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Review Article

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Therapeutic Applications of Nanorobots- Respirocytes and Microbivores

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ABSTRACT

Nano medicine offers the prospect of powerful new tool for monitoring, repair, construction and treatment of human diseases and the improvement of human biological system using molecular nanotechnology. Changes in human behavior and life style over the last century have resulted in a dramatic increase in the diseases world-wide. Among the numerous conditions which can do harm to the human, the most fundamental problem may be due to lack of perfusion of oxygen to the tissue and blood borne pathogens. Insufficient oxygenation can lead to anemia, heart attack and sudden loss of blood supply. To overcome this, one of novel therapeutic technological concept in nanomedicine includes the application of respirocytes and microbivores to treat such conditions in humans.

Key words: Nano medicine, Nanorobotics, Respirocytes, Microbivores.

INTRODUCTION

The 21st century's most hopeful technology is nanotechnology. Nanotechnology is a collective term referring to technological developments on the nanometer scale, usually 0.1-100 nm. The term 'Nanotechnology' generally refers to engineering and manufacturing at the molecular or nanometer length scale [1]. Nanotechnology, 'the manufacturing technology of the 21st century', will offer an opening to build a broad range of economically complex molecular machines. It will lead to the building of computer controlled molecular tools much smaller than a human cell with the accuracy and precision of drug molecules. Nanomedicine, an outgrowth of nanotechnology deals with the prospect of powerful new tool for monitor, repair, construction, and treatment of human diseases and the improvement of human biological system using molecular nanotechnology. The ultimate goal is to improve the quality of life. They could remove obstructions in the circulatory system, kill cancer cells, or take over the function of subcellular organelles. Recently nano robots has been developed, which are of special interest to researchers in the medical industry. Nanorobotics [2] is an emerging field of nanotechnology which deals with design and construction of devices at an atomic, molecular or cellular level. A Nano robot is a tiny machine designed to perform a specific task. This has given rise to the field of Nano medicine. Nano medicine offers the prospect of powerful new tools for the treatment of human diseases and the augmentation of human biological systems. Today's world is suffering an extreme shortage of donor blood, even with Red Cross receiving 36,000 units a day this doesn't satisfy the 80,000 that are needed. People suffering from anemia and microbial diseases also run into a blood problem when their hemoglobin and white blood cell concentration in the blood cells fall below normal, causing severe tissue damage, immunodeficiency and finally lead to death. The root of the problem lies in erythrocytes and leukocytes. A possible future solution to this problem has been purposed by Scientists at the Institute for Molecular Manufacturing with their mechanical artificial red blood cell and white blood cell called a "Respirocytes", and Microbivores. This review is aimed to explore several of the worst medical problems and how Respirocytes and Microbivores can be used to cure them.

Respirocytes
An artificial Nano medical erythrocytes, or "respirocytes" [3], intended to duplicate all of the important functions of the red blood cell could serve as a universal blood supernumerary, preserve living tissue, and provide treatment for anemia, blocking, lung diseases, asphyxia, and other respiratory problems. Respirocytes are micron-scale spherical robotic red blood cells comprised of nanometer-scale components, containing an internal pressure of 1000 atmospheres of compressed oxygen and carbon dioxide. The intense pressure would be safely contained in two separate high pressure vessels likely made of pure diamond. At this intense pressure, a respirocyte could hold 236 times more oxygen and carbon dioxide than our natural red blood cells [4].

Mechanism of respirocytes
Respirocytes consist of oxygen vessel that contains oxygen gas, another is a carbon dioxide vessel that stores carbon dioxide and third is a water ballet that helps maintaining buoyancy [5]. There are specific rotors for the function of controlled uptake and release of oxygen and carbon dioxide. There is also a rotor that allows the passage of glucose into the device, which is combined with the oxygen from the internal storage tank to produce energy required for the working of respirocyte. This is done by an embedded fuel cell.

Applications
The artificial respirocytes is a Nano technological device whose primary applications include trasfusable blood substitution; treatment for anemia, perinatal and neonatal disorders, and a variety of lung diseases and conditions contributing to the success of certain aggressive cardiovascular and neurovascular procedures, tumor therapies and prevention of asphyxia, maintenance of artificial breathing in adverse environments and a variety of sports, veterinary, battlefield and other applications [6].

Transfusions & Perfusions
Respirocytes are used as the active oxygen-carrying component of a universally transfusable blood substitute that is free of disease vectors such as hepatitis, venereal disease, malarial parasites or AIDS, storable indefinitely and readily available with no need for cross-matching. In current practice, organs must be transplanted soon after harvest and respirocytes could be used as a long-duration perfusant to preserve living tissue, especially at low temperature, for grafts (kidney, marrow, liver, and skin) and organ transplantation [7].

Treatment of anemia
Respirocytes in oxygenated from help to treat all forms of anemia, including acute anemia caused by a sudden loss of blood after injury or surgical intervention (Young son C *et al.,* 1993) [8].

Cardio vascular and neurovasular application
Perfusion of respirocytes should be useful in maintaining tissue oxygenation during coronary angioplasty, organ transplantation, and Siamese-twin separation and in cardiopulmonary bypass solutions [9].

Tumortherapy and diagnosis
The formulation of respirocytes have been used to probe tissue oxygen tension. Respirocytes could be used as informer devices to map a patient's whole body blood pressure or oxygenations profile storing direct sensor data in each computer, to be later retrieved by device filtration and data reconstruction [10].

Asphyxia
Respirocytes should enhance and support breathing in case of oxygen-poor environment or where normal breathing is physically impossible.

Under water breathing
Respirocytes act as in vivo scuba device. Their product relives in ease of dangerous hazards of deep sea diving caisson disease, the nitrogen bubbles are formed in blood as a diver rises to the surface, from gas previously dissolved in the blood at higher pressure at greater depth. Respirocytes act as a long-duration perfusion to preserve living tissue (Pearson D *et al.,* 1992).

Other applications
Respirocytes could permit major new sports records to be achieved, because the devices can deliver oxygen to muscle tissues faster than the lungs can provide, for the duration of the sporting event. This would be especially

useful in running, swimming, and other endurance-oriented events, and in competitive sports such as basketball, football and soccer where extended periods of sustained maximum exertion are required. Artificial blood substitutes may also have wide use in veterinary medicine [11-12] especially in cases of vehicular trauma and renal failure where transfusions are required, and in battlefield applications demanding blood replacement or personnel performance enhancement. Swallowed in pill form, respirocytes could be an effective, though temporary, cure for flatulence. With suitable modifications, respirocyte technology could provide a precisely metered ingestible or injectable drug delivery system or could assist in the management of serum glycerides, fatty acids or lipoproteins, diabetic ketosis and gestational diabetes, and other dietary conditions.

Microbivores

A nanorobotic device that could safely provide quick and complete eradication of blood borne pathogens using relatively low doses of devices would be a welcome addition to the physician's therapeutic armamentarium. Such a machine is the microbivore, an artificial mechanical phagocyte. Microbivores [13] are the Nano robots that functions as artificial white blood cell and also known as nanorobotics phagocytes. The microbivore is a spheroid device made up of diamond and sapphire which measures 3.4 µm in diameter along its major axis and 2.0 µm diameter [14] along minor axis and consists of 610 billion precisely arranged structural atoms. It traps in the pathogens present in the blood stream and breaks down to smaller molecules. The main function of microbivore is to absorb and digest the pathogens in the blood stream by the process of phagocytosis.

Applications

The review suggests that existing treatments for many septicemic agents often require large quantities of medications that must be applied over long periods of time, and often achieve only incomplete eradication, or merely growth arrest, of the pathogen. A nanorobotics device that could safely provide quick and complete eradication of blood borne pathogens using relatively low doses of devices would be a welcome addition to the physician's therapeutic armamentarium.

Biofilm digestion

Microbivores, slightly altered, could also be used to digest bacterial biofilms [15]. Biofilms may vary widely in thickness, which is limited more by nutrient transport than by surface roughness. In vitro experiments show that aerobic *Pseudomonas aeruginosa* biofilms can grow to 30-40 microns in depth as monocultures, but may increase in depth to 130 microns when the culture is amended with anaerobic bacteria [16]. Microbivores can digest biomaterial at a rate of ~4 micron^3/min, hence an array of closely packed microbivores (~6.8 micron^2/device) attached to a biofilm can consume the biofilm at a rate of ~10 nm/sec, requiring ~10^5 sec (~3 hr) to consume an entire 100-micron thick biofilm. Again, some means must be found to ensure a watertight seal between partially fragmented organisms and the microbivore ingestion port [17].

Infections of meninges and cerebrospinal fluid

Microbivores could be useful in the treatment of infections of the meninges and the cerebrospinal fluid (CSF) by quickening the kill rate as opposed to typical antibiotic treatments.

Systemic inflammatory cytokine management

Microbivores could also be used in systemic inflammatory cytokine management [18].With minor additions, microbivores could be used to combat toxemia, the distribution throughout the body of poisonous products of bacteria growing in a focal or local site, and other biochemical sequelae of sepsis. Often times even when killing a certain bacteria, byproducts produced can significantly harm the body. Since in the microbivores, all the bacteria components are internalized and fully digested into harmless non antigenic molecules prior to discharge from the device, the Nano robots represent a complete antimicrobial therapy without increasing the risk of sepsis or septic shock.

Bacterial infections in other fluids and tissues

Microbivores could also aid in treatment of bacterial infections of other fluids and tissues [18]. Bacteria present in sputum or in the mucous layers of the throat may be pursued by somewhat larger ambulatory microbivores having an additional array of longer grapples that could serve as locomotive mechanisms (legs), thus permitting the nano robots to engage in microbial search-and-destroy missions along the luminal surfaces of the human trachea, bronchi, and bronchioles. With additional modifications, other variants of microbivores could patrol tissues, organs, and nonsanguinous fluid spaces such as pleural, synovial, or urinary fluids, pursuing bacteria as they disseminate beyond

the bloodstream. Vasculomobile microbivores could follow cytokine gradients and collect at sites of infection, thus increasing their microbicide efficiency.

Viral, fungal, and parasitic infections

Microbivores could also be used to rid the blood of viral pathogens, which are typically present during viremia at concentrations similar to those found in bacteremia. Viruses tend to be much smaller than most bacteria, so processing time per virion may be considerably reduced, perhaps 5-10 seconds or less. Apparently the human body is already fairly efficient at removing virus particles from the bloodstream. The difficulty for the natural defensive systems is that replacement viruses are rapidly replicated and discharged into the blood by infected cells, thus perpetuating the infection. These high production rates are nevertheless easily controlled by a terabot population of microbivores which has a collective digestive capacity of >1015 virions/day. One additional complication, well within the competence of the current microbivore design, is that some viruses like HIV are mutating constantly, so that one patient may have as many as 8-10 different strains concurrently, all of which must be successfully recognized and eliminated.

Fungemias involving particle loads of 1-1000 CFU/ml are rapidly cleared by microbivores. Fungal particles may be up to ~400 micron3 in volume, requiring ~100 min for complete digestion using a microbivores' protocol that employs careful piecewise digestion involving ~800 "bites".

Blood parasites of comparable size may be present at concentrations similar to those found in bacteremia but may be controlled with terabot doses of microbivores. Microbivores also could be helpful in aiding in biofilm digestion, aiding in bacterial Infections in other fluids and tissues, aiding in viral, fungal, and parasitic infections and other useful treatments.

Other applications

Microbivores could be designed to trap and retain (without digesting) samples of unknown microbes found floating in the bloodstream, when those microbes fall within a certain physician-specified size range and are confirmed not to be platelets or chylomicrons. These samples could then be returned to the attending physician for further investigation, following nan apheresis. Ranging still further afield, microbivore-derived devices could be employed in veterinary and military applications; to disinfect surfaces, objects, and volumes (e.g., 102-105 CFU/ml bacteria found in the sink fluid of washbasin drains in a pediatric ward or to sterilize organic samples or edible foodstuffs; to clean up biohazards, bio polluted drinking water, toxic biochemical, or other environmental organic materials spills, as in bioremediation; and in many other useful applications.

CONCLUSION

The nanorobotics are found to exhibit strong potential to diagnose and treat various medical conditions like cancer, heart attack, diabetes, arteriosclerosis, kidney stones etc. The nano robot can allow us a personalized treatment, hence can achieve high efficacy against many diseases. This review presents a preliminary design for a simple nano medical device that functions as artificial erythrocyte and white blood cell. Erythrocyte duplicating the oxygen and carbon dioxide transport functions of red cells largely eliminates the need to manage carbonic acidity because CO_2 is carried mechanically, rather than chemically, in the blood. The respirocytes would be 236 times quicker when compared to normal red blood cells. Microbivores, whose primary function is to destroy microbiological pathogens found in the human bloodstream using a digest and discharge protocol. The device may consume up to 200 pW of continuous power while completely digesting trapped microbes at a maximum throughput of 2 micron^3 of organic material per 30-second cycle. Microbiovores are up to ~1000 times faster –acting than either natural or antibiotic-assisted biological phagocytic defenses, or are ~80 times more efficient as phagocytic agents than macrophages, in terms of volume/sec digested per unit volume of phagocytic agent.

Future advances in the engineering of molecular machine systems permit the construction of the artificial Respirocyte and Microbivores and may find dozens of applications in therapeutic and critical care medicine, and elsewhere. When the severe side effects of the existing therapies are been considered, the Nano robots are found to be more innovative, supportive to the treatment and diagnosis of vital diseases.

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