

Fats and lipid bioactives to quench the fire (inflammation)

Effects of Nutrition and Exercise on Pro-Resolving Lipid Mediators



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Key players in inflammation and its successful resolution



INFLAMMATION

PMN

M1

M2



Endogenous specialized pro-resolving mediator (SPM) families







- Human trials show that supplementation with fish oil containing a mixture of n-3 PUFA can increase blood SPM concentrations.
 - Healthy middle aged adults (Barden et al. 2014)
 - 2.4 g/day for 1 week
 - Subjects with metabolic syndrome (Barden et al. 2015)
 - 2.4 g/day for 4 weeks
 - Chronic kidney disease patients (Mas et al. 2016)
 - 4 g/day for 8 weeks
- Effects on SPM pathway monohydroxy intermediates generally far more consistent and robust than mature SPMs



- Oral supplementation with pure n-3 PUFA in young healthy women
 - Pure n-3 EPA 1g/day
 - Pure n-3 DPA 1g/day
 - Olive oil (placebo) 1g/day



Markworth et al. FASEB J 2016 30(11): 3714-25

•Plasma concentration of the resolvin E intermediate 18-HEPE markedly increased by EPA supplementation

•RvE1 detected in fasting human plasma at ≈ 50 pg/mL

 But no apparent increase in fasting blood with following EPA supplementation

* p<0.05 vs. pre-supplementation #p<0.05 vs. day 7 of placebo (OO) trial



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- A novel resolvin metabolites of n-3 DPA (22:5 n-3) itself was detected in human plasma
 - A n-3 DPA derived analog of the known DHA derived SPM RvD5
- Supplementation with n-3 DPA (but not EPA) greatly increased plasma levels of 7,17-dihydroxy-DPA

* p<0.05 vs. pre-supplementation #p<0.05 vs. day 7 of placebo (OO) trial



Exercise as a human model to study acute self-resolving inflammation?





Paulsen et al. 2009. Medicine and Science in Sport and Exercise.

Anti-inflammatory approach to the treatment of soft tissue injury

- Acute traumatic injury
 - Strains, sprains, contusions, fractures, wounds, burns, post-surgery
- Exercise induced muscle injury
 - Delayed onset muscle soreness (DOMs)
 - Muscle pain associated with unaccustomed activity (i.e. resistance exercise)
- Non-steroidal anti-inflammatory drugs (NSAIDs)
 - Oral or topical delivery
- RICE
 - Rest, Ice, Compression, Elevation



The effect of NSAIDs on the resolution of exercise-induced inflammation in humans





Pro-inflammatory Lipid Mediators

Markworth et al. 2013. Am J Physiol Regul Integr Comp Physiol.

Specialized Pro-Resolving Mediators



***p<0.001, ** p<0.01, *p<0.05 vs. pre-exercise. #p<0.05 vs. placebo group

Markworth et al. 2013. Am J Physiol Regul Integr Comp Physiol.

Impairs muscle recovery



Vella et al Frontiers in Physiol. 2016 7 (86). doi: 10.3389/fphys.2016.00086.

Current and Ongoing Studies

- Cold Water Immersion
 - Delays recovery
 - Impairs muscle gains
 - Roberts J Physiol 2015 593 (18): 4285-301.
 - Peake et al. J Physiol. 2016 Oct 4. doi: 10.1113/JP272881.
- Hot Water Immersion
 - Analysis in progress
- Arachidonic Acid Supplementation
 - Alterations in SRMs
 - Post-exercise actions
 - SRMs
 - Inflammation and recovery



Implications and future directions

- Anti-inflammatory vs pro-resolving therapeutics for the treatment of soft tissue injury
 - Dietary or supplemental n-3 PUFA?
 - Native SPMs/SPM drug analogs?
 - Cold vs heat application following soft tissue injury?
- Do peripheral tissue cells (myocytes, adipocytes, fibroblasts etc.) participate in SPM biosynthetic circuits?
 - Transcellular biosynthetic routes with invading immune cells?
- Do SPMs play direct roles in soft tissue remodelling independent of their immunomodulatory effects?

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