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Gene expression analysis of human primary prostate epithelial and fibroblast cell cultures to an acute dose of 10cGy

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Primary tissue represents a better model for studies than immortalized cell lines that are adapted to culture conditions and may no longer reflect a realistic biological state. In this study, normal tissues from clinically indicated robotic-assisted laparoscopic radical prostatectomy were grossly identified, sectioned into frozen or formalin fixed samples, and processed as primary cultures. Normal epithelial and fibroblast primary cell cultures were derived from regions of normal tissue, as confirmed by analysis on adjacent tissue by hematoxylin and eosin staining, were exposed to acute doses of radiation from a Cs-137 source (0.5cGy per min). Clonogenic survival assays on fibroblasts irradiated with 2 to 200cGy were performed showing minimal cell death up to 10cGy in the primary cultures. This was compared to classical DNA-damage repair foci using gamma-H2AX and 53BP-1 as markers analyzed at 1 hour which showed minimal foci at 10cGy compared to higher doses. Genome-wide expression profiling was then conducted with Illumina human HT-12 v4 chips (~35,000 genes and predicted genes), and data were analyzed for transcriptional programs most differentially modulated following exposure at 24hours, as well as for tissue specific response signatures. Salient genes and biological pathways revealed by expression analyses are now being validated by focused qRT-PCR. Future work will include additional analysis of these primary epithelial and fibroblast cultures in response to chronic daily exposures to ionizing radiation in comparison to acute doses. These results aim to uncover an appreciation of cell-cell signaling within a tissue microenvironment that is critical to understanding cellular response to low-dose ionizing radiation outside the realm of cell death.