Biological response to radiation therapy

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1 Abstract

Radiation therapy, often known as radiation, is an important and integral part of cancer treatment, with the majority of patients experiencing a survival advantage. Radiation therapy kills cancer cells by bombarding them with high-energy radiation. Radiation therapy has evolved throughout time as a result of continual technological advancements, and nearly half of all patients with localised malignant tumours are treated with radiation at some point during their condition. In the field of radiation oncology, research and development during the last three decades has resulted in significant advancements. The linear energy transfer (LET), total dose, number of fractions, and radiosensitivity of the targeted cells or tissues all influence the biological effectiveness of radiation. Radiation can harm a cell's genome either directly or indirectly (by creating free radicals). This has been called into question in recent years by a phenomena known as the radiation induced bystander effect (RIBE). The non-irradiated cells next to or far from the irradiated cells/tissues show similar reactions to the directly irradiated cells in RIBE. Understanding the reactions of cancer cells during fractionation or after irradiation will lead to improvements in therapeutic efficacy, potentially benefiting a large number of cancer patients.

2 INTRODUCTION

The body's reaction to DNA and linage. The present perspective on studies of DNA damage and cell cycle response following ionising radiation (IR) and its application in radiation oncology has been greatly influenced by the avalanche of information in cellular biochemistry and molecular biology. When DNA is damaged by IR, mammalian cells respond by activating two critical physiological functions: cell cycle regulation and DNA repair. Most cells have repair pathways that are always active and are controlled by cell cycle checkpoints. The cell must choose between DNA repair and cell death after recognising damaged DNA and assessing the damage. The goal is to protect the genome's integrity.

2.1 DNA repair:

Effective DNA repair is critical for the genome's long-term stability. The DNA-dsb is the most major DNA damage linked to reproductive cell death in response to IR. Dsb can also be generated by normal endogenous mechanisms such oxygen free radicals, DNA replication, or topoisomerase failure, in addition to IR. Mis rejoining events such as dicentric chromosomes and ring chromosomes, both of which lead to a mitotic catastrophe within 1-2 turns of the cell cycle, are linked to persistent damage. The dsb could also result in significant translocations or the insertion of genetic material outside of its original place. These key events, which may include oncogene activation and deletion or down-regulation of housekeeping genes, are often persistent during the next cell divisions. Biophysical experiments reveal a link between radiosensitivity and both unrejoined dsb fractions and rejoining kinetics. Even while the majority of cells that progressively rejoin the breaks appear to be IR sensitive, other radiosensitive cell lines rejoin the breaks regularly.

2.2 Apoptotic:

In recent years, the manner of cell death caused by DNA damage triggered by anticancer treatments, including radiotherapy, has been highlighted. The discovery of the function of wild-type TP53 in inducing apoptosis in response to DNA damage has sparked a huge interest in programmed cell death. There is clear doubt that after DNA damage that is dependent on wild-type TP53, lymphoid tissues and lymphoma cells die a quick apoptotic death. New ideas have arisen as a result of the fact that apoptosis is thought to be linked to genetically specified pathways. One of these ideas is that the genotype of normal or tumour cells can predict DNA-damaging chemical susceptibility.

2.2.1 Clonogenic:

In a Clonogenic experiment, both genotypes may demonstrate similar cell survival. If clonogenic survival is considered as the endpoint for cell death, neither TP53 status nor the ability of the cells to undergo apoptosis appears to play a significant impact in the susceptibility of these cells to DNA-damaging chemicals, according to the findings of this review. A recent review looked at the ambiguous role of apoptosis in non-lymphoid normal tissues for maintaining the balance between cell production and cell loss. Apoptosis contributes just a small amount to cell turnover in mammalian normal tissues, with a few exceptions. Several processes control cell death in tumours, such as necrosis produced by insufficient angiogenesis.

2.3 Critical issues:

New pathways involved in cell cycle checkpoints and DNA repair will almost certainly be discovered in the near future. However, converting this knowledge into clinically viable medicines faces numerous challenges. —The application of

recent understanding, as seen above, to the in vivo and human condition is still largely unknown. —It is necessary to determine the relative importance of abnormalities in the various signalling pathways involved in cell cycle checkpoints and DNA repair for radiosensitivity. The radiosensitivity of people who are heterozygous or have polymorphisms for some of the genes involved in the complex machinery of cell cycle checkpoints and DNA repair differs from the general population. It is necessary to gain a better understanding of how common these abnormalities are among cancer patients.

3 CELL AND TISSUE RESPONSE TO DOSES ABOVE AND AROUND 1 GY

Radiation destroys cells by causing several types of DNA damage. Damage to DNA appears to be the primary source of IR cell death and mutations, according to the research. In addition to a significant degree of base damage, each 1 Gy dose of low-LET radiation causes roughly 1000 initial single-strand breaks (ssbs) and 25-50 initial double-strand breaks (dsbs). The number of unrepaired or misrepaired dsbs breaks, which are regarded to be the most common type of cellular damage, correlates most strongly with cell death. Only approximately 1-2 percent of dsbs, however, are truly fatal. The majority of ssbs and dsbs are fixed correctly. Various models based on assumptions about target inactivation have been presented to characterise the dose-response relationship for cell death. The exponential and multi-target single hit survival curves are examples of such models. In fact, for most experimental cell survival data produced using clonogenic experiments, a combination of these two is more appropriate. The linear quadratic model provides an even better description of radiation cell killing to single dose fractions of a size for clinical usage. The a/13 ratio, where a and p are cell specific under established conditions, but may vary with radiation quality, dose rate, and other dose modifiers, determines the curvature of the survival curve. There have been suggestions for alternative repair models. The changing of the dose-response function with changes in irradiation volume is known as a volume effect. It is well understood that if the dose-response function is steep, there will be very little volume effect, such as in the case of spinal cord damage. Otherwise, there is a volume effect for most organs and endpoints. There could be a volume effect threshold. Radiation hepatitis, nephritis, and pneumonitis are examples of endpoints where this is most likely the case. The dose-volume effect is also determined by the organ and tissue architecture, as well as the presence of functional subunits. According to the arrangement of the functional subunits, tissue architecture is categorised into serial and parallel types.

4 CELL AND TISSUE RESPONSE TO LOW RADIATION DOSES—HRSIIRR

5 FUTURE ASPECTS AND CLINICAL POTENTIALS

The goal of future study is to figure out how DNA works. Repair can be quantified and modulated to help improve radiation therapy through both rapid and sensitive predictive assays and specific sensitization of tumour cells through knockout of critical repair pathways. Because DNA is the primary target for therapeutic doses of radiation, understanding repair pathways in normal and tumour cells is critical. In 1994, the first gene known to play a substantial role in dsb repair in mammals was discovered, and this field has a lot of study promise. In recent years, major progress in DNA repair research has switched the focus from prokaryotes and yeast to mammalian or human cells. However, there are still a lot of things that aren't evident. The knowledge gathered could pave the way for future advancements in tumour and normal tissue response prediction and prognosis. Identifying key objectives is a similar process. Modulation of the repair, which is preferably down- or up-regulated in tumour cells, may have the potential to improve tumour therapy. There is a need for creative biochemical studies as well as the use of recent discoveries in genomics and proteomics in this study area, which contains intricate interactions between molecular targets.