Carcinogenesis. 2013 May;34(5):1144-9. doi: 10.1093/carcin/bgt017. Epub 2013 Jan 24.

Nicotinamide enhances repair of ultraviolet radiation-induced DNA damage in human keratinocytes and ex vivo skin

Devita Surjana [1], Gary M Halliday, Diona L Damian

Affiliations

Affiliation

1 Department of Dermatology, Sydney Cancer Centre, Bosch Institute, University of Sydney at Royal Prince Alfred Hospital, Camperdown, Sydney, NSW 2006, Australia.

PMID: 23349012 DOI: 10.1093/carcin/bgt017

Abstract

Nicotinamide (vitamin B3) protects from ultraviolet (UV) radiation-induced carcinogenesis in mice and from UV-induced immunosuppression in mice and humans. Recent double-blinded randomized controlled Phase 2 studies in heavily sun-damaged individuals have shown that oral nicotinamide significantly reduces premalignant actinic keratoses, and may reduce new non-melanoma skin cancers. Nicotinamide is a precursor of nicotinamide adenine dinucleotide (NAD(+)), an essential coenzyme in adenosine triphosphate (ATP) production. Previously, we showed that nicotinamide prevents UV-induced ATP decline in HaCaT keratinocytes. Energy-dependent DNA repair is a key determinant of cellular survival after exposure to DNA-damaging agents such as UV radiation. Hence, in this study we investigated whether nicotinamide protection from cellular energy loss influences DNA repair. We treated HaCaT keratinocytes with nicotinamide and exposed them to low-dose solar-simulated UV (ssUV). Excision repair was quantified using an assay of unscheduled DNA synthesis. Nicotinamide increased both the proportion of cells undergoing excision repair and the repair rate in each cell. We then investigated ssUV-induced cyclobutane pyrimidine dimers (CPDs) and 8-oxo-7,8-dihydro-2'-deoxyguanosine (8oxoG) formation and repair by comet assay in keratinocytes and with immunohistochemistry in human skin. Nicotinamide reduced CPDs and 8oxoG in both models and the reduction appeared to be due to enhancement of DNA repair. These results show that nicotinamide enhances two different pathways for repair of UV-induced photolesions, supporting nicotinamide's potential as an inexpensive, convenient and non-toxic agent for skin cancer chemoprevention.

Other Literature Sources

The Lens - Patent Citations