Abstract

"Role of scavenger receptor B1 in cutaneous physiopathology"

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Scavenger receptor B1 (SR-B1) is a trans-membrane protein, known as HDLs main receptor and involved in tissue reverse cholesterol transport. Several studies have demonstrated that SR-B1 is also implicated in other processes, such as regulation of intracellular vitamins levels, recognition of bacteria and apoptotic cells and vesicles uptake. Although this receptor is mainly localized in the liver and steroidogenic tissues, it is significantly expressed also in human skin, especially in the epidermis. The epidermis provides the barrier function of skin, due to the presence of *stratum corneum*, composed by proteins and corneocytes, which are distributed in a lipid envelope. Its localization and composition makes the skin a target for environmetantal stressors. I*n vitro* studies on cultured keratinocytes have shown that SR-B1 protein expression is down-regulated by environmental oxidants such as cigarette smoke. Therefore, the purpose of our study was to evaluate the physiological role of SR-B1 in the skin, with more focus on the not vascularized cutaneous epidermal layer, by using 2D and 3D skin models. We demonstrated that SR-B1 is involved in cellular proliferation and migration, since SR-B1 knockdown keratinocytes presented reduced capacity to proliferate and migrate. In fact, SR-B1 knockdown induced a decrease of Cyclin D1 expression, as well as MMP9 levels accompanied by a defect in cytoskeleton rearrangement, affecting keratinocytes ability to recover from wound scratch. Furthermore, SR-B1 appeared to affect NF-kB activation. SR-B1 knockdown in tridimensional organotypic skin equivalents induced changes in epidermis thickness and deeper layers morphology, together with increased markers of terminal differentiation. Not only, but the scavenger receptor resulted to be essential for lipids expression and epidermal distribution, and it is implicated also in sebocytes lipids metabolism. Moreover, our study demonstrated that environmental stressors down-regulate SR-B1 also in three-dimensional reconstructed epidermis and human skin and, by the use of a natural polyphenol, we showed that such down-regulation was mediated by oxidative damage. Altogether, our findings suggest that SR-B1 plays an important role in keratinocytes recovery from injuries, as well as in epidermal differentiation and lipid composition, therefore its loss induced by oxidants exposure could affect cutaneous homeostasis.