Insights in the molecular basis of a reduced lymphocyte adhesion to irradiated and stimulated primary endothelial cells *

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We reported previously a radiation induced lowered adhesion of immune cells on hybrid endothelial cells (EA.hy.926) as a model of the inner layer of the blood vessel walls [1], which is one possible modification of inflammatory processes in the treatment of chronic inflammatory diseases [2]. Recently, we could further show a relationship between metabolic ROS accumulation and modification of adhesion at low doses in the EA.hy.926 endothelial cell line [3]. We now measured the adhesion of immune cells to primary endothelial cells and assessed NFκB nuclear translocation as a putative molecular basis implicated in the lowered adhesion.

X-ray irradiation (250 kV, 16 mA) of primary endothelial cells (HMVEC) and adhesion assay to TNF-α treated HMVEC was performed with isolated peripheral blood lymphocytes (PBL) according to [1]. TNF-α induced NFκB signalling was analysed in parallel by quantification of the nuclear p65 translocation. Figure 1 shows that the adhesion of non-irradiated PBLs to HMVEC is enhanced by inflammatory TNF-α treatment, whereas the adhesion is reduced in the low dose range (0.1−0.5 Gy) 24h after X-ray exposure. In the presence of TNF-α, non-irradiated EC show nuclear translocation of p65 (not shown), but irradiation did not modify this (Figure 2).

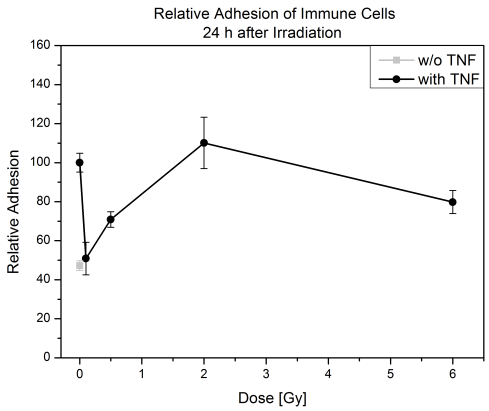

Figure 1: X-ray induced reduced adhesion of PBL to stimulated HMVEC under static conditions normalized to non-irradiated HMVEC. The response for non-stimulated HMVEC is shown as a comparison.

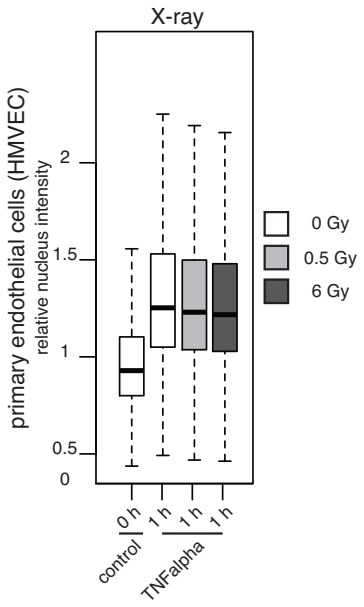

Figure 2: Activation of NFκB signalling via nuclear translocation of p65 in TNF-α stimulated HMVEC 1h after X-ray exposure, normalized to stimulated and non-irradiated HMVEC.

These results confirm that low dose X-ray exposure of primary EC reduces the adhesion of PBL to EC, but rather based on ROS accumulation than on modification of NFκB nuclear translocation.

References

[1] Erbeldinger et al., GSI annual report, 2013

[2] Rödel et al. (2007), IJRB83(6): 357-366.

[3] Large et al. Radiat Oncol (2014), 9:80

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