Postgraduate Student Research Day 2009

Postgraduate Student Research Day
12th June 2009
ILS Seminar Room

9.00am – 9.10am
Welcome

Session One – Chair: Professor Dietrich Mack

9.10am – 9.25am
L Selectin Ligands in Human Endometrium: Comparison of Fertile and Infertile Subjects
Lavinia Margarit

9.25am – 9.40am
Designing Innovative Biocides for Critical Environments
Richard Salvage

9.40am – 9.55am
Design of a Miniaturized Blood Pump with a Hydrodynamically and Magnetically Suspended Impellor
Graham Foster

9.55am – 10.10am
Non-Conveyance of 999 callers: Early findings related to subsequent use of Health Services
Mohammed Al-Sulaiti

10.10am – 10.25am
Prognostic Indicies in Breast Cancer: The Application of Machine Learning Methods
Asmaa Al-Allak

10.30am – 11.00am
Coffee

Institute of Life Science
School of Medicine
Swansea University
L-selectin ligands localized to the luminal epithelium at the time of implantation may support the early stages of blastocyst attachment. We have assessed the expression of two L-selectin ligands defined by MECA79 and HECA452 monoclonal antibodies, and the sulfotransferase GlcNAc6ST-2, involved in generation of L-selectin ligand epitopes, in the secretory phase of the endometrium from fertile and infertile patients.

Endometrial samples were obtained from 33 fertile, 26 PCOS, 25 endometriosis and 33 patients diagnosed with unexplained infertility. L-selectin ligands and GlcNAc6ST-2 expression was assessed by immunohistochemistry and immunoblotting.

Immunohistochemical staining of uterine epithelium, from fertile and infertile women, demonstrated differential expression of MECA79 and HECA452 epitopes. In fertile women in the secretory phase MECA79 was more strongly expressed, particularly on the lumen, than in infertile women. HECA452 staining was significantly stronger in the glands in PCOS and endometriosis patients than in fertile. GlcNAc6ST-2 expression was reduced in infertile patients, correlating with MECA79 expression.

This study demonstrated significant differences in expression of L-selectin ligands between fertile and infertile women in natural cycles and could contribute to patient assessment prior to initiating fertility treatment.
DESIGNING INNOVATIVE BIOCIDES FOR CRITICAL ENVIRONMENTS

Some critical environments, especially life science cleanrooms, demand the use of specifically designed biocides to deal with very specific functions.

In pharmaceutical cleanrooms alcohol is the most commonly used broad spectrum biocide. Without exception it is used in a dilution of 70% alcohol to 30% deionised water. Both 70% Iso Propyl Alcohol and Denatured Ethanol are used routinely. There are a number of denaturants available to render ethanol unpalatable, such as methanol, but they also introduce unwanted impurities into critical environments.

Recently, a new formulation has been approved for Denatured Ethanol creating an opportunity to manufacture a much purer product. TSDA 7 (Trade Specific Denatured Alcohol) is ethanol denatured with 5% IPA thus enabling pure alcohol to be diluted with high grade Water For Injection (WFI) producing a very high standard biocide for the pharmaceutical industry.

Until now the efficacy of all three of these alcohols has not been properly described in terms of the required concentration. The most efficacious concentration has always been understood to be 70% Ethanol, Iso Propyl Alcohol and TSDA 7 have been studied using the harmonised European standard BSEN 1276 and for the first time the efficacy of these biocides can be properly described. Data will show that Ethanol is effective against four standard organisms at 50% concentration, IPA at 35% concentration and TSDA 7 at 44%.

In order to achieve a longer acting broad spectrum biocide, a compound containing a proprionate ammonium quaternary and monovalent silver chloride has been investigated and it has shown to be effective against Aspergillus Niger at 15mins and 8 hours.
There is a need to address the major global health problem of heart failure that affects close to a million people over forty-five years old in the UK alone. Until recently the only way to curatively treat heart failure has been by heart transplant or the implantation of a total mechanical heart. Unfortunately donor hearts are only able to meet a small fraction of the demand and mechanical hearts have yet to gain widespread acceptance due to the technical difficulties with these devices.

Heart assist pumps have emerged more recently as an alternative to complete transplantation and work alongside the diseased heart to boost its output. Clinical studies have proved that heart failure can be halted or in some cases reversed by the fitment of these devices. However, the relatively large size of current devices means that highly invasive surgical procedures are required for their implantation. As a result they are used infrequently as a last resort to bridge the gap between terminal heart failure and receiving a transplant. In addition, the cost of current devices is extremely high and precludes their use by the NHS or being underwritten by medical insurance companies.

It has been speculated that heart assists pumps could become the routine method of treatment for heart failure if two key factors are addressed: 1) reducing cost and 2) making the device suitable for implantation by minimally invasive surgery. This research addresses point 2) above – the miniaturisation of the pump so that it can be made at a size small enough to be implanted via a minimally invasive surgical procedure.
In the UK, up to 30% of 999 patients are not always transported to a medical facility each time the emergency ambulance service is called. This situation is similar to what is being found internationally. The aim was to explore present practice and its consequences in the ambulance service related to non-conveyance of 999 callers. Patient clinical records (PCRs) completed by ambulance crews based at three Swansea ambulance stations for non-conveyed patients during the period 1 July 2006 to 31 December 2006 were collected. PCR data was matched to hospital admission records, A&E attendance, GP in hours contacts data, records of deaths, and GP out of hours contacts data. Further linkage is ongoing – PCR data will be matched if possible, to subsequent 999 calls in order to track patients’ outcomes and to gain a picture of patterns of emergency re-attendance following non-conveyance.

During the six month study period, 734 non-conveyed patients were identified. Half were male. The average age was 60 years (range 1-97).

Chart One: Phase One initial results

This issue of not conveying patients to hospital has become a significant consideration for ambulance services: most ambulance litigation cases have resulted from non-transport of patients.

Early findings indicate that non-conveyance of 999 callers leads to significant utilisation of resources with potential clinical risk. Further detailed assessment of identified calls will now be carried out to identify adverse events.
PROGNOSTIC INDICES IN BREAST CANCER: 
THE APPLICATION OF MACHINE LEARNING METHODS

Over the last few years more concentrated efforts have been made to improve our ability to predict 
the outcome of breast cancer. A number of prognostic indices have been introduced such as the 
Nottingham Prognostic index (NPI) in order to address these needs. With the development of 
machine learning methods there has been a need to introduce more accurate prognostic methods.

Aims:

• Apply machine learning approaches to a large breast cancer data
• Improve approaches taking into account usability and the need for prediction of survival.

The Surveillance, Epidemiology, and End Results (SEER) data was analysed using R and WEKA. 
Classification models applied: decision trees, support vector machines, bagging and NBTree. Results 
were validated using K-fold cross validation.

Table One: Results

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<th>Method</th>
<th>TP Rate</th>
<th>FP Rate</th>
<th>Precision</th>
<th>Recall</th>
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The most optimal model may be a complex unlike the simple NPI. We will often read in the literature 
about a new diagnostic or prognostic model that outperforms a currently used one – but overall 
accuracy is not always the optimal measure of the usefulness of a model.
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Session Two – Chair: Professor Gareth Morgan

11.00am – 11.15am
Dynamics of DNA Topology and the Influences on Gene Expression in Antibiotic producing Streptomyces
Matthew Aldridge

11.15am – 11.30am
Optimising Output Dosimetry of a Broadband Pulsed Light Source and its Role on Clinical Efficacy for Treatment of Skin.
Caerwyn Ash

11.30am – 11.45am
Circadian Rhythms in Adult Attention-Deficit / Hyperactivity Disorder
Alison Baird

11.45am – 12.00pm
Molecular Characterisation of Panton Valentine Leukocidin positive Staphylococcus aureus from Abertawe Bro Morgannwg University and University hospital Wales Cardiff NHS trusts
Naledi Bome

12.00pm – 12.30pm
e-Health Research Exploiting our Potential
Keynote Speaker – Professor Ronan Lyons

12.30pm – 2.00pm
Lunch / Poster Session
Streptomyces coelicolor is a model organism that represents a genus responsible for producing most natural antibiotics used in medicine. DNA in bacteria is maintained in a negatively supercoiled state and this contributes to the organisation of the nucleoid and influences global gene expression patterns.

It has been known for some time that changes in topological state of the chromosome can result in the expression of supercoiling sensitive promoters. Under certain environmental conditions such as osmotic stress an increase in negative supercoiling regulates osmotic stress response genes in E.coli.

Increasing evidence indicates an interaction between histone-like proteins and DNA influencing global and/or local supercoiling of chromosomal DNA resulting in changes of gene expression during the life-cycle of S. coelicolor. A plasmid reporter system has been used to investigate the topological state of the chromosome of several mutants to determine any changes in linking number with or without osmotic stress.
OPTIMISING OUTPUT DOSIMETRY OF A BROADBAND PULSED LIGHT SOURCE AND ITS ROLE ON CLINICAL EFFICACY FOR TREATMENT OF SKIN

High quality Intense Pulsed Light (IPL) systems can offer simple, safe and effective treatments for long-term hair reduction and removal of benign vascular and pigmented lesions. Significant differences in clinical outcomes have been recorded amongst different IPL systems despite comparable display settings.

This investigation focuses on the technical performance of the devices tested and although no clinical data is presented, the measured parameters are those that will directly impact efficacy in hair reduction, efficient coverage of skin and safety in terms of unintentional eye-exposure to the light source or incorrect settings for a given skin type. This study illustrates the variation in pulse structures used by several popular IPL systems available to clinics and estheticians. Using a fast spectrometer, generating 1,000 full spectral scans per second, time resolved spectral data of IPL outputs was captured with a resolution of 0.035 nm.

Spectral outputs are manipulated with an Excel spreadsheet for analysis and results graphically illustrated. A spectral distribution shift that occurs both within a pulse and between pulses is clearly demonstrated and is more prominent with uncontrolled free discharge systems than with square pulsed technology that provides a constant spectral distribution during the pulse duration.
CIRCADIAN RHYTHMS IN ADULT ATTENTION-DEFICIT/HYPERACTIVITY DISORDER

The purpose of this study was to assess circadian rhythmicity in adult ADHD using actigraphy, gene expression and endocrine markers. Patients (n=12) attending an adult ADHD outpatient clinic were recruited, as were healthy age and gender-matched controls (n=24).

Subjects wore an ActiWatch (Cambridge Neurotechnology, UK) on the non-dominant wrist for a period of 7 to 14 days. Gene expression in buccal samples was measured using quantitative PCR. Relative expression levels of the circadian clock genes hPer2 and hBmal1 were examined. Salivary levels of cortisol and melatonin over a 24 hour period were measured.

Preliminary results indicated that the period length was significantly shorter in the patient group compared to the control group and the period deviation was significantly greater in the ADHD group. The relative amplitude of the rhythm, was also significantly weakened. hPer2 and hBmal1 expression were found to cycle in a circadian fashion, however the rhythmic expression of hPer2 and hBmal1 were found to be significantly deregulated in the ADHD patient cohort. Cortisol secretion was shown to oscillate, peaking in the early morning in the majority of the control group, whereas the patient group exhibited varied profiles.

These results provide novel, behavioural and molecular evidence that adult ADHD is associated with less-robust circadian rhythms, and that this circadian dysfunction might contribute to the poor sleep patterns that are associated with adult ADHD.

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MOLECULAR CHARACTERISATION OF PANTON VALENTINE LEUKOCIDIN POSITIVE STAPHYLOCOCCUS AUREUS FROM ABERTawe BRO MORGANNwg UNIVERSITY AND UNIVERSITY HOSPITAL WALES CARDIFF NHS TRUSTS

Epidemic Methicillin Resistant *Staphylococcus aureus* (MRSA) are typically clonal and belong to successful lineages. EMRSA-15 and EMRSA-16; established UK strains, belong to the Barnim-ST22-MRSA-IV and ST30-MRSA-II clones respectively. In the USA, USA300 (ST8-MRSA-IV) a virulent Panton Valentine Leukocidin (PVL) positive Community acquired (CA) MRSA is predominant. Over recent years, in Europe, transmission of USA300 (ST8-MRSA-IV) has been progressive.

80 PVL positive *S. aureus* isolates from Abertawe Bro Morgannwg (n=19) and University Hospital Wales Cardiff NHS trusts (n=61) were characterised by detection of PVL genes and Arginine Catabolic Mobile Element; SCCmec typing; spa typing and Pulsed Field Gel Electrophoresis. PVL positive *S. aureus* of Abertawe Bro Morgannwg NHS Trust, demonstrated great diversity comprising random strains and only 10.5% (2/19) PVL positive MRSA (MRSATIV and MRSATV). Conversely, in the University Hospital Wales Cardiff NHS trust PVL positive MRSA, USA300 confirmed by the 0114 pulsotype was predominant: 45.7% (16/35).

Strains affiliated to the European (ST80-MRSA-IV) and USA800 (ST5-MRSA-IV), accounted for 14.3% and 11.4% of the PVL positive MRSA. 5.7% of the isolates were identified as strains affiliated to USA400 (ST1-MRSA-IV) and EMRSA-15 (ST22-MRSA-IV) respectively. Remaining PVL positive MRSA were random clones, including a strain which was affiliated to the Australian Queensland CA-MRSA (ST93-MRSA-IV).
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Session Three – Chair: Professor Rhys Williams

2.00pm – 2.15pm
Circadian Regulation of P65 in Serum Shocked Fibroblasts.
Amy Beynon

2.15pm – 2.30pm
Investigating the Role of ARF6 and Cytohesin 7 in Cancer
Ben Gosney

2.30pm – 2.45pm
Molecular Epidemiology of Extended –Spectrum beta-lactamase (ESBL) carrying Enterobacteriaceae in Swansea
Caron Jones

2.45pm – 3.00pm
The Expression of the Transcription Factor WT1 (Wilms tumour suppressor gene) within the Human Uterus
Kit Lucas

3.00pm – 3.15pm
Assessing the Medical Costs of Injury using Linked, Anonymised Datasets
Steven Macey

3.15pm – 3.30pm
Interleukin 10 Down-Regulates Thymic Stromal Lymphopoietin-Mediated Chemokine Production
Trisha MacFarlane

3.30pm – 4.00pm
Coffee Break
CIRCADIAN REGULATION OF P65 IN SERUM SHOCKED FIBROBLASTS

In mammals, circadian rhythms have been shown to be generated in a cell autonomous manner by the vast majority of mammalian cell types. Circadian rhythms of cultured peripheral cells is governed by a set of core clock genes whose products oscillate with a circadian periodicity and interact within an interlocked transcriptional/translational feedback loop. The manner and mechanisms of these cycles in cell lines are homologous to those observed in the master brain clock.

Circadian timekeeping is sensitive to immune mediators and there is considerable evidence for their roles in circadian modulation of the immune system. The transcription factor NF-κB has long been implicated in the immune response and there is also evidence for its involvement in the circadian clock.

Circadian oscillations in clock gene expression can be synchronized in cultured cells by incubation with high concentrations of serum, we have used this paradigm to observe whether there is circadian regulation of NF-κB in NIH3T3 fibroblasts.

Nucleic and cytoplasmic extractions were performed every 4 hours for 24 hours following shock treatment with 50% horse serum and analyzed using western blots with semi quantitative relative optical density measurements for total p65 in order to build up a profile of protein expression across the circadian cycle.

Preliminary results indicate a clear temporal regulation of nuclear p65 in the first 24 hours following shock treatment with a peak expression 8 hours after serum shock followed by a second peak in expression 20 hours after the initial serum shock. These results suggest a role for NF-κB in the regulation of the circadian cycle.
INVESTIGATING THE ROLE OF ARF6 AND CYTOHESIN 7 IN CANCER

ADP-ribosylation factor (ARF)6 is a small GTPase that co-ordinates membrane trafficking events and actin cytoskeleton reorganisation by cycling between inactive GDP- and active GTP-bound forms. ARF proteins possess very low intrinsic GTP binding and GTPase activities and therefore require GTP-exchange factors (GEFs) and GTPase activating proteins (GAPs) for their activation and inactivation; the active form binds to downstream effectors giving rise cellular effects. Cytohesin-7 is a GEF, which has been linked to cancer via its upregulation in some cancers and downregulation in others. Therefore, an objective of this project is to investigate more fully the expression pattern of this protein and to investigate its functional role.

This episode of research has been examining expression of ARF6 and cytohesin-7 in various cell lines, particularly breast cancer cell lines MDA-MB-231 and MCF-7. The assessment of cytohesin-7 expression was achieved by characterising the specificity and sensitivity of a polyclonal antibody, before comparing the expression in lysates of various cell lines.

Future work will involve HeLa cells stably transfected with cytohesin-7 and its catalytically inactive mutant, currently in production. This will involve assays investigating migration, invasion and cell-surface expression of proteins such as β1 integrin, as specific examples of how cytohesin-7 putatively may function.
MOLECULAR EPIDEMIOLOGY OF EXTENDED-SPECTRUM BETA-LACTAMASE (ESBL) CARRYING ENTEROBACTERIACEAE IN SWANSEA

Extended-spectrum beta-lactamases (ESBL) mediate resistance to 3rd generation cephalosporins and aztreonam in Enterobacteriaceae and pose major clinical problems. Enterobacteria were collected from Swansea NPHS Microbiology laboratory and ESBL status confirmed by BSAC phenotypic methods.

Of 167 isolates 118 were Escherichia coli, 38 Klebsiella spp., 5 Enterobacter spp., 2 Citrobacter spp., 2 Pseudomonas spp., 1 Morganella morganii and 1 Acinetobacter baumannii. Primer sets were used to specifically amplify TEM, SHV, CTX-M, and plasmid-encoded ampC genes.

The most predominant ESBLs were CTX-M (n=139). 128, 5, 4, and 1 ESBLs belonged to CTX-M groups-1, -9, -25/26, and -2, respectively. 66/128 CTX-M group 1-positive isolates (exclusively E. coli) generated a 400 bp fragment of insertion sequence IS26-CTX-M-15 link region characteristic for epidemic E. coli strain A, which were all clonally related by PFGE. Nucleotide sequencing revealed 7 TEM-116 and 1 TEM-52 ESBLs, 1 TEM-33 (IRT), and 45 non-ESBL TEM-1. 5 SHV-2 ESBLs were found, while 17 SHV-89, 6 SHV-11 and 10 SHV-1 genes, all non-ESBL, were present. 6 isolates carried ampC genes (2 CIT, 1 DHA, 1 EBC, 2 Fox). 83% of isolates carried CTX-M ESBLs, of which 92% belonged to CTX-M group 1. ESBL carrying E. coli outnumber the other Enterobacteriaceae species studied.

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²NPHS Microbiology Swansea, Singleton Hospital, Abertawe-Bro Morgannwg University NHS Trust, Swansea
THE EXPRESSION OF THE TRANSCRIPTION FACTOR WT1 (WILMS TUMOUR SUPPRESSOR GENE) WITHIN THE HUMAN UTERUS

The Wilms tumour suppressor gene (WT1) is located at chromosome 11p13 and encodes a zinc fingered transcription factor. Recent research has shown that WT1 is overexpressed in a wide variety of solid tumours. Such overexpression has been linked to a more severe and aggressive form of these malignancies.

WT1 has also been associated with decidualisation within the human endometrium; this involves a morphological change of endometrial stromal cells into decidual stromal cells. Decidualisation is vital for the implantation of the developing embryo and plays a vital role in sustaining the stability of pregnancy.

Here I illustrate the importance of WT1 within the human endometrium through the use of an in vitro decidual model. This demonstrates that WT1 and a number of its target genes increase expression throughout decidualisation. The role of WT1 on these targets is thus investigated further using plasmid vectors overexpressing the transcription factor. In conclusion WT1 is shown to be of major importance within the decidual process.
ASSESSING THE MEDICAL COSTS OF INJURY USING LINKED, ANONYMISED, DATASETS

The aim of this study is to utilise large scale anonymised datasets, linked via unique patient level identifiers, to estimate the direct medical costs of injury incurred by various sectors within the health care system.

This study will utilise data linkage techniques to join together multiple, large scale, health related databases and population based registries. Longitudinal in design, the investigation will retrospectively approximate the extent of health service utilisation and the demand for health care resources associated with both an injured and uninjured cohort of individuals.

The incidence/cost of injuries in receipt of medical attention at A&E, hospital, outpatients and GPs will be identified and stratified by patient age/gender/social class, injury type and accident category.

Together with identifying high risk injury groups, in terms of the incidence and cost of injuries treated/cared for/rehabilitated by health care providers, thereby allowing injury prevention practitioners to correctly determine the main priority areas in greatest need of intervention, this study will additionally serve to indicate the importance of research investment into injuries in general and add weight to the calls for an increase in research spending on injury prevention so that it corresponds more satisfactorily to the levels directed at other major public health problems.
INTERLEUKIN 10 DOWN-REGULATES THYMIC STROMAL LYMPHOPOIETIN-MEDIATED CHEMOKINE PRODUCTION

Thymic stromal lymphopoietin (TSLP) has a pivotal role in the development of allergic disease via initiation of allergy-favouring immune responses through interactions with multiple cell types. Interleukin (IL)-10 is an immunoregulatory cytokine with anti-inflammatory properties produced mainly by monocytes that is known to inhibit the production of many pro-inflammatory cytokines.

The primary objective of this work was to determine if IL-10 and other cytokines of the IL-10 superfamily might down-regulate the activity of TSLP in adults and neonates. Umbilical cord (CBMCs) and adult peripheral blood (PBMCs) mononuclear cells were cultured with TSLP in conjunction with either IL-10, IL-19, IL-22, IL-26 or IFNγ and levels of an allergy-favouring chemokine - thymus and activation-regulated chemokine (TARC) - were measured using a specific ELISA.

From the cytokines measured, only IL-10 and IFNγ significantly down-regulated TSLP-mediated TARC production by both adult and cord blood mononuclear cells. Similar effects of IL-10 on TARC production induced by other allergy-favouring cytokines were also found. The signalling pathway utilised by IL-10 to down-regulate TSLP-mediated chemokine production is currently being investigated. IL-10 has potential as a treatment for allergic disease in children and adults.
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Session Four – Chair: Professor William Griffiths

4.00pm – 4.15pm
Activation of NFkB by Bile Acids and the influence of Acidity in Barrett’s Oesophagus
Elizabeth McAdam

4.15pm – 4.30pm
The Effects of Advanced Glycation End products in the Endometrium
Amy White

4.30pm – 4.45pm
Magnetic Induction Tomography for Imaging Cerebral Stroke
Massoud Zolgharni

4.45pm – 5.00pm
Synthesis, Characterisation and Applications of Polymeric Organometallic Lewis Acids
Victoria Chislett

5.00pm – 5.15pm
NF-kB Activity in Intestinal Type Gastric Cancer
James Davies

5.15pm – 5.30pm
Molecular Screening of TUBA1A in Neuronal Migration disorders co-morbid with Epilepsy
Thomas Cushion

5.30pm - Close
Prize giving and drinks reception (Café Glas)
ACTIVATION OF NFkB BY BILE ACIDS AND THE INFLUENCE OF ACIDITY IN BARRETT’S OESOPHAGUS

Barrett’s oesophagus is the only known precursor of oesophageal adenocarcinoma, the ninth most common cancer in the UK. Barrett’s involves a change from the normal squamous epithelium of the oesophagus to an intestinal type metaplastic epithelium, initiated by gastroesophageal reflux disease (bile components and stomach acid).

The transcription factor NFkB is well documented as an important regulator of key genes involved in the carcinogenic process. Previous in vitro studies have shown NFkB to be activated by prolonged exposure to the bile acid DCA. However, there is still uncertainty about the effects of short term DCA exposures and acidity.

Using an NFkB transcription factor assay and western blot approach, this study has shown there is a significant increase in activated NFkB after a 30 minute exposure to DCA at neutral pH. This is due to degradation of NFkB’s inhibitor protein IkB, which was seen at lower levels after the same DCA treatment time. Interestingly, DCA treatment at pH5 revealed significantly less activated NFkB when compared with the equivalent neutral pH treatments. This indicates that bile is more damaging in the absence of acid, which could potentially be important to those Barrett’s patients receiving acid suppression therapy.
THE EFFECTS OF ADVANCED GLYcation END PRODUCTS IN THE ENDOMETRIUM

Advanced Glycation End Products (AGE) have been implicated in the high incidence of miscarriage and infertility amongst women suffering from polycystic ovary syndrome (PCOS). It is thought that AGE products can bind to the receptor for Advanced Glycation End products (RAGE) to initiate a signalling pathway that results in the transactivation of the MUC1 gene.

MUC1 protein plays an important role in determining successful implantation of the egg into the endometrium. Therefore, changes in MUC1 expression levels could change the optimum conditions for implantation. It was thus of interest to investigate whether the elevated AGE levels seen in women with PCOS can induce their receptor RAGE in the endometrium.

In previous work, RAGE has been shown to be induced by AGE products in the Ovaries. Here we demonstrate that AGE products can also induce RAGE receptor expression in epithelial endometrial cells both as mRNA transcript and as protein. The effect of known inducers of RAGE in skin endothelial cells was also investigated in parallel.

This study shows Tumour Necrosis Factor alpha (a pro-inflammatory cytokine involved in insulin resistance) and Estradiol (a hormone that targets the endometrium) were also shown to induce RAGE. This study offers a possible explanation for the high incidence of infertility in women with PCOS, who have elevated levels of AGE and RAGE, providing that the AGE-RAGE signalling pathway exists.

Future work will concentrate on MUC1 expression and its induction by AGE products in epithelial endometrial cells.
MAGNETIC INDUCTION TOMOGRAPHY FOR IMAGING CEREBRAL STROKE

Conventional imaging techniques for diagnosing pathologies in the brain (e.g. MRI, CT) are expensive and in some cases inaccessible and Magnetic Induction Tomography (MIT) may be an attractive, low-cost candidate for rapid imaging. MIT is a relatively new imaging modality which is used for imaging the electrical conductivity distribution in an object.

The purpose of this study is to investigate the feasibility of a multi-channel MIT system for imaging haemorrhagic cerebral stroke. A realistic, multi-layered, human-head model is used to simulate the brain. Numerical simulations are used to solve the eddy-current problem and compute the response field measured due to the stroke. Images of conductivity are reconstructed from the values of voltages obtained from simulations. Specific absorption rate is also computed for the head and it was concluded that at present MIT is a harmless and safe imaging method regarding heat generation.
SYNTHESIS, CHARACTERIZATION AND APPLICATIONS OF POLYMERIC ORGANOMETALLIC LEWIS ACIDS

Organometallic polymers represent an interesting class of materials with the potential for novel electronic, optical and magnetic properties, which can be utilized for a range of applications. There are a number of synthetic routes to these polymers, however many face problems such as the use of air sensitive intermediates meaning that a simple and versatile new route is a key target.

Boronic ester condensation chemistry offers a simple and readily tuneable methodology for linking organometallic components, and this can be achieved with high selectivity towards polymeric or macrocyclic products by simple variation of the linker molecule. Resulting air and water stable multi-centre Lewis acids offer a range of applications particularly in anion recognition and sensors.

A range of organometallic polymers can be synthesized using a simple condensation methodology of ferrocenes with varying attached moieties. These new materials can be characterized by a variety of methods, in particular with the use of mass spectrometry, such as MALDI for poly/oligomer characterization. Further testing of physical and electronic properties can also be achieved by employing techniques such as cyclic voltammetry, which in turn can also help identify materials suitable for applications such as anion sensing.
NF-κB ACTIVITY IN INTESTINAL TYPE GASTRIC CANCER

As the world’s fourth commonest malignancy and the second leading cause of cancer-related mortality worldwide, gastric cancer represents a major health concern. The gram-negative, microaerophilic bacterium *Helicobacter pylori* is known to be the cause of acute or chronic gastritis, and a predisposing factor in gastric cancers. As such, *H. pylori* has been classed as a group 1 (definite) carcinogen by the World Health Organisation (WHO).

Long-term *H. pylori* infection causes a carcinogenic environment through inflammation of the gastric mucosa leading to atrophic gastritis and intestinal metaplasia, both of which are precursors of gastric cancer. *H. pylori* infection induces a host inflammatory response involving the infiltration and activation of inflammatory cells, leading to the production of potentially harmful reactive oxygen species (ROS).

Here we assessed NF-κB activation in premalignant gastric epithelium by real-time PCR and immunohistochemistry. Infection with *H. pylori* significantly increased expression of the NF-κB target gene IL-8, whilst activation of p65 increased in both *H. pylori* positive and negative gastritis. NF-κB activation may therefore represent a marker solely of inflammation.
MOLECULAR SCREENING OF TUBA1A IN NEURONAL MIGRATION DISORDERS CO-MORBID WITH EPILEPSY

The development and correct function of the mammalian brain is dependant on the precise arrangement of neurons to assemble its laminar structure. Lissencephaly is a devastating neuronal migration disorder co-morbid with severe epileptic seizures, arising when the strict regulation of cell migration in the developing brain is disturbed. This project intends to determine the role of tubulin genes in Lissencephaly, as mutations in the alpha-tubulin encoding TUBA1A gene have been associated with defective movements of post-mitotic neurons within the developing cortex.

Lissencephaly patient DNA was collected from the Institute of Medical Genetics in Cardiff and the samples were screened for TUBA1A mutations by direct sequencing and using "light-scanner" mutation detection technology. The cohort had previously been examined for LIS1 mutations, an established diagnostic gene, where gene-positive patients share characteristic phenotypes with TUBA1A positive cases. Only LIS1 gene-negative samples were selected for TUBA1A mutation analysis.

Genetic variants were detected and validated appropriately and further functional tests will be carried out to observe how the migration pathway is interrupted. Consequently, if a link between TUBA1A and Lissencephaly is established then the study will characterise the correlations between tubulin gene mutations and case phenotypes, and eventually transferring new genes into the diagnostic domain for cortical malformation syndromes.