Scientific rationale underlying the use of nicotinamide in actinic keratosis

R. Di Caprio¹, A. Balato², N. Balato¹, S. Lembo³, G. Monfrecola¹

¹Department of Clinical Medicine and Surgery, University of Naples Federico II, Italy

²Department of Advanced Biomedical Sciences, University of Naples Federico II, Italy

³Department of Medicine, Surgery and Dentistry, Scuola Medica Salernitana, University of Salerno, Italy

INTRODUCTION:

Besides its known activity in the promotion and progression of non-melanoma skin cancers (NMSCs), cyclooxygenase (COX-2) plays also an important role in modulating inflammatory processes, representing an important link between chronic inflammation and carcinogenesis. Indeed, nicotinamide (NCT), the amide active form of Vitamin B3, has proven to have anti-inflammatory and cancer protection properties, being able to reduce actinic keratosis formation as well as basal- and squamous-cell cancer rate in NMSCs high-risk patients.

AIM OF THE STUDY:

to investigate whether NCT was able to modulate UVB-mediated COX-2 expression in immortalized keratinocytes

MATERIALS AND METHODS:

Immortalized human keratinocytes were pre-incubated with different doses of NCT (0.1, 2.5 and 10mM) for 2h and irradiated in PBS with UVB 10 and 60mJ/cm². Immediately after irradiation, PBS was removed and replaced with the culture medium containing NCT at the above indicated concentrations. COX-2 gene expression was assessed after 6 and 24h, whereas protein levels were measured in cell lysates 24h after irradiation.

RESULTS

The selected *in vitro* doses of NCT of 0.1 and 2.5mM were calculated to approximately reproduce 10 times lower and 2 times higher doses of NCT plasma levels that can be obtained in humans after very high dose oral NCT. UVB dosages were chosen taken into account that they represent the right balance between cell viability (a) and a translational impact since mean UVB minimal erythema dose for a healthy population coming from our area (Southern Italy) is 75.3 mJ/cm²

Pre-incubation for 2h with NCT 0.1, 2.5 as well as 10 mM, strongly down-regulated COX-2 mRNA and protein 24h after irradiation with UVB 10 mJ/cm² (b, d). Irradiation with UVB 60 mJ/cm² resulted in a lower COX2 increase, nevertheless NCT was able to reduce its expression (c). Moreover, NCT treatment at high concentrations without UVB irradiation was able to decrease COX-2 (d).

CONCLUSIONS:

Taken together, these data add another important *tessera* to the complex mosaic of vitamin B3 action mechanism, confirming our hypothesis that NCT efficacy against UV-induced skin damages could occur through COX-2 modulation