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A better understanding of antibiotic resistance

Antibiotic-resistant bacteria already existed in the environment before antibiotics were used in human medicine.¹ Antibiotic resistance-conferring genes are usually located on mobile genetic elements (MGEs). Besides promoting the development of new resistance traits, the way and extent we use antibiotics today also selects for existing resistant clones within microbial populations and promotes their expansion. The spread of antibiotic resistance genes and the development of multidrug resistance represent major threats to public health.²

As antibiotics are not only used in human and veterinary medicine, but also in animal food

production and agriculture,^{3,4} the environment plays an important role in the spread of antibiotic resistances, because it provides a multitude of relevant niches (soil, water, plants, animals) for the spread of resistance. Already in 2001, the European Council Recommendation on the prudent use of antimicrobial agents in human medicine underlined the idea that the occurrence of antibiotic resistance in human pathogens correlates with their occurrence in animals and the environment.⁵ Against this background, also the European Food Safety Authority (EFSA) has re-evaluated antibacterial products used as feed additives and their impact on resistance development to antibiotics of human and veterinary importance.⁶ Based on a recent decision of the European Commission regarding the monitoring of antimicrobial resistance in zoonotic and commensal agents in food-producing animals and meat, the detection of changes in antibiotic resistance patterns in animal populations should help to define future trends in the occurrence of antimicrobial resistance.⁷

So far, microbial pathogens and individual MGEs carrying resistance determinants have been intensively studied regarding the spread of antimicrobial drug resistance. The composition and dynamics of the general bacterial mobile gene pool in a given niche or environment, the so-called 'mobilome', has not been comprehensively studied so far. The mobilome consists of MGEs, including plasmids, bacteriophages, genomic islands (GEIs), integrative and conjugative elements (ICEs), integrons and transposons. These MGEs can frequently carry antibiotic resistance genes and serve as vectors for the lateral dissemination of antibiotic resistance determinants between microbes. Among MGEs, plasmids, which can carry (multiple) resistance determinants, are among the most important vehicles for the spread of antibiotic resistance. In order to better understand the constraints and driving forces of lateral gene transfer (LTG), we have to determine the molecular basis of the bacterial host range of resistance plasmids, the contribution of environmental conditions to the transfer efficiency of such plasmids and the impact that resistance plasmid carriage has on the fitness and competitiveness of the recipient hosts.

The uptake and exchange of bacteria between the environment, animals and humans increases the diversity and dynamics of the mobilome. In the wake of metagenomic analyses, also the prevalence of antibiotic resistance genes in the commensal microbiota is more and more in the research focus. Recent analyses indicate that resistance genes are widely distributed in the intestinal gut microbiota of healthy individuals.^{8,9,10} It has also been shown that the rate of LGT in the gut microbiota is remarkably high, sometimes being much higher than in other environments.^{11,12,13} Accordingly, the detailed analysis of the intestinal mobilome, not only in humans, but also in companion and food animals is critical for our understanding of the spread of antibiotic resistance as well as for relevant preventive approaches.^{10,14} Although we are slowly beginning to elucidate the relevance of certain compositional changes of the microbiota regarding its impact on human health, our knowledge of the mobilome in general, the interplay between different mobilome components, and their transmission and persistence including resistance genes, is still limited.

In summary, there is an urgent need to apply new comprehensive 'omics' approaches to increase our knowledge of the diversity, dynamics and evolution of antibiotic resistance genes including their vectors. We should intensify the analysis of the interplay and exchange of MGEs in complex microbial consortia in relevant reservoirs and environmental niches, including populations of wild and domesticated animals as well as humans.



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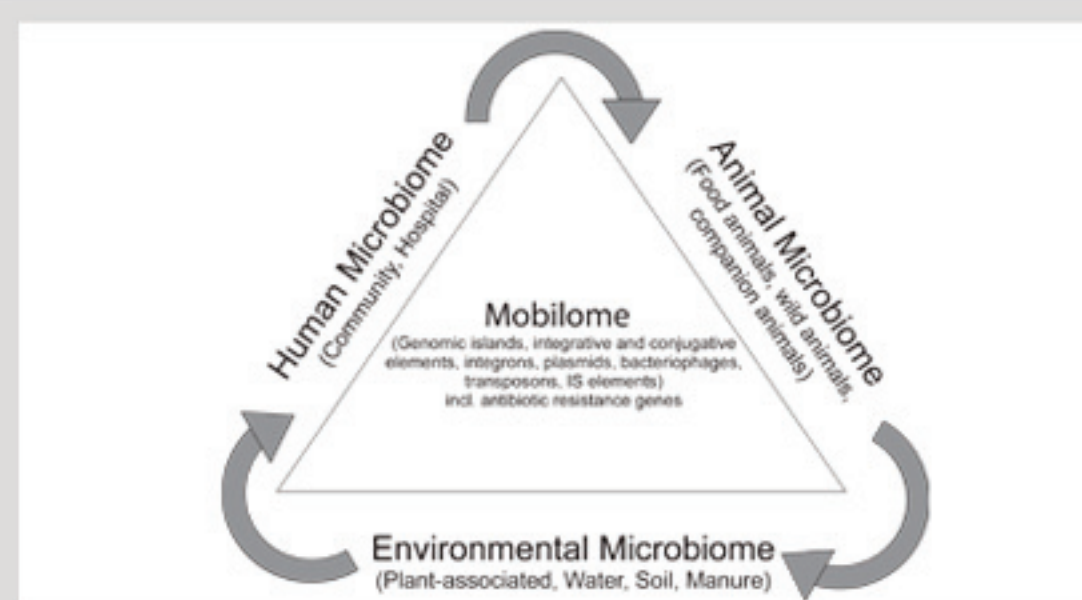


Fig. 1: Interaction between microbial communities from different environments affects the mobilome composition and antibiotic resistance gene reservoir

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