The gut microbiota is composed of different microorganisms that reside in our gut. They serve important functions such as educating our immune system to recognize pathogens, helping to extract energy and nutrients from foods that our bodies otherwise cannot digest, and producing substances that affect our metabolism. At the same time, certain microorganisms and/or their products can harm us and contribute to diseases such as cancer, obesity, diabetes, and even neurological disorders. As one example, colonic bacteria that possess the enzyme urease can convert urea, a waste nitrogen product made by the liver, into ammonia, which is toxic to the body (especially the nervous system) when elevated above normal levels. This leads to conditions where patients with liver diseases or defects in one of the liver enzymes that detoxifies ammonia can exhibit symptoms such as confusion, coma, or even death. Current treatments for these conditions are inadequate. Despite medications that facilitate ammonia excretion from the gut or a low-protein diet to reduce ammonia production, many patients still succumb to the neurological consequences of elevated ammonia circulating in the body.

One novel method developed by our lab to treat these conditions is to replace the normal gut microbiota containing urease with a different gut microbiota that lacks urease. We have accomplished this in mice. We first eradicated the normal gut microbiota of mice with a combination of antibiotics and laxative, then we transplanted in a new group of bacteria called Altered Schaedler Flora (ASF) with minimal urease activity. We showed that this reduced ammonia levels in the gut and protected the mice in the setting of liver injury. We are now looking to see what other effects ASF may have on the body as well as on the gut microbiota. We have previously found that compared to normal mice, mice transplanted with ASF have lower levels of amino acids in their blood. In order to determine why ASF-transplanted mice have lower levels of amino acids in their blood, we used 15N heavy isotope to track nitrogen incorporation into amino acids. We found that the ASF microbiota cannot use the nitrogen from urea to make amino acids given the lack of urease. This may partially explain why ASF-transplanted mice have lower blood levels of amino acids. Additionally, we found that even though ASF-transplanted mice have lower levels of amino acids in blood, they have higher levels of amino acids in their stool compared to control mice. This suggests that the ASF microbiota may compete against the host for amino acids from the diet.

In order to translate our findings from mice to humans, we have created a “custom-made” gut microbiota that lacks urease using bacteria from humans. We have transplanted this group of bacteria into mice and shown that it similarly leads to a long-term reduction in gut ammonia production. We will test whether this group of bacteria can also protect the mice in the setting of liver injury. Eventually, our hope is to be able to use it in patients with liver diseases. By understanding the roles of the gut microbiota both in health and disease, in the future we may be able to create different consortia of bacteria with specific properties for the prevention and/or treatment of various diseases.