Biological Effects of Radiation at the Cellular Level

S. Muise[1], J. Donev[1]
[1] University of Calgary, Alberta, Canada
(jmdonev@ucalgary.ca)

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Summary

The biology of radiation response is a multifaceted issue that informs policies which affect the entire nuclear industry. Ionizing radiation has high enough energy to produce ions and break molecular bonds when it interacts with matter. When these interactions occur in living organisms, cellular damage may result in adverse health effects including, but not limited to, cancer. This paper explores the environmental, genetic and epigenetic factors that affect low-dose biological radiation response, along with the mechanisms through which they act. Understanding these factors could help inform risk assessment and personalized health care.

1. Introduction

Nuclear power has the potential to take the lead in a future low-carbon electricity market, however, it has encountered strong resistance from many sectors. One of the major concerns cited against nuclear power is the production of radioactive substances and the risk of public exposure, now and in the future. Of particular concern are the effects of ionizing radiation on living organisms, especially humans. While the public's perception is out of proportion with the actual dangers, the dangers do exist. This paper will provide an overview of the cellular response to radiation, including genetic, epigenetic and other physiological changes that occur at a molecular level.

2. Motivation

Understanding radiation response at a cellular level could have many benefits for individuals directly involved with handling radiation as well as the population at large. At the moment, the complex mechanisms involved in the biological effects of radiation are insufficiently clear, which indicates an opportunity for the scientific community. Increasing this knowledge base has the potential to improve medical treatment, inform risk assessment in industrial nuclear applications, and shift public perception of radiation.

Radiation response is important for both diagnostic and medical treatment procedures. Many diagnostic imaging techniques involve exposure to a small amount of radiation. Understanding the effect this exposure has on the patient and the technician can improve patient and workplace safety while maximizing benefits and minimizing costs. Identifying and contrasting cellular response in healthy and cancerous cells can help optimize treatment, including level of fractionation, maximum dose given, and co-treatment with resistance-inducing factors. Cataloguing molecular changes may

also provide methods of monitoring individual responses through signalling pathways that are measurable in blood or other samples. A new appreciation for the role of epigenetics in cancer and other diseases could lead to new types of treatments, increasing the survival rate or quality of life for patients.

As for risk assessment, understanding how cells react to varying levels of radiation over time is key for accurate risk analysis. Overall safe exposure limits for everyday, workplace or emergency situations should be based on concrete science. Dose levels, dose rates, and prior exposures for an individual could inform risk for a specific situation. Risk assessment is particularly important for workers in positions requiring exposure to some levels of radiation. To name just a few examples, medical physicists, radiation therapists, diagnostic imaging technicians, mine workers, and nuclear emergency response teams all have to deal with controlling radiation exposure on a routine basis. The current attitude towards radiation exposure is summarized by ALARA (As Low As Reasonably Achievable), which incurs large costs in some cases [1]. More accurate risk analysis from better biological models could save money on unnecessary levels of protection with no increased risk.

Public perception could well be shifted by further understanding of the biological effects of radiation. Increased comprehension about the actual effects of radiation on the body could make the general response to "radiation" more reasonable and less knee-jerk in the long term. Also seeing how science can use radiation to improve health outcomes will help people better appreciate the positive uses of radiation. Improved understanding of cellular response can mitigate the negative effects of radiation, which may help the public feel more at ease with peaceful applications of nuclear technology such as power production and medical procedures.Overall, research in the field of radiation response in relation to outside factors can help reduce risks and improve outcomes in the areas of medicine, energy production, and public perception.

3. Background

In order to explore the cellular response to radiation, there is some important background information to cover. First, the current model of dose-response relationship and possible alternative models will be reviewed, since it could be informed by cellular mechanisms. Second, the field of epigenetics will be briefly reviewed and related to the topic at hand.

3.1 Hormesis and the Linear No-Threshold Model

The currently accepted policy model for the effects of radiation per dose is the linear no-threshold model (LNT) [2]. This describes a linear relationship between the effective dose and the increased risk for cancer due to that dose. This proportional relationship has been well-established for doses greater than 100 mSv through analysis of atomic bomb survivor data. For doses below 100 mSv, however, no significant effect has been observed despite extensive study. For policy purposes, it has been assumed that the proportionality holds through this low-dose range, with no threshold below which there is no increased risk.

An alternative theory describing possible effects at these low doses is known as 'hormesis' [2]. This theory proposes that low doses of radiation actually have beneficial health effects. The basic idea is that humans have evolved in a mildly radioactive environment and thus have adaptations to repair the damage caused by the low levels encountered on a daily basis. These repair mechanisms, activated by low doses of radiation, will also repair DNA mistakes caused by other factors. This theory has been debated for the past several decades, and has resulted in a wide body of literature both in support of and rejecting it. Lately, the idea has gained traction in the scientific community but is far from being accepted by regulatory bodies or the general public.

The debate regarding hormesis and LNT may be well informed by a look at what actually occurs in cells at a molecular level in response to radiation. Regardless of overall trends, it is fascinating to investigate what's occurring at a cellular level when radiation is absorbed by an organism.

3.2 Epigenetics

Epigenetics is the study of how gene expression is modified by molecular interactions with DNA in a mitotically heritable way, meaning that epigenetic changes in a cell can be passed on to its clones during cell replication [3].

Every cell in the average human body contains the same genetic information stored in its DNA, yet every type of cell looks and behaves differently in order to fulfil its distinct role in contributing to the whole. Epigenetics differentiates skin cells, brain cells, liver cells, muscle cells, and so on. Not all genetic data can be read by cell machinery (and thus expressed) in every cell at the same time. In fact, only a small fraction of DNA is in use at any given time in any given cell. The regions of DNA (genes) that are expressed can be controlled in a few different ways.

The main direct controls of gene expression are histone modification and methyl tags [3]. Histones are large protein structures around which DNA strands coil. How tightly the strand is coiled around its histones partly determines how strongly that region of DNA is expressed. Tightly coiled DNA is difficult to access and therefore is not expressed, whereas loosely coiled DNA can be more easily read, leading to greater gene expression. Another level of control is attained by methyl tagging. Methyl groups are small functional groups that can attach to DNA strands, rendering the target section(s) inactive.

These methyl tags and histone states are modified throughout a lifetime and on a minute-to-minute basis as conditions change and signals are received, affecting cell function [3]. These cellular responses are almost certainly affected by radiation, as will be investigated in later versions of this paper.

4. Radiation Response

Cells are complex systems with many components and interactions, therefore their response to radiation is also multifaceted. There are direct effects of radiation, but also protection mechanisms that arise in

response to radiation, effects on cells beyond the target cell, and potentially transfer of radiation effects between generations.

4.1 Direct effects of radiation

Absorbed radiation can directly affect many molecules in the cell. The usual concern is its effect on DNA. Ionizing radiation can cause double or single strand breaks in DNA, base lesions, in which a nucleotide base in DNA is replaced with another, or the loss of a base from a site [4]. These direct effects on DNA may result in cancer or other negative effects. Other direct effects of radiation include the production of free radicals, highly reactive molecules or atoms that cause oxidative stress in cells, indirectly affecting DNA [5].

4.2 Mechanisms of protection

The human body has developed mechanisms to protect itself from a variety of stressors, including oxidation, heat, and radiation. Radiation triggers several protective mechanisms in a cell, the two most important being the antioxidant response and the DNA repair response. The antioxidant defense response involves the activation of enzymes that mop up excess reactive oxygen species, returning the cell to a normal redox state [6]. The DNA repair response involves multiple enzyme pathways depending on the type of DNA damage done, such as non-homologous end joining or homologous rejoinging for double strand breaks, base excision repair, mismatch repair, and nucleotide excision repair [7]. Both of these protective responses are also triggered by other stressors and can repair damage that was previously below the threshold required to initiate them.

4.3 Bystander effect

The absorption of radiation by a cell may not only affect that cell alone. Cells around the target cell have been shown to be affected as well, a phenomenom known as the “bystander effect” [10]. Some research groups have found a negative bystander effect, in which surrounding cells are worse off due to the radiation [11], whereas other groups have found a positive bystander effect, in which surrounding cells benefit from the indirect effects of radiation [12]. The mechanisms by which bystander cells are affected are still being elucidated [10].

4.4 Intergenerational effects

There have also been some observations of radiation effects being passed down to offspring [13][14]. It is thought that the mechanism of transfer is epigenetic, though details are still being fleshed out.

This is an exciting arena for research to investigate in the near future.

5. Conclusion

The cellular response to radiation is a complex subject encompassing direct effects, protection mechanisms, bystander effects and intergenerational effects. The interplay of genetics, epigenetics and physiology make this a fascinating topic of continued research. Understanding molecular effects may inform medical, industrial, and societal issues around radiation dose.

6. References

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