Modulators of Inflammatory Pathways

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Oxidant Stress Modulators

In general: Vitamin A, C, E, melatonin, quercetin, CoQ10, lipoic acid, glutathione, selenium , N-acetyl cysteine, vitamin B3, **Nrf2 induces**: sulfuranes, lycopene. Apo-10'-lycopenic acid

***NADPH oxidase*:** Folate, quercetin, vitamin E, quercetin, lipoic acid, CoQ10, glutathione, vitamin B2, cysteine

Xanthine Oxidase: Folic acid, quercetin, cranberry juice, luteolin,, catechin, epigallocatechin, myricetin.apegenin, kaemferol

Peroxide: glutathione peroxidase, selenium, catalase

Hypochlorite (HOCl): Taurine, r-lipoic acid

Superoxide Anion: Super oxide dismutase with its cofactors copper, zinc and manganese, arginine, gamma tocopherol, folate and vitamin C

Fenton Reaction: Quercetin, resveratrol

Peroxynitrite: Tocotrienols, gamma tocopherol, green tea polyphenols, folate, vitamin B12, r-lipoic acid, vitamin D. Peroxynitrite depletes vitamin C, glutathione, and CoQ10,

Asymmetrical dimethylarginine (ADMA): Arginine, folate, Taurine, vitamin E, reduce homocysteine with vitamin B6, serine, folate, betaine

Inflammation Modulators

C Reactive Protein: Niacin, DHA/EPA, reducing the effect of IL-6. Cod protein

Excessive cortisol activity: Phosphatidyl serine, cysteine, acetyl-l-carnitine and vitamin C and B5

Reduce side effects of corticosteroids: Arginine, vitamin D, C,magnesium, calcium , chromium

Gene transcription:

Genes that are down-regulated by n-3 PUFA are those encoding TNF-α, IL-1, COX-2, 5-LOX, 5-LOX activating protein, certain matrix metalloproteinases, and VCAM-1

Peroxisome proliferator activated receptors (PPAR): [activators of both PPARα and γ have been shown to inhibit the activation of a number of inflammatory genes, including TNF-α, IL-1β, IL-6, IL-8, COX-2 and VCAM]: genistein, EGCG

Hypoxic Inducing Factor: Alpha-ketoglutarate, Vitamin D, C

Heme oxygenase: Curcumin, resveratrol, Green Tea Polyphenols, (-)-Epigallocatechin-3-Gallate, aspirin, statins, L-methionine

Interleukin 6: Vitamin B3, chromium, vitamin E, tocotrienols, grape-seed, procyanidins (GSPE), quercetin (reduces IL6 release) reducing trans fatty acid exposure,

Interleukin 1: quercetin,, DHA/EPA, zinc, glutathione, vitamin D, E and B6, green tea polyphenols.

Interleukin 1B: Omega 3 fatty acids or fish oils, n-acetylglycosamine, niacinamide

Matrix metallo proteinases:

MMP2: quercetin, luteolin, EGCG (epigallocatechin 3-O-gallate)

MMP9: Curcumin, DHA, genistein, quercetin, vitamin D3, EGCG.

Monocyte chemoattractant protein (MCP-1)*:* grape-seed procyanidins (GSPE), quercetin, n-acetylcysteine

Nuclear Factor Kappa B modulators: Vitamin B3, D, omega 3 fatty acids, genistein, Curcumin, indole 3-carbinol melatonin, quercetin, ginger, Caffeic acid phenethyl ester (CAFE), green tea poly phenols, gamma tocopherol, selenium, chromium nicotinate, r-lipoic acid

Poly- ADP-ribose synthetise: niacinamide

peroxisome proliferator-activated receptors (PPARs)[anti-inflammatorymodulator]: genistein, EGCG,

Protein Kinase C: Taurine, n-acetyl cysteine, vitamin E

Tumor necrosing Factor alpha modulators: quercetin, alpha linolenic acid, DHA, EPA, alpha tocotrienols, niacinamide

Trans forming Growth factor Beta: Niacin, luteolin, DHA/EPA, vitamin D, C, E, gamma tocopherol, green tea polyphenols, chromium nicotinate, selenium

NAG-1 (NSAID activated gene-1)[a divergent member of TGF-β superfamily]: Curcumin, resveratrol, green tea polyphenols, Indole -3-carbinol, 6-gingerol, genistein

Prostanoid Metabolism

Supporting Prostanoid metabolism: Gamma linolenic acid, vitamin B6, B3, C magnesium, zinc, omega 3 fatty acids, DHA/EPA, selenium, bromelain

Cyclooxygenase modulators: quercetin, DHA/EPA, soy isoflavones, tea polyphenols, Curcumin, resveratrol, garlic, ginger, tocotrienols

Lipooxygenase: alpha-Tocopherol, green tea polyphenols, garlic, Curcumin, kaempferol, quercetin, morin and myricetin

Phospholipase A2: alpha-Tocopherol, quercetin, Curcumin, licorice

Nitric oxide Metabolism

Supporting Nitric oxide Synthesis: Arginine, biopterin folate, vitamin C, B2, B3

Increasing NO availability: Decrease oxidant stress, decrease ADMA

Decreasing Mitochondrial NOS induction: Melatonin

Reducing NO secretion or synthesis: quercetin, resveratrol, apigenin, ginger and morin

Renin-Angiotensin system: Taurine, DHA, vitamin D, E, C, K

ACE Inhibitors: garlic, tuna muscle protein, sardines, hawthorn berry, pycngenol, gelatine, omega3 fatty acids,, egg yolks

Metabolic Stress Modulators:

Protein urea: Pyridoxine-5-phosphate, vitamin D

Glycotoxicity:

AGEs: Pyridoxine-5-phosphate, lysine, r-lipoic acid, carnosine, vitamin E

Insulin resistance: genistein, chromium, Niacinamide, zinc, glucose tolerance factor, r- lipoic acid, magnesium

Receptor for advanced glycation end products (RAGE): Stimulate PPAR gamma with genistein, EGCG, as this receptor stimulates nuclear factor kappa B, modulation of this transcription factor may reduce AGE toxicity

Lipotoxicity:

LDL oxidation: DHA, L-carnitine, green tea poly phenols, cocoa, proanthocyanidins, selenium, melatonin

High Homocysteine levels: High doses of vitamin B6, vitamin B12, folic acid, and betaine,

Mechanical Stress

Tubula Interstial Damage: Pyridoxal 5-phosphate, selenium, vitamin D

Glomerular hypertrophy: Pyridoxal -5-phosphate, vitamin D

Glomerular sclerosis: Vitamin C, D and E

Mitochondrial or Energy Production Stress

Mitochondrial Support: Acetyl-l-carnitine, lipoic acid, nicotinamide adenine dinucleotide (NAD), vitamin K, B1, B2, C, E, glutathione, CoQ10, selenium, quercetin, taurine, omega 3 oils, phosphatidyl choline, alpha ketoglutarate, malate

AMP-activated protein kinase (AMPK) [a major metabolic-sensing protein implicated in the prevention of metabolic disorders]: resveratrol, epigallocatechin gallate, berberine, and quercetin

Detoxification

Phase 1: Vitamin B2, B3, B6, B12, folate, glutathione, branch chain amino acids, flavonoids, phospholipids

Intermediate metabolites from Phase 1 quenched by: Vitamin C, E, selenium copper zinc, manganese Coq10, bioflavonoids, pycnogenol, thiols (garlic, onions cruciferous vegetables)

Phase 2: SAMe, glycine, taurine, glutamine, folic acid, vitamin B12, betaine, choline, cysteine , methionine

Hyperparathyroidism: Vitamin D

Hyperglycaemia induced apoptosis: Taurine

Reducing inhibition of Complex 1: alpha –ketoglutarate, malate, fumarate, succinate, CoQ10, NAD

Cytoprotection from anoxia: alanine, glycine, glutathione, cysteine

IgA induce nephropathy: Vitamin E, A

Notes

Nicotinamide inhibits the production of a variety of pro-inflammatory agents, such as tumor necrosis factor alpha, interleukin 6, NO, PGE(2), and the generation of ROS.

Arch Immunol Ther Exp (Warsz). 2008 Mar-Apr;56(2):127-34. Epub 2008 Mar 31

Biedroń R, Ciszek M, Tokarczyk M, Bobek M, Kurnyta M, Słominska EM, Smoleński RT, Marcinkiewicz J. 1-Methylnicotinamide and nicotinamide: two related anti-inflammatory agents that differentially affect the functions of activated macrophages. Arch Immunol Ther Exp (Warsz). 2008 Mar-Apr;56(2):127-34. Epub 2008 Mar 31. PubMed PMID: 18373238

Curcumin has been found to induce HO-1 expression by signaling through (NF-E2)-related factor 2 (Nrf-2) and NF-kappaB and thereby has the potential to reduce oxidative stress.[3]

Andreadi CK, Howells LM, Atherfold PA, Manson MM. Involvement of Nrf2, p38, B-Raf, and nuclear factor-{kappa}B, but not phosphatidylinositol 3-kinase, in induction of hemeoxygenase-1 by dietary polyphenols. *Mol Pharmacol*. 2006;69:1033-1040