Synopsis of Original Research Paper

Search for protective compounds against weak ultraviolet light-induced dysfunction of tight junction barrier in skin

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Human skin keratinocytes form a tight junction (TJ) in the lateral membrane between neighboring cells. The TJ restricts the paracellular flux of water, nutrients, and solutes. The architecture of TJ is composed of claudins, transmembrane proteins, and zonula occludens, adaptor proteins. Claudins have four transmembrane domains and comprise a multi-gene family with 27 members. Claudin-1 acts as a physiological barrier in the skin. Ultraviolet (UV) light may disrupt the TJ barrier, but the pathophysiological mechanism has not been clarified well. We found that UVB causes a mislocalization of claudin-1, decrease in transepithelial electrical resistance, and increase in paracellular permeability of lucifer yellow, a hydrophilic fluorescent marker, in human keratinocyte-derived HaCaT cells. Similarly, NOC, a NO donor, and SIN-1, a peroxynitrite donor, caused the mislocalization of claudin-1. PCR showed that opsin (OPN) 2 and 3 mRNAs are expressed in HaCaT cells. UVB increased intracellular Ca^{2+}, nitric oxide, and peroxynitrite concentration, which were inhibited by OPN2 siRNA. In addition, the elevation of Ca^{2+} concentration was inhibited by the siRNA of transient receptor potential vanilloid subtype 1 (TRPV1), suggesting that UVB enhances Ca^{2+} influx mediated through TRPV1. NOC increased the amount of tyrosine nitration and ubiquitination of claudin-1.

Our results indicate for the first time that UVB increases intracellular Ca^{2+}, NO, and peroxynitrite concentration, resulting in the mislocalization of claudin-1. Peroxynitrite may elevate the amount of nitration and ubiquitination of claudin-1. The compounds, which inhibit nitration and ubiquitination of claudin-1, may have a role in preventing the destruction of the TJ barrier caused by UV.