Dietary DHA Promotes an Anti-oxidant Response in Mice Exposed to Environmental Pollutants

Katryn Eiske, Margaret Murphy, Michael Petriello, Bradley Newsome, Sung Gu Han, Bernhard Hennig
University of Kentucky Superfund Research Program, University of Kentucky, Lexington, KY 40536-0200.

Abstract

Consumption of fish oil is associated with improved coronary health outcomes, but the mechanism of protection is not well understood. Environmental stressors, such as polyunsaturated omega-3 fatty acids found in fish oil in reducing the inflammatory response to PCBs. To further our understanding of the mechanism by which the omega-3 fatty acid, docosahexaenoic acid (DHA), is protective, we fed C57BL/6 mice diets enriched in DHA (3% DHA/22% safflower oil, % kcal) or a safflower control diet for four weeks before administration of the coplanar PCB 126 via oral gavage at week five. Liver samples were analyzed by microarray and real-time-PCR to examine the interactive effects of PCBs and DHA on the nuclear factor (erythroid-derived 2)-like 2 (Nrf-2) anti-oxidant response pathway. Microarray data revealed that animals fed DHA and treated with PCBs had decreased expression of kelch-like ECH-associated protein 1 (Keap1), a cytosolic inhibitor of Nrf-2 activity. In addition, an increase in the expression of peroxisome proliferator-activated receptor gamma (PPAR γ), a positive co-activator of Nrf-2, and its chaperone PPARγ co-activator 1a (PPARγca1a). Real-time-PCR analysis revealed increased expression levels of Nrf-2-activated anti-oxidant enzymes, NAD(P)H dehydrogenase (quinone 1) (NQO1) and hemeoxygenase 1 (HO-1) in PCB treated mice on a DHA diet. Together these data suggest that DHA promotes an anti-oxidant response in mice exposed to environmental pollutants such as PCBs. (Supported by grants from NIHES, NIH P42ES07380 and the UK AES.)

Experimental Design and Rationale

Table 1. Experimental design of 6-week DHA feeding study with PCB 126 exposure.

<table>
<thead>
<tr>
<th>Diet</th>
<th>Vehicle</th>
<th>PCB126</th>
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<tbody>
<tr>
<td>Diet*</td>
<td>1</td>
<td>2</td>
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<tr>
<td>Oral Gavage</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Glucose Tolerance Test*</td>
<td>5</td>
<td>6</td>
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<tr>
<td>Blood Collection</td>
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<td>Urine/Feces Collection</td>
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<td>ECHO MRI</td>
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<td>Takedown</td>
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</tbody>
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*A: animals maintained on control diet 25% kcal from fat (safflower oil) or DHA diet 3% DHA/22% Safflower oil diet (% kcal).
*B: oral gavage of 5.0 μmol/kg/PCB 126 or safflower oil, vehicle control.
*C: intraperitoneal injection of 2 mg/g 20% glucose solution.
*D: retro-orbital blood collection used at week 5 and cardiac puncture at takedown.

Methods

Hypothesis

We hypothesize that dietary DHA will promote an anti-oxidant response through modulation of the transcription factors Nrf-2 and PPARγ.

References

10. Statistics: P-value<0.05 was considered significant.