Antibiotic Treatment Drives the Diversification of the Human Gut Resistome

Despite the documented antibiotic-induced disruption of the gut microbiota, the impact of antibiotic intake on strain-level dynamics, evolution of resistance genes, and factors influencing resistance dissemination potential remains poorly understood. To address this gap we analyzed public metagenomic datasets from 24 antibiotic treated subjects and controls, combined with an in-depth prospective functional study with two subjects investigating the bacterial community dynamics based on cultivation-dependent and independent methods. We observed that short-term antibiotic treatment shifted and diversified the resistome composition, increased the average copy number of antibiotic resistance genes, and altered the dominant strain genotypes in an individual-specific manner. More than 30% of the resistance genes underwent strong differentiation at the single nucleotide level during antibiotic treatment. We found that the increased potential for horizontal gene transfer, due to antibiotic administration, was ∼3-fold stronger in the differentiated resistance genes than the non-differentiated ones. This study highlights how antibiotic treatment has individualized impacts on the resistome and strain level composition, and drives the adaptive evolution of the gut microbiota.

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Corresponding author: Sommer, M. O. A.
Contributors: Li, J., Rottedal, E. A., van der Helm, E., Ellabaan, M. M. H., Panagiotou, G., Sommer, M. O. A.
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