MODIFICATION OF RADIATION DAMAGE IN MOUSE LUNG BY DNA-BINDING RADIOPROTECTORS

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Abstract

The limited diffusion of Hoechst 33342 through cell layers, which has been exploited in mapping the location of cells in multi-cellular spheroids (1), and *in vivo* (2), reflects a general characteristic of DNA-ligands. This property may confer special advantages on DNA-binding radioprotectors in the context of radiotherapy, where it is important to minimise delivery of the radioprotector to the tumour. For example, one might expect limited diffusion to capillaries and systemic uptake following topical application to epithelial cells, which can be dose-limiting tissues in radiotherapy. These potential applications will require delivery of sufficient concentrations of the DNA-binding radioprotectors to cells *in vivo*. In this context, the findings of Young and Hill (3), who could not detect any radioprotective effect in an *in vivo* setting, is of concern. We have re-examined this question by investigating radioprotection in the mouse lung model (4). A single intravenous injection of Hoechst 33342 (80mg/kg) given 30min prior to the lung irradiation, extends the radiation dose required for death in 50% of mice at 16 weeks post irradiation, from 19Gy to 23Gy (ie: a DMF of 1.2). This is similar to the extent of radioprotection reported by Travis *et al* (5) for WR2721 (300 mg/kg) in this model. These results auger well for the potential of the more potent radioprotectors, and indeed preliminary experiments with methlyproamine in the mouse lung model suggests a DMF of 1.35.

References

1. Durand, R.E. ***J. Histochem. Cytochem.*, 30,** 117-122 (1982).
2. Chaplin, D.J.*et al* ***Br. J. Cancer,* 51,** 569 (1985).
3. Young, S.D.& Hill, R.P. ***Br. J. Cancer,* 60,** 715-721 (1989).
4. Martin et al, *Brit. J. Cancer* **74**, S99-S101(1996)
5. Travis, *et al.* ***Radiat. Res.* 84,** 133-143 (1980).