Antibiotic resistance is a global problem exacerbated by the use and overuse of antibiotics. Overuse has caused the rapid spread of antibiotic resistant genes (ARGs) and the emergence of multidrug resistant bacteria. Metagenomic analysis of the gut microbiome has shown to be viable method to study the spread of ARGs, mobile genetic elements (MGEs), and bacterial compositional profiles.

This project used next-generation sequencing, a custom-built metagenomics pipeline, and differential abundance analysis to study the effect of antibiotic (ampicillin, ciprofloxacin, and Fosfomycin) combination and monotherapy at high and low doses on resistome and bacterial compositional profiles.

Triple combination, high-dose treatment killed nearly all bacteria and no ARGs were detectable after treatment. Dual combination treatments caused the emergence of clinically relevant multidrug resistant bacteria including Acinetobacter radioresistens, Delftia acidovorans, Enterococcus faecalis, and Stenotrophomonas maltophilia, despite a decrease in microbiota diversity. Only a maximum of 2 ARGs showed enrichment after treatment in any of the dual combination cohorts. Low-dose monotherapy treatments showed little change in microbiome composition but saw enrichment of over 30 ARGs. Relative abundances of MGEs either decreased or remained unchanged for combination therapy with increases in low-dose monotherapy.

Combination therapy appears to be a feasible option to prevent the spread of ARGs, but caution needs to be taken to prevent possible superinfection. Low-dose monotherapy did not greatly change bacteria diversity but did cause an increase in ARGs that could cause cross-resistance of antibiotics.