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Protein Nanotechnology- An Overview

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INTRODUCTION

The combination of nanotechnology and molecular biology has led to a new generation of nanoscale-based devices and methods for probing the cell machinery and elucidating intimate life processes occurring at the molecular level that were heretofore invisible to human inquiry.

HISTORY OF NANOTECHNOLOGY

Nanotechnology involves research and development on materials and species at length scales between 1 and 100 nm. The term *nano* is derived from the Greek word meaning "dwarf." In dimensional scaling, *nano* refers to 10–9, i.e., one billionth of a unit. *Nanotechnology* therefore, refers to the techniques and methods for studying, designing, and fabricating things at the nanometer scale. The initial concept of investigating materials and biological systems at the nanoscale dates to more than 40 yr ago, when Richard Feynman presented a lecture in 1959 at the annual meeting of the American Physical Society at the California Institute of Technology. Nanostructures are similar in size to many biological species such as proteins. These species comprise a wide variety of basic structures such as carbohydrates (sugars), and lipids; thus, they have a great variety of chemical, physical, and functional properties. To understand complex biological nanosystems at the cellular level, we urgently need to develop a next-generation nanotechnology tool kit.

THE IMPORTANCE OF PROTEIN NANOTECHNOLOGY

The living cell, with its myriad of biological components, may be considered the ultimate nanoscale device. Chemistry also deals with atoms and molecules, which are of nanometer sizes. However, nanotechnology differs from chemistry in a very fundamental aspect. Whereas chemistry deals with atoms and molecules at the bulk level (we do not see the molecules in chemical solutions), nanotechnology seeks to actually "manipulate" individual atoms and molecules in very specific ways. Proteins are major cellular components that play an essential role in maintaining the functioning of the cell. Proteins have a number of functions. They can function as enzymes, which are the driving force for biochemical reactions. Also, they can serve as antibodies that recognize invading elements and allow the immune system to neutralize and eliminate unwanted invaders.

Proteins have functions within physiological as well as pathophysiological processes in a cell or organism. Because diseases, therapy, and drugs can alter protein profiles, a determination of protein profiles can provide useful information for understanding disease and designing therapy. Therefore, understanding the structure, metabolism, and function of proteins at the molecular (i.e., nanoscale) level is absolutely critical to our understanding of biological processes. This knowledge will contribute to improving our ability to manipulate biological species in molecular manufacturing, enhancing energy production using biofuel-based microbial systems, or detecting the health status of a living organism in order to effectively diagnose and ultimately prevent disease. Proteins and genes are closely related. Thus, knowledge of the sequence information in genes is not sufficient to describe life. It is also critical to determine the function of the corresponding proteins, which are the actual players in the process of life.

PROTEIN STRUCTURE: THE BASIC BUILDING BLOCKS

Proteins are long chains of molecules consisting of polymers assembled from a large number of amino acids like beads on a necklace. The sequence of the amino acids in the polymer backbone is the *primary structure* of any given protein. Since amino acids have hydrophilic, hydrophobic, and amphilic groups, in an aqueous environment they tend to fold to form a locally ordered, 3D structure, called the *secondary structure*, that is characterized by a low-energy configuration with the hydrophilic groups outside and the hydrophobic groups inside. Folded proteins, such as egg albumin, can be unfolded by heating. Diseases such as Alzheimer's disease, cystic fibrosis, mad cow disease, an inherited form of emphysema, and even many cancers are believed to result from protein misfolding. Extensive experimental and theoretical research efforts have been devoted to determine the structure of proteins.

The goal of understanding the structure and function of proteins as integrated processes in cells, often referred to as "system biology," presents a formidable challenge, much more difficult than that associated with determination of the human genome. Therefore, proteomics, which involves determination of the structure and function of proteins in cells, could be a research area that presents more challenges than genomics. Proteomics research directions can be categorized as structural and functional. Structural proteomics, or protein expression, measures the number and types of proteins present in normal and diseased cells. This approach is useful in defining the structure of proteins in a cell. However, the role of a protein in a disease is not defined simply by knowledge of its structure. An important function of proteins is in the transmission of signals through intricate protein pathways. Proteins interact with each other and with other organic molecules to form pathways. Functional proteomics involves the identification of protein interactions and signaling pathways within cells and their relationship to disease processes. Elucidating the role that proteins play in signaling pathways allows a better understanding of their function in cellular behavior and permits diagnosis of disease and, ultimately, identification of potential drug targets for preventive treatment. Protein nanotechnology holds the promise of providing the critical tools needed to obtain real-time information about the signaling processes in cells.

PROTEIN MACHINES: NATURE'S ENGINES OF LIFE

Life is made possible by the action of a series of biological molecular nanomachines in the cell machinery. By evolutionary modification over trillions of generations, living organisms have perfected an armory of molecular machines, structures, and processes. The simplest cells used nanoscale manipulators for building molecule-sized objects. They are now used to build proteins and other molecules atom by atom according to defined instructions encrypted in the DNA. The cellular machinery uses rotating bearings that are found in many forms; for example, some protein systems found in the simplest bacteria are used as clamps that encircle DNA and slide along its length. Human cells contain a rotary motor that is used to generate energy. A wide variety of molecule-selective pumps are used by cells to absorb ions, amino acids, sugars, vitamins, and all of the other nutrients needed for living. Cells also use molecular sensors that can detect the concentration of surrounding molecules and compute the proper functional outcome. Over the last several years, Noid and Sumpter have investigated the performance of nanobearings, nanomotors, and fluid flow through nanotubes using fully dynamic (molecular dynamics) simulation. Various types of molecular bearings and other mechanical devices have recently been proposed in the growing nanotechnology literature.

Final Fact

The study of biological applications of nanotechnology will be important to the future of biological research and medical science. Medical applications of nanomaterials will revolutionize health care in much the same way that materials science changed medicine 30 yr ago with the introduction of synthetic heart valves, nylon arteries, and artificial joints. The protein nanotechnologies discussed previously are just some examples of a new generation of nanotools that have the potential to detect, identify, and manipulate single proteins in vivo and drastically change our fundamental understanding of the life process itself. They could ultimately lead to the development of new modalities of early diagnostics and medical treatment and prevention beyond the cellular level to that of individual proteins, the building blocks of the life process.