# CELL SURVIVAL IN IRRADIATED MOUSE INTESTINE IS INCREASED BY DNA-BINDING RADIOPROTECTORS

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Crypt survival in the mouse intestine has been used to examine effects of bisbenzimide radioprotectors. The DNA-binding ligand Hoechst 33342 was serendipitously observed to protect against radiation in cultured cells in 1984 (1) but *in vivo* radioprotective effects were not seen, possibly because insufficient concentrations of drug were delivered to the cells (2). Recently, however, *in vivo* radioprotection by Hoechst 33342 has been demonstrated both in mouse lung (3) and in brain endothelium using i.v administration.

Intravenous delivery has again been used for the present study in which the effects of methyl proamine (MP), a second generation Hoechst 33342 analogue have been examined. Recent results using the lung model suggest that MP is both more potent as a protector and less toxic than H 33342. The rapid nature of the crypt microcolony survival assay (e.g. 3) in mouse intestine provides an efficient way to examining factors which could impinge on the extent of radioprotection, for example, the interval between protector administration and radiation exposure. It is expected that once optimal timing of drug delivery and radiation exposure have been determined, topical delivery will be used to exploit fully the limited diffusion properties through cell layers of the bisbenzimides. This should permit the mitigation of normal tissue epithelial reactions without engendering unwanted concomitant protection of tumour cells

In our earlier studies on lung and vascular endothelium (see accompanying presentations) the location of the protected target cells was either in, or immediately adjacent to the vasculature through which the drug was delivered, a situation in which the limited diffusion of Hoechst 33342 through cell layers was unlikely to inhibit maximal delivery of the ligand to the target cell population. The present investigation also uses intravenous delivery but here delivery to the target crypt cell population is likely to be less efficient. The data clearly show however that for MP at 100 mg/kg, there is substantially increased crypt survival equivalent to a dose modification of about 1.33. The crypt scoring methods used indicate that protection is throughout the small intestine and preliminary data indicate that colon is also protected to a similar or slightly greater extent.

References

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3. Withers, H.R. & Elkind, M.M. ***Int.J.Radiat.Biol.*** 17, 261 (1970)