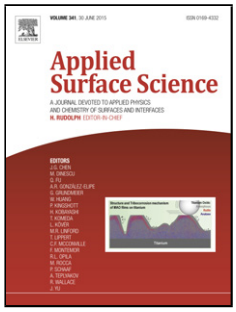

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Probing Stem Cell Differentiation Using Atomic Force Microscopy

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Abstract: A real-time method using atomic force microscopy (AFM) was developed to probe stem cell differentiation by measuring the mechanical properties of cells and the extracellular matrix (ECM). The mechanical properties of stem cells and their ECMs can be used to clearly distinguish specific stem cell-differentiated lineages. It is clear that AFM is a facile and useful tool for monitoring the differentiation of stem cells in a non-invasive manner.

Keywords

Atomic force microscopy, stem cell differentiation, cell mechanical property, extracellular matrix

Introduction

Recognition of the importance of mechanical signals from the microenvironment for various biological processes (e.g., tissue organization, tumorigenesis, and diseases) has increased in the last decade [1]. Mechanical loads on tissues or organs are transmitted to individual cells, leading to various physiological responses, such as orientation of cells, cell factor release and extracellular matrix (ECM) synthesis.[2-4] Therefore, how the physical interactions between cells and the ECM affect the mechanical properties of cells and how these mechanical interactions are transduced in mesenchymal tissues are important but still unanswered questions.[5-8] Moreover, recent progress in the study of cell behaviour has demonstrated a strong association between the mechanical properties of cells and tissue regeneration and some diseases.[9-13] For example, the cytoskeleton undergoes dynamic reorganization during stem cell differentiation.[14,15] Stem cells divide and create fully differentiated daughter cells during tissue and organ regeneration and/or repair as well as during normal cell turnover. After differentiation, cells show very different physical and biological characteristics (e.g., mechanical properties, ECM components, and cell structures) despite sharing the same genome.[16-19]

Probing the differentiation of stem cells prior to their *in vivo* application for stem cell therapies and tissue repair is of great importance. Striking evidence has shown that implanting stem cells with indefinite potential into the human body may result in tumorigenesis.[20] Researchers have well-established techniques, including gene expression and immunohistology, for controlling stem cell differentiation. However, the current analysis