BIOLOGICAL EFFECTS OF ISOPROSTANES AND NEUROPROSTANES: FROM RETT SYNDROME TO BRAIN DISEASE

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F_4-neuroprostanes (F_4-NeuroPs) and F_2-dihomo-isoprostanes (F_2-dihomo-IsoPs) are known as non-enzymatic oxidized products from the adrenic acid (AdA) and docosahexaenoic polyunsaturated fatty acid (DHA), respectively.

Our keen interest in the F_4-NeuroP field moves from the relevant role of DHA, highly concentrated in the nervous system and whose oxidation generates F_4-NeuroPs, thus allowing neurons to work at their best [Dyall SC 2015; McNamara 2012; Bradbury 2011; Bazan 2011]. The selective role for the F_4-NeuroPs in indicating the brain tissue oxidative status is also evidenced by the major increase of F_4- NeuroPs levels, rather than F_2-IsoPs, in brain injury conditions [Montine 2002, Milne 2006]. F_4-NeuroPs involvement in the clinical history has first been shown for Rett syndrome (RTT), a severe neurodevelopmental disease caused by mutations in the X-linked *MECP* gene. Likewise, F_2-dihomo-IsoPs, deriving from a specific component of myelin, are shown to be an early marker of lipid peroxidation in RTT [De Felice et al. 2011]. Intriguingly, patients with *MECP2* gain-of-function mutations show increased levels of F_4-NeuroPs as compared to healthy controls [Signorini et al. 2016]. Overall, a finely tuned balance of *MECP2* expression appears to be critical to oxidative stress homeostasis, thus shedding light on the relevance of the redox balance in the central nervous system integrity. On the other hand, emerging data are becoming available concerning other neurodegenerative diseases, or clinical conditions in which a nervous system damage is invoked. Certainly, F_4-NeuroP and F_2-dihomo-IsoPs evaluations are considered to be specific and accurate when carried out in brain tissue or cerebrospinal fluid [Łuczaj W 2016], whereas determinations of these molecules in plasma samples could be considered as an inadequate proxy of what is going on in the brain. Nevertheless, our group has repeatedly explored the relevance of plasma levels of F_4-NeuroPs and F_2-dihomo-IsoPs in RTT [De Felice et al. 2014], and other authors have confirmed the importance of monitoring the plasma levels of NeuroPs in Parkinson's disease [Seet 2010].

Our studies underline the key role of interaction between organic chemists, OS biochemists, and clinicians in the discovery of new markers of disease and potential targets for new interventional strategies