SKIN CANCER (OTHER THAN MELANOMA)

NICOTINAMIDE REDUCES ULTRAVIOLET-INDUCED DNA DAMAGE IN HUMAN SKIN: EX VIVO IMMUNOFLOURESCENCE STUDY AND CLINICAL OUTCOME OF NON-MELANOMA SKIN CANCER PATIENTS

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Introduction: Ultraviolet (UV) radiation is the main extrinsic factor causing skin cancers; the photocarcinogenetic process involves oxidative DNA damage and photochemical reactions. Nicotinamide (NAM), the active amide form of vitamin B3, is a precursor of nicotinamide adenine dinucleotide (NAD+), the only substrate for the DNA-repair enzyme poly-ADP-ribose polymerase. NAM enhances DNA repair in UV-irradiated HaCat keratinocytes and ex vivo human skin, probably due to its ability to prevent UV-induced ATP depletion. However, a precise description of NAM effects on human skin isolated from non-melanoma skin cancers (NMSCs) patients is still pending.

Objective: To investigate NAM effects in reparation of UV-induced DNA damage on photodamaged ex vivo skin obtained from NMSCs patients. We correlated experimental data with clinical outcomes of the skin-donor patients, treated with oral NAM.

Materials and Methods: Full-thickness biopsies from photodamaged skin surrounding NMSCs and actinic keratosis (AKs) obtained from 10 patients were cultured for 24h in DMEM 10% FBS with or without NAM 50μM. Then, we investigated the immunofluorescence expression of Cyclobutane pyrimidine dimers (CPDs) and OGG1 (markers of DNA damage and oxidative stress, respectively). The same patients received oral NAM (250 mg twice daily) for 12 months.

Results: Non-treated ex vivo human skin expressed both OGG1 and CPDs in the cytoplasm of granular layer keratinocytes. Conversely, both antigens were absent after treatment with NAM. Clinical data showed a significant reduction in AKs count and new NMSCs during the treatment period, without side effects.

Conclusions: This is the first study investigating NAM effects on DNA repair of human photodamaged skin surrounding AKs and NMSCs. We suggest that NAM can reduce UV-

induced DNA damage in keratinocytes from skin areas near to NMSCs and AKs. Moreover, oral NAM significantly reduced premalignant AKs and new NMCS in the same patients, suggesting its role as chemopreventive agent.