

(様式4) (Form 4)

学位論文の内容の要旨

Dissertation Abstract

Sangeeta Kakoti

印

(学位論文のタイトル)

p53 deficiency augments nucleolar instability after ionizing irradiation
(p53欠損は放射線照射後の核小体不安定性を増大させる)

(学位論文の要旨) 2,000字程度、A4判 (approx. 800 Words in English /A4 size)

Ribosomes are important cellular components that maintain cell homeostasis through overall protein synthesis. The nucleolus is a prominent sub-nuclear structure that contains ribosomal DNA (rDNA) encoding ribosomal RNA (rRNA), an essential component of ribosomes. Despite the significant role of the rDNA- rRNA- ribosome axis in cellular homeostasis, the stability of rDNA in the context of the DNA damage response has not been fully investigated. In this study, we examined the number and morphological changes of nucleolin, a marker of the nucleolus, following ionizing radiation (IR) to investigate the impact of DNA damage on nucleolar stability. We found an increase in the number of nucleoli per cell in HCT116 and U2OS cells following IR. Interestingly, the IR-dependent increase in nucleolar fragmentation was enhanced by p53 deficiency. In addition, the morphological analysis showed several distinct types of nucleolar fragmentation following IR. The pattern of nucleolar morphology differed between HCT116 and U2OS cells, and the p53 deficiency altered the pattern of nucleolar morphology. Furthermore, carbon-ion particle irradiation induced more nucleolar fragmentation than X-ray in HCT116 cells. Finally, we found a significant decrease in rRNA synthesis in HCT116 *p53*^{-/-} cells following IR suggesting that severe nucleolar fragmentation down-regulates rRNA transcription. Our study suggests that p53 plays an essential role in protecting transcriptional activity of rDNA in response to DNA damage.