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a gut's tale

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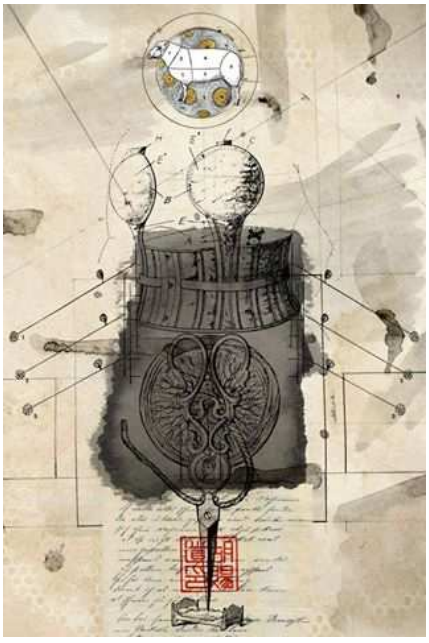
Many of our cells are not…us… Besides the cells we produce, we carry around an awful lot of bacteria. In reality, 90 percent of the cells that make us up are bacterial, that is to say about one billion billion (10^{12}). That's a lot. A large proportion of these bacteria are part of our gut, add an average of 2 kg to our adult weight and form what has been termed our gut microbiome. Why have they set up camp inside us? Because we need them… And vice versa. The human gut hosts bacteria that are able to break down all sorts of molecules we cannot. In exchange, we offer them an environment to thrive in. This mutual parasitism has evolved over time, and is a consequence of the various surroundings humans have lived in, especially the kinds of food we have eaten, and eat. Recently, scientists discovered that a group of Japanese were able to digest polysaccharides westerners are unable to. It turned out that this was most probably the result of the long Japanese tradition of eating 'nori', an edible seaweed species of the red algae, and is due to specific seaweed carbohydrate active enzymes which have become an integral part of their digestive system.



The Pain, by Alvaro Sanchez

Courtesy of the artist

Nori is the Japanese word for the species of red algae – of the genus *Porphyra* – which has been part of Japan's cuisine for centuries, even millennia. The first description of nori dates back to the eighth century when it was already being harvested and imposed on for taxation purposes. It was mentioned for the first time in a European publication in 1796 following the travels of Carl Peter Thunberg (1743-1828), a Swedish naturalist and physician. It then became popular outside of Japan in the 1960s with the macrobiotic movement, and then again in the 1970s with the advent of sushi bars and Japanese restaurants, especially in the United States. Paper techniques – such as shredding and rack-drying – are used to prepare the red algae for the traditional sushi everyone has become accustomed to.

Terrestrial plants have been part of the human diet for as long as humans have existed, yet our body is unable to produce the array of carbohydrate active enzymes – or CAZymes – it needs to breakdown plant polysaccharides and use them. Evolution solved this by introducing bacteria into the human gut, who do the job for us. Not so long ago, scientists discovered that the Japanese seem to have gone one step further because of their taste for seaweed, i.e. a marine plant. Two CAZymes – porphyranase and agarase – which, until recently, had only been found in the marine bacterium *Zobellia galactanivorans*, were also found in the Japanese gut bacterium *Bacteroides plebeius*. As a consequence, the Japanese are able to take advantage of the polysaccharides found in red algae. Something no other human population – to date – is able to do.

How did the Japanese gut bacteria acquire the capacity to synthesize these particular CAZymes? Red algae are covered with the marine bacterium *Zobellia galactanivorans*. With the Japanese taste for uncooked foods, eating sushis, for instance, is an

open invitation to any bacteria that comes with them. Over the many years that red algae bacteria and human gut bacteria have been rubbing shoulders, it is thought that a plasmid carrying the genes for the red algae porphyranases and agarases must have found its way into the *Bacteroides plebeius* gut bacteria, and became part of its genome.

The marine CAZyme porphyranase is active on the sulphated polysaccharide porphyran from marine red algae. These polysaccharides are the major matrix polysaccharides – along with agars and carrageenans – found in the cell walls of red algae, which all contain sulphate esters that are unknown in terrestrial plants. Typically, the polysaccharide slips into a positively charged, hydrophobic pocket of the porphyranase, which is critical for porphyran recognition. In the catalytic cleft, the porphyranases present a closed ring structure, the centre of which harbours the catalytic residue for porphyran cleavage. Here, the six sugar rings of the polysaccharide are bound, and split into oligosaccharides, which are then imported into the bacteria and catabolized.

Much has been said about our microbiome – i.e. the collection of bacteria we host in our gut – in the past years. A foetus has no microbiome, but rapidly collects bacteria as it begins to travel down the uterus at birth. After that, the amount and type of bacteria we host will vary with age, time and the environment we happen to be in. Given a little thought, we are, in fact, hosting a whole microsystem. We do this for our benefit but, like any microsystem, if something is altered, or goes wrong, there is a great chance that it will have an effect on its immediate surroundings. In this case, these surroundings are us, and it is argued that our microbiome could be the cause of physical and perhaps even mental drawbacks. We are all aware of our feelings being translated into stomach aches, diarrhoea and the like. But there is evidence that things may go in the other direction too; that the state of our microbiome may influence our feelings for instance… Stretch the notion a little further and, in time, the microbiome could become a way of measuring a person's health.

It all sounds very engaging but the notion must be handled with care. The microbiome involves very complex exchanges of which we know very little. What is more, it has to be taken as a community and not one single member at a time. But the connections between health and microbiome have been demonstrated and studies are ongoing to establish the diversity – and the plasticity – of the human gut. The degradation of seaweeds by intestinal microbes may have health implications. Indeed, the red algal porphyrans, for example, have been associated with a wide range of pharmacological activities: antiviral, anticancer, anti-inflammatory, anti-oxidative and anti-coagulative. These activities are dependent on the porphyran's weight and the number of sulfatations it carries – both of which are also modulated by specific CAZymes. The idea that altering our microbiome could alter our state of health is hugely intriguing and attractive, but it will take many more years to discover the many tales our guts have to tell.

Cross-references to UniProt

Beta-porphyranase B, *Bacteroides plebeius* : B5CY92
Beta-porphyranase A, *Bacteroides plebeius* : B5CY96
Beta-agarase, *Bacteroides plebeius :* B5CY73

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