INVESTIGATION OF MITOCHONDRIAL NETWORK IN KERATINOCYTES WITH PSORIATIC PHENOTYPE

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Psoriasis is an inflammatory skin disease whose pathogenesis is driven by IL-17, IL-22, and TNF-α, which potently activate keratinocytes, causing hyperproliferation and abnormal differentiation [1]. Adaptive responses to psoriasis involve alterations in mitochondrial morphology, reflecting dynamic cellular adaptation based on external stimuli [2]. Therefore, mitochondrial dysfunction leads to inflammation and potential damage to the cell [3].

This study aims to investigate how the morphology of mitochondria in human keratinocytes (HaCaT) is affected by individual cytokines (IL-17, IL-22, and TNF-α) and cytokine mixture with 1, 3, and 24-hour stimulation time.

Two study groups of keratinocytes included treatment of individual cytokines and cytokine mixture. Mitochondrial morphology was analyzed using Live Mito Orange, STED nanoscopy, and fluorescence microscopy with Zeiss Axio Observer.Z1. A quantitative analysis of mitochondrial morphology was performed with the mitochondrial network analysis toolset (MiNA) in Fiji [4].

Cytokine mixture reduced mitochondrial area, branch lengths, and number of network branches, which is characteristic of mitochondrial fragmentation. Analysis of the impact of specific cytokines revealed IL-22 and TNF-α as the primary effectors in changing mitochondrial morphology. However, the cytokine mixture caused more pronounced changes, suggesting synergistic effects, that amplify the loss of network integrity. Furthermore, the most significant changes were seen after 1 hour of incubation, and although a significant decrease persisted after 24 hours, the trend indicated a restoration toward the baseline level.

The study results show that psoriatic phenotype-inducing cytokines cause the fragmentation of mitochondria in keratinocytes, where IL-22 and TNF-α play a crucial role. Further investigation of mitochondrial changes occurring in psoriasis under inflammatory conditions can offer valuable insights into the diseaseś pathogenesis.

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