10th Jubilee

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INTERNATIONAL CONFERENCE ON RADIATION IN VARIOUS FIELDS OF RESEARCH

Spring Edition

June 13-17, 2022
Hunguest Hotel Sun Resort
Herceg Novi, Montenegro

BOOK OF ABSTRACTS

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Hypoxia affects the expression of SOX genes and induction of neural differentiation of human embryonal carcinoma NT2/D1 cells

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https://doi.org/10.21175/rad.spr.abstr.book.2022.22.2

The family of *SOX* genes encodes proteins that display properties of both classical transcription factors and architectural components of chromatin. During development of nervous system, as well as adult neurogenesis, SOX transcription factors govern diverse cellular processes such as maintaining the multipotency of neural stem cells, cell proliferation, cell fate decision, migration as well as terminal differentiation of neurons. Despite their well-known function in development and brain homeostasis, the expression and role of these genes in pathology- induced neural stem cell plasticity is poorly understood. Reduction in oxygen supply or ischemia are involved in various pathological conditions, such as stroke, traumatic brain injury and cardiac arrest, which promotes neurogenesis, angiogenesis, cell proliferation and other cell mechanisms for survival under the stress. The aim of the present study was to analyze the expression of SOX genes during *in vitro* neurogenesis following chemical hypoxia.

Neuronal differentiation of human pluripotent embryonal carcinoma stem cell line NT2/D1 was used as an *in vitro* model system for studying the process of human neurogenesis. Depending on different concentration, RA directed the differentiation of NT2/D1 cells into neurons with a different phenotype. The effect of stress caused by hypoxia on the properties of pluripotent cells as well as the induction of neural differentiation was monitored *in vitro* by culturing NT2/D1 cells in the presence of cobalt chloride, a chemical inducer of hypoxia. The results of the analysis showed that the effect of hypoxia on the expression of SOX2 and OCT4 proteins involved in maintaining the pluripotency of cells depends on the duration of action of cobalt chloride. After short-term exposure of the cells, an increase in the levels of expression of SOX2 and OCT4 proteins was detected, while long-term treatment of the cells led to a decrease in the expression of these proteins. Furthermore, results showed that depending of duration of cobalt chloride treatments, the level of expression of miR-21 in undifferentiated NT2/D1 cells significantly changed. In addition, long-term pretreatment of pluripotent cells with cobalt chloride resulted in increased expression levels of SOX2, SOX3 and GAD67 proteins in neural progenitors induced for 7 days in the presence of, either low or high concentration of retinoic acid, indicating that hypoxia causes increased efficiency of NT2/D1 cell neural differentiation.

Damage of brain tissue caused by reduction of oxygen and/or blood flow to the tissue is the leading cause of death worldwide and the leading cause of disability in humans. Our results contributes to the research focused on discovering the roles of SOX TFs and their gene targets in ischemia related pathologies, making them promising biomarkers and potential targets for future diagnostic and therapeutic strategies.