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Evaluation of FDXR gene expression in human lymphocytes after exposure to ionizing radiation

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1. Introduction

Ionizing radiation has undeniable medical benefits as well as biological harms to humans when exposed to high doses. Thus, it is important to evaluate exposure to ionizing radiation in order to minimize biological damage and maximize the benefits of its use. The fundamental physical quantity in monitoring individuals exposed to ionizing radiation is the absorbed dose, which is defined as the average energy deposited by ionizing radiation per unit mass of the irradiated volume [1]. Determination of the absorbed dose of ionizing radiation can be performed directly with the help of sensitive devices called dosimeters. Recently, the evaluation of biological parameters sensitive to radio-induced effects has been used in individual monitoring called biodosimetry, thus becoming a complementary tool to physical dosimetry. Currently, the most widely used and well-established method of biological dosimetry is the dicentric chromosome assay.

In addition to the evaluation of biological parameters sensitive to radio-induced effects, recent research has been directed towards identifying genes that correlate with exposure to ionizing radiation. The selection of the control gene is essential for the interpretation of the quantification of interest´s genes; ionizing radiation induces leukocyte gene expression among others, CDKN1A, FDXR, SESN1, BBC3 and PHPT1 [2,3]. Therefore, the FDXR protein function is the transfer of electrons from NADPH to cytochrome P450 via ferredoxin in the mitochondria, and can be induced by DNA damage in a p53-dependent manner that sensitizes cells to apoptosis [4].

2. Methodology

This is a literature review of FDXR gene expression after exposure to ionizing radiation. The search was conducted by crossing the following Health Sciences Descriptors (DeCS): ionizing radiation, X-ray, FDXR gene, RT-PCR, low doses and high doses. The studies were identified through extensive searches of online databases such as Library Online such as Library Online (SciELO), Latin American and Caribbean Literature on Health Sciences Information (LILACS); between the years 2013 and 2021.

3. Results and Discussion

Gene expression is a method of high sensitivity for assessing radiation exposure. The FDXR gene, responsive to ionizing radiation, is considered an efficient biomarker in estimating both low and high doses of ionizing radiation [5]. The study by White et al. (2016) [6] reported the function of FDXR protein; this protein enables electron transfer from NADPH to cytochrome P450 via ferredoxin in mitochondria, and can be induced by DNA damage in a p53-dependent manner that sensitizes cells to apoptosis.

To confirm the gene expression characteristics of the FDXR gene, Brzóska, et al. [7] performed blood collection from three healthy volunteers followed by the same methodology as this research work. The samples were exposed to 0, 0.6 and 2 Gy doses of x-ray, and RNA was extracted after 6, 12, 24 or 48 h irradiation. Gene expression was measured by the quantitative transcription PCR (RT-qPCR) method, using ACTB, GAPDH, HPRT1 genes as reference genes. Interestingly, the RT-PCR technique allowed differentiation between irradiated and non irradiated samples, therefore, FDXR gene expression was positively regulated 8-10 times higher than that of reference genes and other genes, with a peak expression at 6h after exposure.

Furthermore, when comparing the non-irradiated and irradiated samples, the studies detect a time-dependent increase in the FDXR gene expression profile. Analysis of the studies (Strunz et al., 2013 [8]; Macaeva, et al., 2016 [9]; Beer et al., 2014 [10]; Ghandhi, S. A., et al., 2015 [11]; Ostheim, et al., 2021 [12]; Kabacik, S., et al., 2015 [13]) report greater detectable differences 20 hours after exposure to low doses and lower doses in FDXR gene expression. The study by Beer et al. (2014) [10] reveals that very early events (up to 4 hours) after irradiation were specifically associated with p53 signaling and apoptotic pathways, while a large number of diverse cellular processes were downregulated after 20 hours, which explains why the peak expression is between 4 to 20 hours after low dose exposure. However, high doses of ionizing radiation induce significant changes in gene expression only after 20 hours of exposure [10].

Furthermore, studies have shown that all FDXR gene variants show a clear dose-dependent response with large variability in the range of responses among them to external ionizing radiation exposure. After in vivo irradiation, the expression profiles dependent on FDXR-201 and FDXR-208 variants show a high gene expression responsiveness 24 hours after radiation exposure [14].

4. Conclusions

Based on current literature studies about the FDXR protein, the observations made through the correlation of results concluded that FDXR gene responsive to ionizing radiation is considered as an efficient biomarker in estimating both low dose and high dose ionizing radiation. Therefore, gene expression analysis using the RT- PCR technique is a method of high specificity and sensitivity for radiation exposure assessment.

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