



Electricity auto-generating skin patch promotes wound healing process by activation of mechanosensitive ion channels

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ARTICLE INFO

Keywords:

Wound healing
Electricity generation
Enzymatic biofuel cell
Ion channel
Piezo1

ABSTRACT

Electricity constitutes a natural biophysical component that preserves tissue homeostasis and modulates many biological processes, including the repair of damaged tissues. Wound healing involves intricate cellular events, such as inflammation, angiogenesis, matrix synthesis, and epithelialization whereby multiple cell types sense the environmental cues to rebuild the structure and functions. Here, we report that electricity auto-generating glucose-responsive enzymatic-biofuel-cell (EBC) skin patch stimulates the wound healing process. Rat wounded-skin model and *in vitro* cell cultures showed that EBC accelerated wound healing by modulating inflammation while stimulating angiogenesis, fibroblast functionality and matrix synthesis. Of note, EBC-activated cellular behaviors were linked to the signalings involved with calcium influx, which predominantly dependent on the mechanosensitive ion channels, primarily Piezo1. Inhibition of Piezo1-receptor impaired the EBC-induced key functions of both fibroblasts and endothelial cells in the wound healing. This study highlights the significant roles of electricity played in wound healing through activated mechanosensitive ion channels and the calcium influx, and suggests the possibility of the electricity auto-generating EBC-based skin patch for use as a wound healing device.

1. Introduction

Human body and tissue generate electrical signals, which is considered a natural phenomenon to maintain homeostasis [1–3]. When tissues or cells in the body experience a loss of anatomical integrity or are exposed to toxin, homeostatic imbalance occurs and inherent electrical cues are also impaired [4,5]. Thus, applying electrical stimulus has been considered an effective way of accelerating tissue repair and regeneration in preclinical and clinical settings by modulating intracellular

biophysical/biochemical signals (*i.e.* ions transport, action potential, secretomes, etc.), ultimately dictating various cell functions [6,7]. For example, medical devices used for nerve and heart apply electricity for the purpose of rehabilitation, regeneration, and repair of tissue and organ functions [8]. A recent development of implantable-wireless electricity generator is a notable example of providing electrical cue that is cariable without an external connection.

Wound healing is also merited by the electrical cues. Skin is considered a sort of natural battery [9], and wounding is a breakdown of

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