RADIOPROTECTION OF MOUSE CNS ENDOTHELIAL CELLS *IN VIVO.*

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Abstract

Radioprotection using the minor groove binding DNA ligand Hoechst 33342 has been demonstrated *in vitro*, and more recently *in vivo*, in mouse lung (1). Intravenous administration was used for the lung studies, and both endothelial and alveolar epithelial cells showed good up-take. Radiation damage to the endothelial cell population has also been postulated as important in late developing radionecrosis of spinal cord and brain. Endothelial cell density in brain can be readily determined by a fluorescent-histochemical technique. Treatment with a monoamine oxidase inhibitor and subsequent injection with L-DOPA results in an accumulation of dopamine (DA) in CNS endothelial cells. DA is converted to a fluorophore by exposure to paraformaldehyde, and cell numbers assayed by fluorescence microscopy.

Earlier studies used this technique to monitor post-irradiation changes in endothelial cell density in rodent brain and showed the loss, within 24 hours, of a sensitive subpopulation comprising about 15% of the endothelial cells (2). Ten minutes after intravenous injection of Hoechst 33342 (80mg/kg) the ligand is confined by its limited penetration to the endothelial cells in mouse brain. When we irradiated at this time, there was protection against early endothelial cell loss. Ablation of the sensitive subpopulation in unprotected mice takes place over a dose range of 1 to 3 Gy γ-rays, but doses between 12 to 20 Gy are required in the presence of ligand. This protection equates to a very high dose modification factor of about 7 and possibly reflects a suppression of apoptosis in the sensitive endothelial subpopulation.

The extent to which there is enhanced survival in the endothelial population as a whole and how the observed protection affects late CNS necrosis development has yet to be determined. However present results clearly show potential for the use of DNA-binding radioprotectors with limited penetration for investigations into the relative significance of endothelial and parenchymal damage in normal tissues responses to ionising radiation.

References

1. Martin et al, *Brit. J. Cancer* **74**, S99-S101(1996)
2. Lyubimova et al, *Brit.J Radiol.* **64**, 934(1991)