

The role of persisting phenotypes on radiation-induced genomic instability

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Our laboratory is involved in elucidating the role of reactive oxygen species in the cellular response to DNA damage and the resulting genomic instability following exposure to radiation. We have previously found that human immortalized bronchial epithelial cells exposed to a single dose of 1Gy of low (X-rays) or high (Fe ions) LET radiation exhibit multiple persisting phenotypes as part of a stress response, which is resolved within 2 weeks after exposure and affects distinctly the expression of genomic instability. Some of these phenotypes, such as elevated reactive oxygen species (ROS) and nitric oxide are radiation quality independent, while genomic instability and the appearance of senescence and pro-inflammatory biomarkers are radiation quality dependent. We found that ROS added exogenously or increased by inhibiting catabolism, reduced genomic instability measured by micronucleus formation and gamma-H2AX-53BP1 foci. This result indicates an adaptive role for ROS production and provides an explanation for the weak effect of antioxidants as radiation countermeasure agents. In contrast, senescence-like responses and pro-inflammatory cytokines driven by p38 MAPK activity, increased the expression of genomic instability. These findings implicate a more specific and effective target to reduce radiation-induced genomic instability and inflammation.

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