

Real-world Applications of Microbiome in Bladder Cancer. What should patients know?

Dr. Laura Bukavina, MD, MPH



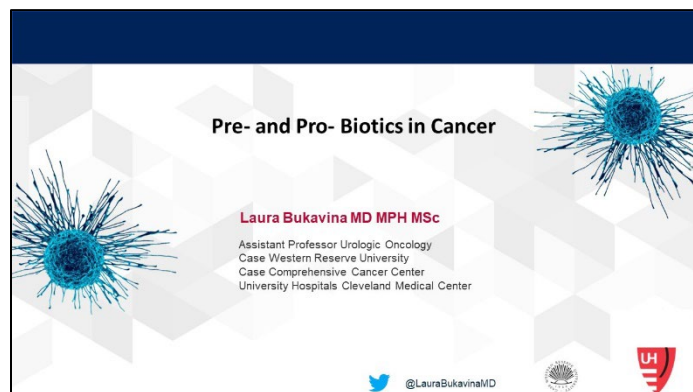
Stephanie Chisolm:

Welcome to Real World Applications of the Microbiome in Bladder Cancer. What Should Patients Know? Scientists have been looking at the relationship between the microbiome, probiotics and bladder cancer. That relationship is very complex and it's not well understood. Today's program is really intended to shed some light. It's not going to give you all the answers. It might give you some good questions to bring back to your healthcare provider, that really look at the potential impact of your gut bacteria on the tumor development and your treatment responses.

We're delighted to have urologist and scientist, Dr. Laura Bukavina from Case Western Reserve University Hospitals Cleveland Medical Center. In 2022, Dr. Bukavina received one of BCAN's Young Investigator Awards to support her research, and today she's going to explain that cutting-edge research that she did on the microbiome and it was showcased in BCAN's 2023 Bladder Cancer Think Tank.

Dr. Laura Bukavina:

Hi everyone. My name is Laura Bukavina. As Stephanie has said, I am a urologic oncologist. I do a lot of work in bladder cancer research and I'm at Case Western University Hospitals. So today's focus really is to talk a little bit about the research that we have been doing in bladder cancer, but also, I wanted to just give an overall presentation of what is microbiome. What is probiotics, prebiotics? Because I think having that level of understanding really



allows you to be able to transition to microbiome and ask the appropriate questions. So we have to start at the bottom and work our way up to what microbiome is.

So as I said, we're going to talk about the pre- and the pro- and the syn- and the post-biotics, which are a lot of confusing language, and I think everyone who looks at this is really confused. I know even a couple of years ago when I was looking into it, this was a very confusing topic overall.

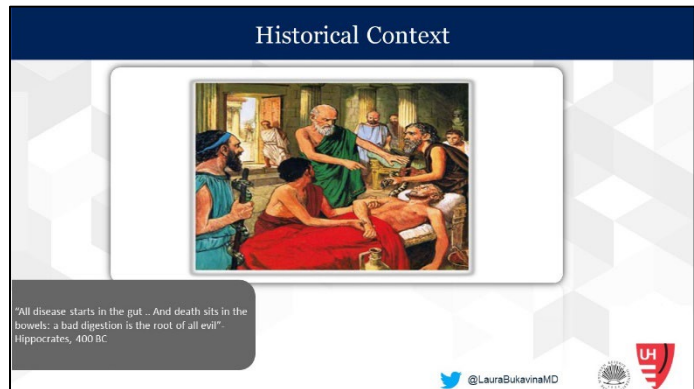
Dr. Laura Bukavina:

So there are no disclosures that are relevant to this presentation. As Stephanie has said, a lot of the research that I have presented is supported by BCAN Young Investigator.



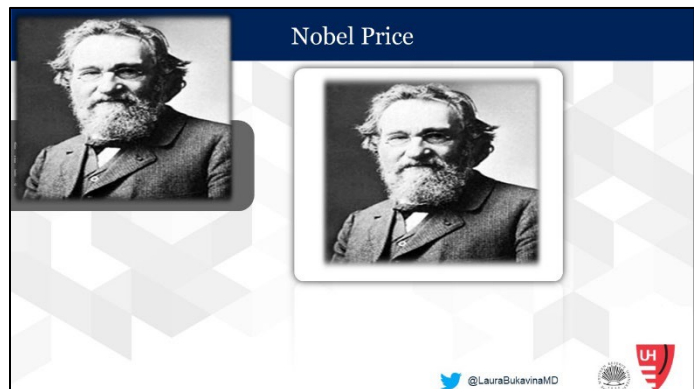
Dr. Laura Bukavina:

So in terms of historical context, the concept of probiotics and prebiotics really started a long time ago. As Hippocrates was a huge proponent of probiotics, he said on multiple occasions that, "All disease starts in the gut." That's one of his quotes, and, "Death sits in the bowels and bad digestion is the root of all evil." So clearly he was a fan of microbiome and probiotics even before the term was coined.



Dr. Laura Bukavina:

And really not until about late 1800s, 1900 was the father of modern immunology, Ellie Metchnikoff coined that term of probiotics. He is considered to be the father of immunology and he's the one that started looking at the relationship between the gut and how your immune system develops.



Dr. Laura Bukavina:

So what are prebiotics and probiotics? The simplest way to explain it is prebiotics are not alive. Those are the potential things that bacteria might digest, that help certain types of bacteria grow. Now, probiotics really do mean that it is a live organism. Typically, they're considered to be the good type of organisms within your gut that have a host bug positive relationship.

What are prebiotics and probiotics?

Prebiotics

- Apple
- Artichoke
- Banana
- Onion
- Tomato

Probiotics

- Yogurt
- Miso
- Kimchi
- Pickles
- Tempeh

PrObiotics are live microorganisms
PrEbiotics are types of fiber that feed the "good" bacteria in the gut

@LauraBukavinaMD

Dr. Laura Bukavina:

Everything in-between is highlighted here. So the synbiotics are the combination of the bacteria as well as the food for the bacteria that sometimes you see manufactured and marketed. And then the postbiotics, which are in that purple right here are the byproducts of bacteria. For example, vitamin K, which is produced by bacteria, is one of the postbiotics. So this is just a wording game. A lot of the research has been focused on the probiotics, which means live bacteria. But the Nalo research really recognizes that in order for us to really move forward with microbiome, we have to almost focus on the pre and the probiotics together.

What are prebiotics and probiotics?

Prebiotics

- Plant-based prebiotics
- Non-fermentable prebiotics
- Plant-based prebiotics
- Plant-based prebiotics
- Plant-based prebiotics
- Plant-based prebiotics
- Plant-based prebiotics
- Plant-based prebiotics
- Plant-based prebiotics
- Plant-based prebiotics

Probiotics

- Fermented foods
- Fermented foods
- Fermented foods
- Fermented foods
- Fermented foods
- Fermented foods
- Fermented foods
- Fermented foods
- Fermented foods
- Fermented foods

Synbiotics

- Plant-based prebiotics + Fermented foods
- Plant-based prebiotics + Fermented foods
- Plant-based prebiotics + Fermented foods
- Plant-based prebiotics + Fermented foods
- Plant-based prebiotics + Fermented foods
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PrObiotics are live microorganisms
PrEbiotics are types of fiber that feed the "good" bacteria in the gut

@LauraBukavinaMD

Dr. Laura Bukavina:

So prebiotics, short version is anything that is resistant to digestion. So I think the most commonly way we think about it is fiber. Some fiber is digested, some fiber is not digested. However, the things that are not digested by us, by our own enzyme will be tolerated and digested by bacteria. The most commonly are what called inulin and some of the carbohydrates. Now those are used as food by the bacteria which are further broken down into other metabolites that can affect your immune system.

Prebiotic

Carbohydrates that are resistant to digestion and are instead fermented by gut microbiota in the colon; these can be both soluble and insoluble fibers in foods or supplements

Soluble prebiotic fibers form viscous gels when dissolved in water, whereas insoluble prebiotic fibers do not dissolve in or gel in water

Fiber, trans-galacto-oligosaccharide & Inulin are widely recognized

PRE-biotics (Pre-Before; Biotic-life) is a selectively fermented ingredient that allows specific changes, both in the composition and/or activity of the GI microflora that confers benefits to host well being and health - Roberfroid MD

@LauraBukavinaMD

Dr. Laura Bukavina:

Prebiotics are really in every vegetable possible. The most common vegetables that have a high concentration of prebiotics are your berries, your bananas, your green vegetables, your artichokes and onions. Now, the stimulation of the flora is thought to be accomplished by these prebiotics really being beneficial at increasing the growth of the good bacteria, which are your Lactobacillus. I'm pretty sure everyone has heard of Lactobacillus species being good. Your Akkermansia, which has been shown in research in humans and in mice to be beneficial to our cancer patients. And really, it selects specific bacteria because those bacteria are able to digest these prebiotics much more efficiently.

Prebiotic

- Selective growth stimulation of beneficial bacteria in the colon
- Stimulation of beneficial flora that promotes colonization resistance
- Focused on promotion of Akkermansia spp, Propionibacterium spp, Lactobacillus spp

@LauraBukavinaMD

Dr. Laura Bukavina:

Research has shown that these prebiotics, which is a healthy diet, a combination of high fiber diet and not digestible carbohydrates, not only decrease the risk of multiple cancers, bladder, melanoma, colon, pancreas, I think, but also other diseases including inflammatory bowel disease and Parkinson's disease. And then if you look at overall infection complication, children who have a high prebiotic diet have less need for antibiotics and have decreased number of total infections in their lifetime. So if you look at many of these studies in history that looked at having a good diet, balanced diet, high in vegetable content, high fiber diet decreases the risk of colon and many of these diseases, this really pinpoints to the fact that many of these are because of the prebiotic potential to increase the growth of these good bacteria.

Prebiotic

- Decrease in cancer risk including colon, pancreas, melanoma, and bladder*
- Decrease in inflammatory bowel disease
- Decrease in number of infectious episodes needing antibiotics and total number of infections in children and adults

@LauraBukavinaMD

Dr. Laura Bukavina:

Now, I wanted to dig a little bit deeper into what actually is happening within the science on the prebiotic research base. So right now as we look, there's over 265 trials that are looking at prebiotics, probiotics, or combination of two within multiple disease states. Many of them are in cancer. The limitation of a prebiotic is that you can only eat so many leafy green vegetables and so many vegetables overall to be able to reach that five-gram recommendation of a prebiotic.

Prebiotic

- There are over 265* registered trials on use of prebiotics alone or with combination across all disease states
- Limitation of natural occurring vs isolated
- dietary fiber modulation could enhance therapeutic response to ICB in preclinical melanoma model
- Mice receiving a fiber-rich diet demonstrated delayed tumor outgrowth compared with mice who received a fiber-poor diet when treated with anti-PD-1

@LauraBukavinaMD

Now, dietary fiber modification, meaning that if patients or mice are given fiber in a clinical trial have been shown to correlate to response not only with development of cancer but also because it increases your response to many, many immunotherapy types. And this is one of the study that I highlighted here in melanoma. And melanoma really has been the poster child for a lot of these studies because it's such a high morbidity disease, but also some patients have an amazing response to immunotherapy.

Now, what Dr. Vargo's team looked at is that they noticed that mice who received a fiber rich diet in combination with probiotics, so in addition to giving supplements of healthy microbiome, really had almost an exaggerated response to immunotherapy, in compared to those mice who had a fiber poor diet. And what they're doing now is they're actually translating these findings to humans, to patients who are receiving immunotherapy within the clinical trial.

So I wanted to highlight this because I wanted to make sure that patients and overall public understands that microbiome modulation or supplementation with prebiotics and probiotics is never a single therapy. It is never meant to be a therapy taken alone. It is a therapy meant to be taken in combination with what we consider to be standard of care because it's never going to be curative. However, it increases the efficacy of current therapy and it decreases the number of side effects associated with that therapy.

Dr. Laura Bukavina:

So this is a trial that I was talking about in melanoma and prebiotic, and really, they're currently recruiting many patients and some of the early results they presented that I was able to see had incredible response to immunotherapy while patients were taking fiber supplementation. However, the limitation is that as soon as the patient are off the trial, the fiber intake drops dramatically and back to baseline. So it's a catch 22. We know that this helps. There is a high fiber intake to better immune response. However, it's very difficult for patients, really for anyone to have such level of dedication and to continue that high fiber intake throughout their daily life.

A slide titled "Prebiotic" with a blue header. The main content is a white box with a grey border containing the following text: "RECRUITING", "Effect of Diet on the Immune System in Patients With Stage III-IV Melanoma Receiving Immunotherapy, DIET Study (DIET)", "ClinicalTrials.gov ID: NCT04640950", "Sponsor: UH, Anderson Cancer Center", "Microbiome provided by: UH, Anderson Cancer Center (Sheepskin Park)", and "Last Update Posted: 2022-04-06". Below this box is a list of bullet points: "Early results are promising", "Limited Fiber intake adverse events", and "Inability for patients to continue with high fiber diet after trial". The slide also features a Twitter handle "@LauraBukavinaMD", a logo for the University of Houston, and a small number "11" in the bottom right corner.

Dr. Laura Bukavina:

So what do we know about prebiotics and bladder cancer? We really don't. So prebiotics research and bladder cancer is non-existent. There is some research that I'll share with you that we have done on probiotics. However, prebiotics has not been explored and really should be the target of more research within bladder cancer in combination with probiotics.

A slide titled "Prebiotic and Bladder Cancer" with a blue header. The main content is a white box with a grey border containing a cartoon stick figure with a question mark above its head, pointing towards the right. The slide also features a Twitter handle "@LauraBukavinaMD", a logo for the University of Houston, and a small number "12" in the bottom right corner.

Dr. Laura Bukavina:

As I said, prebiotics dose recommended by the Gastrointestinal Society is five grams. So just to highlight how varying amounts of this probiotic is actually listed within the supplements that we currently get, this is an example of a very popular pre and probiotic supplement on the market. And you can see here that's highlighted by an arrow, the recommendation is five grams versus the actual content within that one capsule is 362 milligrams. That's less than one-tenth of the recommended dose. So for one to be able to even obtain the necessary prebiotic fiber that's recommended, you have to take 10 of these capsules, which you understand that's highly unrealistic.



Dr. Laura Bukavina:

This is other examples. This one's even worse. It's a 100 milligrams and you can see this one, the prebiotic fiber is 377 milligrams. So for anyone going to the store and considering buying any probiotic or prebiotic supplementation, I wanted to highlight a couple of the things that everyone should look out for because a lot of this is unregulated and really heavily marketed towards people without really any justification for what the guidelines recommend. So one of the things you should definitely look at when you look at probiotic and prebiotic pills is the amount of prebiotic fiber that's within these capsules.

Prebiotic and Bladder Cancer

Supplement Facts	
Serving Size: 1 Capsule	
Amount Per Serving	
Proprietary Probiotic Blend	100 mg (100% DV)
L. plantarum (DSM 4980)	
L. casei (DSM 9842)	
L. rhamnosus (DSM 5092)	
L. reuteri (DSM 16209)	
L. acidophilus (DSM 3322)	
Fructooligosaccharide (FOS)	100 mg

*Daily value (DV) not established.

Dr. Laura Bukavina:

So I want to move on to probiotics and talk a little bit about probiotics because that's where a lot of the research is. So probiotics are live, these are live bacteria. Typically, they're the good type, the good bacteria such as Lactobacillus, they typically do not cause disease. They don't cause sepsis, they don't cause urinary tract infections. These are bacteria that are living in tune with your body and stimulate your immune response. And they're almost always capable of exerting some sort of beneficial effect on the host.

Probiotics

Probiotic microorganisms are:

- Able to survive the passage through the digestive system
- Able to attach to the intestinal epithelia and colonize
- Able to Maintain good viability
- Able to utilize the nutrients and substrates in a normal diet
- Non-pathogenic and non-toxic
- Capable of exerting a beneficial effect on the host

Probiotics are live microorganisms

Dr. Laura Bukavina:

These are some of the commonly listed probiotics. Lactobacillus species really dominates this field as well as Bifidobacterium, which has been known to be prevalent in children who are breastfed and have multiple immunomodulatory, meaning stimulating the immune response, but also got protective effects.

Probiotics

Lactic acid bacteria (LAB) and Bifidobacteria spp are the most common types of microbes used as probiotics; but certain yeasts and bacilli may also be used

- Lactobacillus acidophilus
- Lactobacillus rhamnosus
- Lactobacillus paracasei
- Lactobacillus plantarum
- Lactobacillus bulgaricus
- Bifidobacterium infantis
- Bifidobacterium longum
- Bifidobacterium breve
- Streptococcus Thermophilus

Product images: Culturelle, NOW Probiotic-40, align Probiotic.

@LauraBukavinaMD

Dr. Laura Bukavina:

And I wanted to throw this out there, and this is really just an association, but I thought this was an interesting finding when I heard is that we hear of colon cancer fairly often in terms of the incidents and the prevalence. However, if you look at the diversity of bacteria from small bowel to large bowel, which is your colon, the microbial density within the large intestine is about 12 times higher than that of the small intestine. However, if you look at the cancer prevalence, the cancer prevalence within small intestine is almost 12 to 15 times decrease compared to colon cancer. And that really is thought to be secondary to multiple bacteria that is within the colon in addition to other factors. And also the metabolites that are produced by this high burden of bacteria.

Probiotics: Food for Thought

Intestine is composed of over 1000 different bacterial species and the microbial population is heterogeneous in nature

The microbial density within large intestine is 12-fold beyond that in the small intestine

So there is an estimated 12-fold increase in cancer risk in the large intestine compared with the small intestine

Diagram of the digestive tract showing higher bacterial density in the large intestine.

@LauraBukavinaMD

Dr. Laura Bukavina:

And how do the bacteria really cause cancer? In addition to the immune stimulation, the bacteria do. They also have the ability to produce multiple byproducts. So those prebiotics, they're not digested, can sometimes be digested by the bad bacteria, by these enzymes that it can later produce these toxic metabolites that cause then immune dysfunction. It can cause genetic mutations and it can cause cancer down the line.

Probiotics: Food for Thought

Microflora resident in colonic region are able to convert harmless compounds into metabolites that causes inflammation or tumorigenesis

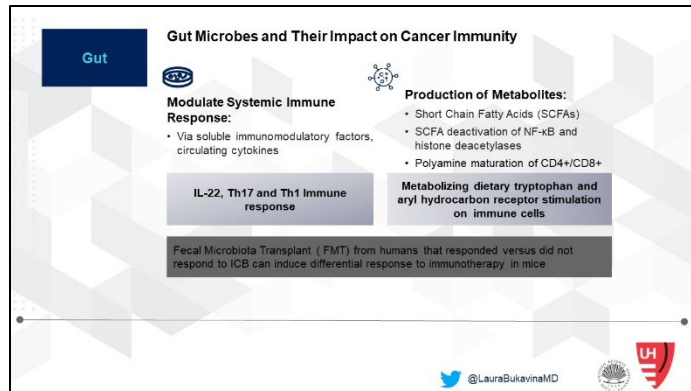
Microflora in intestinal region can contribute to carcinogenesis by producing enzymes like β -glucosidase, β -glucuronidase, nitroreductase and azoreductase

Diagram of the digestive tract showing bacterial activity in the large intestine.

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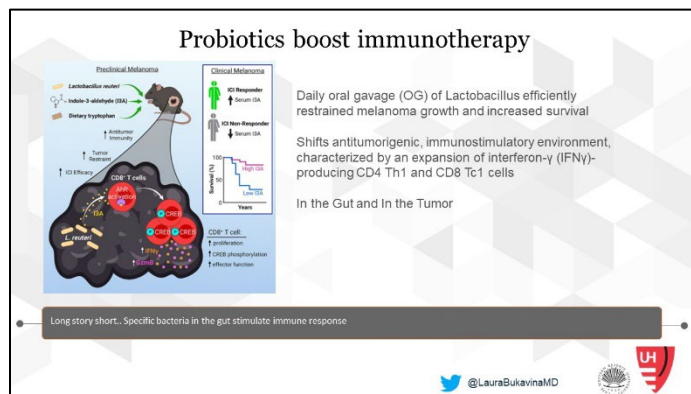
Dr. Laura Bukavina:

This is some of the things that I talked about within bladder cancer, additional ways that your gut microbes can impact cancer immunity. Not only can they... As I talked about enzymes, can they really produce those metabolites, but also these microbes can also produce short-chain fatty acids. So short-chain fatty acids, depending on the fatty acid can actually be protective against cancer development.



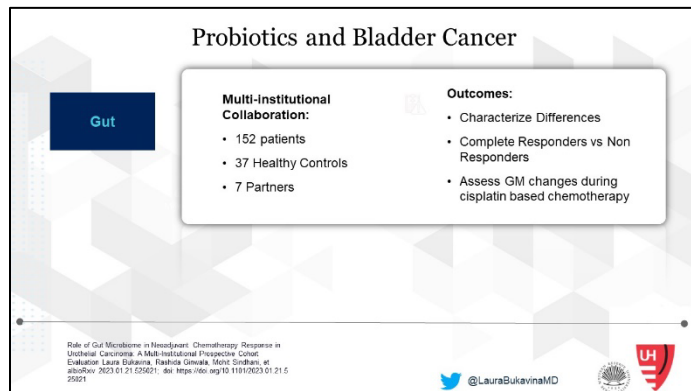
Dr. Laura Bukavina:

So I wanted to dive into a little bit into the research again within melanoma and immunotherapy. So another story is combination of prebiotics and probiotics. So when we look at just supplementing someone with, for example, Lactobacillus, without supplying the necessary digestive nutrients for that bacteria, which are your prebiotics, the effect on immunotherapy response is much lower. However, if you have a mouse with cancer and you give them prebiotics and probiotics, so combination of Lactobacillus, in addition, you can see here Indole, which is the most common prebiotic, this really shifts your immune response to cancer. In this study, you can see that the mice who had melanoma when they were supplied with both Lactobacillus, which is the probiotic and the prebiotic Indole, in combination, their survival almost doubled over their duration because of this immune response.



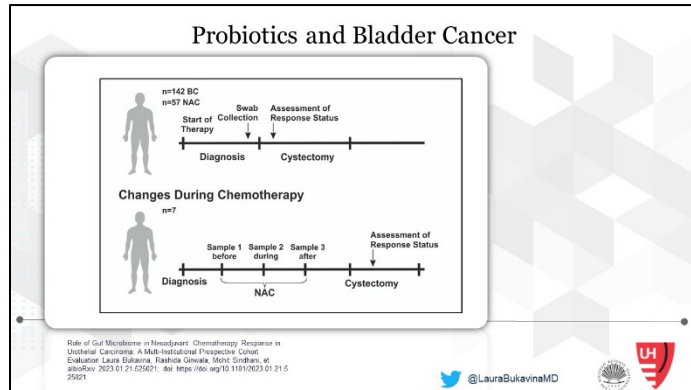
Dr. Laura Bukavina:

So we did something similar in bladder cancer by first looking at the differences in microbiome. So we wanted to see if there's specific bacteria that provide a signature for patients who respond to chemotherapy. A lot of you know that if you have muscle invasive bladder cancer, your treatment really starts with chemotherapy if you're able to receive chemotherapy followed by surgery. So we wanted to see in addition to just the tumor differences, are there differences in the gut microbiome in our patients who respond to neoadjuvant chemotherapy better than others.



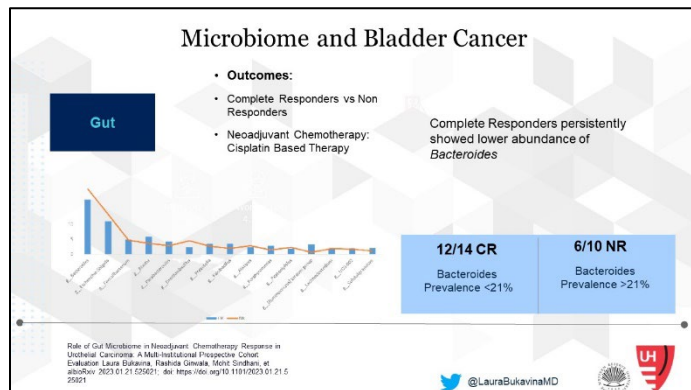
Dr. Laura Bukavina:

And what we did is we collected several stool samples and urine samples throughout the study to see if there are differences.



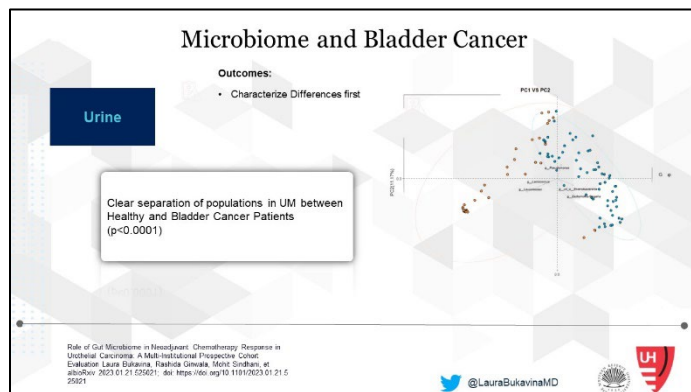
Dr. Laura Bukavina:

And we did find a difference in one bacteria that was very interesting, which is *Bacteroides*. Again, going back to melanoma. This previously has been shown in melanoma as well where patients with a high *Bacteroides* count were less likely to respond to neoadjuvant chemotherapy. In fact, the response was so strong that we found that patients who did not respond continued to have increased number of that *Bacteroides* throughout their therapy, while patients who are going to respond to chemotherapy actually had a significant decrease in that bacteria. So that was very interesting to us and that's something that we continue to explore right now with other studies.



Dr. Laura Bukavina:

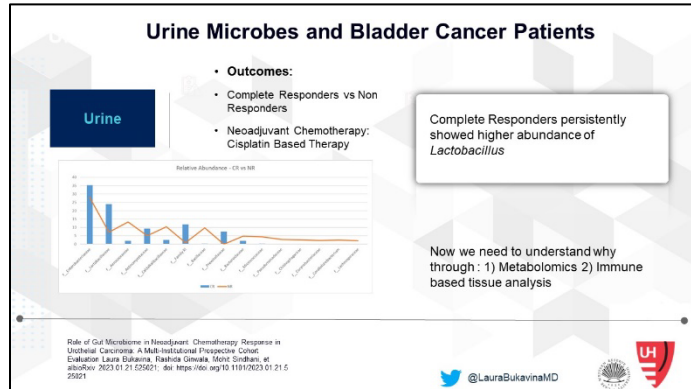
As I mentioned, we also collected urine as bladder. We have the ability to really collect the urine from these patients and we know that there's a clear difference in the composition of the bacteria in patients with bladder cancer and without bladder cancer.



Dr. Laura Bukavina:

And we continue to look at response status. Again, patients who received neoadjuvant chemotherapy and had a response, had a much, much higher Lactobacillus in their urine. And this is males and females. I think we typically think of Lactobacillus to be associated with females, with vaginal flora. But really, this was within urine and actually about 60% to 70% of our patients were male.

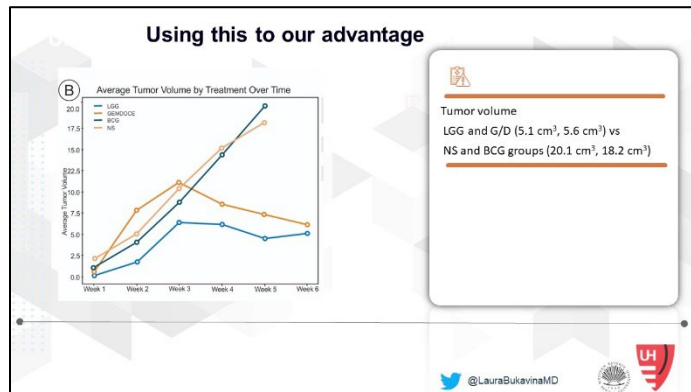
And so Lactobacillus continued to be present in urine in many, many of our responders.



Dr. Laura Bukavina:

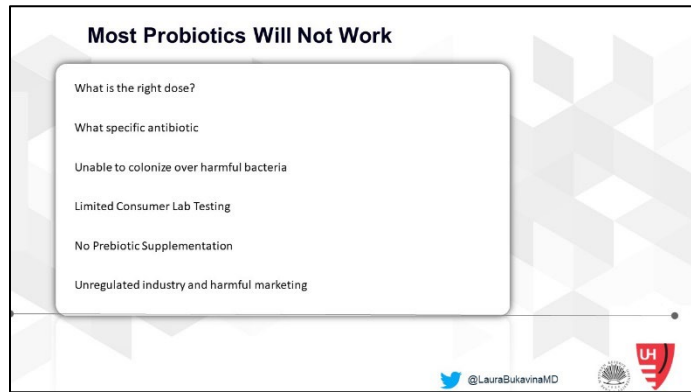
So based on this finding, we actually applied this to our mice and what we found is that supplementing mice with Lactobacillus specific species called Lactobacillus Rhamnosus, which is the LGG. Intravesically, so instilling this Lactobacillus during treatment, we were able to obtain a 50% complete response in these mice.

So just to interpret that, if you compare that to chemotherapy, just giving someone intravascular installation of LGG, meaning we put into the bladder the LGG and compared it to BCG and compared it to chemotherapy, gemcitabine docetaxel, the two best responses we've seen was actually with LGG and with chemotherapy and they were almost equivalent. BCG on the other hand did not work so well.



Dr. Laura Bukavina:

However, if you are considering going to the store and buying probiotics off the shelf, I do want to warn you that there's a lot of difficulties in finding the right probiotic and really understanding that there's a lot of nuances behind it. We really don't know what the right dose of probiotic is. We know that there is a certain amount called colony forming units that has been used previously, that we have used in our studies, which is 10 to the six.



What specific antibiotics affect what microbiome? And if you are an antibiotic at the same time as your probiotic, does that affect it? If you take probiotics right now and you are already colonized with many, many harmful bacteria, it really is very difficult to change your microbiome because there's no room for the good bacteria really to sort of colonize. So does that mean that we have to clear, sort of reset our gut before we even start to think about taking probiotics? Which is in mice studies, which is what exactly happened. You have to be able to completely clear your existing microbiome, almost like a colonoscopy prep, before you start taking probiotics.

A lot of these companies are really targeted to marketing and less so towards actual consumer testing. So their reported number on the bottle might actually be different than what is actually in the pill. A lot of them don't have the prebiotic supplementation. So taking probiotics without really providing the food necessary for these bacteria really has limited response overall. And a lot of this is just harmful marketing over promising to many of the patients because they are just aimed for their financial incentives.

Dr. Laura Bukavina:

So there are some recommendations currently out there from many of the societies in terms of what has been very rigorously tested and is currently recommended for treatment. As you can see, a lot of these recommendations are again focused on Lactobacillus. And again, this is that Lactobacillus GG, the LGG that I talked about, in addition to the Bifidobacterium. But again, many of these recommendations are within the infectious space. None of the recommendations currently exist for any of our cancer patients.

Some Recommendations

Indication	Recommended Regimen
Prophylaxis	Primary prophylaxis: VSL#3 3 g/d for 12 mo
Infectious diarrhea	Lactobacillus casei GG 6x10 ⁹ CFU twice per day for 6 d
Clostridium difficile-associated diarrhea	L. acidophilus 25x10 ⁹ CFUs for 3 d, then 25x10 ⁹ CFUs for the duration of antibiotic OR L. casei 1x10 ¹⁰ CFUs, L. bulgaris 1.8x10 ⁹ CFUs, and Streptococcus thermophilus 1.9x10 ⁹ CFUs, all starting within 48 h of antibiotic and continued for 7 d after antibiotic
Multibacter pylori infection	Prophylaxis of treatment associated diarrhea: Lactobacillus GG twice daily for the duration of treatment and for 7 d thereafter
Constipation	L. casei 200m 8.5x10 ⁹ CFUs for 4 wk, OR E. coli Nissle 1917 25x10 ⁹ CFUs for 8 wk
Irritable bowel syndrome	Bifidobacterium infantis 35624 1x10 ¹⁰ CFUs for 4 wk OR B. bifidum MM02 75 1x10 ⁹ CFUs for 4 wk
Neutropenic enterocolopathy	No recommended regimen
Crohn's disease	No recommended regimen
Ulcerative colitis	E. coli Nissle 1917 200 mg/d for maintenance of remission

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Dr. Laura Bukavina:

So just as we did with prebiotics, I wanted to take some of the most commonly used probiotics out there and look at the composition. As I said, CFU, which stands for Colony Forming Units, is typically how we look at the content of bacteria per milliliter. So if you think of BCG as bacteria, the typical amount of BCG per milliliter is 10 to the six, and that's the minimal amount that has been shown to be effective. Now, some of these probiotics have 50 billion CFUs and some of them have 50 billion and some of them have 10 to the two CFUs. So it's very important to look at the CFU content in the back.

Lets Look Again

SUPPLEMENT FACTS

Gut Health Probiotic Blend 400 mg 50 Billion CFU (minimum 100 billion per serving)

Contains: Lactobacillus acidophilus, Lactobacillus casei, Lactobacillus rhamnosus, Bifidobacterium infantis, Bifidobacterium bifidum, Lactobacillus bulgaricus, Streptococcus thermophilus, Lactobacillus reuteri, Lactobacillus fermentum, Lactobacillus plantarum, Lactobacillus gasseri, Lactobacillus helveticus, Lactobacillus delbrueckii subsp. bulgaricus, Lactobacillus acidophilus, Lactobacillus casei, Lactobacillus rhamnosus, Bifidobacterium infantis, Bifidobacterium bifidum, Lactobacillus bulgaricus, Streptococcus thermophilus, Lactobacillus reuteri, Lactobacillus fermentum, Lactobacillus plantarum, Lactobacillus gasseri, Lactobacillus helveticus, Lactobacillus delbrueckii subsp. bulgaricus.

Supplement Facts

Serving Size: 1 Capsule Servings per container: 30

Amount Per Serving	% Daily Value*
Probiotic Blend	100 mg
Total Cultures	15 billion CFU*

Other Ingredients: microcrystalline cellulose, capsule (pregelatinized cellulose), magnesium stearate, silica. No gluten, milk derivatives, wheat, soy, or artificial colors or flavors.

Minimal recommended dose 10⁶ CFU (colony forming units)

1,000,000/ml

Some advocate up to 50 billion/ml

Unclear how many CFU of each Variety of CFU

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In addition, as you notice, a lot of these probiotics actually lump all of these cultures together and give you a lump sum. So if you see in the gut health probiotic blend, there's a 400 milligram probiotic blend with 50 billion CFUs. However, it's a combined CFU, so you're not really getting the information on each individual bacteria. And I've looked through about 15 of these and I really couldn't find one that actually

gives you specific number per each bacteria. And a lot of this has to do with marketing, a lot of it has to do with just not understanding the process. But if you find one that specifically lists CFU per each bacteria, would love to see it.

Dr. Laura Bukavina:

Now, this is what someone called the best probiotic out there and it's called synbiotic. So I wanted to dissect this synbiotic. It's what they consider to be the pre, pro and the post-biotic supplementation. I do like that they only list two probiotic blends, which is your Lactobacillus Rhamnosus, which is great. They also listed it as compounded. So you see that they only have 11 billion CFUs. But again, this is combined. Again, let's go look at the prebiotics. Remember we said five grams is a recommended dose. Here they have 15 milligrams is all you're getting. And then the post-biotic, which we didn't talk about much, but this Tributyrin, the post-biotic has never really been shown to really affect much of the outcomes within cancer outcomes. However, they also listed it here.

So as I finish up this talk, I really wanted to make sure that many of you understand that there are a lot of nuances to these supplements and when you consider buying any pre or probiotic supplement next, it's really important to turn the bottle and question what is in the back, what is marketing and what is real and how much of this is really going to help me?


Lets dissect further

Best overall: Ritual Synbiotic*

- Price: \$54
- Quantity: 30 capsules (30-day supply)
- Daily dose: 1 capsule
- CFU: 11 billion
- **Bacteria strains:** Lactobacillus rhamnosus, Bifidobacterium animalis

Ritual Synbiotic* contains prebiotic, probiotic, and postbiotic bacteria.

Learn about prebiotics vs. probiotics here.



What is CoreBiome?
How Many CFU of each?
15 mg of Prebiotics?

Supplement Facts


Serving Size: one (1) vegan capsule
Servings Per Container: 30

	Amount Per Serving	% DV*
Calories		
5		
Prebiotic Blend		
Lactobacillus rhamnosus (LGG) ¹	100mg	**
Bifidobacterium animalis ssp. lactis (BB-12) ²	(11 billion CFU) ³	**
PostKyrusTM		
LSM ¹ - Mucorhizella, L.1 - Eubacterium, T40 - Mucorhizella, L.12 - Mucorhizella	15mg	**
Tributyrin (as CoreBiomeSM)	300mg	**

*% Daily Value (DV) are not established.

1. An Equivocal Data under recommended storage conditions.


Other ingredients: Stearic acid, resistant outer veggie capsule (Ergonomics, gallic acid, inner veggie capsule (Ergonomics), coconut medium chain triglycerides (MCT), oil, cellulose, silica.

[@LauraBukavinaMD](#)


Dr. Laura Bukavina:

I looked at another one just to highlight, and this is number one seller on Amazon currently. I'm not sure why it's just for men. I couldn't find anything that's men specific except Selenium in this. However, again, if you look at this probiotic blend and the prebiotic. So again, they're lumping everything together and this one gives you 85 million CFUs, but there's 85 different bacteria in this. In addition, if you look at their prebiotic, which they list as a fruit and veggie blend, which it doesn't necessarily mean it's a prebiotic. There's only 207 milligrams within this supplement.

Lets dissect further




Supplement Facts

Suggested Use: Adults take 3 capsules per day. Best taken as divided servings. Can be taken with or without food. Best absorbed for digestion.

Amount Per Serving	% Daily Value*
Probiotic Blend	
Probiotic Blend	85 Billion CFU
Prebiotic Blend	207 mg
Other Ingredients	50 mg

*Percent Daily Values are based on a diet of other people's secrets.

Recommended up to 3 pills per day
Unclear individual CFU




[@LauraBukavinaMD](#)



Dr. Laura Bukavina:

So to finish off, there is a clear and well-documented role of pre and probiotics in cancer development response. It's a well-studied phenomenon in melanoma and we're starting to understand it in bladder cancer. And I really look forward to exploring LGG more in bladder cancer patients, seeing how we can use this to our advantage. The use of pre- and probiotics is always in addition to current therapy. This is not meant to be a standalone therapy.

However, it is meant to augment and increase the efficacy of the current therapy and decrease the side effects. And I think overall as society, we need to focus on more studies and really more trials within microbiome modulations and the use of prebiotics within the clinical trial setting. So we're able to do vigorous signs and really be able to provide the results for our patients. And with that, I am happy to take some of these questions.

To summarize

-  There is a CLEAR and WELL DOCUMENTED role of pre- and pro- biotics in cancer development and response
-  We need to invest in more studies within bladder cancer and microbiome modulation And use of Prebiotics
-  Use of pre- and pro-biotics in addition to current therapy



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