Radiation response related to inflammation and differentiation in human skin*

J. Wiedemann[1,2], *P. Simoniello*[1], *E. Thönnes*[1], *A. Benzer*[1], *M.Durante*[1,2], *M. Kovacs*[4], *M. Podda*[4], *and C. Fournier*[1,3]

[1]GSI, Darmstadt, Germany; [2]TU Darmstadt, Germany; [3]Hochschule Darmstadt, Germany; [4]Department of Dermatology, Darmstadt Hospital

Introduction

The balance between apoptosis, proliferation and differentiation is important for the homeostasis of healthy skin [1]. In psoriatic skin this balance is disturbed and shifted in the direction of proliferation [2].The symptoms of psoriasis can be alleviated by irradiation with low intensities of UV-light [3] or low doses of ionizing irradiation, such as alpha-particels emitted from a radon source [4]. These effects of UV exposure in skin are quite well understood [3], whereas alterations in skin induced by low doses of ionizing irradiation which explain the clinical effectiveness of radon treatments remain to be elucidated.
We investigated if irradiation with low and clinically used fractionated doses shifts the disturbed balance of apoptosis, proliferation and differentiation back to a normal level by enhancing apoptosis and/or reducing proliferation.

Material and Methods

Human full-thickness skin equivalents (EFT400; MatTek; Ashland) were irradiated using low versus high and single versus fractionated X-ray doses. Samples were fixed 3 days after irradiation and processed for immunohistchemistry. Proliferation was assessed microscopically and Ki67$^+$ cells per field of view were counted. To analyse the status of differentiation sections were stained with Hematoxylin and Eosin.

Results and Discussion

Histological analysis (H&E staining) shows that after low dose X-ray irradiation the basal cells loose their palisadic shape and become more rounded up. This effect is more pronounced after a single dose of 0,5 Gy compared to a fractionated irradiation with 3x 0,17 Gy. The cobblestoned morphology can be related to proliferation of the basal cells which can be a sign of a faster or impaired differentiation process. An enhanced proliferation in the basal layer after a low dose of irradiation could be confirmed by quantification of Ki67 (Figure 2) but was not observed for high X-ray doses like 10 Gy (data not shown). Interestingly, also for a fractionation of 0,5 Gy in 3 doses of 0,17 Gy this effect didn't occure pointing to that a single treshold dose has to be delivered to trigger proliferation .
In addition to the observed changes in morphology of the basal cells which have an impact on tissue organisation and

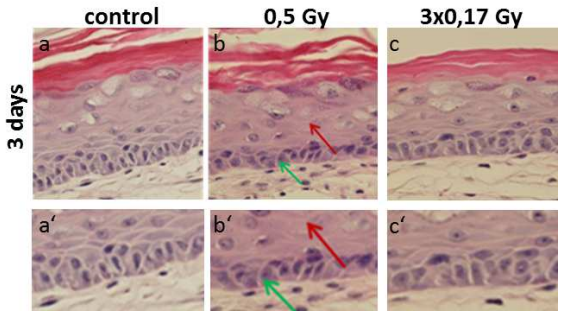

Figure 1: H&E staining of sections from skin equivalents. Changes in the shape of the basal cells (green) and the stratification (red) are indicated with arrows. Pictures a' to c' show a magnification of the basal cells

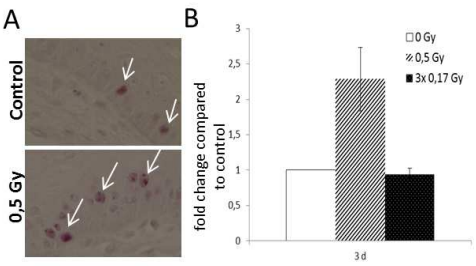

Figure 2: (A) Ki67 staining of skin equivalents. Proliferating cells are labeled in pink and indicated with an arrow. (B) Statistical analysis of Ki67 staining

the enhanced proliferation for a low X-ray dose we could show in previous studies that there is no enhancement of cell death (apoptosis and necrosis) after low dose of irradiation. This argues against a irradiation induced shift to enhanced apoptosis and reduces proliferation after low doses. These effects has to be further investigated in a model system which mimics the inflammatory state of psoriatic skin.

References

[1] P. Kolarsick et al.,J Dermatol Nurses Assoc, Volume 3, 2011

[2] M. Lowes et al., NATURE Vol 445—22 February 2007, doi:10.1038/nature05663

[3] K. Stein., J Dermatolog Treat.. 2008; 19: 141–145

[4] P. Deetje et al., Verlag Dr. Kovac, 2005

* Work supported by GREWIS No. 02NUK017A; DFG (GRK 1657) and HGS-HIRe.

DOI:10.15120/GR-2015-1-APPA-HEALTH-26