Our annual meeting, IVTS 2011, took place this year amid the seafaring exhibits of The Merseyside Maritime Museum on 08–09 November 2011. Nearly 100 delegates (from academia, industry, regulators and other organisations), speakers and sponsors enjoyed a varied programme covering Nanotoxicology, Organelle Toxicity, Regulatory Aspects and Emerging Liver Technologies, plus Free Communication and Poster sessions. In addition, there was the opportunity for sponsors to showcase related topics and technologies in a series of integrated workshops.

The full two day meeting was opened by the Society Chairman, James Sidaway, and started with the very topical subject of Nanotoxicology in a session chaired by Alfred Thumser and Rosemary Gibson. Vicki Stone, (Herriot-Watt University, Edinburgh), opened the session with an excellent introduction to the field, focussing on how the physico-chemical properties of nanomaterials can influence their inflammatory and oxidative properties, e.g. through the activation of the NFkB and/or ROS pathways, and GSH depletion. Vicki also summarised her involvement with several EU projects, such as ENPRA (comparing the impact of nanomaterials upon cell viability, and pro-inflammatory cytokine production) and InLiveTox (developing multi-cellular microfluidic systems to assess the uptake of nanomaterials across tissues and subsequent pro-inflammatory gene expression in vitro and in vivo).

Martin Clift (University of Bern) discussed in vivo vs. in vitro approaches and the setup of sophisticated co-culture and 3D human cell culture systems in his research group, for example to mimic the epithelial airway barrier in vitro. Many challenges need to be overcome to develop good in vitro systems, but it will be worth the effort
to provide models more relevant to investigate the human exposure to nanoparticles. Geja Oostingh (University of Salzburg) provided a different immunological perspective, focussing on the toxicology of diesel exhaust particles and engineered nanoparticles. Geja highlighted a number of *in vitro* assays being developed to assess immunotoxicity induced by nanomaterials, but included a note of caution. Nanomaterials, contamination with chemicals used for synthesis and/or stabilization, and bacteria attached to the particles, can interfere with many of these *in vitro* methods (especially those that rely on optical readout parameters) and induce immunological responses. Issues related to batch-to-batch variation, solvent effects and endotoxin contamination were also discussed.

Delegate at the break and poster session

After lunch and poster viewing, the second session (chaired by Dan Antoine and James Sidaway) moved on to Organelle Toxicity, focusing on mitochondrial and endoplasmic reticulum (ER) toxicity. The topic was given an excellent introduction by James Dykens (EyeCyte Therapeutics) focussing on the concept that mitochondrial disruption may be the mechanism behind many idiosyncratic drug reactions. During his talk, James provided examples of such off-target effects induced by the thiazolidinelones and statins, and highlighted the technology available to measure mitochondrial function and energetics. Kelvin Cain (MRC Toxicology Unit, University of Leicester) continued the cell bioenergetics theme, describing how his group are profiling mitochondrial proteins in the search for new targets aimed at disrupting mitochondrial function in malignant B-cells. Of particular interest to him in this regard are the intrinsic cell (mitochondrial-mediated) death pathway and BCL-2 proteins. Kelvin described extracellular flux assays in the Z138 lymphoma cell line showing how presence and absence of glucose in medium (i.e. aerobic glycolysis) modulates cell death in these cells.

James Dykens

George Kass

George Kass (European Food Standards Agency) switched the discussion to ER stress and the Unfolded Protein Response (UPR) caused by disruption of normal ER functioning that in the short term seems to help with cell survival but on prolongation
can lead to cell death. UPR may have a role in both disease and drug toxicity. George described in vitro studies in HuH7 liver cells demonstrating possible ER effects of paracetamol and thapsigargin. Amy Mercer (MRC Centre for Drug Safety Science, University of Liverpool) finished the session with a talk on her work with ρ₀ cells, which lack a functioning electron transport chain, to investigate clinical agents associated with mitochondrial dysfunction. As an example Amy focussed on the mechanism by which the Artemisinin class of anti-malarial drugs cause toxicity via endoperoxide activation mediated by heme within the mitochondria. Amy was the IVTS poster prize winner at the March 2010 British Toxicology Society Spring meeting.

Two workshops were held during the afternoon which linked with the session subject and described new technologies available for measuring mitochondrial function. Silke Schwengberg (representing Axiogenesis and Lonza) described a mouse ES-derived cardiomyocyte model assay for the detection of mitochondrial toxicants using continuous electric cell-substrate impedance measurement. Alex Liversage from Seahorse Bioscience described the company’s technology (quoted by several meeting speakers) for measuring mitochondrial respiration and glycolysis simultaneously in cultured cells through extracellular measurements of oxygen consumption and extracellular acidification.

The first day ended with the IVTS 2011 Annual General Meeting giving members an opportunity to engage with the Committee and discuss Society matters. This was followed by a drinks reception for delegates hosted by the IVTS Committee members and a conference dinner in the Maritime Dining Room at the Museum. Enthusiastic discussions were continued after dinner by those delegates keen on sampling the Liverpool nightlife that has grown up around the dockside developments.

A Regulatory session (chaired by Rosemary Gibson and Anthony Holmes) kicked off the second day of the meeting with an excellent talk from Penny Jones (Unilever). Penny summarised how toxicological assessment of new ingredients that are intended for use in consumer products has shifted from purely hazard-based to
overall risk-based approaches at Unilever. For this risk characterisation, the Unilever team makes full use of all data that is available from relevant *in vitro* and *in silico* techniques, as well as information on likely levels of human usage. Penny illustrated the approach with examples, and also discussed more challenging and complex endpoints such as dermal allergic responses that require more creative approaches to characterise risk *in vitro*.

Ian Indans (Health and Safety Executive (HSE)) gave the second talk of the session. Ian explained in detail the long and tortuous journey required of a new method before it gains regulatory acceptance. He illustrated this with anecdotes and examples of where methods have run into difficulties, and where even methods that technically have gone through the process successfully are then not used. This may arise where regulators deem they were not necessary in the first place (emphasising how important it is to involve them in early discussions of ideas for new methods) or are not fit-for-purpose in terms of giving useful information about the endpoint in question.

Georgios Katalagarianakis (European Commission (EC)) concluded the regulatory session with a discussion of the EC’s strategy to investigate the toxicology of nanomaterials; this talk was closely linked with the Nanotoxicology session on the first day of the meeting. The EC has made huge investment in this area, funding numerous projects of all types (e.g. large and small research, coordination actions) in recognition of the fact that gaining a thorough assessment of potential health and safety implications is key to achieving the promised economic and societal benefits of nanotechnology. The latest calls for proposals aim to develop a new safety culture, partnering academic and industrial centres to work together to develop a testing and communications strategy that will result in an adequate risk management framework for nanomaterials.

Following coffee, the meeting topics were opened up with a selection of free communications, introduced by Alfred Thumser and Jeff Penny. Ezequiel Mas del Molino from Barcelona (LEITAT Technological Center) highlighted the importance of nanoparticle functionalisation, as in the production of composites, in affecting toxicity in a number of cell lines. Mark O’Connor, from Asterand, talked about a proliferation assay using valvular interstitial cells to investigate potential cardiac side effects. This is of importance as valvular heart disease has led to the withdrawal of several drugs from the market. Finally, Hemad Yasaei (Brunel University) presented a new assay for carcinogen screening that is based on shRNA knockdown of a telomerase repressor gene which his group has developed.
Two workshops followed the free communications. Antony Rutt (InSphero) discussed scaffold-free hanging drop technology to produce microtissue spheroids. Anthony Holmes (National Centre for the Replacement, Refinement and Reduction of Animals in Research (NC3Rs)) introduced the CRACK IT funding competition designed to stimulate open innovation and problem solving in 3Rs research.

The final session of the meeting highlighted Emerging Liver Cell Technologies, focussing particularly on stem cells and 3D culture models. Lorraine Young (University of Nottingham) began the session by providing an introduction to induced pluripotent stem (iPS) cells, highlighting that differences in the cell production methods used by individual groups can give rise to experimental variability. Lorraine then gave examples of how revealing the use of specific markers of differentiation is and how these can be used to improve the purity of populations used in assays. Christopher Goldring (University of Liverpool) continued the discussion of iPS cells and focused on the important topic of drug induced liver injury (DILI). Christopher explained some factors contributing to the complexity of DILI and population variability in drug toxicity, suggesting that panels of iPS-derived hepatocytes from DILI patients would be a useful tool for in vitro toxicology.

Cliff Rowe (University of Manchester) began by discussing the research fields where in vitro organ models would be most useful, highlighting that different applications may require models at different places on the spectrum between simple ‘fit for purpose’ screening assays and accurate physiological models. Cliff then discussed his own work phenotyping hepatocytes using proteomics to help characterise the differentiation status of liver models. Simon Messner (InSphero) then continued the 3D model theme, describing examples of applications of liver microtissues in toxicology including screening and pathway analysis.

In addition to the oral presentations, 24 posters were exhibited covering a wide range of subjects relevant to in vitro toxicology. All posters were eligible for a poster competition, judged by members of the IVTS Committee, and congratulations are
due to the winner, William Dott (University of Leicester) for his poster “Development of in vitro models with metabolic capability for cardiac and skeletal muscle toxicity testing”

William Dott (on the left) being presented with his prize, by Alfred Thumser