Sinister blastocystis: A clandestine killer of good bacteria revealed

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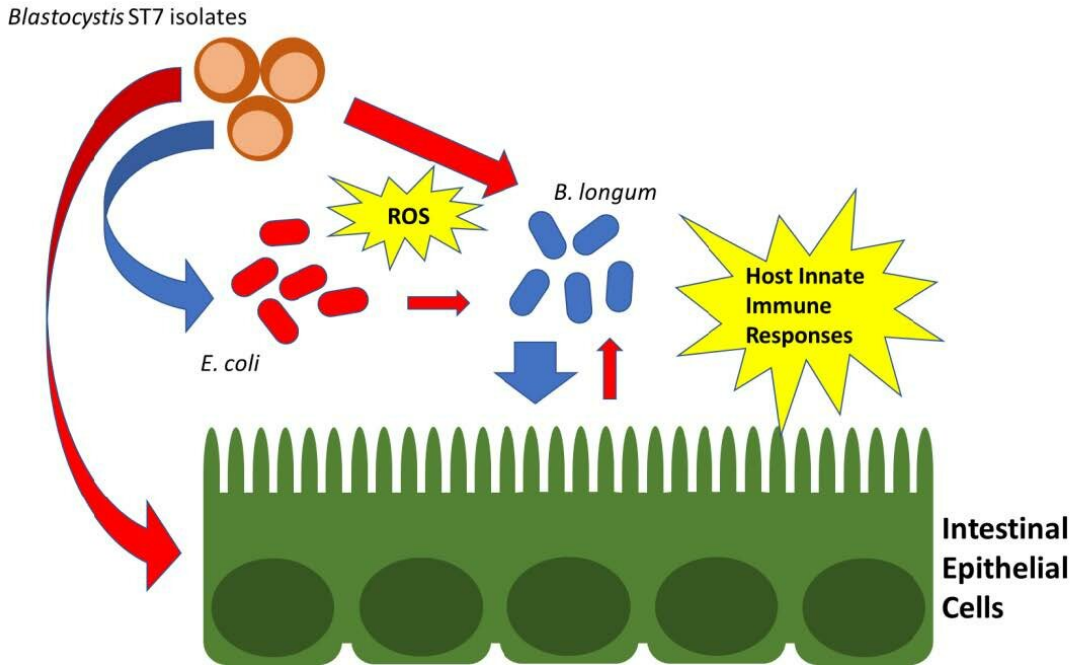

Blastocystis could disrupt gut microbiota selectively. In this study, *Blastocystis* caused reduction of *Bifidobacterium longum* but an increase in *E. coli*. This could happen by several mechanisms. There is a direct effect of *Blastocystis* through oxidative stress, limiting the viability of obligately anaerobic bacteria. Host immune responses as induced by *Blastocystis* could also limit Bifidobacterium. This bacterium is important to protect the epithelial barrier from *Blastocystis*-mediated damage. Red and blue arrows signify negative and positive interactions respectively. Credit: Dr. Kevin S.W. Tan

Since most of the microbes in our gut are bacteria, they tend to hog much of the microbiome research limelight. But lurking amongst the bacteria are other microbes such as single-cell eukaryotes (SCE) and viruses, which have been largely ignored until now. Doctors and scientists have previously regarded Blastocystis, among the most common gut SCEs, as a harmless commensal organism, peacefully co-existing with its bacterial neighbors. However, that could change with the publication of a new study from NUS Medicine in *Microbiome* demonstrating that a subtype of Blastocystis isolated from Singapore can actually harm its neighbors and its home in an insidious way.

Associate Professor Kevin Tan and Associate Professor Zhang Yongliang from the Department of Microbiology and Immunology at NUS Medicine, together with postdoctoral research associates John Yason and Chin Wen Png, report that Blastocystis subtype 7 (ST7) selectively caused the death of Bifidobacterium (one of the "good" bacteria in the body) in cell culture and in vivo.

The ST7 strain of Blastocystis appeared to induce oxidative stress mechanisms, which involve the release of reactive oxygen species (ROS). These killer molecules caused the death of the good Bifidobacterium. Interestingly, the Blastocystis ST7 organisms also reduced the population of Lactobacillus (another good bacteria) in vivo, although the mechanism of killing is still unknown.

Bifidobacterium and Lactobacillus are considered "good bacteria" because they maintain the integrity of the intestinal lining by supporting tight junctions, which act like cement between the cells that make up the lining. They are also commonly used as probiotics to promote gut health. Besides killing Bifidobacterium directly, Blastocystis ST7 can also gang up with E. coli in the gut to kill even more of these protectors. Ironically, Bifidobacterium and E. coli both help Blastocystis grow better. In other words, Bifidobacterium promotes the growth of its own killer.

To make matters worse, Blastocystis ST7 injures the gut lining directly as well as indirectly by triggering an inflammatory response (Figure), causing lesions (ulcers) and a disordered structure of the intestinal lining in vivo. Combined with the loss of the protective good bacteria, an infection with Blastocystis ST7 could be a recipe for long-term damage to the gut lining, possibly contributing to inflammatory bowel disease, irritable bowel syndrome, as well as gastrointestinal and colon cancers.

Previous studies did not consider this Blastocystis subtype. Some subtypes are likely to be harmless, but this study shows that ST7 is unique. Not only does ST7 have harmful effects, it is also resistant to metronidazole, the typical treatment for Blastocystis. Like other Blastocystis subtypes, ST7 is transmitted through eating food that has been contaminated with feces from infected animals, especially birds. Although ST7 has been reported mainly in Singapore, it has also been described in Japan and at least one Danish study. Thus, this pathogenic Blastocystis subtype could be found in other ethnicities and geographic locations as it becomes more widely studied.

Assoc Prof Tan is already developing tools to study the mechanisms by which Blastocystis cause disease in greater depth. He and his team have established a genetic modification system for Blastocystis, whereby foreign genes can be introduced into and expressed in Blastocystis and the effects of these changes can be studied. They hope to use this system to illuminate how Blastocystis interacts with its host to cause disease and to explore ways to combat the microbe.

Associate Professor Tan says, "This is the first detailed study to show a causal link between Blastocystis, a common single cell eukaryote of the human gut, and the host microbiota. We reveal how it reduces the numbers of beneficial bacteria, which may in turn lead to an unbalanced gut microbiome and poorer gut health."

The detrimental effects of Blastocystis on Bifidobacterium and Lactobacillus could facilitate the development of inflammatory bowel disease and irritable bowel syndrome, in which the good bacteria play a protective role. Based on these results, clinicians could also consider whether to exclude fecal transplants that contain specific subtypes of Blastocystis during fecal microbiota transplantation.

More information: Yason JA, Liang YR, P'ng CW, Zhang Y, Tan KSW. Interactions between a pathogenic Blastocystis subtype and gut microbiota: in vitro and in vivo studies. *Microbiome* 2019.

Li FJ, Tsaousis AD, Purton T, Chow VTK, He CY, Tan KSW. Successful genetic transfection of the colonic protistan parasite Blastocystis for reliable expression of ectopic genes. *Sci. Rep.* 2019;9:3159.

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