PHOTOBIOLOGY AND PHOTOPROTECTION

IMPACT OF NIACINAMIDE ON KERATINOCYTE METABOLISM AND STRESS RESPONSE UNDER PHYSIOLOGICALLY RELEVANT OXYGEN TENSION CONDITIONS.

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Introduction: In contrast to dermis, skin's epidermis is devoid of a direct vasculature network. Gas and metabolite exchange are dependent on active and passive diffusion from the dermis or from the environment. Oxygen tension levels were evaluated to ensure in vitro models were at physiologically relevant conditions for mechanistic based research and technology screening.

Objective: Evaluate impact of O2 on metabolism in keratinocytes and under stress conditions. Additionally, evaluate niacinamide's (Nam) effect on metabolism and under metabolic and inflammatory stress.

Materials and Methods: Keratinocyte monolayer cultures were grown at 5% and 20% O2 and cellular metabolism was measured in Seahorse Flux Analyzer. Cultures were treated with Nam to monitor impact on basal metabolism and under stress conditions (Mitostress and Glycostress). Solar simulated radiation (SSR) was used to induce inflammation and measured by PGE2 synthesis.

Results: Keratinocytes grown at 5% O2 have decreased mitochondrial activity and under stress a lowered ability to produce ATP as measured by spare respiratory capacity (SRC). Keratinocytes compensate for this decrease by increasing basal glycolysis. Under stress conditions, there is an increase in glycolysis but a loss of glycolytic reserve, presumably due to need for glycolysis to run at capacity to produce ATP. Treatment with Nam increases mitochondrial function, both on basal as well as SRC and increases basal glycolysis and under stress. SSR significantly increases PGE2 levels at 5% O2, Nam treatment significantly mitigates the increase.

Conclusions: Skin's epidermis is exposed to a range of 3-7% O2 compared to ambient levels of 20% O2. In vitro models grown at this lower oxygen tension should be more predictive of in vivo. As predicted, keratinocytes grown at 5% O2 show greater reliance on glycolysis compared to metabolism at 20%. Nam treatment can enhance basal metabolism

as well as rescue from stress induced alterations on metabolism and inflammation.