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REVIEWS

Healthcare Revolution: The Power of Nanosensing

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ABSTRACT

Now days era of average life expectancy of 100 is just around the corner. Everyone desires life without any diseases. Nanotechnology is developing faster than our expectation for disease free world. The essence of nanotechonogly is a nanosensor in which environment within the cell can be monitored in real-time. It is nearly impossible for us to avoid getting disease completely. However, if the symptoms of disease can be detected as early as possible, disease can be completely prevented. Disease is induced from a cell, which is the smallest unit of our body. If the nanosensing, which enables us to monitor the situation of cell metabolism in real-time, is combined with internet of things, a patient can easily check their health status through mobile devices on their hand and communicate with doctors who can also check the patients' health in real-time. The health care revolution through nanosensing will soon become realized.

KEYWORDS

Nanotechnology, Nanosensing Nanosensor, Nanorobot, Nanoscale

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INTRODUCTION

Biology has entered a new era with the recent advances in nanotechnology, which have recently led the development of nanosensor devices having nanoscale dimensions that are capable of probing the innerspace of single living cells [1]. Nano is now a popular label for much of modern science, and many nano- words have recently appeared in dictionaries, including: nanometer, nanoscale, nanoscience, nanotechnology, nanostructure, nanotube, nanowire, and nanorobot. Nanotechnology gives us ability to fabricate productive machines and devices that can manipulate things at the atomic level [2]. The purpose of developing nanotechnology is to have tools to work on the molecular level analogous to the tools we have at the macro world level.

One area of nanotechnology application that holds the promise of providing great benefits for society in the future is in the realm of medicine [3]. Nanotechnology has been described as the next the medical revolution, It includes manipulating properties and structures at the nanoscale, often involving dimensions that are just tiny fractions of the width of a human hair [4]. Nanotechnology is already being used as the basis of new and more effective drug delivery systems [5]. The purpose of this research is to understand current and future applications of nanotechnology in various fields of medicine.

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MAIN BODY

The Potential on the Nanoscale

A nanometer (nm) is 1,000 times smaller than a micrometer. It is equal to 1/1,000,000,000th or one-billionth of a meter (Figure 1). When things are this small, you can't see them with your eyes, or even with a light microscope. Objects this small require a special tool. Things on the nanometer scale include: Virus (30-50 nm) and DNA (2.5 nm). To see anything smaller than 500 nm, an electron microscope is required. Nanoscale objects have at least one dimension (height, length, depth) that measures between 1 and 999 nanometers (1-999 nm).

Nanomaterials are materials that have structural components smaller than 1 micrometer in at least one dimension. Nanoparticles are particles with at least one dimension smaller than 1 micron and potentially as small as atomic and molecular length scales (~0.2 nm). Nanoparticles (NPs) are of similar size to typical cellular components and proteins, and can efficiently intrude living cells [6]. At the molecular level, It is important for developing NPs designed for selective uptake by specific cells(1000nm-5000nm) [6]. The lymphatic capillary (Figure 2) is uniquely adapted for

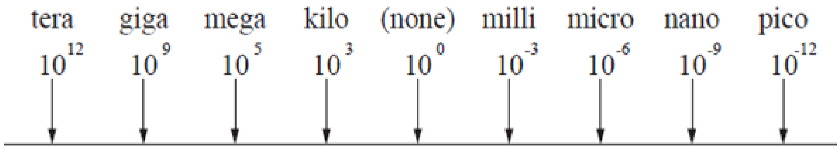

Fig.1. Unit of nano

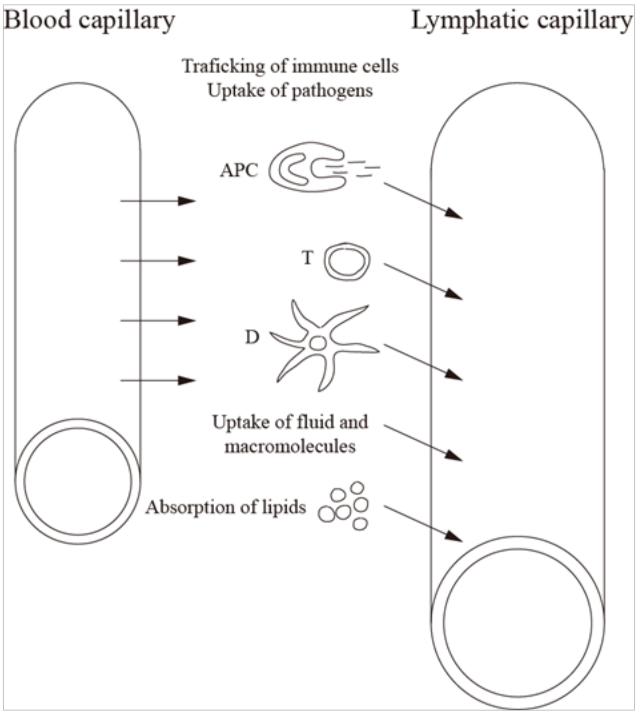

Fig.2. Characteristic structure and function of the lymphatic microvasculature

the uptake of fluid, lipids, macromolecules, and cells from the interstitium [7]. By directing leukocytes and antigens from tissues to lymph nodes, lymphatic vessels play an essential role in initiating the immune response [7]. Lymphatic capillaries are slightly larger in diameter than blood capillaries, But, The lymph nodes and lymphatic vessels, which consist of a single layer of thin-walled, and non-fenestrated lymphatic endothelial cells are more difficult to access than most vascular structures [8]. NPs also provide the capability of accessing into lymphatic vessels. Lymphatic capillaries are extremely porous because the gaps between lymphatic endothelial cells are roughly 30-120 nm in size, thus allowing the entry of large particles, cells, and interstitial fluid [8].

Generally, the sizes of nanomaterials are comparable to those of viruses, DNA, and proteins, while sizes of microparticles are comparable to those of cells, organelles, and larger physiological structures [7]. A red blood cell is approximately 7 µm wide, a hair 60 µm, while lung alveoli are approximately 400 µm [7]. Compared to microparticles, nanoparticles have a very large surface area and high particle number per unit mass. The ratio of surface area to volume (or mass) for a particle with a diameter of 60 nm is 1000 times larger than a particle with a diameter of 60 µm. A clear distinction should be marked between what we call nanoparticle and nano-organisms or their components(including bacteria, viruses, cells, and their organelles) [7]. Nano-organisms generally dissipate when their supply of energy is exhausted. In contrast, nanoparticles are typically inorganic solids that require no supply of energy to maintain their stable form [7]. Nanobacteria are ubiquitous within living organisms, humans and animals, and they are found in blood, serum, and organs. These very small bacteria are suspected of being the cause (at least in part) for many diseases. Advancement in the field of nanotechnology and its applications to the field of medicines and pharmaceuticals has revolutionized the twentieth century. Nanotechnology works on matter at dimensions in the nanometer scale length (1-100 nm), and thus can be used for a broad range of applications and the creation of various types of nano materials and nano devices [9].

The Final Goal of Nanosensing

In age of the 100 year life, everyone wants a life without illness. Health is one of the global challenges for humanity. To keep individuals healthy an effective and readily accessible modern healthcare system is a prerequisite [10]. Currently, the healthcare system is undergoing a cultural shift from a traditional approach to a modernized individuals centered approach [10]. The key element of Healthcare Revolution is a reliable and readily available body monitoring system. Diagnostic nanosensors will allow for the early detection of various diseases, like cancer, at the very onset of the symptoms, before the disease is perceived by the patient. Early detection means higher chances of successfully treating and overcoming the disease.

Nanosensor in which the condition of blood vessels, lymphocytes, extracelluar matrix, and cytoplasm can be measured in real-time is needed and nano robot that cleans up the waste in the body will also be needed. Moreover, nano capsule that transports the necessary material to tissue in which medicine treatment is also needed. It could be considered implantable nano sensor that is used to measure and collect physiological data [10]. IOT (Internet of Things) is used to transmit data from nanosensor to a mobile device or desk top of doctor [10]. Nano sensor in body is able to monitor the physiological data of individuals under 24hr real time condition. some problems that wearable sensors generate are many false alerts. Hence, these sensors are unsuitable for predicting the risk level of individuals. By using nano sensor Inserted into the body of individuals, the healthcare doctor can monitor, diagnose, and advice their clients from a remote location all the time.

Real-time observation of single-molecule activities in living cells by nano sensor is another important aspect of providing fundamentally new information about intracellular processes. One such nano ensor can be inserted into single living cells to monitor and measure, in vivo, molecules and chemicals of biomedical interest without disrupting normal cellular processes. Nano sensor potentially provide unprecedented insights into living cell function, allowing studies of molecular functions such as apoptosis-signaling process. An interesting biological target using nanosensor is programmed cell death, also known as apoptosis [11]. Apoptosis is an extensively regulated programme for the safe removal of cells and is essential for normal tissue homeostasis and tissue differentiation [11]. Only if the apoptosis rate equals the rate of cell division (mitosis) does the number of cells in an organ remain constant (homeostasis). Changes in apoptosis play a very important role in the pathology of many diseases such as atherosclerosis, myocardial infarction, stroke, neurodegenerative diseases and cancer [11]. Moreover, the induction of apoptosis is the goal of most cancer therapies. Currently, the effectiveness of anti-cancer treatments is evaluated by measurements of size reductions of the tumours [11].

The induction of apoptosis and necrosis usually occurs within hours after treatment begins [11]. Therefore nanosensing of apoptosis allows real-time monitoring of treatment outcome and identification of the most effective anticancer regimen for an individual patient [11]. Nanosensing enables us to have glimpses of the inner life of cells and insight into molecular mechanisms and dynamics of subcellular systems with unprecedented details. The ultimate goal of nanosensing is to design a truly personalized healthcare platform that can intelligently cater to each unique individual's healthcare needs [12].

Feasibility of Nanosensing

Cells must move materials through membranes and throughout cytoplasm in order to maintain homeostasis. The movement is regulated because cellular membranes, including the plasma and organelle membranes, are selectively permeable. The cellular environment is aqueous, meaning that the solutes dissolve in water, which is the solvent. In living cells, the movement of water into and out of a cell is affected by the relative solute concentration on either side of the plasma membrane. As water moves out of the cell, the cell shrinks, whereas when water moves into the cell, it swells. However, It cannot be monitored all of inside cells by nanosensor, Therefore, There are different kinds of possibility: real possibility and potential possibility. In dealing with the possibilities of nanosensor, real possibility should be considered first. Inside a living cell, numerous biological processes and biochemical reactions occur in the subcellular organelles, which are often compartmentalized and dynamically change intracellular physical and chemical properties such as temperature, pressure, mechanical and electrical characteristics, pH, viscosity, Osmolality and concentrations of ions and other molecules [13]. It is required for intracellular homeostasis to maintain normal cellular functions. Tracking the regulation of quantities on intracellular physical and chemical properties using nanosensor could reveal largely underexplored subcellular functions and mechanisms [13]. Moreover, an increasing body of evidence indicates a close correlation between intracellular disorders and diseases [13]. Thus, monitoring intracellular environments and quantitatively measuring intracellular properties would enable us to better understand subcellular activities and disease mechanisms and potentially develop new therapies via rescuing/altering subcellular functions [13]. Intra

cellular pH (pH_i) has an important role in the maintenance of normal cell function, and hence this parameter has to be tightly controlled within a narrow range, largely through the activity of transporters located at the plasma membrane [14]. Therefore, it appears that such a pH_i change might represent a more generalized apoptotic feature [14]. Apoptosis can be initiated by a wide variety of intracellular and extracellular stimuli and is a mechanism that removes unnecessary, aged, or damaged cells shrinkage, followed by widespread membrane blebbing, chromatin condensation, and DNA fragmentation.

For example, abnormalities in cell apoptosis, which can result from pH regulation disorders, can lead to cancers [13]. Cells maintain intracellular pH (pH_i) within a narrow range (7.1–7.2) by controlling membrane proton pumps and transporters [15]. pH-mediated changes affect processes such as migration and metastasis in cancer cell [15]. Cancer cells have a reversed pH gradient compared with normal cells in that Cancer cells having a higher intracellular pH and a lower extracellular pH than normal cells [15]. Measurements of the physical properties of cells with nanosensor indicate that the interior of a cell departs from these ideal conditions in several important ways [8]. The total concentration of macromolecules inside cells is very high, with proteins by far the most abundant species. Increasing of protein concentration in cytoplasm induces the osmotic response of all cellular water molecules [16]. In cell, cytosolic viscosity depends on the concentration of the solutes, The cytosol viscosity increases monotonically from with increasing osmolality [16]. Large viscosity variations within a cell can influence diffusion and bimolecular reaction rates and must be considered when developing strategies for drug delivery and cancer therapy [17].changes in the intracellular viscosity can be monitored through nanosensing [18].

Temperature is a fundamental physical quality that governs every biological reaction within living cells [19]. Thus, temperature distributions inside a living cell reflect the thermodynamics and functions of cellular components [19]. Temperature nanosensors are under development to meet the urgent demand for measuring temperature in a tiny intracellular space between cancer and normal cell [19]. Cancer cells favor low body temperature which means low oxygen levels and high acidity [20]. The point is that by increasing the body temperature, the the immune system is strenghtened because more enzymes become available. Proteins that are secreted by cancer cells paralyze the thermoregulation function. Cancer cells protect themselves from immune cells attack by lowering host's body temperature [20].

Methods of Nanosensing

In order to monitor the environment of inside cell, Nano sensor should be able to access into cytosol of target cells. Therefore, nano-robot is necessary. The feasibility of nano robots is inspired by existence of biological organisms at same size scales performing very efficiently, in robust manner and intelligently [21].

The flagellar motor of bacteria is a specialized and particularly interesting nanomachine, because it seems so similar to human-scale motors. The flagellar motor is a highly structured aggregate of proteins anchored in the membrane of many bacterial cells that provides the rotary motion that turns the flagella—the long whip-like structures that act as the propeller for these cells and allow them to propel themselves through water [22]. The flagellar motor is not activated by electric current to generate magnetic fields; instead it uses the decomposition of ATP to cause changes in the shape of the molecules that, when combined with a sophisticated molecular ratchet, make the protein shaft revolve [22]. Recent advancements in nanotechnology indicate that the nano robots might be capable of more than drug delivery. The main reasons of advancing attempts in nano robot are the unique applications in medical, health care and environmental monitoring [21]. A nanorobot is essentially a controllable machine at the nano meter or molecular scale that is composed of nano-scale components. Nanorobots are theoretical microscopic devices measured on the scale of nanometers, and would constitute any smart structure capable of sensing for processing of information and swarm behavior at nano scale. The development of nano robots is a technological breakthrough that can enable real time *in vivo* prognosis for application in a variety of biomedical problems [23]. Nanorobots could propose solutions at most of the nanomedicine problems. Nano robots integrated with nanosensors can help to transmit real time information in a single cell In fact, nano robots should be an efficient and powerful clinical device for monitoring [23]. The use of nano robots for *in vivo* monitoring chemical parameters should significantly increase fast medical decisions by doctors. The nano robot used for cellular level scale is a special and useful technological device to sense the nano environment and to monitor on living cell [23]. In the future, nano robot could deliver important medicines to previously inaccessible parts of the body (such as inside cell) or monitor direct cellular status in real time.

The power of Autonomous Nanosensing

Nanosensors provide new and powerful tools for monitoring *in vivo* processes within living cells, leading to new information on the inner workings of the entire cell [24]. They have the potential to become a key tool for health monitoring based on molecular information. The use of nanosensor could help save lives, and could detect and warn of early symptoms of impending cardiac (or other) problems, enabling the patient to receive potentially life-saving treatments earlier [25]. The nanosensor can also provide doctors with real bio-signal information on body. The field of Healthcare is entering a new era where technology is starting to handle Big Data, bringing about unlimited potential for information growth [26]. Data mining and Big Data analytics are helping to realize the goals of diagnosing, treating, helping, and healing all patients in need of healthcare [26]. Big Data occurs when new data is coming in at high speeds, which can be seen when trying to monitor real-time events whether that be monitoring a patient's current condition through medical nanosensors [26]. Data streams coming from nanosensors inside body require continuous analysis that gives the possibility for real-time results and predicting patient's conditions [26]. In the future, data mining technology will be developed with the goal of analyzing patient data in order to make real-time prognosis and diagnosis. Nanosensors allow for building integrated devices, providing an elemental base for intelligent sensors. Intelligent sensors are characterized as having significant data storing, processing, and analyzing capacity. Intelligent sensors can be utilized as autonomous systems or they can be spread out in large numbers to form networks [27]. In the future, many nano-robots with sensor will be stationed in cell, and blood throughout the body, where they would monitor various physiological parameters and periodically communicate their findings, The actual communication network would also be made up of nanosensors [27]. Twenty-four hours a day, year-in, year-out, nanosensors in tissue could measure every conceivable variables of a human body, at whatever scale might be appropriate. New computers would take the form of networks of sensors with data-processing and transmission facilities built in [27]. The interconnection of nanosensors with existing communication networks and ultimately the Internet defines a new networking paradigm that is further referred to as the Internet of Nano-Things [28]. In IOT networks, nanosensors deployed inside the human body are remotely controlled by an external user such as a healthcare provider. The nanoscale is the natural domain of molecules, proteins, DNA, organelles and the major components of cells. Amongst others, existing biological nanosensors provide an interface between biological phenomena and electronic devices, which can be exploited through this new networking paradigm [28, 29]. Recent researchers are underway to determine the communication architectures that could adequately support endeavors, like continuous remote patient monitoring and real-time analytics of biomedical signals through cloud computing and the Internet of Things [12].

When nanosensing is combined with wireless communication, it can also collect a range of valuable cell-level data for early detection of diseases [30]. Under networking in the Internet of Things, it is possible for nanosensors to accurately detect and predict the timings of good and bad on cell states [30].

CONCLUSION

Many of the cells are very tiny, and very active; they manufacture various substances; they walk around; they wiggle; and they do all kinds of marvelous things – all on a very small scale. Also, they store information. One of the major advantages of using nanosensor is its ability to collect real time data on cell *in vivo* [31]. Preventive diagnostic based on nanosensors could help reduce hospital admission and allow patients to be cared for at home, for longer period of time. The essence is keeping patients out of hospitals. In the near future, it is expected to emerge simple diagnostic nanosensor at the personal level that can universally monitor the health status of individuals in a relaxed atmosphere at home in real time. These diagnostic nanosensors should be able to digitize the collected information and use the internet to transfer data and communicate with the doctor's offices. One great possibility of healthcare cost reduction is to find a solution to the fact that much time and money is spent on patients visiting their doctors or a clinic and too little attention is afforded to preventive care. The nanosensor technology is one of the best solutions.

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