Ionizing Radiation on Nuclear Inherent Radio Sensitivity Is Correlated with Radio Responsiveness of Plasma Membrane

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Abstract— Therefore, among the biological effects caused by ionizing radiations have called Probabilistic (Stochastic), because the probability of occurring increases with the doses of these rays, not presenting dose threshold from which can be produced. They include the leukemia and cancer and genetic effects on future populations. There are also called Probabilistic No effects (not Stochastic), whose presence or not depends on the dose received, its severity increases with the dose received and there is a dose threshold, below which there is demonstrate these effects. Among them we can mention hair loss, sterility, aplastic anemia, lens opacity, death, etc. Another classification of risks or adverse effects of ionizing radiation, would be to consider the action of the same cells on which they act. If these cells were germ cells (cells involved in reproduction) risks could be genetic and inherited alterations in these cells. If the cells affected by ionizing radiation were somatic (non-germ cells) could then consider the undesirable effects

Index Terms— angiogenesis; Doppler sonographer; radiotherapy, Rad

I. INTRODUCTION

The action of ionizing radiation on specific organs may cause alterations on these bodies, some of which may be affected greater extent by its greater sensitivity to radiation because at one time or are particularly affected given (critical organ). These bodies may be considered more affected by ionizing radiation due to their increased radio sensitivity or more affected at certain times, such are the skin, which causes acute or chronic involvement. The skin is quite affected by ionizing radiation, because the body is the same input in external irradiation and also has a constantly updated, making it particularly sensitive to radiation because of its high number of cell mitosis. In physics, radiation describes a process in which energetic particles or waves travel through a medium or space. Radiation can be classified according to the effects it produces on matter, into ionizing and non-ionizing radiation. Ionizing radiation includes cosmic rays, X-rays and the radiation from radioactive materials. Non-ionizing radiation includes ultraviolet light, radiant heat and microwaves. The word radiation is commonly used in reference to ionizing radiation only (i.e., having sufficient energy to ionize an atom), but it may also refer to non-ionizing radiation (e.g., radio waves or visible light). The energy radiates (i.e., travels outward in straight lines in all directions) from its source. This geometry naturally leads to a system of measurements and physical units that are equally applicable to all types of radiation. Both ionizing and non-ionizing radiation can be harmful to organisms and the natural environment. All life on Earth has evolved in presence of this radiation. Figure 1.1 shows the percentage contribution of various sources of ionizing radiation to which

human beings are exposed. Over 85 percent of total exposure is from natural resources with about half coming from radon decay products in the home. Medical exposure of patients accounts for 14 percent of the total, whereas all other artificial sources – fallout, consumer products, occupational exposure, and discharges from nuclear industries account for less than 1 percent of the total value. Of all the exposures, medical exposure is of the main interest to scientists all over the world because of the ability of radiation to treat dreaded disease like cancer, for which, ironically it is a cause as well.

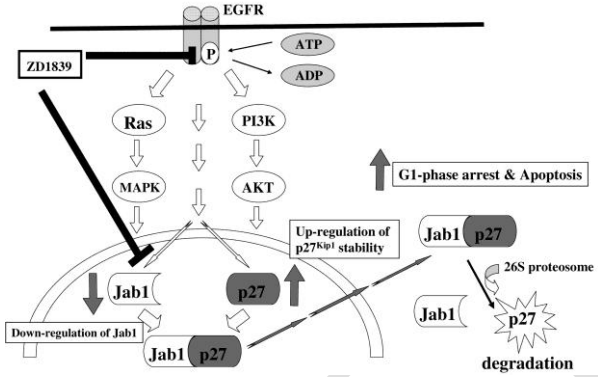

Fig 1. Enhances Radio sensitivity in Cell Lines

It has also recently been found that nitro tyrosine. The first response to radiation induced DNA damage is the activation of the alarm sensors. As the name indicates, these are proteins which detect the damage and set off the alarm signals, thereafter, the cell readies itself for subsequent action. Interestingly, it is the proteins involved in DNA repair, like (DNA-PK, ATR, ATM, BRCA-1, PARP etc.), which scan the genome, detect the damage and act as alarm sensors.

II. OVERVIEW OF RADIATION INDUCED CELL SIGNALING

According to the results of large multicenter Exposure of cells to ionizing radiation results in complex cellular responses resulting in cell death and altered proliferation states. The underlying cytotoxic, cytoprotective and cellular stress responses to radiation are mediated by existing signaling pathways, activation of which may be amplified by intrinsic cellular radical production systems. These signaling responses include the activation of plasma membrane receptors, the stimulation of cytoplasmic protein kinases, transcriptional activation, and altered cell cycle regulation. There is increasing evidence for the functional links between cellular signal transduction responses and DNA damage recognition and repair, cell survival, or cell death through apoptosis or reproductive mechanisms.

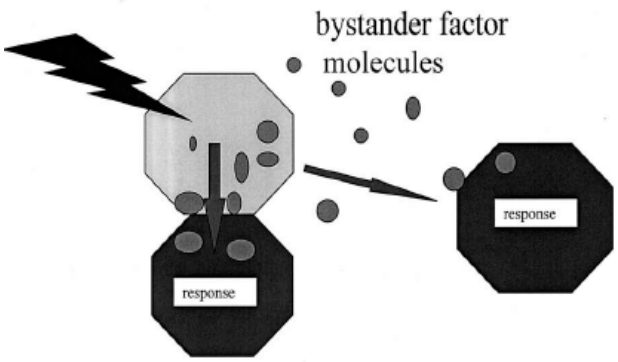

Fig 2. Radiation induced bystander effect.

Recent radiobiological studies have demonstrated that the exposure of mammalian cells to ionizing radiation over a wide dose range results in activation of existing cellular response pathways. These pathways, dominantly involving protein kinases, mediate the cytoprotective and cytotoxic responses of cell survival and cell death, respectively. Cytoprotective responses involve pathways of the mitogen activated protein kinase (MAPK) and phosphatide inositol- 3-phosphate kinase (PI3 kinase) cascades which activate the machinery of biosynthesis and may stimulate cell proliferation if radiation-induced damage is successfully repaired. The most direct consequence of cytotoxic or stress responses is thought to involve Jun N-terminal kinase (JNK, now known as MAPK8) and results in apoptosis and/or other forms of cell death. Although general statements may be premature, current data suggest that cells of the hematopoietic lineage and fibroblasts or other normal cells are substantially more prone to undergo radiation-induced apoptosis than many carcinoma cells. The goal of this chapter is to describe the complexity of the responses of cells to exposure to ionizing radiation. Links between the mechanisms of various sensors of radiation effects and the activation of major cellular response pathways will be emphasized where possible (Fig. 1.4). The response networks include cytokines and plasma membrane receptors, effector protein kinases, and phosphatases in the cytoplasm or at the interfaces of plasma membrane and nucleus. The extent of radiation-induced changes in proteins, lipids and nucleic acids, the latter recognized by defined proteins as DNA damage, is likely to determine the relative balance between plasma membrane events, mitochondrial reactions, and nuclear responses

III. METHODOLOGY

Fractionated irradiation induced signaling events. The contribution of these events to the increased cell survival. High LET induced signaling and variance from low LET gamma radiation. Contribution of radiation induced bystander effect to cell survival and its mechanism.

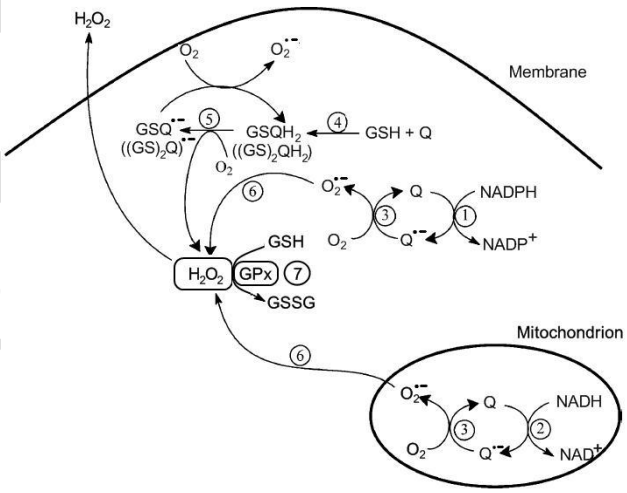

Fig 3. GSQH2 or ((GS) 2QH2) represent mono conjugated hydroquinone respectively 1 Diabetic retinopathy: Fluorescein angiography showing multiple microaneurysms

Despite improvements in the ability to shape and target radiation beams to deliver higher doses to tumor tissue and lower doses to the surrounding normal tissues, In other words, cancer begins whe n a cell breaks free from the normal restraints on cell division and begins to follow its own agenda for proliferation. From a clinical point of view, cancer is a large group of diseases, perhaps up to a hundred or more, that vary in their age of onset, rate of growth, state of cellular differentiation, diagnostic detectability, invasiveness, metastatic potential,

response to treatment, and prognosis. The malignant transformation of cells is collectively determined by six essential alterations (commonly shared by all types of human tumors) to cell physiology: self-sufficiency in growth signals, insensitivity to growth-inhibitory (antigrowth) signals, evasion of programmed cell death (apoptosis), limitless replicative potential, sustained angiogenesis, and tissue invasion and metastasis. Each of these physiologic changes represents the successful breaching of an anticancer defense mechanism hardwired into cells and tissues.

IV. RESULT

Serine translocation from inner part of plasma membrane to outer part is believed to be an early event in apoptosis. Binding of Annexing V to serine in presence of calcium ions, results in green fluorescence. During late apoptosis or necrosis, owing to increased membrane permeability, P I also enters the cell and binds to cellular DNA and stains the nucleus red. Results from the present study Figure 3 shows that treatment resulted in significant elevation in the percentage of Annexing V-FITC (+)/PI(+) cells (upper right quadrant), both in a time and concentration dependent manner indicating late apoptotic/secondary necrotic death. About 30.64% cells were present in upper right quadrant after treatment with 5 µM for 12 h. This figure drastically increased to 67 % after 24 h incubation. however, at a higher dose (10 µM) of, no significant time- dependent increase was observed in the percentage of Annexing V-FITC(+)/P I(+) cells.

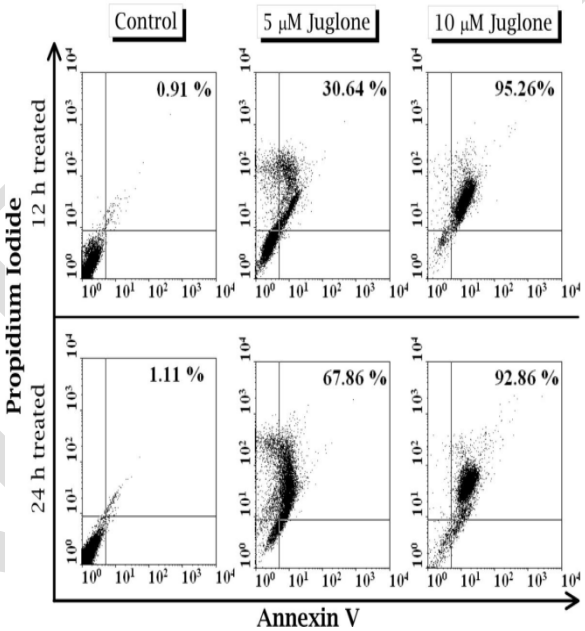

Fig 4. Flow analyses of apoptosis and necrosis using Annexing V

The result of DCF H-DA assay gives an idea about the ability of to induce formation of intracellular ROS, which substantiated the findings of GSH studies. A concentration-dependent depletion of GSH levels with corresponding elevation in intracellular ROS levels after treatment with in the present study indicates that oxidative stress could be an important mechanism by which exerts its toxic activity against melanoma cells as well. In general, toxicity of quinines is known to depend mainly on two mechanisms such as, the redox cycling resulting in production of semi Quinone radicals and reactive oxygen species leading to depletion of glutathione in the cells. The former leading to the latter. Further, the structure-activity relationship studies on the toxicity of have revealed that 1, 4-naphthoquinones with a hydroxyl group at position 5 at position.

V. DISCUSSION AND CONCLUSION

Radiation induced signal transduction, as understood presently, is an activation of the existing network, where both positive and negative signals converge and these are interpreted as cell survival and cell death. In spite of the fact that mere phosphorylation by kinases seem to be the basic theme, it is crucial as based on this life or death decisions are taken. Hence enormous cross checking of the ultimate signal must exist. The lung carcinoma cell line A549, a highly radio resistant cell line could be effectively made radiosensitive by inhibiting Rad52, one of the components of its repair pathway. The survival of the cells decreased significantly after doing so.

The survival of the A549 cell line could also be significantly decreased by heavy ion irradiation. The mechanism of which seems to be a lack of repair, despite the activation of some of the component of the repair pathway. Besides the microenvironment of the cells and the LET of the radiation, even transfer of medium from irradiated cells to non-irradiated cells can alter the pattern of signaling in a cell. Radiation induced signal transduction, as understood presently, is an activation of the existing network, where both positive and negative signals converge and these are interpreted as cell survival and cell death. In spite of the fact that mere phosphorylation by kinases seem to be the basic theme, it is crucial as based on this life or death decisions are taken. Hence enormous cross checking of the ultimate signal must exist. The lung carcinoma cell line A549, a highly radio resistant cell line could be effectively made radiosensitive by inhibiting Rad52, one of the components of its repair pathway. The survival of the cells decreased significantly after doing so.

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