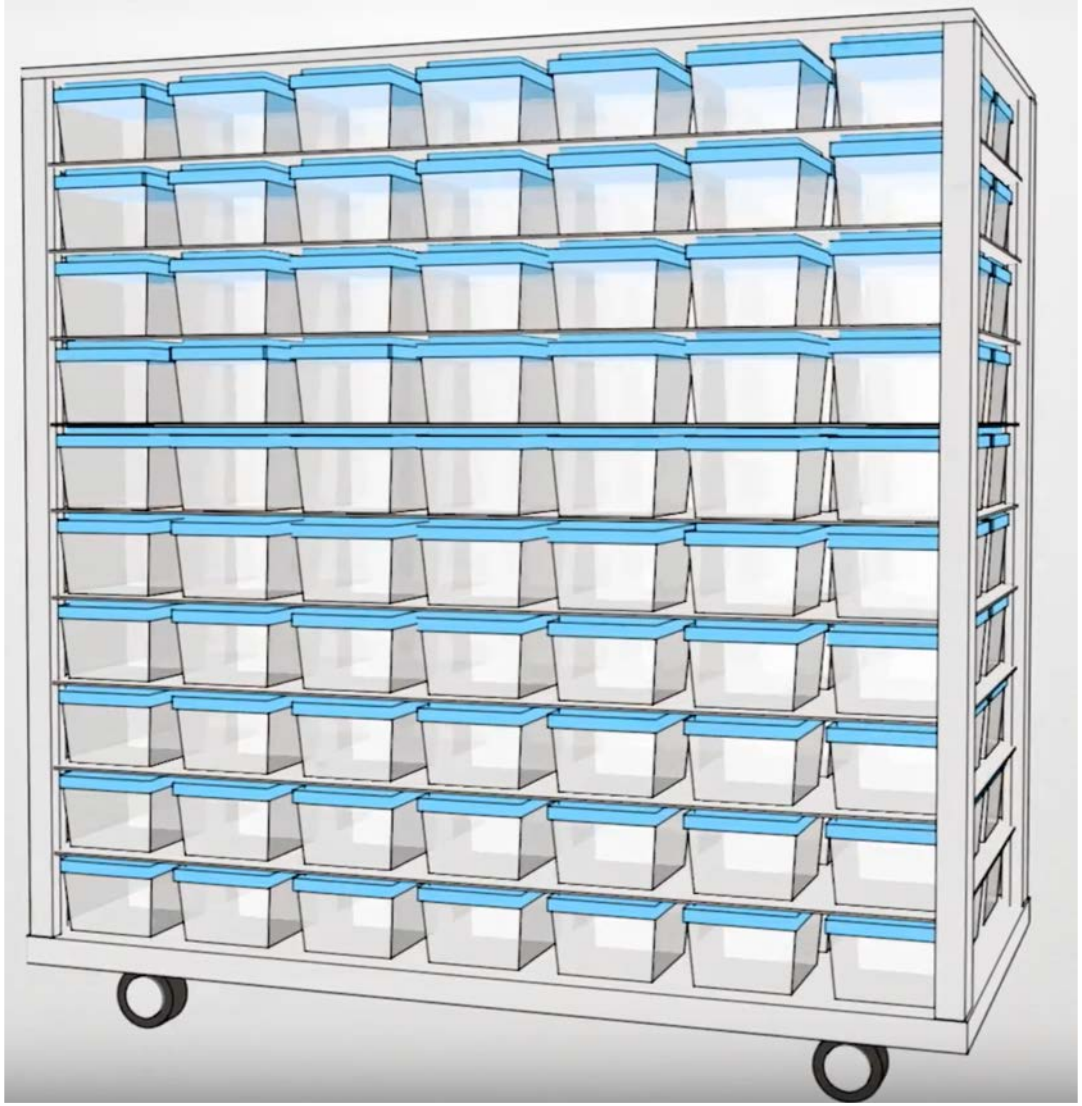


Natural World

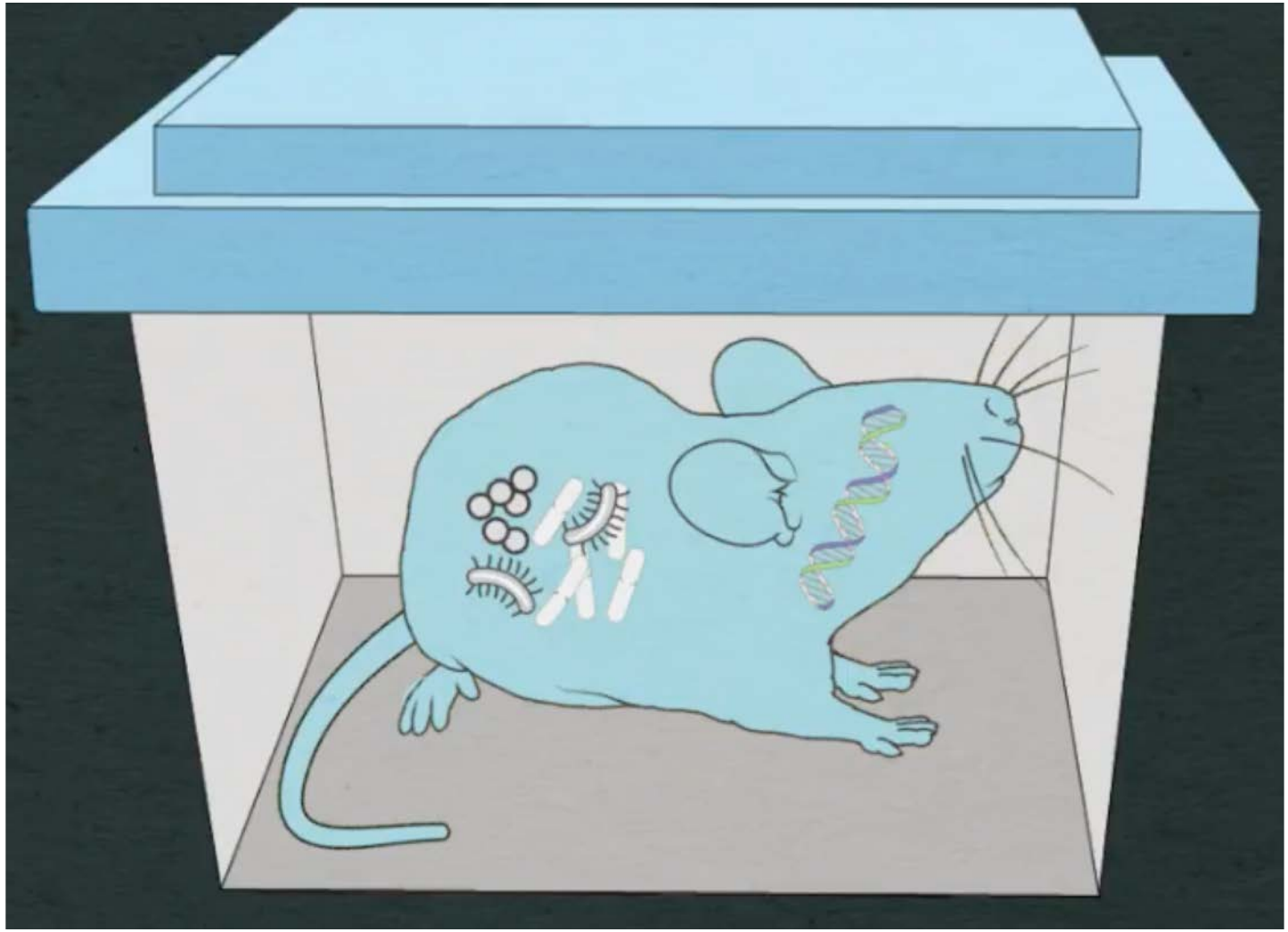


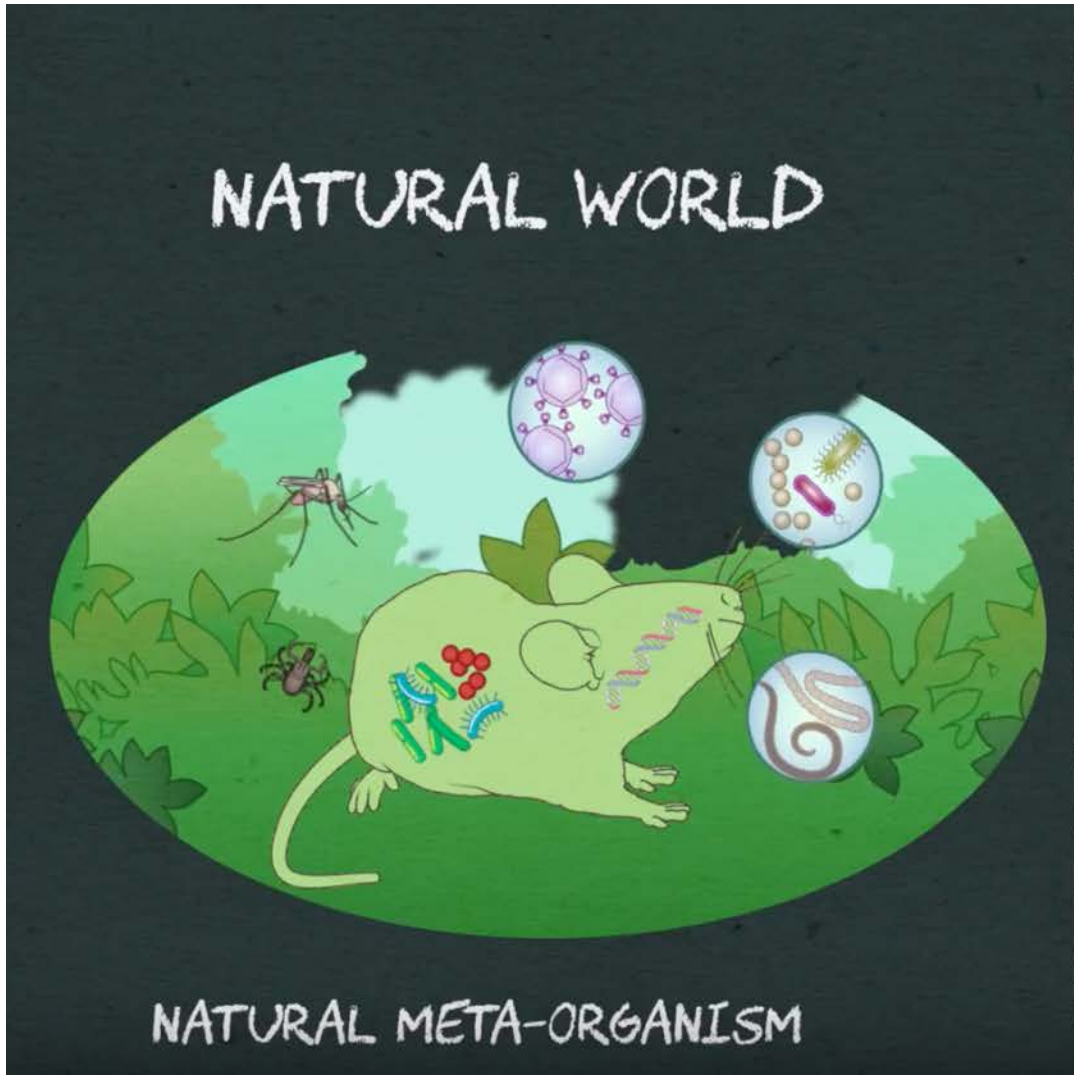
Natural World

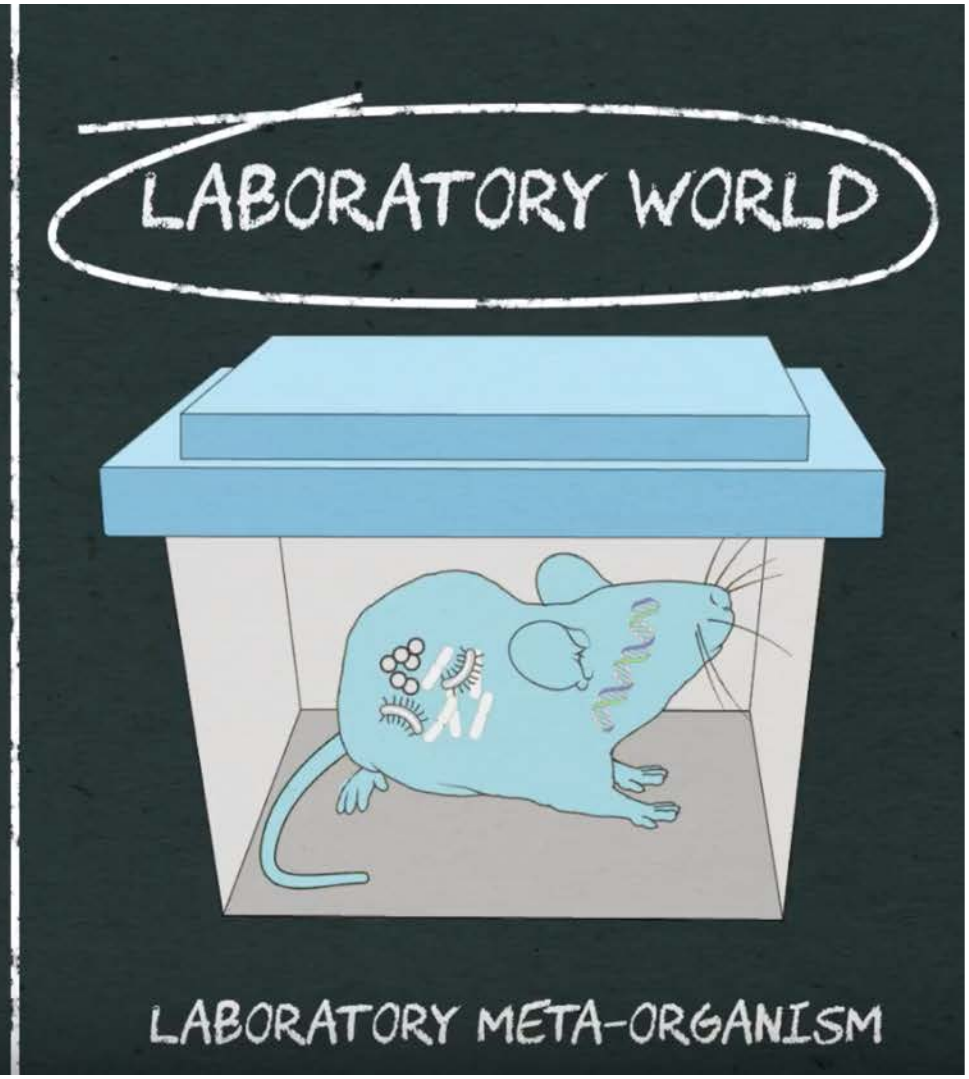
Laboratory World



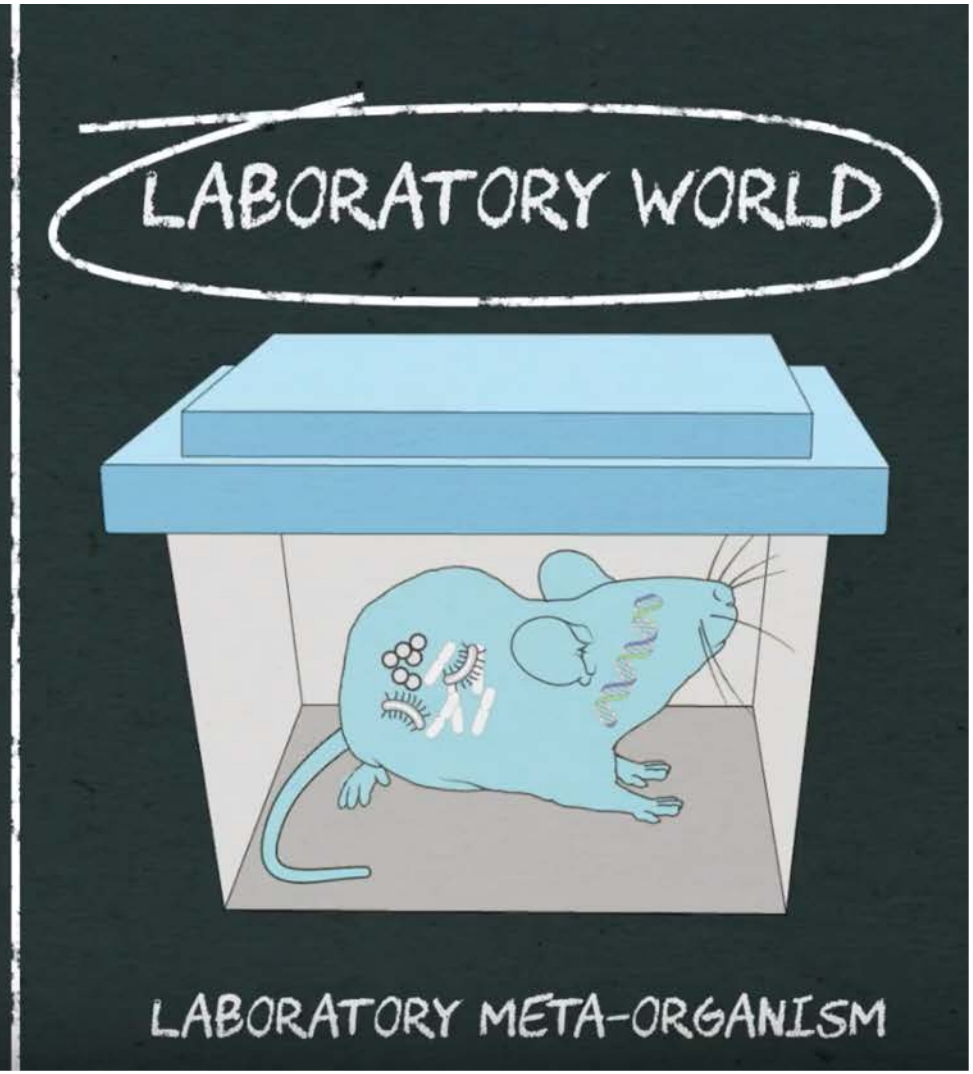
Normalized and Restrictive Environment




NATURAL WORLD
NATURAL META-ORGANISM


LABORATORY WORLD
LABORATORY META-ORGANISM

NATURAL WORLD
NATURAL META-ORGANISM


LABORATORY WORLD
LABORATORY META-ORGANISM

Hypothesis

Laboratory mice lack host-microbe interactions that are physiologically important and found in the natural world.

Question

Can we learn anything from a naturally co-evolved microbiome?

Stephan Rosshart, MD

NIH Intramural Research Program
Our Research Changes Lives
one program
many people
infinite possibilities

Studies on Microbiome

Germfree or
antibiotic treated

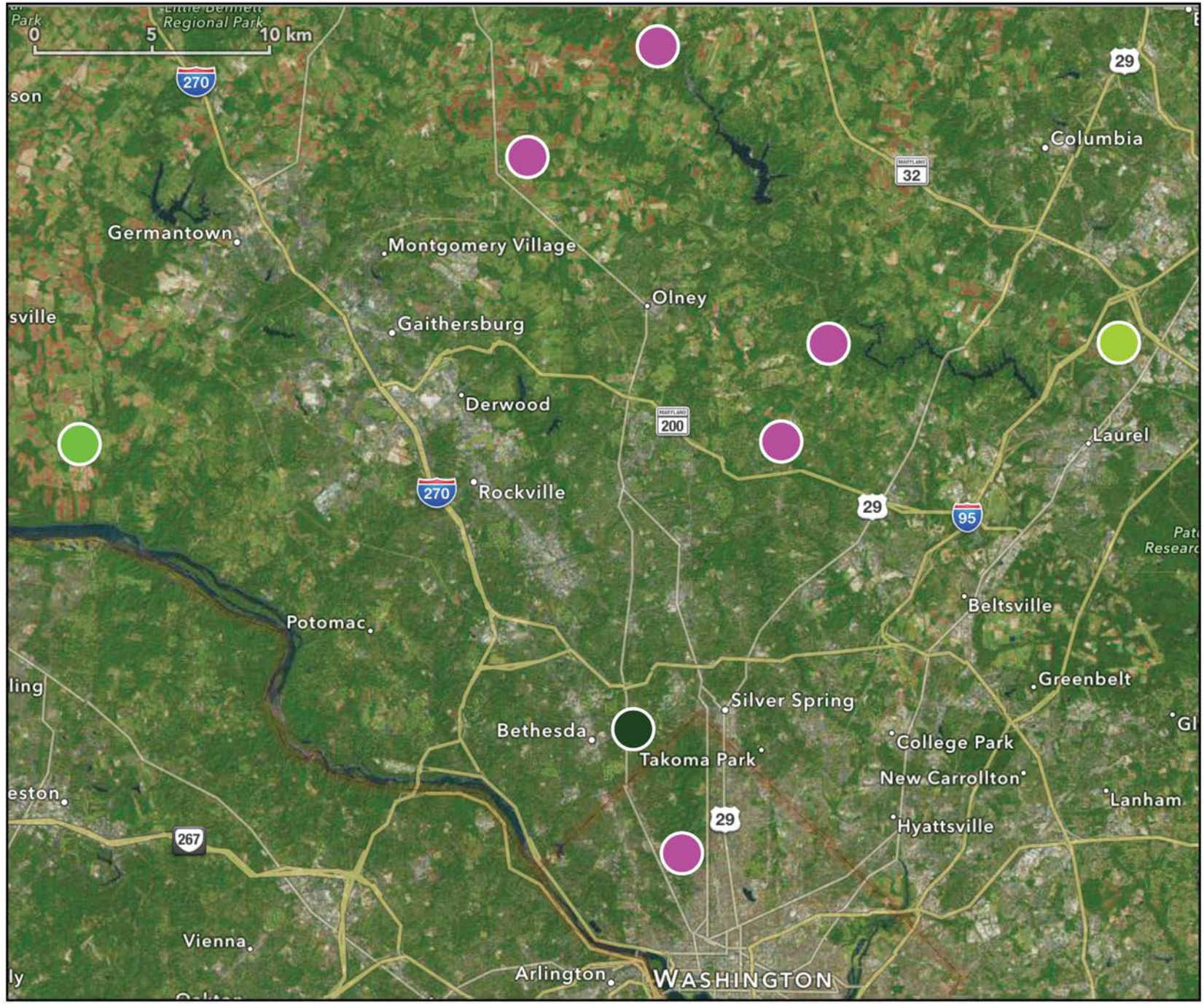
Lab mice in
barrier facility

Studies on Microbiome

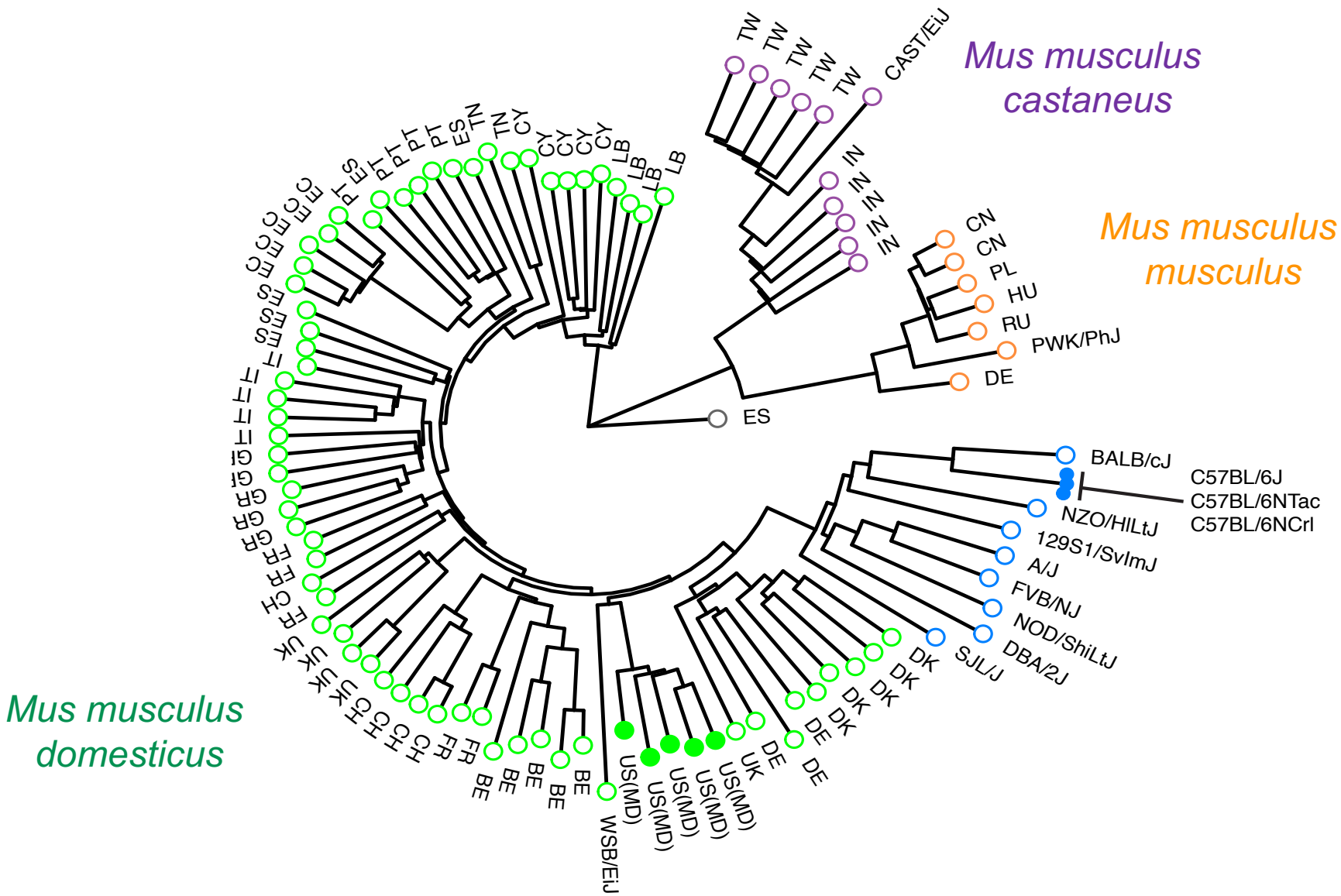
Germfree or
antibiotic treated

Lab mice in
barrier facility

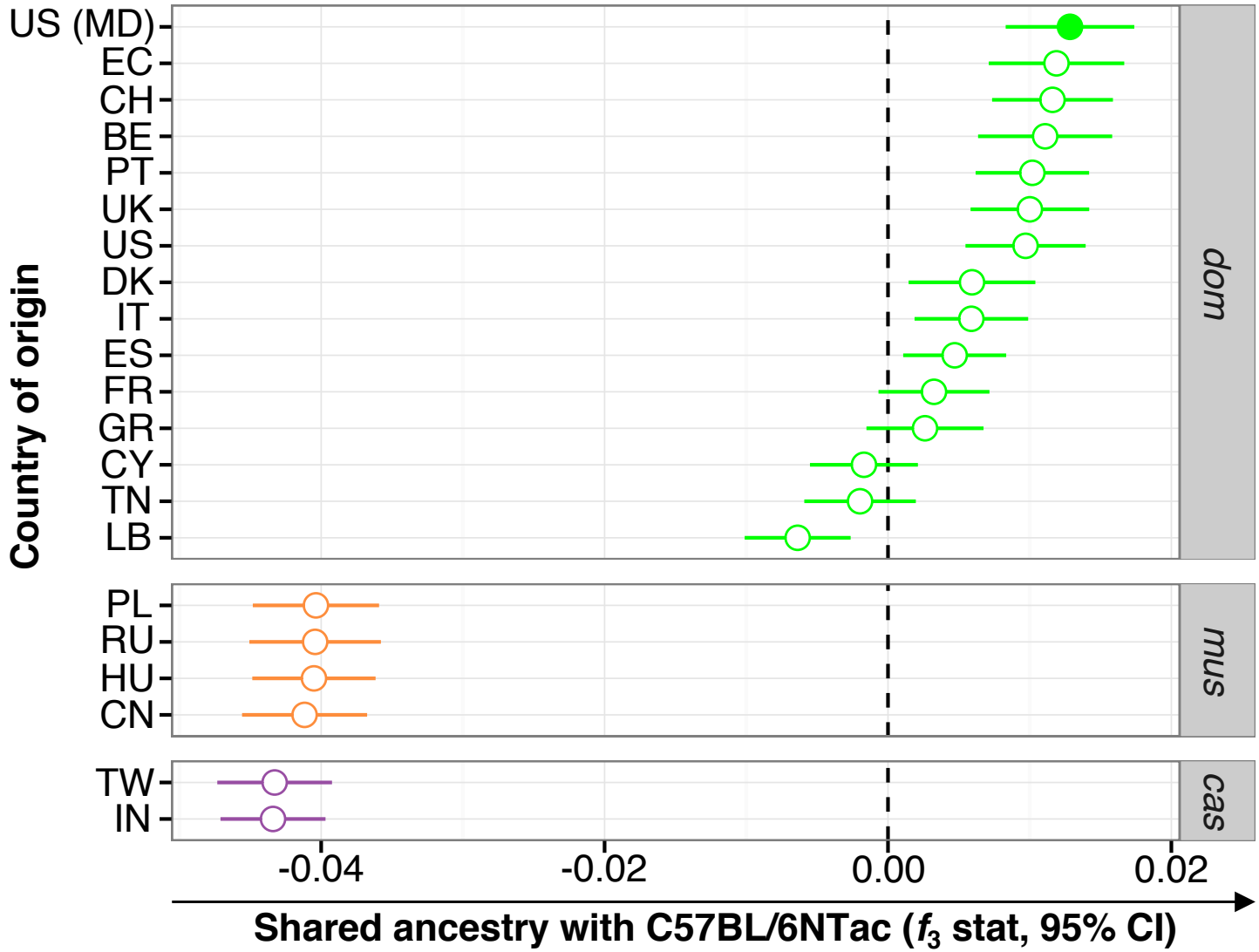
Wild mice
Mus musculus domesticus


0
5
10 km
Little Bennett Regional Park
270
29
Columbia
32
Germantown
Montgomery Village
Olney
Gaithersburg
Derwood
200
Laurel
270
Rockville
29
95
Beltsville
Potomac
Greenbelt
Silver Spring
Bethesda
College Park
Takoma Park
New Carrollton
Lanham
29
Hyattsville
267
Vienna
Arlington
WASHINGTON

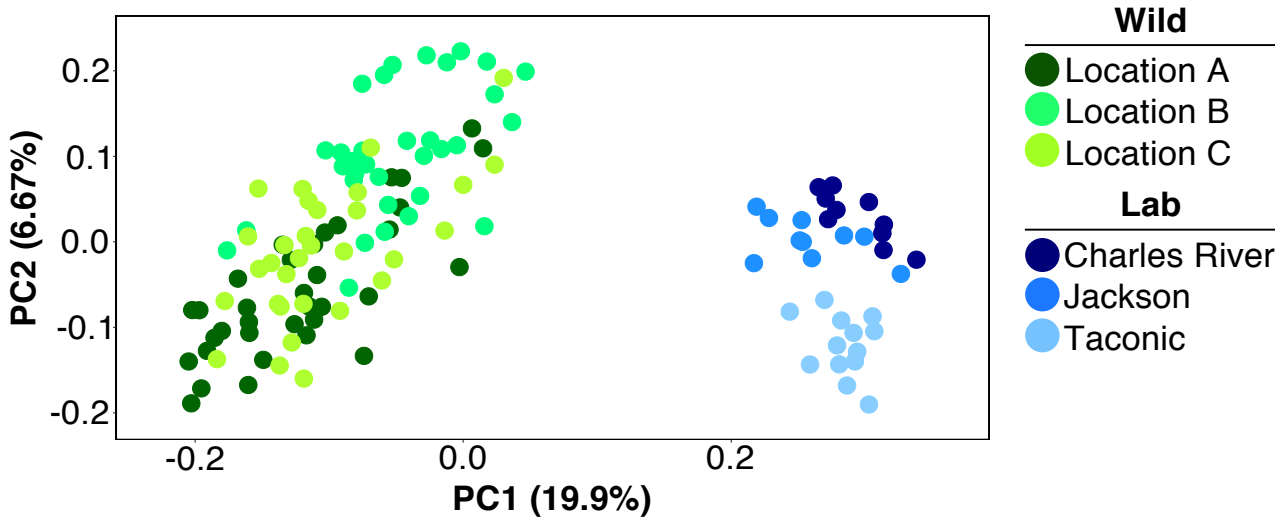
Mus Musculus Domesticus from Maryland are Close Relatives to Standard Laboratory Strains



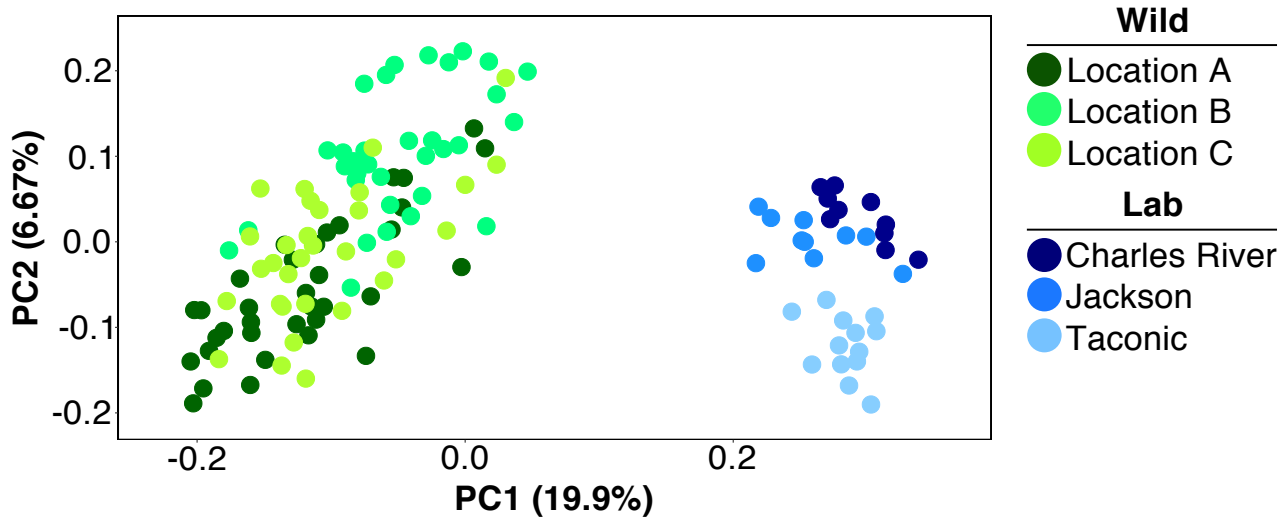
Mus Musculus Domesticus from Maryland are Close Relatives to Standard Laboratory Strains

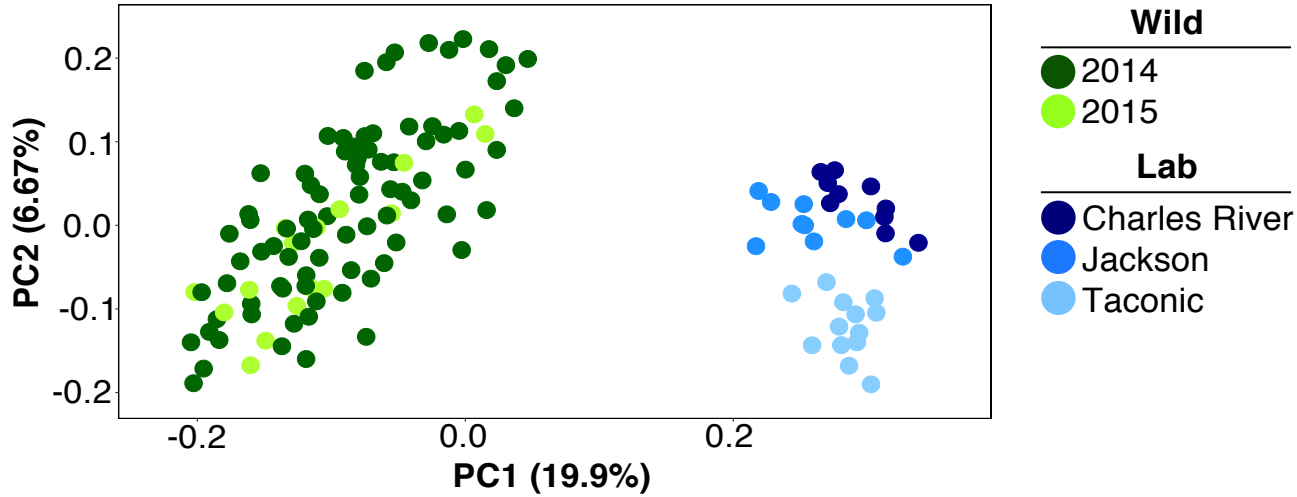


The Lab Mouse Gut Microbiome Differs from that of their Wild-Living Kin

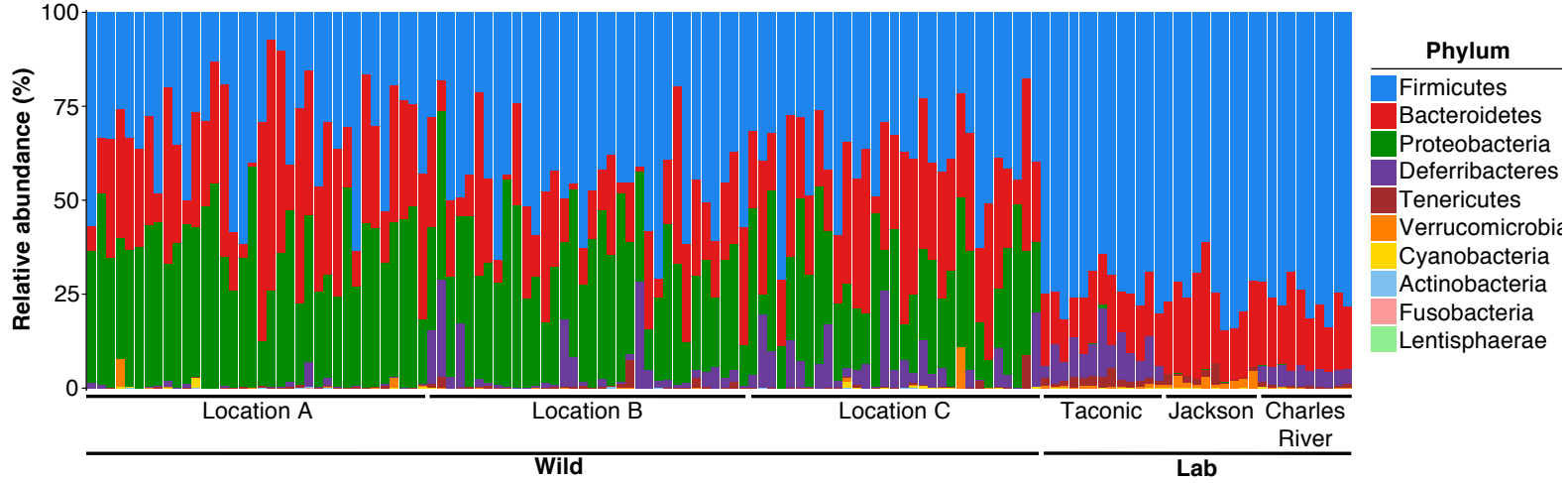


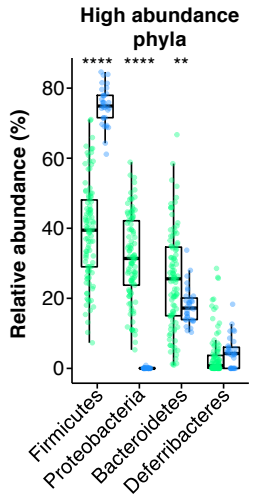
The Lab Mouse Gut Microbiome Differs from that of their Wild-Living Kin

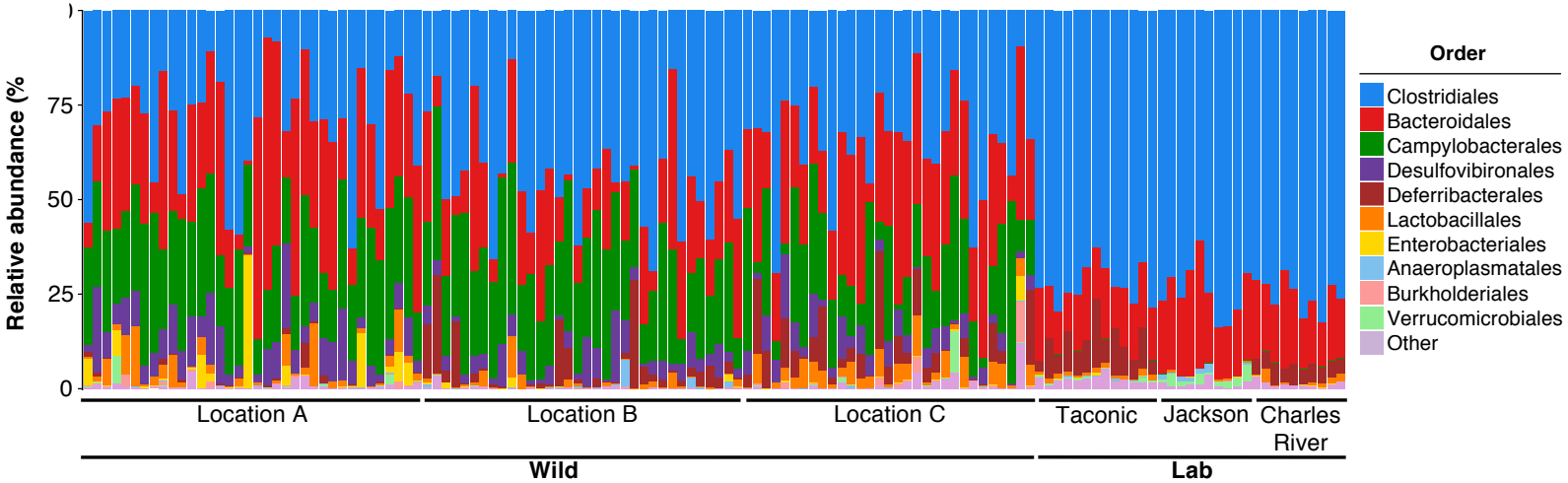


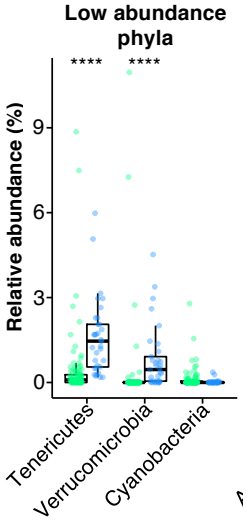


The Lab Mouse Gut Microbiome Differs from That of their Wild-Living Kin

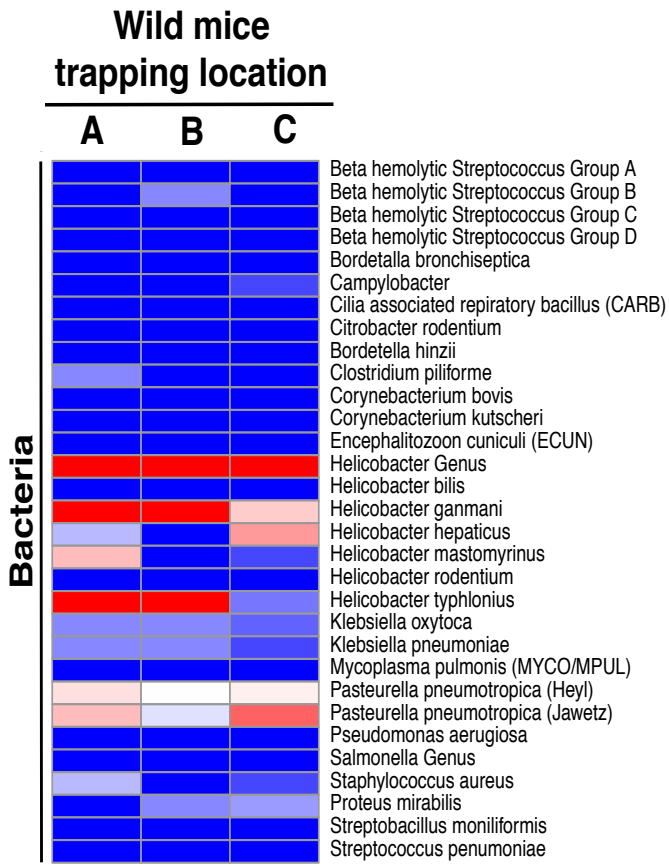


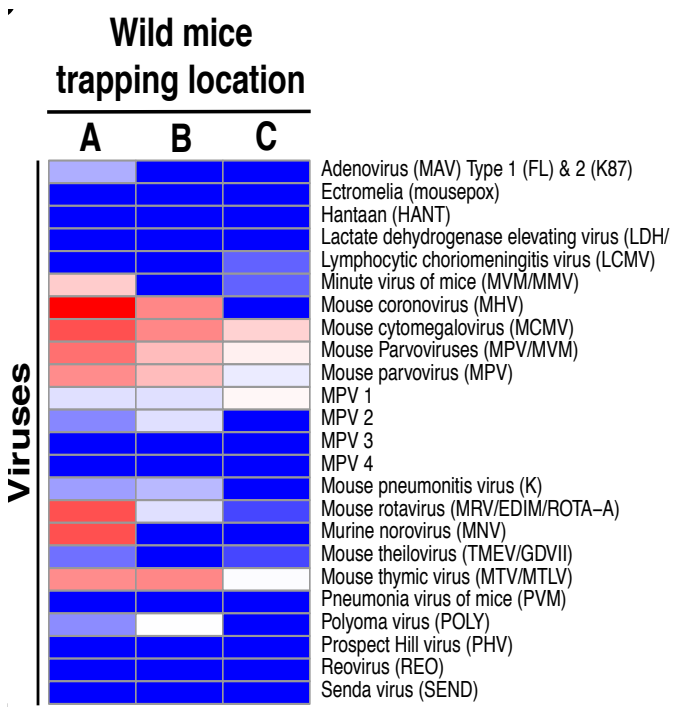


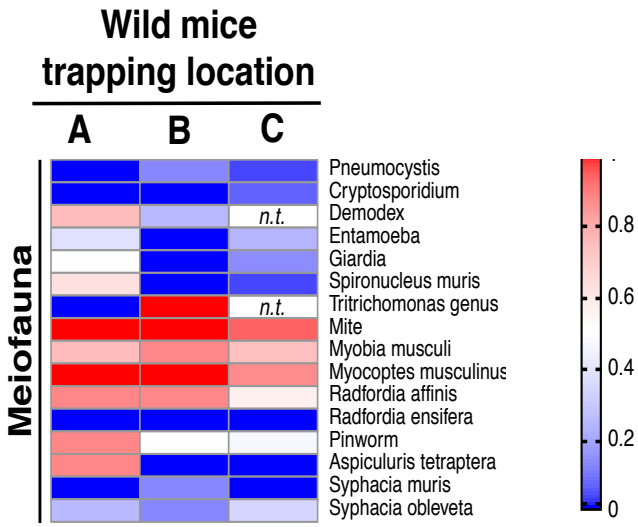




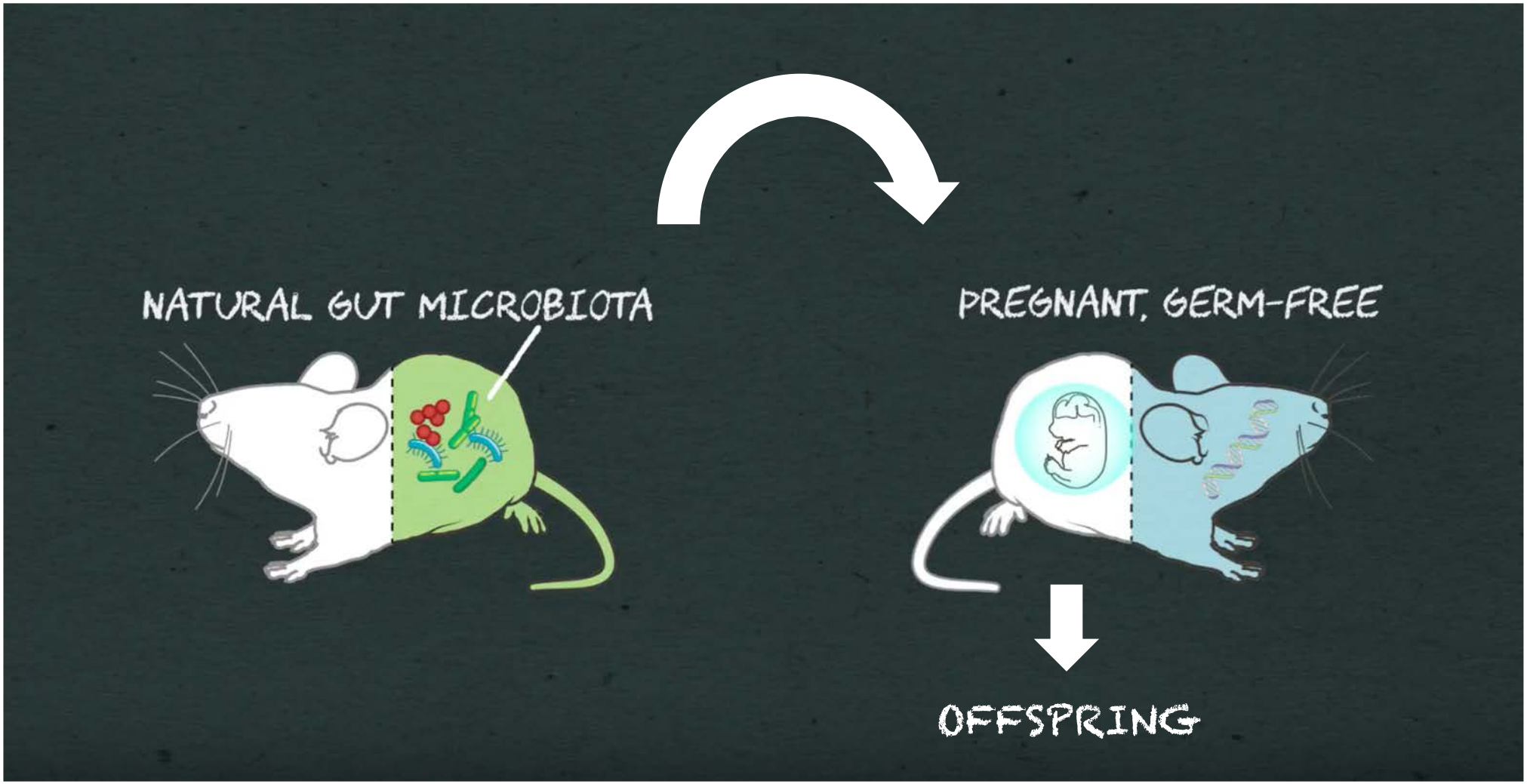
Bio-banking and Selection of Ileocecal Material



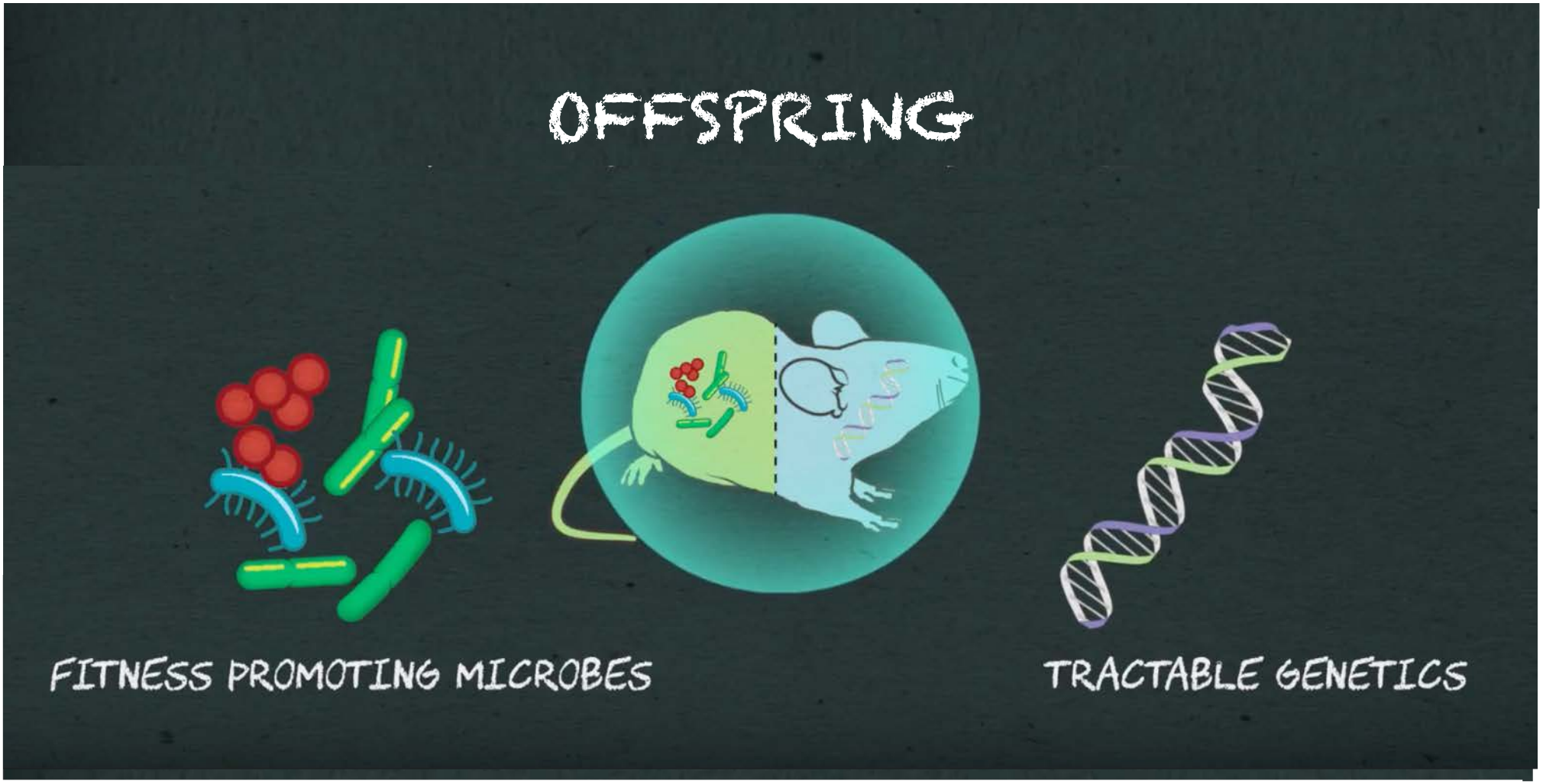




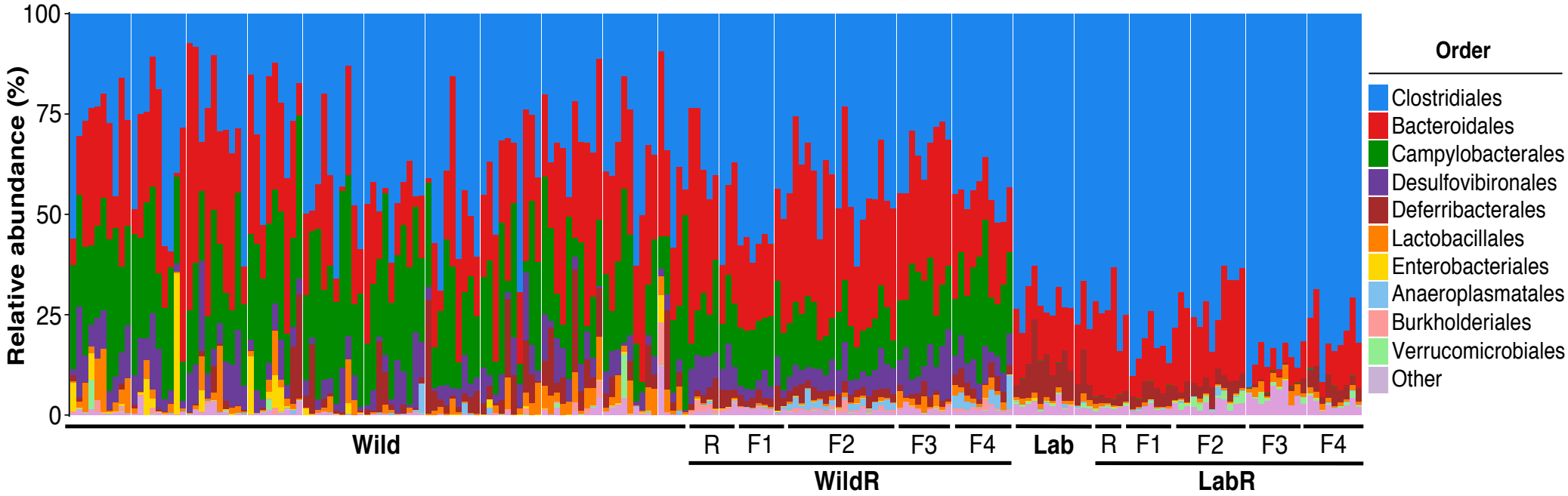
Transfer of Natural Gut Microbiota into Pregnant Germ-free Mice



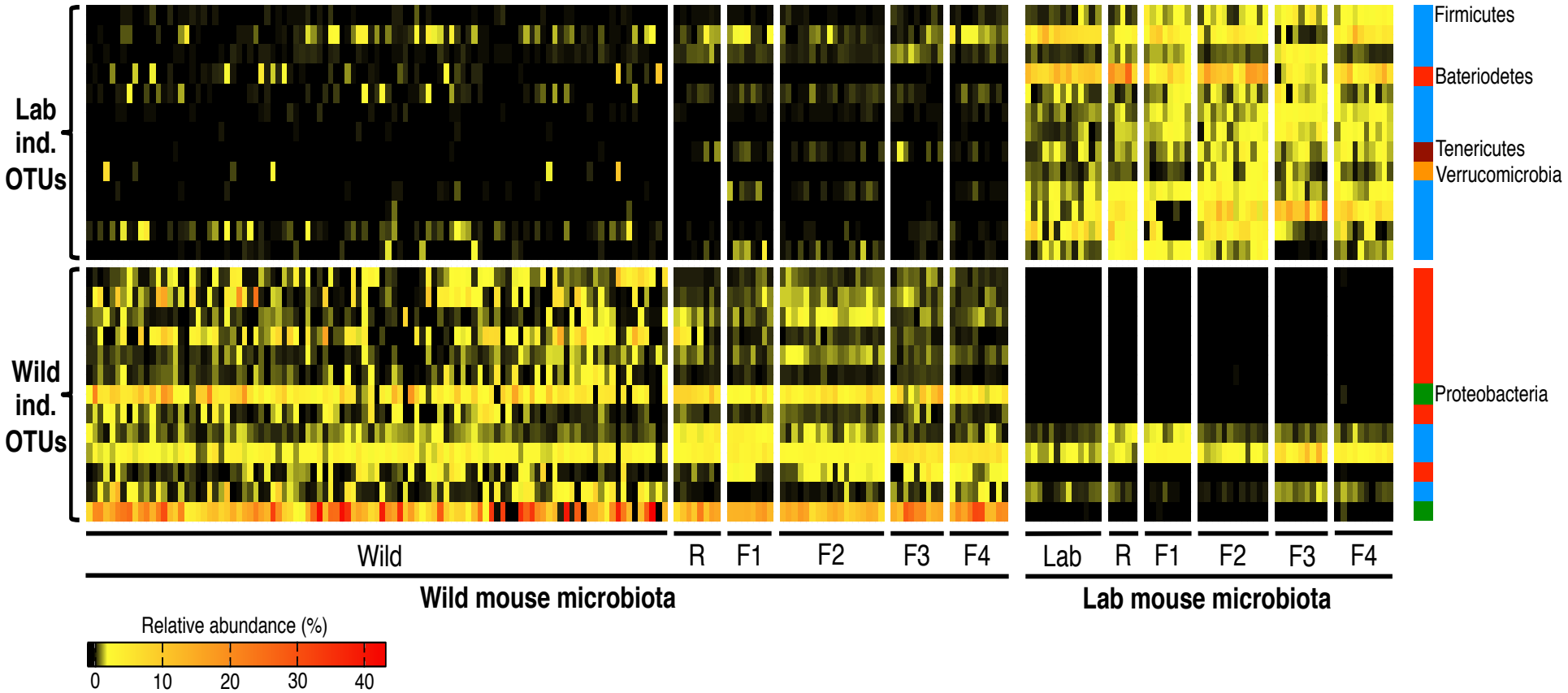
Chimeric Metaorganism



The Wild Mouse Gut Microbiome can be Maintained in a Laboratory Mouse Colony



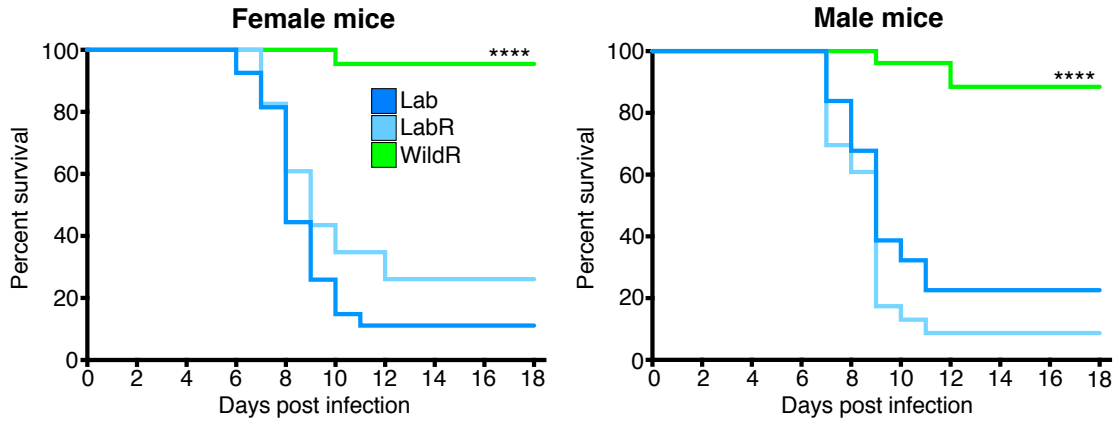
Machine Learning: Indicator Species Analysis



Do Natural Microbiota Promote Host Fitness?

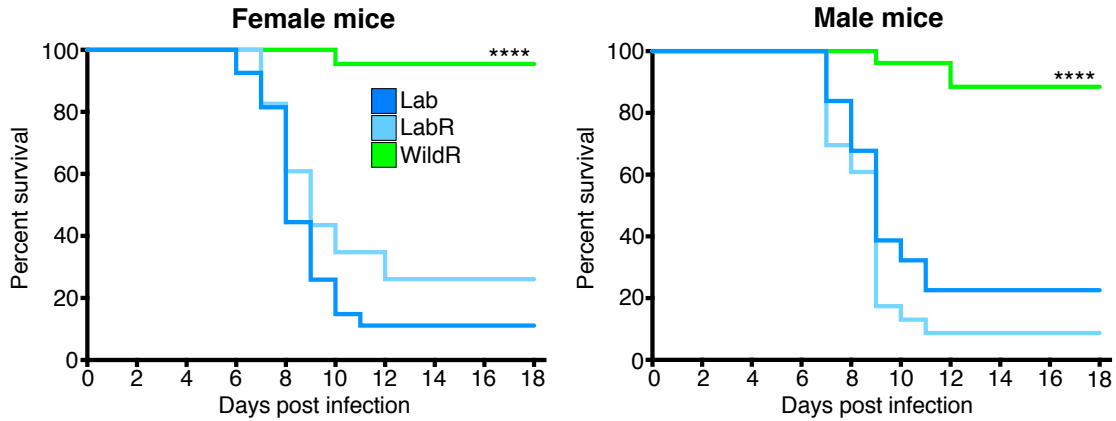
The Wild Mouse Gut Microbiome Confers a Survival Advantage Upon Influenza Virus Infection

Survival

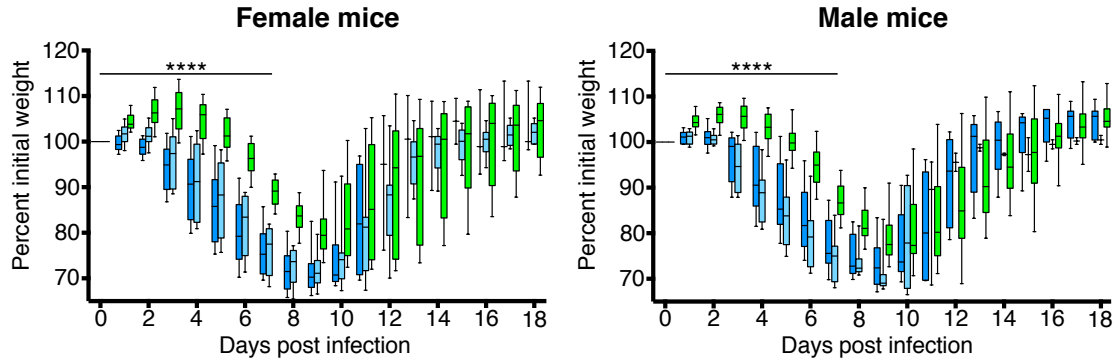


The Wild Mouse Gut Microbiome Confers a Survival Advantage Upon Influenza Virus Infection

Survival

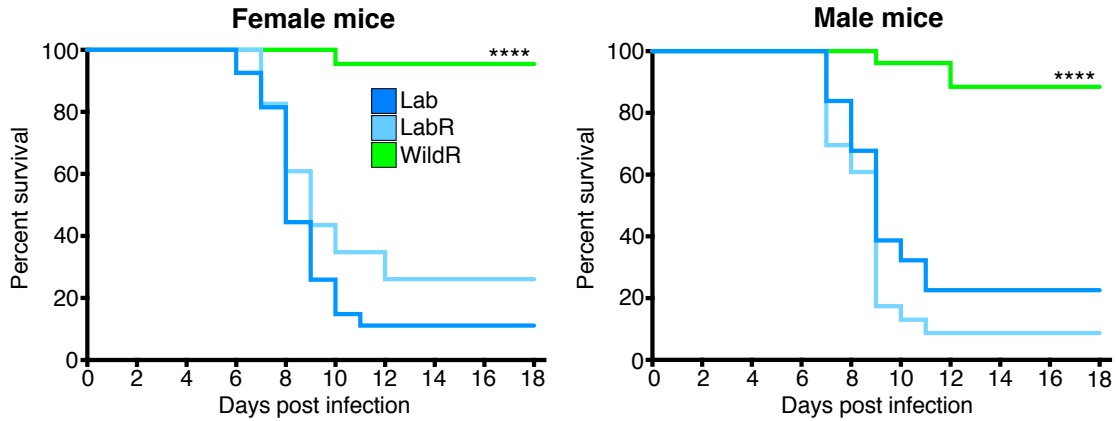


Weight Loss

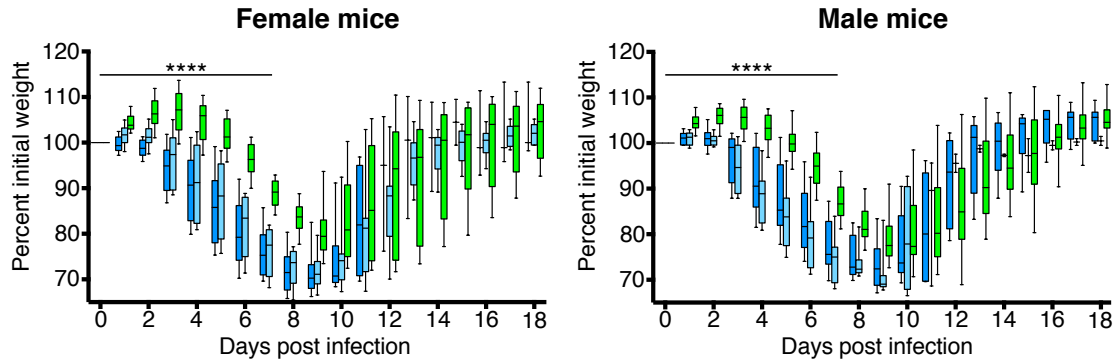


The Wild Mouse Gut Microbiome Confers a Survival Advantage Upon Influenza Virus Infection

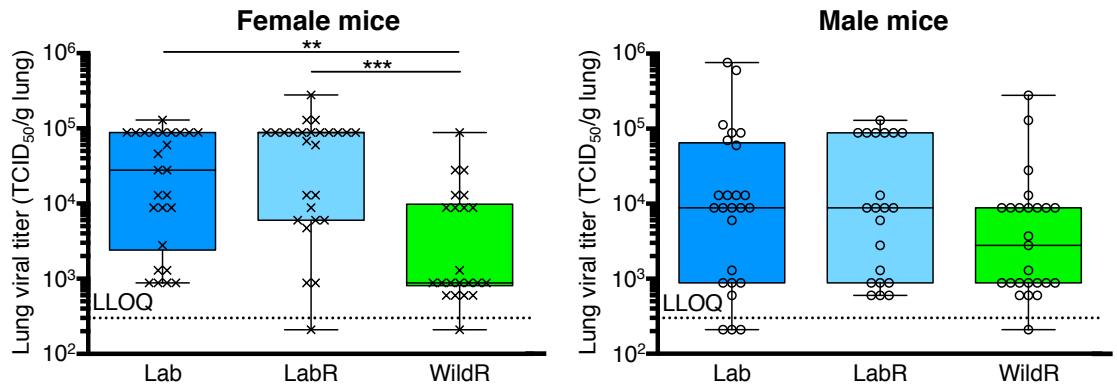
Survival



Weight Loss



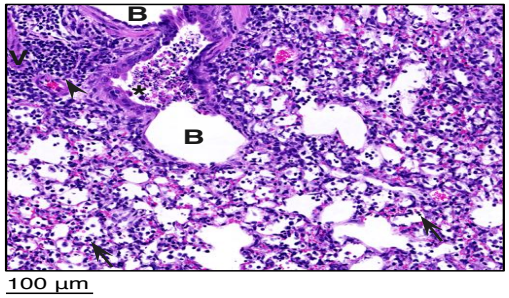
Virus Titer



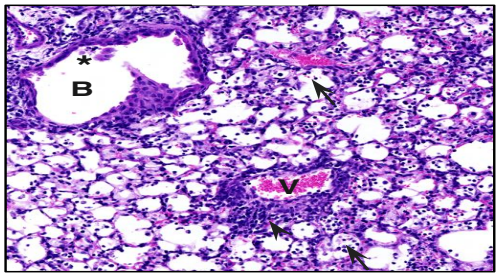
The Wild Mouse Gut Microbiome Confers Traits that Abrogate Excessive Inflammation

Lung Histology

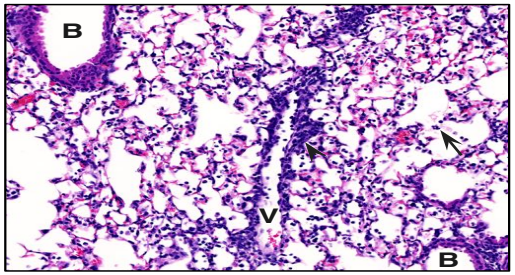
Lab



LabR



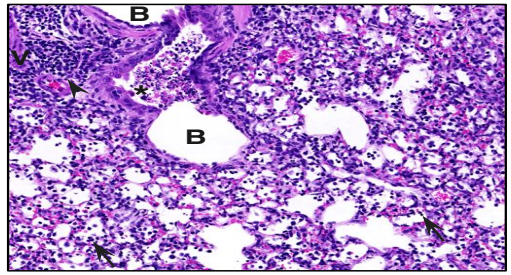
WildR



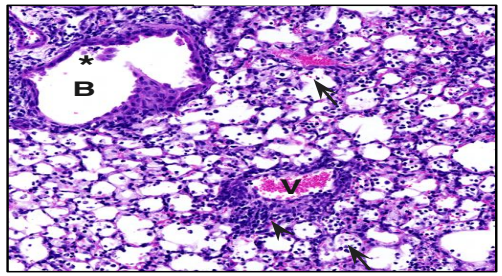
The Wild Mouse Gut Microbiome Confers Traits that Abrogate Excessive Inflammation

Lung Histology

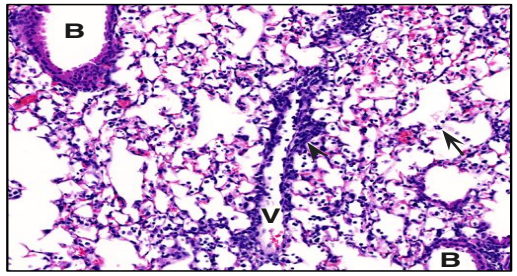
Lab



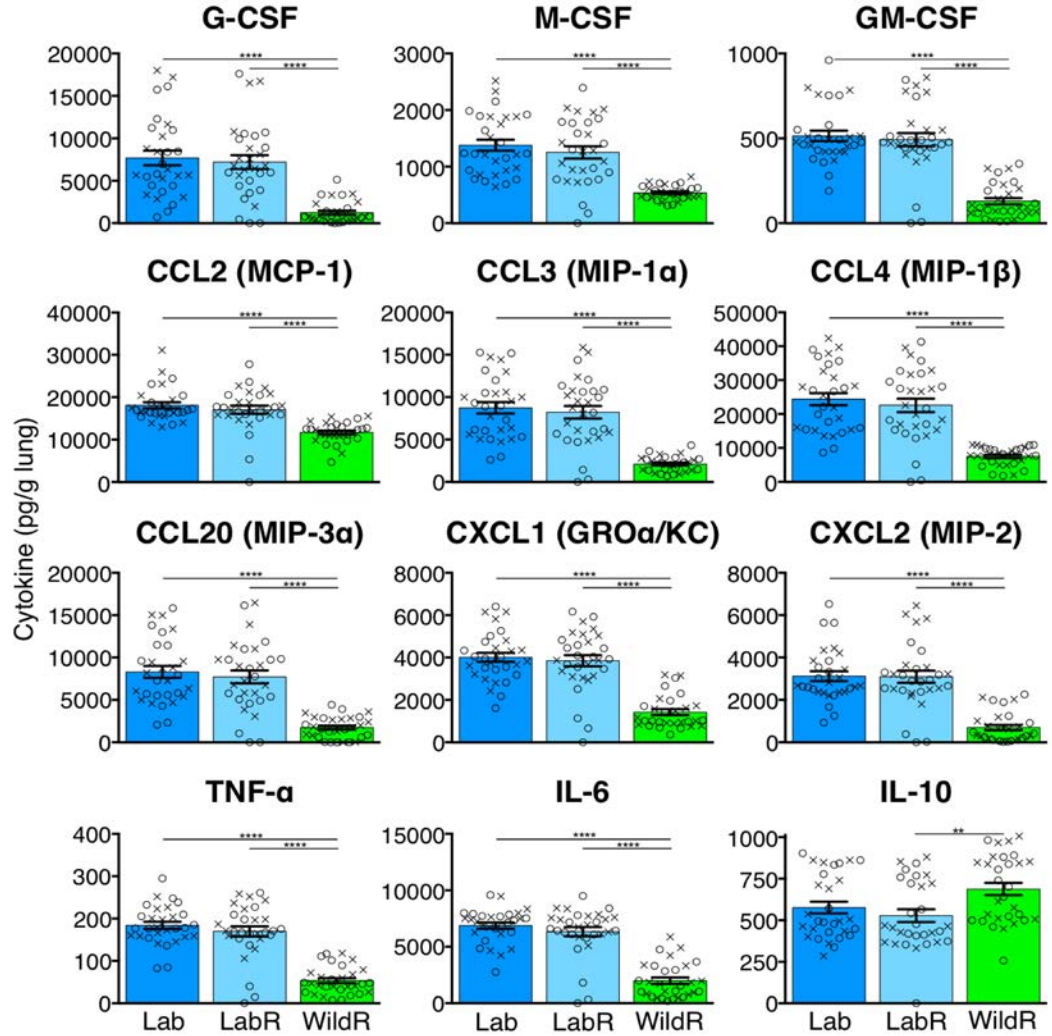
LabR



WildR

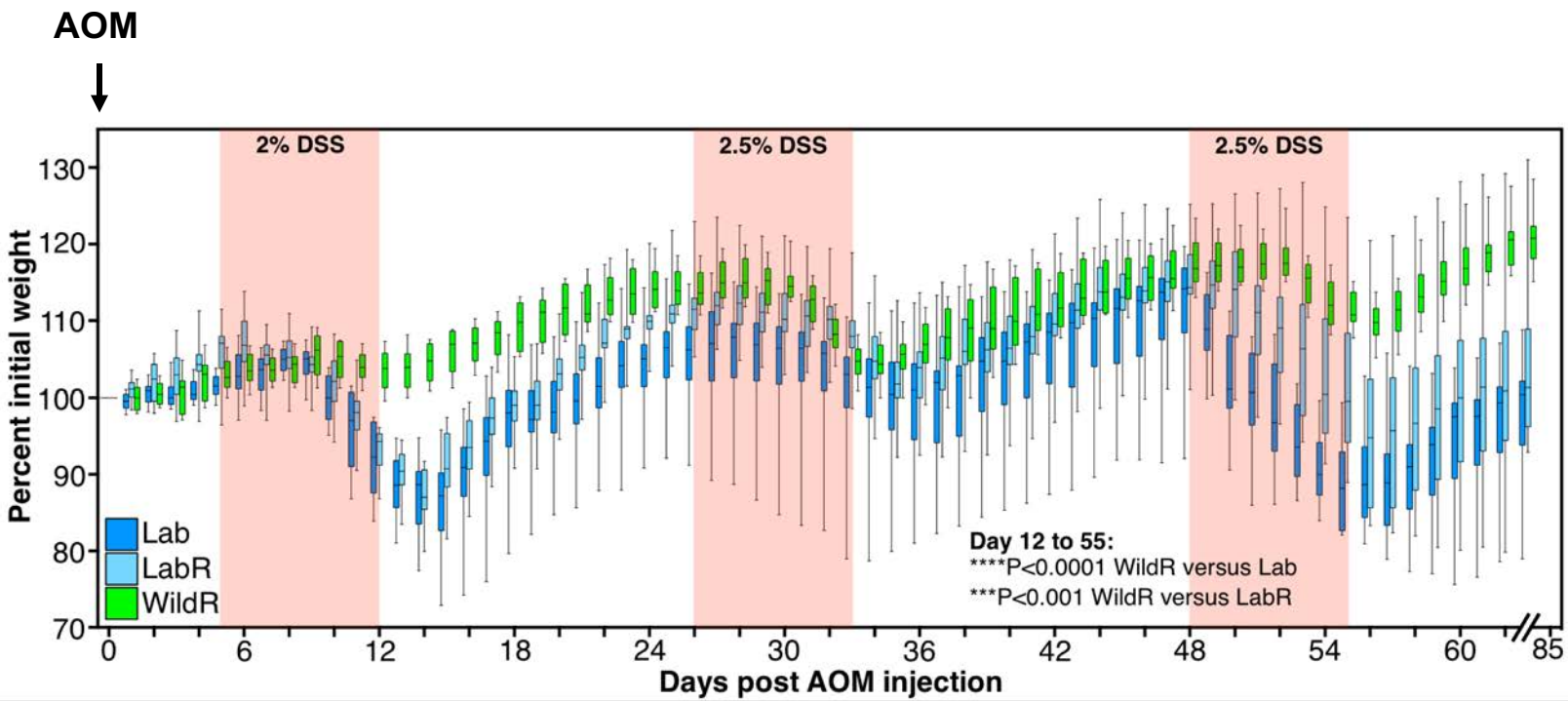


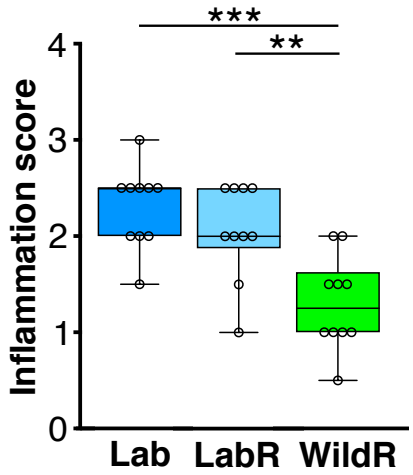
Lung Cytokines and Chemokines



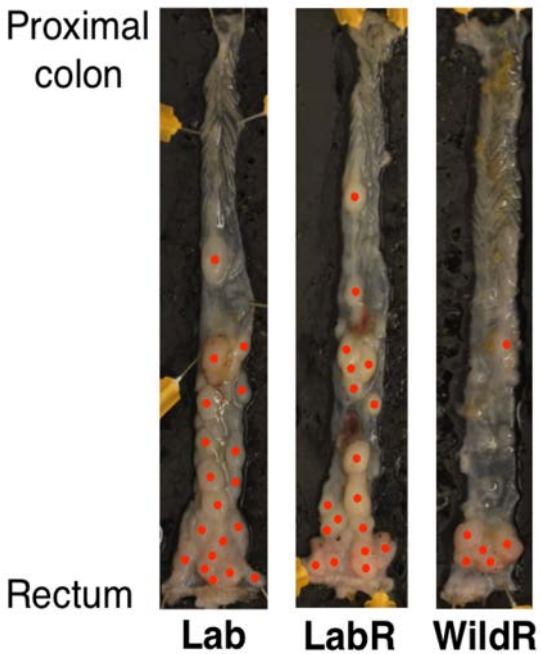
Do Natural Microbiota Promote Host Fitness?

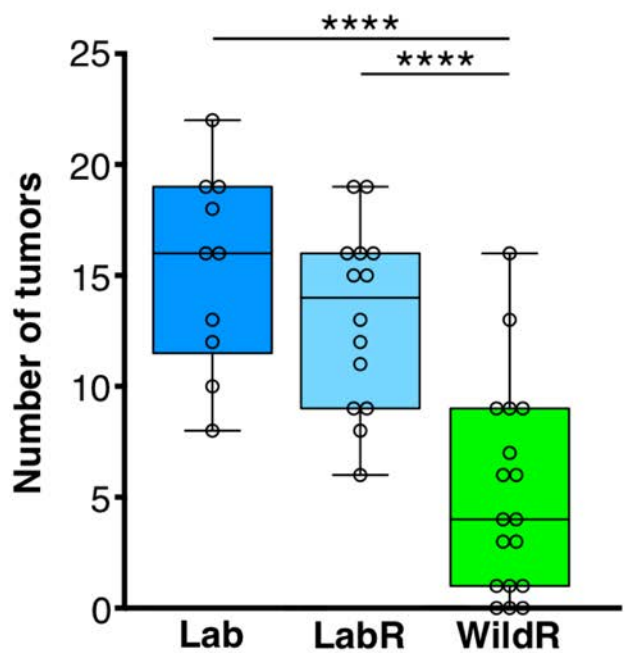
The Wild Mouse Gut Microbiome Protects from Colitis

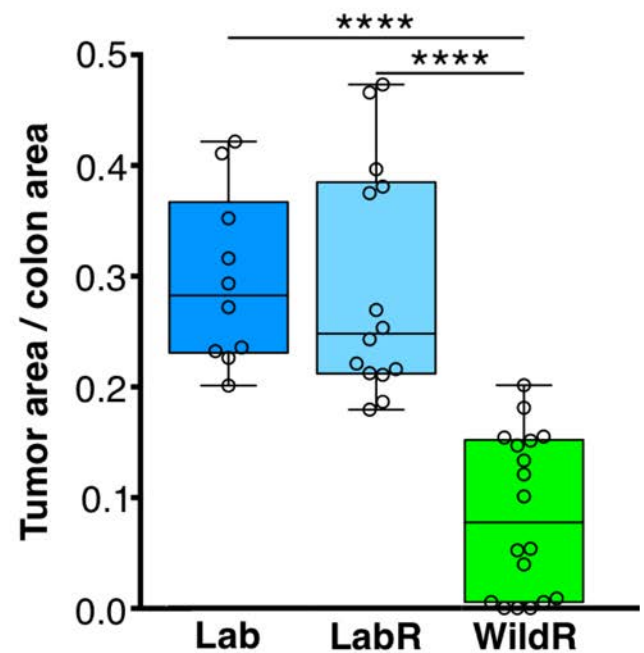




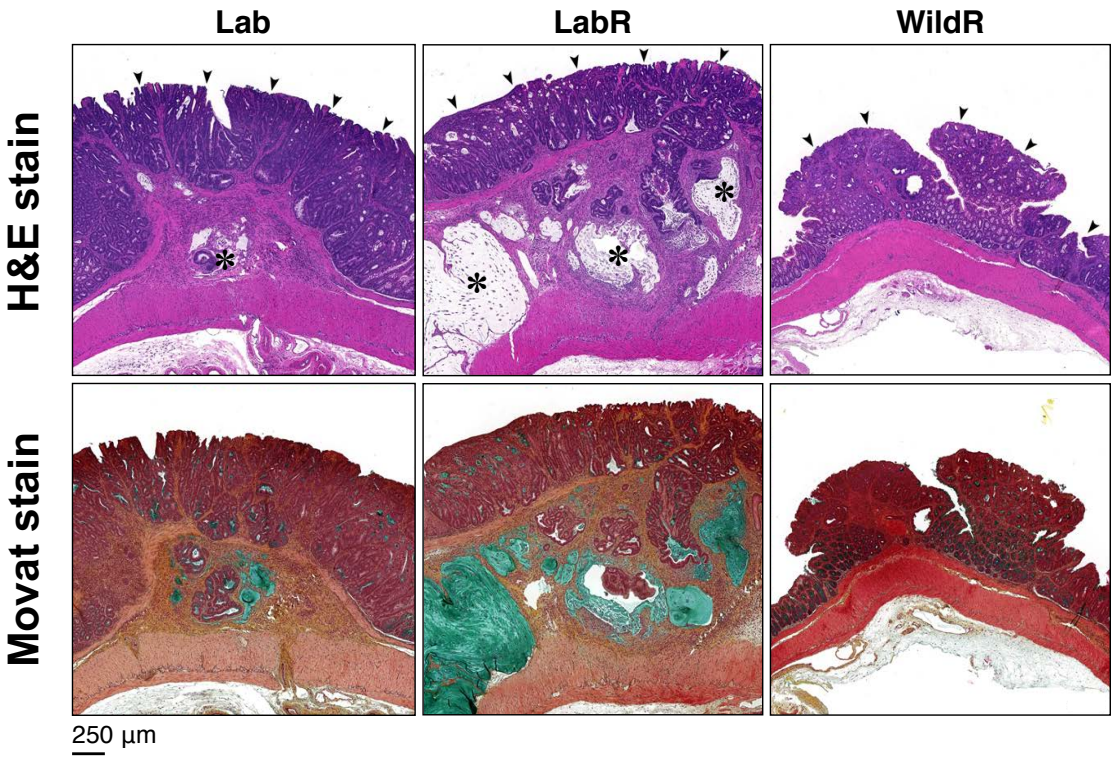
The Wild Mouse Gut Microbiome Protects from Colorectal Tumorigenesis

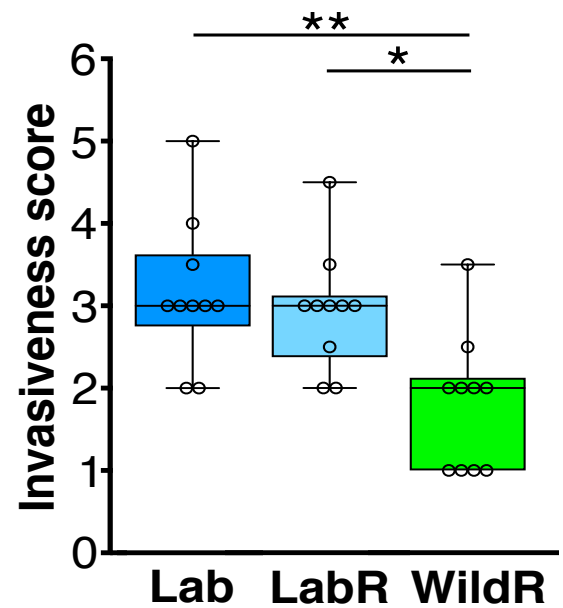




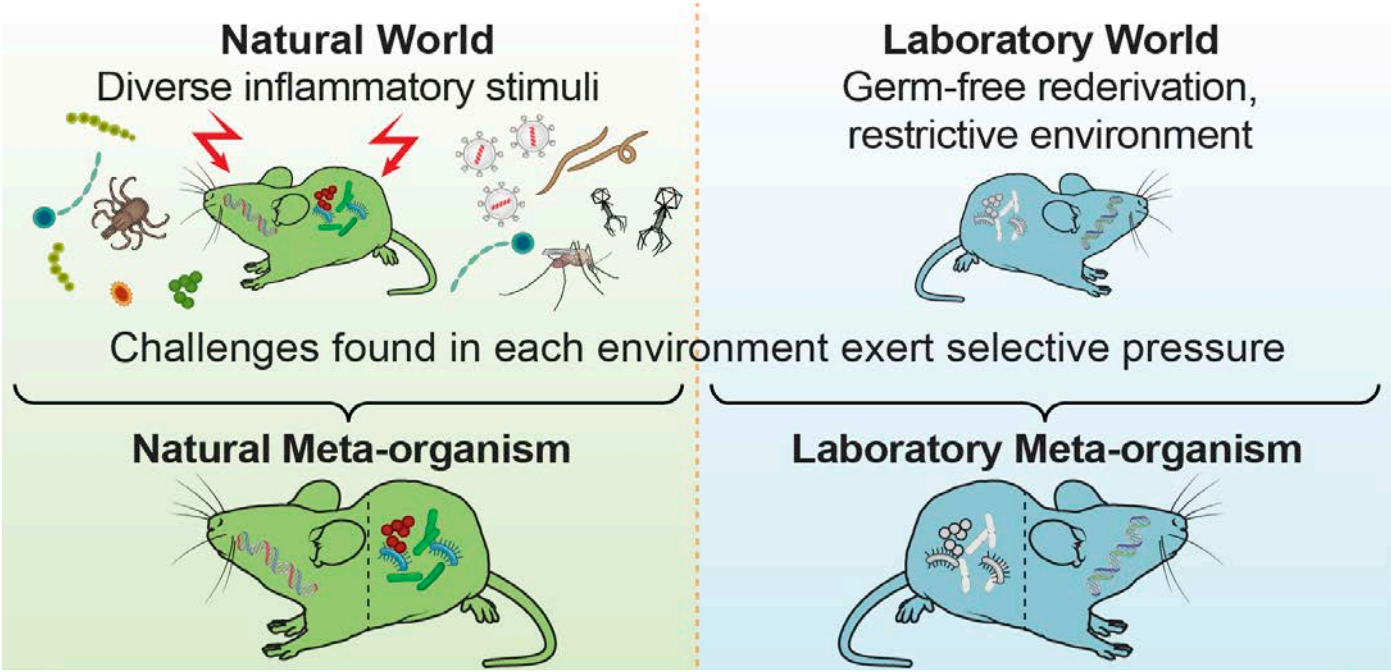


The Wild Mouse Gut Microbiome Protects from Colorectal Cancer

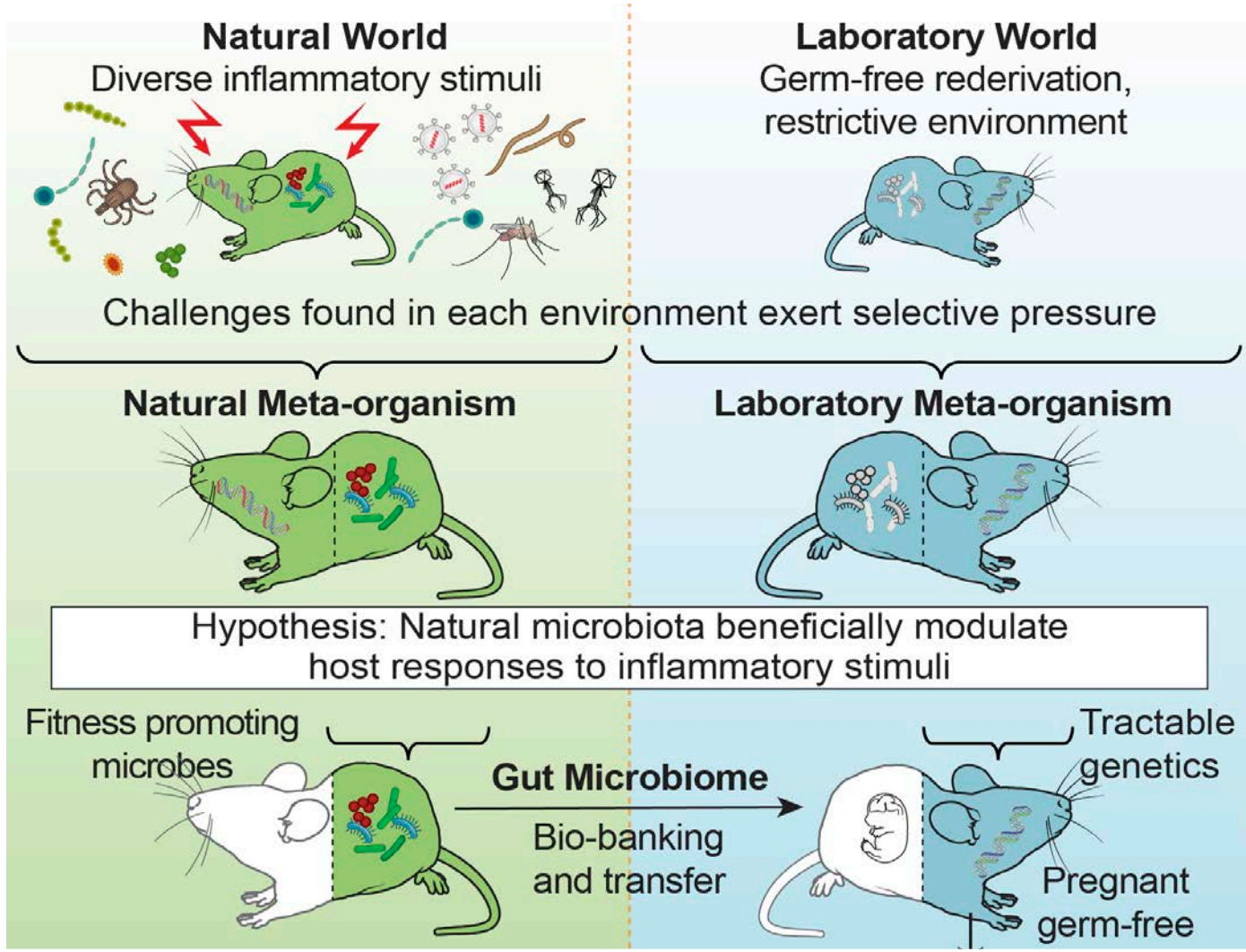




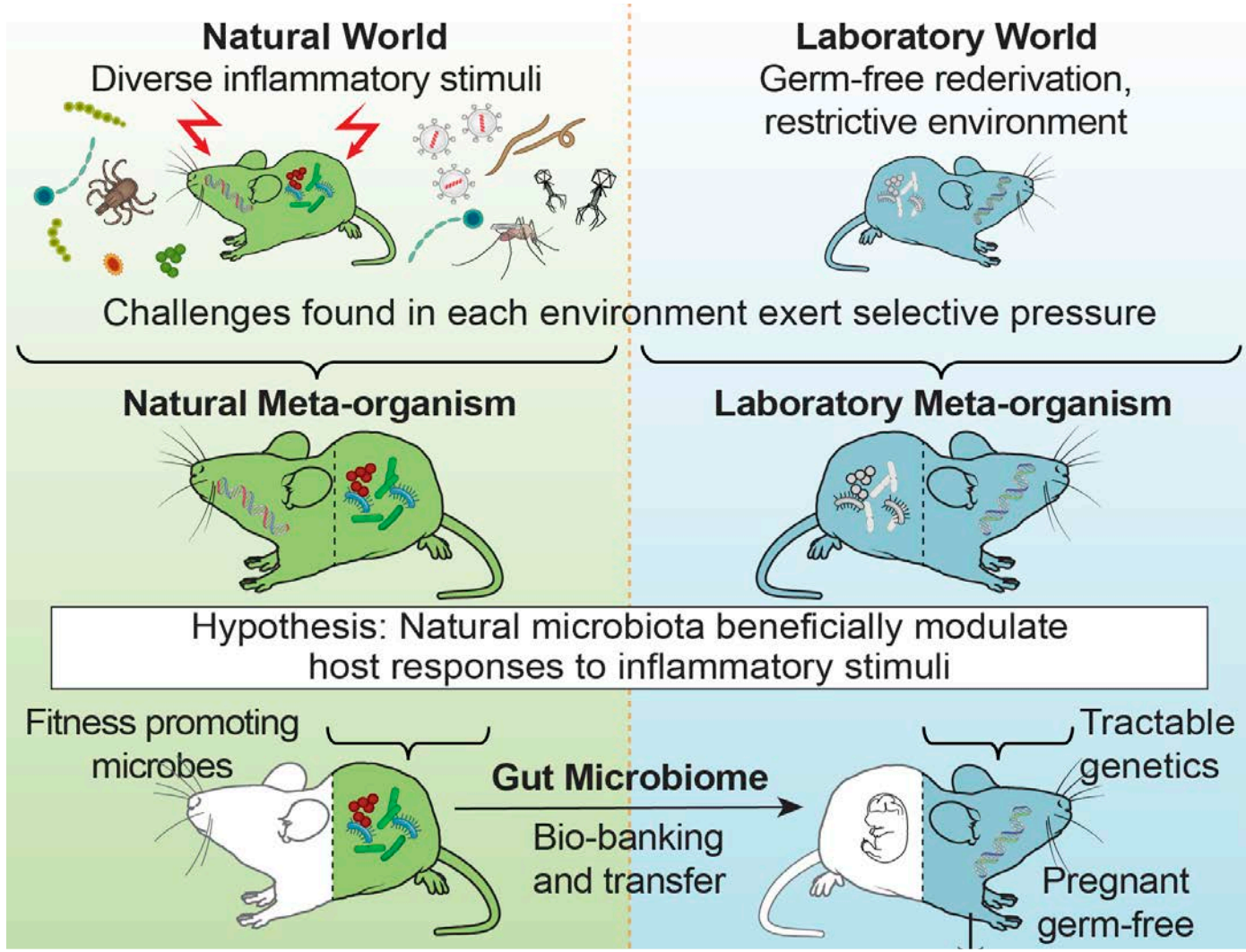
Summary



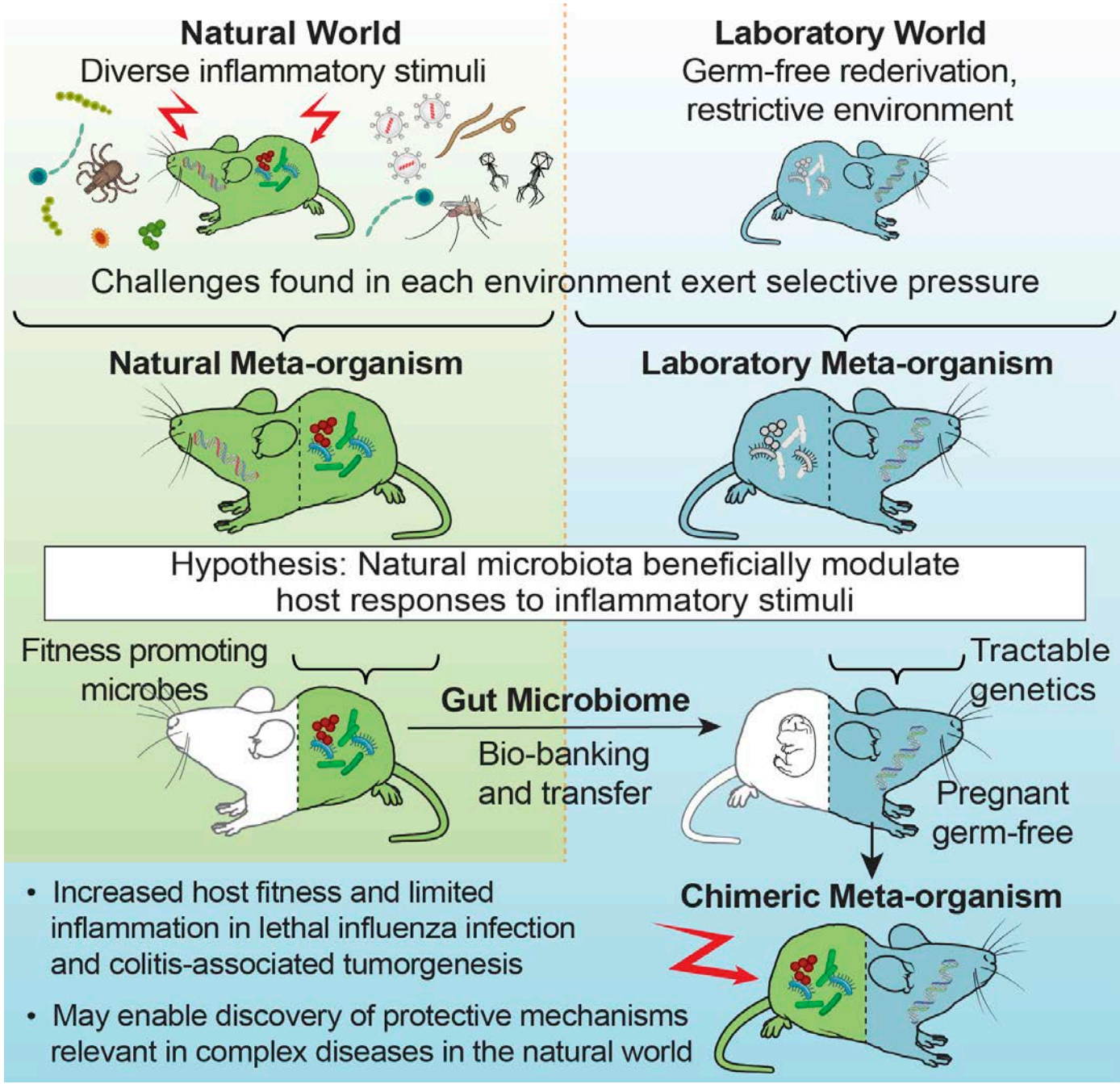
Rosshart et al., Cell 2017



Rosshart et al., Cell 2018



Rosshart et al., Cell 2018



Rosshart et al., Cell 2018

Acknowledgements

NIH Intramural Research Program
Our Research Changes Lives
one program
many people
infinite possibilities

THE UNIVERSITY of NORTH CAROLINA at CHAPEL HILL

Liver Diseases Branch, NIDDK

Stephan Rosshart
Brian Vassallo
Ashli Hunter

Collaborators
NIAID

Davide Angeletti
Heather Hickman
Jon Yewdell

Yasmine Belkaid

FDA
Kazuyo Takeda

NCI

John McCulloch
Jonathan Badger
Giorgio Trinchieri

Andrew Morgan
F. Pardo-Manuel de Villena

Baylor College of Medicine
Diane Hutchinson
Nadim Ajami