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Potential impact of nanotechnology in the control of infectious diseases.

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Summary

Nanotechnology encompasses those technologies to fabricate materials, including sphere, cubic and needle-like nanoscaled particles (approximately 5 to 100nm), and near-nanoscaled devices (up to 500 nm). In comparison mycoplasma are approximately 200 nm in length and a nanometre is 10^{-9} of a metre. The field of nanotechnology is experiencing rapid growth, with many & diverse potential applications being explored in the biomedical field, including the control of infectious diseases. Nanotechnology has the potential to offer not only improvements to current approaches for immunisation, drug design and delivery, diagnostics and cross infection control, but is unexpectedly delivering many new tools and capabilities. (102 words)

Immunisation

The potential of nanoparticles as novel adjuvants and the use of nanoemulsions as colloidal vaccine carriers are being explored in the field of immunisation against infectious diseases. Calcium nanoparticles have been examined as a vaccine adjuvant of anti-idiotypic antibody against schistosomiasis (Fang *et al*, 2004). Nanoemulsions, which consist of minute droplets of oil suspended in water and stabilized by detergents, are finding applications for both prevention and treatment of a wide variety of infections. Droplets in nanoemulsions are surface active and react specifically with the outer membrane of infectious organisms. In pre-clinical trials with animals at the University of Michigan mixtures of the nanoemulsion with either whole virus or protein have been tested as potential vaccines. Such vaccines, which do not require cold storage and can be administered via the mucosal route, are particularly suitable for applications in developing countries.

Cross Infection Control

Exploitation of the toxic properties of nanoparticulate metals and metal oxides, in particular those that produce reactive oxygen species under UV light, are finding increasing use in antimicrobial formulations and dressings within and outside the hospital environment. Silver, copper and their compounds have been widely used. In particular, nano silver particles (5-40 nm) have been reported to inactivate most microorganisms, including HIV-1. The high reactivity of titanium dioxide and silicon dioxide is also exploited extensively for their bactericidal purposes in filters and coatings on substrates such as alumina (Han *et al* 2005). Significant activity using the latest generation of nanoparticles, and their compound clusters, against fungal and bacterial pathogens, such as Methicillin resistant *Staphylococcus aureus* (MRSA) and *Escherichia coli* has recently

been demonstrated at Queen Mary. Research carried out by Retroscreen Virology, Queen Mary and QinetiQ Nanomaterials has also shown the capability to inactivate viruses, including SARS, bird flu, and HIV. For example, specially developed nanoparticle clusters can reduce virus levels by 80-100% through direct contact.

Detection

Nanotechnology is finding uses in the rapid diagnosis of infectious diseases, whereby the increased functional surface area per unit volume can be exploited for use in diagnostics. Biosensors, devices in which a biological sensing element is either intimately connected to or integrated within a transducer, are being developed. Nano-fabricated structures, coated with elements such as gold that have affinity for biomolecules, are incorporated into these biosensors. For example, a rapid method for the detection of urinary tract infection, caused by *Escherichia coli*, has been developed with the application of such a nanotechnology approach (Basu *et al*, 2004). The detection system, partly based upon enzyme-linked immunosorbant assay technology, utilises anti-*E. coli* antibody-bound Gold Nanowire Arrays (GNWA) on an anodized porous alumina template. It has also been shown possible to detect minute amounts of target DNA strands with complementary DNA linked to gold nanoparticles (Cao *et al*, 2002). This particular approach is also finding applications in the detection of single-nucleotide polymorphisms (SNPs) in microarray-based systems. It has even been possible to distinguish antibiotic resistant bacteria, such as *Staphylococcus aureus*, from non-resistant strains. Biosensors and nucleic acid detection methods are also finding applications for the rapid detection of biological warfare agents.

Treatment

The fundamental properties and bioactivity of drugs and other materials can be changed at the nanometre level. In theory it should be possible to control the characteristics of drugs including solubility, controlled release and specific site-targeted delivery. A nanotechnological approach to formulate suitable colloidal carriers for the delivery of drugs and genes is currently under investigation by many laboratories. Chitosan-coated nanocapsules as triclosan carriers have been found to be particularly effective in this capacity. This approach may be of use in the delivery of triclosan as an effective anti-malarial drug by inhibiting the growth of *Plasmodium falciparum* (Maestrelli *et al*, 2004). Chitosan can also effectively bind DNA and protect it from nuclease degradation *in vivo*. The application of DNA-chitosan nanospheres for gene delivery is currently under investigation.

Safety Issues

In theory certain nanoparticles may be retained within the body for longer than is desirable, thus the safety profile becomes a matter of overriding significance. Nanomaterials are able to cross biological membranes and gain access to cells, tissues and organs that larger-sized particles normally cannot. Nanomaterials can gain access to the blood stream following inhalation or ingestion. Some nanomaterials can even

penetrate the skin. Recent studies have found that a particle's surface chemistry can govern whether it will be suitable for biomedical applications. It remains to be determined how potential toxicity issues will impact on the use of nanotechnology in the control of infectious diseases. (861 words – total)

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