INFLAMMATORY SKIN DISEASES (OTHER THAN ATOPIC DERMATITIS & PSORIASIS)

FUNCTIONAL HUMAN PERIPHERAL SENSORY NEURONS DERIVED FROM STEM CELL TO STUDY REACTIVE SKIN DISORDERS

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Beyond its protective barrier function, human skin makes a sensorial interface with the environment. Sensory neurons such nociceptors, pruriceptors and mechanoceptors allow our skin to react to external conditions such as pollution, UV and temperature, involving a crosstalk between sensory neurons and skin cells, mainly keratinocytes. These two cell types are involved in the reactiveness of the skin, via signaling and transduction mechanisms that can contribute to reactive skin disorders like eczema, contact dermatitis and rosacea, involving discomfort sensation such as urticaria. Few studies addressed the generation of peripheral sensory neurons (PSNs) from human induced Pluripotent Stem Cells (hiPSCs) aiming in vitro modelling of skin disorders, but the functionality of these cells remain challenging. Human neurons are hard to obtain, but consist in a powerful tool to investigate somatosensory biology and pathology in skin models reconstructed from human epidermal keratinocytes. We developed an efficient protocol to obtain PSNs from hiPSCs, using chemically defined media enriched with small-molecule compounds to achieve efficient differentiation into neurons. These sensory neurons are functional in response to capsaicin, pungent principle of peppers, triggering the release of substance P, a neurotransmitter involved in neurogenic inflammation. After testing neuronal functionality in vitro, measuring expected stimuli responses to different agonists and antagonists such anandamide and rimonabant, we proceeded to the integration of the neurons in the reconstructed human epidermis model. The goal is to reach a model predictivity similar to the human skin in living conditions. In conclusion, this protocol creates a source of human neurons to be used in skin disease modelling, serving as a powerful tool to model human diseases for drug discovery, to deepen our understanding of a key component of the skin physiology and to develop reconstructed a reconstructed human skin model with enhanced neuro-inflammation predictivity to develop products for sensitive and aged skin.