

Study sheds light on antibiotics-associated diarrhea

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SMART AMR researchers Xiaoqiong Gu (right) and Wei Lin Lee (left) set up assays for measuring the levels of gut bacteria Ruminococcaceae in a stool sample. Credit: Singapore-MIT Alliance for Research and Technology (SMART).

A joint study by the Singapore General Hospital (SGH) and Singapore-

MIT Alliance for Research and Technology (SMART), MIT's research enterprise in Singapore, may have found the reason why some patients experience diarrhea after taking the antibiotic, amoxicillin-clavulanate, commonly known as Augmentin. It is a widely prescribed antibiotic used to treat many infections including pneumonia and urinary tract infections.

The team of researchers found that the level of gut Ruminococcaceae, a family of bacteria that plays an important role in maintaining an individual's gut health, strongly impacts diarrheal outcomes following [antibiotic treatment](#).

"The problem is very real for patients who are unable to take amoxicillin-clavulanate because it gives them [diarrhea](#), even though it is an effective and affordable antibiotic for their infection. Knowing why may help us identify those at risk of antibiotic-associated diarrhea, and devise treatment strategies in the future to minimize or avoid such adverse effects," said Dr. Shirin Kalimuddin, Consultant, Department of Infectious Diseases, SGH, and Principal Investigator of the study.

A total of 30 healthy volunteers were recruited for the study. They each received a three-day oral course of amoxicillin-clavulanate. Their [stool samples](#) were collected on stipulated days over a period of four weeks and analyzed using gene sequencing to look for changes in the [gut microbiome](#) during the study period.

Results showed that Ruminococcaceae levels in the stools of study volunteers who developed diarrhea were significantly lower when compared to those who did not, both before and during treatment with amoxicillin-clavulanate. This suggests that individuals may, depending on their gut composition, be predisposed to antibiotic-associated diarrhea. The team further devised a simple polymerase chain reaction (PCR) test based on levels of *Faecalibacterium prausnitzii*, a species

within the Ruminococcaceae family, that could potentially be used in [clinical settings](#) to quickly determine an individual's risk of developing diarrhea with amoxicillin-clavulanate treatment.

"People respond differently to medication. Understanding this response and the ability to predict those at risk will help guide the development of point-of-care diagnostics," said Professor Eric J. Alm, Professor of Biological Engineering at MIT, Principal Investigator at SMART Antimicrobial Resistance (AMR) interdisciplinary research group, and co-corresponding author of the study.

"While a lot of attention has been paid to how DNA influences a person's response to medication, the impact of the gut microbiome on the human drug response has not been widely researched. Our findings provide evidence that an individual's gut microbial composition can influence the risk of developing [antibiotics](#)-associated diarrhea. Tested against amoxicillin-clavulanate, the study provides a framework to identify other potential causes of antibiotic-associated diarrhea in relation to other classes of antibiotics," added Professor Alm.

Globally, one in three patients prescribed amoxicillin-clavulanate will develop diarrhea. In some cases, their diarrhea may be so severe that doctors have to stop the antibiotic prematurely, resulting in inadequate treatment of the infection, or the need to switch to another antibiotic that may be more costly or can only be given intravenously. The diarrhea could also prolong patients' hospital stays, leading to an increased risk of other infections as a result.

Building upon what is now known, the team now hopes to conduct a clinical trial to see if certain species of bacteria within the Ruminococcaceae family could be used as a probiotic to prevent diarrhea in patients receiving antibiotics.

The study findings were published in the peer-reviewed scientific journal *iScience* in January 2022.

More information: Xiaoqiong Gu et al, Gut Ruminococcaceae levels at baseline correlate with risk of antibiotic-associated diarrhea, *iScience* (2021). [DOI: 10.1016/j.isci.2021.103644](https://doi.org/10.1016/j.isci.2021.103644)

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