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Involvement of olfactory receptor OR2AT4 in skin aging and the response to environmental pollution

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Olfactory receptors (ORs) are 7-transmembrane G protein-coupled receptors expressed in the olfactory epithelium and mediate the odor perception. Around 400 ORs are known in humans and their expression has been evidenced in various peripheral tissues such as intestinal epithelium, prostate, spermatogenesis, liver, and skin. These ectopic receptors might regulate physiological functions beyond olfaction. The OR called OR2AT4 is expressed in the skin, especially the epidermal keratinocytes, melanocytes, dendritic cells, and hair follicles. Its activation increases the proliferation and migration of keratinocytes, allowing faster re-epithelialization during wound healing. OR2AT4 downregulation decreases the induction of IGF-1 expression in hair follicles suggesting its link with hair growth. However, the roles of ORs in the skin are still incompletely described, especially the possible link with intrinsic and extrinsic aging.

In this study, OR2AT4 expression was investigated in various senescent skin models in vitro such as murine dermal fibroblasts. Besides, the consequences of ultrafine particle-induced skin damage were studied via the evaluation of OR2AT4 expression level and on markers involved in skin senescence and differentiation. In parallel, botanical extracts were screened for their ability to modulate the expression of OR2AT4 and related markers. Our results showed that the expression of OR2AT4 was inversely correlated with aging and UFP-induced skin damage, suggesting that its modulation could be beneficial to limit the consequences of intrinsic and extrinsic aging into the skin.

Keratinocyte media differences uncovered during COVID-19 supply shortages

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Skin barrier properties are critical for maintaining epidermal water content, protecting from environmental factors, and providing first line of defense against pathogens. In this study, the epidermal differentiation influences epidermal barrier function. Barrier disturbances are known to contribute to and promote the inflammatory process. While the cytokine milieu in skin can vary between individuals, acute innate immune responses cause increases in tumor necrosis factor α (TNFα), interleukin (IL)-1β, IL-6, and interferon γ (IFNg). We asked what the single or combined effects of these pro-inflammatory cytokines on epidermal barrier function and the expression of key elements of tight junctions and the cornified envelope in single donor-derived 3D human epidermal equivalents (N = 8 individuals).

Transcript analysis by qPCR shows a significant negative impact of TNFα and a combination of all four cytokines on the expression of cornified envelope elements filagrin and loricrin. Although IL-1β, IL-6, or IFNγ alone did not affect filagrin or loricrin, the combination of four cytokines reduced the expression of these cornified envelope transcripts by more than 50-fold. Conversely, TNFα and the combination of four did not affect the expression of tight junction components claudin 1, occludin, or zona occludens 1, while claudin 4 was significantly upregulated by both treatments (p < 0.01). Using transmembrane electrical resistance (TER) assays, we found that concurrent treatment with TNFα, IL-1β, IL-6, and IFNγ significantly decreased TER (p < 0.01). As a single treatment, TNFα alone significantly reduced TER (p < 0.05). Only the dual combination of IL-6 and TNFα significantly reduced TER (p < 0.05). The number of simple biomers collected in each condition and the sequences-based assay was used to quantify the enzymatic activity of 12R-LOX, another lipoxigenase critical for maturation of skin barrier ceramides. Significant increase in 12R-LOX activity was measured after L4 treatment vs. vehicle (+31%) with a stronger effect in subjects 40 years-old or older (+56%). In conclusion, cytokine modulation in 3D human skin models uncovered important effects that may impact barrier disruption factor in acute inflammation but that IL-6 may have protective effects. Further, TNFα specifically disturbs gene expression of the cornified envelope, not the tight junction barrier.