Radiation induced genomic instability in bystander cells

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There is considerable evidence that exposure to ionizing radiation may induce a heritable, genomic instability that leads to a persisting increased frequency of genetic and functional changes in the non-irradiated progeny of a wide variety of irradiated cells. Genomic instability is measured as delayed expressions in chromosomal alterations, micronucleus formation, gene mutations, and decreased plating efficiency. During the last decade, numerous studies have shown that radiation could induce bystander effect in non-irradiated neighboring cells; similar endpoints have also been used in genomic instability studies. Both genomic instability and the bystander effect are phenomena that result in a paradigm shift in our understanding of radiation biology. In the past, it seemed reasonable to assume that the production of single- and double-strand DNA breaks are due to direct energy deposition of energy, by a charged particle, to the nucleus. It turns out that biology is not quite that simple. Using the Columbia University charged particle microbeam and the highly sensitive human hamster hybrid (AL) cell mutagenic assay, we irradiated 10% of the cells with a lethal dose of 30 alpha particles through the nucleus. After overnight incubation, the remaining viable, bystander cells were replated in dishes for colony formation. Clonal isolates were expanded and cultured for 6 consecutive weeks to assess plating efficiency and mutation frequency. Preliminary results indicated that there was no significant decrease in plating efficiency among the bystander colonies when compared with their parental controls. In contrast, a progressive increase in mutant fraction over the background re-emerged 5 to 6 weeks post-irradiation among the bystander clones. Further experiments are on-going to confirm this interesting finding. The bystander effect and genomic instability both contribute to our understanding of low dose radiobiological effects. If phenomena demonstrated in vitro are applicable in vivo, then the genomic instability and bystander effects imply that a linear extrapolation of risks from high to low doses may underestimate rather than overestimate low-dose risks.