

Wound Pathophysiology: Insights of Ca²⁺ Signalling and Cellular Senescence Mechanisms in Healing and Regeneration

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Abstract

Cellular senescence and calcium signalling are interrelated phenomena of cellular events. As, cellular senescence is associated with stress, alongside it, intracellular calcium signalling has a concern with cellular senescence. Henceforth, both events participate in wound regeneration and governed few of its phases (re-epithelialization, tissue remodelling, inflammation and granulation). Despite it, mitochondrial Ca²⁺ uptake influences the phenomena of fibroblast and myofibroblast differentiation. Quantitative imaging and computational modelling expose hidden features of calcium signalling route. A proper investigation of the role of calcium in specific senescence-associated routes and physiopathological conditions will expose forefront of calcium signalling and its association with cellular senescence.

Keywords

Inflammation • Epithelialization • Autophagy • Epithelial cells • Tissue remodeling

Description

The phenomenon of intercellular communication is a key feature of a cellular system in the pathophysiology conditions for the transfer of various messages. The pharmacological molecules influence the above-referred communication by hindering the release of some factors that play a part in these communications [1]. Senescent cells participate in many phenotypic alterations such as metabolic reprogramming, and autophagy modulation. Therefore, the senescent cells govern many physiological and pathological processes, as well as participate in anti-senescent therapies [2]. After wounding, epithelial cells communicate via cell-cell communication and coordinate with the migrant cells. Here, the injury-induced sustained Ca²⁺ travel between cells and generate communication within the wound edge and prevent further injuries and associated with changes in cell morphology (Figure 1).

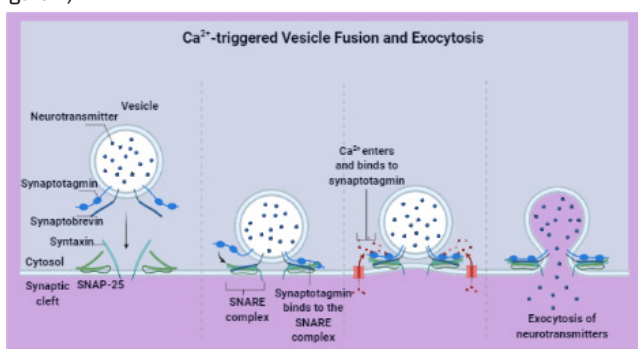


Figure 1. Illustrate the phenomenon of Ca²⁺ signaling in cellular events. "Adapted and created with permission from [biorender.com] and acknowledged.

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The role of skeletal muscle in regeneration is pivotal where interminably the muscle plasticity initiates the mechanism, thus, it is there as an essential element to regulate activities according to specific signalling mechanisms transpired within to govern various pathways and interrelated mechanisms [3]. By elucidating these signalling and other inter concerned, mechanisms, there is a possibility to find out the answer for the query, how calcium signalling regulates skeletal muscle development, homeostasis, and regeneration. Besides it, the calcium dynamics and calcium-dependent play a crucial role in these mechanisms [4]. It is a well-known fact that calcium governed myoblast proliferation and differentiation in growth. In an emergency, the injury-induced calcium signalling deals with originating harsh conditions. The most important phenomena of calcium signalling and cellular senescence ensued to initiate the satellite cells to participate in the aforementioned signalling pathways to inductee muscle regeneration [5]. It is a challenging task to decode these pathways in which the multiple spatial and temporal scales take part in all these signalling processes [6]. Here, the main component is the epithelial cells that can interpret these routes (Figure 2).

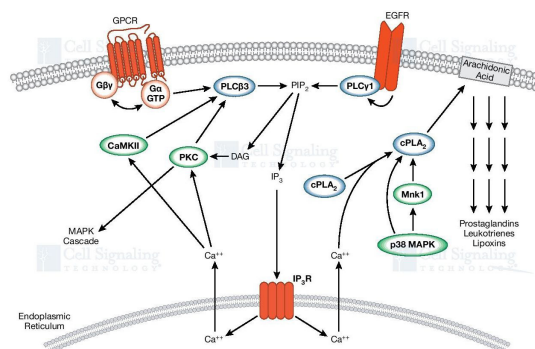


Figure 2. Calcium signaling and cellular senescence, receptor non receptor tyrosine kinases during activation. Members of the PLCβ subfamily are activated by α- or βγ-subunits of proteins and play an important role in signaling cascades.

The importance of calcium signalling is highlighted here because it regulates many featured activities in the cellular process, i.e., division, differentiation, migration, and death [7]. Therefore, the insights of these multiple signalling mechanisms that were transduced by calcium transients in the generation of epithelial tissues, are essential [8]. Using modern techniques, i.e., quantitative imaging and computational modelling, it is possible to expose different features of calcium signalling. These findings will boost the research efforts that are necessary for developing regenerative medicine. In wound repair, several cell signalling pathways are there to contribute and complete it, but calcium signalling predominantly participates

in it [9]. The epidermal cell migration and regeneration patterns are there to follow until the final stage is not achieved. At this point, the author underlined the important role of calcium signalling and how it influenced cell migration, and remodelling, same is explained in this section in brief (Figure 2). Besides it, the other interrelated factors are not yet exposed nor investigated in detail [10]. But, it is clear from the discussion that the role of calcium and its management is important in healing of wounds.

The role of the molecular and cellular mechanisms of cellular senescence is critical in calcium signalling and how it controlled it, explained by conducting extensive research that helped in detecting concerned pathways and routes [11]. Scientifically, it is proved that cellular senescence has a key involvement and is interlinked to age-related diseases. It has also been acted to stabilize the proliferation arrest tempted by many stresses [12]. Recently, it was reported that the calcium signalling participates in the form of a key promoter in all routes of cellular senescence, and it was also evidenced that the rise and fall in the concentration of intracellular calcium levels affected cellular senescence [13]. When any disease persists, to encounter it, the cells generate various movements on cellular environment for altering the local environment to remodel cellular metabolism [14]. Further, a decrease in mitochondrial Ca^{2+} uptake also affected metabolic remodelling, and alters gene expression associated with the processes of fibroblast and myofibroblast differentiation.

Conclusion

Damage-associated molecular patterns communicate among damaged cells/tissues and neighbouring healthy cells. During these changes and computations, ATP receptors monitor damages activate a Ca^{2+} channel in the surrounding healthy cells, and propagate further according to the release and diffusion model that stop harmful inflammatory responses. Therefore, these findings will be helpful in the identification of specific features of cells *in vivo* to be considered during the planning of strategies for altering senescence features for therapeutic for healing chronic tissue senescence. Overall, the quickly tempted senescence is helpful for regeneration and acute wound repair. The author underlined the importance of planned strategies for managing senescence in chronic wounds and interrelated cutaneous pathologies depending on the physiological conditions.

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