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Long term co-culture of human adipocytes and dermal fibroblasts: a new predictive system for modelling hypodermis-dermis interactions and for screening compounds on the skin biology

Abstract:

Human skin is composed of three layers: epidermis, dermis and hypodermis. For many years, the therapeutic strategies to improve skin health and appearance were focused on the superficial layers composed by the epidermis and dermis. However, the recent advances in adipocyte biology and cellular biotechnologies increased the interest of the subcutaneous adipose tissue, referred as hypodermis, in skin properties. Adipose cells from the hypodermis play a crucial role in the mechanical and physiological properties of the skin. The role of these cells is not limited to their capacity to fill volumes by accumulating lipids, but they also regulate the mechanical properties of the dermis thanks to their endocrine function. In this context, we have set-up a novel in vitro model allowing us to assess the bi-directional interactions between the hypodermis and the dermis, and to propose a suitable tool to screen and evaluate efficacy of new compounds to maintain skin quality. Technically, we isolated adipocytes and fibroblasts from skin tissue of human donors undergoing aesthetic or reconstructive surgery. To preserve their viability and their metabolism up to 3 weeks, the isolated adipocytes were embedded in a gel mixture to form 3D capsules and cocultivated in 96-well plates containing adherent dermal fibroblasts. The culture conditions were initially validated to maintain the biological properties of each cell type. The DIVA Skin-Caps model preserved cell viability and did not exhibit cytotoxicity after 22 days in culture while maintaining the adipocyte metabolism (adiponectin secretion and lipolytic activity). Moreover, we showed that the presence of mature adipocytes modulated over time the secretion of extracellular proteins (hyaluronic acid, fibronectin and procollagen I) and stimulated the organization of the matrix network into fibres (collagen I, elastin and fibronectin). This novel 3D co-culture system combining human mature adipocytes and skin fibroblasts provides an original and unique approach to screen active compounds and assess their impact on the bi-directional interactions between the hypodermis and the dermis. This multiparameter model allows the high throughput screening of ingredients or molecules and the evaluation of their potential efficacy on skin biology :slimming, anti-cellulite, anti-aging, and plumping effects.