would, in fact, pose serious problems with regards to toxicity.

The safety of macro- or micro-sized particles of the same materials does not necessarily translate into the safety of nanomaterials. Early work by Casley-Smith [4] demonstrated the widespread distribution of particles in the body, thus highlighting the tracking of systems as an essential consideration during early clinical studies.

At the extreme, of course, systems with diameters of the order of 5–10 nm, are at a boundary between the molecular and the particulate state. This is especially true with dendrimers; therefore, the question posed is, at what point does a system become particulate?

Of particular interest to my group is the fate of nanosystems after oral administration. Nanoparticles can be absorbed via M cells of the gut-associated lymphoid tissues, albeit in low amounts, if they have hydrophobic exteriors. There are both beneficial and adverse possibilities as a result [5]. It is the gradual piecing together of information about the fate of these particles that will lead to a better understanding of the relationships between nanoparticle diameter, surface character, interactions and transport, leading to the optimal choice of systems for therapy and diagnosis.

Ultimately, the principal challenge with nanoparticles containing active agents is to design systems that protect the active from degradation, but enable it to be released at the appropriate site at the appropriate rate; but, even then, the release of a drug from a carrier at the site of action does not necessarily, or always, lead to lower systemic levels [6] because free drug is just that – it can freely diffuse.

We must ensure that, as pharmaceutical scientists, we do not inadvertently add to the hype surrounding nanotechnology.

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Advancing applications of microarrays

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This year, *Chips to Hits* (October 28–31, 2002) moved to Boston and attracted an audience of ~1600 delegates and 90 exhibitors, discussing latest developments and applications within the field of microarray and biochip technologies. The conference, itself, has morphed over the years from a purely technology-driven discussion into an applications-oriented forum, which continues to seek out emerging technologies. It has provided a valuable forum for both developers and users of microarrays to present their latest developments and applications.

Innovations in tools and methods

The extremely popular pre-conference workshop, 'Innovations in tools and methods for clinical and biomedical applications', provided an excellent basis for the discussion on the needs and demands of microarray technology. This session was opened by Guido Grandi of Chiron Vaccines (http://www.chiron.com), who discussed the application of microarrays in vaccine development. Sanford Simon of Rockefeller University (http://www.rockefeller.edu) provided an insight into approaches using luminescent quantum dots to label live cells and their use in the long-term imaging of living cells. Christian Hennig of Genovoxx GmbH (http://www.genovoxx.de) gave an outline of massive paralleled single-molecule sequencing, which was followed by an intriguing insight into a carbohydrate-based microarray technology, presented by Denong Wang of Columbia University (http://www.columbia.edu). The session closed with a presentation by Cleo Salisbury of the University of California (http://www.ucla.edu) on how substrate specificity of a protease can help in the design of potent and selective substrates and inhibitors.

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Surface chemistry and surface-engineering

The 'Surface chemistry and surface-engineering techniques' session posed some interesting challenges, in particular, how to retain the native structure and activity of immobilized biomolecules when improving the performance of solid-phase assays. Proposals for ways to tackle these problems were presented, including: a) MALDI (matrix-assisted laser desorption/ionization) MS-based approaches (Milan Mrksich, University of Chicago; http://www.uchicago.edu), b) the design of surfaces that inhibit non-specific interactions (Michael Lochhead, Accelr8 Technology, http://www.accelr8.com) c) the improved immobilization of antibodies and proteins (Lawrence Cohen, Zyomyx; http://www.zyomyx.com; Enoch Kim, Surface Logix; http://www.surfacelogix.com) and d) the anticipated use of lipid membrane arrays in industrial drug discovery programs.

Protein microarrays

The 'protein microarray' session focused, primarily, on how the major bottlenecks – density, large numbers of capture molecules required, target validation and sensitivity – are currently being addressed. Although all of the solutions that were presented here would help in the pursuit of high-throughput analyses using protein microarrays, the approach presented by Rules-Based Medicine (http://www.rulesbasedmedicine.com) and their partner, Charles River Laboratories (http://www.criver.com), seems to be the most promising. Founded on the bead-based Luminex technology, Rules Based Medicine are analyzing ~90 mouse serum parameters and ~170 human serum parameters from minute amounts of sample volumes. Using these technologies, thousands of samples can be screened within a day. For the bead-based systems, throughput and sample volume no longer seem to pose a problem. By contrast, Markus Ehrat from Zeptosens AG (http://www.zeptosens.com), described a microarray platform that combines state-of-the-art planar wave-guide detection, surface chemistry, assay design, fluidics and image analysis, thus, expanding the range of microarray applications. The company plans to use reverse screening assays to follow the up- and down-regulation of cell-signalling molecules in treated and non-treated cell lines. Soonkap Hahn, from Biocept (http://www.biocept.com), provided insights into the 3D HydroArray™ surface coating technology. Hollis D. Kleinert from Protometrix (http://www.protometrix) demonstrated the use of comprehensive protein microarrays in the achievement of simultaneous screening of several thousands of proteins for drug binding, molecular interactions or enzymatic activity.

Intellectual property

Intellectual property is a highly controversial subject and has often led to legal disputes or difficulties, arising from material transfer agreements, questions on how research tool patents can be adequately exploited or how interference proceedings can be strategically used to acquire rights to a competitor's intellectual property. The intellectual property (IP) workshop, chaired by Linda E. Alcorn (Sterne, Kessler, Goldstein & Fox; http://www.skgf.com), brought together a thorough overview on building a patent portfolio, by Matt Murphy (Nanosys; http://www.nanosysinc.com), followed by an interesting perspective on resolving patent disputes that concern contemporaneous invention, by Andy Filler (Caliper Technologies; http://www.calipertech.com). The workshop then delved into the more specific areas of enforcement and licensing of research 'tool' patents. Ray Salemme (consultant to J&J Pharma; http://www.jnj.com) and Jorge Goldstein (Sterne, Kessler, Goldstein & Fox) discussed the impact of the clinical research exemption to patent infringement, as presented by Anthony Miele of Palmer & Dodge (http://www.palmerdodge.com). Concluding the workshop, was a presentation on Material Transfer Agreements, presented by Marv Guthrie (Sterne, Kessler, Goldstein & Fox).

Emerging technologies

The main conference was opened with a keynote address from Dalia Cohen (Novartis Pharma; http://www.novartis.com), who clearly showed how genomics technologies are rapidly filling the drug pipeline with information on important pathways in disease. She indicated that the challenge facing the industry now is how to improve detection and understanding of the next proteomics phase of drug discovery. The new technologies will not only be used for target identification, but more so for target validation approaches to eliminate false positive targets at an early stage of the drug discovery process. The session 'Emerging technologies' gave some new insights into multiplexed assay systems, with presentations by Aclara Biosciences (http://www.aclara.com), who focus on fluidic phase assays, and SmartBead Technologies (http://www.smartbead.com), another company focusing on bead-based approaches and using microscopy and image analysis to track their photolithography-derived bar-coded tags, instead of the FACS (Fluorescence Activated Cell Sorting), as currently used in many applications. The topic of scanner calibration was discussed by Youxiang Wang of Full Moon Biosystems (http://www.fullmoonbio.com) and was well received by the audience, many of whom are looking to use this approach in the future for more regulated diagnostic assay formats.

As research moves from the discovery or hypothesis generation phase to a

more focused screening or hypothesis testing phase, there is a greater need to assay many more biological samples and screen relatively small target gene sets to test hypotheses or screen for a specific biological outcome. GeneXP Biosciences (http://www.genexpbio.com) offers a solution for focused high-throughput, low-cost gene expression analysis, which enables researchers to profile gene expression patterns of large numbers of biological samples in a compact and affordable format that is compatible with installed laboratory automation. The resulting increases in reliability, reproducibility and sample throughput, as well as the significant reduction in cost, now allows the serious consideration of many gene expression experiments that were previously not feasible.

This meeting has long attracted technology developers, who, this year, presented some interesting new platforms. On the recurring theme of multiplex technologies, Eli Glezer of Meso Scale Discovery (http://www.meso-scale.com) described electrochemiluminescent (ECL) detection in a microplate format with screen-printed electrodes fabricated in the bottom of a plate well. Hugh Daniels of Nanosys explained how the creation of nanostructures on the surface of silica can be exploited to create an increased spot surface area, while maintaining spot uniformity for microarray applications; although, such applications still need to address the 'noise' within a perfect round microspot. On the same theme, Andy McShea of CombiMatrix Corporation (http://www.combimatrix.com) gave a well-attended talk on the extent to which industry standard CMOS fabrication has been applied to microarray technology development. Using fabricated microstructures, he described how electron flow could be coupled to redox chemistry on a reactive surface to detect labelled probes in some diagnostic applications. This technology is being commercialised by Roche Diagnostics (http://www.roche-diagnostics.com) and is attracting bioterrorism funding to develop rugged detection platforms. Whether this will be a robust, reliable and cheap technology is yet to be proven. Applications of multi-antibody microarrays, together with resonance light scattering particles, were described by Bernard H. Geirstranger of Genomics Institute of the Novartis Research Foundation (http://www.gnf.org). Using minute amounts of material that were available in their mouse models, they were able to measure up to 36 markers in multiplexed assays. However, they are currently limited by the availability of efficient antibody detection reagents, which do not show cross-reactivity in these multiplexed assay formats. The final talk of the session, given by Luke Schneider of Target Discovery (http://www.targetdiscovery.com) concluded the technology developers' part of the meeting, with some intriguing insights into a new MS approach. He introduced a paradigm shift, by presenting his work on interaction proteomics in which mass defect tag technology can be used to enable MS detection in a microarray format. The potential of this technology is exciting but it could hold a high cost of entry, due to the complexity of the instrument hardware.

Clarifying the regulatory role

The inclusion of an FDA session in Chips to Hits 2003 attracted an extensive audience, clearly hoping for insight into where this regulatory body can play a role in product development. The first speaker, Joseph Hacket of the FDA (http://www.fda.gov), gave a helpful overview of the review process and invited technology developers to look to the FDA for help at an early stage of the product life cycle. Clearly, both parties are in initial phases, with regards to some of the new format diagnostic platforms that are based on microarrays, and need to work as a team. The questions surrounding analyte-specific reagents (ASR's) were discussed and will be resolved by the FDA, shortly, in response to market pressure to move some tests into the MDx marketplace. The technical presentations by the FDA's Emanuel F. Petricoin and Kostantin Chumakov gave some insight into new proteomic and viral genome sequencing technologies. This session was well attended and elicited some lively questions during the panel discussion that concluded the morning's sessions.

Leading the way…

Three of the many poster presentations were honoured an award: Dong-Ki Lee's poster (Korean Advanced Institute of Science and Technology; http://www.kaist.edu) on the identification of genetic modules in human cells using a large scale gene perturbation by artificial transcription factors; Kerring Gunning's poster (Integrated DNA Technologies; http://www.idtdna.com) on improved print and QC methods for oligonucleotide microarrays; and Manessh Jain's poster (ParAllele Bioscience; http://www.p-gene.com) on comprehensive genetic analyses using highly multiplexed SNP discovery and genotyping. BioTechniques (http://www.biotechniques.com) selected the winning posters on the basis of the promise and potential for wide application of the technologies described.

Concluding remarks

Chips to Hits 2003 attracted a large group of delegates who are clearly looking to this area of technology to meet some of the future drug discovery and molecular diagnostic needs. The conference provided a good forum for presentation and discussion on new developments in the microarray field. We look forward to the next conference, again in Boston, on 19–22 September 2004.