




UVB stimulates production of enkephalins and other neuropeptides by skin-resident cells

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While studies on the ultraviolet B (UVB)-induced expression of proenkephalin (PENK) in murine regulatory T (Treg) cells with their possible role in regulation of skin homeostasis (1) are of interest, several very important issues have to be addressed to establish their significance. First, PENK is expressed and processed to the final opioid peptides including Leu- and Met-enkephalins in the resident skin cells such as keratinocytes, melanocytes, and fibroblasts, and this expression and production of enkephalins are stimulated by UVB (2). Since in murine skin, the UVB penetrates deeply into the dermis and hypodermis (3), it is likely that PENK-derived peptides will be produced by most resident skin cells (of neuroectodermal and mesenchymal origin) at total levels higher than reported PENK⁺ UVB-skin Treg cells. Second, the authors did not consider the fact that local neuroendocrine activity of skin cells is regulated by UVB, which also involves regulating proopiomelanocortin expression and its processing to different neuropeptides including endorphins (4, 5). Third, cortisol is not produced in mice; therefore, their conclusion on the lack of effect of glucocorticoids is

incorrect. In fact, similar doses of the UVB do stimulate local and central elements of hypothalamic–pituitary–adrenal axis with increased levels of corticosterone (6). It must be noted that when measuring adrenocorticotropic hormone or corticosteroids, the circadian rhythm has to be taken into consideration, since improper timing may generate a high level of values variability, preventing any conclusion. Here, precise timing is crucial. Last, mice are nocturnal species; therefore, it has to be mentioned that the significance of these findings must be validated in humans or in free-running animals active during daytime. In addition, UVB can stimulate glucocorticoid production in the human skin (7). In summary, while this paper provides an impressive amount of data (1), the authors should address adequately the above problems to place their work in the proper context but not drive the reader to the wrong conclusions.

Acknowledgments

Writing of this Letter was in part supported by NIH Grants 1R01AR073004 and R01AR071189 (to A.T.S.), R21AI149267-01A1 (to C.R. and A.T.S.), and R21MD015319 (to C.R.).

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The authors declare no competing interest.

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Published January 7, 2021.