

PRESS RELEASE

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Not mere gut feeling: *Blastocystis* unmasked as clandestine killer of good bacteria

Singapore, 14 March 2019 – 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. If doctors and scientists think of *Blastocystis* (one of the most common gut SCEs) at all, they often regard it as a harmless commensal organism, peacefully co-existing with its bacterial neighbours. However, that could change with the publication of a new study from NUS Medicine (online in *Microbiome* on 11 March 2019), which shows that a subtype of *Blastocystis* isolated from the stools of a hospital patient with gastrointestinal problems in Singapore can actually harm its neighbours and its home in an insidious way.

In fact, Associate Professor Kevin Tan and Associate Professor Zhang Yongliang from the Department of Microbiology and Immunology at NUS Yong Loo Lin School of Medicine (NUS Medicine), together with postdoctoral research associates John Yason and Chin Wen Png, demonstrated 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 *Bifidobacteria*. 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. The researchers also found that 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, causing lesions (ulcers) and a disordered structure of the intestinal lining in vivo. Add to this 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.

Part of the reason for the unclear role of *Blastocystis* in disease is that previous studies did not consider the *Blastocystis* subtype that was being investigated. Some subtypes are likely to be harmless, but this study shows that ST7 is uniquely different. 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 faeces from infected animals, especially birds. Although ST7 has been reported mainly in Singapore, it has also been described in Japan and in 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* causes 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.

“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,” he said.

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, doctors may want to consider excluding faecal transplants that contain specific subtypes of *Blastocystis* during faecal microbiota transplantation.

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Our multidisciplinary and real-world approach to education, research and entrepreneurship enables us to work closely with industry, governments and academia to address crucial and complex issues relevant to Asia and the world. Researchers in our faculties, 29 university-level research institutes, research centres of excellence and corporate labs focus on themes that include energy, environmental and urban sustainability; treatment and prevention of diseases common among Asians; active ageing; advanced materials; as well as risk management and resilience of financial systems. Our latest research focus is on the use of data science, operations research and cybersecurity to support Singapore's Smart Nation initiative.

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It admits 300 students to the MBBS degree programme annually and its principal missions are to educate and train the next generation of healthcare professionals, and foster research that will help to advance the practice of medicine.

The 18 NUS Medicine departments in the basic sciences and clinical specialties work closely with the Centre for Medical Education, the Centre for Biomedical Ethics, the Centre for Healthcare Simulation as well as the restructured public hospitals to ensure that teaching and research are aligned and relevant to Singapore's healthcare needs. The School is a founding institutional member of the National University Health System.

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