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Editorial
Fighting microbes with microbes

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One of the most fascinating topics of human medicine is the relationship between microorganisms in maintaining the balance between health and disease[1]. Indeed, microorganisms have been living in harmony with our body since the beginning of the human history and they have developed well refined mechanisms of adaptation toward our immune system during millennia[1]. Innate immunity plays a very important role in defining the individual level of tolerance towards all kinds of microorganisms, such as pathogens, pathobionts and symbionts[2]. This explains why some subjects are particularly prone to acquire infections, of viral, bacterial or fungal origin, while others seem to be more protected. This is particularly true for urinary tract infections or respiratory viral infections, including the recent SARS-CoV2[2]. One of the most common questions asked by patients is whether the mechanism of tolerance is only innate[3]. Some recent studies[4] focused on this question and showed that tolerance is not only related to a host genetic predisposition but may also be linked to the relative abundance of the various species composing the microbiota. This is very clear in the field of gut microbiota, where several species may trigger a high number of immunomodulatory mechanisms and modulate the production of butyrate, a major anti-inflammatory metabolite. Experiencing an overgrowth of these species may result in boosting their immunological effect, possibly resulting in an increased pathogenic activity, which can disrupt the mechanism of tolerance[5]. In this case, we may need to use antibiotics to downregulate their concentration[5]. But what happens when those strains show antibiotic resistance?

There is increasing evidence supporting the role of some 'microbes' to fight other 'microbes'. Some of them are able to produce naturally occurring antibiotics, while others may decrease the concentration of pathogens by competing for space and nutriments[6]. Yeasts surely represent the best example of microorganisms able to produce antibiotics. One must always remember that penicillin is produced by a fungus, *Penicillium notatum,* and that yeasts are able to create their own space inside our body by producing antibacterial substances[7]. We also know that some probiotics produce antimicrobial compounds; such is the case of *Lactobacillus reuteri*, which produces reuterin, and *Bacillus clausii* producing clausin, as well as *Bacillus subtilis* 3 producing amicoumacin A[8]. Those antimicrobials are effective against a wide range of bacteria, including *Escherichia coli*, *Helicobacter pylori* and *Clostridia* species[9,10]. Even prebiotics may exert an active action against pathogens, since they promote the growth of competitive bacterial species[11]. Finally, fecal microbial transplantation showed a very effective activity against pathogens, such as *Clostridioides difficile*, which may be completely eradicated without the use of antibiotics[12].

As we are faced with growing evidence of antibiotic resistance, we should encourage trials able to test the efficacy of such biotherapies to fight infections. This will increase the success of our therapies and reduce, whenever possible, the use of antibiotics and then antibiotic resistance.

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