Programming Macrophage Inflammation Resolution: The Role of Omega-3 Polyunsaturated Fatty Acids

Boris Krasnov  
*St. John Fisher College, bak07784@students.sjfc.edu*

Mathew Lombardozzi  
*St. John Fisher College, msl09713@students.sjfc.edu*

Maria Caraballo  
*St. John Fisher College, mlc00400@students.sjfc.edu*

Ramil Sapinoro  
*St. John Fisher College, rsapinoro@sjfc.edu*

How has open access to Fisher Digital Publications benefited you?  
Follow this and additional works at: [http://fisherpub.sjfc.edu/pharmacy_facpub](http://fisherpub.sjfc.edu/pharmacy_facpub)

Part of the Pharmacy and Pharmaceutical Sciences Commons

Publication Information  
Krasnov, Boris; Lombardozzi, Mathew; Caraballo, Maria; and Sapinoro, Ramil, "Programming Macrophage Inflammation Resolution: The Role of Omega-3 Polyunsaturated Fatty Acids" (2015). Pharmacy Faculty Publications. Paper 60.  
http://fisherpub.sjfc.edu/pharmacy_facpub/60  
Please note that the Publication Information provides general citation information and may not be appropriate for your discipline. To receive help in creating a citation based on your discipline, please visit [http://libguides.sjfc.edu/citations](http://libguides.sjfc.edu/citations).

This document is posted at [http://fisherpub.sjfc.edu/pharmacy_facpub/60](http://fisherpub.sjfc.edu/pharmacy_facpub/60) and is brought to you for free and open access by Fisher Digital Publications at St. John Fisher College. For more information, please contact fisherpub@sjfc.edu.
Programming Macrophage Inflammation Resolution: The Role of Omega-3 Polyunsaturated Fatty Acids

Abstract
It was previously thought that resolution of inflammation was a passive process, but recent emerging research has identified that resolution is an active process and that dual acting lipid mediators derived from essential omega-3 polyunsaturated fatty acids (PUFAs) have both anti-inflammatory (reducing neutrophil access to the inflamed tissue) and pro-resolving (removal of apoptotic cells by macrophages in the inflamed site) actions. The objective of our study was to determine the role of omega-3 PUFAs in programming phenotypic changes in treated macrophages. The polarization of macrophages during inflammatory responses to functionally distinct phenotypes may play a role in both inflammation and resolution of inflammation following treatment with omega-3 PUFAs for chronic inflammatory diseases.

Keywords
fsc2015

Disciplines
Pharmacy and Pharmaceutical Sciences

Comments
Programming Macrophage Inflammation Resolution: The role of omega-3 polyunsaturated fatty acids
Boris Krasnov, Mathew Lombardozzi, Maria Caraballo, and Raml Sapinoro, Ph.D.
St. John Fisher College, Wegmans School of Pharmacy, Rochester, NY

Introduction

The objective of our study was to determine the role of omega-3 polyunsaturated fatty acids in programming phenotypic changes in treated macrophages.

It was previously thought that resolution of inflammation was a passive process, but recent emerging research has identified that resolution is an active process and that dual acting lipid mediators derived from essential ω-3 PUFAs have both anti-inflammatory (reducing neutrophil access to the inflamed tissue) and pro-resolving (removal of apoptotic cells by macrophages in the inflamed site) actions.

Omega-3 PUFAs have anti-inflammatory and pro-resolving activity in preclinical disease models (e.g. peritonitis, colitis, asthma).

Chronic inflammation is a key factor in the pathogenesis of numerous diseases (e.g. COPD, RA, IBD).

The M2 Macrophage Phenotype

- Role in allergic responses driven by IL-4 and IL-13
- Involved in the development of TH2-dependent immune response to extracellular parasites
- M2 macrophages are associated with an anti-inflammatory state

DHA treatment reduces IL-6 production in product in LPS-stimulated RAW264.7 macrophages

IL-6 production was measured in the supernatant fraction of treated cells by ELISA. RAW264.7 macrophages were seeded at a density of 200,000 cells/ml and pre-treated with the indicated concentrations (μM) and combinations of ω-3 PUFAs ~18 hours prior to a 24 hour LPS (1 μg/ml) stimulation. Data is represented as mean ± SEM for n=3. **p<0.01 versus LPS-treated cultures by one-way ANOVA; ***p<0.001 versus LPS-treated cultures by one-way ANOVA. (DHA (500μM) + LPS = not detected by lower sensitivity of assay)

DHA drives polarization of alternatively activated (M2) macrophages

Quantitative RT-PCR. Total RNA was extracted from non-treated, LPS treated (500 ng/ml), and DHA pre-treated (500 μM) RAW264.7 macrophages to measure mRNA levels of Arg-1 and FIZZ-1. Data is represented as mean ± SEM for n=4. **p<0.01 versus LPS-treated cultures by one-way ANOVA; ***p<0.001 versus LPS-treated cultures by one-way ANOVA.

Exposure to DHA following inflammatory insult attenuates COX-2 expression on LPS-stimulated RAW264.7 macrophages

Western blot: RAW264.7 macrophages were seeded at a density of 200,000 cells/ml and pre-treated with DHA ~18 hours prior to a 24 hour LPS (500ng/ml) stimulation or treated with DHA 30 minutes after LPS stimulation. Non-treated cultures were treated with the same final concentration of ethanol as vehicle. Cell lysates were collected and subjected to western blot analysis using an anti-COX-2, or anti-beta-tubulin antibody. The antibody-specific bands were quantified by densitometry and were normalized to beta-tubulin (numerical values above COX-2 band.) Blot shown is a representative image from 3 independent experiments.

Conclusions

- The action of ω-3 PUFAs drives the decrease in the proinflammatory mediator COX-2 and IL-6
- M2 markers, Arg-1 and FIZZ1, are up-regulated in DHA treated macrophages
- The polarization of macrophages during inflammatory responses to functionally distinct phenotypes may play a role in both inflammation and resolution of inflammation following treatment with ω-3 PUFAs.