6 times in the southern clade. "This difference is due primarily to the disparity in the number of new species created per progenitor that diversified," they say.

However, three of these four southern clade speciation events resulted in widespread species that now range across much of eastern North America and a species that is restricted to the Atlantic coastal plain. "The fourth event led to the splitting of a progenitor into three species that all now inhabit this same coastal plain," they say.

Importantly, the differences between the northern and southern clades suggests that local biogeography and climate change were critical for the macroevolutionary dynamics of these organisms. "Both the northern and southern clades showed a recent elevation in speciation rate and, as expected, the northern clade showed a substantially greater increase than the southern clade," the authors say.

Changing climates may be more likely to drive members of some groups with particular features extinct, simply shift the ranges of others, and spark diversification in still others, the authors say. "Focused studies comparing clades with different responses will allow us to to determine how biogeography may interact with the ecological and phenotypic properties of various clade members to determine these responses," they say. "Such studies will be invaluable as guides to conservation efforts as we try to anticipate species' response to climate change in the future."

Although for many species, climate change spells trouble, for others, local factors and evolutionary mechanisms may provide an opportunity for exploitation of a changing climatic world.

Quick guide

Intestinal microbiota

Claudia Lupp and B. Brett Finlay

Who are they? Our intestinal system harbors an enormous number of non-pathogenic bacteria, eukaryotic microorganisms, archaea, viruses and bacteriophages, comprising a community collectively referred to as the intestinal microbiota. Bacteria account for the majority of these microorganisms: their total number in the human gut is estimated at 10^{14} cells, which roughly equals the number of human cells in our body. Over 500 different bacterial species build a dynamic community consisting of both persistent and transient members. The microbial community structure is influenced by genotype, immune status, age, diet and environmental factors, and consequently varies among different people. Also, changes in nutrient availability and oxygen concentration along the gastrointestinal tract are reflected in regional differences in bacterial concentrations and community composition.

Our relationship with the entire intestinal microbiota can be described as symbiotic, with both partners benefiting. At present, however, direct evidence for the beneficial nature of only a few species within the community exists. Thus, many bacterial species may be classified as commensals, as they benefit from the nutrient-rich environment in the intestine yet their presence has no beneficial consequence to the host. The intestinal microbiota also harbors opportunistic pathogens, which have the potential to cause disease if the human host defenses are compromised.

Where do they come from? The association of bacteria with the intestinal tracts of animals is far older than human life itself, and the bacterial communities have presumably co-evolved with their animal and human hosts. Our first encounter with microorganisms occurs in the birth canal, when the colonization of the formerly sterile gastrointestinal tract is initiated by the maternal vaginal and intestinal microbiota. Interactions with humans and animals, food ingestion, and other environmental contacts define successive gastrointestinal colonization events, establishing persistent community members and periodically introducing transient bacterial species, resulting in a dynamic association throughout life.

What do they do? The intestinal microbiota, together with gut epithelial and immune cells, comprise a complex ecosystem that is important for many physiological processes. Intestinal epithelial cells with their junctional complexes, the associated apical mucus layer, and the luminal and mucosa-associated bacteria provide a selective physical barrier between the lumen and systemic sites, which allows the absorption of water, electrolytes and nutrients but discourages the translocation of harmful microbial products. Thus, treatments affecting the microbiota, as for example antibiotics, increase the chance of host colonization by infectious agents.

The intestinal microbiota improves digestion and absorption of nutrients by increasing the intestinal surface area and through fermentation of otherwise non-digestible food components, such as starch and fibre, thereby liberating additional energy for the host. The presence of bacteria in the intestine promotes the establishment of a resident population of immunocytes, keeping the intestinal epithelium in a state of 'physiological inflammation', which is required for the generation of a rapid defense response against invading pathogens. Intestinal bacteria also actively prevent infection with invading pathogens by competing for nutrients, space

and host receptors, and by secreting antimicrobial substances.

What would we do without them? Because we are constantly exposed to the environment, and thus to microorganisms, we cannot avoid bacterial colonization. Nor should we, as studies conducted in germ-free animals suggest. For example, when compared to conventionally raised rodents, their germ-free counterparts excrete more calories, require a higher energy intake to maintain their body weight, and need vitamin K and in some cases special vitamin B supplements. Germ-free mice also demonstrate morphological abnormalities of the intestine and gut motor dysfunction. Furthermore, the intestinal immune system is immature at birth and requires exposure to colonizing bacteria in order to fully develop. Germ-free animals thus display an enhanced susceptibility to enteric infections and are prone to develop allergies.

How do we tolerate them? As long as we are healthy, the intestinal immune response to bacteria or bacterial products has two principal outcomes: tolerance to the microbiota and response to pathogenic bacteria. There are many contributing factors allowing the immune system to distinguish between pathogenic and non-pathogenic bacterial stimuli to ensure the proper response. The most significant distinguishing feature is the ability of pathogenic bacteria to invade spaces that are usually devoid of bacteria, such as epithelial crypts, the epithelial surface, epithelial cells and the lamina propria.

Tolerance to the intestinal microbiota is thus maintained partially by ignorance of the host to bacterial products in the lumen. In addition, the microbiota actively places constraints on the host immune system by down-regulating inflammatory immune responses. Maintaining a fine balance between immune tolerance and response is extremely important, as hypersensitive responses to the microbiota have been implicated as the cause of inflammatory bowel disorders such as Crohn's disease and ulcerative colitis.

What if they turn against us? We normally coexist peacefully with our microbiota. However, any factor disturbing the intestinal ecosystem has the potential to lead to disease. For example antibiotic treatment, infection, surgery, chemotherapy or other medical procedures or diseases that weaken the immune system may cause the escape of opportunistic pathogens from the intestinal lumen, resulting in systemic infection. While the net metabolic activity of the microbial community in a healthy host appears to be health-promoting, individual metabolic products may be toxic and have been connected to gastrointestinal cancers. Epidemiological studies have linked an altered composition of the intestinal microbiota with the development of atopic eczema, arthritis and allergic diseases.

How can we support them? Many factors such as our diet, diseases and drug treatments can disturb the intestinal microbiota composition and thus cause disease or intestinal discomfort. To alleviate the symptoms of conditions linked to an altered microbiota, treatments are being developed with the general goal of increasing the number of beneficial bacteria at the cost of those bacteria having neutral or detrimental effects. The major approaches are: prebiotics, which are dietary supplements that are preferably metabolized by health-promoting bacteria; probiotics, which are based on direct administration of beneficial bacteria; or synbiotics, which is a combination of these.

What else do we need to learn about them? Because our intestinal microbiota is incredibly diverse and dynamic, and we each host a unique community of bacteria, it is problematic to interpret epidemiological data and thus to determine the cause–effect relationship of diseases and an altered microbiota. Additionally, most intestinal bacteria are strictly anaerobic and/or are not culturable in the laboratory, making it difficult or even impossible to access them experimentally. To overcome these constraints, gnotobiotics — the study of germ-free or ex-germ-free animals that have been colonized with a defined microbiota usually consisting of one or a few bacterial species — have been used to elucidate many molecular and physiological aspects of beneficial host-bacteria interactions.

However, questions concerning bacteria–bacteria interactions within the intestinal microbial community cannot be addressed using these techniques, and it is most likely that the impact of a community consisting of more than 500 diverse members is different from that of a single bacterial species. An alternative approach is to use culture-independent molecular methods, such as sequencing bacterial 16S rRNA genes, to define the microbial community. However, molecular information does not necessarily relate to bacterial physiology. Thus combining existing methods and developing new methods are necessary to address the many complex questions that remain to be answered concerning our microbial gut community.

Where can I find out more?

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