**Dr. Guandalini Discusses His Other Expertise:**
**PROBIOTICS AND HOW THEY RELATE TO CELIAC DISEASE**

A little over a year ago, Dr. Stefano Guandalini sat down with The University of Chicago Medicine’s *Science Life* to discuss probiotics. This is an updated version of that interview:

Walk past the dairy case or health food section of any grocery store and you’ll see a variety of yogurts, milk, shakes and even granola bars that say they contain probiotics. These “good” bacteria are added to foods to promote a healthy environment of microorganisms in the digestive tract, supposedly to aid in digestion and promote good gastrointestinal health. Are these claims based in real science, or are they just another food fad to squeeze money out of consumers?

We spoke to Stefano Guandalini, MD, Founder and Medical Director of the Celiac Disease Center at the University of Chicago and Section Chief of Pediatric Gastroenterology, Hepatology, and Nutrition about probiotics and prebiotics, the precursor that provides fuel for the supposedly beneficial bacteria. He and his colleagues published a review paper recently looking at various studies and clinical trials that used pre- and probiotics to treat symptoms of inflammatory bowel disease (IBD) and irritable bowel syndrome (IBS) in children.

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**Q / HOW ARE PROBIOTICS DIFFERENT FROM PREBIOTICS?**

Prebiotics are basically the metabolic fuel for probiotics. It’s a term that encompasses a number of mostly carbohydrates that are present in vegetables and grains, for instance in wheat, artichokes, legumes, etc. They are only partially digested by the human intestinal tract, so they reach the colon where they are fermented by bacteria. We have trillions of bacteria happily living in our colon, and they ferment these substrates. They’re happy with them, and so they thrive. The idea of taking prebiotics is that you can encourage the growth of good bacteria in the gut by providing them the food they like. If your diet is rich in things like onions, garlic, wheat, legumes and artichokes, then you ingest a lot of prebiotics already. But there are also chemically identifiable supplements that also serve the same purpose.

Probiotics are microorganisms that, if ingested in adequate amounts, confer a health benefit to the host beyond the nutritional value. In practical terms, it’s a class of mostly live bacteria that have been studied for a long time and been found useful for treating or preventing a number of clinical conditions.

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**Q / HOW EFFECTIVE ARE PREBIOTICS AND PROBIOTICS?**

In theory [prebiotics] are a good way of promoting a healthy microflora in your gut, and one would expect beneficial effects, but in reality it has been quite disappointing. There’s not a lot of practical use for prebiotics as we speak, in terms of clinical effectiveness. The only niche in which we found them to be successful is as an additive to formula for premature babies, because human milk actually contains plenty of prebiotics. Other than that, there hasn’t been much practical use. In fact, our search shows that prebiotics have been tried for treating irritable bowel syndrome, but actually with mostly negative results.

On the other hand, for IBS, we have some good evidence in adults that some probiotics actually seem to be effective in relieving some of the symptoms, mostly the bloating and abdominal pain that accompanies IBS, especially when there is either diarrhea or constipation that goes along with it.

And in the case of ulcerative colitis, there is a growing body of evidence supporting the efficacy of some specific strains as an adjuvant in the course of the therapy. Crohn's disease is different, however. People have tried multiple ways of addressing the problem with different strains of probiotics, different clinical settings, different endpoints, but none of the researchers were able to show any efficacy with probiotics in Crohn’s disease patients.

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Q / YOU CAN GO INTO ANY GROCERY STORE AND FIND YOGURT AND OTHER FOODS THAT HAVE PROBIOTICS ADDED TO THEM. DO THOSE PRODUCTS DO ANY GOOD?

Not all probiotics are equal, that’s an important thing to stress. People think they can walk into a store and pick any probiotic from the shelf and they’re just the same. That is not the case. Different probiotics have different strains and concentrations of bacteria that have different properties. Only a minority of them has been tested properly in clinical trials to find if they were indeed effective.

In reality, yogurt by definition has to have two strains of bacteria—Lactobacillus bulgaricus and Streptococcus thermophilus—to create the yogurt. However, these strains do not pass the gastrointestinal tract intact. They are destroyed by the acidity of the stomach and the enzymes of the pancreas, so nothing reaches the colon and it’s not beneficial. But some yogurts are now enriched with other live bacteria of different strains. Some of them indeed include strains that survive the passage through the intestinal tract and then can potentially be beneficial, although for none we have as of today a strong evidence of clinical efficacy.

Q / IS A FOOD PRODUCT THE BEST WAY TO TREAT SYMPTOMS OF IBS OR IBD, OR DO YOU NEED A SPECIAL PREPARATION IN A PILL?

The best way is to use specific strains that have been validated through clinical trials and published in peer-reviewed journals to show efficacy, and if possible reproduced by different groups using the same preparations. So the list of probiotics that have gone through this process is actually very short:

- There is a product called Align, based on a specific Bifidobacterium, which is mostly for adults with IBS.

- For infants and colicky babies there is proof of effectiveness for a product called Biogaia, which has the bacterium Lactobacillus reuteri in it.

- Then we have Culturelle with Lactobacillus GG, another one with a long record of scientific, well conducted studies, which has been found effective in treating diarrheal diseases.

- Florastor, which contains a yeast [Saccharomyces boulardii] instead of bacteria, is also effective in treating and preventing antibiotic associated diarrhea. Children who get antibiotics often develop diarrhea, and in many cases that can be prevented by the use of Florastor.

- Finally there is a preparation called VSL #3, which is a highly concentrated preparation of 8 different strains of probiotics. This has received a great deal of attention by the scientific world to treat a number of conditions. It seems to be effective for ulcerative colitis, both in adults and children, and it has been found effective in irritable bowel syndrome as well.

Outside of this incredibly short list, however, there is really very little. This is not to say they aren’t working, it’s just to say we don’t have any solid scientific proof yet.

Q / ARE PROBIOTICS SAFE FOR CELIAC DISEASE PATIENTS?

One thing that all these probiotics have in common is that they are safe and gluten free. They are very tolerable and basically create no side effects. One caveat is for premature babies and people with profoundly depressed immune systems. Some of these preparations might be contaminated by yeasts, which can be dangerous in those cases. But with these two exceptions, probiotics have been used in large amounts for generations now. So they are safe, but if there is no clear cut indication, I wouldn’t necessarily recommend them. That’s a question I often get from patients, “Could we use probiotics?” And if it’s not to treat a specific condition and they just think it will improve health, I tell them it’s not necessary.

Q / WHERE IS THE RESEARCH ON PROBIOTICS AND PROBIOTICS HEADED?

It’s interesting. There was a boom for years and then it died down quite a bit. From a laboratory standpoint, we don’t understand a lot about how the probiotics work. So the attention of scientists now is more focused on understanding the mechanisms of the interactions between these bacteria and the host, which are different between different individuals. Each one of us has a unique composition of intestinal flora. The same probiotics may have a different effect for you and me, because they interact with trillions of other bacteria, which are different for each person. So all of these nuances are going back to basic science before moving further to the clinical arena.

Q / THAT SEEMS TO BE A THEME OF MICROBIOME RESEARCH. EVERYONE AGREES ON ITS PROFOUND EFFECT ON OUR HEALTH, BUT GETTING TO WHERE YOU COULD CHANGE SOMETHING MEANINGFULLY TO TREAT A DISEASE IS A DIFFERENT THING. TRUE?

Right, we are not there yet. It’s very complicated. As we have said, the genome of the microbes is much more complex than the human genome. When we are talking about personalized medicine, we are really talking about the microbiome: how to understand all the subtle interactions with the human host, and how to possibly exploit this for health reasons.

In fact, it is indeed in celiac disease that the possible use of probiotics has an area of great potential: babies born in family where there is already celiac disease and who have the “right” genes to develop it, may or may not end up developing celiac disease in large part due to how their microbiota is composed! As you can see, possessing the “good” microbiota helps preventing celiac, while having an “unfavorable” microbiota may be favoring its development.

Once we will have a fuller understanding of this situation, then we would be able to identify which probiotics could be used for which baby in order to help preventing completely the development of this condition: a very exciting proposition! We aren’t there yet, but we will get there. I have great enthusiasm in this. I think this is the medicine of the future.
DIETITIAN’S CORNER

With this issue we introduce a new feature, called Dietitian’s Corner. Our registered dietitian and expert on the gluten-free diet, Lori Welstead, has answered hundreds of questions from our readers over the years. In this feature, Lori will answer specific and timely questions about the gluten-free diet. But in this debut installment, Lori would like to share her recent and unexpected story of her diagnosis.

Lori, who presented a session on “Pitfalls of the Gluten-Free Diet” at our 2015 Celiac Education Day event, had not been feeling well and took the initiative to sign herself up for the free antibody screening test that October morning, in spite of the fact that she had been tested nearly two years earlier. Here is her story, in her own words:

Just 18 months ago I tested negative when my antibodies were drawn. But since that time, I had not been feeling well. During that period, I have been on three international trips (two to Italy in which I was quite sick), and have had two devastating miscarriages and a hernia surgery. It’s been a whirlwind. My symptoms included fatigue, borderline anemia, miscarriages, eczema and anxiety.

Well, on November 9th, I received a life-changing call from Dr. Guandalini. He told me my celiac serologies from our screening came back positive. I quickly scheduled an endoscopy with Dr. Kupfer, and just two weeks later got the definitive diagnosis of celiac disease. As you may imagine, the ten days between the bloodwork and the endoscopy included many questionable “last meals” and I got in my favorites before confirming I had celiac disease and would now be gluten free for life. After so many years of advising patients about the gluten-free diet and researching and writing about it, I would now be experiencing it and living with it, just as they do every day.

My husband, a chef, initially found the diagnosis too coincidental to be believed. But we have come to accept it, and have worked together to clean up our kitchen and make it entirely gluten free. We hope to someday collaborate on delicious but nutritious gluten-free food in the future, to turn this diagnosis into a positive for us both.

Indeed, this was beyond a shocker, but I know it will make me a stronger specialist in this insidious disease.

I am so thankful to everyone working with our Center, and I am gratified to be a part of it myself, where I have access to so much excellent information and am in the position to help others in my situation as well. Finally, I am happy I had the intuition to get checked in October and that we offer this important service to so many each year. I look forward to addressing the most interesting and significant questions from our readers in Dietitian’s Corner, but my tip for this issue is:

Trust your intuition and if you are experiencing symptoms, get tested!

Calendar of Upcoming Events

**February 21, 2016:** Celiac Skate, in Highland Park, IL. Visit [www.celiacskate.com](http://www.celiacskate.com) for more information.

**May 6, 2016:** Spring Flours! Tickets will go on sale on April 1. Visit [www.cureceliacdisease.org](http://www.cureceliacdisease.org) for more information.

Celiac Skate

Please note: Tickets for Celiac Skate are on sale now! Spend a wonderful afternoon skating and helping to raise awareness about celiac disease on February 21, in Highland Park, IL. For more information or to buy tickets, please visit: [www.celiacskate.com](http://www.celiacskate.com).

Proceeds benefit research at The University of Chicago Celiac Disease Center.
THE ULTIMATE FACS MACHINE

We recently sat down with Cezary Ciszewski, MS, Lab Manager for The Celiac Center’s research department, to learn more about the Fluorescence Activated Cell Sorter (FACS) machine that the Center acquired last year, thanks to the donations of three generous families. After the machine arrived, Cezary spent a week at the manufacturer’s offices in San Jose, CA, to train on it and learn how to use, troubleshoot and maintain the instrument. He trained the rest of the staff upon his return. He explained to us how the machine brings us closer to our goals of finding better treatments for celiac disease and a cure. “[The FACS machine] helps us look for new combinations of known things,” says Cezary. “For example, you can identify known markers and see how they come together in undiscovered ways.”

Different groups of scientists in the lab work on various aspects of celiac disease research. Cezary noted that the group that focuses on the mouse model can use the FACS machine for myriad applications. The machine also helps validate the mouse model to make sure the specimens are valid, by matching cell characteristics between human and animal samples.

Cezary himself is currently involved in a multi-center trial on refractory celiac disease. He receives tissue of refractory patients from the Mayo Clinic at the beginning and end of treatment and blood samples throughout, at specific intervals. He looks for cells that he would expect to be there, that are not normally found in the intestines. The scientists can test various therapies on these cells in vitro, that may eventually move forward into a clinical trial and lead to better in vivo therapies. By examining samples throughout the treatment, it also helps scientists and clinicians evaluate treatment options.

Because the FACS machine can identify 18 different molecules at one time, as opposed to the six that its predecessor could handle, it helps the scientists identify much more precisely which abnormal cells are relevant to the celiac diagnosis, and what therapies will target those cells. The machine looks at 10,000 cells per second, and gives researchers tremendous power to identify those cells, any one of which might have an impact on celiac disease. Another significant benefit of having this machine is that word has gotten around the research community, says Cezary. Researchers from different departments and labs have contacted the celiac research lab to see if they can examine specimens in the machine. This, says Cezary, “is leading to more collaboration, which is what scientific research is about.” Who knows what information and cures are yet to be discovered through this amazing gift?

ADOLESCENTS WANTED!

The University of Chicago Celiac Disease Center is currently conducting a research study for teenagers with celiac disease and their parents, to better understand the feelings and coping skills of our adolescent patients with celiac disease and how this affects their adherence to a gluten-free diet later in life. Our goal is to use this information to improve adherence to a gluten-free diet for these patients as they get older. If your child is between the ages of 12 and 18 and is a celiac patient at The University of Chicago Medicine, he or she may qualify.

Parents should contact Celiac Center Research Coordinator Diane McKiernan by phone at 773-702-3572 or by e-mail at dmckiernan@peds.bsd.uchicago.edu for more information.
PREMIERE PARTNERS

The University of Chicago Celiac Disease Center is proud to recognize its Premiere Partners, listed below. This is a highly dedicated group of companies, both large and small, that truly understands and champions the University of Chicago Celiac Disease Center and its important work.

We thank them for their generous support.

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THE CHEFS’ STATIONS ARE BACK!
Spring Flours will take place on May 6 at the Chicago Cultural Center, with approximately 20 delicious gluten-free tasting stations.

TICKETS WILL BE AVAILABLE STARTING APRIL 1.
Please check our website in the coming months for more details. www.cureceliacdisease.org

A Cure for Celiac Disease is possible ...

We are making it happen.

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