

Paper 2

Title:	Antibiotic resistance and dissemination potential in the human gut resistome are promoted by antibiotic treatment
Author keywords:	antibiotics resistome gut microbiome metagenomic variation analysis horizontal gene transfer
Abstract:	Submission for a keynote talk: Disruption of the gut microbiota and increased resistance of gut microbes by antibiotic treatment has been frequently documented; however, the impact of antibiotic intake on the resistance gene reservoir and its dissemination potential remains poorly understood. In this longitudinal study, we performed comprehensive analyses to unravel the dynamics of the resistome and its dissemination potential upon antibiotic administration by combining cultivation-based multiplex phenotyping, functional and shotgun metagenomics. Our results demonstrated that a 5-day cefuroxime treatment reshaped the bacterial community drastically and significantly increased the resistance levels within 12 bacteria species, which persisted for at least 1-3 months. Single nucleotide variant analysis revealed that <i>Escherichia coli</i> and <i>Enterococcus faecium</i> experienced genome-wide selective sweeps in response to the antibiotic pressure. Additionally, over 50% of the functionally validated antibiotic resistant genes underwent strong selection at single nucleotide level. Further phylogenetic analysis indicated the increased potential for horizontal gene transfer during treatment with the antibiotic differentiated resistant genes to be 2-fold more likely to be horizontally transferred than non-differentiated ones. These findings were validated using independently published metagenomic data sets. This study provides strong evidence for the amplified antibiotic resistance and increased risk of disseminating antibiotic resistance via horizontal gene transfer upon short time antibiotic treatment.
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