Organ Specific Gene Expressions in C57BL6 Mice

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1. Introduction

Cellular and tissue sensitivity against ionizing radiation depends on many endogenous gene expression patterns. It is well known that tissue or cells responds differently to various stimuli, including ionizing radiation according to the genetic background and the decision whether the damage is dealt with by apoptosis or whether rescue or repair is attempted is critical. Death of the individual cells removes the problem from the tissue but if the cell does not die, it may acquire genomic instability and lead to a population of cells with abnormally high susceptibility to chromosomal instability mutation and other delayed effects.

Studies using inbred strains of rodents have clearly shown genotype-dependent differences in response to radiation exposure, including susceptibility to radiation-induced cellular transformation and tumor formation, as well as differences in susceptibility to radiation-induced chromosomal instability. In experiment systems, mouse models have proven very useful in identifying genes that modify radiation sensitivity. For instance, p53 deficient mice are strongly influenced by genetic background. Another importance aspect is that particular type of tumor that arises is dependent on the genetic background.

In this study, we analyzed the genes which were previously reported to be overexpressed by radiation in human peripheral blood lymphocytes, in brain, spleen and lung which have different intrinsic radiosensitivity, and examined the correlation between gene expression patterns and organ sensitivity and identified the possible genes which are responsible for organ sensitivity.

2. Results and Discussion

In the present study, we analyzed 24 genes which are overexpressed in human peripheral blood lymphocytes in microarray system in brain, lung, and spleen which showed different sensitivity to radiation exposure; brain showed the most resistant and spleen showed the most sensitive. We want to know if these genes are differently expressed according to the organs and regulate organ sensitivity by radiation. Twenty-four genes include diverse functions such as antioxidation system, cell surface marker, chaperone function, and cell cycle regulation etc.

Expression pattern of each gene was different in 3 organs of 3 individual mouse. Expression of APO-1 cell surface antigen, HSP70, nuclease sensitive element binding protein-1, cannabinoid receptor, Na, K-ATPase alpha-subunit, cyclin protein gene, nucleolar protein hNop56, and paraxonase (PON2) were not different depending on the sex, suggesting that these gene expression may not involve in sex difference and may be candidates for universal markers for radiation exposure independently to sex.

Expression of mRNAs, sialytransferase, delta7-sterol reductase, leptin receptor splice varian form 12.1, and Cu/Zn superoxide dismutase showed the highest expression in spleen, while □B crystalline showed the lowest expression. Spleen is one of the radiosensitive organ in TUNEL staining and these genes may play role in controlling susceptibility to radiation exposure. In the case of brain, one of radioresistant organ, Na, K-ATPase □-subunit, delta7-sterol reductase, cyclin G and nucleolar protein hNop56 were specifically over or underexpressed. Since delta7-sterol reductase was the highest expressed in spleen and the lowest in brain, this gene is the most possible candidate for controlling radiosensitivity. Lung is known to show moderate radiosensitivity when compared to the spleen and brain and is also known as a target organ to induce complication such as fibrosis after radiation treatment. Therefore, further study if lung specific genes involve in radiation induced complication and radiation response, will be needed. We do not know exactly if organ specific genes which examined in this study are involve in organ sensitivity by radiation. However, there genes may give a clue of regulating organ sensitivity and gene expression profiles after radiation, especially low dose radiation is under progressing now.

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