Who is running your gut? The gut-brain axis in brain metastasis formation by polychlorinated biphenyls

Toborek M

Department of Biochemistry and Molecular Biology, University of Miami School of Medicine, USA

The gut microbiome is a dynamic bacterial community that interacts with the host and closely relates to human health by regulating energy metabolism and immune functions. Each host has a unique composition of gut microbiota, which implies highly individual responses to environmental stressors and suggests a role for gut microbiota in future personalized health strategies. However, the influence of the microbiome on the toxicity of environmental pollutants and its role in risk assessment are largely unknown. In addition, there is an emerging interest in the role of behavioral factors in modulating toxicity of environmental pollutants. While the role of nutrition has been explored, the impact of exercise on the health effects of toxicants is not known. Because exercise can influence the outcomes of disorders known to be associated with alterations of the gut microbiome, we hypothesized that physical activity may affect the composition of the gut microbiota and thus influence the impact of environmental toxicants. In order to address this hypothesis, we investigated the effects of polychlorinated biphenyls (PCBs) and exercise on the composition and structure of the gut microbiome. In addition, we related these results to PCB-induced development of brain metastases [1,2]. Mice exercised voluntarily for 5 weeks, followed by the exposure to a mixture of environmentally relevant PCB congeners (PCB153, PCB138 and PCB180) for 48 h. The microbiome was assessed by determination of 16S rRNA. Oral exposure to PCBs disrupted the integrity of the gut barrier function and significantly altered the abundance of the gut microbiome primarily by decreasing the levels of Proteobacteria. The activity level correlated with a substantial shift in abundance, biodiversity, and microbiome composition. Importantly, exercise attenuated PCB-induced changes in the gut microbiome. Oral exposure to PCBs facilitated the development of brain metastases, the effects that was attenuated by exercise. This study provides the first evidence that oral exposure to PCBs can induce substantial changes in the gut microbiome, which may then influence their systemic toxicity. Importantly, these changes can be attenuated by behavioral factors, such as voluntary exercise.

References:

1. Choi JJ, Eum SY, Rampersaud E, Daunert S, Abreu MT, Toborek M. Exercise attenuates PCB-induced changes in the mouse gut microbiome. Environ Health Perspect. 2003; 121: 725-730
2. Sipos E, Chen L, Andras IE, Wrobel J, Zhang B, Pu H, Park MS , Eum SY, Toborek M. Proinflammatory adhesion molecules facilitate polychlorinated biphenyl-mediated enhancement of brain metastasis formation. Toxicol Sci 2012; 126: 362-371