Analysis of Individual Difference of Radiosensitivity using Genome-editing Technique

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Current standards for radiological protection are applied uniformly to the public. However, the radiosensitivity of individual people can vary; this might depend on the nucleotide variants on the individual's DNA repair genes. To verify that these variants indeed result in a difference of radiosensitivity, it is useful to introduce such nucleotide variants into cultured human cells and evaluate their radiosensitivity. This will allow for a precise analysis of the effect of candidate nucleotide variants on individual radiosensitivity, independently of the diverse genetic background. However, having efficient gene targeting of cultured human cells has been difficult due to the low frequency of homologous recombination repair. Therefore, development of artificial nucleases enabled efficient homologous recombination-mediated genome editing to be performed in cultured human cells. Recently, we developed a novel genome editing strategy, called "TALEN-mediated two-step single-base-pair editing" and biallelically introduced a nucleotide variant associated with chromosomal instability into cultured human cells. The single-base-pair editing technique is now used to generate human model cells carrying the candidate nucleotide variants on DNA repair genes and to investigate their radiosensitivity.