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Stress on Stem Cell

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Abstract

Stem cells are sensitive to stress because of their properties and functions. The presence of growth factors, cytokines, oxidative stress and mechanical stresses stimulate cell division and differentiation. Several signaling pathways that regulate the self-renewal and differentiation of stem cells are stress response pathways. Stem cells have a long life span and have the potential to divide. These properties cause transformation on cells, create specific stress responses such as apoptosis and senescence.mAging is an important source of stress for stem cells. Repetitive divisions, epigenetic irregularities, mutations and telomere erosions that occur in stem cells can cause cumulative effects on cells. In addition, chronic inflammation and oxidative stress cause impairment of systemic signals of the stem cell niche. In addition to generating serious damage to biological macromolecules, oxidative stress can cause genomic instability and cellular senescence by affecting cell proliferation. There are two different types of stress in stem cells: external stress caused by environmental factors that cause a potentially harmful change in a biological system, and internal stress that causes the accumulation of waste products during normal metabolism and the formation of reactive metabolites. Internal and external stresses that occur in stem cells cause different damages according to tissue-specific stem cell types. In this review; stress, factors causing stress and some therapeutic agents used against stress were taken in stem cells.

Keywords: Stem cells, stress, therapeutic, agents

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Introduction

The cells from which all cells of the organism originate, which can differentiate into different cell types, which have the ability to renew themselves and form clones, are called stem cells. They support continuous tissue regeneration throughout the adult's lifespan. However, they show a limited proliferation ability (Hoffman and Carpenter, 2005). Stress manifests itself in various ways at the cell and organism level. The types of stress occurring in SCs are divided into internal and external stress. Environmental factors that cause a potentially harmful change on a biological system are defined as external stressors. Internal stress factors are the accumulation of metabolic wastes during normal metabolism, the formation of reactive metabolites, and the damage and stresses caused by repeated cell division (Kirkwood, 2005, Tower, 2012). Replicative stress and cellular aging affect stem cell viability and function (Green et al., 2011).

Types of Stress in Stem Cells

Intrinsic Stress in Stem Cells: Cell divisions made by stem cells in order to regenerate tissues result in replication-related stress on cells. Replicative Aging (or 'Hayflick limit') refers to the limited number of divisions of normal cells before they enter an irreversible arrest in the cell cycle (Tower, 2012). Changes in the morphology and gene expression levels of cells with replicative aging make cells resistant to apoptosis. In addition to cell division; It also causes an aging phenotype with the stresses that occur. This is also known as cellular aging. These stresses include telomere shortening, DNA damage, expression of active oncogenes and oxidative stress (Goligorsky et al., 2009). Cellular senescence is also associated with normal chromatin modifications and disruptions in gene expression (Krizhanovsky et al., 2008). Oxidative stress, especially related to stem cells, damages all cellular macromolecules, including DNA, causing both apoptosis and cellular senescence (Pollina abd Brunet, 2011; Zhang, 2010).

Extrinsic Stress for Stem Cells: Extrinsic stress for stem cells includes environmental stresses that cause tissue and cellular damage in addition to systemic stresses. Radiation and xenobiotic toxins used in cancer treatment are environmental stress factors. Cancer treatments typically function in suppressing apoptosis in dividing cells or hyperstimulation of senescence pathways. Because stem cells divide, they are particularly susceptible to damage from these agents. Physical interactions with the extracellular matrix and biomechanical stresses are important factors in the regulation of stem cell biology (Tower, 2012).

Agents Used Against Stress in Stem Cells

Metformin: In a study to determine the effect of periodontal ligament stem cells (PLKH) on bone regeneration, the proliferation and differentiation abilities of PLCHs, the protective effects of Metformin against hydrogen peroxide-induced oxidative stress on PLCHs, and the mechanisms associated with the Akt-Nrf2 signaling pathway were investigated. In conclusion; low Metformin concentrations have been shown to stimulate osteogenic cell differentiation and inhibit adipogenic cell differentiation of PLCHs without affecting cell proliferation in vitro. Moreover, it has been reported that Metformin reduces the production of ROS induced by H2O2, increases antioxidant capacity, alleviates oxidative stress damage on proliferation and osteogenic cell differentiation in PLCHs. It was concluded that these beneficial effects of metformin are partially due to the activation of Akt-Nrf2 (Akt; Protein kinase B, NrF2; Nuclear factor erythroid 2-associated factor 2) signaling pathway, and that metformin administration may facilitate PLKH-based alveolar bone regeneration in the treatment of periodontitis (Jia et al., 2020).

Rosiglitazone: In a study evaluating the effect of neural stem cells on mitochondrial dysfunction and oxidative stress in the treatment of Alzheimer's disease; Two neuroprotective factors (Bcl-2 and CREB (CRE-binding protein)) were seen to reduce the levels of messenger RNA (mRNA) in neural stem cells, but it was reported that the use of Rosiglitazone significantly reduced these effects. However, it has been reported to reduce Amyloid beta-induced oxidative stress (Chang et al., 2016).

Curcumin: In an in vivo study on bone marrow mesenchymal stem cells (MSCs); It has been reported that pretreatment with curcumin significantly inhibits hypoxia and reoxygenation (H/R)-induced loss of viability and caspase-3 activity in bone marrow MSCs, and inhibits H/R-induced mitochondrial dysfunction by suppressing ROS accumulation and mitochondrial membrane potential reduction by accelerating ATP production (Wang et al., 2019).

Vitamin E: In a study evaluating the effect of MSCs in improving the resistance to oxidative stress that occurs during osteoarthritis; MSCs treated with vitamin E were exposed to oxidative stress with hydrogen peroxide in vitro and implanted in a rat model of osteoarthritis. Analyzes were made in terms of cell proliferation, apoptosis, cytotoxicity, chondrogenesis and repair of cartilage tissue. In conclusion; It has been shown that vitamin E has a significant effect on improving the repair potential of MSCs, and it has been reported that these effects occur with increased anabolic reaction and decreased catabolic reactions in cartilage tissue (Bhatti et al., 2017).

Apigenin: To evaluate its neuroprotective activity, in a study with neurons produced from induced pluripotent stem cell (iPKH) from healthy controls and familial sporadic Alzheimer's patients; It has been reported that it has strong anti-inflammatory properties with its ability to protect neurons and cell viability by regulating cytokine and nitric oxide release in inflammatory cells. In addition, it has been reported that Apigenin has the ability to protect iPKH-induced Alzheimer's neurons by significantly reducing spontaneous calcium signals and caspase-3/7-mediated apoptosis, and that Apigenin has a broad neuroprotective effect against Alzheimer's pathogenesis (Balez et al., 2016).

Conclusion

Stress is a common mechanism involved in stimulating stem cell division and differentiation in response to stem cell homeostasis and injury repair. Response to internal and external stress is important in the long-term culturing, repair and maintenance of stem cell populations. In particular, oxidative stress emerges as a common feature that limits stem cell culture and impairs function. In stem cell biology; The control of emerging stresses, the production and maintenance of functional cell reagents and the controllability of cell differentiation are becoming more and more important.

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