Review article

Nanomedicine: diagnosis to therapy

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Abstract

It can be said that "small technology" becomes a very useful technology and is replacing the classical technology. Nanotechnology is an applied technology relating to management, construction, synthesis of devices in atomic or molecular level that poses the size between 1 and 100 nanometers. In this short article, the author will summarize important advent in nanodiagnosis and nanotherapy then further extrapolate this for the tropical medicine aspect.

Keywords: nanomedicine; diagnosis; therapy

INTRODUCTION

It can be said that "small technology" becomes a very useful technology and is replacing the classical technology. Nanotechnology is an applied technology relating to management, construction, synthesis of devices in atomic or molecular level that poses the size between 1 and 100 nanometers. In medicine, present molecular biology technique is often made of the microlevel technology which is about 100 times larger than this new kind of technology. Measurement in nanometer is widely used in nanoscience. In addition to length, area as two-dimensional aspect and volume as three-dimensional aspect are also focused in nanoscience. Of interest, nanoobjective is not a new thing. Human beings have ever used nanoobjects for a long time. In the West, Lycurgus cup, a magic golden cup which could automatic change its color and was made in A. D. 300[1-3], is the best example. The technique used to grind Roman diatreta glasses is elucidated with the aid of reproductions of both the network diatreta from Cologne-Braunsfield and Niederemmel as well as the Lycurgus beaker[3].

The nanoparticle has its significant change in its property comparing to larger size particle. In brief, the nanoparticle has its own new property due to the change of 1) contact surface area, 2) electrostatic property and 3) quantum property. Simply, it means that nanoparticle has incresed reaction possibility due to significantly increase of contact surface area and it also pose new color and other physical properties due to the chance of electrostatic and quantum properties. Of several nanotechnology, nanomedicine is a new branch of medical science. Nanomedicine embraces five main sub-disciplines: 1) analytical tools, 2) nanoimaging, 3) nanomaterials and nanodevices, 4) novel therapeutics and drug delivery systems and 5) clinical, regulatory and toxicological issues. It can be said that the potential of nanotechnologies raises great hopes. In this short article, the author will summarize important advent in nanodiagnosis and nanotherapy then further extrapolate this for the tropical medicine aspect.

NANODIAGNOSIS

Based on advanced nanotechnology, nanoanalytical tools and nanoimaging are available. Nanoparticles, such as gold nanoparticles, silver nanoparticles and quantum dots, are the most widely used, but various other nanotechnological devices for manipulation at the nanoscale as well as nanobiosensors are also promising for potential clinical applications[4]. Gold nanoparticle is one of the most widely used nanoma-

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terial at present[5,6]. Due to the very small size of gold nanoparticle, the surface area significantly increases comparing to general gold. Therefore, it can be used as sensor. Of interest, the different size gold nanoparticle results in difference colors. The change of the color of gold nanoparticle from pink at very small to gray at larger size can be seen. Silver nanoparticle is another widely used nanomaterial[7,8]. The different size silver nanoparticle also results in different colors. It should be noted that silver nanoparticle, which has the size lower than 10 nm has golden yellow color while the color change into red and black in the larger size. In conclusion, nanotechnologies will extend the limits of current molecular diagnostics and help in point-of-care diagnostics, integration of diagnostics with therapeutics, and development of personalized medicine[4]. In addition, nanoparticles can also be used as ybridization probes in single nucleotide polymorphism screening and to detect biological markers for cancer, infection, and cardiovascular diseases. Indeed, nanobiosensor is a new hope in diagnostic technology. Various types of transducer and bioreceptor molecule are presently used for nanosensor and nanobiosensor fabrication [9-11]. In the biochip, flow splitting nanochannels, chaotic nanomixers, reaction nanochambers and detection nanofilters are fully integrated. Several biochips are assuming an important role in submolecular diagnostics, and their application in point-of-care diagnosis is expected to facilitate the development of personalized medicine[12].

Quantum dot is another important nanoparticle, mainly used for imaging purpose. Quantum dot is a synthesized nanopolymer with semiconductor property. Quantum dot is a novel class of inorganic fluorophore which is gaining widespread interest as a result of its exceptional photophysical properties. Semiconductor quantum dots are inorganic nanoparticles with unique photophysical properties [13]. In particular, their huge one- and two-photon absorption cross sections, tunable emission bands and excellent photobleaching resistances are stimulating the development of luminescent probes for biomedical imaging and sensing applications [13]. With the nanoproperty of quantum dot, electron and energy transfer processes can be designed to interprete the luminescence of semiconductor quantum dots in response to molecular recognition events[13]. On the basis of these operating principles, the presence of target analytes can be transduced into detectable luminescence signals. The quantum dot is proved to be better than classical fluorecence imaging because it has longer half life, therefore, allows following up of dynamicity in the cellular process of the focused stained celled. At present, quantum dots have been increasingly employed in measuring the dynamic behavior of biomacromolecules using fluorescence correlation spectroscopy[13]. This brings a challenge, because quantum dots display their own dynamic behavior in the form of intermittent photoluminescence, also known as blinking [13].

NANOTHERAPY

The important query "How can we search the site and size specific therapy?" has been searched for its answer for years. Luckily, due to the advanced nanobiotechnology, the answer seems to be reached. The core concept of nanotechnology is the "small". In one sense, small means specific: focus on a limited scoped site and size. Nanopharmacology is a very useful medical science. It can be applied for nanotherapy. New specific drug design can be performed at presented[14,15]. Nanopharmacology is the hope for treatment of presently untreatable diseases such as cancer and human immunodeficiency virus infection. The application of nanotechnology on drug delivery can be seen in four important areas as controlled release of drug, prolongation of drug life-time, acceleration of drug absorption and drug targeting.

There are many nanomaterials that are presently applied for drug delivery. However, the most widely used ones are aptamer, liposome and dendrimer. Neverthess, the best known nanoparticle is liposome, a spherical shape nanopolymer. Liposome´s main composition of liposome is sugar and protein that can act as the receptor. The good property of liposome can help accelerate drug absorption as previously mentioned. In many cases liposomal drugs are administered *via* the bloodstream [16]. The stability in the bloodstream, clearance, and biodistribution are dependent on the composition, size, and charge of the liposomes[16]. Three kinds of functional long-circulating liposomes are available at present, namely, thermosensitive liposomes for delivering macromolecules, pH-sensitive liposomes for the cytosolic delivery of encapsulated materials, and reticuloendothelial system - avoiding liposomes for the passive targeting to tumor tissues [17]. In addition, it has become increasingly evident that tissues utilize specific localization of enzymes to perform certain tasks, often associated with various types of tissue remodeling[18]. The ubiquitous presence of such enzymes, along with their specific localizations, provides an ideal opportunity to elicit specific delivery *via* an enzyme-triggered mechanism[18].

APPLICATIONS OF NANODIAGNOSIS AND NANAOTHERAPYU IN TROPICAL MEDICINE

As previously mentioned, it can be seen that nanotechnology can be applied for diagnosis and therapy for many diseases including tropical diseases[19]. For nanodiagnosis, there are some recent reports and most are the new diagnostic alternatives. For example, progression of respiratory syncytial virus infection monitored by fluorescent quantum dot probes was recently reported by Bentzen *et al*[20]. In another study, Agrawal *et al*[21] reported that antibody-conjugated nanoparticles rapidly and sensitively detected the virus and estimated relative levels of surface protein expression. Agrawal *et al*[21] proposed that a major development was the use of dual-color quantum dots or fluorescence energy transfer nanobeads that can be simultaneously excited with a single light source[21]. The good property of gold nanoparticle reported in the quoted articles[20,21] is not surprised because the finding is due to the basic property of nanoparticle as mentioned in the early part of this article. It seems that there will be enormous new diagnostic tools, enzyme linked immunoassay or molecular based tools, for diagnosis of several tropical infections within a next few years. However, an important concern in developing of such new diagnostic tests kit is the specificity of the test. Because most reactions in nanodiangosis are based on the electrostatic reaction the specifit of which is actually lower than basic molecular immunological reaction. This follows the basic fact in laboratory medicine that the sensitivity and specificity are usually discordant.

For therapy, there are many reports on new drugs and vaccine for tropical diseases based on the nanotherapy technology. An interesting advent is the success in nanovaccination for Japanese encephalitis. Okamoto *et al* recently reported that single dose of inactivated Japanese encephalitis vaccine with poly(gamma-glutamic acid) nanoparticles could provide effective protection from Japanese encephalitis virus[22]. Several attempts are also mentioned for other important diseases including influzenza virus and human immunodeficiency virus[23,24]. It is no doubt that the nanoparticle can be succussfully used as molecular tool for gene transferring in vaccine production. However, there is still a big concern on the usage of nanoparticle because the nanotherapy is quite a new technique and there is no complete report on its long toxicity and teratogenicity.

REFERENCES

1 **Esser A**. The one-eyed Lycurgus and other deities of light. *Klin Monatsblatter Augenheilkd Augenarztl Fortbild*. 1954; **125**: 361-3.

2 **Weyant RG**. Lycurgus: the father of applied psychology? *Am Psychol*. 1967; **22**: 432-4.

3 **Josef W**. Grinding technique of the diatreta glasses. (Schleifiechnik der Dlatretglaeser). *Glastech Ber*. 1978; **51**: 130-136.

4 **Jain KK**. Applications of nanobiotechnology in clinical diagnostics. *Clin Chem*. 2007; **53**: 2002-9.

5 **Guo S**, Wang E. Synthesis and electrochemical applications of gold nanoparticles. *Anal Chim Acta*. 2007; **598**: 181-92.

6 **Han G**, Ghosh P, Rotello VM. Functionalized gold nanoparticles for drug delivery. *Nanomedicine*. 2007; **2**: 113-23.

7 **Evanoff DD Jr**, Chumanov G. Synthesis and optical properties of silver nanoparticles and arrays. *Chemphyschem*. 2005; **6**: 1221-31.

8 **Lee KS**, El-Sayed MA. Gold and silver nanoparticles in sensing and imaging: sensitivity of plasmon response to size, shape, and metal composition. *J Phys Chem B*. 2006; **110**: 19220-5.

9 **Cullum BM**, Vo-Dinh T. The development of optical nanosensors for biological measurements. *Trends Biotechnol*. 2000; **18**: 388-93.

10 **Cui D**, Gao H. Advance and prospect of bionanomaterials. *Biotechnol Prog*. 2003; **19**: 683-92.

11 **Cui D**, Gao H. Advance and prospect of bionanomaterials. *Biotechnol Prog*. 2005; **21**: 650.

12 **Jain KK**. Applications of biochips: from diagnostics to personalized medicine. *Curr Opin Drug Discov Devel*. 2004; **7**: 285-9.

13 **Heuff RF**, Swift JL, Cramb DT. Fluorescence correlation spectroscopy using quantum dots: advances, challenges and opportunities. *Phys Chem Chem Phys*. 2007; **9**: 1870-80.

14 **Dutta RC**. Drug carriers in pharmaceutical design: promises and progress. *Curr Pharm Des*. 2007; **13**: 761-9.

15 **Dobson J**. Magnetic micro- and nano-particle-based targeting for drug and gene delivery. *Nanomedicine*. 2006; **1**: 31-7.

16 **Oku N**, Namba Y. Long-circulating liposomes. *Crit Rev Ther Drug Carrier Syst*. 1994; **11**: 231-70.

17 **Oku N**. Basic study and application of functional liposomes. *Yakugaku Zasshi*. 1995; **115**: 483-98.

18 **Meers P**. Enzyme-activated targeting of liposomes. *Adv Drug Deliv Rev*. 2001; **53**: 265-72.

19 **Pedroso S**, Guillen IA. Microarray and nanotechnology applications of functional nanoparticles. *Comb Chem High Throughput Screen*. 2006; **9**: 389-97.

20 **Bentzen EL**, House F, Utley TJ, Crowe JE Jr, Wright DW. Progression of respiratory syncytial virus infection monitored by fluorescent quantum dot probes. *Nano Lett*. 2005; **5**: 591-5.

21 **Agrawal A**, Tripp RA, Anderson LJ, Nie S. Real-time detection of virus particles and viral protein expression with two-color nanoparticle probes. *J Virol*. 2005; **79**: 8625-8.

22 **Okamoto S**, Yoshii H, Ishikawa T, Akagi T, Akashi M, Takahashi M, *et al*. Single dose of inactivated Japanese encephalitis vaccine with poly(gamma-glutamic acid) nanoparticles provides effective protection from Japanese encephalitis virus. *Vaccine*. 2008 ; **26**: 589-94.

23 **Wang X**, Uto T, Akagi T, Akashi M, Baba M. Poly(gamma-glutamic acid) nanoparticles as an efficient antigen delivery and adjuvant system: potential for an AIDS vaccine. *J Med Virol*. 2008; **80**: 11-9.

24 **Okamoto S**, Yoshii H, Akagi T, Akashi M, Ishikawa T, Okuno Y, *et al*. Influenza hemagglutinin vaccine with poly(gamma-glutamic acid) nanoparticles enhances the protection against influenza virus infection through both humoral and cell-mediated immunity. *Vaccine*. 2007; **25**: 8270-8.