Alternative splicing and radiobiology

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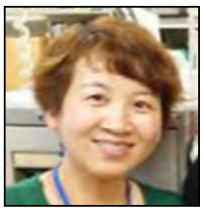

Abstract

Alternative splicing is a key molecular mechanism for increasing the functional diversity of the eukaryotic proteomes, but it also often altered in cancer. Mounting evidence indicates that alternative splicing, the process that allows production of multiple mRNA variants from each gene, contributes to the heterogeneity of the disease. Although the mechanism of alternative splicing variant in cancer is unclear, the cancer-specific alterntive splicing variants have been observed in a variety of human cancers and have been connected to tumorgenesis. In recent years several reports have uncovered how DNA damage can induce splicing changes that give rise to mRNA variants encoding different protein isoforms with the potential to affect the cellular response and the cell fate2. However, the role of alternative splicing in radiobiology remains enigmatic.

Hence the aim of our work is to study the radio-specific isoforms status in cancer cell lines related to apoptosis. For example, p73 isoforms can be divided into two groups: transcriptionally active p73 isoforms (TAp73) which induce apoptosis and activate transcription of cell cycle regulators, and N-terminally truncated variants (referred to as DNp73) which lack the N-terminal transactivation domain and inhibit TAp73 and p53 activity. Our findings have been reported that there is a differential ΔNp73 expression in response to different LET radiations, and down-regulated ΔNp73 expression might play a critical role in sensitivity of tumor cells2,3,4. Additionally, we tried to find new way used for detecting alterative splicing variants. We created an antibody microarray for the analysis of the expression of splice variants associated with cancer. Furthermore, we tried to find potential use of therapeutic approaches that target alternative splicing to enhance the radiosensitivity. Thus our work highlights the significance of variants in radiobiology and it might be targets for future therapeutic strategies.

Biography

Cuixia Di has been engaged in research on radiation sensitized tumor biology for many years. In recent years, she has published more than 60 articles in international well-known journals such as cell death and differentiation, FASEB Journal and so on. She has participated in many academic conferences hosted at home and abroad and made invitation reports. She won the second prize of medical science and technology of Gansu Province and the third prize of scientific and technological progress of Gansu Province. She has close cooperation with the cancer research center in Germany and the National Institute of radiology in Japan in heavy ion therapy for tumors and other diseases.

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