Exploring interactions between microbes and environmental exposures

By Audrey Pinto

Cutting-edge research on microbial communities in the intestine and how they may contribute to obesity and brain metastases were highlighted in a May 21 NIEHS Partnerships for Environmental Public Health webinar. Recent studies, including the National Institutes of Health Human Microbiome Project, *(http://commonfund.nih.gov/hmp/index)* indicate that the microbiome, or all the microorganisms that live in and on the human body, can trigger disease as well as promote health. However, the role of these microbes and how they interact with the environment is poorly understood.

The webinar, hosted by Lisa Chadwick, Ph.D., health scientist administrator in the NIEHS Genes, Environment, and Health Branch, featured John Rawls, Ph.D., and Michal Toborek, M.D., Ph.D., both of whom study the role of intestinal microbes in human health and disease.

"Recent increases in the prevalence of obesity among adults and the tripling of rates in one generation among children and adolescents suggest a strong contribution from environmental factors," said Rawls. (Photo courtesy of Duke University)

Fighting the obesity epidemic

"Evidence indicates that the complex interactions between the gut microbiota, diet, and the human or animal host contribute to a spectrum of human diseases including obesity," said Rawls, *(http://rawlslab.duhs.duke.edu/People/People.html)* associate professor in the Department of Molecular Genetics and Microbiology, and director of the Center for Genomics of Microbial Systems at Duke University.

"Our goal is to understand the mechanisms by which environmental factors regulate fat storage, so that effective microbiome strategies can be developed, and even tailored for individuals, to reduce obesity," he continued.

"For example, in both mice and zebrafish models, researchers have shown that increases in dietary intake are often associated with an increase in the abundance of Firmicutes - a large phylum of bacteria linked to obesity in humans - suggesting that this bacterium is instrumental in increasing the absorption of fat."

With NIEHS funding, Rawls is now researching tributyltin (TBT), an environmental toxin known to promote obesity in vertebrates. Using the zebrafish model system, he hopes to define the impact of TBT on the obesogenic activity of gut microbiota. Developing techniques to moderate the effects of TBT and other obesogens could help prevent obesity.

Toborek's lab evaluates how certain properties of the brain endothelium can influence migration of tumor cells into the brain, and how exercise can help protect against the development of brain metastases. (Photo courtesy of University of Miami)

PCBs, the gut microbiome, and brain metastases

Toborek, *(http://biomed.miami.edu/?p=491&pid=230&m=facultyph&mid=1&item=516)* professor in the Department of Biochemistry and Molecular Biology at the University of Miami Miller School of Medicine, and his team study the associations between the changes in the gut microbiome and the blood-brain barrier (BBB), which protects the brain's internal environment. Toborek discussed the effects of PCBs on gut microbes and the BBB.

"We are all exposed to PCBs, which continue to be used in the United States. The main route of exposure to PCBs is through the food chain, and many studies show that there is a broad range of health effects from exposure to these toxicants that includes cancer and brain metastasis - a leading cause of cancer-related morbidity and mortality," said Toborek.

Toxicity, the gut-brain axis, and exercise

According to Toborek, he and his team are the first to suggest a link between the gut microbiome and brain metastases. "Our research indicates that both the intestinal epithelium and the brain epithelium are highly susceptible to the toxicity of PCBs. Exposure to these toxicants alters protein expression and increases permeability of the gut and the BBB, which, in turn, disrupts their protective microenvironments," he said. "We are now finding that alterations in the gut permeability have a profound effect on the BBB and influence the development and growth of metastases."

In previous research, Toborek showed that exercise had a profound effect on the gut microbiome, reducing the PCB-induced changes. Taking these findings a step further, he then demonstrated that moderate to vigorous exercise - a powerful, modifiable behavior - helps increase the growth of beneficial bacteria, which protect against the development of brain metastases.

(Audrey Pinto, Ph.D., is technical editor for the journal Environmental Health Perspectives.)

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