Podcast Interview: Akiko Iwasaki

PNAS: I’m your host Ann Griswold, and welcome back to Science Sessions. Bacteria vastly outnumber human cells in the gut and play an important role in digestive health. But what’s less clear is whether gut bacteria can boost immunity in other parts of the body. That is the focus of research by Akiko Iwasaki, a professor of Immunobiology at Yale University. In a 2011 paper in PNAS, Iwasaki showed that commensal bacteria can evoke an immune response to influenza—not in the digestive tract where the bacteria reside, but in the mucosal surfaces of distant organs such as the lungs. Iwasaki spoke to PNAS about the importance of commensal bacteria and their role in defending the body against viruses like influenza.

Iwasaki: The commensal bacteria are an integral part of the human body, and we have coexisted for as long as there have been humans. Essentially, they perform many functions that are classically understood such as helping with digestion and generating certain key vitamins, and their metabolites are important for our function. But in addition to that, more recent work has revealed their functions in the immune system. In particular, the gut-associated immune system as well as the systemic immune response.

PNAS: Iwasaki’s group showed just how important commensal bacteria are when it comes to regulating the immune response. From the cells lining the walls of the small intestines to the gut’s immune system, everything, she says, seems to rely on signals from the body’s natural flora.

Iwasaki: What we found was that likely the gut commensal microbiota provides a key stimulus to the lung, in sort of a remote-control manner, to prepare the lung for infection by viruses such as influenza. And it seems to induce basal expression of key genes that are involved in what’s called the inflammasome pathway. So for instance when we treated mice with antibiotics, these mice now have reduced expression of these key genes in the lung, which then makes them more susceptible to influenza infection. So I think our paper was one of the first to show that in fact there is a distal relationship between organs that are not related to the gastrointestinal tract but are reaping the benefit of the bacteria in the gut, and so our data suggests there is systemic or remote control of the immune system by the commensal bacteria in the gut. If we can find the right way of triggering these responses in everybody, then we might be able to fight influenza infection better.

PNAS: I asked Iwasaki whether these findings lead to improved vaccinations or antiviral therapies.

Iwasaki: The key thing that we need to understand is what component of the bacteria is triggering this steady-state level of expression of the key genes in the lung. If we can
understand that, then we might be able to mimic that without having to alter the actual gut microbiota. For instance, what we did in our paper is that we used toll-like receptor ligands to restore immune response in mice that have been treated with antibiotics. So at least we know that those type of agents can restore immune response. But again, triggering the same set of genes that I’m talking about, the inflammasome-related genes. But that might not be great in humans because these are also quite toxic and inflammatory. So if we can understand the downstream signaling that allows expression of these genes in the lung, we might be able to actually either preventatively or therapeutically treat people against influenza infection.

**PNAS:** Should we begin taking probiotics to boost immunity?

**Iwasaki:** Altered microbiota in the gut might affect susceptibility to influenza infection, for instance, in people who are on chronic antibiotic treatment. And there’s no evidence for that in humans yet but I suspect that that might have an effect on the respiratory tract. So there’s a lot of effort, I think, by the community, to understand the benefits of the probiotics. And currently there are a lot of associated benefits to eating yogurt and taking probiotics. I suspect that not all probiotics will provide all the benefits that we’re looking for. So the key is, again, to understand the molecular pathways triggered by a certain type of bacteria that may allow protection against different kind of diseases. But I think probiotics, if we can do this in a successful manner, will help.

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