Characterizing the radioresponse of pluripotent and multipotent human stem cells.

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Authors: Mary L Lan, Munjal M Acharya, Katherine K Tran, Jessica Bahari-Kashani, Neal H Patel, Jan Strnadel, Erich Giedzinski, Charles L Limoli

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Public Summary:
The potential capability of stem cells to restore functionality to diseased or aged tissues has prompted a surge of research, but much work remains to elucidate the response of these cells to genotoxic agents. To more fully understand the impact of irradiation on different stem cell types, the present study has analyzed the radioresponse of human pluripotent and multipotent stem cells. Human embryonic stem (ES) cells, human induced pluripotent (iPS) cells, and iPS-derived human neural stem cells (iPS-hNSCs) cells were irradiated and analyzed for cell survival parameters, differentiation, DNA damage and repair and oxidative stress at various times after exposure. While irradiation led to dose-dependent reductions in survival, the fraction of surviving cells exhibited dose-dependent increases in metabolic activity. Irradiation did not preclude germ layer commitment of ES cells, but did promote neuronal differentiation. ES cells subjected to irradiation exhibited early apoptosis and inhibition of cell cycle progression, but otherwise showed normal repair of DNA double-strand breaks. Cells surviving irradiation also showed acute and persistent increases in reactive oxygen and nitrogen species that were significant at nearly all post-irradiation times analyzed. We suggest that stem cells alter their redox homeostasis to adapt to adverse conditions and that radiation-induced oxidative stress plays a role in regulating the function and fate of stem cells within tissues compromised by radiation injury.

Scientific Abstract:
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