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BIOBOTS ADVANCE IN ATHEROSCLEROSIS AND IN CANCER: REVIEW

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Abstract: Biobots a kind of nanorobots, another application of nanotechnology, is the creation of muscle-powered nanoparticles having the ability to transfer information into cells, gives the potential of replacing lost biological function of many tissues such as sinoatrial node. This effect can lead to treatment of diseases which otherwise would be fatal or difficult to cure for human. Nanotechnology mainly consists of the processing, consisting of processing of separation, consolidation and deformation of materials by one atom or by one molecules. Many novel nanoparticles and nanodevices are expected to be used, with an enormous positive impact on human health. The vision is to improve health by enhancing the efficacy and safety of nanosystems and nanodevices. Products based on nanotechnology in medicine and medical technology are reaching the market, with an anticipated enormous positive impact on human health, in the coming years. Nanotechnology also plays a key role in the interventional therapeutic approach of atherosclerosis and Coronary Artery disease (CAD), by improving the biocompatibility of intracoronary stents and by regulating the main limit factors for Percutaneous Trans luminal Coronary Angioplasty(PTCA) at a molecular level via nanoparticles.

Keywords: Nanotechnology, Nanorobot, Tumour cell

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INTRODUCTION

Nanotechnology:

Nanoscale devices could be 100 to 10,000 times smaller than human cells but are similar in size to large bio molecules such as enzymes and receptors. Nanoscale is generally considered to be at a size below 0.1 μm or 100 nm (a nanometer is one billionth of a metre, 10-9 m) (Figure 1). Nanoscale science (or nanoscience) studies the phenomena, properties and responses of materials at atomic, molecular and macromolecular scales, and in general at sizes between1-100 nm. In this scale, and especially below 5 nm, the properties of matter differ significantly (i.e. quantum scale effects play an important role) from that at a larger particulate scale. Nanotechnology is then the design, the manipulation, the building, the production and application, by controlling the shape and size, the properties responses and functionality of structures, devices and systems of the order or less than 100 nm.

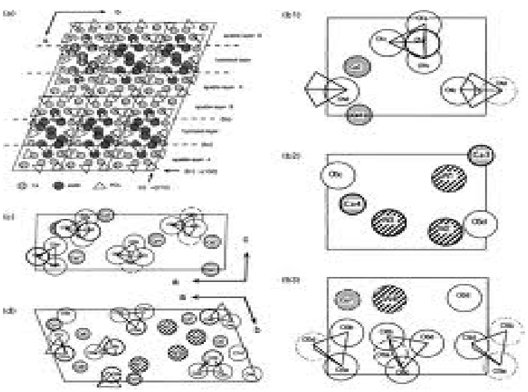

Figure 1: Objects and living organism that size occur at nano scale

Nanotechnology is considered an emerging technology due to the possibility to advance well established products and to create new products with totally new characteristics and functions with enormous potential in a wide range of applications. In addition to various industrial uses, great innovations are foreseen in information and communication technology, biology and biotechnology, medicine and medical technology, in metrology, etc. It is anticipated that nanotechnology can have an enormous positive impact on human health. Relevant processes of living organisms occur basically at nanometer scale, elementary biological units like DNA, proteins or cell membranes are of this dimension.

The potential medical applications are predominantly in diagnostics (disease diagnosis and imaging),monitoring, the availability of more durable and better prosthetics, and new drug-delivery systems for potentially harmful drugs[1], as shown in Figure 2. For example, nanoscaled diagnostics are expected to identify in the becoming, giving the opportunity to intervene specifically prior to a symptomatically detected onset disease. Biomedical nanotechnology presents revolutionary opportunities in the fight against many diseases. An area with near-term potential is detecting molecules associated with diseases such as cancer, diabetes mellitus, neurodegenerative diseases, as well as detecting microorganisms and viruses associated with infections, such as pathogenic bacteria, fungi, and HIV viruses. For example, in the field of cancer therapy, promising novel nanoparticles will respond to externally applied physical stimuli in ways that make them suitable therapeutics or therapeutic delivery systems. Another important field of application for nanotechnology are biomaterials used for example in orthopedic implants or as scaffolds for tissue engineered products.

Nanotechnology might yield nano-structured surfaces preventing non-specific protein adsorption. Control of surface properties at nanolevel was shown to increase the biocompatibility of the materials[2]. While products based on nanotechnology are actually reaching the market, sufficient knowledge on the associated toxicological risks is still lacking. Reducing the size of structures to nanolevel results in distinctly different properties.

While products based on nanotechnology are actually reaching the market, sufficient knowledge on the associated toxicological risks is still lacking. Reducing the size of structures to nanolevel results in distinctly different properties. As well as the chemical composition, which largely dictates the intrinsic toxic properties, very small size appears to be a dominant indicator for drastic or toxic effects of particles. From a regulatory point of view, a risk management strategy is already a requirement for all medical technology applications[1].

The impact of nanotechnology in medicine and medical technology is presented first with the introduction of nanomedicine and the “nanorobots”, and then through some of myriad applications in diagnosis and treatment (such as biocompatibility and implants, cardiology, cancer, the ranostics, etc). The future nanoparticles used in treatment of diseases like, gene therapy and in cancer. They are used in cancer mainly, as shown in figure: 2.

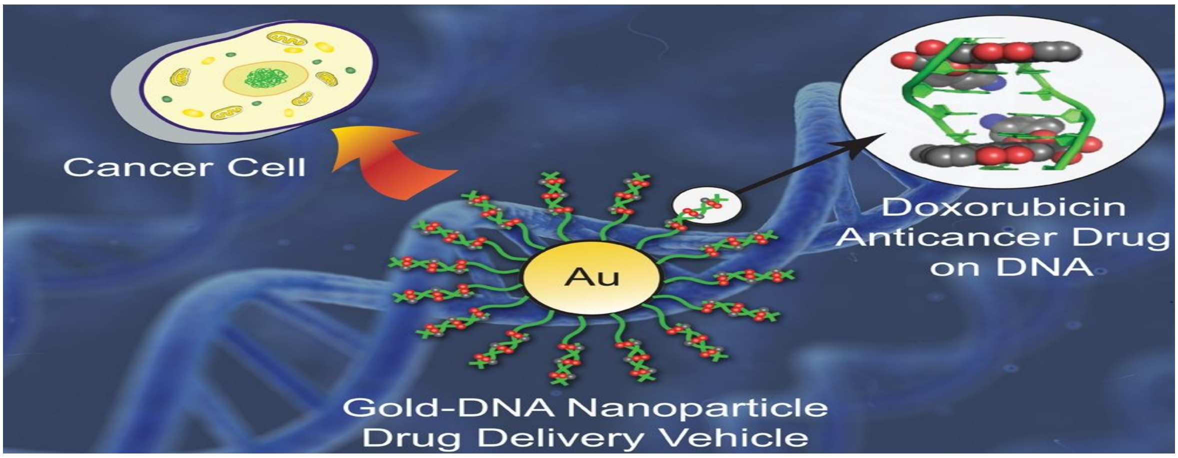

Figure 2: Use of nanoparticle in treatment of disease

Future nanoparticles should act as drug-delivery and drug- targeting systems. Due to their smallness they are not recognized by the human body, migrate through cell membranes beneath a critical size and are able to pass the blood - brain barrier. These characteristics are used to develop nanoscaled ferries, which transport high potential pharmaceutics precisely to their destination. There are different kinds of nanoparticles which are suitable to be applicable in drug- and gene- delivery, probing DNA structures, etc, and are categorized as: liposomes, polymer nanoparticles (nanospheres and nanocapsules), solid lipid nanoparticles, nanocrystals, polymer therapeutics such as dendrimers, fullerenes (most common as C60 or buckyball, similar in size of hormones and peptide a-helices), inorganic nanoparticles (e.g. gold and magnetic nanoparticles). Individual nanoparticles, novel biomaterials can be constructed using structural surface modifications of macro-, microas well as nanomaterials. Control of surface properties at nanolevel was shown to increase the biocompatibility of the materials.

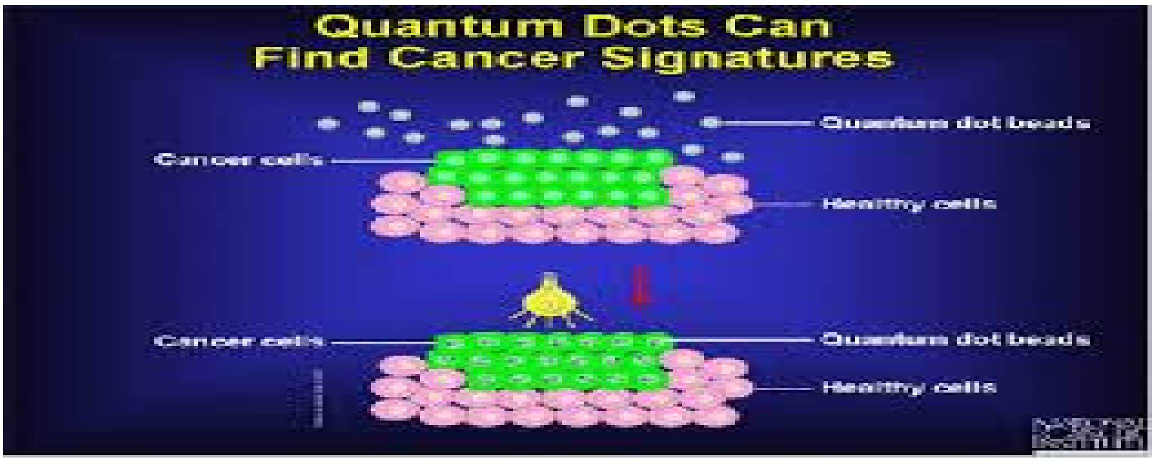

Figure 3: Quantum dots used to locate and kill cancer cells

The synthesis and properties of semi-conductor nanocrystals was studied; this led to a fast and increasing number of metal and metal oxide nanoparticles and quantum dots, which in the future could be applied to treat cancer, as shown in Figure 3. The advantage that this treatment, like other nanotechnology research is that it aims therapies directly and selectively at cancerous cells. As one of the primary tools for imaging, measuring and manipulating matter at nanoscale it has been particularly important in the study of cancer, HIV, genetics and stem cell research. Quantum dots can be made to emit light at any wavelength in the visible and infrared ranges, and can be inserted almost anywhere, including liquid solution, dyes etc. Quantum dots can be attached to a variety of surface ligands, and inserted into a variety of organisms for in-vivo research[2,3].

Nanorobot

Nanorobots are theoretical microscopic devices measure the scale of nanometers (1nm equalsonemillionthof1millimeter). When fully realized from the hypothetical stage, they would work at the atomic, molecular and cellular level to perform tasks in both the medical and industrial fields that have here to fore been the stuff of science fiction. Nanomedicine's nanorobots are so tiny that they can easily traverse the human body. Scientists report the exterior of a nanorobot will likely be constructed of carbon atoms in a diamondoid structure because of its inert properties and strength. Super-smooth surfaces will lessen the likely hood of triggering the body' simmune system, allowing the nanorobots to go about their business unimpeded. Glucose or natural body sugars and oxygen might be a source for propulsion and the nanorobot will have other biochemical or molecular parts depending on its task. Nanomachines are largely in the research but some primitive molecular machines have been tested. An example is a sensor having a switch approximately 1.5nanometersacross,capableof counting specific molecules in a chemical sample. The first useful applications of nanomachines, if such a ever built, might be in medical technology, where they might be used to identify cancer cells and destroy them. Another potential application is the detection of toxic chemicals, and the measurement of their concentrations, in the environment. Recently, Rice University has demonstrated a single-molecule car which is developed by a chemical process and includes bulky balls for wheels. It is actuated by controlling the environmental temperature and by position in gas canning tunnel in microscope tip[4].

Since nanorobots would be microscopic in size, it would probably be necessary for very large numbers of them to work together to perform microscopic and macroscopic tasks. These nanorobots warms, both those which are in capable of replication(as inutility fog) and those which are capable of un constrained replication in the natural environment (as ingrey go and its less common variants), are found in many science fictionstories, such as the Borg nanoprobes in Star Trek. The word "nanobot"(also "nanite", "nanogene", or"nanoant") is often used to indicate this fictional context and is an inform alor even pejorative term to refer to the engineering concept of nanorobots. The word nanorobotis the correct technical term in the nonfictional context of serious engineering studies. Some proponents of nanorobotics, in reaction to the grey goo scare scenarios that they earlier helped to propagate, hold theviewthatnanorobotscapableofreplication outsideofarestrictedfactoryenvironmentdon otformanecessarypartof a purported productive nano technology, and that the process of self-replication, if it were ever to be developed, could be made inherently safe. They further assert that free-for aging replicator sare in fact absent from their current plans for developing and using molecular manufacturing.

Biobots

Biobots is the creation of muscle-powered nanoparticles having the ability to transfer information into cells, gives the potential of replacing lost biological function of many tissues such as sinoatrialnode. This effect can lead to treatment of diseases which otherwise would be fatal or difficult to cure for human beings (Figure 4).

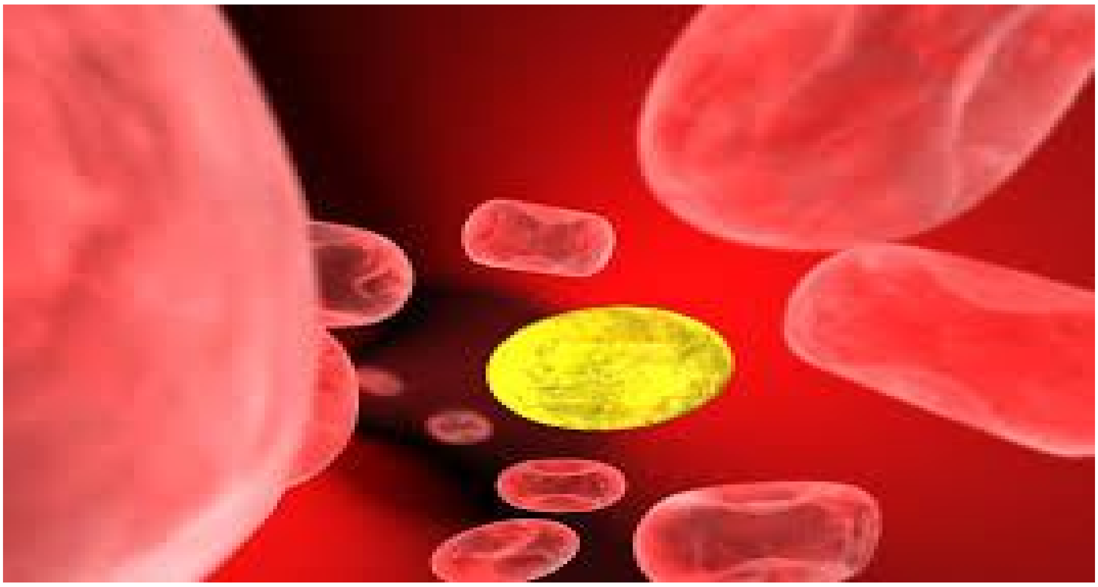

Figure 4: A futuristic representation of biobots in area of red cell within the blood vessels

Elements of Biobots:

Carbon will likely be the principal element comprising the bulk of a medical biobot, probably in the form of diamond or diamondoid/fullerene nano composites. Many other light elements such as hydrogen, sulfur, oxygen, nitrogen, fluorine, silicon, etc. will be used for special purposes in nanoscale gears and other components. The chemical inertness of diamond is proved by several experimental studies. Morphological examination revealed no physical damage to either fibro blasts or macrophages, and human osteo blast like cells confirming the biochemical indication that there was no toxicity and that no inflammatory reaction was elicited in vitro. The smoother and more flawless the diamond surface, the lesser is the leukocyte activity and fibrinogen adsorption. An experiment by Tang et al. showed that cardiovascular disease diamond wafers implanted intraperitoneally in live mice for 1 week revealed minimal inflammatory response. Interestingly, on the rougher “polished” surface, a small number of spread and used macrophages were present, indicating that some activation had occurred. The exterior surface with nearnano meter smoothness results in very low bio activity. Due to the extremely high surface energy of the passivated diamond surface and the strong hydrophobicity of the diamond surface, the diamond exterior is almost completely chemically inert.

The typical size of a blood born medical biobot will be 0. 5-3micrometersasit is the maximum size that can be permitted due to capillary passage requirement. These nanorobots would be fabricated in desktop nanofactories specialized for this purpose. The capacity to design, build, and deploy large numbers of medical nanorobots into the human body would, make possible the rapid elimination of disease and the effective and relatively painless recovery from physical trauma. Medical nano robots can be of great importance in easy and accurate correction of genetic defects, and help to ensure a greatly expanded health span. More controversially, medical nanorobots might be used to enhance natural human capabilities. However, mechanical, medical nano devices would not be allowed to self-replicate inside the human body, nor would there be any need for self-replication or repair inside the human body since these nanobugs are manufactured exclusively in carefully regulated nano factories without most precision.

Advantages of Biobots:

- Useful for monitoring, diagnosis and fighting sickness.
- To cure HIV, Cancer and other harmful diseases and research under progress.
- Biobot will treat and find disease, and restore lost tissue at the cellular level.

Disadvantages of Biobots:

- The initial design cost is very high.
- The design of the biobot is a very complicate done. Electrical systems can create stray fields which may activate bioelectric-based molecular recognition systems in biology. Electrical biobots are susceptible to electrical interference from external sources such as electric fields, and stray fields from other in vivo electrical devices.
- Hard to Interface, Customize and Design, Complex.
- Biobots can cause a brutal skin the field of terrorism. The terrorism and anti-groups can make use of bio bots as a new form of torturing the communities as nanotechnology also has the capability of destructing the human body at the molecular level.
- Privacy is the other potential risk involved with Biobots. As Biobots deals with the designing of compact and minute devices, there are enhances for more eaves dropping than that already exists.

Approaches of Biobots:

Biochips:

The joint use of nano electronics, photolithography, and new biomaterials, can be considered as a possible way to enable the required manufacturing technology towards biobots for common medical applications, such as for surgical instrumentation, diagnosis and drug delivery. Indeed, this feasible approach towards manufacturing on nanotechnology is a practice currently in use from the electronics industry. So, practical biobots should be integrated as nano electronics devices, which will allow tele-operation and advanced capabilities for medical instrumentation.

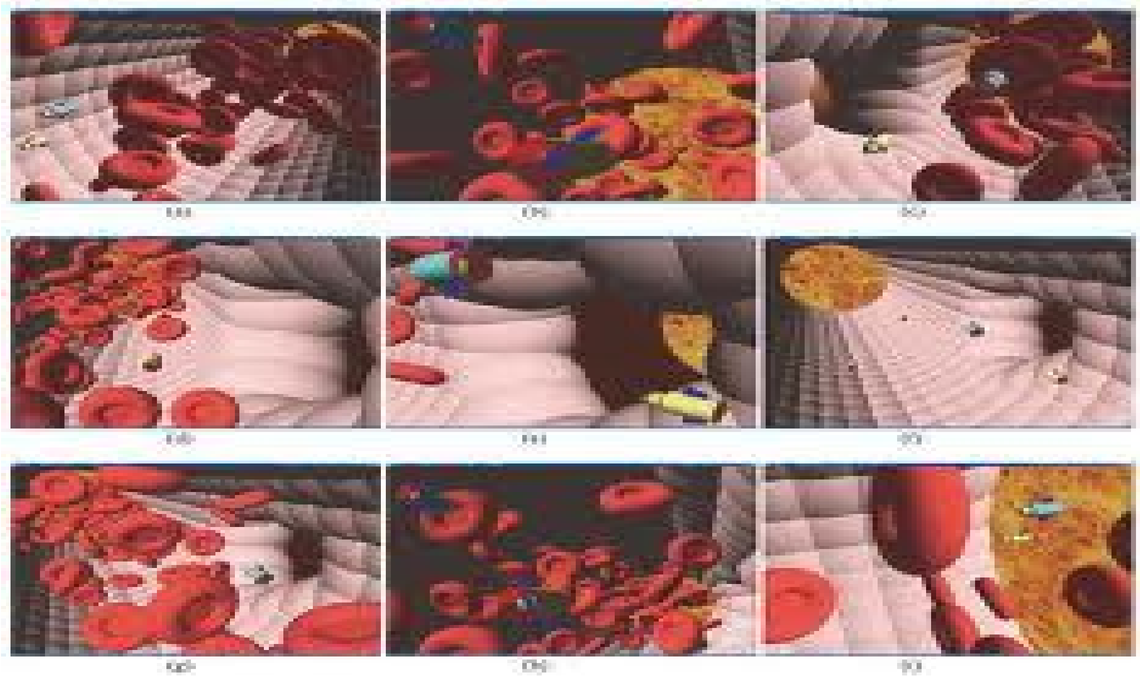

Figure 5: Biochips

Nubots:

Nubotisan abbreviation for" nucleic acid robots." Nubotsare synthetic robotics devices at the nanoscale. Re presentative nubots include the several DNA walkers reported by Ned Seeman's group at NYU, Niles Pierce's group at Cal tech, John Reif's group at Duke University, Chengde Mao's group at Purdue, and Andrew Turberfield's group at the University of Oxford.

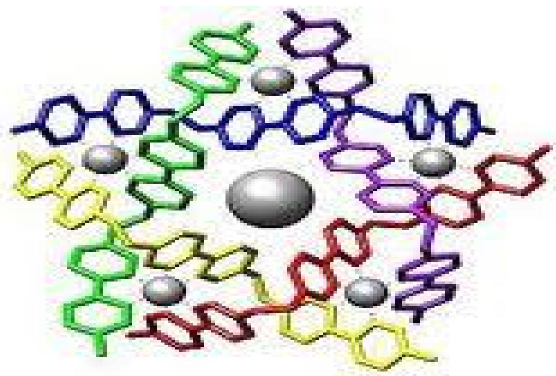

Figure 6: Nubots

Positionalnanoassembly:

Nano factory Collaboration, founded by Robert Freit as and RalphMerklein2000,isa focused ongoingeffortinvolving23 researchersfrom10 organizations and4countriesthatisdevelopinga practical research agenda specifically aimed at developing positionally-controlled diamond mechano synthesis and a diamondoid nanofactory that would be capable of building diamondoid medical biobots.

Bacteriabased:

This approach proposes the use biological microorganisms, like Escherichia coli bacteria. Hence, the model uses a flage lumfor propulsion purposes. The use of electromagnetic fieldsarenormally applied to control the motion of this kind of biological integrated device, although his limited applications.

Open Technology:

A document with a proposal on nanobiotech development using open technology approaches has been addressed to the United Nations General Assembly. According to the document sent to UN, in the same way Linux and Open Source has in recent years accelerated the development of computer systems, a similar approach should benefit the societyatlargeandacceleratenanoroboticsdevelopment.Theuseofnanobiotechnologyshould be established as a human heritage for the coming generations, and developed as a open technology based on ethical practices for peaceful purposes. Open technology is stated as a fundamental key for such aim.

Application of Biobots:

Biobots in Atherosclerosis and Coronary Artery disease:

Nanotechnology also plays a key role in the interventional therapeutic approach of atherosclerosis and Coronary Artery disease(CAD), by improving the biocompatibility of intracoronary stents and by regulating the main limit factors for Percutaneous Transluminal

Coronary Angioplasty(PTCA) at a molecular level via nanoparticles (Figure 7).

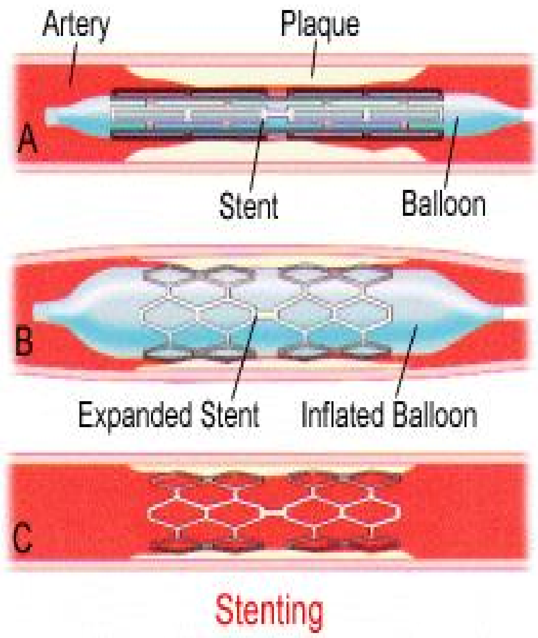

Figure 7: Percutaneous transluminal coronary angioplasty with stent implantation

The introduction of intracoronary bare metal stents reduced the restenosis rate within 6 months, however a smaller portion of the patients (20–30%) still suffered of so called “in-stent” restenosis. Recently, drug eluting stents loaded with the anti-proliferative compounds paclitaxel and rapamycin have lead to the reduction of restenosis rate to 1–3% at 1 year. However, “in-stent” restenosis remains the major limiting factor of percutaneous interventions for Coronary Artery Disease. That is the reason that makes nanotechnology necessary for improving biocompatibility of stents. Many nanocoatings have been evaluated *in vivo* and *in-vitro* and have been proposed to improve the biocompatibility of metallic stents or to serve as matrix for drug delivery. Recent research data involving surface modifications of these prostheses at nanoscale as well as the loading of an antiproliferative and anti-inflammatory drug onto a stent via nanoparticles such as liposome's may lead to the prevention of early thrombus formation and late neointima development, which are the major side effects of PTCA with stent implantation[5]. Going beyond drug-eluting stents, many nanoparticle carrier systems may be developed in order to transfer molecules via blood stream that block both neointimal hyperplasia and negative remodelling. In Figure 7, we can see these molecules that can be used as stand-alone and without being necessary to be loaded onto stents and their potential molecular targets could be endothelial cells, vascular smooth muscle cells, adventitial fibroblasts, leukocytes and platelets which are the main cells involving in acute thrombosis and neointimal hyperplasia after PTCA with stent implantation.

In particular, in a mouse model of vascular injury, the injection of endothelial progenitor cells was associated with endothelization of the injured segment of the artery and with reduced neointimal proliferation. Many anti apoptotic agents such as caspase inhibitor or an antiapoptotic gene targeting against the activation of vascular smooth muscle cells, transferring via nanoparticles to the arterial wall being injured by stent implantation, might reduce restenosis. It can be concluded that a highly effective molecular coronary intervention by means of nanotechnology may eliminate the need for stents themselves [6].

Diagnosis of cardiovascular diseases:

Itis an application of recent advances in nanotechnology as well. Many monoclonal antibodies, peptides and carbohydrates for non-invasive targeting of atherosclerotic lesions, myocardial necrosis, brain infarction and various tumours can be used for their detection. As an example, an antibody specific for the proliferating smooth muscle cells of the human atherosclerotic plaque was standardized for imaging experimentally-induced atherosclerotic lesions in rabbits. The antibody after successful preclinical trials in

North-eastern University is already being used for clinical studies in Italy and Spain[7,8].

Figure: 8 illustrate very small atherosclerotic lesions in-vivo, using bi specific antibodies targeted with very high specific radio activitiy nano-polymers.

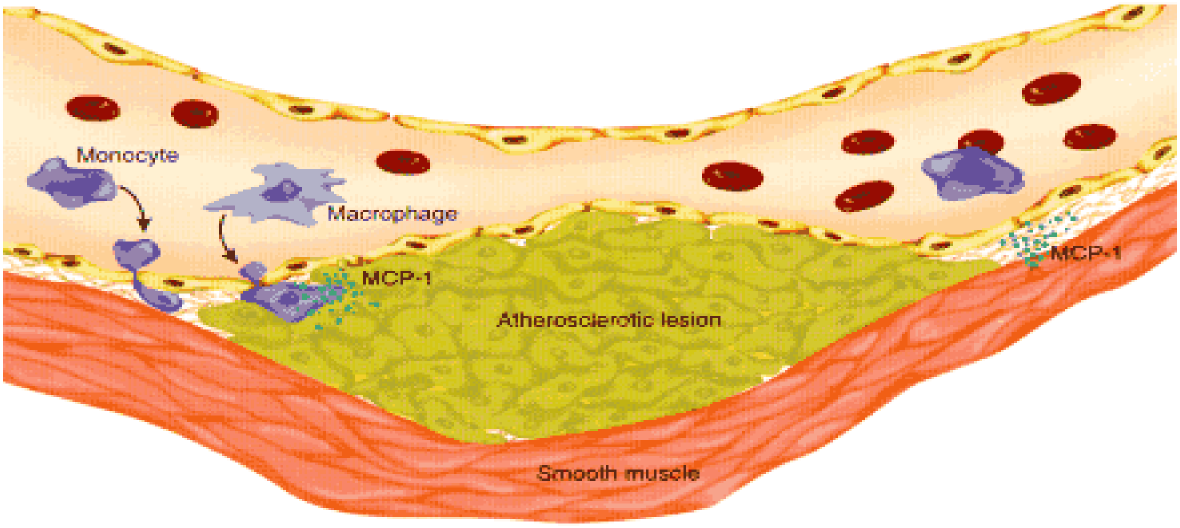

Figure 8: Atherosclerotic lesion by antibody targeting with nano-polymers

By screening tests which are based on the above application of Nanomedicine, individuals that are prone to develop atherosclerosis might be detected and by controlling the main risk factors for CAD (hypertension, diabetes mellitus, smoking, hyperlipideamia, obesity) a long-term acute coronary syndrome may be avoided. This approach can also be used for a variety of other diseases, leading to the earlier diagnosis and prevention.

Diagnosis of Tumour:

The vascular permeability of the tumour influence the retention of intravenously administered nanoparticles, and the subsequent nanoparticle drug-delivery are shown in Figure 9 [10,11]. Tumour diagnosis and prevention is the best cure for cancer, but failing that, early detection will greatly increase survival rates with the reasonable assumption that an in situ tumour will be easier to eradicate than one that has metastasized. Nanodevices and especially nanowires can detect cancer-related molecules, contributing to the early diagnosis of tumour**.** Nanowires having the unique properties of selectivity and specificity, can be designed to sense molecular markers of malignant cell. They are laid down across a microfluidic channel and they allow cells or particles to flow through it. Nanowires can be coated with a probe such as an antibody or oligonucleotide, a short stretch of DNA that can be used to recognize specific RNA sequences. Proteins that bind to the antibody will change the nano wire's electrical conductance and this can be measured by a detector. As a result, proteins produced by cancer cells can be detected and earlier diagnosis of tumour can be achieved.

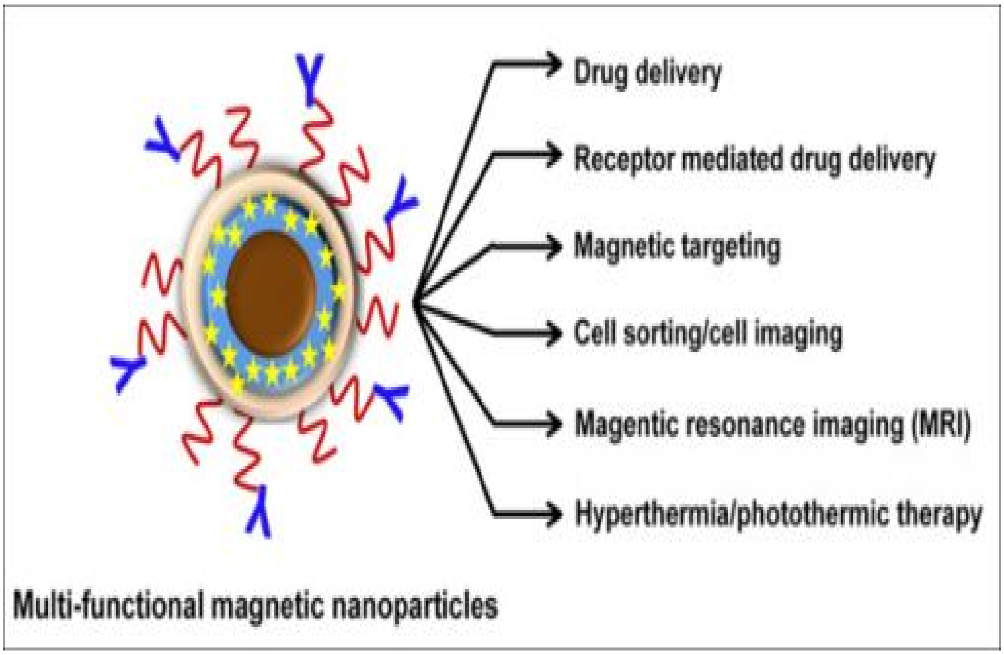

Figure 9: Nanoparticle drug – delivery accumulation at tumour site.

In addition to this, laser-induced thermal effects around nanoparticles attached to specific targets have recently been used for the treatment of cancer. The basic concept for this application of Nanotechnology is the fact that nanoparticles of different properties (magnetic, optical etc.), due to their size, can be delivered more easily to target cells than can larger particles, via conjugation with antibodies, conjugation to viruses and physiological transportation as shown in Figure 9. After reaching target cells, these nanoparticles are then self-assembled into larger nanoclusters within cells. Afterwards, these nanoclusters can be activated by laser irradiation, microwaves or magnetic fields, depending of the nanoparticles' synthesis. By this process and its photo thermal effects, destruction of cancer can be achieved.

Conclusion:

Biobots can be applied for analytical, imaging, detection, diagnostic and therapeutic purposes and procedures, such as targeting cancer, drug delivery, improving cell material interactions, scaffolds for tissue engineering, and gene delivery systems, and provide innovative opportunities in the fight against incurable diseases. Biobots will play a key role in the medicine tomorrow providing revolutionary opportunities for early disease detection, diagnostic and therapeutic procedures to improving health.

Acknowledgements:

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