Effects of microbiome diversity and indole on *Candida albicans* infections in *Caenorhabditis elegans*

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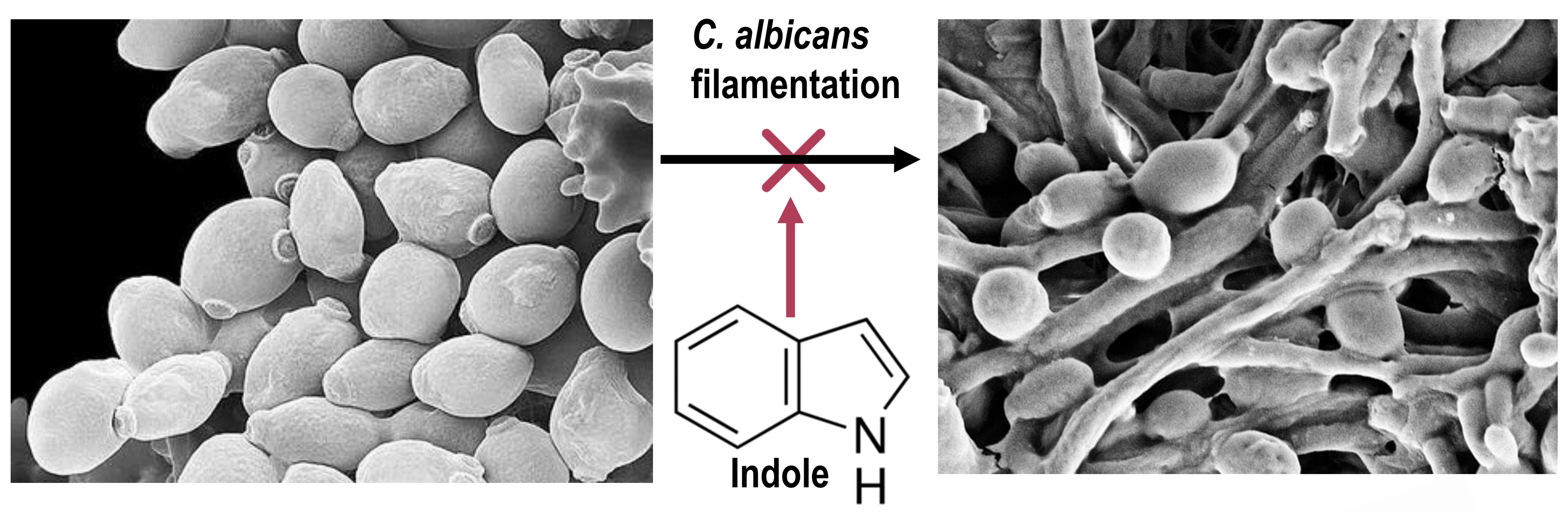
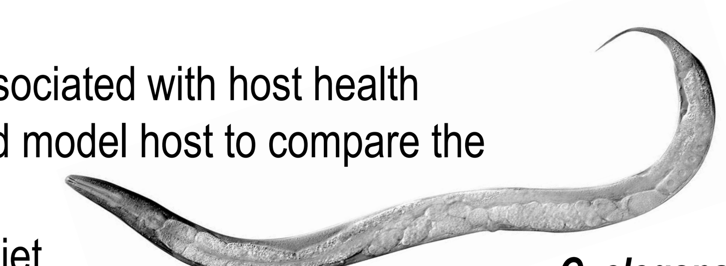
Background

- ~1.2 billion people are suffering from a fungal infection at any given time[1]
- Resistance to antifungal drugs is on the rise[2]
- The most prevalent fungal pathogen is *Candida albicans*, which must produce filamentous appendages to infect host tissues[3]
- The bacterial quorum-sensing molecule indole inhibits *C. albicans* filamentation and therefore its virulence[3]



- Microbiome diversity is also generally associated with host health
- *Caenorhabditis elegans* serves as a good model host to compare the effects of indole and diversity
  - Its microbiome can be controlled via diet
  - *C. albicans* infections are fatal (alive/dead scoring system)
  - It has genes (*cnc-4, cnc-7,* and *fipr-22/23*) that produce antifungal immune molecules, so immune response can be measured



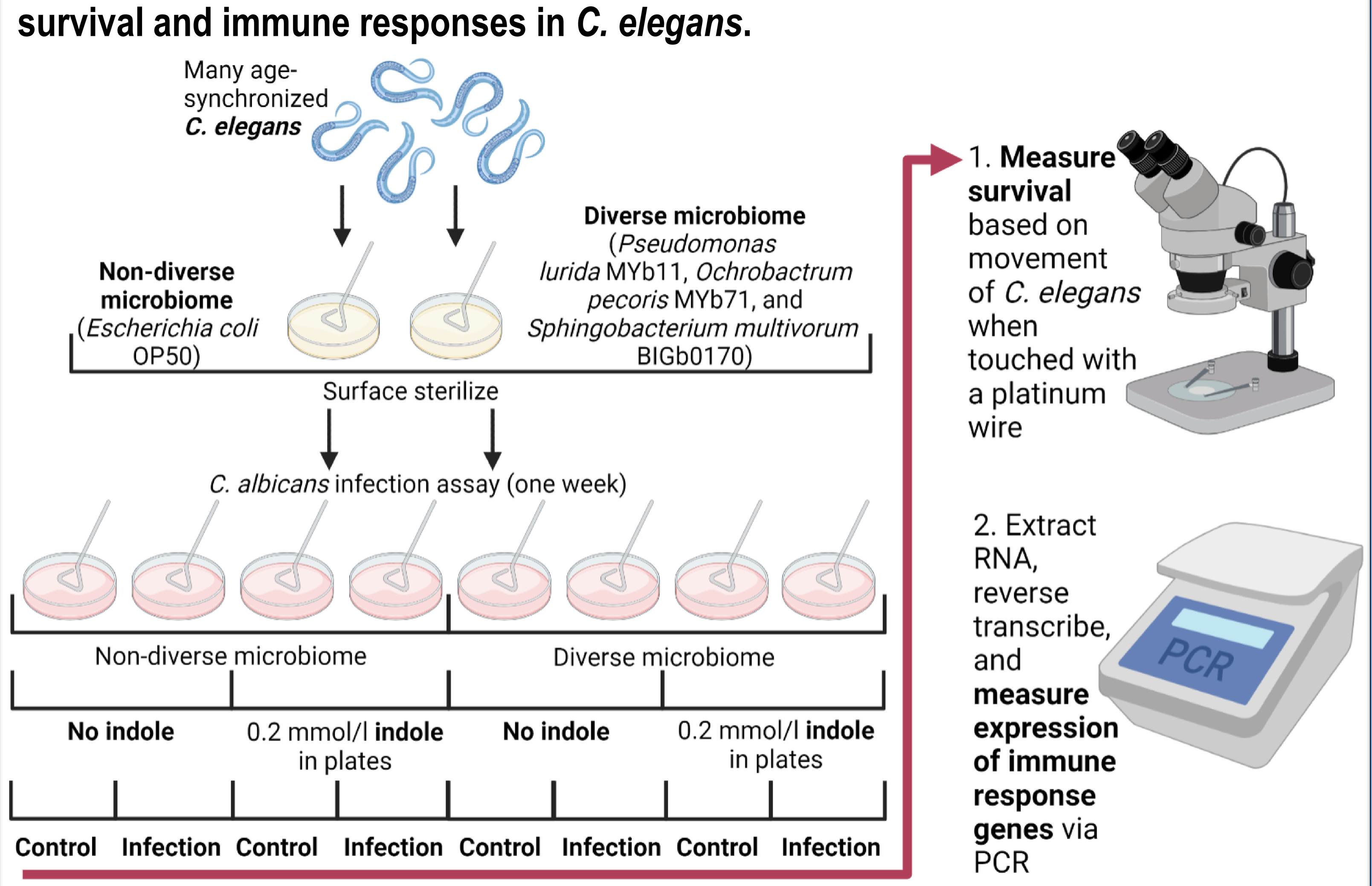
C. elegans nematode worm

Significance

Comparing the relative effects of microbiome diversity and the presence of supplemental indole on *C. elegans* survival and immune responses during *C. albicans* infections will link these two topics to fill current knowledge gaps. This information could one day extend to the development of more effective anti-fungal treatment methods for human patients.

Methods

Objective: Compare effects of microbiome diversity and supplemental indole on survival and immune responses in *C. elegans*.



Results

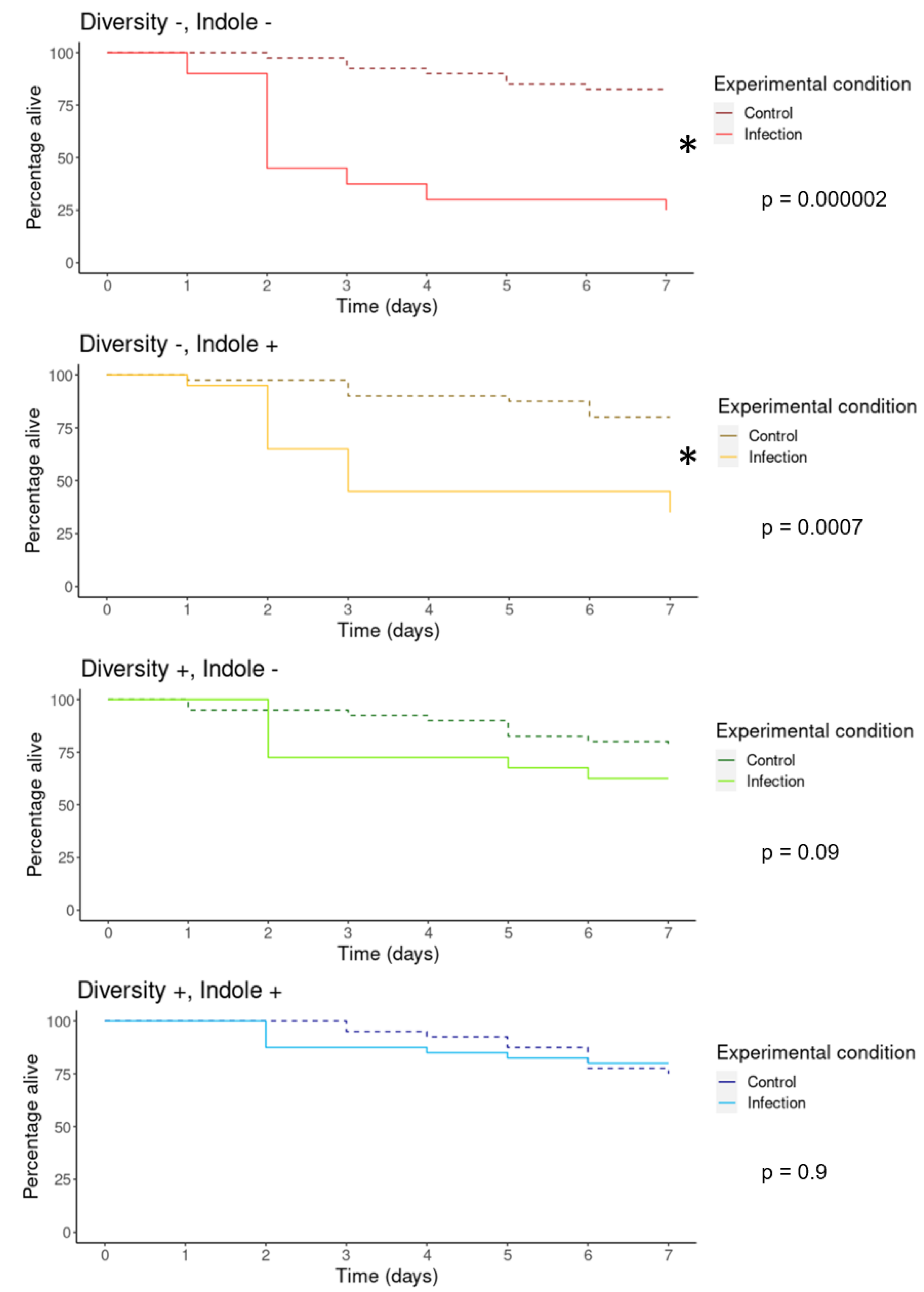


Figure 1. Microbiome diversity has a stronger protective effect on C. elegans survival than the presence of exterior environmental indole does. Ten or 30 worms were present on each plate in different experimental replicates. Survival was scored every 24 hours by assessing presence or absence of movement after the prick of a platinum wire. The entirety of the assay took place at room temperature. P-values included above were determined between control and infection groups in each graph condition by log rank tests, and statistically significant groups are signified with asterisks (alpha = 0.05).

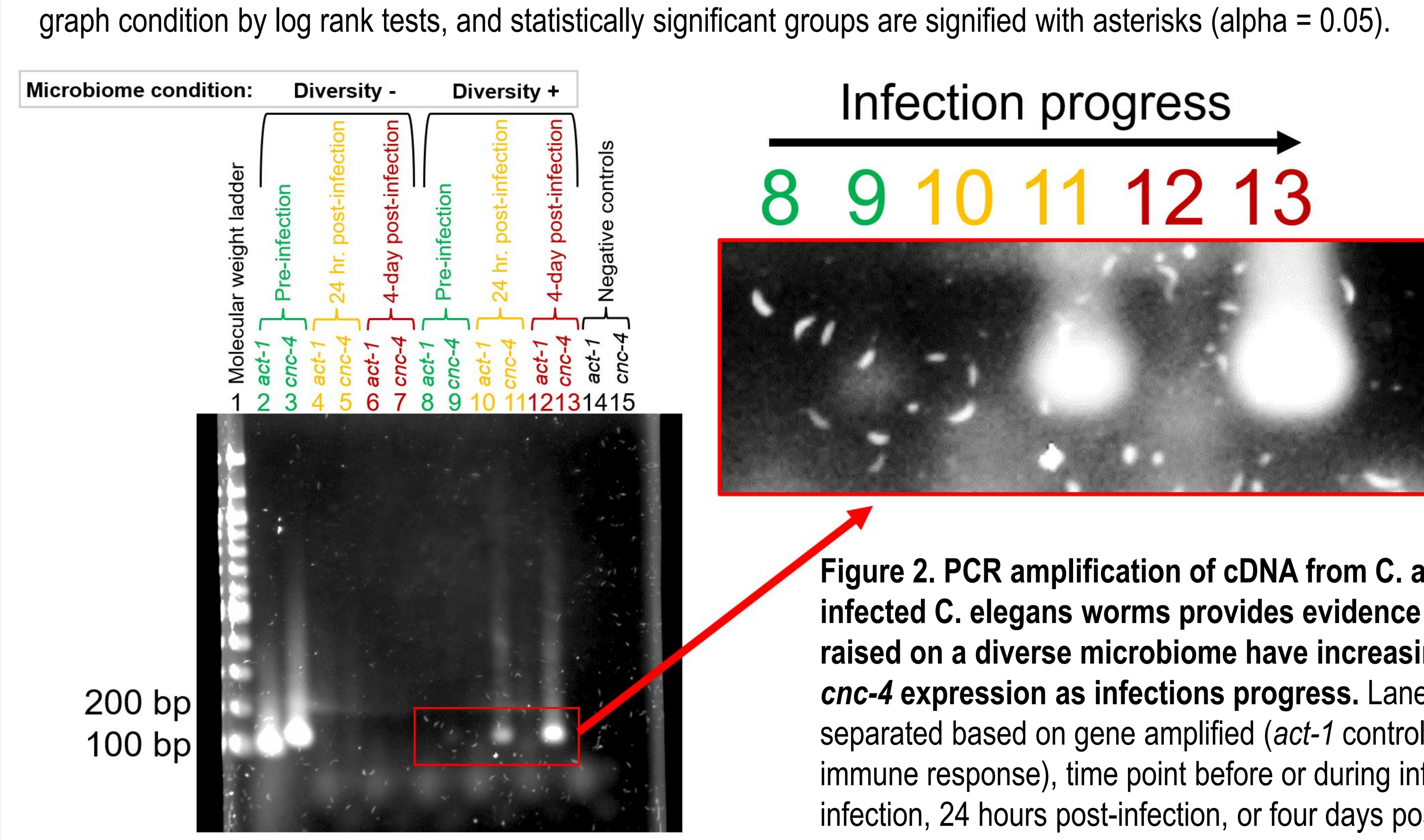
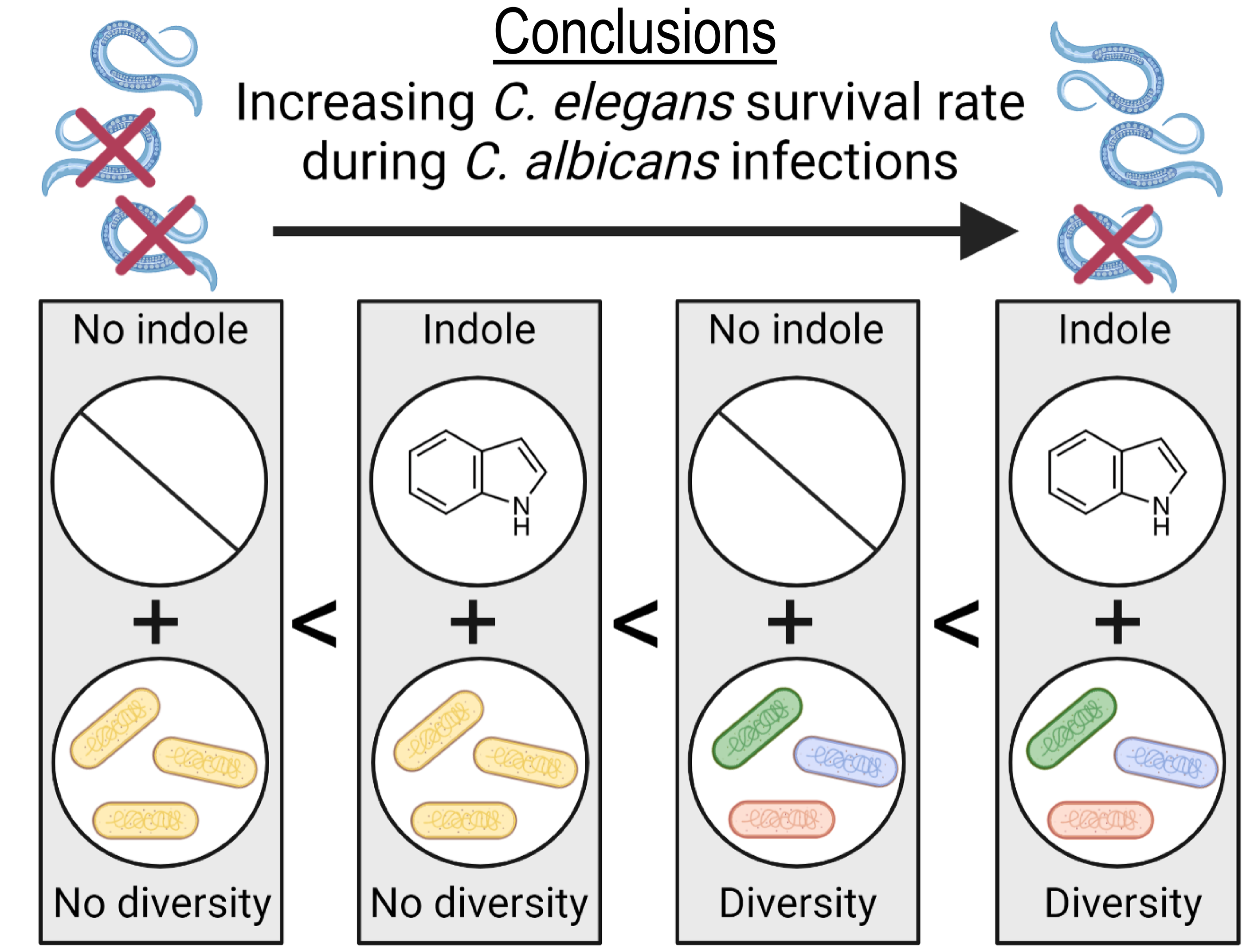


Figure 2. PCR amplification of cDNA from C. albicans-infected C. elegans worms provides evidence that worms raised on a diverse microbiome have increasing levels of *cnc-4* expression as infections progress. Lanes are separated based on gene amplified (*act-1* control or *cnc-4* immune response), time point before or during infection (pre-infection, 24 hours post-infection, or four days post-infection), and microbiome diversity condition. The inset highlights consistent *act-1* expression throughout infection but increasing *cnc-4* expression throughout infection in diversity-raised worms.

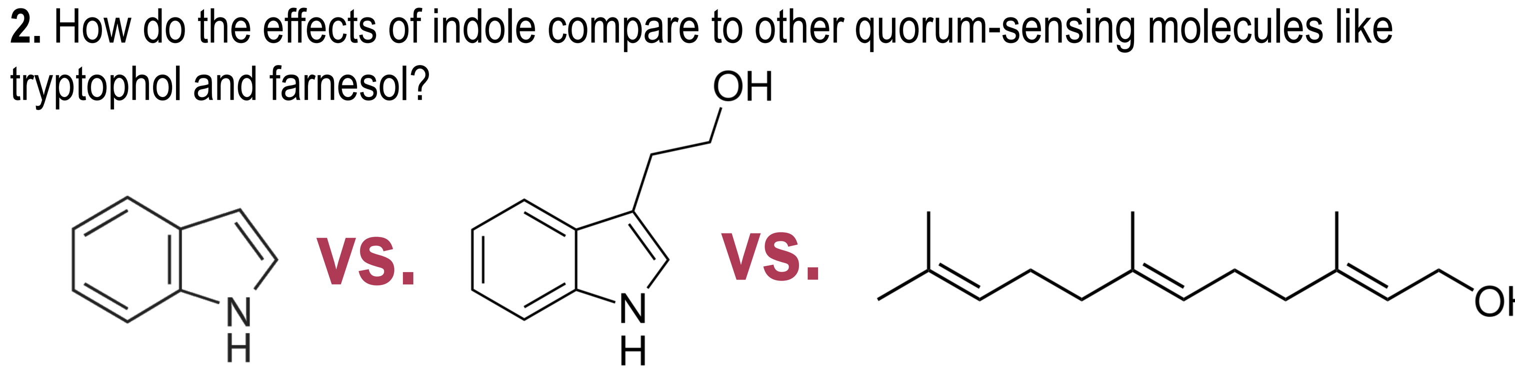
Conclusions



Both microbiome diversity and supplemental indole had beneficial effects on host survival, but effects of diversity were more significant. Microbiome diversity benefits may be due in part to enhanced biofilms, metabolite interactions, or priming of host immunity. For example, data in this study may suggest increasing *cnc-4* expression throughout infection in *C. elegans* raised on diverse microbiomes.

Future Directions

1. Examine differences in antifungal gene expression between conditions
2. How do the effects of indole compare to other quorum-sensing molecules like tryptophol and farnesol?



References

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