The effects of Residential Gut Microbiota on an Infectious E. coli strain in the presence of Antibiotics

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**Introduction**

The residential gut microbiota has a very important role in humans such as aiding in digestion and as a part of the innate immune system. The microbiota is a diverse dense group of bacteria that is present and has mutually beneficial relationship with the host. It is colonized by a rich diversity of bacteria, eukarya, and viruses that have biotic interactions (Ley et al. 2006). The relationship is very important to prevent infectious disease in humans. One of the mechanisms in which the microflora does this is by colonization resistance. Colonization resistance is the failure of pathogenic or infectious bacteria to colonize the gastrointestinal tract and cause enteric disease (Stecher and Hardt 2008). Therefore, any lack of this normal microbiota increases the likelihood of enteric infection.

Despite microbiota having the ability to defend against infectious bacteria, pathogens are still able to cause gastrointestinal infections. The ability of pathogens to evade the normal gut microbiotas defense mechanism causes us to use antibiotics to treat these gastrointestinal infections. With the increase usage of antibiotics, bacterial pathogens have developed more antibiotic resistance which cause them to be more difficult to treat. Antibiotics may also have roles in disrupting the normal gut microbiota causing an increased risk of gastrointestinal infection. The usage of antibiotics cause the gut microbiota to lose the ability of colonization resistance (Bohnhoff and Miller 1962). Another example of this is in the usage of common beta-lactam antibiotics such as ampicillin actually lead to an overgrowth of resistant Enterobacteriaceae (Edlund and Nord 2000). Therefore, the interactions between beneficial gut microbiota and antibiotics needs to be more understood.

In this analysis, I intend to explore the effects of residential gut microbiota on an infectious *E coli.* strain in the presence of antibiotics. The analysis will be done to determine what effects the residential microbiota has on the concentration of infectious *E coli.* and also determine what happens to that concentration when adding a common antibiotic such as ampicillin along with the residential microbiota collected from human donors. I hypothesize that the fitness of infectious *E coli.* strain decreases when in the presence of human residential gut microbiota and ampicillin. Fitness is broadly defined here as the concentration of the infectious *E coli.* The purpose is to determine if the human residential gut microbiota is capable of fighting off infectious *E coli.* and look at the interaction between antibiotics and the normal human residential gut microbiota to understand how we can better treat enteric infection.

**Materials and Methods**

To run this analysis and test the hypothesis, data was collected by (Baumgartner et al. 2020) in which I obtained from the paper “Resident microbial communities inhibit growth and antibiotic-resistance evolution of *Escherichia coli* in human gut microbiome samples” through the dryad repository. The data chosen for this was the measured abundance (cfu) of the infectious *E coli.* strain over a 7-day time period in the presence of either a basal medium, faecal slurry, or residential microbial community (gut microbiota) from each of the three human donors in the absence or presence of the antibiotic ampicillin. The basal medium was used as control to use to compare how the values differ because we know the bacteria will grow in the medium. The no antibiotic group with all the same treatments is used to determine if it is solely the antibiotic acting on the infectious *E coli*. strain or if the residential microbial communities can decrease the fitness of the infectious *E coli.* alone. By performing with antibiotic we can also determine how the antibiotic is acting along with the residential microbiota communities and maybe allowing for better survival of the infectious *E coli.*

Once data was obtained in an excel file, we ran it through Rstudio to make a boxplot of the values to determine what was happening to the infectious E coli strain in each treatment to test the hypothesis. After boxplot was performed, an anova was performed to look at significance and the effect size of the data points to determine if there were any importance’s between the group with no gut microbiota vs the groups with gut microbiota. This was performed to determine if the hypothesis that fitness of infectious *E coli.* decreases in the presence of residential gut microbiota.

**Results**

**Chart

Description automatically generated**

Figure 1. Concentrations of Infectious e coli shows some decrease in the presence of Residential gut microbiota and ampicillin.

Infectious *E coli.* concentration showed lower values most consistently when it was in the presence of both the ampicillin and the residential microbial communities that were sampled from the human donors. We can also see that in some instances that it was extremely low when in the presence of both of those. However, we can also determine that sterile slurry from the human donors was not able to decrease infectious *E coli.* concentration, therefore needing the actual residential microbiota communities is important.

The residential human donor 1 gut microbiota community showed the lowest mean (-1.6610) which shows that this residential microbiota community was able to decrease the infectious *E coli.* strain the most. This was also the only instance in which adding the antibiotic did not help decrease the concentration of *E coli*. even further. Whereas in both human donor 2 and 3 residential microbiota communities upon addition of the antibiotic were able to decrease infectious *E coli.* strain further with means of (0.1081 to -1.9035 and -0.1558 to -1.5774) respectively. The antibiotic alone did show a decrease in infectious *E coli.* concentration with a mean of (-0.3164). This was relatively higher compared to the residential gut microbiota communities with the exception of human donor 2’s sample.

Human donor 1’s residential microbiota community sample showed a significant difference (P < 0.05). Upon the addition of the antibiotic ampicillin, both human donors 2 and 3 also showed there was a significant decrease in the infectious *E coli.* strain. However, neither residential microbiota community alone showed a significant decrease in *E coli.* concentration.

**Discussion**

This analysis of the residential gut microbiota’s ability to decrease the fitness of infectious *E coli.* did show some ability in decreasing bacterial concentration. In each of the residential microbiota communities, infectious *E coli.* shows a decrease. Upon the addition of antibiotic there is an even larger decrease in concentration. In human donor 1, we see that infectious *E coli.* has a decrease in growth (Figure 1). Therefore, residential gut microbiota shows to some extent to have the ability to suppress the growth and colonization of infectious pathogens of the gastrointestinal system (Stecher and Hardt 2008). We can also see this trend in the human donor 2 and 3 residential communities combined with antibiotics.

There are a lot of possible mechanism as to how the gut microbiota are able to suppress the growth of pathogenic bacteria such as nutrient competition, niche competition, and even the production of bile acids in larger concentrations (Kamada et al. 2013). In this analysis we are not trying to develop a possible explanation on the mechanisms by which gut microbiota can do this. No matter how gut microbiota executes the suppression of pathogens its expected that reduced population growth, size, and replication to also reduce the supply of new genetic variation in invading pathogens (Baumgartner et al. 2020).

Upon addition of ampicillin with the residential gut microbiota community treatments showed to have limited the growth of infectious *E coli*. even further (Figure 1). Therefore, there is some need in the use of antibiotics along with residential gut microbiota communities to better treat enteric infection. That is because we have suppression of infectious *E coli.* in presence of these communities, but the suppression was always stronger with the addition of the antibiotic to the treatment. Although, more research needs to be done to determine what interactions between the rich microbiota and antibiotics plays in the suppression of the pathogens. It could be to due to particular antibiotic/species interactions, host immune response, and could be the possible mechanism to colonization resistance (Zheng et al. 2008).

In conclusion, the results of this analysis show that the residential gut microbiota communities sampled from live human gastrointestinal tracts does have the potential to decrease fitness of an infectious *E coli.* strain in the means of decreasing its concentration. The addition of antibiotic makes the decrease of infectious *E coli.* stronger. Some limitations are can this be consistent throughout because of what lineages of commensal bacteria are present in the residential gut microbiota. Also, is the effect due to more ecological interactions rather than host immune response or vice versa. There needs to be experiments done to expand on the mechanism by which we see the decrease of infectious E coli strains in the presence of residential gut microbiota communities.

**Literature Cited**

Baumgartner M, Bayer F, Pfrunder-Cardozo KR, Buckling A, Hall AR. 2020. Resident microbial communities inhibit growth and antibiotic-resistance evolution of Escherichia coli in human gut microbiome samples. PLOS Biology. 18(4):e3000465. doi:10.1371/journal.pbio.3000465.

Bohnhoff M, Miller CP. 1962. Enhanced Susceptibility to Salmonella Infection in Streptomycin-Treated Mice. The Journal of Infectious Diseases. 111(2):117–127.

Edlund C, Nord CE. 2000. Effect on the human normal microflora of oral antibiotics for treatment of urinary tract infections. Journal of Antimicrobial Chemotherapy. 46(suppl\_1):41–48. doi:10.1093/jac/46.suppl\_1.41.

Ley RE, Peterson DA, Gordon JI. 2006. Ecological and Evolutionary Forces Shaping Microbial Diversity in the Human Intestine. Cell. 124(4):837–848. doi:10.1016/j.cell.2006.02.017.

Stecher B, Hardt W-D. 2008. The role of microbiota in infectious disease. Trends in Microbiology. 16(3):107–114. doi:10.1016/j.tim.2007.12.008.