Lipid Mediators of the Sunburn Response: A Lipidomic Approach

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Ultraviolet radiation (UVR) produces many damaging effects in the skin and is the major aetiological factor in all the main types of skin cancer. Sunburn is one of the first signs of this damage; it occurs within a few hours of UVR exposure and its central features are vasodilatation and leucocyte chemotaxis. Bioactive lipid mediators play pivotal roles in this process, following their metabolism by cyclooxygenases, lipoxygenases and CYP450. We therefore investigated the profile of lipid mediators produced during the progress of UVR-induced erythema development in human skin, aiming to assess the contribution of various pro-inflammatory and anti-inflammatory metabolites, and identify biomarkers characteristic of the underlying biochemical mechanisms.

A lipidomic approach based on electrospray liquid chromatography tandem mass spectrometry (ESI/LC-MS/MS) analysis was applied to screen for the presence and quantitation of 47 bioactive lipid mediators including prostaglandins, thromboxanes, prostacyclines, dihydro-prostaglandins, isoprostanes, hydroxy fatty acids, leukotrienes, resolvins and protectins. Human volunteers were irradiated with 4 minimal erythemal doses of UVR and the erythema quantified over 72 h. Suction blisters were raised at various time points post-UVR and suction blister fluid was collected for analyses.

Omega-6 PUFA derived vasoactive prostaglandins PGE₂ and PGF₂₅ were significantly raised in the first 18h, while the n-3 PUFA-derived partial agonist PGE₃ was significantly raised at 48h. The potent neutrophil chemotactins 8-, 11- and 12-HETE showed significant increase from 18 h onwards. Conversely, the neutrophil chemotactin LTB₄ was not detected. Furthermore, the potent anti-inflammatory 15-HETE (inhibitor of 12-HETE and LTB₄ synthesis) was increased at later time points peaking at 72 h.

Our results suggest that the combined influence of a series of UVR-induced prostaglandins may contribute to vasodilatation during the sunburn response. Furthermore, temporal profiles of eicosanoids with pro- and/or anti-inflammatory activities indicate a differential regulation of the early and late stages of the inflammatory response supporting the monohydroxy-eicosatetraenoic acids 12-HETE, 11-HETE and 8-HETE, rather than LTB₄, as candidate mediators of UVR-induced neutrophil chemotaxis, while the anti-inflammatory metabolite 15-HETE may provide regulation of the inflammation. (Project funded by the Wellcome Trust)