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Inventive appliance of nano medicine via artificial red blood cell respirocytes

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ABSTRACT

The present manuscript concerns the formation of artificial red blood cells and blood substitutes An alternative method for synthesis of erythrocyte models for simulating cellular pathology in clinical hematology as proposed precise control of matter at the atomic and molecular level, allowing the construction of micron-scale machines comprised of nanometer-scale components. The complex human body with its interdependent physiological subsystems can be scaled down to a collection of various types of molecules. The accessibility to the molecular and atomic components of the body can resolve a variety of constraints faced in the medical field and can provide a tremendous breakthrough for the treatment of a variety of diseases which are considered incurable in the present scenario. The artificial red blood cell or "respirocyte" proposed here is a blood borne spherical 1-micron diamond 1000-atm pressure vessel with active pumping powered by endogenous serum glucose, able to deliver 236 times more oxygen to the tissues per unit volume than natural red cells and to manage carbonic acidity. An on board nanocomputer and numerous chemical and pressure sensors enable complex device behaviors remotely re programmable by the physician via externally applied acoustic signals. Primary applications will include transfusable blood substitution; partial treatment for anemia, perinatal/neonatal and lung disorders; enhancement of cardiovascular/neurovascular procedures, tumor therapies and diagnostics; prevention of asphyxia; artificial breathing; and a variety of sports, veterinary, and other uses. Even though the respirocytes have not been practically implemented wide research is going on for the design of these promising artificial red blood cells. The major problem in the design of these nanorobots is their manufacturing in the nano scale using materials and components which are physically and chemically compatible with the human body with minimum after effects. The respirocytes thus give us huge hopes for the elimination of many currently untreatable diseases with added advantages of precise and effective resolution

KEYWORDS

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INTRODUCTION

Molecular manufacturing promises precise control of matter at the atomic and molecular level. One major implication of this realization is that it may become possible to construct machines on the micron and the nanometer scale. Sub assemblies of such devices may include such useful robotic components designed for molecule-by-molecule reagent purification, and smooth superhard surfaces made of atomically flawless diamond[1,2]. Such technology has clear medical implications as It would allow to perform precise interventions at the cellular and molecular level. Medical nanorobots have been proposed for gerontological applications[3], in pharmaceutical research and to diagnose diseases, mechanically reverse atherosclerosis[4-8], supplement the immune system[9], rewrite DNA sequences *in vivo*[10], repair brain damage[11], and reverse cellular insults caused by "irreversible" processes[12] or by cryogenic storage of biological tissues[1,13,14]. The goal of the present manuscript is to present one such nanotechnology design for a specific medical nanodevice that would achieve a useful result as An artificial mechanical erythrocyte termed as "respirocyte." At the present moment, the fundamental problem of hematology is the development of biologically compatible non-heme protein-free blood substitutes with the same functional properties as red blood cells. There were several attempts to create alternative blood substitutes based on perfluorocarbon emulsions in order to avoid the intoxication by hemoglobin-containing blood substitutes[2-5]. However, the oxygen capacity of perfluorocarbon does not correspond to the oxygen capacity of native blood and plasma. Besides, the practical application they are accompanied by a number of medical problems like wise phylactic reaction[7]. Perfluorocarbons are not stable enough due to their lipophilicity[8,9] and thus tends to interact with plasma membrane lipids and receptors. The creation of new nanomechanical devices[10,11] that mimic the functions of blood cells, both erythrocytes and lymphocytes are termed as Respirocytes – they are carbon nanomachines with a diameter of 1 micron, containing mesoscopic tanks - reservoirs of O2, CO2, water and glucose for respiration and energy supply.

The transportation of respiratory gas transport in the blood is well understood. In brief, oxygen and carbon dioxide are carried between the lungs and the other tissues, mostly within the red blood cells. Hemoglobin, the principal protein in the red blood cell, combines reversibly with oxygen, forming oxyhemoglobin. About 95% of the O_2 is carried in this form, the rest being dissolved in the blood. At human body temperature, the hemoglobin in 1 liter of blood holds 200 cm^3 of oxygen, 87 times more than plasma alone (2.3 cm^3) can carry. Carbon dioxide also combines reversibly with the amino groups of hemoglobin, forming carbamino hemoglobin. About 25% of the CO_2 produced during cellular metabolism is carried in this form, with another 10% dissolved in blood plasma and the remaining 65% transported inside the red cells after hydration of CO_2 to bicarbonate ion. The creation of carbamino hemoglobin and bicarbonate ion releases hydrogen ions which, in the absence of hemoglobin, would make venous blood 800 times more acidic than the arterial[12-15]. This does not happen because buffering action and isohydric carriage by hemoglobin reversibly absorbs the excess hydrogen ions, mostly within the red blood cells. Respiratory gases are taken up or released by hemoglobin according to their local partial pressure. There is a reciprocal relation between hemoglobin's affinity for oxygen and carbon dioxide[17]. The relatively high level of O_2 in the lungs aids the release of CO_2, which is to be expired, and the high CO_2 level in other tissues aids the release of O_2 for use by those tissues[18].

PRESSURE VESSEL

Given the goal of oxygen transport from the lungs to other body tissues, the simplest possible design for an artificial respirocyte is a microscopic pressure vessel, spherical in shape for maximum compactness. Most proposals for durable nanostructures employ the strongest materials, such as flawless diamond or sapphire constructed atom by atom, In the simplest case, oxygen release could be continuous throughout the body. Slightly more sophisticated is a system responsive to local O_2 partial pressure, with gas released either through a needle valve (as in aqualung regulators) controlled by a heme protein that changes conformation in response to hypoxia, or by diffusion via low pressure chamber into a densely packed aggregation of heme-like molecules trapped in an external fullerene cage porous to

environmental gas and water molecules[19-21]

THERAPEUTICS AND PERFORMANCE

Artificial mechanical red cells can give physicians the ability to precisely control saturation curve profiles independently for oxygen and carbon dioxide, either to maximize gas transport efficiency or to meet specialized demand functions imposed by emergency situations, unusual activities, or specific medical treatments. The artificial respirocyte is a simple nanotechnological device whose primary applications include transfusable blood substitution[22]; treatment for anemia, perinatal and neonatal disorders, and a variety of lung diseases and conditions; contribution to the success of certain aggressive cardiovascular and neurovascular procedures, tumor therapies and diagnostics; prevention of asphyxia; maintenance of artificial breathing in adverse environments; and a variety of sports, veterinary, battlefield and other applications.

TRANSFUSIONS AND PERFUSIONS

Respirocytes may be 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. Mechanical red cells, like other artificial blood substitutes, may permit treatment and In current practice, organs must be transplanted soon after harvest; 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[7,9,21].

Treatment of anemia

Oxygenating respirocytes offer complete or partial symptomatic treatment for virtually all forms of anemia, including acute anemia caused by a sudden loss of blood after injury or surgical intervention; secondary anemias caused by bleeding typhoid, duodenal or gastric ulcers; chronic, gradual, or post-hemorrhagic anemias from bleeding gastric ulcers, hemorrhoids, excessive menstrual bleeding hereditary anemias including hemophilia, leptocytosis and sicklemia, thalassemia and anemias resulting from infectious diseases including rheumatism, scarlet fever and cancer, or from hemoglobin poisoning such as by carbon monoxide inhalation; hemolytic anemias including chemical hemolysis (including malarial, snake bite, etc.)[23], paroxysmal hemoglobinuria, and chronic hemolytic anemia from hypersplenism due to cirrhosis of the liver[9].

Fetal and child-related disorders

Respirocytes may be useful in perinatal medicine, as for example infusions of device suspension to treat fetal anemia (erythroblastosis fetalis), neonatal hemolytic disease, or *in utero* asphyxia from partial detachment of the placenta or maternal hypoxia, to restore the oxygen-carrying ability of fetal blood[24-26]. Asphyxia neonatorum, as from umbilical cord compression during childbirth, may fatally deprive the infant of oxygen; prenatal respirocyte treatment could be preventative. Many cases of Sudden Infant Death Syndrome (SIDS) or crib death. Respirocytes could also aid in the treatment of childhood afflictions such as whooping cough, cystic fibrosis, rheumatic heart disease and rheumatic fever, congenital heart disorders and laryngo trachea bronchitis[23].

Respiratory diseases

Current treatments for a variety of respiratory viruses and diseases, including pneumonia, bronchopneumonia and pleuropneumonia; pneumoconiosis including asbestosis, silicosis and berylliosis; emphysema, empyema, abscess, pulmonary edema and pleurisy; epidemic pleurodynia; diaphragm diseases such as diaphragmatic hernia, tetanus, and hiccups; blood flooding in lungs (hemoptysis, tuberculosis, chronic histoplasmosis, and bronchial tube rupture). The devices could provide an effective long-term drug-free symptomatic treatment for asthma, and could assist in the treatment of hemotoxic (pit viper) and neurotoxic (coral) snake bites[27]; hypoxia, stress polycythemia and lung disorders resulting from cigarette smoking and alcoholism; neck goiter and cancer of the lungs, pharynx, or thyroid; pericarditis, coronary thrombosis, hypertension, and even cardiac neurosis; birth traumas leading to cerebral palsy, and low blood-flow conditions seen in most organs of people as they age. Even poliomyelitis, which still occurs in unvaccinated Third World populations, could be treated with respirocytes and a diaphragmatic pacemaker[5,9].

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Cardiovascular and neurovascular applications

Respirocyte perfusion could be useful in maintaining tissue oxygenation during anesthesia, coronary angioplasty organ transplantation, siamese-twin separation, other aggressive heart and brain surgical procedures in postsurgical cardiac function recovery, and in cardiopulmonary bypass solutions. The device could help prevent gangrene and cyanosis[28].

Asphyxia

Respirocytes make breathing possible in oxygen-poor environments, or in cases where normal breathing is physically impossible. Prompt injection with a therapeutic dose, or advance infusion with an augmentation dose, could greatly reduce the number of choking deaths and the use of emergency tracheostomies, artificial respiration in first aid, and mechanical ventilators. The device provides an excellent prophylactic treatment for most forms of asphyxia, including drowning, strangling, electric shock (respirocytes are purely mechanical), nerve-blocking paralytic agents, carbon monoxide poisoning, underwater rescue operations, smoke inhalation or firefighting activities, anaesthetic/barbiturate overdose, confinement in airtight spaces (refrigerators, closets, bank vaults, mines, submarines), and obstruction of breathing by a chunk of meat or a plug of chewing tobacco lodged in the larynx[29]. Respirocytes augment the normal physiological responses to hypoxia, which may be mediated by pulmonary neuroepithelial oxygen sensors in the airway mucosa of human and animal lungs[27]. A design alternative to augmentation infusions is a therapeutic population of respirocytes that loads and unloads at an artificial nanolung, implanted in the chest, which exchanges gases directly with the natural lungs or with exogenous gas supplies.

Tumor therapy and diagnostics

Cancer patients are usually anemic. X-rays and many chemotherapeutic agents require oxygen to be maximally cytoxic, so boosting systemic oxygenation levels into the normal range using respirocytes might improve prognosis and treatment outcome. Fluorocarbon emulsions have been used to probe tissue oxygen tension; similarly, respirocytes could be used as reporter devices to map a patient's whole-body blood pressure or oxygenation profile, storing direct sensor data in each computer along with positional information recorded from a network of precisely positioned acoustic transponders, to be later retrieved by device filtration and data reconstruction. A similar network of acoustic transmitters, making possible respirocyte autotriangulation hence precise internal positional knowledge, could allow preferential superoxygenation of specific tissues, enhancing treatment effectiveness[22-25].

Further 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[8,11]. 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. They could improve geriatric sports participation. Hyperbaric oxygenation by respirocytes could help treat anaerobic and aerobic infections such as clostridial myonecrosis, chronic refractory osteomyelitis[30-33], and necrotizing soft tissue infections including cutaneous ulcers, and could assist in burn recovery by reducing fluid requirements, improving microcirculation, and reducing the need for grafting[34]. Artificial blood substitutes may also have wide use in veterinary medicine, especially in cases of vehicular trauma and renal failure where transfusions are required. Swallowed in pill form, respirocytes could be an effective, though temporary, cure for flatulence, which gas is largely swallowed air and CO_2 generated by fermentation in the stomach. 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.

REFERENCES

[1] K.E.Drexler; Engines of Creation: 'The Coming Era of Nanotechnology', New York: Anchor Press/ Doubleday, **(1986)**.

[2] R.C.Merkle; 'The molecular repair of the brain', Cryonics, Part I, 16-31, Jan. (1994); Part II 20-32, Apr. **(1994)**.

[3] G.M.Fahy; Possible medical applications of

nanotechnology. In: B.C.Crandall, J.Lewis, (Eds); 'Nanotechnology: Research and Perspectives', Cambridge MA: MIT Press, 251-267 **(1992)**.

[4] R.C.Merkle; The technical feasibility of cryonics, Med.Hypoth, **39**, 6-16 **(1992)**.

[5] G.M.Fahy; A realistic scenario for nanotechnological repair of the frozen human brain. In: 'Alcor Life Extension Foundation. Cryonics: Reaching for Tomorrow', Appendix B. Scottsdale AZ, Alcor Foundation, **(1993)**.

[6] B.Wowk; 'Cell Repair Technology', Cryonics, July **(1988)**.

[7] T.M.Devlin, (Ed); 'Textbook of Biochemistry with Clinical Correlations', New York, John Wiley & Sons, **(1986)**.

[8] K.E.Drexler; Molecular engineering: an approach to the development of general capabilities for molecular manipulation, Proc. NAS USA, **78**, 5275-5278 **(1981)**.

[9] K.E.Drexler; 'Nanosystems: Molecular Machinery, Manufacturing, and Computation', New York, John Wiley & Sons, **(1992)**.

[10] GM.Fahy; Short-term and long-term possibilities for interventive gerontology, J.Med., **58**, 328-340 **(1991)**.

[11] G.M.Fahy; Molecular nanotechnology, Clin.Chem., **39**, 2011-2016 **(1993)**.

[12] G.M.Fahy; Molecular nanotechnology and its possible pharmaceutical implications. In: C.Bezold, J.A.Halperin, J.L.Eng, (Eds); 2020 Visions: 'Health Care Information Standards and Technologies', Rockville MD, U.S. Pharmacopeial Convention, 152-159 **(1993)**.

[13] C.Lampton; Nanotechnology promises to revolutionize the diagnosis and treatment of diseases, Genetic Eng News, **4**, 23, 1 Apr **(1995)**.

[14] R.A.Freitas Jr.; The future of computers, Analog, **116**, 57-73 Mar. **(1996)**.

[15] A.K.Dewdney; Nanotechnology — wherein molecular computers control tiny circulatory submarines. Sci.Am., **258**, 100-103 Jan. **(1988)**.

[16] R.C.Merkle; Nanotechnology and medicine. In: R.M.Klatz, (Ed); 'Advances in Anti-Aging Medicine', Liebert Press, http://nano.xerox.com/nanotech/nanotechAndMedicine.html, **1**, 277-286 **(1996)**.

[17] J.C.Clark Jr, F.Gollan; Survival of mammals breathing organic liquids equilibrated with oxygen at atmospheric pressure. Science, **152**, 1755-1757 **(1966)**.

[18] R.P.Geyer; Bloodless rats through the use of artificial blood substitutes. Fed.Proc., **34**, 1499-1505 **(1975)**.

[19] C.Marwick; More than a trickle of interest in blood substitutes. JAMA, **271**, 895 **(1994)**.

[20] E.Griffiths, A.Cortes, N.Gilbert, P.Stevenson, S.MacDonald, D.Pepper; Haemoglobin-based blood substitutes and sepsis. Lancet, **345**, 158-160 **(1995)**.

[21] M.S.Litwin, C.W.Walter, P.Ejarque, E.S.Reynolds; Synergistic toxicity of Gram-negative bacteria and free colloidal hemoglobin. Annals Surg., **157**, 485-493 **(1963)**.

[22] G.H.Bornside, I.Cohn; Hemoglobin as a bacterial virulence-enhancing factor in fluids produced in strangulated intestinal obstruction, Am.Surg., **34**, 63-67 **(1968)**.

[23] A.M.Sellards, G.R.Minot; Injection of haemoglobin in man and its relation to blood destruction, with special reference to the anemias. J.Med.Res., **34**, 496-594 **(1916)**.

[24] J.Hodgson; Substitutes for human blood. Biotechnology, **9**, 69 **(1991)**.

[25] S.R.Eastaugh; Valuation of the benefits of risk-free blood. Intl.J.Technol.Assess Health Care, **7**, 51-57 **(1991)**.

[26] J.A.Jones; Red blood cell substitutes: current status. Brit.J.Anaesthes, **74**, 697-703 **(1995)**.

[27] T.F.Zuck, J.G.Riess; Current status of injectable oxygen carriers. Crit.Rev.Clin.Lab.Sci., **31**, 295-324 **(1994)**.

[28] (a) T.M.S.Chang, R.Geyer, (Eds); Blood Substitutes. New York: Marcel Dekker, **(1988)**; (b) T.M.S.Chang, (Ed); 'Blood Substitutes II', New York: Marcel Dekker, **(1992)**.

[29] E.Tsuchida, T.Komatsu; Synthetic hemes. Meth Enzymol, **231**, 167-193, 685-687 **(1994)**.

[30] T.M.S.Chang; Artificial cells: 35 years. Art Organs, **16**, 8-12 **(1992)**.

[31] C.A.Hunt, R.R.Burnette, R.D.MacGregor, A.E.Strubbe, D.T.Lau, N.Taylor, H.Kawada; Synthesis and evaluation of a prototypal artificial red cell. Science, **230**, 1165-1168 **(1985)**.

[32] A.S.Rudolph, R.O.Cliff; Dry storage of liposome-encapsulated hemoglobin: a blood substitute. Cryobiology, **27**, 585-590 **(1990)**.

[33] A.S.Rudolph, L.P.Stratton, B.Goins, F.Ligler; Liposome-encapsulated hemoglobin: efficacy and stabilization. In: 'The Red Cell', Seventh Ann Arbor Conference. New York: Alan R. Liss, 435-455 **(1989)**.

[34] R.F.Service; Small spheres lead to big ideas. Science, **267**, 327-329 **(1995)**.