



To engraft or not to engraft: an ecological framework for gut microbiome modulation with live microbes

Jens Walter^{1,2}, María X Maldonado-Gómez³ and Inés Martínez^{1,4}

Strategies aimed at modulating the gut microbiota by using live microbes range from single strains (probiotics or live biotherapeutics) to whole non-defined fecal transplants. Although often clinically efficacious, our understanding on how microbial-based strategies modulate gut microbiome composition and function is vastly incomplete. In this review, we present a framework based on ecological theory that provides mechanistic explanations for the findings obtained in studies that attempted to modulate the gut microbiota of humans and animals using live microbes. We argue that an ecological perspective grounded in theory is necessary to interpret and predict the impact of microbiome-modulating strategies and thus advance our ability to develop improved and targeted approaches with enhanced therapeutic efficiency.

Addresses

¹ Department of Agricultural, Food, and Nutritional Science, University of Alberta, AB, Canada

² Department of Biological Sciences, University of Alberta, AB, Canada

³ Department of Food Science and Technology, University of California, Davis 95616, United States

⁴ Sacco System, Cadorago 22071, Italy

Corresponding author:

Current Opinion in Biotechnology 2018, **49**:129–139

This review comes from a themed issue on **Food biotechnology**

Edited by **Maria Marco** and **Eddy Smid**

<http://dx.doi.org/10.1016/j.copbio.2017.08.008>

0958-1669/© 2017 Elsevier Ltd. All rights reserved.

Using live microbes to modulate the gut microbiota

The gut microbiota is a critical determinant of human health by directly contributing to pathologies, influencing host predisposition to disease, and providing cues to maintain metabolic and immunological functions [1]. The crucial role of the microbiome in disease has been clearly proven in various animal models, providing a compelling case to design strategies that modulate gut microbiota composition and function. Such modulations can range from small temporary alterations in

the composition and/or metabolic output of the community to a more permanent and global transformation of microbiome structure and functional configuration. Although our mechanistic understanding on how the microbiota relates to human health is still in its infancy, and few cause-and-effect relationships have been established, microbiome-modulating strategies are increasingly aimed to redress dysbiotic patterns in both composition and function that are associated with disease [2].

One approach to modulate the gut microbiota is through the oral administration of live microorganisms [3]. These strategies range from pure cultures or consortia thereof, which are referred to as probiotics or live bio-therapeutics [4], to complex preparations of whole stool, such as Fecal Microbiota Transplants (FMT), or stool components (microbial cells, spores) [5]. Together, these strategies have been tested in a wide range of clinical contexts, with varying degree of success. Although various mechanisms have been established or suggested by which administered microbes exert their benefits, a modulation of gut microbiota is often one of the driving motivations to apply these approaches [3]. Novel technologies based on next-generation sequencing now provide unprecedented insight into the effect of live microbes on the gut microbiome. There is substantial literature published describing the effects of probiotics on the gut microbiota composition, and although most strains show good survival during gastrointestinal passage and remain metabolically active, most human studies have shown extremely short persistence [6] and little effect on the composition of the resident microbiota [7]. FMTs appear to be much more successful in engrafting bacterial strains into an established gut microbiota [8,9], but the reasons for these differences have been hardly studied and poorly understood. What the field currently lacks is a conceptual understanding of the effect of live bacteria on the gut microbiota and their potential to modulate the community.

Given that the digestive tract and its microbiota operate as a highly interconnected and co-evolved ecosystem in which interactions among members and community characteristics are governed by the principles of community ecology [10], we argue that the modulation of gut microbiomes can only succeed when based on ecological and evolutionary criteria. The introduction of a microorganism into a gut ecosystem can be considered a biological

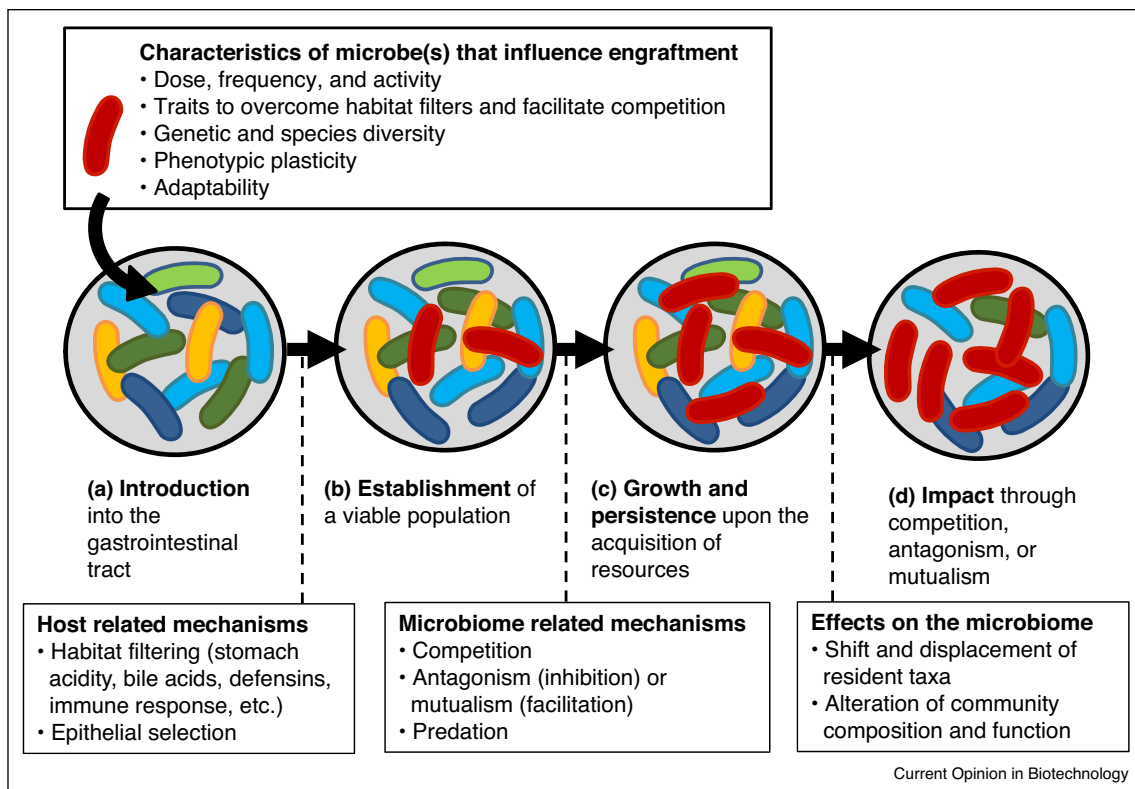
invasion of non-native microbes into a highly adapted resident microbial community [11]. Here we apply concepts from invasion and general community ecology to develop a theoretical framework to understand the success of live microbes introduced into the digestive tract and their ecological impact on the resident microbial community. We then apply this framework to explain the findings that have been obtained with currently used microbiome-modulating interventions (probiotic strains and mixtures, synbiotics, and FMTs) in different contexts, and discuss its implications for the development of improved strategies and the open questions and challenges that remain.

An ecological framework

Biological invasions can be conceptualized as a multifaceted process that can be broken down into a series of at least four stages [12]. This framework, which has been recently extended to microbial invasions [13^{*}], can be directly adopted toward microbiome-modulating strategies (Figure 1). Invasion stages are associated with barriers that must be overcome by the incoming microbe to

allow colonization and an impact on community composition and/or function. From the incoming microbe's perspective, the organism must be first introduced in an active form and in sufficient numbers (step 1), and secondly overcome the immediate habitat filters of the gastrointestinal tract to become established (step 2). Once established, the microbe must be able to gain access to resources under the competitive conditions of at least one site within the gastrointestinal tract to become metabolically active within the resident microbial community (step 3). If the local conditions allow the potential colonist to satisfy its minimum requirements so that replication is equal or greater to wash-out, the incoming microbe has successfully occupied an ecological niche and persists, resulting in colonization [4,14]. Although colonization might not be necessary for ecological impact, it is still required that the invader is able to attain sufficient metabolic activity at a local site to engage in interactions with the resident members of the community (e.g. through competition, antagonism, or mutualism) that will ultimately cause changes to microbiota composition and/or function (step 4).

Figure 1



Successful invasion of a microorganism conceptualized as a 4-stage process. **(a)** The microbe needs to be introduced in sufficient numbers and in an active form, and possess the traits to withstand the pressures of the gut environment. **(b)** Habitat filters will select for microbes that possess the traits necessary to overcome them, while the host specifically selects for symbionts by a variety of mechanisms (glycans, epithelial capture, etc.). **(c)** The microbe needs to compete with resident members to access resources to grow and persist in an ecological niche. **(d)** Successful occupation of niches may result in metabolic activities and/or competitive, antagonistic, or mutualistic interactions that impacts the resident community's composition and/or function. Adopted from Mallon et al., 2015 [13^{*}].

Download English Version:

<https://daneshyari.com/en/article/6451481>

Download Persian Version:

<https://daneshyari.com/article/6451481>

[Daneshyari.com](https://daneshyari.com)