

TIME-DEPENDENT EFFECTS ON MITOCHONDRIAL FUNCTIONS INDUCED BY PSORIASIS-LIKE INFLAMMATION IN HUMAN KERATINOCYTES AND FIBROBLASTS

Martyna Uldukytė¹, Gabrielė Kulkovienė^{1,2}, Ramunė Morkūnienė², Aistė Jekabsone^{1,3}

¹Laboratory of Pharmaceutical Sciences Institute of Pharmaceutical Technologies, Lithuanian University of Health and Sciences, Kaunas, Lithuania

²Department of Drug Chemistry, Faculty of Pharmacy, Lithuanian University of Health and Sciences, Kaunas, Lithuania

³Preclinical Research Laboratory for Medicinal Products Institute of Cardiology, Lithuanian University of Health and Sciences, Kaunas, Lithuania
martyna.uldukyte@stud.lsmu.lt

Psoriasis is a chronic inflammatory skin disease driven by excessive keratinocyte proliferation, psoriatic fibroblasts, and key cytokines such as TNF- α , IL-17, and IL-22 [1]. *In vivo* studies have shown that mitochondrial dysfunction, marked by increased ROS production and metabolic alterations, plays a critical role in psoriasis progression [2]. It has been discovered that skin cells exhibit different sensitivities to psoriasis inflammation, with keratinocytes showing a more immediate and intense response than fibroblasts [3]; however, the underlying mechanisms of these mitochondrial responses remain insufficiently investigated.

The aim of this study is to examine the impact of psoriasis-like inflammation (PLI) on mitochondrial functions in human keratinocytes and fibroblasts over 24, 48, and 72 hours, specifically assessing mitochondrial membrane potential, mtROS production, and cellular respiration.

PLI was induced by treating keratinocytes and fibroblasts with a cytokine mixture consisting of TNF- α , IL-17, and IL-22. Mitochondrial membrane potential and mtROS levels were assessed at 24, 48, and 72 hours using TMRM and MitoSox Red staining, respectively, with fluorescence microscopy performed on an Olympus APX100 microscope and image analysis conducted via Fiji software. Cellular respiration was measured at 24 and 72 hours using the Seahorse XFp Analyzer and Mito Stress Test Kit, with data normalized to total protein content using the Bradford assay and analyzed with the Infinite 200 Pro Nano Plex reader.

The results demonstrated that keratinocytes exposed to PLI exhibited a transient increase in mitochondrial membrane potential at 24 and 48 hours, accompanied by a peak in mtROS production at 24 hours that remained stable thereafter. These mitochondrial alterations were linked to significant reductions in cellular respiration, and glycolytic activity at 24 hours, all of which returned to baseline levels by 72 hours. In PLI-treated fibroblasts, mitochondrial membrane potential increased at 24 hours but normalized by 72 hours, alongside a progressive rise in mtROS production that reached its peak at 72 hours. Unlike keratinocytes, fibroblast cellular respiration and glycolysis remained stable initially but showed a decline in respiration and an increase in glycolytic efficiency at 72 hours.

This study reveals that PLI induces distinct time-dependent mitochondrial responses in keratinocytes and fibroblasts, with rapid dysfunction in keratinocytes and delayed impairment in fibroblasts, providing insights into mitochondrial mechanisms in psoriatic skin cells and potential therapeutic targets for restoring mitochondrial homeostasis.

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