

Review on Application of Nanotechnology in Animal Health and Production

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ABSTRACT

Nanotechnology is research and technology development at the atomic, molecular and macromolecular levels at the scale of approximately 1 - 100 nanometer range, to provide a fundamental understanding of phenomena and materials at the Nano scale and to create and use structures, devices and systems that have novel properties and functions because of their small and/or intermediate size. Nanotechnology has the potential to solve many more puzzles related to animal health, products and breeding. The applications of nanotechnology become the proving ground for untried and more controversial techniques from Nano capsule vaccines to sex selection in breeding. There are numerous applications of nanotechnology in veterinary medicine including disease diagnosis, treatment, drug delivery, animal breeding and improving and boosting animal origin food product. It provide variety of new nanomaterial and nanoparticle including Nano chips, nanosenser, liopsoms, quantum dot, gold nanoparticle, magnetic nanoparticle etc for vaccination, pathogen detection, disease diagnosis, animal breeding and provide polymeric nanoparticle, carbon nanotube, Nano shell dendrites, etc for delivering antimicrobial nanoparticle and Nano medicine for treatment of disease. It is swiftly changing the diagnosis and treatment patterns at faster and low cost in less time duration.

Keywords: Diagnosis, Nanomaterial's, Nanotechnology, Treatment

INTRODUCTION

Nanotechnology is an exciting and rapidly emerging technology allowing us to work at the molecular level, often atom by atom, to create and manipulate tools, materials and functional structures that have nanometer dimensions. Nature has been performing 'Nano technological feats' for millions of years. Through the arrangement of atoms and molecules, biological systems combine wet chemistry and electro-chemistry in a single living system. It used within the body, within the cells for diagnosing and treatment of diseases. It has the potential to have great impact on diagnosis and treatment of animals. Unique size dependent properties of nanoparticles have numerous diagnostic applications such as diagnostic biosensors, imaging Nano probes for magnetic resonance imaging contrast agents [1]. Using nanotechnology multifunctional nanomaterial's can be designed to image a specific organ, target tissue, access deep molecular targets and provide drug at controlled release. Great advances have been and are being made in Nano biochip materials, Nano scale biomimetic materials, Nano motors, Nano composite materials, interface biomaterials and Nano biosensor with enormous prospect in veterinary medicine application [2].

It is a research and development aimed at understanding and working with seeing, measuring and manipulating at the atomic, molecular and supramolecular levels. This correlates to length scales of roughly 1 to 100 nanometers. At this scale, the physical, chemical and biological properties of materials differ fundamentally and often unexpectedly integrated sensing, monitoring and controlling system could detect the presence of disease and notify the farmer and veterinarian to activate a targeted treatment delivery system. This is possible with nanotechnology and could permit a wide range of advances in the field of agriculture, animal and veterinary sciences such as conversion of agricultural and food wastes to energy and other useful by-products through enzymatic Nano bioprocessing, development in reproductive science, breeding management, disease prevention and treatment in animals and public health [3]

Applications of nanotechnology and nanoparticles in food, animal breeding and animal productivity such as in meat production, milk production are emerging rapidly. It used to create materials and change structure, enhanced quality and texture of foodstuffs at the molecular level. This technology has a major impact on production, processing, transportation, storage, traceability, safety and security

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of food.

The objective of this paper is to review about the application of nanotechnology on the:

- ❖ Drug delivery system
- ❖ Animal disease diagnosis and treatment and
- ❖ Animal breeding and productivity

LITERATURE REVIEW

Definition of Nanotechnology

The term 'nanotechnology' was first applied in 1970 and was used to describe production technology at ultrafine dimensions, hence the use of the Greek word 'Nano' - meaning dwarf. According to the published document of International Organization for Standardization, nanotechnology is defined as a scientific knowledge application for matter's manipulation and control in Nano metric scale [4]. The most widely use definition of nanotechnology is provided by the United States Government's National Nanotechnology Initiative. According to the researchers, nanotechnology is defined as: "Research and technology development at the atomic, molecular and macromolecular levels at the scale of approximately 1 - 100 nanometer range, to provide a fundamental understanding of phenomena and materials at the Nano scale and to create and use structures, devices and systems that have novel properties and functions because of their small and/or intermediate size [5]. The generic term of 'Nano-object' as defined by the European Union Commission recommendation on a code of conduct for responsible Nano sciences and nanotechnologies research will include all nanomaterial's, nanostructured materials, nanoparticles and their aggregation at the Nano scale, Nano-systems, and Nano products [6].

Application of Nanotechnology in Disease Diagnosis

Nanotechnology has the potential to provide cheaper, fast and precise diagnostic tools. These days, nanomaterials are playing a key role in imaging and monitoring and hence earlier detection of disease. Better diagnosis has a positive effect in the cost of animal health care. Bio nanomaterial based research has emerged as a new exciting field and DNA, RNA and peptides are considered as important bionanomaterials for the fundamental development in life sciences. The nanomaterial's such as quantum dots, Nano shells, carbon nanotubes can be synthesized and functionalized which may couple with the imaging sources and accompany the molecule with ultrasound, magnetic resonance, X-rays techniques to diagnose the targeted organ effectively [7]. Diagnosis at molecular level as well as single cell can be detected by Nano sensors and Nano chips. These help to diagnose monitor and treat diseases. Various nanomaterial's are discussed below that are used for diagnosis. Of all the discussed nanomaterial's, quantum dots and gold nanoparticles show finest results in diagnosis.

Nano chips

Earlier and rapid detection of disease causing pathogens was done by wide range of assays like enzyme immunosorbent assay, western blot assay, polymerase chain reaction, neutralization, agar-gel immuno diffusion. The above named assays suffer from varied drawbacks that can be overcome by Nano chips providing rapid and specific diagnosis. Nano chips have diverse range of applications ranging

from recognizing genes, guiding drug delivery to monitoring body functions and perceive life science and chemical pathogens. Nano chips are also applied for identification of certain diseases like cystic fibrosis and scanning of DNA for signs of predispositions of other ailments [8]. Nano chips have been employed to detect gene mutations responsible for monogenic disorders that help to determine etiology of complex diseases including heart disease, diabetes and neuropsychiatric traits. Recently, researchers developed silver sputtered Nano chip that mimic the connectivity between neurons in the brain [9]. Thus, Nano chip technology has tremendous potential as a diagnostic tool which will also be effective for targeted drug delivery in future.

Nano sensors

Nano sensors are miniature devices that can diagnose samples which use biological material or tissue based on bio recognition element which is immobilized on the surface of physicochemical transducer. Applications of Nano sensors open great prospective ranging from whole body monitoring to diagnosing various diseases due to their unprecedented sensitivity. Majorly, Nano sensors are based on two detection principles - catalytic and affinity sensing. Catalytic sensors utilize enzymes, cells, tissues/organelles and microorganisms as the recognition agent. Affinity sensors are those which utilize whole antibodies, antibody fragments, nucleic acid/aptamers, receptors, lectins, phages, novel engineered scaffold derived bonding proteins, molecular imprinted polymers, plastic antibodies and synthetic protein binding agents as the recognition agent [10]. Nano sensors have major role in veterinary sciences, they use very small amount of a chemical contaminant, virus or bacteria which is helpful for agriculture and food systems that in return improves the feedstock [11].

Liposomes

Liposomes are small artificial vesicles of spherical shape composed of single or multiple concentric bilayers, size ranging from 50-500 nm. Liposomes play a key role in diagnosis as they can be used as carriers for radioisotopes and contrast agents. Liposome can be used in blood pool or perfusion and lymphatic imaging based on contrast enhancement. The potential of paramagnetic liposomes in blood pool, lymphatic and perfusion imaging was proven by various ex vivo and in vivo animal studies [12].

Quantum dots

Quantum dots are semiconductor Nano crystals having unique properties like high level of photostability, tunable optical properties, single-wavelength excitation and size-tunable emission. Due to their extremely small size (around 10 nm in diameter), they are used as fluorescent probes for bimolecular and cellular imaging [13]. A quantum dot enables high sensitive detection of analytes at low concentrations due to their similar quantum efficiencies. Diseases involving large number of genes and proteins can be detected by multicolor quantum dot probe that helps in imaging and tracking multiple molecular targets simultaneously [14].

Gold Nanoparticles

The attractive features of gold nanoparticles such as ease of synthesis, non-cytotoxicity, high biocompatibility, broad optical properties make them fascinating for diagnosis. Gold nanoparticles have proven to be the most flexible nanostructures, due to their ability to control size, shape, composition, structure, assembly,

encapsulation thereby resulting in enhanced optical properties. Gold nanoparticles can be functionalized easily with biological molecules such as antibiotics and nucleic acid using various strategies and employed for diagnosis. Gold nanoparticles upon aggregation change its color as an example when gold nanoparticles are functionalized with DNA, which is capable of specifically hybridizing to a complementary target for the detection of specific nucleic acid sequences in biological samples; their properties change [15].

Magnetic nanoparticles

Magnetic nanoparticles are finding increasing applications in the areas of diagnostic and therapeutic because of the advantageous properties associated with the lesser dipole dipole interactions, lower sedimentation rates, facilitation in tissue diffusion, high magnetization so as to be controlled by external magnetic fields and to reach the targeted pathologic tissue and their small size that make them available for circulation through the capillary systems of organs and tissues [16]. Magnetic nanoparticles have been widely used in the early diagnosis of diseases. They are especially important for some fatal diseases such as cancer. Some magnetic nanoparticles like iron oxide nanoparticles have been used in perfusion imaging for in-vivo characterization of tumors [17].

Application of Nanotechnology in Drug Delivery Systems and Treatment of Disease

Application of Nanotechnology in drug delivery systems

Considering the Pharmacology area, nanotechnology allows the development of new products and also the possibility to rework conventional substances in order to obtain better efficacy results, by loading drugs into nanoparticles through physical encapsulation, adsorption, or chemical conjugation, the pharmacokinetics and therapeutic index of the drugs can be significantly improved in contrast to the free drug counterparts. Drug-loaded nanoparticles can enter host cells through endocytosis and then release drug payloads to treat microbes-induced intracellular infections [18].

Nanoparticle-based drug delivery provides many advantages, such as enhancing drug-therapeutic efficiency and pharmacological characteristics. The utility of nanoparticles in improving pharmacokinetics, reducing unwanted side effects, and improving delivery to disease sites has been demonstrated for a number of Nano drug delivery systems [19]. For example, nanoparticles improve the solubility of poorly water-soluble drugs, modify pharmacokinetics, increase drug half-life by reducing immunogenicity, increase specificity towards the target cell or tissue (therefore Reducing side effects), improve bioavailability, diminish drug metabolism and enable a more controllable release of therapeutic compounds and the delivery of two or more drugs simultaneously for combination therapy [20].

Generally, the practical consequences of a pharmaceutical nanostructure substance are:

- a) Providing a rational use of the active ingredient, considering that both the number of doses and the concentration of the drug may be reduced during the treatment;
- b) "Renewing" of old pharmaceutical bases which were continued used;
- c) Prolonging the systemic circulation lifetime of drug;

d) Releasing drugs at a sustained and controlled manner, preferentially delivering drugs to the tissues and cells of interest;

e) Delivering multiple therapeutic agents to the same cells for combination therapy [21]

f) Providing new perspectives of administration routes for medicines and vaccines;

g) Reducing stress for drug administration;

h) Reducing toxicity and collateral effects of conventional pharmaceutical actives;

i) Providing the use of new molecules and actives in animal therapeutic and

j) Producing low (or none) residues in animal products, resulting in no withdrawal needed [18]

Application of Nanotechnology in Treatment of disease

The effective delivery of therapeutic molecules has been a major barrier to obtain targeted response against the disease agent. Many drugs are effective in treating diseases but most of them also have certain limitations with regard to toxicity, poor aqueous solubility and cell impermeability. The drawbacks discussed above can be solved by Nano medicine. Nano medicine has the potential to solve unique biological challenges. New drugs and new delivery systems both come under "Nano medicine" umbrella. Therapeutic and diagnostic agents are at the forefront projects of Nano medicine and research is focused on rational delivery and targeting of pharmaceuticals in animals [22]. Nano pharmaceuticals, the most promising and productive area of nanotechnology application in animal treatment involves nanoparticles and hence they are available for broad range of biological targets owing to their small size and higher mobility. Nano pharmaceuticals engross encapsulating the material to generate nanoparticle which thereby improves solubility, diffusion and degradation characteristics of the encapsulated material and, nanomaterial's that can carry drugs to the targeted site [23]. Various nanomaterial's are used in the treatment of veterinary diseases like polymeric nanoparticles, carbon nanotubes, liposomes, dendrimers, Nano shells, Nano pores, magnetic nanoparticles, etc.

Polymeric nanoparticles

Strategies for controlled drug-delivery have made a considerable progress in the field of veterinary medicine where polymeric nanoparticles play a key role. They deliver drugs for long periods, increasing the drug efficacy, maximizing the patient compliance thereby enhancing the ability to use highly toxic, poorly soluble or relatively unstable drugs. They are used for the development of highly selective and efficient therapeutic and diagnostic modalities [24]. Polymeric nanoparticles can circulate freely in the body and penetrate tissues by means of mechanisms such as endocytosis.

Carbon nanotubes

Carbon nanotubes have potential therapeutic applications in the field of drug delivery. They can be functionalized by various biomolecules such as bioactive peptides, proteins, nucleic acids and drugs, and are used to deliver their cargos to cells and organs [25]. Carbon nanotubes show effectiveness in treatment of wide range of diseases but its major role is in cancer treatment. Carbon nanotubes on combination with anticancer drugs, enhances their chemotherapeutic effects.

Nano shells

Nano shells are concentric particles in which one material is coated with a thin layer of another material by various synthesis methods. Nano shells are currently being used in cancer chemotherapy and still more applications are conceived in the treatment of diseases. . Gold Nano shells destroy the cancer completely. They can also be used to immobilize cells or viruses, to trap and embed small and macromolecules on surfaces [26].

Dendrimers

Dendrimers have a range of applications from drug delivery to drug diagnosis. It considered as potential drug carriers for treatment of diseases with the capability to provide a sustained release along with reduced side effect and rapid pharmacological response with improved efficacy. Dendrimers are effectively used in drug delivery as they deliver a drug at controlled rate by chemically modifying them either by fine tuning of hydrolytic release conditions and the selective leakage of drug molecules on the basis of their size or shape or by pH-sensitive materials [27].

Antimicrobials Nanoparticles in Veterinary Medicine

The field of veterinarian sciences stands to gain with nanotechnology diagnostic tools (Nano probes) that can be used in vitro and on living animals, targeted delivery of medications, therapeutic nanomaterial's, vaccine antigen vectors, in vivo imagery, or traceability of products of animal origin. An important increase of scientific researches for nanostructured products development in the last years has been verified in Veterinary Medicine, especially using antimicrobials actives. Conventional synthetic and natural antimicrobial substances are being tested, and have shown excellent results against multi-resistant microorganisms and bacteria strains that are normally hard to eliminate by using the conventional treatment, like *Brucella*, *Mycobacterium bovis*, *Staphylococcus aureus*, *Salmonella*, *Ehrlichia*, *Ana plasma*; *Rhodococcus equi*, etc. [28].

In vitro studies – conventional antimicrobials

Nanostructured streptomycin and doxycycline were tested against *Brucella melitensis* strains, and the efficacy results of nanoparticles were better than the conventional antimicrobials [29]. This specific pathogen usually stays inside animal's macrophages, and its pharmacological control is very hard. In this *in vitro* study, both antimicrobial actives were encapsulated in anfililic polymers, allowing the nanoparticles to reach the interior of murine macrophages. When tested *in vivo* (in infected murines), the nanostructured formulation determined reduction of the number of colony-forming unities and also with a better efficacy compared to the conventional formulation. *Escherichia coli* and *Salmonella typhi* bacteria are two common pollutants and they are developing resistance to the most used bactericide. New biocide materials are being tested. Thus, gold nanoparticles are proposed to inhibit the growth of these two microorganisms. Gold nanoparticles dispersed on zeolites eliminate *Escherichia coli* and *Salmonella typhi* colonies at short time [30]

In Vitro Studies with Ag Nanoparticles

The antimicrobial effects of silver ion or salts are well known, and the silver nanoparticles show efficient antimicrobial property compared to other salts. The Ag nanostructures are most effective on *E. coli*, yeast *S. aureus*, *Klebsiella* and *Pseudomonas*. These

nanoparticles preferably attack the respiratory chain and cell division, finally leading to cell death. Ag nanoparticles can be used as effective growth inhibitors in various microorganisms, making them applicable to diverse medical devices and antimicrobial control systems. The scanning transmission electron microscopy confirms the presence of silver in the cell membrane and inside bacteria [31].

In vitro studies of nanoparticles composed by natural antimicrobial actives

The antimicrobial activity and bactericide effect of propolis against a wide range of bacteria, fungi, yeasts and viruses has been investigated since the late 1940s and it showed variable activity against different microorganisms. The alcoholic extracts of propolis inhibited the growth of various bacteria, including strains of streptococci and *Bacillus*. The inhibition of bacterial RNA polymerase by the components of propolis is probably due to the loss of their ability to bind to DNA [32].

Nano Vaccines and Vaccine Adjuvant

Vaccination is one of the important methods of prevention of disease in advance by developing antibody against the particular pathogen. Nanoparticles used as vaccine carriers and adjuvants. Synthetic oligodeoxynucleotides and antigens in biodegradable Nano spheres used for immunization .A better immune response seem to be obtained with biodegradable Nano spheres vaccines produced by conventional methods. These new perspectives for vaccines development are contributing with better efficacy and safety results, both in pets and livestock animals [33].

Liposomal vaccines can be made by associating microbes, soluble antigens, and cytokine. Liposomes as vaccine adjuvants, liposomes have been firmly established as immunoadjuvants (enhancers of the immunological response), potentiating both cell mediated and humoral immunity. Liposomal immunoadjuvants act by slowly releasing encapsulated antigen on intramuscular injection and also by passively accumulating within regional lymph nodes [34].

Adjuvants are agents added to a vaccine to augment immune responses toward antigens. A number of studies describe the use of nanoparticles as adjuvant. Immunization of animals with both complete antigens and happens (small molecules that can elicit an immune response only when attached to a large carrier such as a nanoparticle or a protein) conjugated to the surface of colloidal gold particles generated higher levels of specific antibodies than immunization of the same antigens with classical adjuvants. Furthermore, the amount of antigen required to achieve a high antibody response was an order of magnitude lower than for immunization with Freund's adjuvant [35].

Application of Nanotechnology in Animal Breeding

Management of breeding is an expensive and time-consuming problem for canine, dairy and swine farmers. One solution that is currently being studied is a nanotube implanted under the skin to provide real time measurement of changes in the level of estradiol in the blood. The nanotubes are used as a means of tracking oestrus in animal because these tubes have the capacity to bind and detect the estradiol antibody at the time of oestrus by near infrared fluorescence. The signal from this sensor will be incorporated as a part of a central monitoring and control system to actual breeding [36].

Microfluidics is used today in animal science to significantly simplify traditional *in vitro* fertilization procedures used in animal breeding. It is being used in livestock breeding to physically sort sperm and eggs. Geneticists are now rapidly sequencing the genomes of cattle, sheep, poultry, pig and other livestock hoping to identify gene sequences that relate to commercially valuable traits such as disease resistance and leanness of meat. By including probes for these traits on biochips, breeders will be able to speedily identify champion breeders and screen out(remove) genetic diseases [36].

Application of Nanotechnology in Animal and Chicken Product

Meat production/industry sector (Nano meat)

Nanotechnology study individual nanoparticles and their unique application for meat industry ranging from meat design, achieving food security, meat safety, overcoming food allergies, eliminating pesticide use, meat packaging, restoring meat damage and sensory evaluation to processes such as filtration, separation, encapsulation etc [37]. One of the more futuristic applications of nanotechnology lies in the production of “interactive” poultry meat that change colour, flavor or nutrients depending on diner’s taste or health [38].

There were many methods to improve livestock meat products by nanotechnology.

Encapsulation system, at present spray drying, melts extrusion, co-acervation, coating with fat and sprays chilling are commonly employed encapsulation techniques. The encapsulation system using nanotechnology has numerous benefits as detailed below [39].

- a) Taste masking,
- b) Head-triggered release
- c) Consecutive delivery of multiple active ingredients,
- d) Change in flavor character and
- e) Long lasting organoleptic perception

Nanotechnologies ranging from the actual to the speculative promise a variety of ways to create real meat without killing animals. On top of this, add the promise that genetic engineering could produce cells that have a variety of new qualities that would make meat even healthier and tastier: higher protein, lower fat, high omega 3 acid levels or other healthful concoctions [40]. Some of the researchers in this field, for instance, are so committed to the development of cultured meat—largely out organizations to pursue the technology. For example, New Harvest is a “non-profit research organization working to develop new meat substitutes, including cultured meat—meat produced *in vitro*, in a cell culture, rather than from an animal. Cultured meat has the potential to make eating animals unnecessary, even while satisfying all the nutritional and hedonic requirements of meat eaters. It also has the potential to greatly reduce animal suffering [41].

Milk production/industry sector (Nano milk)

Nanotechnology is a new technological tool in modern raw milk production and pasteurization, recent and ongoing advances in biomedical technology will assist in advancing our understanding of disease prevention and health promotion, as well as medical diagnostics and therapeutics [42].

Recent developments of Nano technological tools begins to

bring sophisticated Polymerase Chain Reaction (PCR) methods, cantilever systems, various micro array systems, new biosensors, etc. This substantiates an intensified research in new solid on-line/at line methods, which can measure critical points throughout the milk production chain (e.g., feed, cow, raw milk, milk tank, throughout the processing chain, during storage and distribution with regard to pathogens, indicator organisms of contamination, antibiotics, toxins, chemical contaminants, and allergens). This support the development of hazard analysis critical control points (HACCP)-based quality management systems. Development of mentioned HACCP-based quality management systems as well as shelf-life prediction systems also calls for development of sophisticated modelling of growth and decline of pathogens, spoilers and contaminants in the milk and dairy products [43].

Liposomes micelles used to encapsulate both water and lipid soluble compounds. The dissolution of fat-soluble nutrients in water-based drinks is one of the key applications of liposomes. Examples of current research into the use of liposome technology in food are the encapsulation of enzymes, lactic acid bacteria extracts and/or antimicrobials for accelerated cheese ripening. Liposome technology can be used potentially to target specific sites within a food product for enzymatic degradation [44].

Egg production/industry sector (Nano egg)

Poultry meat and eggs are often the source food borne pathogens, like *salmonella*. Early detection of food borne pathogenic bacteria is critical to prevent disease outbreaks and preserve public health. Now, a novel nanotechnology-based biosensor is showing great potential for forborne pathogenic bacteria detection with high accuracy [45].

Nanotechnology has to supply cholesterol free eggs, yolkless or reduced yolkeggs which can be the high value protein source, immune eggs which can supply the predetermined antibodies and therapeutic eggs with supply the predetermined physiological factors for treatment purposes. The tools and techniques currently with us will not give the solution for these challenges. They can only be meeting out by the emerging nanotechnology, which deals not merely at the molecular level but at the atomic level [46].

CONCLUSION

Nanotechnology has emerged as one of the most innovative technology. The applications of this technology are immense. The nanotechnology or Nano science which is so full of potential that it has been called ‘the next industrial revolution’ will impact society, the environment, the animal, the economy or even global politics in profound ways.

In the future, nanotechnology has the potential to provide cheaper, fast and precise drug delivery and diagnostic nanomaterial tools and therapeutic nanoparticle and Nano medicine (Nano drug). These nanomaterials are playing a key role in imaging, monitoring and earlier and faster detection of disease. It is possible to diagnose disease at molecular level as well as at single cell by using that nanomaterials. It provide smart drug delivery and effective treatment through nanoparticle and Nano medicine. The high variety of nanoparticles engineering has allowed the development of a great number of new antimicrobial products, with excellent efficacy results; quick and specific action, and also high bioavailability and biodegradability levels. It has advances impact on less production/economic losses and better health conditions

for animal. Also nanotechnology in livestock product, such as in meat and milk, has key role. In the future it provide new products and new processes, with the goal of enhancing the performance of the product, prolonging the product shelf life and freshness, and improving the

Safety and quality of animal origin food.

RECOMMENDATIONS

Based on the above conclusion the following recommendations are forwarded:

- ❖ Continuous research should be conducted on nanotechnology, particularly on Nano biotechnology in animal science and veterinary medicine in order to increase production of low fat and low cholesterol animal products.
- ❖ More advanced research should be conducted on nanoparticle, nanomaterial and Nano medicine to improve effective diagnosis and treatment of animal diseases.
- ❖ The governments should give a great attention to nanotechnology and they must support the Scientists and researchers who investigate nanotechnology.

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