Visualization of DNA double-strand breaks induced by heavy ions in murine tissues

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DNA double-strand breaks (DSBs) constitute the most lethal and hence the biologically most significant damage in response to ionizing radiation (IR). Particle radiation results in DNA damage that is more complex than the damage evoked by photon radiation, therefore these DSBs are repaired with much slower kinetics [1].

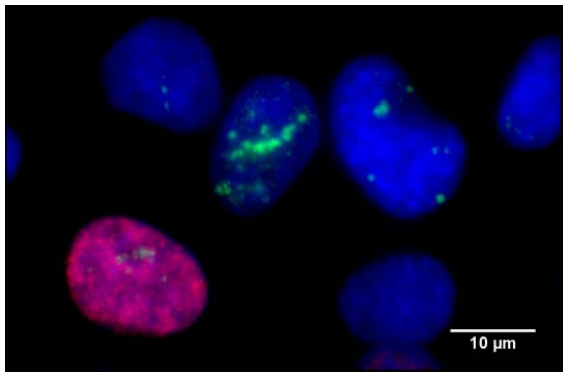
As part of the GREWIS project, the goal of this study is the biodosimetric measurement of inhaled radon gas in different mouse tissues. Radon (Rn-222) is a radioactive noble gas that has been used for its therapeutic anti-inflammatory effects in Central Europe for over a century. Patients with painful inflammatory or degenerative joint and spine diseases are treated in radon therapy caves in Bad Gastein and Bad Kreuznach [2]. During the radioactive decay of radon and radon progeny, three biologically relevant α-particles are emitted. In this project, the goal is to detect α-particle induced DSB tracks in various murine tissues to gain insight into the diffusion patterns of radon gas inside the body and information about potential accumulation in specific organs.

An ^{241}Americium source was used for preliminary *in vitro* experiments with α-particles. Due to the low penetration depth of α-particles, HeLa cells were seeded on Mylar® polyester film (2 µm thickness). The cells were irradiated with up to 300 mGy, and α-particle induced DNA DSBs were visualized by γH2AX immunofluorescence staining. We were able to successfully visualize tracks of DNA DSBs in HeLa cells after α-particle irradiation (Fig. 1 A).

Prior to *in vivo* radon experiments, wild type C57BL/6 mice were irradiated with low fluence carbon ions at the GSI particle accelerator. This experiment served as a positive control to assess the staining efficacy of heavy ion induced DNA DSB tracks in various murine tissues. Using 53BP1 immunofluorescence staining, paraffin embedded sections of murine brain tissue was analyzed. We were able to visualize ion tracks in brain tissue, especially in the granular cell layer of the cerebellum, as this region contains very densely packed cell nuclei (Fig. 1 B).

Future efforts will focus on the visualization and quantification of carbon ion induced DNA DSBs in other murine tissues, such as lung, kidney, and intestine. Upon completion of the radon exposure chamber, *in vivo* radon experiments will be conducted.

A) α-particle tracks in HeLa cells



B) Carbon ion tracks in murine brain tissue

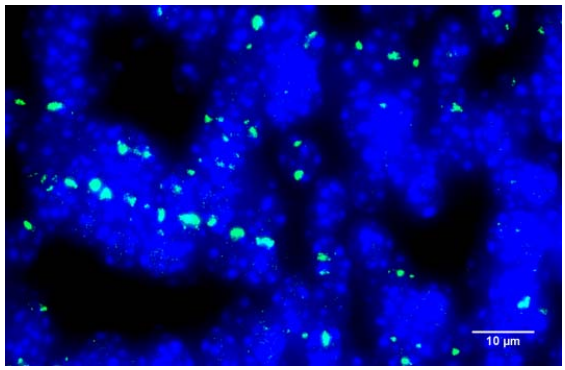


Fig.1: Visualization of DNA DSBs: (A) γH2AX foci in HeLA cells after α-particle irradiation. (B) Tracks of 53BP1 foci in murine brain tissue (granular cell layer of the cerebellum) after carbon ion irradiation.

References

[1] R. Okayasu. Int. J. Cancer:130 (2012) 991-1000
[2] K. Becker. Int. J. Low Radiation Vol. 1 (2004) 334-356

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