Low dose radiation effects of multipotent neural stem and progenitor cells

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Multipotent neural cells (both stem cells and their precursor cell progeny) retain their capacity to proliferate and differentiate throughout the mammalian lifespan. High numbers of these cells are located within the dentate subgranular zone (SGZ) of the hippocampus and the subventricular (SVZ) zone adjacent to the lateral ventricles, where they produce cells that can migrate away and differentiate into neurons (neurogenesis) and glia (gliogenesis). The realization that the brain contains such cells has sparked intense interest and speculation regarding their potential function. While significant data indicates that these cells participate in the repair of normal tissue injury in the CNS, these very properties may prove deleterious from a cancer perspective. Multipotent neural cells may represent a latent reservoir of brain tumor stem cells, an idea supported by data from us and others that show normal and cancerous precursors from the brain to share many immature expression profiles, a rapid proliferation, marked radio/chemoresistance, and similar redox properties.

We have recently demonstrated that exposure of primary multipotent neural cells to dose fractionation leaves a surviving population enriched for both nestin and prominin-1/CD-133. This finding is significant since several reports have shown that a subpopulation of brain tumor stem cells isolated from primary glioblastoma multiforme (GBM) express these very same markers. Further analysis of our primary multipotent neural cells has indicated that neural precursor cells are more radiosensitive than neural stem cells, a finding consistent with recent reports analyzing the radiosensitivity of multipotent cells derived from other tissues. Multipotent neural cells and glioma cells also show increased oxidative stress following irradiation, a characteristic not found in normal brain cells. Given the foregoing, along with our past data showing irradiation of multipotent neural cells leads to both acute (days) and chronic (months) increases in oxidative stress, suggests that changes in redox state are critical in reshaping the stress response of the CNS. New data collected after low dose ($\leq$ 10 cGy) photon irradiation indicate that redox changes still operate to influence cellular physiology, and suggest the possibility that activation of redox sensitive pathways may alter the susceptibility of multipotent neural cells to transformational events.