Opinion

The role of microbiota in infectious disease

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The intestine harbors an ecosystem composed of the intestinal mucosa and the commensal microbiota. The microbiota fosters development, aids digestion and protects host cells from pathogens – a function referred to as colonization resistance. Little is known about the molecular basis of colonization resistance and how it can be overcome by enteropathogenic bacteria. Recently, studies on inflammatory bowel diseases and on animal models for enteric infection have provided new insights into colonization resistance. Gut inflammation changes microbiota composition, disrupts colonization resistance and enhances pathogen growth. Thus, some pathogens can benefit from inflammatory defenses. This new paradigm will enable the study of host factors enhancing or inhibiting bacterial growth in health and disease.

Introduction

Most bacterial pathogens infect their hosts via mucosal surfaces of the respiratory, urogenital or gastrointestinal tracts. Mucosal surfaces are protected against infection by several mechanical and immunological barriers, which have recently been reviewed elsewhere [1,2]. Here, we focus on an additional protective mechanism – colonization resistance – which is characteristic of the heavily colonized intestinal mucosa (Box 1). Colonization resistance describes the failure of most pathogenic bacteria to colonize the normal gut and cause enteric disease (Box 2). It results from the presence of a dense (10^{12} organisms per ml) microbial community called the microbiota (see Glossary). In the normal gut the relationship between the microbiota and the host is mutually beneficial. The microbiota is provided with steady growth conditions and a (somewhat limited) nutrient supply. In return, the microbiota contributes to the host's nutrition, immune system development, angiogenesis and fat storage [1,3–9]. This complex network of interactions is thought to stabilize the population structure of the microbiota and to prohibit colonization by intruding pathogens. The molecular basis of colonization resistance is still poorly understood.

In spite of colonization resistance and numerous other defenses, some pathogens are still capable of infecting the gut. The mechanisms that pathogens use to overcome these barriers, to compete against the intrinsic microbiota and to guarantee successful infection also remain elusive. One such mechanism has recently been shown in studies on the enteropathogenic bacteria *Citrobacter rodentium* and *Salmonella enterica* spp. I serovar Typhimurium (*S.* Typhimurium) [10,11]. Remarkably, both enteropathogens were shown to rely on the inflammatory host response, which they evoke in the gut: inflammation changed the composition of the commensal gut microbiota and concurrently fostered pathogen growth. Similar observations were made in patients and animal models for inflammatory bowel diseases (IBD). In this case, the gut inflammation also coincided with altered population structure of the microbiota [11–14]. These findings identify a shared mechanism of gut ecosystem intrusion by enteropathogens: that is, triggering the host's inflammatory response to overcome colonization resistance. The molecular basis of this strategy is still unclear and might involve different molecular mechanisms. The inflamed gut might offer altered conditions such as changes in the available nutrients and adhesion sites that can be exploited by the pathogen but not by the microbiota (the 'food hypothesis'). Alternatively, changes in antimicrobial compounds such as lectins and defensins released by the inflamed tissue might be detrimental for the microbiota but not for the pathogen (the 'differential killing hypothesis').

In this review, we describe the 'classical' observations linking a disturbed gut microbiota to increased susceptibility to gut infections. We then discuss how inflammation might alleviate colonization resistance and how these basic findings can be extended to help elucidate the interactions between bacteria and the gut mucosa in health and disease.

Glossary

Axenic or germfree: animals that have been raised in a sterile environment without microbiota. Axenic mice differ from colonized mice in many ways. They have an underdeveloped immune system, no colonization resistance, and require higher caloric intake than normal mice to maintain body weight.
Commensal: Originating from the Latin meaning 'sharing the same table'; an alternative term for microbiota.
Gnotobiotic: animals colonized with a defined microbiota.
Inflammation: host response following extraneous insults such as lesions, bacterial or viral infections or the introduction of foreign substances. The innate immune system reacts with the localized production of cytokines, dilatation of blood vessels, edema and leukocyte infiltration into the affected tissue (Table 1) to eventually antagonize the insulting agent.
Microbiota: all microbial species present in the intestine. Prominent eubacterial phyla are the Bacteroidetes and the Gram-positive Firmicutes. The microbiota reaches a high concentration (10^{12} gram^{-1}) in the lower parts of the human intestine and has various beneficial effects for the host.
Mucosa: intestinal tissue composed of a single layer of epithelial cells and underlying tissue (lamina propria) containing vessles and various types of immune cells.

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0966-842X/$ – see front matter doi:10.1016/j.tim.2007.12.008 Available online 14 February 2008

Box 1. The gut microbiota

Classical bacterial culture methods [44], fluorescent *in situ* hybridization (FISH), molecular fingerprinting [45], microarray techniques [46], high-throughput 16S rRNA gene sequence analysis, and metagenomic approaches [47–49] have revealed the population structure of the microbiota.

The microbiota is introduced at birth, undergoes a maturation phase and assumes a stable population structure in adults [50,51]. It is mainly composed of eubacteria and its general composition at the phylum level is fairly similar even between different species [48,52]. Compared with other habitats, the phylum-level diversity is low (Firmicutes, Cytophaga-Flavobacterium-Bacteroides [CFB], Proteobacteria, Actinobacteria, Fusobacteria, Deferribacteres, Spirochaetes, Cyanobacteria and Verrucomicrobia) and few archaebacteria (e.g. *Methanobrevibacter* spp.) are represented. Taxonomic diversity at the species and strain level is immense with >7000 unique strains in human feces [48]. Some differences in the population structure have also been detected in different regions of the intestine [44,48,53]. Nevertheless, the Firmicutes and Bacteroidetes represent the predominant phyla making up 90–99% of total intestinal microbiota in humans and mice [54].

Classical observations linking the microbiota to colonization resistance

It has long been recognized that disruption of the normal microbiota by antibiotics increases the risk for gut infections. The classic example is pseudomembranous colitis, a frequent form of infectious diarrhea caused by *Clostridium difficile* in hospitalized patients [15]. Pseudomembranous colitis occurs after broad-spectrum antibiotic treatment (e.g. ampicillin, cephalosporins and clindamycin). Similar observations have been made for several other pathogens [16]. Several animal models for enteric infections are based on the same principle of disruption of the normal microbiota: antibiotic-treated mice are currently used to study *Salmonella* spp.-induced colitis and *Shigella* spp. and *Escherichia coli* infections (Box 3) [17–19]. Thus, reduction of the normal microbiota by antibiotics disrupts colonization resistance. However, it is still unclear which effect accounts for the increased susceptibility to enteric infection – selective eradication of specific species or genera (which would normally confer colonization resistance) or simply overall reduction of microbiota density or indirect effects on mucosal physiology.

Box 2. Colonization resistance

The normal gut eco-system can efficiently block intrusion of many pathogenic bacteria. This has been termed 'microbial interference' or 'colonization resistance' [16,55] (Figure 3). The lack of an intact microbiota (e.g. in axenic mice raised under sterile conditions and antibiotic-treated mice) dramatically increases susceptibility to enteric infection (e.g. *Salmonella* spp., *Streptococcus mutans, Clostridium difficile, Shigella flexneri*) [56–58]. Conversely, selected commensal species, such as *Lactobacillus* spp. or *Bifidobacterium* spp. have therapeutic and/or prophylactic effects against enteric infection [59]. Some have been commercialized as probiotics or live microbial food supplements with health-promoting attributes.

The molecular basis of colonization resistance is probably multifactorial and might involve: (i) the production of antimicrobial or toxic substances by the flora (bacteriocins, short chain fatty acids [SCFA]), (ii) competition with pathogens for adhesion receptors, (iii) stimulation of mucin secretion or antimicrobial peptide production, (iv) stabilization of the gut mucosal barrier and improvement of gut motility and (v) overall nutrient limitation by the elaborate microbial food-web (reviewed in [59,60]). These mechanisms are not mutually exclusive: for example, butyrate was found to induce the antimicrobial peptide cathelicidin LL-37, thereby eliminating *Shigella* spp. and protecting against infection [61]. The complexity of the microbiota–host interactions represents a major obstacle for analyzing the molecular basis of colonization resistance.

Box 3. Animal models for enteropathogenic bacteria

The majority of enteropathogens is host-adapted and as a result causes no disease or a different type of disease in laboratory animals. *Yersinia* spp. seems to represent an exception [62]. This has limited the development of appropriate animal research models for human gut infections. Only a few robust small animal models are available. *Citrobacter rodentium*, the causative agent of transmissible colonic hyperplasia in mice, causes disease even without previous disruption of the flora by antibiotics [20]. This infection serves as a mouse model for diarrheal diseases caused by enterohemorrhagic (EHEC) and enteropathogenic (EPEC) *E. coli* in humans [63,64]. *Shigella* spp., *V. cholerae* and *Salmonella* spp. cannot colonize the intestinal tract of normal adult mice. Therefore, the *Shigella* infection is studied in rabbit ileal loops, newborn mice, streptomycin-treated mice and mice rectally pretreated with the human proinflammatory chemokine IL-8, or rectally infected guinea pigs [65–68]. *V. cholerae* pathogenesis is analyzed in rabbit ileal loops or a suckling mouse model [69,70]. Bovine infection models and streptomycin-treated mice are used to investigate *Salmonella* enterocolitis [17,71]. These animal models have allowed the study of bacterial virulence factors and host factors involved in disease, and will be valuable tools for investigating the influence of microbiota composition, antibiotic treatment, inflammation, immune responses and nutrient availability on microflora–pathogen crosstalk in infectious disease.

Disrupting colonization resistance by triggering mucosal inflammation

Recent work has shown that colonization resistance can be disrupted by gut inflammation. This strategy is used by at least two enteropathogenic bacteria, *Citrobacter rodentium* (a close relative of enteropathogenic *E. coli*) and *Salmonella enterica* spp. I serovar Typhimurium (*S.* Typhimurium) [10,11]. In mouse infection models, pre-existing or pathogen-induced inflammatory conditions in the large intestine drastically boosted colonization by the pathogen. Conversely, both pathogens failed to colonize the gut in the absence of inflammation. Avirulent *S.* Typhimurium, which does not induce inflammation owing to the absence of both type three secretion systems, were outgrown by the microbiota within four days post infection. By contrast, wild type *S.* Typhimurium induced inflammation, dramatically altered microbiota composition and represented the predominant bacterial species after four days of infection [10] (Figure 1). Importantly, colonization of avirulent *S.* Typhimurium could be rescued by induction of inflammation '*in trans*', for example by co-infection with wild type *S.* Typhimurium in IL-10 knockout (KO) mice suffering from chronic colitis or by inflammation induced in a T-cell transfer model.

In murine *Citrobacter rodentium* infections, pathogen colonization peaks at day seven post infection. This correlates with changes in the microbiota composition (reduced total density and relative increase in γ-proteobacteria) and first manifestations of colitis symptoms [11,20]. Decline of *C. rodentium* colonization again coincided with the resolution of inflammation by day 28 post infection. Lupp et *al.* [11] found that *C. rodentium* induced similar changes in microbiota composition as observed in mice suffering from

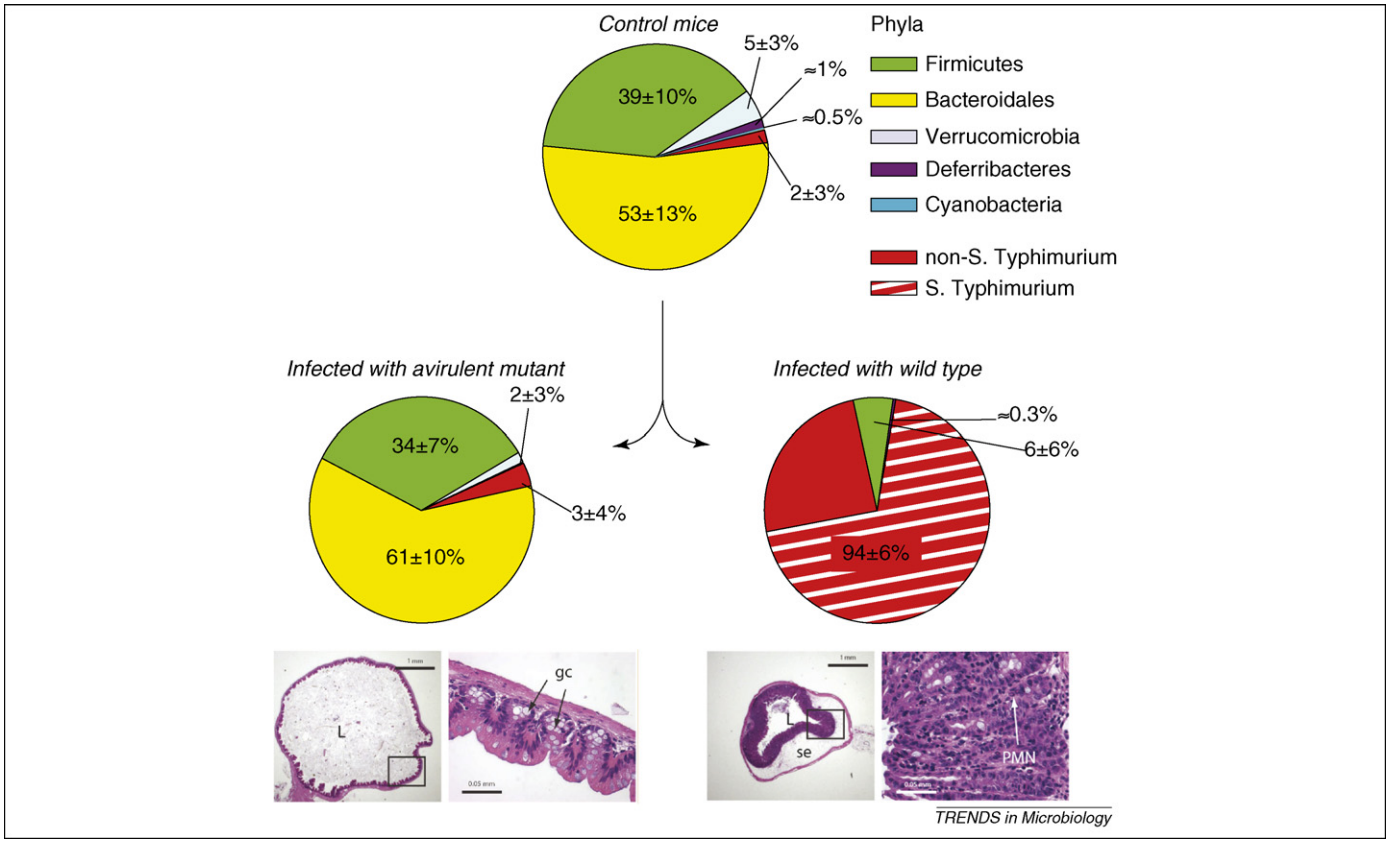

Figure 1. S. Typhimurium out-competes the microbiota in the inflamed gut. In the streptomycin mouse model the normal microbiota (top) is severely altered in the case of an infection with wild type *S.* Typhimurium, which triggers acute mucosal inflammation (histology of inflamed cecum, bottom right). In the case of an isogenic *S.* Typhimurium mutant incapable of triggering inflammation (bottom left), the microbiota suppresses pathogen growth [1]. Abbreviations: se, submucosal edema; g, goblet cells; L, lumen; PMN, polymorph nuclear leucocyte.

IBD (IL-10 KO mouse model) and in patients suffering from IBD or acute colitis [12–14].

These data have established a novel paradigm in infection biology – intestinal inflammation can disrupt colonization resistance, alter microbiota composition and foster pathogen growth. In addition, these observations point towards an additional function of some of the virulence factors expressed by enteropathogenic bacteria – they might enhance the pathogen fitness by deliberately triggering gut inflammation.

Possible mechanisms of disruption

What is the causal link between gut inflammation and disruption of colonization resistance? There are several plausible hypotheses:

- The inflamed mucosa might release antibacterial factors that could kill or retard growth of certain members of the microbiota that would normally inhibit enteropathogen growth under steady-state conditions. However, the pathogen would be able to resist these factors (see 'differential killing hypothesis', following section).
- There could be a loss of key species (i.e. secondary fermenters, Figure 2) that might be required for efficient growth of other groups of microbiota that retard pathogen growth in the normal, healthy intestine. ('commensal-network-disruption' hypothesis).
- The altered overall microbiota density might improve the conditions for pathogen growth (higher nutrient availability, fewer inhibitory substances).
- An altered nutrient mix, increased oxygen levels or increased availability of surface adhesion sites might prevail in the inflamed mucosa and foster pathogen growth. Under these conditions, microbiota might simply be overgrown by the pathogen ('food hypothesis'; see following section and Figure 3).

It will be an important objective of future research to disentangle the possible direct and indirect effects of inflammation and microbiota composition on colonization resistance. However, the current evidence suggests that nutrient availability and selective susceptibility to antimicrobial compounds are particularly important.

The food hypothesis

The large intestine represents an anaerobic bioreactor synthesizing essential amino acids, vitamins and short chain fatty acids (SCFA) while breaking down a variety of proteins and otherwise indigestible polysaccharides, including plant-derived pectin, cellulose, hemicelluloses and resistant starches [21]. This 'bioreactor' is fuelled only by those parts of the diet that cannot be processed or resorbed by the small intestine and by glycoconjugates, proteins and cellular debris released by the mucosa. Thus, high energy nutrients are scarce and the available nutrients are used up efficiently by the microbiota (Figure 2). Any incoming pathogen faces severe nutrient limitation, which slows pathogen growth.

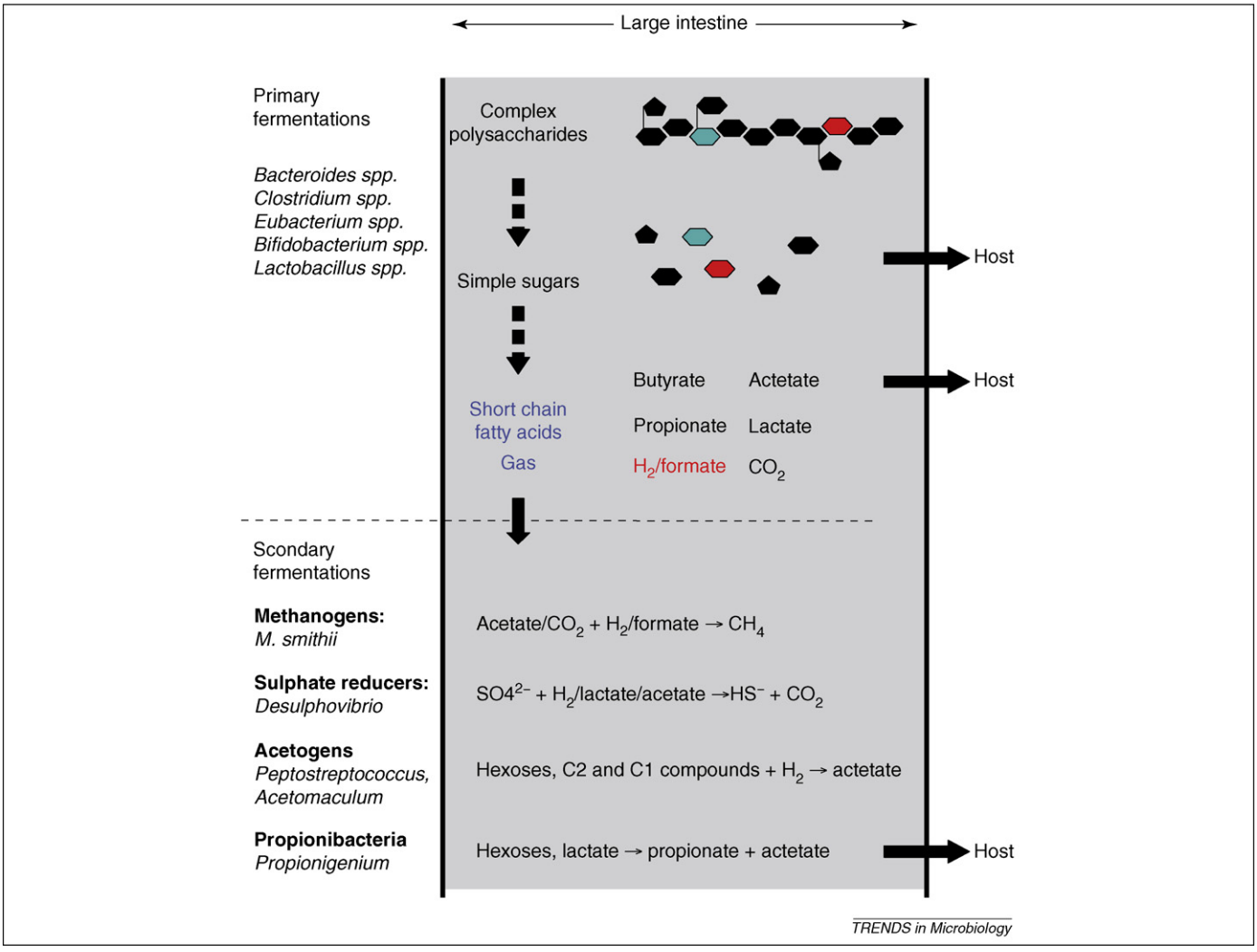

Figure 2. The intestinal foodweb. The intestinal microbial community is organized as a complex food web in the large intestine (grey). Nutrients that are not consumed by the host in the upper intestinal tract (ileum), such as complex polysaccharides, reach the large bowel, which contains the highest density of microbiota. Prominent and highly abundant species, such as *Bacteroides* spp., synthesize enzymes to break down the otherwise indigestible dietary compounds into simple sugars. The anaerobic milieu in the gut restricts metabolism to fermentations or anaerobic respirations. The main products of bacterial fermentations are short chain fatty acids (SCFA) of acetate, butyrate, formate, lactate and the gases CO_2 and hydrogen. SCFA are energy sources for the host and can make up 10% of the daily caloric intake (right). Accumulation of hydrogen thermodynamically inhibits primary fermentations. However, in the gut, most hydrogen is removed via interspecies hydrogen transfer by secondary fermenters. Typically, these secondary fermentations use the products of the primary fermentations (i.e. SCFA) as substrates. Secondary fermenting species include sulphate reducers, homo-acetogens, methanogens and propionibacteria (left). Products of the secondary fermentations include SCFA (acetate and propionate) and gas (methane and hydrogen sulfide).

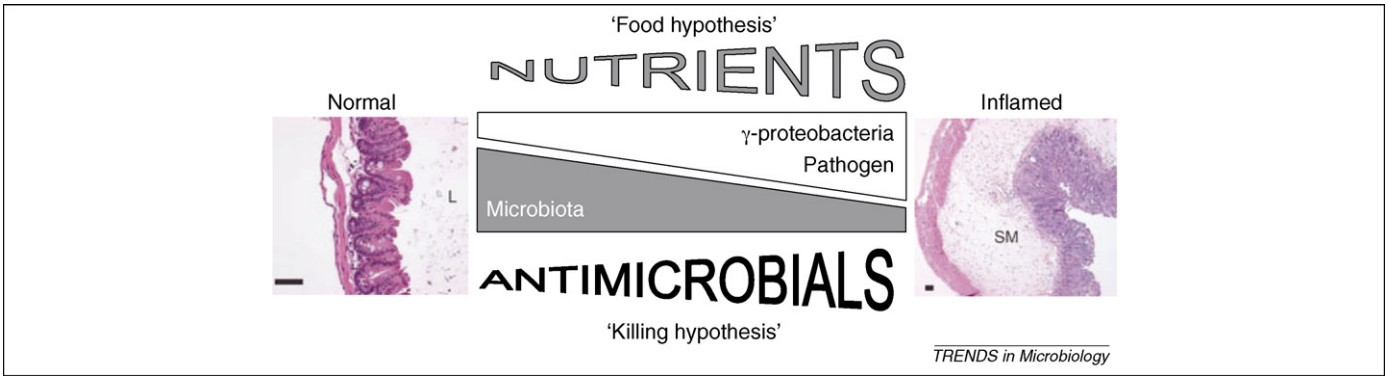

Figure 3. Interaction of host, microbiota and pathogens in health and disease: the 'nutrient hypothesis' and the 'food hypothesis'. The normal healthy intestine ecosystem is characterized by a mutualistic interaction between the host and microbiota which prevents colonization by incoming pathogens (left). In diseases such as IBD or pathogen-induced inflammation, the microbiota–host–pathogen interaction shifts in favor of the pathogen (right). This might be because of enhanced antibacterial defenses, such as neutrophil effector mechanisms, antimicrobial peptide production and mucus secretion (i.e. the; 'killing hypothesis'), or because of changes in nutrient availability, including cellular debris and secreted mucins (i.e. the 'food hypothesis'). Both mechanisms could contribute to alteration of microbiota composition, disruption of colonization resistance and pathogen overgrowth.

Table 1. Factors affecting the microbiota–pathogen competition in an inflamed intestine

Molecule	Function	Disease and host organism		Refs
Antimicrobial factors				
Mucosal epithelium				
MMP-7 (Matrilysin)	Antimicrobial peptide maturation	IBD[a], *Listeria*	Hu[b]	[72,73]
Defensin 5 and 6	Antimicrobial peptides	UC[c], CD[d]	Hu	[74]
RegIIIγ,	Antibacterial lectin	IBD, DSS colitis	Hu	[75]
Mucins (MUC-1, MUC-2, MUC-13)	Mucosal barrier	UC, CD DSS[f] colitis	Hu Mu[e]	[74,76,77]
Trefoil factor 1, 3	Mucosal barrier	UC, DSS colitis	Hu Mu	[74,77]
Lipocalin 2	Bind bacterial lipophilic ligands	UC, *Listeria*	Hu, Mu	[74,78]
Phospholipase A2	Bactericidal, increases membrane permeability	UC, CD	Hu	[74,76]
Phagocytes				
IL-8	Neutrophil chemotaxis	UC, CD	Hu	[74]
Myeloperoxidase	Neutrophil function	DSS, TNBS[g], IL-10 KO *Salmonella*	Mu Ra[h]	[79–81]
MyD88	Toll-like receptors	*Listeria*	Mu	[78]
Nitric oxide synthase 2	Nitric oxide production, antibacterial	UC, *Listeria*	Hu, Mu	[74,76,78]
Neutrophil lipocalin	Binds lipophilic ligands	UC	Hu	[74]
Lysozyme	Bacteriolytic	UC	Hu	[74]
Lymphocytes				
IgA	Binds bacterial surfaces	UC, CD	u	[74,76]
Complement system				
C3, C4B	Complement system	*Listeria*	Mu	[78]
Decay accelerating factor (DAF)	Decay accelerating factor, complement system	CD	Hu	[76]
Nutrients				
Molecule	**Components**			**Refs**
Secreted mucins	Sugars (fucose, galactose, N-acetyl glucosamine), amino acids (i.e. threonine, serine)			[82,83]
Serum, blood	Proteins, ions, heme			
Cellular debris	Lipids, sugars, proteins vitamins and nucleic acids			[65,84]

[a]Inflammatory bowel disease
[b]Human
[c]Ulcerative colitis
[d]Crohn's disease
[e]Mouse
[f]Dextrane sulphate sodium
[g]Trinitrobenzene sulfonate
[h]Rat

Triggering inflammation shifts the nutrient availability in this ecosystem. The inflamed mucosa releases increased amounts of fluids (i.e. serum and blood), mucin, shed epithelial cells and transmigrated neutrophils (Table 1). High energy substrates such as glycoproteins are probably more abundant in the inflamed gut. The shifted nutrient range accessible for bacterial degradation will lead to overgrowth of those bacterial species growing at high rates on these substrates. Enteropathogens such as *Salmonella* spp., pathogenic *E. coli* spp., *Shigella* spp., *Citrobacter* spp. and *Vibrio cholerae* are known for their fast growth rates in rich media. Shifts in species abundance might have further effects on the intestinal trophic chain and gut ecology. Decreased abundance of key primary or secondary fermenters might further alter the substrate range, thus increasing high nutrient availability and decreasing the concentrations of growth-inhibitory fermentation products such as SCFA, or of toxic products such as bacteriocins. The improved pathogen growth in the inflamed gut might be largely attributable to improved nutrient availability.

What is the experimental evidence? Nutrient availability in the infected gut has not been analyzed quantitatively. Analysis of nutrient concentrations and their utilization by incoming pathogens and by the resident microbiota will be an important topic for future studies. Most of the available evidence comes from histopathological and *in vitro* studies (Table 1). Increased oxygen availability and the presence of additional receptors for pathogen adhesion might also enhance colonization. The increased population sizes of the γ-proteobacteria and other facultative anaerobic species (certain Lactobacillaceae) in *Salmonella*- or *Citrobacter*-infected guts [10,11] and in inflammatory bowel diseases [11–14] would be in line with this hypothesis. The γ-proteobacteria include a variety of prominent pathogenic species, including some enteropathogens (e.g. *Salmonella* spp., *Shigella* spp., *Yersinia* spp. and *E. coli* spp.) and some commensal strains ($\sim 10^4$–10^6 colony forming units per gram in the normal gut). It is conceivable that conditions prevailing in the inflamed intestine (e.g. oxygen availability) specifically foster growth of this facultative anaerobic group. Thus, inflammation might improve nutrient availability and thereby weaken colonization resistance simply by enabling fast pathogen growth.

The differential killing hypothesis

The differential susceptibility towards host defenses might provide an alternative explanation for the loss of colonization resistance in the inflamed gut. At the cellular level inflammatory responses are well understood. Immune effector cells such as macrophages, dendritic cells and neutrophils are attracted to the site of bacterial intrusion. They produce lysozyme, acidic hydrolases, nitric oxide, cationic antimicrobial peptides, iron-scavenging

lactoferrin and the respiratory burst consisting of superoxide anions, hydroxyl radicals, singlet oxygen, hydrogen peroxide and halide products. These antimicrobial molecules act inside the phagosome and are also released to take effect extracellularly. Furthermore, the intestinal mucosa expresses a diverse repertoire of α- and β-defensins. In mice, α-defensins (cryptidins) are expressed in paneth cells of the small intestine (Table 1). Beta-defensins and the cathelicidin CRAMP are also secreted by large intestinal epithelial cells. CRAMP contributes to mucosal defense against epithelial-adherent bacterial pathogens and can restrain intracellular survival – even of *S.* Typhimurium to some extent [22,23]. In the inflamed gut, the expression of many antimicrobial compounds is further increased. This holds true for several defensins [24–26] and for the antimicrobial lectin RegIIIγ[11]. Comprehensive data for the acutely infected gut are still unavailable but the antibacterial effector mechanisms upregulated in the inflamed gastrointestinal mucosa in inflammatory bowel diseases might serve as a general guide (Table 1). Based on this evidence, there are numerous antimicrobial effector mechanisms operating in parallel. It will be an important task to understand these mechanisms in more detail.

In general, antimicrobial defenses act non-specifically. However, the binding affinity of defensins and lectins towards the bacterial surface and/or their killing efficiency differs between bacterial species. In the gut lumen the microbiota are exposed to antimicrobial defenses to the same extent as the pathogen. Thus, it is conceivable that the microbiota suffers 'collateral damage'. In particular, those members of the microbiota that mediate colonization resistance might be affected whereas pathogens might resist [27]. This is in line with the presence of numerous genes enhancing antimicrobial peptide-resistance and radical detoxification in the *S.* Typhimurium genome [28–30]. Thus the differential susceptibility to killing mechanisms might explain the loss of colonization resistance in the inflamed gut.

Altered microbiota composition in inflammatory bowel disease

Altered population structures of the gut microbiota are also observed in inflammatory bowel diseases. In this case, the inflammation is triggered by exaggerated immune defenses directed against members of the commensal microbiota and not by pathogen insult. It is assumed that similar antibacterial defenses are induced as in the case of an acute enteropathogenic infection (Table 1). Interestingly, the fraction of γ-proteobacteria was increased in the microbiota of IBD patients [12–14]. Similar observations were made in IL-10 knockout mouse models of this disease [11] and in experimental infections with avirulent *Salmonella* strains [10]. This indicates a general mechanism favoring the growth and/or survival of certain γ-proteobacterial species in the inflamed gut. In the case of IBD, the inflammation seems to favor the growth of commensal γ-proteobacteria.

In conclusion, gut inflammation affects the intestinal ecosystem and shifts the population structure of the bacterial gut community. In particular, intestinal pathogens (and other γ-proteobacteria) seem to benefit from this. These observations are in line with the 'differential killing' hypothesis and with the 'food hypothesis'. It seems likely that both mechanisms contribute to the loss of colonization resistance in the inflamed gut.

Concluding remarks and future directions

Is the triggering of gut inflammation a common strategy used by enteropathogenic bacteria to invade the intestinal ecosystem? In most cases this question has not been addressed directly. However, there are multiple reports providing circumstantial evidence to support this concept: mutations attenuating mucosal inflammation often result in reduced gut colonization levels. These examples include *Salmonella* infections in the calf model [31,32], *S. flexneri* infections [33], *V. cholerae* infections [34] and *C. rodentium* infections in the mouse gut [35]. The data suggest that inflammation-inflicted alleviation of colonization resistance might represent a common strategy used by enteropathogenic bacteria to colonize a niche that is already occupied by the microbiota.

The complexity of the microbiota–pathogen–host interactions has been the prime obstacle in defining the mechanisms of colonization resistance at the molecular level. The recent technical advances in analyzing bacterial genomes, complex bacterial consortia [36–39] and intra- and interspecies metabolic networks [40–42], along with proteomics [43] and differential bacterial and host gene expression profiling, will help to tackle this problem. This will enable systems-level analyses of the three-way cross-talk between the microbiota, the host and the pathogen. It will be important to identify the regulating parameters of the functioning intestinal ecosystem and the bottlenecks restricting pathogen intrusion are also of particular interest. This information will be of great value for elucidating how pathogens benefit from the inflammatory response in the gut. Knowledge of the molecular details of this process might open new doors for novel antimicrobial therapeutics and prevention of enteric infection.

Update

It was demonstrated recently that S. Typhimurium can benefit form sugars (i.e. galactose) released as a component of the mucosal defence in the inflamed gut. Stecher B. *et al.* (2008) Motility allows S. Typhimurium to benefit from the mucosal defence. *Cellular Microbiology* (in press).

Acknowledgements

This work was funded by a grant from the Swiss National Foundation (SNF) 310000–113623/1 and a grant from the European Union 'SavinMucoPath' FP6–2004-INCO-DEV-3, both to Wolf-Dietrich Hardt.

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