

### Unique-to-Salmon Compounds Increase in Plasma and Are Associated With Cardiovascular Health Following a Mediterranean Diet Intervention

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**Objectives:** Salmon consumption may promote cardiovascular (CV) health through nutrients such as omega-3 fatty acids (n-3 FAs) or other yet unidentified compounds. Metabolomics allows for the comprehensive analysis of small molecules in foods and human samples. The objectives of this study were to: 1) identify compounds present in salmon that were increased in plasma after consumption of a salmon-containing Mediterranean-style eating pattern (MED); and 2) evaluate associations between salmon compounds detected in plasma and CV biomarkers.

**Methods:** Individuals ( $n = 41$ ) completed a 16-week randomized, crossover, controlled feeding study of a MED containing 2 servings salmon/week. Assessments were completed pre- and post-intervention, where CV biomarkers (e.g., blood pressure, lipid profile) were measured

and fasting plasma collected. Samples of participants' plasma, salmon, and 99 other foods in the trial were analyzed in triplicate via liquid chromatography-mass spectrometry (LCMS). Compounds were determined to be unique-to-salmon (UTS) if detected in all replicates of salmon but none of the other 99 foods. For UTS compounds that were found in plasma, linear mixed effects models were used to assess change from pre- to post-intervention and the association between this change and changes in CV biomarkers. Significance was assessed after adjustment for false discovery rate.

**Results:** Relative to the other 99 foods, 508 compounds were determined to be UTS, and 143 of these UTS compounds were detected in plasma. Forty-eight UTS compounds significantly increased in plasma from pre- to post-intervention. Two compounds, a phosphatidylglycerolphosphate (40:4) and a triglyceride (58:11), were associated with improvement in  $\geq 1$  CV biomarker. The former, a cardiolipin precursor, was associated with improvements in total cholesterol, LDL cholesterol, and Apolipoprotein B.

**Conclusions:** Salmon compounds are detectable in human plasma after consumption within a complex diet and increase after intervention, suggesting potential as intake biomarkers. Further, bioactive compounds beyond nutrients such as n-3 FAs may be associated with CV benefits. Future studies should be conducted to quantify concentrations and define dose-response.

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