A new insight of skin organoids

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Abstract: Organoids refer to bioengineered small organs that mimic the characteristics and functions of body tissues or organs . The skin is the largest organ of the human body. Designing different skin organoids models can gives researchers a new insights into skin development and disease, potentially revolutionizing drug discovery and opening new approaches to personalized skin care. In this study, we briefly introduce the types of skin organoids, their uses in different fields such as evolutionary biology, disease modeling, regenerative medicine and the progress made in this field.

1. INTRODUCTION

Skin performs wide range of functions including: protection, sensation, and thermoregulation. This organ consists of three layers surrounded by a membrane: epidermis, dermis and hypodermis. The epidermis is composed of connected keratinocytes that produce stratum corneum to resist environmental factors. The dermis is a complex structure that contains mechanoreceptors, sensory nerves, blood vessels, sweat glands and, hair follicles. The hypodermis contains subcutaneous adipose tissue that stores energy and growth factors [1, 2].

Organoids refer to 3D cell cultures that can mimic the specific characteristics of human organs or tissues. The skin organoids discussed in this review are in vitro 3D tissue constructs that contain a variety of skin cells and demonstrate morphological and functional competence as organ replacements [3].

2. TYPES OF BIOENGINEERED SKIN ORGANOIDS

sweat gland organoid

Sweat glands originate from epidermal stem cells during embryonic development and consist of a duct portion and a secretory portion surrounded by myoepithelial cells that contribute to sweat secretion [4, 5]. By using 3D bioprinting techniques, mesenchymal stem cells can be differentiated into mouse sweat glands, and this differentiation leads to the repair of damaged sweat glands in the body after organoid transplantation [6].

Hair follicle organoid

One of the common approaches to achieve human hair follicle formation in vitro involves combining dermal papilla cells with epithelial components. Isolated human dermal papilla cells can partially recover their inducibility when grown as spheroids, leading to the induction of human hair follicle neogenesis [7].

Vascularized skin organoid

Due to the lack of an efficient vascular system for the exchange of substances, the organoids do not overgrow. It is very important for the proliferation of cells, the internal structure of organs, the regeneration of intercellular communication and blood vessels. Therefore, vasculature is essential for the use of skin organoids in wound healing as well as long-term culture [8, 9]. Self-assembly of vascular cells to form new blood vessels is called vasculogenesis. Co-culture of organoids with vascular cells is a good method to introduce blood vessels in different organoids, including liver organoids [10].

Sebaceous gland organoid

In a complex skin organoid following organogenesis, sebaceous glands were observed after approximately 140 days of incubation, along with the presence of hair follicles [11]. However, it is difficult to produce human sebaceous gland organoids alone. One approach involves the use of immortalized cell lines [12].

4. USES OF SKIN ORGANOIDS

Organoids provide a powerful platform, researchers can artificially manipulate cell populations and cell environments, greatly contributing to the study of a diverse range of physiological and pathological contexts [13, 14].

Developmental biology

Examining the effects of microenvironment and cell-to-cell interactions on stem cells during skin development is one of the future research avenues. Epidermis induction involves various signaling pathways, including Wnt, FGF, and BMP, which induce early differentiation of ectodermal and mesenchymal cell lineages. Although the role of developmental cues has been studied in mice, few studies directly examine these cues in human skin development [15-18].

Disease modeling

To investigate structural and cellular changes in human skin under different conditions, organoids are versatile tools and provide detailed studies on the effects of different interventions at the cellular level. In addition, the cells derived from the patient are used in the production of skin organoids, which provide researchers with the possibility of personalized treatments and drug screening, and are very valuable in clinical applications [19].

Regenerative medicine

Skin damage caused by burns or surgery can have negative effects on the human psyche [20]. To study wound healing in laboratory conditions, skin organoids are good models that researchers use to examine biophysical and biochemical signs without the need to use animals [21].

Human face skin transplant, which is a form of removing tissue from other parts of the body and transplanting it to the face, can lead to immune system rejection and wounds due to its different function from facial skin tissue [22]. In recent years, the use of skin organoids derived from hiPSCs has been proposed for facial repair and skin regeneration. This approach greatly reduces scar formation and provides a valuable model in the field of regenerative medicine [22, 23].

Alopecia is a common disease that affects both men and women worldwide and significantly affects their physical appearance. Fortunately, skin organoids offer a promising solution for treating alopecia and restoring natural hair growth [11].

5. CONCIUSIONS

In summary, skin organoid models provide a deeper understanding of how human skin forms and fetal skin develops. Technical advances in the field of organoids allow us to achieve a variety of organoid cultures, from simple in vitro cultures to complex systems involving the epidermis, dermis, and skin appendages. This advance in skin organoids is expected to provide new insights into the field of human skin.

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