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Polyamine Depletion and Drug-Induced Chromosomal Damage: New Results

During studies to establish why pretreatment of 9L cells with α-difluoromethylornithine (DFMO) enhanced cell killing induced by 1,3-bis-(2-chloroethyl)-1-nitrosourea (BCNU) (*1*) and reduced cell killing induced by *cis*-platinum (*2*), we reported, in 1982, an enhancement of BCNU-induced sister chromatid exchanges (SCE's) and a reduction in *cis*-platinum–induced SCE frequency with DFMO pretreatment (*3*). Subsequently, we could neither replicate the DFMO enhancement of BCNU-induced SCE's in separate experiments (*4*) nor confirm those findings by rescoring the slides from the original experiments. In 1989, we therefore retracted our report of DFMO enhancement of BCNU-induced SCEs in 9L cells (*4*). The enhancement of BCNU cell killing by DFMO pretreatment had proved certain, however, and the discrepancy was puzzling in view of repeated confirmation of the correlation between reduced cell killing and SCE frequency with *cis*-platinum (*3*).

New experimental results reported by others (*5*) show that when DFMO remains in the cell culture medium during the period of BCNU treatment, the procedure enhances the number of BCNU-induced SCE's in 9L cells. When the DFMO-containing medium is removed and the cells are rinsed before BCNU is added, however, the additional rinsing procedure greatly diminishes or eliminates the enhancement. We believe that our replicate experiments (*4*) deviated from our original protocol (*3*) by the introduction of an additional rinsing procedure, thereby accounting for the discrepant results. There is now evidence that slides containing DFMO-treated cells degrade over time (*6*). Such a degradation over the 5 years between the original scoring of the slides and the rescoring attempts could have contributed to our inability to confirm the original findings.

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