

# Home-site advantage for host-species specific gut microbiota<sup>1</sup>

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## Question

### What Drives Host-Specificity During Microbiome Assembly?

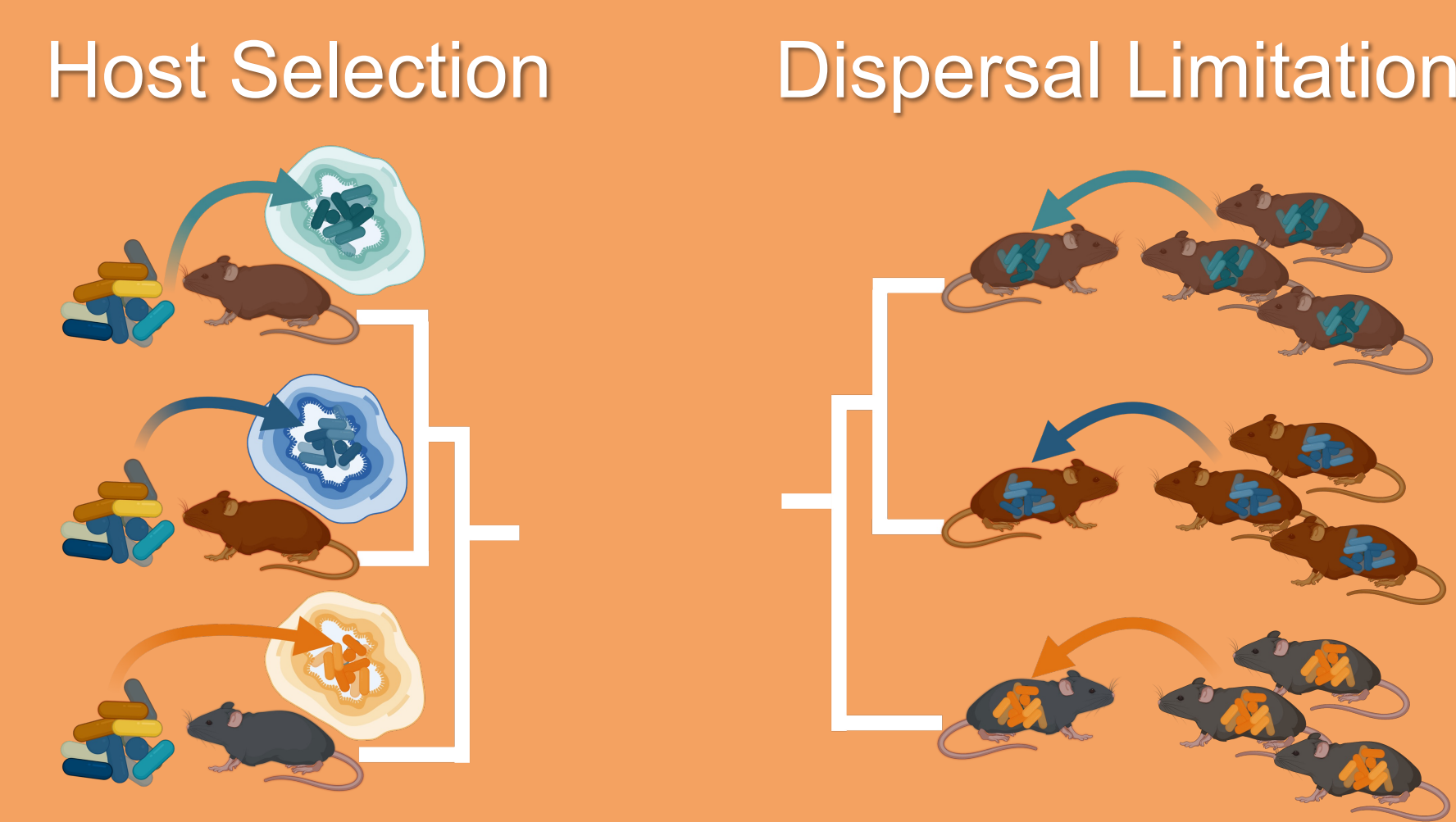


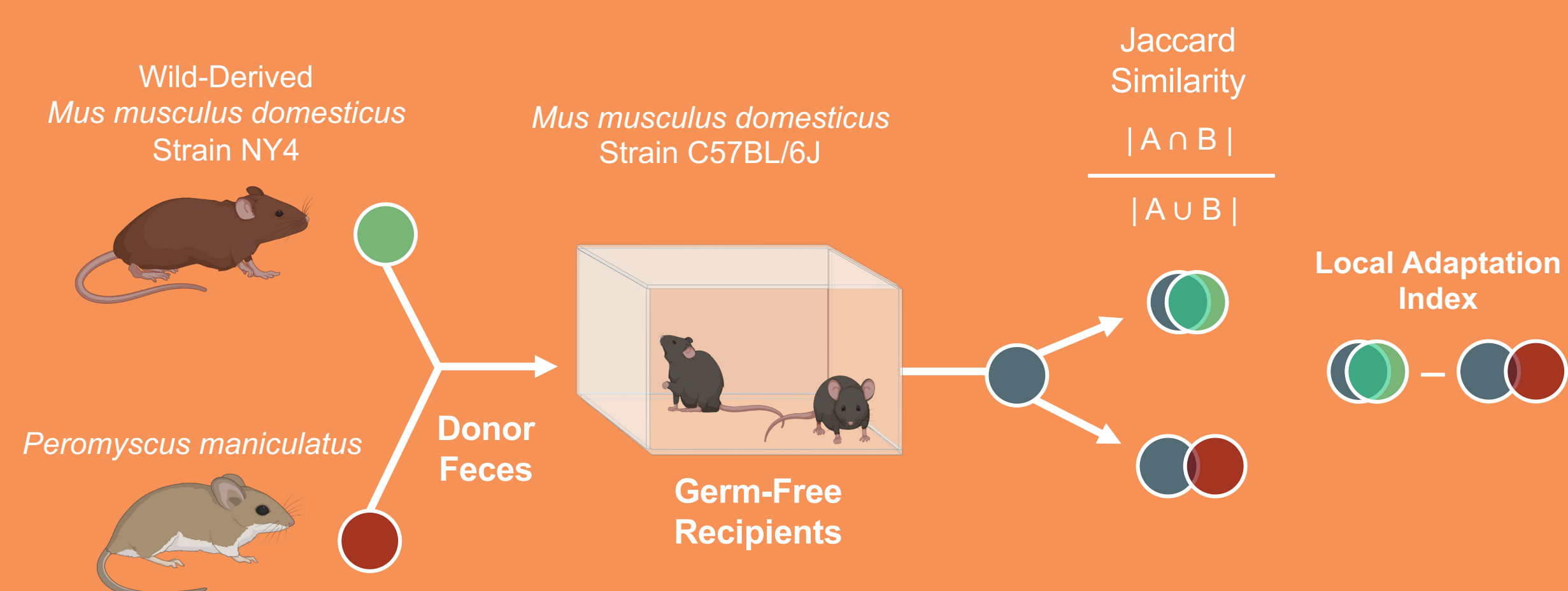
Figure Adapted from Kohl (2020)<sup>2</sup>

The mammalian gut harbors species-specific microbial communities that reflect their hosts' evolutionary histories, although the forces that generate host-species specific gut microbiotas remain poorly understood. Quantifying the relative influences of these two ecological mechanisms remains a critical gap in understanding the assembly of host-species specific microbiota in mammals<sup>3</sup>.

## Methods

### Hypothesis:

### Locally-Adapted Native Microbiotas Outcompete Non-Native Microbiotas



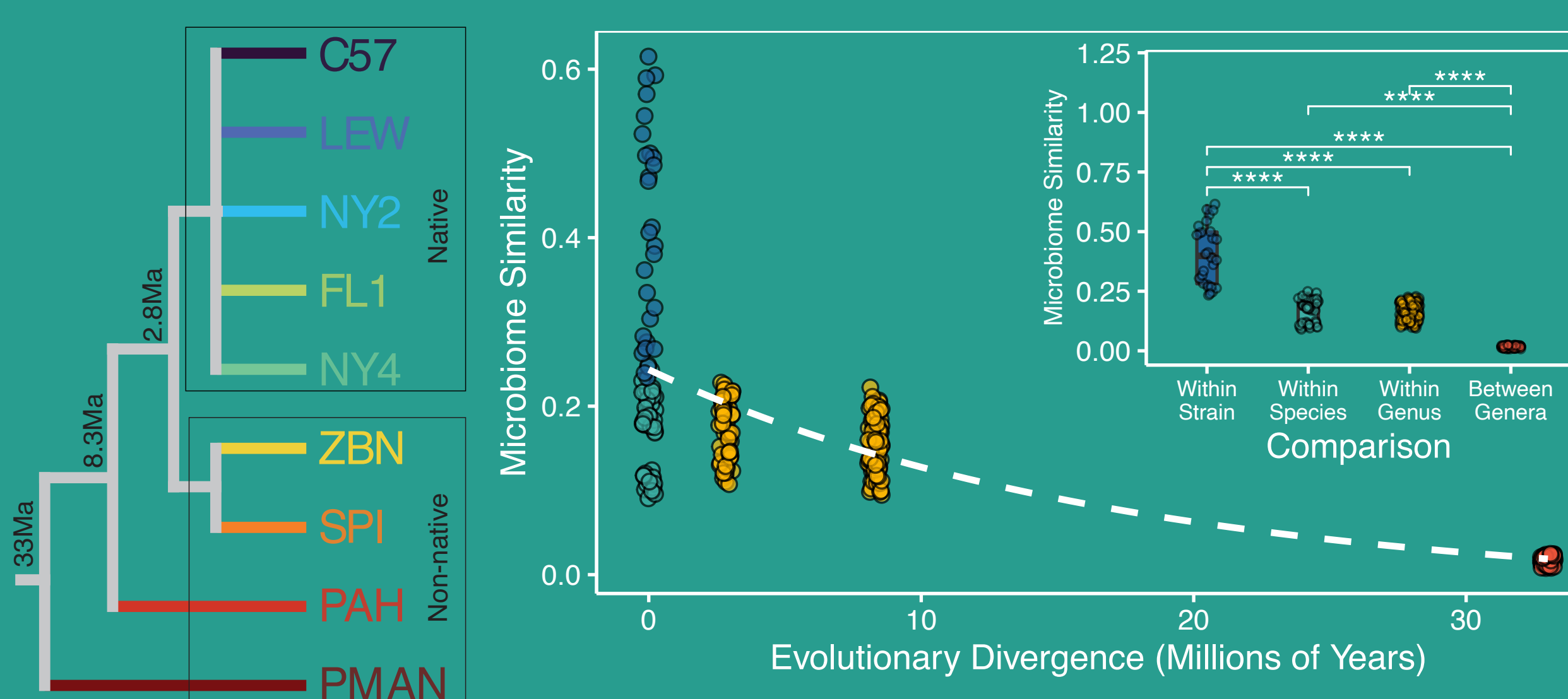
We conducted a series of pairwise *in vivo* microbiota competition experiments in germ-free mice designed to measure the degree of local adaptation of gut microbiota to their host species while explicitly controlling for dispersal limitation. We used 16S rRNA profiling to characterize the microbial community structure in the feces of ex-germ-free mice, and then quantified their similarity to each donor by developing the Local Adaptation Index<sup>3</sup>.

## References

1. Sprockett *et al.* (2023) Home-site advantage for host species-specific gut microbiota. *Science Advances*. DOI: 10.1126/sciadv.adf5499
2. Kohl (2020) Ecological and evolutionary mechanisms underlying patterns of phyllosymbiosis in host-associated microbial communities. *Philosophical Transactions of the Royal Society B*. DOI: 10.1098/rstb.2019.0251
3. Diagrams created with BioRender.com

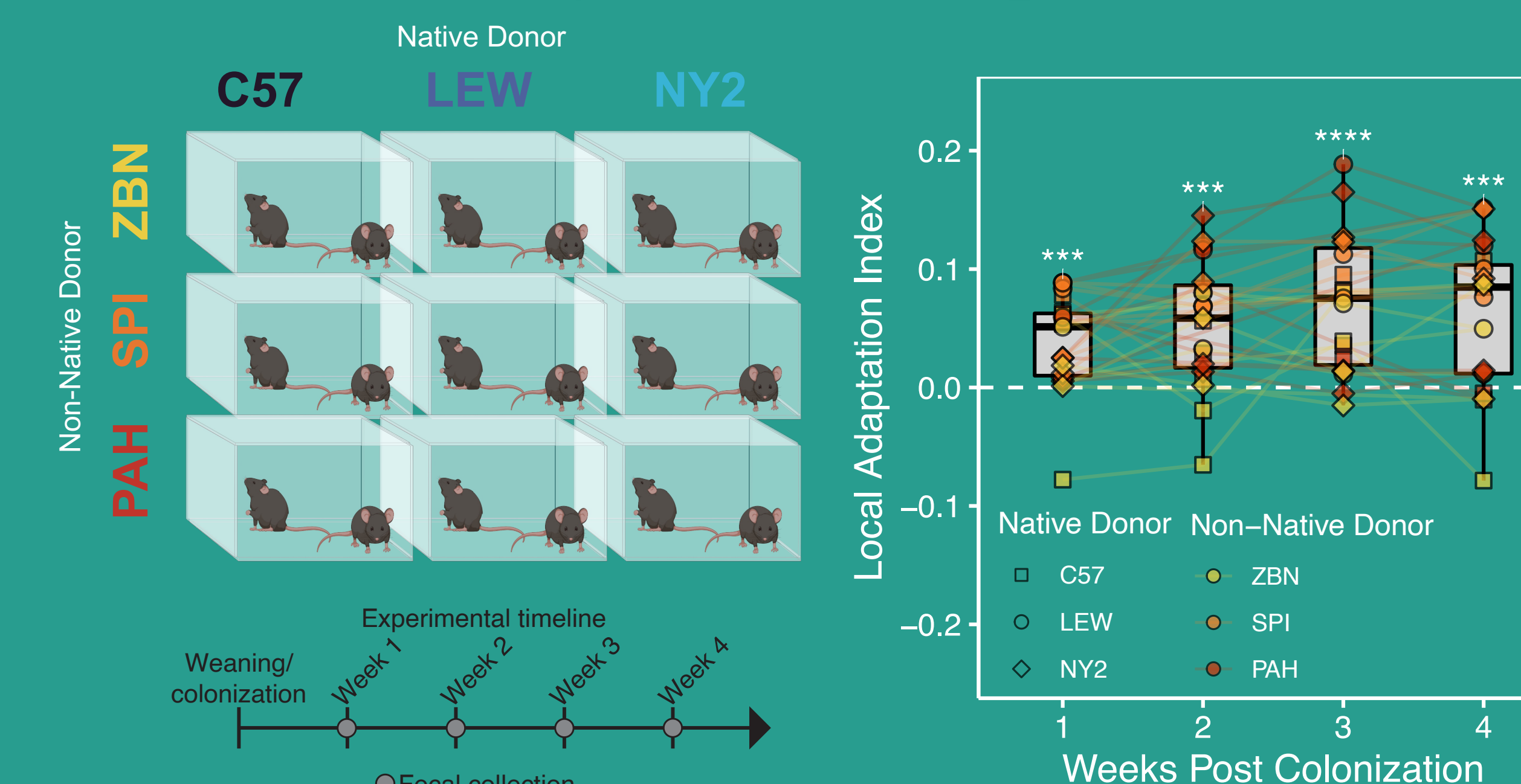
## Results

### Rodent Microbiotas Show Host-Species Specificity



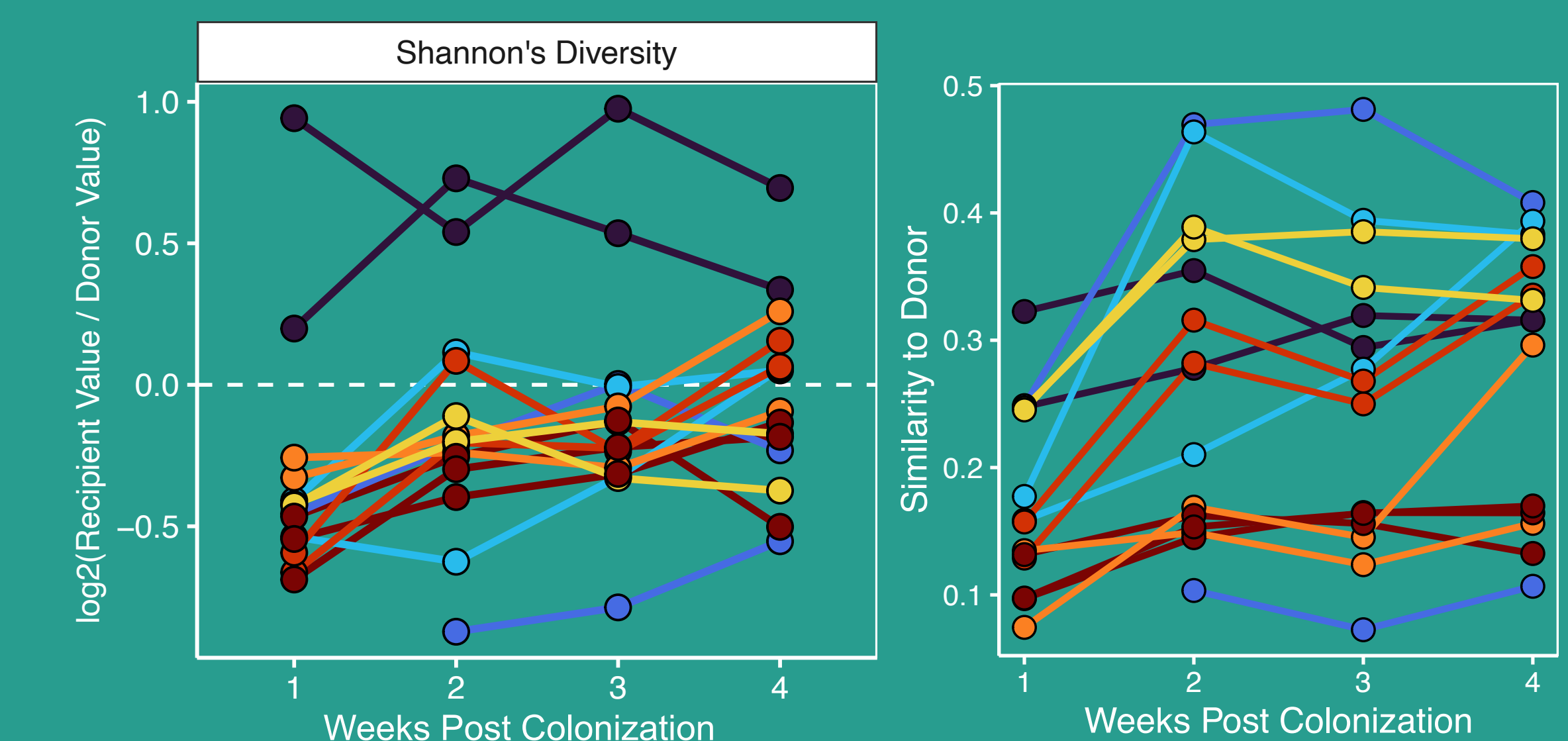
Microbiota similarity of 9 mouse strains decayed exponentially as a function of host evolutionary divergence time, indicating a degree of host-microbe association over evolutionary time scales ( $p < 0.001$ ,  $R^2 = 0.57$ ).

### Native Microbiomes Dominate During *in vivo* Competition



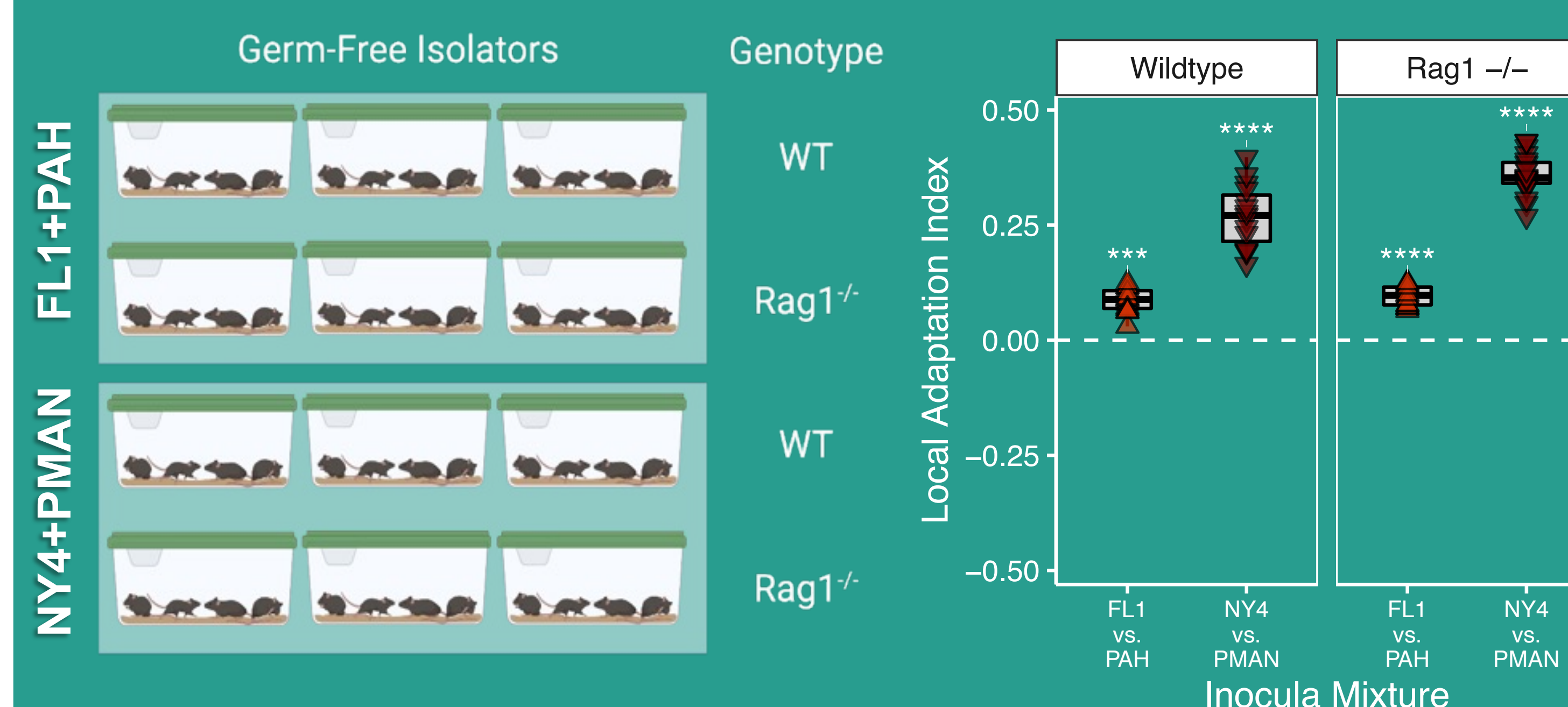
Germ-free mice were inoculated with mixtures of fecal samples from native and non-native mouse donors. The resulting communities were more similar to their native donor than their non-native donor ( $p < 0.001$  for all time points).

### Monocolonized Native and Non-Native Microbiomes Colonize Equally Well



Germ-free mice were inoculated with fecal samples from a single native or non-native rodent donor. The resulting communities reached comparable levels of diversity ( $p > 0.05$ ), and microbiota of mice colonized by native microbes were not more similar to their donors than those colonized by non-native microbes at weeks 2-4 ( $p > 0.05$ ).

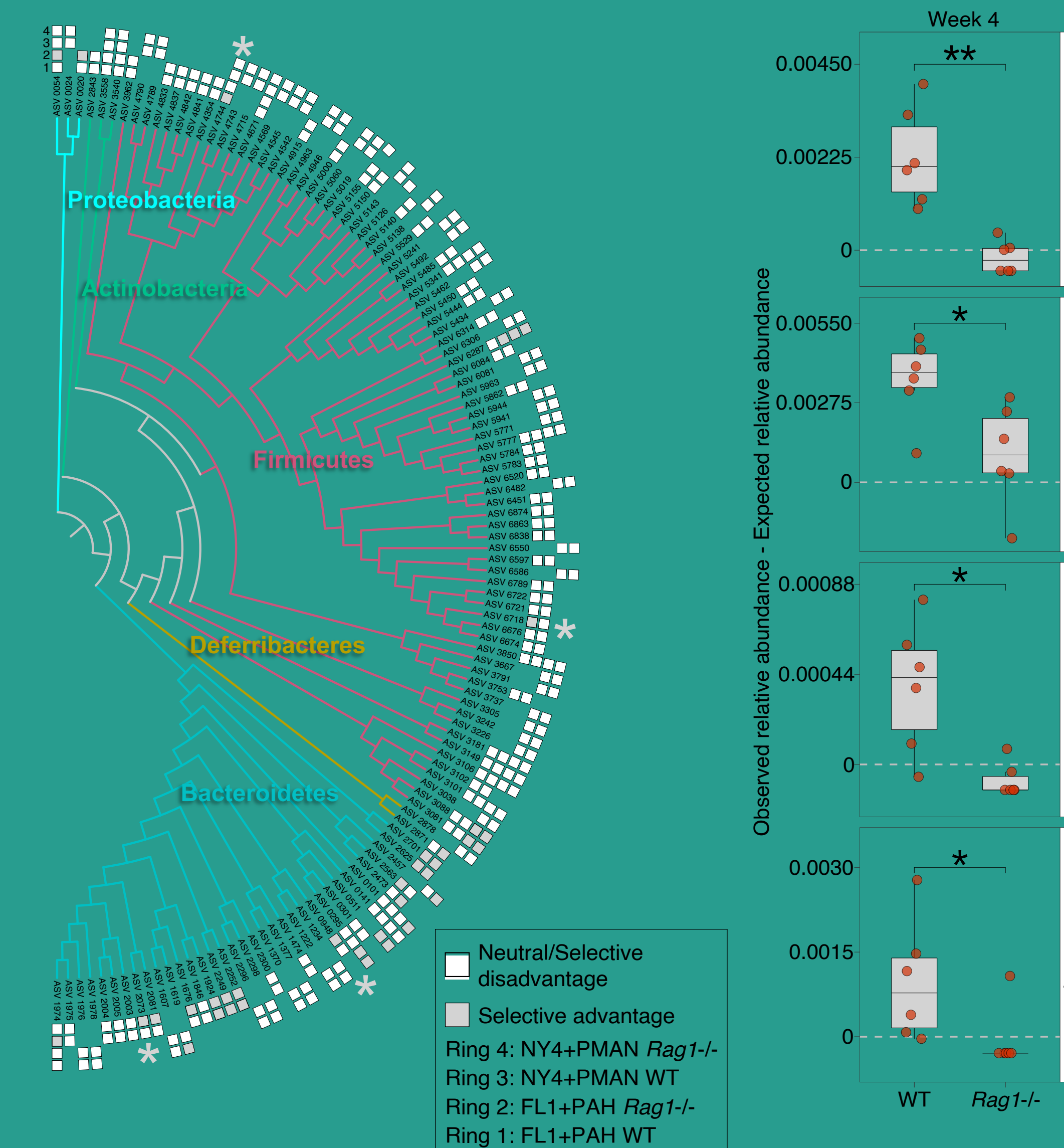
### Adaptive Immunity Does Not Mediate Fitness Advantage of Native Microbiotas



Two different native vs non-native microbiota mixtures were inoculated into both wildtype and Rag1 deficient mice, and fecal samples were collected at 4 and 6 weeks. The resulting communities were more similar to their native donor than their non-native donor ( $p < 0.001$ ).

We then developed a neutral model of community assembly with which we could calculate the expected relative abundance of each ASV based on their relative abundance in the input inoculum. Four ASVs were found to have a selective advantage in wildtype mice, but not Rag1<sup>-/-</sup> mice, indicating that Rag1 mediates the selective advantage of these microbes.

### Selective advantages for a subset of native ASVs is depended on Rag1



## Conclusions

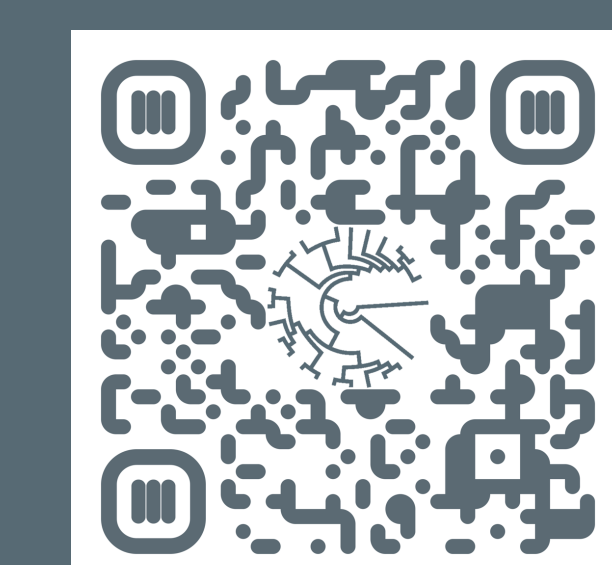
*Our findings provide the first experimental evidence that the endogenous gut bacterial lineages of house mice have adapted to their host species.*

Native gut microbiota outcompeted non-native gut microbiota in gnotobiotic mice, and the degree of local adaptation observed in competition experiments was positively associated with the divergence time of the hosts from which competing microbiotas were obtained. This work indicates that, in the absence of dispersal limitation, natural selection is sufficient to generate the emergence of host-species specificity and phylogenetic signal in the mammalian gut microbiota.

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