Dr. Lightfoot: We're really excited to lead off with this first speaker, Dr. Jeff Woods, from the University of Illinois Urbana-Champaign. Doctor Woods, please welcome.

Dr. Woods: Thank you, Tim. Howdy, Aggies.

[Audience]: Howdy.

Dr. Woods: Ready to get this party started?

[Audience]: [inaudible]. Yeah.

Dr. Woods: All right. All right. So for about 45 years now, my gut's been pretty solid. I could eat anything I wanted, drink beer in any quantities I wanted. But in the last 10 years, something's changed. Spicy barbecue, IPAs, not so much. What the heck is going on with my gut? "Why, for 10 years now, I've put up with this. I must stop gut pain from coming, but how?" How many in here have had gut pain like I have? Stomach aches, or even worse? Truth is, in industrialized nations like ours, gut problems are on the rise. Gut diseases are increasing. So really, we're not alone. What if I told you that transferring someone else's poop into your gut might solve your gut problems? Yummy. [laughter] Gross. Amazing, if it worked. What if I also told you if that poop was from somebody who exercised regularly, the benefits might be even greater. The story I want to tell you today is about the emerging power of poop. To understand the story, I need to tell you you're in a relationship. Whether you like it or not, you're in a relationship with your microbes. These are the little bacteria, viruses, and other things that live in and on you. These microbial hitchhikers are very important for your health. They have powerful effects on your health. What you do also has powerful effects on them.

Today, I want to focus on the gut. Most of the microbes in your body or on your body are in your gut. About 10 to the 12th in your colon. Huge numbers. I want to focus on the bacteria in your gut because we know the most about them. We know most about their health effects. There are about 500 to 1,000 different species of bacteria in your gut. I may have some that you have, but I may have some that are different than you, and vice versa. What I'm saying is that the community that you have is uniquely you, like your fingerprint. We need to depend on these little guys. You can see some of the beneficial things they do for us up here. For example, they help us in digestion, and they help us harvest energy from the food we eat. When we're young, they help us develop our immune systems.

A lot of things can go wrong in your gut. You can see the list here. It's endless. I'm sure you've experienced some of these things. The question is, do microbes cause these problems? And for some problems, the answer is yes. So for example, salmonella is causative related to food poisoning. But for other diseases, we don't know if the microbe causes the disease or the disease causes changes in the microbes. Dysbiosis is defined as an imbalance in the composition of our good and bad microbes associated with a disease, like inflammatory bowel disease or obesity or a condition like aging.

So who are the bad guys, and who are the good guys? Well, first, bacteria aren't inherently bad or good, right? They're just living in a very hostile environment. Believe me, your gut's a pretty hostile place. Here's some of the bad guys. Students, there's not going to be a quiz on this, so you don't have to know the names. But do remember I said salmonella's one of the bad guys. Who are some of the good guys? You may recognize a couple of these, like bifidobacteria or lactobacilli. So these are

used as probiotics. They're also found in yogurts. Problems arise when we've got more of the good guys than the bad guys. So we really want to make sure we have more good guys than bad guys.

What's the good news? The good news is, what you do can affect your microbes. There are modifiable factors, your lifestyle, that can change the microbes in and on your body. Look at this baby. The mom has an important relationship with this baby and also establishes this baby's microbiota. If the baby is formula-fed or breast-fed, that establishes the gut microbiota for this baby for quite a while in its life. There are other lifestyle factors, as you can see here, that have good or bad effects on your microbes. Diet is an especially important lifestyle factor that is particularly influential of your gut microbiota.

For this Hilliard Discussion, what about exercise? Can exercise change your gut microbiota? So what I want to do today is share with you three studies from our lab that we've done over the last five to six years. The question we're trying to answer is, can you exercise-train your microbes? One way we can answer that is to ask the question, who's there? Which bacteria are in your gut, and do they change? For you scientists out there, what we can do is isolate DNA from fecal samples, feces, sequence the bacterial 16S rRNA gene. And when we do this, the result, we call our microbiomes. So you may have heard these terms microbiome and microbiota used synonymously, but they're a little different. When we do this microbiome analysis, it tells us who's there, and it tells us relatively how many bacteria are there compared to the other bacteria. And then we can visualize the data. Let me show you.

So on this graph, each point represents a person's or an animal's individual bacterial community. So each point represents kind of like your zoo of microbes. So each dot represents your community. Dots that are closer together on the graph are more similar. Dots that are farther apart are more different. In our first study with mice, we looked at three groups of mice: sedentary mice shown in red, mice that were run on a treadmill shown in blue, and mice that were voluntary wheel-exercised shown in orange or yellow. What you can see is that they clearly differed from one another. They differed from one another, and they also differed from the sedentary group. We concluded that forced and voluntary running differentially altered the gut bacterial community structure of these animals. And we did this because they all ate the same food, so we controlled for that influence. Well, as you might suspect, mice have very different microbiotas than humans do. What about people?

Two of my doctoral students, Jacob Allen and Lucy Maling, thought this question was so important that they spent two years of their lives formulating a study they cleverly called Fit Gut. Our primary aim was to understand whether six weeks of endurance exercise could change the gut microbiomes of previously sedentary, lean, and obese adults. We used obese adults because obesity leads to dysbiosis. But also, people who are obese have gut problems at a higher incidence rate than those who are not. So we've recruited 32 sedentary, lean, and obese adults and had them exercise for six weeks at a moderate intensity, about 45 minutes a day, and we collected fecal samples before and after the exercise. Importantly, we had them eat the same foods for three days before each fecal sample. In this way, we could attribute the changes in the gut microbiome to the exercise and not to some other compounding factor, like diet.

Using the same graph as I showed you minute ago with the mice, we compared lean in red and obese people in blue, before and after exercise. So this is the graph before exercise. And you can see that the gut microbiomes of lean and obese differed significantly even before the exercise. This was not something that we found initially. Other groups had found this before. But the amazing thing was, the innovative thing

and the novel thing that we found, was that after the six weeks of endurance exercise, their gut microbiomes were no longer different. Pretty cool.

Okay. For you aspiring microbiologists there, what bacteria specifically changed? So on the left, you can see the lean, and on the obese, you can see the right. And you can see the names there. I'm not going to go through them. Again, no quiz. Those that are shown in green were elevated in response to exercise. Those shown in orange or yellow were reduced. More importantly than their names, though, is what they're doing. And we found that exercising creates bacteria that specifically produced the beneficial molecule, or a group of beneficial molecules, called short-chain fatty acids. Exercise also decreased two bacteria in the obese individuals implicated in gut disease.

So, bottom line, endurance exercise appears to increase the good and decrease the bad bacteria in our gut and perhaps correct dysbiosis in obesity. We wanted to convince ourselves this was pretty novel stuff. And so what we did is we asked our participants to stop exercising after they had already trained for six weeks. And then we took another fecal sample to see if we could make the effect appear with exercise and then disappear with return to sedentary behavior. And that's exactly what we found. The bacteria, the good guys that increased with exercise, decreased when they went back to a sedentary lifestyle and vice versa. The bad guys decreased with exercise and went back up when they returned to a sedentary lifestyle. So we can make this appear and disappear.

Another important question is, what are they doing? Because we saw that exercise increased bacteria that produce short-chain fatty acids, we wanted to measure these short-chain fatty acids, and we hypothesized that they would increase. And guess what? Looking at concentration of short-chain fatty acids in both the lean and obese adults, after exercise, there were higher levels. And after they returned to a sedentary lifestyle, those levels came down, much like is what happened with the bacteria. So the take-home message from this study that we published in Medicine Science in Sports & Exercise just this year was that six weeks of moderate endurance exercise independently affected our gut microbes. It changed who's there, and it changed what they're doing. More good short-chain fatty acids were produced. Well, because this was the first longitudinal trial that has shown this, this got a lot of interest from the lay press, including from the New York Times. In fact, Gretchen Reynolds, who was a speaker here last year, wrote an insightful article about it in January. My mom was really excited about this. It was insightful because she asked a really important question. "Is that one of the reasons that exercise is good for us?" In other words, are exercised-induced changes in our gut microbiomes responsible for the health benefits of exercise? This is a really hard question to address in people. But it's a really important question.

The tool we have as researchers seems to be inspired by the 1976 movie, The Boy in the Plastic Bubble, where John Travolta had a defect in his immune system that required him to live in a sterile environment at all times. The tool we have as researchers are called germ-free mice. Like the bubble boy, these mice live in a sterile environment. They're born and raised in a sterile environment. They lack microbiota completely. Totally sterile. And we use these special mice because we can transplant microbes into them and then determine whether or not they affect the health of the animals. And that's exactly what we did. In a paper we published this year in collaboration with the Mayo Clinic, because they had the germ-free facility where the animals were housed, we took microbiotas from sedentary and exercised animals, transplanted them into the germ-free mice, and then looked at their colon health, both in the absence and presence of a drug that caused ulcerative colitis. Importantly,

these transplanted mice did not exercise. So what we were trying to do is transplant the beneficial effects of exercise by just transplanting the microbes. Guess what we found? Amazingly, we found that these mice had overall healthier colons, as evidenced by some of the things that are up here in green: reduced colon inflammation, increased regenerative signals. If that doesn't demonstrate the power of poop, I don't know what does.

You might be wondering, are poop transplants being used right now to treat diseases? And actually, there's one instance where that is happening. Does anybody know? Clostridium difficile, C. diff. This is a very nasty infection of the colon, causes a lot of inflammation, a lot of problems. And indeed, fecal microbial transplants cure recurrent C. diff infection to the tune of about 90%, greater than 90%. Even better than antibiotics. Experimentally, fecal microbial transplants are also being used to try and treat obesity, Parkinson's disease, and many other things. Again, power of poop.

I hope you've learned today that your microbes are very important in your health. Hope you've also learned that you have some control over this. What you do affects them. Also, I hope you've learned that we can add regular endurance exercise to the list of modifiable factors that can beneficially affect your gut microbes. So we all know exercise is good for us, right? The problem that we have as researchers is we don't really know how it works. It's my gut feeling that this effect comes through your microbes, at least some of it. So in this election season, I want to kind of close on a quote. "My fellow Americans, ask not what your microbes do for you, but ask what you can do for your microbes." Thank you.

Dr. Lightfoot: Great job, Dr. Woods. Thank you.

Dr. Woods: Thank you, Tim.

Dr. Lightfoot: We have a couple questions for you that have come in.

Dr. Woods: Absolutely.

Dr. Lightfoot: So one of the questions from Faith is, would the composition of the new six-week diet while during the study have affected the results?

Dr. Woods: So we controlled for that the best we could. We had them fill out food records before they even entered the study. We kind of looked at their normal diets, and we had them eat that normal diet for three days before each fecal sample. And then we asked them not to change their diet across the six-week period, and we had recordings throughout. Other than putting them in a metabolic ward and feeding them ourselves, I think we had really good control over the diet.

Dr. Lightfoot: Excellent. We had a question from CJ, and I'm going to actually use this question to lead into a longer question. How can poop be used to treat diseases?

Dr. Woods: So as I just mentioned, fecal microbial transplants - that's the scientific name for a poop transplant - is being used for C. diff and perhaps some other diseases of the gut. But there's a lot of research going on right now with a lot of other diseases, like obesity, I mentioned. I think what happens is, as we get older, or as we have complications, we get dysbiotic, and perhaps rewriting the ship, rebooting, if you will-- I know there's some people that are actually saving their healthy poop now, frozen, so that they can put it back into them if they have problems later, so.

Dr. Lightfoot: Interesting. A little bit longer question here from Ed, from northern Ohio. Given the novelty of your topic, what's the opinion on the value of gut bacteria on diseases such as Crohn's and their fairly specific inflammatory origins?

Dr. Woods: Yeah. So I mentioned in one of the slides that we really don't know if the microbes cause the disease or the disease processes affect the microbes. And so with Crohn's and with colitis, we're at the stage now where we know that there are changes in the gut biota with these diseases. We just don't know if it's causative or not. And that--

Dr. Lightfoot: Chicken and egg syndrome.

Dr. Woods: It's the classic chicken and egg argument. Exactly.

Dr. Lightfoot: Fabulous. One last question from Rick here in the audience. Is there evidence that acute exercise affects the microbiota and the nutrient absorption? If so, how would post-exercise nutrient timing be affected?

Dr. Woods: So bacteria do proliferate fairly rapidly. And there is actually one paper that's published that looks at the effects of acute exercise. I forget the duration of the bout. But they did see some changes. Certainly with-- it probably affects more what they're doing as opposed to who's there, because it takes a while to establish a bacterial community, so a single bout of exercise may not do that. But it may affect the metabolism of the microbes in a short time frame that could have some impact on the host.

Dr. Lightfoot: Super. Thank you, Dr. Woods. Please join me in thanking Dr. Woods.

Dr. Woods: Thank you.