ATOMIC FORCE MICROSCOPY STUDY OF HUMAN MESENCHYMAL STEM CELLS

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The mesenchymal stem cells (MSCs) are the undiferentiated cells that can self-renew and diferentiate into tissue-specific cell types. MSCs, which possess self-renewal potential and multipotent properties, have recently been identified as a potential novel therapeutic strategy for various degenerative and autoimmune disorders, including multiple sclerosis [1]. The aim of the mesenchymal stem cell replacement therapy is to overcome central nervous system cell loss and remyelination failure. Moreover, due to their immunomodulative properties, MSCs can resolve inflammation triggered by injury or degeneration.

Nevertheless, a number of questions about the cellular and molecular biology of MSCs are not yet understood. Study in details of human mesenchymal stem cells (hMSCs) mechanical properties such as elasticity, adhesion and stiffness, cytoskeleton organization and cell shape are required to realize their promising potential for development of new therapies. In this work the actin cytoskeleton and mechanical properties of hMSCs were studied by fluorescence microscopy and atomic force microscopy. For atomic force microscopy (AFM) investigations the hMSCs were fixed with 2% glutaraldehyde for 30 min. All data were obtained on a Nanoscope (R) IIIa MultiMode atomic force microscope. Force modulation mode was used to study mechanical properties (local stiffness and adhesion) of the hMSCs. The images were acquired by using silicon nitride cantilevers (NSC12/50) with a nominal force constant of 0.65 N/m (NT-MDT, Zelenograd, Russia). The measurements were performed in air at room temperature. The AFM investigations of hMSCs exhibited a considerable range of morphologies. Cells possess irregularly shaped flat lamellipods. Lamellipodia contain orthogonally arranged actin networks at the hMSC peripheries. For the spindle shaped cells the height of the nuclear region varies from 400 nm to1 μm, whereas lamellipodia thickness varies from 150 to 340 nm. For the star shaped cell nuclear region height is about 400–800 nm with the lamellipodia thickness from180 to 300 nm. The area around nucleus looks like a smooth fiber mesh. AFM images demonstrate many parallel actin bundles with granule size of from 20 to 70 nm extending throughout the nuclear region. Darker parts in the adhesion image correspond to low adhesion value. The nucleus appears to be distinctly softer than the flat lamellipodia. According to the hMSC fluorescent images the microfilaments are linear in form and mostly is localized over the nucleus. The microtubules more often appear curved in form and span large regions of the hMSCs. Mechanical properties of hMSC most likely are regulated by the actin cytoskeleton, its structure and dynamics.

This study demonstrates that the AFM study of the structure and mechanical properties of MSCs can help in elucidating the mechanisms behind the beneficial effects of

stem cell transplantation leading to immunomodulation, transforming the central nervous system microenvironment from hostile to supportive and neurotrophic action, promoting the diferentiation and regeneration of endogenous oligodendrocytes.

References

1. The use of stem cells as a potential treatment method for selected neurodegenerative diseases: review / E. Cecerska-Heryc [et al.] // Cellular and molecular neurobiology. 2023. Vol. 43. P. 2643–2673.