U251 and U87, the two human glioma cell lines differ significantly in their radio-sensitivity to low LET (X-rays) and high LET radiation like Fe 26+. Radiosensitivity of the two cell lines does depend on the cell cycle stage they were in when exposed to ionizing radiation. U251, when exposed to X-rays after 1 day of split (when they are about 27% in G1, 26% in S and about 46% in G2/M phase) were most sensitive to low LET (X-rays, ~1 keV/n) and higher LET (Si (60keV/n) and Fe (150 keV/n)) radiations where as when they were exposed to same X-rays and heavy ions day 2 after split (60% G1, 25% S and 15% G2/M) they were only sensitive to higher LET radiations. The prolonged G2/M arrest seen with Si and Fe could be due to lack of IR (ionizing radiation) induced S phase check point which may result in these cells going into prolonged arrest in G2/M phase since they did not get arrested in S phase, in order to rectify the damage made by the heavy ions prior to cells entering the cell division stage. U87, on the other hand had most of its cells in G1 phase on day1 (G1 60% S 30%, G2/M 10%) and on day 2 most were in S phase(G1 35%, S 50% and G2/M 15%) and did not show much alteration in cell cycle stages after exposure to X-rays but showed similar alterations like U251 when exposed to heavy ions; this is indicative of the more significant and longer lasting effects of heavy ions as opposed to lower LET radiations. We determined the BER enzyme Apurinic Endonuclease1 (APE1) activity changes between the two cell lines and found that U87 had 3-4 fold higher APE1 activity than U251! U251 also underwent apoptosis at earlier time points as opposed to U87 which did not undergo any significant apoptosis even at 96h post 5 Gy dose of X rays. Even with heavy ions U251 showed higher apoptosis as compared to U87.

In order to determine the effect radiation has on synaptic activity of these glioma cells, the two cell lines were analysed for intracellular and released ATP where we found that U87 has about 10 fold lower intracellular ATP as opposed to U251 (none of these cell lines released any ATP due to lack of connexins). There was a significant drop in intracellular ATP of U251 when exposed to 50cGy of X rays where as a decrease in ATP in U87 was seen only after 500 cGy of X rays.

Thus, we hypothesize that U251 is more radiosensitive due to 1) lower APE1 activity which may not correlate with cell cycle stage and 2) higher intracellular ATP (as gliomtransmitter) which may cause U251 to apoptose much rapidly than U87. Currently studies are underway to 1) determine whether the APE1 expression is cell cycle dependent in order to explain the differences in radiosensitivity between the two cell lines and 2) to determine whether radiation has any effect on APE1 activity in these two cell lines.

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