Abstract

Nutrition and lifestyle are well-defined modulators of chronic diseases, and evidence is accumulating that dietary components can modulate toxic insults mediated by environmental pollutants. Results from epidemiological studies support the hypothesis that cardiovascular diseases such as atherosclerosis are linked to environmental pollution. There is also evidence linking the arachidonic acid receptor (AHR) with mechanisms associated with cardiovascular diseases and that AHR ligands such as polychlorinated biphenyls (PCBs) may be atherogenic by disrupting the functions of endothelial cells in blood vessels. Because PCBs are in general very persistent and proinflammatory, life-long exposure to these pollutants may fuel vascular inflammation and the pathology of atherosclerosis. We are exploring the paradigm that nutrition can modulate environmental insults in the vasculature and thus modulate endothelial dysfunction induced by exposure to PCBs. Nutrition can dictate the lipid milieu, oxidative stress, and antioxidant status within cells. Therefore, nutritional interventions may influence the ability of environmental pollutants to cause disease such as vascular dysfunction. For example, certain dietary fats increase the risk to environmental insults induced by PCBs, while fruits and vegetables, rich in antioxidants and anti-inflammatory nutrients or bioactive compounds, may provide protection. Our studies indicate that an increase in cellular oxidative stress and an imbalance in antioxidant status are critical events in PCB-mediated induction of inflammatory genes and endothelial cell dysfunction. We have demonstrated that diet-derived lipids and bioactive compounds can alter the cellular lipid milieu, oxidative stress and antioxidant status, and thus modulate mechanisms of cytotoxicity mediated by PCBs. We also have evidence that the plasma membrane microdomains called caveolae play an important role in endothelial activation and toxicity by mediating PCBs. Caveolae are particularly abundant in endothelial cells and play a major role in endothelial trafficking and the regulation of signaling pathways associated with the pathology of vascular diseases. There is a great need to further explore this nutritional paradigm in environmental toxicology and to improve our understanding of the relationship between nutrition and lifestyle, exposure to environmental toxicants and disease.

Results

PCB77 increases extent of atherosclerosis

Vehicle PCB77

PCB77 increases abdominal aortic aneurysms (AAA)

A

B

PCB77 vs. control

PCB77 increases pro-inflammatory events

High omega-6 oil (corn oil) increases PCB77 induced vascular cell adhesion molecule-1 and decreases major serum fatty acids

References


Conclusions

- PCB77 increases the incidence and severity of atherosclerosis and AAA.
- High omega-6 fatty acids increase the pro-inflammatory properties of PCB77, whereas omega-5 fatty acids protect against these events.
- PCB77 and AHR are localized to caveole domains.
- Dietary compounds can modulate expression of caveolin-1, the structural component of caveolae.
- Abolition of caveolin-1 protects against PCB77-induced pro-inflammatory events.
- These data suggest that caveolae are a critical signaling platform in the interactive regulation of environmentally-induced pro-inflammatory events.

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