The silent go-between - the role of the microbiota as intermediator in horizontal gene transfer

Horizontal gene transfer (HGT) (also known as lateral gene transfer) is a powerful genetic process, in which DNA is transmitted from a donor organism to a recipient organism that is not its offspring. Thus, acquisition of DNA through HGT is distinguished from the transmission of genetic material from a parent to descendants during reproduction, which is known as vertical gene transfer. HGT often occurs between different bacterial species, and even between bacteria and unicellular eukaryotic organisms and is facilitated by mobile genetic elements including plasmids (extra-chromosomal DNA entities), transposons (transposable DNA elements that can move to new positions within or between genomes), and bacteria-infecting viruses, called bacteriophages. These mobile genetic elements can moved between organisms via distinct mechanisms, known as conjugation, transformation and transduction, respectively.

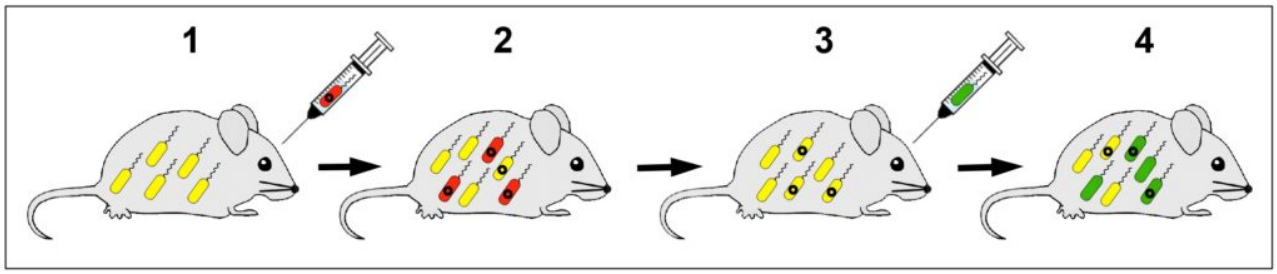

Fig. 1. Dissemination of virulence and resistance genes via the microbiota.
Mice were orally infected with Salmonella Infantis (red rods) harboring a plasmid (black circle) that carries antibiotic resistance and virulence genes (stage 1). These bacteria were able to colonize the mouse intestines (stage 2) and the plasmid was transferred to the natural mouse microbiota (yellow rods; stage 3). When these mice were reinfected with a different bacteria (green rods; stage 3), the plasmid was able to retransfer to this new bacteria providing the bacteria new antibiotic resistance and additional virulence traits (stage 4).

HGT plays a fundamental role in the evolution of bacteria and particularly in the emergence of new virulent and resistant strains. In a single genetic event, a bacterium can acquire a genetic element that encodes multiple (sometimes hundreds) genes and by that changes its genetic landscape (genotype) and its overall composition of traits (phenotype). Therefore, HGT is considered a quantum leap in the evolution of bacteria. If the acquired mobile genetic happens to encode virulence factor genes (such as toxins, colonization factors, or translocated effector proteins that manipulate host pathways), the recipient bacteria may change its ecological niche, host range or its virulence potential (its ability to cause diseases) and transform from an environmental organism to a pathogen. Similarly, if the acquired element harbors antibiotic resistance genes, then the recipient bacterium becomes tolerant to particular antimicrobial compounds.

Microbiota refers to the entire communities of microorganisms (bacteria, archaea, protists, fungi and viruses) colonizing multicellular hosts. In the last decade or so, the importance of the microbiota in health and disease is becoming more and more evident. Microbiota have been found to play important roles in host metabolism, physiology, nutrition, hormonal and immune functions. Nevertheless, their involvement in the evolution of pathogens and emergence of resistant strains was overlooked. In a recent paper published by Gili Aviv and colleagues in *mBIO*, we demonstrated the possible role of the gut microbiota as intermediator of horizontally acquired virulence and resistance genes

Salmonella enterica serovar Infantis (*S*. Infantis) is one of the most prevalent *Salmonella* serovars worldwide. Healthy humans infected with *S*. Infantis will develop, in most cases, a self-limiting gastroenteritis (food poisoning). Interestingly, recent emergent populations of *S*. Infantis in different regions of the world were found to harbor a large conjugative plasmid called pESI. This plasmid provides multidrug resistance phenotype and was shown to increase the virulence and the tolerance to certain environmental stresses of *S*. Infantis strains harboring this mega-plasmid.

When we studied the conjugation frequency of pESI (i.e. the number of the plasmid transfer events from *S*. Infantis to a different bacterium species), we found that the conjugation rate increases at 37-41°C and under microaerobic conditions. This set of environmental conditions is known to characterize the gut of warm-blooded hosts. Furthermore, when mice were orally infected with *S*. Infantis carrying the pESI plasmid, it was disseminated to the mouse natural microbiota and from there to a secondary pathogen (*S. enterica* serovar Typhimurium) that was used to infect the mice at a later time point (Fig. 1). In this experiment we were able to show a complete cycle of HGT of a large plasmid, which contain multiple resistant and virulence genes, from a pathogen to the mouse microbiota and from there further to a different pathogen. These results demonstrate that the commensal microbiota may play a part as intermediator of gene flow from one pathogen to another and by that contribute to resistance and virulence genes dissemination among bacteria.

Ohad Gal-Mor
The Infectious Diseases Research Laboratory, Sheba Medical Center, Tel-Hashomer, Israel
Department of Clinical Microbiology and Immunology, Sackler Faculty of Medicine,
Tel-Aviv University, Tel-Aviv Israel

Publication

Horizontal Transfer of the Salmonella enterica Serovar Infantis Resistance and Virulence Plasmid pESI to the Gut Microbiota of Warm-Blooded Hosts.
Aviv G, Rahav G, Gal-Mor O
MBio. 2016 Sep 6