



HAL
open science

Neuroprostanes, produced by free-radical mediated peroxidation of DHA, inhibit the inflammatory response of human macrophages

Cécile Gladine, Laurie L. Joumard-Cubizolles, G. Chinetti, Dominique Bayle, C. Copin, N. Hennuyer, B. Staels, G. Zanoni, A. Porta, Jm Galano, et al.

► To cite this version:

Cécile Gladine, Laurie L. Joumard-Cubizolles, G. Chinetti, Dominique Bayle, C. Copin, et al.. Neuroprostanes, produced by free-radical mediated peroxidation of DHA, inhibit the inflammatory response of human macrophages. SFRR-E-Meeting Paris 2014. Free radicals: insights in signaling and adaptive homeostasis, Society for Free Radical Research Europe (SFRR). FRA., Sep 2014, Paris, France. 1 p., 10.1016/j.freeradbiomed.2014.10.590 . hal-02744292

HAL Id: hal-02744292

<https://hal.inrae.fr/hal-02744292>

Submitted on 3 Jun 2020

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

Neuroprostanes, produced by free-radical mediated peroxidation of DHA, inhibit the inflammatory response of human macrophages.

C Gladine¹, L Joumard-Cubizolles¹, G Chinetti², D Bayle¹, C Copin², N Hennuyer², B Staels², G Zanoni³, A Porta³, JM Galano⁴, C Oger⁴, T Durand⁴, A Mazur¹

¹UMR1019 INRA/Clermont Université, Clermont-Ferrand, France ; ²UMR1011 INSERM/Université de Lille 2/Institut Pasteur, Lille, France ; ³Université de Pavie, Pavie, Italie ; ⁴IBMM, UMR 5247 CNRS/UM I/UM II, Montpellier, France

The anti-inflammatory properties of DHA have been largely demonstrated *in vitro* and *in vivo* but research gaps remain regarding the contribution of the oxygenated metabolites. Among them, we are focusing on prostaglandin-like molecules termed Neuroprostanes (NeuroPs) which are produced through free-radical-mediated peroxidation of DHA. We hypothesized that these specific molecules which are highly reactive and produced in abundance during oxidative stress and inflammation could contribute to the anti-inflammatory properties of DHA.

Human peripheral blood mononuclear cells were isolated from healthy donors by Ficoll density gradient centrifugation. Monocytes were differentiated into resting macrophages (RM) for 6 days (37°C, 5% CO₂). RM were exposed to 2 different types of NeuroPs (i.e. 14-A₄-NeuroP and 4-F_{4t}-NeuroP, 10 µM) or ethanol (vehicle 0.15%) during 30 min. Then LPS (100 ng/mL) was added for 6 hours to induced inflammatory response.

Both types of NeuroPs (14-A₄-NeuroP and 4-F_{4t}-NeuroP) significantly decreased the mRNA levels of IL-6 (-49% and -26% respectively) and MCP-1 (-55% and -24 % respectively). Secretion of TNFα and MCP-1 was also reduced when RM were exposed to 14-A₄-NeuroP (-10%, ns and -34%, p<0.05) and 4-F_{4t}-NeuroP (-12%, p<0.01 and 25%, ns). Preliminary results regarding the expression and phosphorylation of IκBα suggest that 4-F_{4t}-NeuroP could exert its anti-inflammatory effects through the inhibition of IκBα phosphorylation. Finally, cotransfection of luciferase reporter vector with hPPAR_γ expression vector performed on Cos-7 cells suggests that NeuroPs probably act independently of PPAR_γ.

In conclusion, these results suggest that the anti-inflammatory properties of DHA could be mediated, at least in part, by NeuroPs which corroborates the importance of oxidative stress in cell signaling.