

EFFECTS OF LOW DOSE RADIATION ON DEVELOPING HUMAN RETINAL GANGLION CELLS FROM INDUCED PLURIPOTENT STEM CELLS

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Retinal ganglion cells (RGCs) are essential components for vision, whose long axons link to the visual field in the brain. Loss of RGC is often in the eyes observable in the eyes with various visual disorders, such as glaucoma and ischemia. Developments of RGCs start at gestational 5 weeks earlier than other kinds of neural cells in the retina. However, regeneration of RGC has never been reported in mammalian eyes so far. Instead, small amount of loss in RGC does not cause visual disturbance which may be supported by some surplus of RGCs in retina. To validate the effects of low dose radiation on the differentiation of RGC, we have established a protocol to differentiate iPS into RGCs within 35 days. We applied low dose irradiation of 30 mGy and 180 mGy for 24 hours from day 4 to day 5 and observed that the axagonal elongation was interfered. To dissect molecular mechanism of this finding, we performed a series of transcriptome analysis and extracted a group of genes, including PAX6, which were down regulated in a dose dependent manner. To identify radiation dependent gene regulation, we performed epigenetic analysis to identify active enhancers in affected genes. Based on H3K4me3 and H3K27ac localization, we work on motif analysis to identify consensus transcription factor binding sites could be observed. Currently, we are recollecting time course data and trying to find the earliest responsive transcription factor in low dose irradiation stimulation.

BIOGRAPHY

Mari Katsura is graduated from Hiroshima University Medical School, Hiroshima, Japan. She has been an ophthalmologist after graduation. Now her work is research for the effects of low dose radiation on human health, especially in neural cells. Her laboratory is in Isotope science center, The University of Tokyo, where many researchers from different fields are working cooperatively.

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