

Materials for biological modulation, sensing, and imaging

Hyunjoon Kong and Joyce Y. Wong, Guest Editors

Biological cells are major building blocks of tissues and organs of living organisms. These cells are also being used as biomarkers for diagnosis and sources for regenerative medicine. To better understand and even regulate diverse activities of cells, materials capable of interacting with cells have been designed by integrating various material chemistry, characterization, and processing techniques. These materials are often integrated with various nano- and microscale engineering devices. In this article, we provide an overview of materials for biological modulation, sensing, and imaging and also discuss opportunities for the future development of multifunctional materials for sensing and therapies.

Introduction

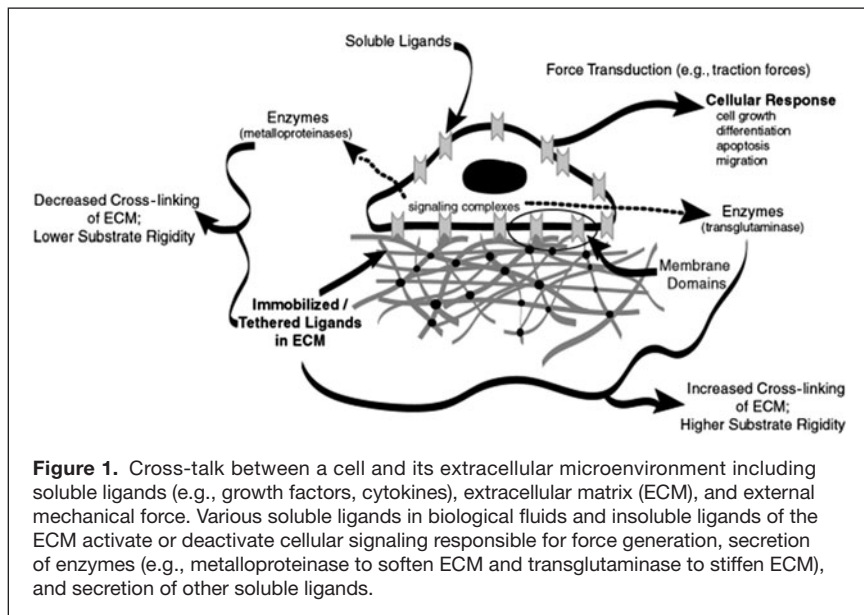
Biological cells are fundamental building blocks of tissues and organs of living organisms.¹ Over their lifetimes, cells are responsible for the development, programmed remodeling, and regeneration of tissues and organs. In addition, cells play crucial physiological roles, such as transport of oxygen and carbon dioxide, signal transduction, muscle contraction/relaxation, homeostasis, immune response, and metabolic activities. In addition, a number of chronic and malignant diseases result from a wide range of genetic abnormalities and the conversion of normal cells to cancer cells.

Therefore, cells have been studied extensively as biomarkers for early detection, therapeutic targets, and even as sources for regenerative medicine that can take current levels of diagnosis and disease treatment to the next level.^{2–7} In these efforts, cells are typically isolated from tissues of interest and cultured *in vitro*. Alternatively, various pluripotent and multipotent stem cells are being studied to generate specific cell types for use both in understanding their diverse emergent behavior and for treating disease and tissue defects via their *in vivo* transplantation.^{8–10} Efforts to directly convert fibroblasts (main component of connective tissue) to neuronal cells (i.e., nerve cells) are also under way.^{11,12} Additionally, these cells are actively being used to assemble *in vitro* platforms, such as “body-on-a chip” that can screen newly designed drug molecules, including recombinant proteins and genes.^{13,14} From these studies, there

is a growing consensus that the successful use of cells in fundamental studies and translational clinical treatments greatly depends on the ability to retain cell viability and to regulate cellular activities in a controllable and predictable manner.

It is well understood that the diverse activities of cells, including growth, gene expression, migration, differentiation, and even programmed death, are regulated by multifaceted extracellular microenvironmental factors and genetic influences (**Figure 1**). The characteristics of the microenvironment include various soluble biochemical factors, biochemical and biomechanical properties of the surrounding extracellular matrix, and intercellular adhesion.^{15–22} These factors also influence cellular binding and uptake of drug molecules and subsequent therapeutic activities.^{23,24} Major goals in the regenerative medicine field have been to recapitulate the extracellular microenvironment *in vitro* for specific diagnostic applications. In addition, a major goal for *in vivo* applications to regenerate damaged or diseased tissue has been to recapitulate specific tissue functions *in vivo* by first developing proper *in vitro* cell culture and subsequent *in vivo* transplantation tools and biomolecular carriers.^{21,25–27} Aligned with these efforts, various materials, either alone or integrated with other engineering devices such as microelectromechanical systems, are also being explored to analyze and control chemical, mechanical, and biological interactions inside and between cells.^{28–34}

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Interactive biological materials

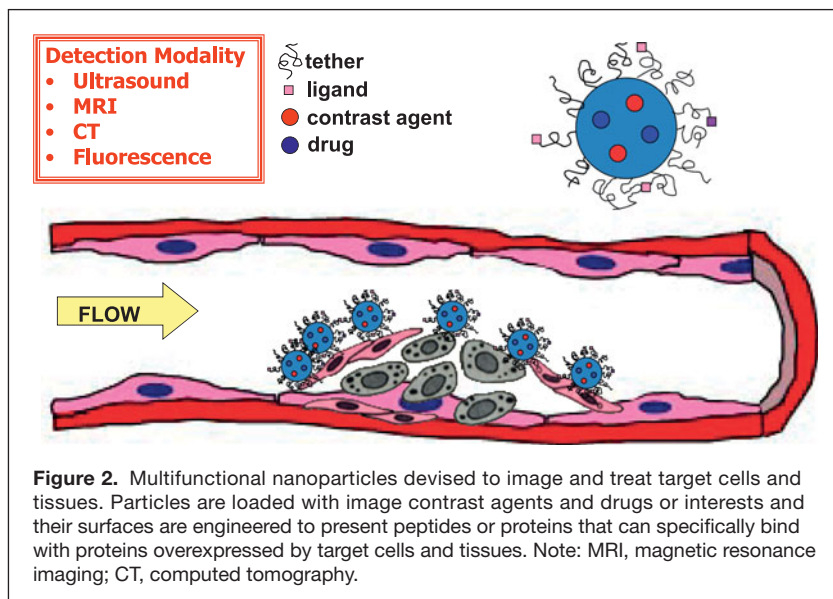
For the last few decades, there has been significant growth in designing such interactive biological materials by introducing or creating novel materials chemistry, characterization, and processing techniques. For instance, materials designed to present cell adhesion ligands found in the native extracellular matrix with mechanical properties similar to specific tissues were found to improve viability, modulate cellular adhesion machinery, and further stimulate or inhibit diverse cellular activities of various normal and pathologic cells.^{35–37} Additionally, various nanoscale materials (e.g., bioconjugated quantum dots, superparamagnetic iron oxide nanoparticles, carbon nanotubes) with unique photonic activities, as well as microfabricated materials coupled with electromechanical sensors

were proposed to analyze cellular mechanics and signaling.^{31,38–43} To this end, nano-sized biomolecular carriers were developed to facilitate binding to target cells and subsequent intracellular drug transport (**Figure 2**).^{44–47} However, there are still significant grand challenges in assembling such material systems that interface with biological cells. These challenges include overcoming both the difficulty of assembling multifunctional materials at varied length scales and the limited controllability of the feedback mechanism between cells and materials, and realizing the ability to sense and detect cellular near- to mid-term activities *in vivo*.

This issue of *MRS Bulletin* addresses these scientific and engineering challenges. The articles in this issue first critically explore the design of materials that have proved capable of reporting biological activities of cells, and second, identify challenges that are currently being faced. In addition, recent work that incorporates molecular and cellular biology techniques, specifically genetic engineering and strategies that harness the immune system into materials design, is described. The articles also include a discussion of opportunities for the future development of multifunctional materials for sensing and therapies. Finally, clinical perspectives and opportunities for the future development of these materials are discussed.

Overview of the articles

Kuo and Smith discuss perspectives on natural tissues as materials and also discuss how to develop novel synthetic materials that guide cell function. Next, Lewis et al. introduce efforts to design materials capable of modulating the immune response: (1) materials capable of suppressing immune response and (2) materials capable of activating or enhancing immune response. Then, Mastria and Chilkoti present a body of work based on genetically encoded elastin-like polypeptides that offer a route to modular, multifunctional drug delivery systems. Hwang et al. discuss the area of nanotheranostics and give examples of their recent work on genetic modification of cells and molecular imaging. Lee et al. introduce material considerations for vascularized organs-on-a-chip, which is rapidly emerging as a promising tool for fundamental and applied biological studies. Finally, Gomes et al. present their perspective on the potential barriers for translating gene therapies into clinical practice and what must be overcome for clinical translation.



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Glossary

Apoptosis: The process of programmed cell death.

Extracellular matrix: It is composed of proteins and other molecules (including polysaccharides) that surround cells.

Signal transduction: The cascade of processes by which an extracellular signal (typically a hormone or growth factor) interacts with a receptor at the cell surface, causing a change in the level of a second messenger and ultimately affects a change in the cell function.

Homeostasis: The tendency of an organism or a cell to regulate its internal conditions.

Pluripotent stem cell: A cell that possesses the potential to take on many fates in the body, including all of the more than 200 different cell types.

Multipotent stem cell: A cell that possesses the ability to differentiate into a various but limited number of cell types, especially into cells of a closely related family of cells.

Gene expression: The conversion of the information from the gene into mRNA (messenger RNA) via transcription and then to protein via translation.

Cell differentiation: The normal process by which a less specialized cell develops or matures to possess a more distinct form and function.

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