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ABR001. Functional nanocoatings for biotechnology

Over the years, several methods have been developed to coat solid surfaces for biotechnological applications. Success has primarily been achieved by using wet chemical methods employing solvents, or strong acid/base media, some of which are becoming increasingly unacceptable due to environmental and safety concerns. An alternative approach is to employ non-isothermal plasmachemical processing. This technology offers many potential benefits including low energy consumption, absence of solvents, minimal waste, rapid treatment times, ambient temperatures, applicability to a whole host of different substrate materials, and control of surface functionality. Specific examples will include high throughput and low-cost technological solutions for preparing re-writable DNA microarrays, protein chips, antibacterial surfaces, thermo-responsive protein resistant coatings for tissue engineering, and substrates for rapid cell growth.

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ABR002. DNA hybridization detection using a piezoelectric quartz crystal transducer with a nanoparticle-protein scaffold amplification system

A DNA hybridization sensor for single-stranded DNA (ssDNA) detection was developed using a piezoelectric quartz (pzq) crystal with nanoparticle–protein-based mass amplification. 21-mer 5′ thiolated-oligonucleotides were immobilized onto Au-coated 10 MHz pzq crystals to act as capture probes for complementary 21-mer target sequences. Hybridization of target to probe produced a limit-of-detection (LOD) of 10 ng of target DNA. Subsequent colloidal Au-nanoparticle attachment to hybridized DNA led to an increase in LOD to 0.5 ng. Biotin-streptavidin binding to attached Au-nanoparticles further increased the LOD to 0.05 ng. This scheme has proved to be highly reproducible and has demonstrated its ability for simple regeneration of probe DNA by heating the crystal to the duplex melting temperature (T_m). A scanning electrochemical microscope (SECM) was used for surface interrogation of the monolayers to produce electrochemical topographs. This allowed determination of the uniformity and robustness of the receptor layer.

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ABR003. Production of biodegradable nano- and microparticles via ultrasonic atomization for biopharmaceutical delivery

Biopharmaceuticals have been shown to have low delivery and transformation efficiencies. To overcome this, larger doses are administered in order to obtain the desired response which may lead to toxicity and drug resistance. This paper reports on a continuous particle production method utilizing surface acoustic wave atomization to reliably produce nano- and microparticles with physical characteristics to facilitate the cellular uptake of biopharmaceuticals. By producing particles of an optimal size for cellular uptake, the efficacy and specificity of drug-loaded nanoparticles will be increased. Better delivery methods are an important technological development for pandemic preparedness, as reducing the amount of antigen (biomolecule) required to produce immunity will enable more people to be vaccinated in the case of vaccine shortages. Better delivery reduces the amount required per dose (hence cost per dose), reduces toxicity, and reduces problems associated with multi-drug resistance due to overdosing.

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ABR004. Nanoparticle delivery for RNA interference (RNAi)-based therapeutics

While RNA interference (RNAi) has reinvigorated therapeutic prospects of nucleic acid inhibitor, nanotechnology for construction of nanometer-sized carrier with advanced properties has accelerated the development of small interfering RNA (siRNA) therapeutics. Using a ligand-directed nanoparticle (LDN) approach, we are able to systemically deliver siRNA and achieve strong anti-angiogenesis and anti-tumor efficacies in two ocular neovascularization mouse models and three mouse xenograft models. To evaluate our anti-cancer drug candidate, ICS-283, in a clinical scenario, we conducted a study using a combined regimen of bevacizumab and ICS-283 with a mouse xenograft model. The treatment resulted in a stronger anticancer efficacy indicating that siRNA and monoclonal antibody can work in concert to achieve better efficacy and safety outcomes. Further molecular and histological analyses revealed its anti-angiogenesis efficacy without IFN induction. The LDN delivery of siRNAs targeting multiple genes within VEGF pathway has further exhibited the unique advantage of the siRNA drug with much more potent anti-angiogenesis activity. In addition, we lately found that polymer-siRNA nanoparticles can effectively down regulate expression of C3 protein through perfusion medium treatment which brings a potential approach for improving organ transplantation. The LDN delivery of siRNAs illustrated capabilities of "targeted" therapeutics offering promise for revolutionary medicine.

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ABR005. Nano-scaled ZnO particles for antibacterial applications

This work deals with formulation of functionalized nanoparticles for antibacterial applications in for example medical devices, food wrapping and packaging, decorating materials and prevention of bioterrorism. Focus of the work is on nanosized ZnO

particles. These materials have the advantages of being low cost, light in weight, and perceived by the public as safe to human beings. Experimental work has been carried out on testing the effectiveness of these materials against model bacteria particularly *E. coli*. The tests are based on minimum inhibiting concentration and growth curve. The effects of particle size, shape, and crystalline structure are examined. The results show that the effectiveness of the metal oxide particles increases with decreasing particle size. This has significant implication in terms of minimizing the amount of antibacterial agent used in practical applications. SEM analysis of the bacteria before and after treatment with ZnO suspensions shows the presence of ZnO particles creates damages to the membrane wall of the bacteria.

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ABR006. Electronic nanomedical data and images: privacy and security issues

As healthcare providers begin the movement towards a paper-less clinical environment, large amounts of nanomedical data and images will be stored, accessed, and shared electronically. Electronic nanomedical data processing will affect key processes such as appointment scheduling, admissions of patients, and clinical reporting of images. In recent times legal and regulatory requirements have driven compliance in medical imaging and electronic clinical data processing to the forefront. The processes of clinical data collection, clinical trial management, and storage and sharing of clinical data must be compliant with relevant regulations as non-compliance could result in huge fine or even cessation of business. The need to ensure the privacy and security of electronic clinical data is now a priority for all healthcare providers. Patients have certain rights over the use of their clinical data and these rights need to be taken into consideration in nanomedical data processing and imaging. Patients' data need to stored in secure, reliable, long-term media. Where nanomedical images have to be distributed outside an organization, privacy and security issues have to be effectively addressed. To ensure that they are legally compliant, healthcare providers must have appropriate policies and procedures in place to address access control, information security, authentication, confidentiality, information integrity, and electronic communications. This paper will focus on the various information privacy and security requirements that are relevant to electronic nanomedical data processing and imaging. It will highlight acceptable practice in electronic clinical data and image management.

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ABR007. A novel method for micro-pattern transfer on substrates without photolithography

Newcastle University has invented a new process and technology which eliminates photolithography on each substrate as an essential process step to transfer micro patterns. The advantage of the process is that the surface of the work-piece is modified at the nanometric level by choosing the appropriate electrolyte and current or potential, at the micrometric level by controlling the tool to work-piece distance, and at the macrometric level by controlling the reactor geometry. The process therefore structures a surface at the nano-, micro-, and macrolevels in a single step. One of the advantages of this method is that it can be used to pattern steel, titanium, and tantalum substrates

– the materials of choice in medical implants. In addition, it can structure substrates of complex geometry – shapes such as cylinders, spheres can be structured by this method. Our experiments involving copper as the tool as well as substrate material, show that micro-scale patterns can be transferred with good reproducibility. We have successfully transferred micro-patterns between 200 and 10 µm. At present we are exploring the possibility of using our process technology for tissue engineering. We will discuss the process and it usefulness in medical implant structuring during the presentation.

ABR008. Nano- and microstructured PVD coatings on coronary stents

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Coronary stenting saves many lives, is a minimally invasive technique, and is a billion dollar business. However, there remain problems of medium- and long-term effectiveness and no one has yet designed the perfect system so that failure rates of at least a few percent still occur. Drug-eluting stents have taken the market by storm but other approaches are being pursued by smaller players. One such is the deposition of biologically inert coatings onto bare metal stents to, firstly, isolate the foreign body and, secondly, to act as a binding surface for slow-release drugs that inhibit the processes of restenosis, the reblocking of the stented artery. This paper will discuss some of the issues to be resolved and then focus on some promising results of magnetron-sputtered TiN coatings on stainless steel stents. Physical characterization using SEM and nano-indentation techniques will be described and also some early results of in vitro tests will be presented.

ABR009. Novel water carbosilane dendrimers as antisense oligodeoxynucleotides delivery

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Water-soluble ammonium terminated carbosilane dendrimers (CBS) containing Si-O bonds in the outer branches have recently been synthesized. We tested these CBS for cytotoxicity in T cell and MT-2 cell cultures finding good biocompatibility at potential therapeutic concentrations. Next, gel electrophoresis was utilized to characterize the binding between CBS and antisense oligodeoxynucleotides (ODNs) at various charge ratios by examining ODN migration patterns. The CBS were determined to bind the ODNs even in the presence of a ubiquitous serum protein (albumin). To understand the possible protective effects these dendrimers could have on ODNs, we studied the interactions between various combinations of CBS, ODNs, and albumin via fluorospectrophotometry and obtained the binding constant and the number of binding centers. Together these binding characteristic studies revealed that CBS could protect ODNs from serum proteins. A main drawback to therapies with ODN is that only the free ODN (not bound to albumin) will have any biological effect. Finally, the ability to transfect cells in vitro with dendrimers was tested. We found the CBS capable of transfecting PBMC and MT-2 with fluorescein-labelled ODNs. These results lend evidence that CBS could be useful drug delivery molecules and allow for a reduction in the administered ODN dose.

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ABR010. Application of porous Si in chronotherapeutic drug delivery

Many human diseases such as asthma and heart attack show a circadian (daily) pattern of their symptoms. It is recognized that their treatment can be made more effective if the drug dosage can be controlled to match their circadian pattern. These time-of-day-dependent treatments are described as chrono-therapeutics. Porous Si material has been demonstrated to be biocompatible and biodegradable in the human body. In this presentation, we describe our study of the enhanced erosion of porous Si structure in electrolytes such as body fluids through a pH modulation at the cathodic electrode when an electric current is flowing. In conjunction with this study, we describe the concept and the prototype of an electronic time-controlled drug delivery capsule incorporating porous Si and using primarily of commercial off-the-shelf (COTS) electronic components. Use of COTS components offers the advantage of a fast and cost-effective route to proof-of-concept prototyping, though with a penalty in the optimum device miniaturization. The drug release can be achieved by either a controlled volume erosion of a drug-containing porous Si structure or the erosion of a porous Si membrane covering the orifice to a drug reservoir.

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ABR011. Silicon quantum dots as labels

Alkylated silicon quantum dots (alkyl-SiQDs) are being developed as luminescent labels in biological applications. The alkyl monolayer surrounding the Si core is anchored by an inert Si-C bond which protects the luminescent core from corrosion and provides a platform upon which to attach useful species such as DNA probes or antibodies. Although the best understood and most commonly employed quantum dot labels are based on CdSe, they have various limitations and other materials are being actively investigated. The absence of leachable metals ions and the small particles size of red SiQDs could be a significant advantage; however, the low water solubility of alkyl-SiQDs is a problem. Nevertheless, we have found that alkyl-SiQDs can be dispersed in aqueous solutions containing <1% organic solvent (tetrahydrofuran or DMSO) and are taken up by cultured cells. The luminescence intensity is linear in particle concentration and independent of pH over the range 5–9; this allows reliable quantitation of the luminescence intensity from confocal microscopy. The aqueous sols are stable against flocculation and retain their photoluminescence for at least 4 months. Recent work also has demonstrated an automated solid-phase synthetic route to the fabrication of SiQD-DNA conjugates.