

Contribution of Tissue Level Organization to Genomic Stability Following Low Dose Gamma Irradiation

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Our study proposes that the level of tissue organization will affect the induction and persistence of low dose radiation-induced genomic instability. To investigate this hypothesis, we are using rat thyroid cells grown in vitro as three-dimensional (3D) tissue analogs in bioreactors and as traditional two-dimensional (2D) flask grown cultures. We postulated that cells grown as tissue analogs will exhibit a reduced expression of genomic instability as compared to aliquots of the same cells grown in two-dimensional tissue culture flasks. Analysis of reverse DAPI-banded and painted chromosomes has been performed using an Applied Spectral Imaging system. Aberrations have been scored and differences documented. Percentage active caspase 3 levels, indicating apoptosis, have also been determined from immunocytochemistry analysis. We have conducted replicate experiments of 2D and 3D cultures exposed to acute low dose (1, 5, 10 and 200 cGy) gamma rays with harvests taken at 2, 10 and 30 days post irradiation. Data assessing the percentage caspase 3 activity levels show that, initially, the 3D cultures display more immediate (2 days) genomic instability (as shown by the higher levels of apoptosis) compared to the 2D cultures. The intermediate time point of 10 days reveal little differences in apoptosis between the 2D and 3D cultures overall and by day 30, the 3D cultures have switched from being initially more unstable to becoming less unstable than the 2D cultures. Further analysis of chromosomal aberration among the dose and time points is currently underway and will be reported at the time of this meeting.