Recent Advances in Molecular and Cellular Pathology

Friday, 06 December 2013
The O2, London. SE10 0DX, United Kingdom
This new conference will feature current topics presented by experts in their fields of research and practice. Placed in the context of molecular cellular pathology presentations will explore disease mechanisms, clinical advances and latest technology breakthroughs. This event has **CPD accreditation.**

Who Should Attend
All who need to be at the leading edge of developments in this area will find this attendance at this conference rewarding. Accordingly, attendance is recommended to students and professionals within the diagnostic and research communities that engage with molecular aspects of cellular pathology.
The deadline for abstract submissions for oral and poster presentation has now passed.

09:00 – 09:45 **Registration**

09:45 – 10:00 **Introduction by the Chair:** *Dr Anthony (Tony) Warford,* Senior Lecturer in Cellular Pathology, University of Westminster, UK

10:00 – 10:40 **Update in the molecular pathology of uveal melanoma**
Professor Sarah Coupland, Professor and Honorary Consultant in Pathology, University of Liverpool, UK
Uveal Melanoma (UM), the most common primary intraocular cancer in adults, is fatal in 50% of patients, because of metastatic spread involving the liver. Chemotherapy of metastases has limited success and disseminated disease occurs in most patients <2 years of diagnosis. Clinical, histopathological and genetic risk factors for UM metastasis are documented. UM is characterised by frequent non-random gross chromosomal changes, the most common being monosomy 3, gain of 8q, loss of 1p, gain of 6p and loss of 6q. The first two chromosomal abnormalities in particular are the strongest predictors for metastasis development. The purposes of this presentations are to review: a) described genetic abnormalities of UM, and relate these to hypotheses regarding tumour development and spread; b) current methods used in UM prognostication.

10:40 – 11:20 **The modification of proteins by glycosylation: the bitter-sweet tale of breast cancer metastasis.**
Dr Miriam Dwek, Reader in Biochemistry, Group Leader - Against Breast Cancer Research Unit, University of Westminster, UK
Alterations in the post-translational modification of proteins by the attachment of sugars (glycosylation) is a hallmark of both tumorigenesis and metastasis. This relatively complex modification offers potential for development of assays and identification of targets associated with metastatic cancer. We have focussed on identification of glycosylation changes influencing the outcome of patients with breast cancer, in particular characterisation and validation of serum biomarkers and potential cell surface targets in metastatic cancer cells. The approaches taken for this, include the use of a novel cellular-biosensor to monitor the kinetics of carbohydrate protein interactions. Recent developments that we have made in this area will be described in this presentation.

11:20 – 11:50 **Speakers' photo then mid-morning break and trade show/poster viewing**
Please try to visit all the exhibition stands during your day at this event. Not only do our sponsors enable Euroscicon to keep the registration fees competitive, but they are also here specifically to talk to you.

11:50 – 12.15 **Developments in Nucleic Acid Extraction & Quantification**
Dr Fiona Marshall, Promega, UK
Recent developments in nucleic acid extraction and quantitation enable high quality genomic DNA to be purified from FFPE samples in less than two and a half hours, with minimal hands on time and without the use of hazardous solvents. Subsequent accurate quantitation of DNA concentration is critical for many applications, traditional spectrophotometric assays have a practical lower limit of detection at ~1µg/ml; however, many isolated DNA samples have concentrations well below this level. Here we'll present new dye formats allow accurate fluorescent quantitation of extracted DNA, especially of low concentration samples, in a simple add-and-read formats which simplify and speed up workflow and maximise efficiencies.

12.15 – 12.55 **Lineage tracing in normal and neoplastic human tissues**

Professor Malcolm Alison DSc, FRCPath: Professor of Stem Cell Biology, Centre of Tumour Biology, Barts Cancer Institute, Barts and the London School of Medicine and Dentistry, London, UK

Through the ability to detect neutral mutations in mitochondrial DNA within individual cells. we have identified clones of cells within human tissues with an ordered structure for the first time. These can be illustrated in a variety of tissues including the stomach, intestines, liver, pancreas, bladder and prostate. Furthermore, the origins of tumours can be inferred, including the outer root sheath for basal cell carcinomas and PIN for prostate cancer. Using this technique, we have also proven the existence of a multipotential stem cell in neoplastic colorectal epithelia.

12.55 – 14.00 **Lunch and trade show/poster viewing**

14.00 – 14.25 **No Antibody? No Problem.**

Mr Barry Lynch, Advanced Cell Diagnostics, Inc

Because over 70% of protein-coding genes have no reliable antibody for immunohistochemistry (IHC), research can come to a screeching halt while you wait for new antibodies to be developed. Whether your target is a novel gene with no commercial antibody available, a secreted protein with poor-quality antibodies for IHC, or a non-coding RNA our universal assay workflows and rapid probe design for any gene, eliminates the hassles of antibody screening, saving you precious time and effort, while delivering publication quality data today.

14.25 – 15.05 **Towards earlier diagnosis of oesophageal adenocarcinoma**

Professor Rebecca Fitzgerald, Programme Leader, University of Cambridge, UK

Survival rates in cancer are directly related to the degree of disease spread at the time of diagnosis. Oesophageal cancer is a prime example of this problem. We have developed a screening test for the pre-malignant stage called Barrett's oesophagus. This comprises a device, CytospongeTM, coupled to a molecular marker which is a less invasive and cost-effective alternative to endoscopy. Our current work is focussing on how to effectively risk-stratify patients according to their likelihood of cancer progression and apply these to the CytospongeTM. This methodology could provide an alternative to the controversial endoscopic surveillance practices.

15.05 – 15.45 **The role of digital pathology and image analysis in tissue research and companion diagnostics**

Professor Peter Hamilton, Centre for Cancer Research and Cell Biology Queen's University Belfast, PathXL Ltd, Innovation Centre, Belfast, Northern Ireland

The ability to stratify patient populations into well-defined subgroups which respond to targeted therapy and have a better clinical outcome, is the basis of stratified medicine. Drug discovery and associated clinical trials in cancer now go hand in hand with the development and validation of "companion" biomarkers. It is increasingly evident to the Pharma, Diagnostic and academic research centres that digital pathology has an extremely important role to play in biomarker discovery, validation and in patient stratification using tissue-based markers. This talk will outline the key roles for digital pathology and image analysis in tissue-based research, drawing on experiences within the Northern Ireland Molecular Pathology Laboratory, the Northern Ireland Biobank and PathXL Ltd. Biobanks now more than ever rely on digital scanning and archiving to support their sample collections and pathological review. The ability to store and share digital slides for remote diagnostics and biomarker scoring is a key advantage supporting multisite integration and international biomarker trials. Digital pathology also underpins automation in pathology which has developed rapidly over the last number of years. We have developed high performance computing solutions to speed up IHC biomarker image analysis in tissue microarrays and developed PICAN (Pathology Integromics in Cancer), a data integration platform to support convergence of biomarker, clinical pathological and genomic data for biomarker discovery. Digital pathology and image analysis also has a role to play in molecular testing. A collaborative research programme between PathXL and QUB has developed TissueMark™ – a highly performant solution for automated tumour identification and for measuring % tumour cells. Precise tumour estimation is essential for the discovery and translation of new molecular tissue markers in solid tumours. Automation of tumour analysis will help remove the considerable bottle-necks that exist and improve the reliability and reproducibility of molecular testing in cancer. It is evident that digital pathology and image analysis is now coming of age and is going to help fast-track new methods of drug/diagnostic development.

15:45 – 16:15 **Chairman's summing up and Close of Meeting followed by afternoon tea**

Registration Website: www.regonline.co.uk/Pathology13

Keywords: signalling, mTOR, cancer, protein kinase, therapeutic drugs, Ocular melanoma; monosomy 3; BAP1; MLPA; GEP, Barrett's oeosphagus, oesophageal adenocarcinoma, biomarkers, screening, glycosylation, glycobiology, proteomic, cancer, metastatic, Stem cells, Lineage tracing, mitochondrial DNA, Human epithelia, Tumour origins.

About the Chair

Anthony (Tony) Warford expertise is in molecular histopathology. He has set up and managed laboratories in the UK health service, academic institutions, biotechnology and Pharmaceutical companies. Technology developments he has spearheaded include the introduction of diagnostic immunohistochemical methods, validation of antibodies for use as biomarkers, production of probes and methods for in situ hybridisation and supervision and interpretation of GLP tissue based safety studies of potential therapeutic antibodies. Concurrently he has championed quality assurance programmes in histopathology and automation of immunohistochemistry coupled with image capture and analysis. He has also run laboratory safety and human bio-banking programmes. He has published in these fields and shared experience with fellow scientists by organising wet workshops, chairing symposia and lecturing in many countries.

About the Speakers

Sarah E. Coupland, MBBS, PhD, is a senior pathologist at the Royal Liverpool University Hospital, and Professor and Academic Lead of Pathology at the University of Liverpool. She is the lead pathologist in Ocular Oncology, which receives patients and tumour specimens from all over the world, and she heads a team of nine students and scientists as chair of the Liverpool Ocular Oncology Research Group (www.loorg.org), which she established together with Prof. B Damato. She is the also the lead hematopathologist in the region, Director of the Liverpool Tissue Bank of the Royal Liverpool University Hospital, and Deputy Head of the Dept of Molecular and Clinical Cancer Medicine. Prof. Coupland has given more than 90 invited lectures around the world, with several of these presentations being prestigious keynote lectures. Prof. Coupland has published more than 140 scientific articles, with at least 68 of these as first or senior author, with an H-index of 28. This is in addition to 16 textbook chapters. Her major scientific achievements include devising the first TNM staging system for ocular adnexal lymphomas; developing a novel grading system for malignancy of in situ conjunctival melanomas; revitalizing the European Ophthalmic Oncology Group; and successfully translating molecular typing of uveal melanoma from a research tool into routine clinical practice.

On graduation, **Miriam Dwek** joined the biotech company Oxford Glycosystems (subsequently part of the CellTech group), this was followed by a PhD undertaken at UCL with Dr Leathem on glycosylation changes in breast cancer. After post-doctoral work with Dr Leathem she moved from to the University of Westminster as a Senior Lecturer and set up her own laboratory in 2002. She is Principal Investigator of the Against Breast Cancer Unit at the University of Westminster, currently comprising 3 researchers and a research administrator. The research work continues in the area of Cancer Glycobiology. Most of the work has been focussed on proteins that show alterations in glycosylation in cancer using HPLC, lectin and proteomic technologies with a view to developing blood and urine tests for breast cancer. The aim is to develop strategies for targeting breast cancer and boosting the immune response to carbohydrate antigens. A further aspect of the research is the interplay between diet and lifestyle and outcome following breast cancer.

Fiona Marshall is currently Business Development Clinical Diagnostics at Promega UK. She has PhD in Molecular Biology/Virology from Oxford Brookes University and has previously worked in Field Applications Specialist roles at Promega UK, Tebu-Bio and in management consultancy to support small businesses' commercialising Intellectual property from research.

Malcolm Alison is Professor of Stem Cell Biology at Barts Cancer Institute, Barts and The London School of Medicine and Dentistry. He is Assistant Editor of the International Journal of Experimental Pathology, a member of the Steering Committee of the UK Stem Cell Bank, a member of the Scientific Advisory Committee of Yorkshire Cancer Research, the Finnish Academy of Sciences' (Chairman: Stem Cell Panel) and 'Health Research Board' Ireland'. Member of FACULTY OF 1000 in MEDICINE. He is an editorial board member of numerous Journals including The Journal of Pathology and The American Journal of Pathology and author of over 240 scientific articles. In 2012 he was awarded the Doniach Lectureship of The Pathological Society of Great Britain and Ireland for his life-long contribution as a Senior member of the Society to the science of Pathology and to the Scientific activity of the Pathological Society.

Rebecca Fitzgerald is a tenured Programme Leader at the MRC Cancer Cell Unit, Hutchison-MRC Research Centre and Honorary Consultant in Gastroenterology and Oncology, Addenbrooke's Hospital, Cambridge (appointed 2001). She graduated from Cambridge University in 1992, performed a research degree at Stanford University, California (1995-1997) and was then awarded an MRC Clinician Scientist Fellowship to enable her to undertake specialist clinical training in parallel with postdoctoral research at St Barts and The London Hospitals (1997-2001). Her research focuses on malignant transformation processes in the oesophagus and the development of novel clinical methods for early cancer detection incorporating devices and molecular technologies.

Peter Hamilton's research interests focus on the development and application of new bio-imaging modalities in cancer, cell biology and tissue diagnostics. This includes automated machine vision in histopathology, 3-D visualisation and quantitation of cell and molecular events and gigapixel image processing. In addition he is the Academic lead for the Northern Ireland Virtual Tissue Archive (NIVTA) housed within the Bioimaging Unit. This is a new initiative funded by the HPSS R&D Office, Queen's University Belfast and supported by Hewlett Packard.

POSTER PRESENTATIONS

DIMETHOATE INDUCES REDOX STATE IMBALANCE, DISRUPTS MEMBRANE BOUND ATPASES AND CONFERS NEUROTOXICITY THROUGH DNA DAMAGE. PROTECTIVE EFFECTS OF VITAMIN E

Ibtissem ben amara[1], Awatef ELWEJ[1], Dorra Driss[2], Semia Ellouze Chaabouni[2], & Najiba ZEGHAL [1]*
1: Animal Physiology Laboratory. Sfax Faculty of Science. BP1171, 3000 Sfax. University of Sfax. Tunisia. 2: Enzymes and Bioconversions Laboratory, National Engineering School of Sfax, BP 1173, 3038-Sfax, University of Sfax, Tunisia.

Pesticides have been used in agriculture to enhance food production by eradicating unwanted insects and controlling disease vectors, nevertheless occupational exposure to high levels of these compounds can lead to neurodegenerative disorders, characterized by serious oxidative and neurotoxic effects. However, there is a lack of consensus as to which determinations are best used to quantify future risks arising from xenobiotic exposure and natural antioxidant interventions. Our study aims to determine the potential ability of vitamin E, used as nutritional supplement, to alleviate oxidative stress in cerebellum tissue induced by dimethoate, an organophosphorus pesticide. Fur this purpose, vitamin E, dimethoate, vitamin E+dimethoate, vitamin E were given to adult rats for 4 weeks. Exposure to dimethoate increased malondialdehyde levels, H_2O_2 and advanced oxidation protein products, while Na^+K^+-ATPase, Mg^{2+}-ATPase, acetylcholinesterase and butyrylcholinesterase activities decreased in the cerebellum. A decrease in glutathione peroxidase, superoxide dismutase and catalase activities and in glutathione, non protein thiols and vitamin C levels were observed. A smear without ladder formation on agarose gel was also shown in cerebellum, indicating random DNA degradation, a hallmark of necrosis. Administration of vitamin E through the diet in dimethoate treated rats ameliorated the biochemical parameters cited above and were found to be effective in preventing DM-induced smear formation. The mechanisms, which contribute to it effectiveness, involve free radicals quenching and antioxidant status improvement. Thus, vitamin E appear to be promising agents for protection against DM induced neurodegenerative effects.

PHENOTYPING TILS *IN SITU*: AUTOMATED ENUMERATION OF FOXP3+ AND CD69+ T CELLS IN FOLLICULAR LYMPHOMA

R.C. Lloyd, 1 J.R. Mansfield,2 C.M. van der Loos,3 , L.S. Nelson,4 C. Rose,4 H.E. Sandison,4 S. Usher,4 J.A. Radford,4 K. M. Linton,4 R.J. Byers, 4

1) PerkinElmer, Chalfont Road, Seer green, Beaconsfield, Bucks, HP9 2FX, 2) PerkinElmer, Hopkinton, USA, 3) Academic Medical Center, Amsterdam, Netherlands; 4) University of Manchester, UK

Background: In many cancers, tumor-infiltrating lymphocytes (TILs) indicate levels of tumor immunogenicity and predict survival. In particular, increased levels of regulatory T cells (Tregs) are associated with poorer prognosis, whilst CD69+ T-cells may also be prognostic. Understanding the phenotype and pattern of TILs in situ within tumors would be advantageous. However, visual TIL assessment cannot easily determine the type of lymphocyte in situ and multimarker quantitation is difficult with standard methods. We present a multi-marker, computer-aided event-counting method for determining the phenotypes of lymphocytes in follicular lymphoma using a multispectral imaging (MSI) automated tissue segmentation and counting approach. Material and methods: A tissue microarray containing follicular lymphoma (FL) cores from 70 patients was chromogenically immunostained for CD3, CD69 and FOXP3, counterstained with hematoxylin, of which 40 cores were informative for both triplex staining and clinical follow-up. Each core was imaged using MSI and the individual staining of each marker separated from each other using spectral unmixing. Images were analyzed using software trained to recognize different tissue compartments based on morphology, specifically based on CD3 rich (extra-follicular) and poor (intra-follicular) areas. The FOXP3 or CD69 status of each CD3+ TIL was then determined and number Treg (FOXP3+/CD3+) and CD69+ T-cells counted in the intra- and extra-follicular areas. Results: The intra-follicular (CD3 poor) and extra-follicular (CD3 rich) regions were accurately recognized within each core, based on abundance of CD3 cells. MSI enabled the accurate quantitation of CD3, CD69 and FOXP3 without crosstalk. The number of FOXP3+/CD3+ Tregs and CD69+ T-cells were counted in each core and used in Kaplan-Meier survival analysis, which demonstrated association of FOXP3+/CD3+ Tregs with favourable outcome in both the intra- (p=0.0173) and extra-follicular (p=0.0173) areas, as well as CD69+ T-cells in intra-follicular (p=0.0175) areas; CD69+ T-cells were not prognostic in extra-follicular areas (p=4509). Conclusions: This study demonstrates use of an automated method for counting Tregs in follicular lymphoma, showing association of FOXP3+ Tregs with good outcome. Given the generic nature of the method automated multiplexed tissue cytometry analyses are feasible for routine clinical studies and work with many multiplexed IHC staining methodologies, of importance for translational cancer studies in general.

DETECTION OF P53 249SER POLYMORPHISM AND HBV IN HEPATOCELLULAR CARCINOMA PATIENTS FROM DARFUR:-

Badreldin Yousif[1], Salma Mahmoud[1], Hiba Salah[1].

Elfasher Teaching Hospital , P.O Box 125, Darfur Sudan

Hepatocellular carcinoma (HCC) is among the most lethal and prevalent cancers in the human population. HCC has been reported to show an increasing pattern in the past two decades especially in western Sudan, this alongside the recorded data of the high exposure to aflatoxin in that area may underlie possible relationship. Specific polymorphism at codon 249 of the *P53* tumor suppressor gene was found to present in patients with hepatocellular carcinoma (HCC) in regions with high levels of dietary exposure to the fungal toxin, aflatoxin B1. Our main objective in this study was to examine the presence of P53 codon 249 polymorphism and HBV in DNA samples of HCC patients from western Sudan, where incidence of HCC and HBV infection are very high in addition to high level of aflatoxin B1 exposure. *Methods*: DNA was extracted from the serum of 58 patients with HCC and 40 control subjects was amplified by the polymerase chain reaction assay using primers specific for exon 7 of the P53 gene, and submitted to endonuclease cleavage with HaeIII to identify the 249serine *P53* polymorphism using RFLP. HBV infection were detected using PCR *Results*: The specific polymorphism was detected in 5.1% of the HCC patients and no polymorphism was found among control subjects although all of them were exposed to high level of aflatoxin. Further experiments will be carried out for HBV detection. *Conclusions*: The 249serine *P53* polymorphism is found less often in HCC patients from western Sudan.

BOTANICAL HEPATOTOXICITY – EVIDENCE-BASED MEDICINE AND SYSTEMATIC REVIEW

Consolato Sergi and Reem J. Abdualmjid.
Department of Laboratory Medicine and Pathology, University of Alberta, Edmonton, Alberta, Canada

Aim. Herbal medicines have been increasingly used worldwide. However, the potential harms of these herbs have been noticed only occasionally. The aim of this review is to evaluate the evidence of hepatotoxic effects linked to use of herbal preparations. Method. Electronic search was performed by searching several databases: PubMed, HerbMed, Google Scholar, Scopus, Cochrane Database of Systematic Reviews and Cochrane Library using both Latin and common names of several herbs. Language was restricted to English and articles were selected for relevance reporting incidence of hepatotoxicity associated with use of herbal products in human. Results. A total of 565 relevant reviews and articles were found, whose 254 met our inclusion criteria and were analyzed. Serious hepatotoxic events associated with various herbal products alone or in combination with other drugs have been collected and summarized. The spectrum of liver toxicity includes elevated liver enzymes, acute or chronic hepatitis, cholestasis, hepatic necrosis, fibrosis, and cirrhosis, as well as acute liver failure and hepatic veno-occlusive disease. Conclusion. Botanical hepatotoxicity seems to be extensively acknowledged, although most probably in a fragmentary way. As the use of natural medicine increases, the risk of liver toxicity and drug interaction increase as well. Herbal remedies are probably useful in several fields of medicine, but botanicals may indeed cause several liver damages. Further scientific studies with high and good quality are needed to selectively identify toxic compounds and understand the exact mechanism of hepatotoxicity-induced by herbs. The adverse effects of herbal products should be fully reported worldwide and professional / college regulations should be uniform, because they are different from country to country. In our opinion, extensive education of healthcare providers by pathologists or liver specialists with a major interest in pathology must be provided in order to reduce danger of alternative medicines.

HYDROALCOHOLIC EXTRACT OF *LIGUSTRUM VULGARE* FLOWER INDUCES CYTOTOXIC EFFECT ON GLIOBLASTOMA CELLS *IN VITRO*

SO, Purcaru,SA. Buteica, GD. Mogoşanu, DE. Tache, and A. Dricu.
University of Medicine and Pharmacy Craiova, Str. Petru Rares nr. 2-4, Craiova, Romania. e-mail: anidoth@yahoo.com, anica.dricu@webmailumfcv.ro

Glioblastoma (GB) is very aggressive brain tumour and despite current advances in multimodality therapy, outcome for patients with this malignant disease remains uniformly fatal with a median survival of 9–15 months. Resistance to conventional therapies has posed major challenges for these patients' treatment. *Ligustrum vulgare*. extracts were reported to be used for prevention or treatment of several diseases including cancer. The aim of this study was to investigate the effect the *Ligustrum vulgare* hydroalcoholic extract (LHAE) effect on GB cell viability. GC–MS analysis of LHAE revealed 28 compounds, the most abundant being *trans*-1,3-dimethyl-cyclohexane (5.44%), octahydropentalene (4.68%), 1-methyl-2-methylene-cyclohexane (4.24%), 4-hydroxy-3-hexanone (4.23%), *n*-butyl acetate (4.12%) and 2,3,5-trimethyl-decane (3.98%), most of them from the volatile oil of *L. vulgare* flowers. In our study, we have analyzed the effect of LHAE alone and in combination with helianthine (HL), temozolomide (TMZ) or doxorubicine (DOXO) on a primary GB cell line *in vitro.* The cells were incubated with the drugs and the antiproliferative effect was examined using MTT assay. LHAE displayed inhibition property against GB cells. Depending on drug concentration and period of treatment, LHAE induced *40–60*% cytotoxicity in GB cells. Combining different compounds has been reported to enhance tumour cell death and to prolong survival of patients with malignant disease. However, in our study, the combination of LHAE with HL, TMZ or DOXO did not induced synergistic cell death in the GB cells *in vitro*.

POTENTIAL PROGNOSTIC AND THERAPEUTIC IMPORTANCE OF MTOR COMPLEXES RELATED ACTIVITIES IN HUMAN LYMPHOMAS

A. Sebestyén[1,2,*], Á. Márk[1], N. Nagy[1], A. Molnár[1], T. Sticz[1], M. Hajdu[1], B, Timár[1], M. Csóka[3], L. Kopper[1]

**Ist Department of Pathology and Experimental Cancer Research, Semmelweis University, Budapest, 1085 Üllői út 26, Hungary. [1]Ist Department of Pathology and Experimental Cancer Research, Semmelweis University, Budapest,; [2]Tumor Progression Research Group of the Hungarian Academy of Sciences and Semmelweis University, Budapest; [3]2nd Department of Pediatrics, Semmelweis University, Budapest;*

Deregulation of signaling network, especially the increased activity of mTOR kinase could be an important event in tumor growth. The mTOR pathway has recently attracted attention as a potential target in oncological therapy, rapalogs are in therapeutic protocol of renal cell carcinomas and mantle cell lymphomas. However, limited data exist about the activity of different mTOR kinase complexes and their role in potential therapeutic effectivity of different mTOR inhibitor treatments. In our work we tried to characterise the mTOR activity of different human lymphomas, leukemias, we study the effects of different mTOR inhibitors and the activity of C1 and C2 complexes in lymphoma, leukemia cells. We characterised the expression of mTOR activity dependent phospho-proteins and the elements of different mTOR complexes by several technics (ELISA, Western blot, different immunohistochemical technics) in fresh leukemic cells and in archive tissue biopsy materials as well. The activity and expression were analysed to find statistical correlation between clinical/survival data. Moreover, we studied the mTOR inhibitor sensitivity of different human lymphoma cell lines (Hodgkin lymphoma - HL, Diffuse large B cell lymphoma DLBCL, Burkitt lymphoma, T- and B-ALL) and isolated pediatric ALL cells in vitro. The biological effects (proliferation, apoptosis) were detected by alamarBlue® test and flow cytometry. We established mTORC1, C2 complex measurment by Duolink technique to compare the effectivity of the studied inhibitors to the mTORC1/C2 complex availabilty in cells. We found that all ALL cases and the majority of mantle cell lymphomas, Burkitt lymphomas, DLBCLs, anaplastic large cell lymphomas and HLs showed high mTOR activity. Further characterisation of HLs, DLBCLs and ALL cases showed that mTORC2 related high mTOR activity is a sign of worse prognosis. We found that: 1. High mTORC1 activity (high mTOR activity without Rictor expression) was observed in more than 90% of HL cases with both favorable and unfavorable (few cases) clinical response; 2. mTOR activity was characteristic in 80% of non-germinal center DLBCLs and Rictor overexpression was detectable in more than 60% of these cases (these patients have significantly worse prognosis and shorther survival); 3. mTOR activity dependent phospho-protein expression was significantly higher in ALL patients with poor prognosis at diagnosis. Increased mTOR activity was found in all studied cell lines and we found alteration in the expression of Rictor, Raptor and mTOR-Rictor complex expression. In vitro treatment showed different mTOR inhibitor sensitivity correlated to the expression of different mTOR complex elements. The increased mTOR activity in different lymphomas may be useful as a potential therapeutic target. According to our results, analysis of the expression and activity of different mTOR complexes related proteins should have prognostic value and great importance before mTOR inhibitor therapy in lymphomas and ALLs. Supported by OTKA81624 and OTKA84262 project of Hungarian Scientific Research Funding.

BREATHE EASY WITH QUANTITATIVE IMAGE ANALYSIS – QUANTIFYING HISTOLOGICAL EFFECTS OF RIA TARGETS IN PRE-CLINICAL RESPIRATORY MODELS

S. C. Heasman, D L. Clarke, N. H. E. Davis, J. B. Majithiya, A. Carruthers, M. A. Sleeman and D. J. Corkill, L. Murray, R. May, A. Lewis

MedImmune, Milstein Building, Granta Park, Cambridge, CB21 6GH

Respiratory disease processes such as asthma and idiopathic pulmonary fibrosis (IPF) can be modelled and assessed pre-clinically using a range of in vivo and ex vivo measurements. Quantitative histopathological assessment of these models is critical in demonstrating that the classical hallmarks of peri-bronchiolar inflammation in asthma or pulmonary fibrosis in IPF that correlates to clinical disease and has a measurable response to treatment. Mouse models of asthma exacerbations using the aeroallergen house dust mite and the TLR3 agonist polyI:C, were established and histological Haematoxylin & Eosin or Massons' Trichrome stained lung sections were prepared. A set of image analysis algorithms were developed and used, to quantify the number of peri-bronchiolar inflammatory cells present within the digital histological images across multiple in vivo studies. We intend to use this methodology to demonstrate measurable differences in the models in the number of peri-bronchiolar inflammatory cells in response to HDM/polyI:C and extend this to quantitatively assess the changes in pulmonary fibrosis in response to bleomycin exposure. Development of automated image analysis enables quantitative assessment of different therapeutic strategies across our respiratory disease models in a standardized process. This is enhancing both our understanding of these models and the clinical disease and supports the characterization of the disease relevant targets being evaluated for their importance in the disease process.

Don't forget to sign up to Euroscicons' e-newsletter at www.euroscicon.com/signup.htm to keep up to date with European Life Science news and events and to be notified of the follow up to this event. This meeting was organised by Euroscicon (www.euroscicon.com), a team of dedicated professionals working for the continuous improvement of technical knowledge transfer to all scientists. Euroscicon believe that they can make a positive difference to the quality of science by providing cutting edge information on new technological advancements to the scientific community. This is provided via our exceptional services to individual scientists, research institutions and industry.

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