Phosphokinome Profile Of Human Keratinocyte Metabolic Reprogramming To Different Stressors

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Biochemical and mechanical properties of skin are important for protection against diverse types of stress. Among the different skin cells, in keratinocytes, the stress induces signal transduction pathways involving differentiation, senescence and programmed cell death. Most of these cellular processes are regulated by protein kinases via phosphorylation of specific tyrosine, serine, and threonine residues. Therefore, the goal of this work was to define the phosphoproteome profile of human keratinocytes (HaCaT cells) in response to 3 types of stress, using peptide arrays (PepChip). We evaluated the *in vitro* phosphorylation of peptide arrays exhibiting the majority of PhosphoBase-deposited protein sequences on lysates from HaCaT cells submitted to hyperosmotic stress (1.0 mol/L sorbitol for 2 h), oxidative stress (2.0 mol/L H_2O_2 for 4 h) and UVA exposure (5.0 J/cm² for 50 min). Protein kinase C was mainly activated by all types of stress. Interestingly, when the hyperosmotic and oxidative conditions were compared, a set of protein kinases displayed higher activity: Janus kinase 1, Src, protein kinase A, fibroblast growth factor receptor 3, casein kinase 2 and death-associated protein kinase 1. Our findings clearly indicate a kinome-based metabolic reprogramming mediating survival and death processes in keratinocytes exposed to different stressors. Besides, under kinomic aspect, the response of these cells to hyperosmotic and oxidative stimuli is apparently similar.

Key words: oxidative stress, hiperosmotic stress, UVA, phosphokinome, keratinocytes.

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