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The skin-brain connection hypothesis, bringing together CCL27-mediated T-cell activation in the skin and neural cell damage in the adult brain

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Abstract

© 2017 Blatt, Khaiboullin, Lombardi, Rizvanov and Khaiboullina. Recent discovery of an association of low serum melatonin levels with relapse in multiple sclerosis (MS) opens a new horizon in understanding the pathogenesis of this disease. Skin is the main organ for sensing seasonal changes in duration of sunlight exposure. Level of melatonin production is dependent on light exposure. The molecular mechanisms connecting peripheral (skin) sensing of the light exposure and developing brain inflammation (MS) have not been investigated. We hypothesize that there is a connection between the reaction of skin to seasonal changes in sunlight exposure and the risk of MS and that seasonal changes in light exposure cause peripheral (skin) inflammation, the production of cytokines, and the subsequent inflammation of the brain. In skin of genetically predisposed individuals, cytokines attract memory cutaneous lymphocyte-associated antigen (CLA+) T lymphocytes, which then maintain local inflammation. Once inflammation is resolved, CLA+ lymphocytes return to the circulation, some of which eventually migrate to the brain. Once in the brain these lymphocytes may initiate an inflammatory response. Our observation of increased CC chemokine ligand 27 (CCL27) in MS sera supports the involvement of skin in the pathogenesis of MS. Further, the importance of our data is that CCL27 is a chemokine released by activated keratinocytes, which is upregulated in inflamed skin. We propose that high serum levels of CCL27 in MS are the result of skin inflammation due to exposure to seasonal changes in the sunlight. Future studies will determine whether CCL27 serum level correlates with seasonal changes in sunlight exposure, MS exacerbation, and skin inflammation.

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Keywords

Brain, CCL27, Inflammation, Light, Melatonin, Multiple sclerosis, Skin

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