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Simulated Microgravity Inhibits the Proliferation of Chang Liver Cells by Attenuation of the Major Cell Cycle Regulators and Cytoskeletal Proteins

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Abstract: Simulated microgravity (SMG) induced the changes in cell proliferation and cytoskeleton organization, which plays an important factor in various cellular processes. The inhibition in cell cycle progression has been considered to be one of the main causes of proliferation inhibition in cells under SMG, but their mechanisms are still not fully understood. This study aimed to evaluate the effects of SMG on the proliferative ability and cytoskeleton changes of Chang Liver Cells (CCL-13). CCL-13 cells were induced SMG by 3D clinostat for 72 h, while the control group were treated in normal gravity at the same time. The results showed that SMG reduced CCL-13 cell proliferation by an increase in the number of CCL-13 cells in G0/G1 phase. This cell cycle phase arrest of CCL-13 cells was due to a downregulation of cell cycle-related proteins, such as cyclin A1 and A2, cyclin D1, and cyclin-dependent kinase 6 (Cdk6). SMG-exposed CCL-13 cells also exhibited a downregulation of α-tubulin 3 and β-actin which induced the cytoskeleton reorganization. These results suggested that the inhibited proliferation of SMG-exposed CCL-13 cells could be associate with the attenuation of major cell cycle regulators and main cytoskeletal proteins.

Keywords: Chang Liver Cells; cell cycle regulators; cytoskeleton; proliferation; simulated microgravity

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1. Introduction

Simulated microgravity (SMG) can be generated through several mechanisms, such as rotating wall vessels [1], 2D clinostats [2], 3D clinostats [3–6], or random positioning machines [7,8]. The model clinostat environment consists of purely rotational flow that is perpendicular to the gravitational field to interfere with the recognition of the gravitational acceleration vector of a biological system [9]. Clinostat with a rotating axis is called clinostat 2D. Meanwhile, in clinostat 3D, a second shaft is installed perpendicular to the first, operating at a constant speed and orientation. The slow rotation of clinostat could prevent the responses triggered by gravity [10]. These systems can modulate the orientation of the research object, in which this object cannot perceive the gravitational acceleration vector [11]. Previous studies have reported that microgravity inhibits the proliferation of several cell lines, such as human hematopoietic progenitor cells [12], bone marrow mesenchymal stem cells [13], and mouse mesenchymal stem cells [14]. SMG was also reported inducing markedly changes in cytoskeleton of many cell types. The remodeling of tubulin has been demonstrated in endothelial cells under microgravity