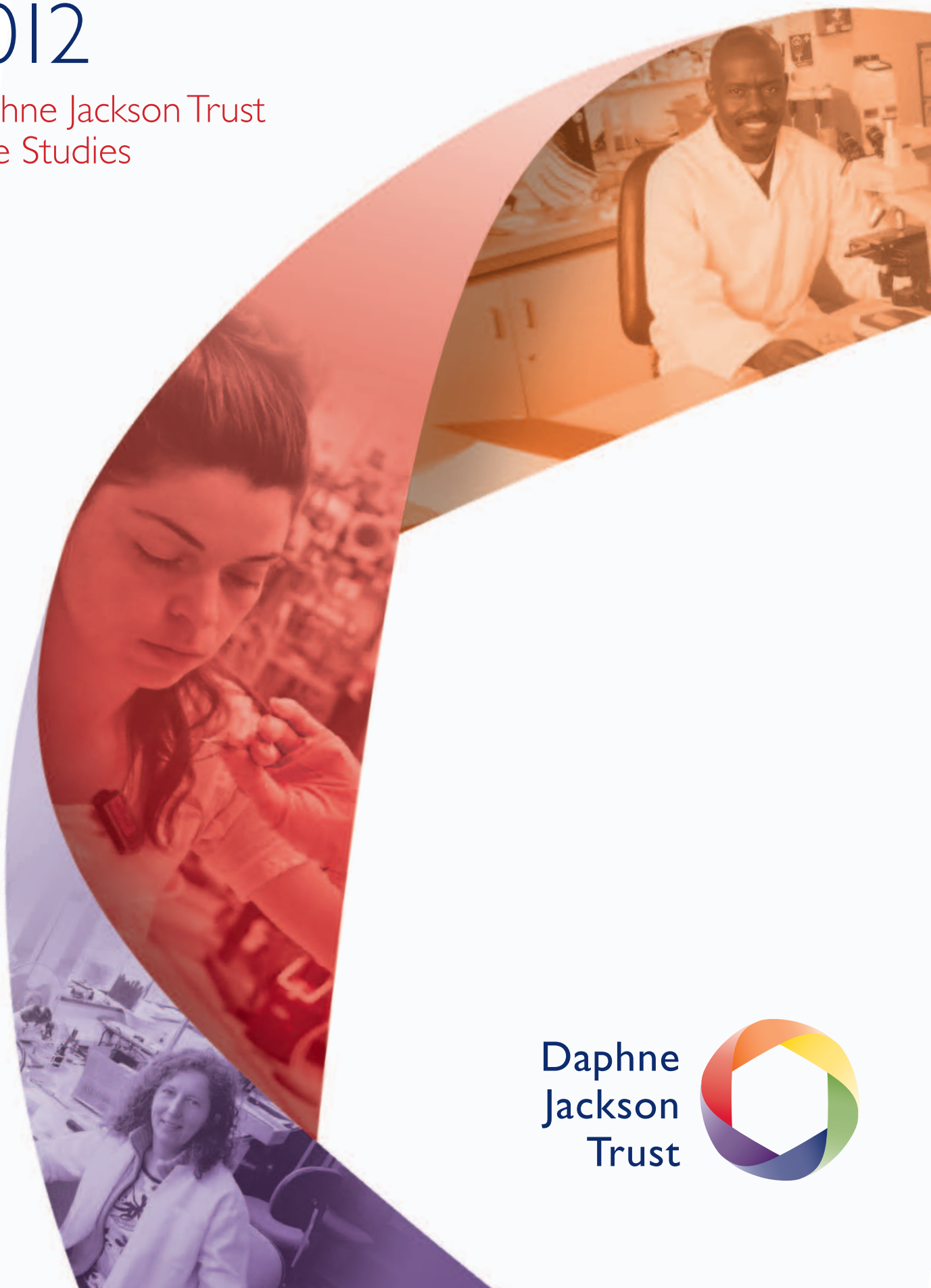
RESEARCH CONFERENCE 2012

Daphne Jackson Trust Case Studies



Daphne Jackson Trust

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DR KATE O'NEILL

Dr Kate O'Neill is a biomedical researcher and a former Daphne Jackson Fellow who investigated the causes of childhood cancers during her fellowship.

She was hosted by the University of Oxford and sponsored by GlaxoSmithKline.

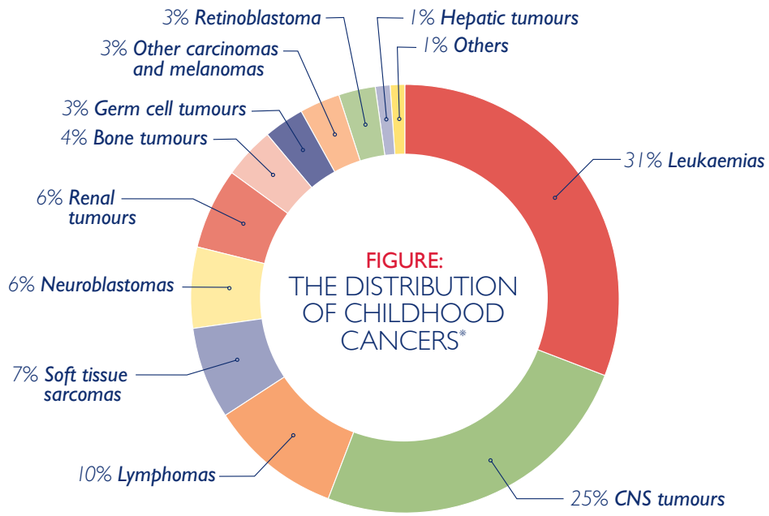
Cancer affects 1 in 500 children, leukaemia being the most common subtype (Figure). Though treatment has seen massive improvement over recent decades, the causes of childhood cancer remain unknown.

Numerous studies have noted that cases of childhood leukaemia have higher birthweights than controls, suggesting that growth in utero may play a role in its development. However, low case numbers have prevented in depth analysis of this risk association, as well as exploration of its association with other, rarer, childhood tumours.

Kate circumvented the problem of low case numbers by looking at the effect of infant birthweight on the risk of developing childhood cancer for which she could obtain data from the UK National Registry of Childhood Tumours and from linking birth and cancer registry records across the US. Using this method she obtained an impressive total of more than 40,000 cases and 86,000 controls.

From the data, Kate was able to show that higher weight at birth resulted in an increased risk of developing cancer in childhood with every 0.5 kg increase in birthweight increasing the risk by 6%. However, birthweight does not have the same effect for all cancer subtypes. There is a positive correlation between birthweight and cancer risk for leukaemia, tumours of the central nervous system, renal tumours, soft tissue sarcomas, neuroblastoma, lymphomas, and germ cell tumours. However, there is a negative correlation for hepatic tumours and no relationship between birthweight and the risk of developing retinoblastoma or malignant bone tumours.

"Birthweight is a significant risk factor for half of all childhood tumours. Future work will be aimed at understanding the biology behind this risk relationship, and our identification of unaffected subtypes may facilitate these studies. Given that birthweights and childhood obesity are steadily rising, our findings may also have a clinical and public health impact," concludes Kate.



**Based on the National Registry of Childhood Tumours in Great Britain 1991-2000*

DR JACKIE FERGUSON

Dr Jackie Ferguson is a biomedical researcher and a Daphne Jackson Fellow who is investigating reactions to treatments with the protein hormone, erythropoietin, in anaemic patients at the cellular level.

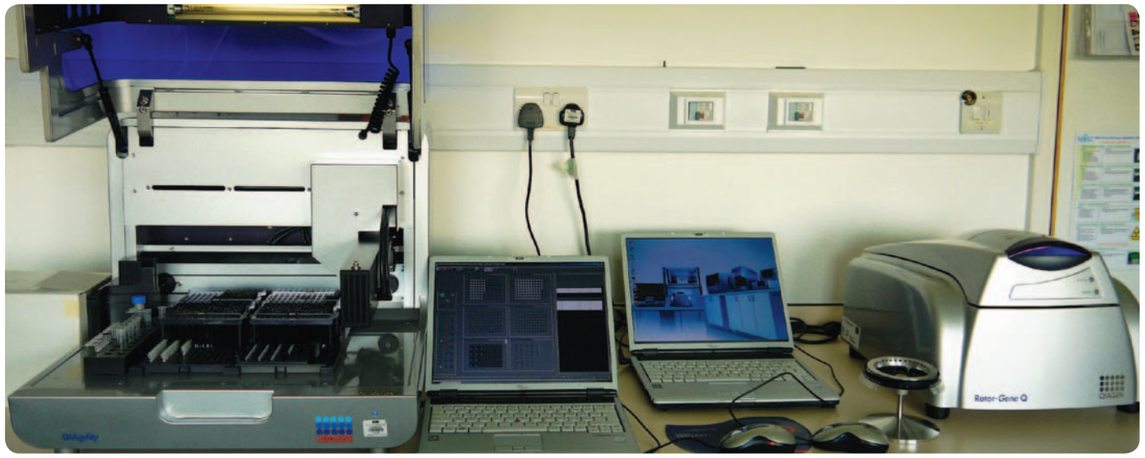
She is hosted by the National Institute for Biological Standards and Control and is sponsored by the Biotechnology and Biological Sciences Research Council.

Erythropoietin (EPO) is a protein hormone produced in the kidneys which stimulates cells in the bone marrow to develop into red blood cells.

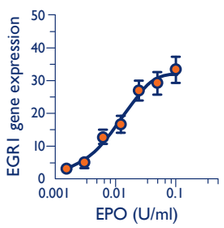
Since 1988, preparations of EPO produced in genetically engineered cell lines have been approved for the treatment of anaemia. In rare cases, therapeutic EPO has elicited an immune response in patients, resulting in the generation of anti-EPO neutralizing antibodies. These inhibit the activity of EPO resulting in the development of pure red cell aplasia (PRCA), a severe anaemia characterised by a drastic decline in red blood cell production.

Jackie aims to develop a cell-based bioassay to detect anti-EPO antibodies by using EPO-stimulated gene expression as a measure of EPO bioactivity.

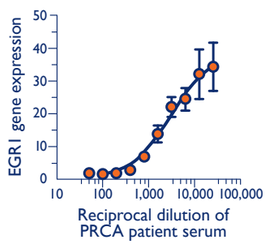
Jackie is nearing the end of her fellowship and has identified that the Egr-1 gene, which is involved in co-ordinating the cellular response to EPO, is expressed in a dose-responsive manner to EPO. She explains: *"Egr-1 is rapidly and robustly induced by EPO, such that we routinely measured a maximal fold-change in Egr-1 gene expression of >50-fold over unstimulated cells after 50 minutes of stimulation with EPO."*



ABOVE: QIAgility benchtop instrument for high precision automated PCR set up and Rotorgene 6000 real-time PCR system.



^ *The EGR1 gene is expressed in response to EPO in the human leukaemic cell line, UT-7/EPO*



^ *The expression of the EGR-1 gene in response to EPO is inhibited in a dilution-dependent manner by serum which contains anti-EPO neutralizing antibodies*

Furthermore, Jackie has found that gene expression was inhibited by dilutions of serum from a patient with PRCA, suggesting that the inhibition of EPO-stimulated Egr-1 gene expression could provide a widely-available, rapid and automatable bioassay to monitor patients for the development of neutralizing antibodies to EPO.

In the remaining time of the project, Jackie hopes to further investigate the potential of this assay method using patient samples and purified antibodies which exhibit varying degrees of binding and neutralization of EPO activity.

DR BEATE NÜRNBERGER

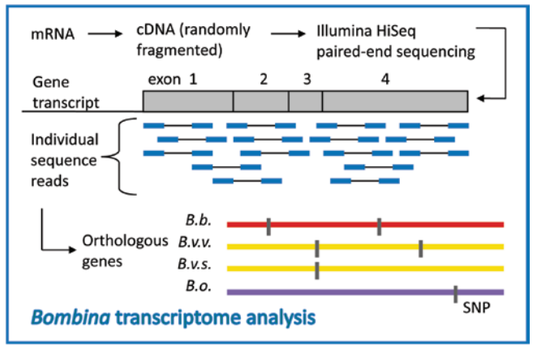
A genomic approach to study the genetics of speciation in the hybridising toads *Bombina bombina* and *B. variegata.*

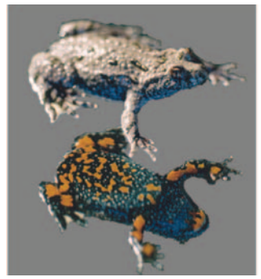
The process of speciation underlies the diversity of all living things on earth. The concept of 'ecological speciation' is of particular current interest. It suggests that adaptation to varying environmental conditions across a species range can not only give rise to genetic differences between populations but may also reduce the rate of gene exchange between differently adapted populations. This may happen, for example, if the offspring from inter-population crosses have reduced Darwinian fitness.

Understanding if and how speciation evolves from these tentative beginnings requires a genomic perspective, because initially only the handful of genes that directly underpin 'hybrid' fitness are barred from crossing into the respective other population. So what determines whether these genetic barriers spread across ever larger parts of the genome until genetic exchange ceases altogether and new species are formed? According to population genetic theory, this should largely depend on the particular genetic architecture of adaptive divergence.

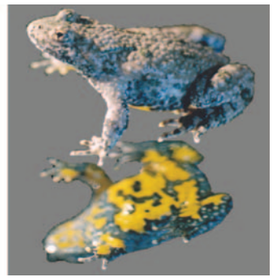
One intriguing test case of this theoretical prediction features the anciently diverged fire-bellied toads *Bombina bombina* and *B. variegata*. Their adaptation to reproduction in lowland ponds versus upland puddles, respectively, is manifest in a whole suite of adaptive trait differences. And yet, wherever their distribution ranges meet across Central and Eastern Europe, abundant fertile hybrids are produced in typically narrow (2-9 km wide) zones of overlap. To determine the genetic basis of incomplete reproductive isolation in these toads, very many genetic markers are needed that collectively identify the patchwork of ancestry across a given hybrid's genome and that ultimately allow us to generate genomic maps of adaptive traits and of natural selection in the hybrid zone.

Beate is a Daphne Jackson Fellow in the School of Biological Sciences at the University of Edinburgh, sponsored by NERC. The aim of her project is to identify such markers from DNA sequences of expressed genes. Modern high-throughput sequencing technology is key to this endeavour: in a single experiment, it captures information on thousands of genes of these non-model organisms. Datasets have been generated for *B. bombina* and *B. variegata* as well as the nearest relative





^ *B. bombina*



^ *B. variegata*

B. orientalis and the subspecies *B. v. scabra*. The latter two taxa allow her to address two evolutionary questions: a) Is there a dichotomy of anciently diverged versus recently introgressed genes in the hybridising taxa? This analysis will provide a first estimate of the 'porousness' of the *Bombina* genome across zones of contact and uses *B. orientalis* as an outgroup. b) Is the greater ecological divergence between *B. bombina* and *B. variegata* reflected in greater sequence divergence relative to the two ecologically similar lineages within *B. variegata,* which are of a comparable age.

Each dataset consists of millions of 100 bp-long sequences that first need to be assembled into presumptive gene transcripts. She is currently applying dedicated software and her new-won bioinformatics knowledge to this task. The completed assemblies of the four taxa will be aligned to each other to extract sets of orthologous genes. These will be scanned for single nucleotide polymorphisms (SNP) for marker development and subjected to evolutionary sequence analyses to address the two questions posed above.

DR NAHLA EL-TAI

Dr Nahla El-Tai is a fellow in the Department of Health and Life Sciences at the University of the West of England.

Her project is *'Assessment of the efficacy of oregano oil as a biocidal agent against in vitro pathogens using lux reporter gene technology'.*

The project evaluates the real-time, in-situ pharmacodynamics of novel antimicrobial agents derived from Himalayan oregano oil using bioluminescent reporter bacteria.

Health care-associated infections such as *MRSA, E. coli, P. aeruginosa* and *C. albicans* spread by hand contact pose a serious health problem. Compliance with hand hygiene procedures, including washing with medicated soap or use of alcohol rubs, can be very low and may only give transient decontamination. Nahla's project evaluates a novel method for sustained hand decontamination, with none of the deleterious effects caused by soap or alcohol-based products, using Oregano essential oil which has been shown to have potent biocidal activity, is heat stable and is effective as a vapour.

Samples of Himalayan oregano oil (HOO) and Mediterranean oregano oil (MOO) have been analysed using gas chromatography to determine the percentage contents of the bio-active agents thymol and carvacrol, which were found to be significantly higher in the HOO.

In order to assess the real time *in vitro* bacterial killing rate of the oils and their bio-active components, Nahla has used representatives of the common UK bacterial pathogens *E. coli* and *Staphylococcus aureus* which have been genetically modified to express bioluminescence as reporters of viable metabolically active cells. Light output from bioluminescent bacteria correlates with their metabolic activity and therefore measurement of light provide a rapid means of collecting data on the sustained biocidal action of the substances in terms of their minimum inhibitory concentrations (MIC). The traditional bacterial viable count method was also used in conjunction with bioluminescence to evaluate the correlation between light output and bacterial viability over a range of oil concentrations.

Nahla's work to date has demonstrated that Himalayan oregano oil may have potential as a potent natural bactericide in the health care setting, as it has demonstrated bactericidal action towards significant pathogens.

Compared to the conventional viable count method, the bioluminescent reporter technique provided a rapid means of collecting data on the bacterial action of oregano oil and could replace the plate culture method for evaluating the efficacy of a new antimicrobial product.

"My plan for the second year of the project is to determine the safety of using Oregano oil as a topical antimicrobial agent by performing the toxicity test on human keratinocytes," says Nahla. *"The technique will involve cell culture. In addition to bacteria I will extend the investigation to study the susceptibility testing of Oregano oil against some fungi namely Candida albicans, Malassezia furfur and Aspergillus oryzae. Finally I will use bioluminescent constructs of non-pathogenic strains of bacteria (E. coli) to show in-situ survival and inhibition on volunteers' hands, with and without application of Oregano oil."*

Nahla feels that obtaining a fellowship has impacted on her life in different ways, commenting, *"The Daphne Jackson fellowship has given me a great opportunity to return back to the field of science after a long career break. During my return I have managed to refresh my skills, master and learn new techniques. Day after day I found myself going back to the right track and building up my self-esteem and confidence. I have achieved a substantial improvement in my performance since I received the fellowship. During that period I have succeeded to update my knowledge by attending many relevant lectures, workshops and conferences. I have really enjoyed the past 14 months of this fellowship and now I feel that I can compete for relevant jobs that otherwise could have not been possible for me. I would like to take this chance to express my deepest gratitude to Daphne Jackson trust for awarding me this prestigious fellowship and to the University of the West of England (UWE) for funding this project."*

DR CAROLINE TAYLOR

Dr Caroline Taylor is a Daphne Jackson Fellow based at the Centre for Child and Adolescent Health in the School of Social and Community Medicine at the University of Bristol, where she is investigating how maternal blood lead levels (BLL) during pregnancy can be used to predict later adverse outcomes in children.

Low-level chronic lead exposure in children remains a serious and largely undetected problem in the UK. It is well known that such exposure has irreversible effects on the developing central nervous system, which can affect academic performance and behaviour.

Low-level chronic lead exposure in children remains a serious and largely undetected problem in the UK. It is well known that such exposure has irreversible effects on the developing central nervous system, which can affect academic performance and behaviour. Although levels of environmental lead have been reduced by the removal of lead from petrol, paint and water pipes, the persistent nature of the metal means that it could still have significant long-term health effects. During pregnancy, the contribution to the unborn baby's lead load by maternal transfer is likely to be significant. Since lead is mainly stored in bone, increased bone turnover during pregnancy releases lead that crosses the placenta and accumulates in the baby.

Using data from the Avon Longitudinal Study of Parents and Children (ALSPAC), a unique population-based study investigating environmental and genetic influences on the health, behaviour and development of children, Caroline intends to model correlations between social and clinical factors as determinants of BLL in mothers and children and to assess the effect on umbilical cord tissue lead levels. It has been previously been reported that academic performance and behaviour of children in this study can be adversely affected even by low blood lead levels of 5–10 µg/dl, so the aim of the project is to identify appropriate interventions to limit childhood damage from lead.

Whole blood samples from a large cohort (n=4472) of pregnant women enrolled in ALSPAC have been analysed by inductively coupled plasma dynamic reaction cell mass spectrometry to determine BLL. Data on lifestyle and environmental factors during pregnancy were provided by the participants using self-completion postal questionnaires.

During the first 6 months of her fellowship, Caroline has established that the mean BLL for the group was 3.67±1.47 (median 3.41, range 0.41–19.14) µg/dl, which is greater than has been found previously in similar but smaller cohorts of pregnant women. Six-hundred and twenty women (14.5%) had BLL >5 µg/dl and 15 (0.4%) had levels above the USA level of concern (>10 µg/dl).

In the present study, BLL >5 µg/dl was significantly associated with being older, having higher social class and education level, lower parity, coffee and alcohol intake, and smoking. Caroline's findings that higher social class and educational attainment were associated with higher BLL were unexpected and she intends to explore this further using multiple linear regression analysis to determine the independent contributions of these factors to BLL in pregnancy.

"I am exceptionally lucky to have been given an opportunity to pick up the threads of my research career after some time away working in medical publishing", comments Caroline. *"I have found it both challenging and exciting to be able to immerse myself in a project that I find completely fascinating. I have really enjoyed learning new skills and updating old ones, and pushing myself out of my comfort zone. I am looking forward to continuing to work on the project and I am starting to think about my future beyond the Fellowship."*

BELOW:
Caroline is pictured below against the background of the Grade II listed lead shot tower in the centre of Bristol, which is one of only three left in the UK. She comments, "The tower closed as a lead shot works in about 1990 and is now used as offices. Bristol has a long history of lead mining and working, and this activity could have contributed to the relatively high levels of blood lead that I have found in a large group of pregnant women living in the Bristol area."

DR MIRANDA SMALLWOOD

Dr Miranda Smallwood is a biomedical researcher and a Daphne Jackson Fellow who is investigating the mechanism by which organisms remove dead cells.

She is hosted by the Peninsula Medical School, which also sponsor her fellowship together with the Medical Research Council.

Cell death in organisms is a normal process, but it is necessary for systems to be in place to remove these dead cells without causing inflammation.

Apoptosis is a programmed form of cell death, and death by this pathway provides the opportunity for the non-inflammatory removal of cells. Macrophage cells recognise dead or dying cells through signals generated on the surface of apoptotic cells and remove them by engulfing and 'eating' them in a process known as of phagocytosis. The process by which an apoptotic cell is recognized prior to phagocytosis is triggered by binding of the protein C1q to oxidised lipids.

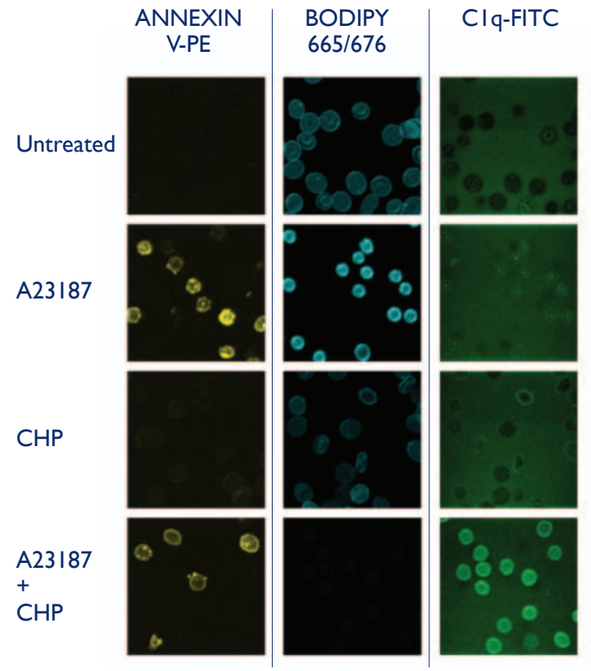
Miranda investigates the signals used in the C1q pathway such as lipids and oxidised lipids on the surface of neutrophils – a cell type associated with the inflammatory response. In particular she is interested in the process, during apoptosis, the phospholipid, phosphatidylserine (PS), becomes externalised on the surface of the cell.

Miranda is nearing the end of her fellowship, which has generated clear findings. From measurements on the binding process of C1q on red blood cells she has found that effective C1q binding to apoptotic cells requires PS to be in an oxidized form, in order for C1q to aid apoptotic removal (Figure).

Her research is interesting not only for its intrinsic scientific value, but may also have applied medical relevance. Miranda explains: *"This work is important in systemic lupus erythematosus (SLE), as a key feature of this disease is a deficiency in the clearance of apoptotic cells by membrane-bound C1q. A build-up of apoptotic cells in the blood of SLE patients is thought to result in a 'reservoir' of post-translationally modified autoantigens presented by the unremoved apoptotic cells and consequently organ failure."*

Miranda is currently investigating lipid peroxidation in neutrophils from control people and SLE patients, working with a summer project student James Richardson-May, funded by ARUK. Preliminary findings are showing that controls have lower amounts of neutrophil peroxidation which can be increased with chemical oxidants, but SLE patients have higher amounts of neutrophil peroxidation which cannot be increased any further – so there are clear and interesting differences.

CONFOCAL MICROSCOPE IMAGES OF RED BLOOD CELLS



ABOVE:
These images show RBCs labelled with annexinV-PE, BODIPY or C1q-FITC.

a) Untreated cells do not show any annexinV-PE or C1q-FITC binding. The BODIPY staining shows they are not peroxidised (BODIPY staining reduces as peroxidation increases).

b) Calcium ionophore, A23187, increases annexinV-PE binding only (RBCs shrink with A23187 & BODIPY staining appears slightly brighter).

c) Cumene hydroperoxide caused oxidation (lowering of BODIPY staining).

d) It is not until the RBCs are both peroxidised (no BODIPY staining) & bind annexinV-PE that C1q-FITC binds to the RBCs.

DR FRANCES PEARL

Dr Frances Pearl is a Daphne Jackson Fellow in the Section of Cancer Therapeutics at The Institute of Cancer Research, and is sponsored by the MRC.

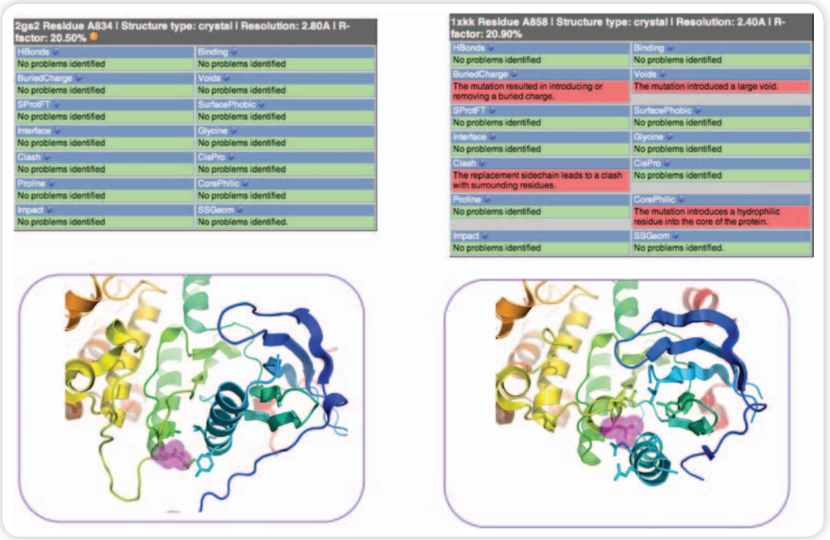
Cancer is a genetic disease, caused by mistakes termed 'mutations' in the DNA, which are caused by carcinogens such as cigarette smoking and sunlight, or inherited from your parents.

As a cancer progresses and becomes more aggressive, it becomes genetically unstable and more mutations occur. Consequently large-scale re-sequencing of cancer genomes have revealed many thousands of mutations. Knowledge of these mutations is key to both understanding the biology of cancer initiation and progression, and to the development of targeted therapeutic strategies.

Although some of these mutations are well characterised, for the majority their contribution to disease has not yet been established. In all cases the key to understanding the contribution of a disease-associated mutation to the development and progression of cancer, comes from an understanding of the consequences of that mutation on the function of the affected protein, and the impact on the pathways in which that protein is involved. Frances's project is to extend the MOKCa database (http://strubiol.icr.ac.uk/extra/mokca) and to provide assessments from multiple sources and algorithms for each potential cancer-associated mutation, and present these together in a consistent and coherent fashion to facilitate authoritative annotation by cancer biologists and structural biologists, directly involved in the generation and analysis of new mutational data.

An automatic pipeline has been developed that structurally and functionally annotates all the genes and proteins that are mutated in cancer. Somatic mutation data from tumours and tumour cell lines from the COSMIC database have been mapped onto UniProt protein sequences and positions of the mutations highlighted on a sequence-based domain pictogram. Mutated amino-acids are highlighted on a 3D-image of the protein structure, and in a molecular graphics package, integrated for interactive viewing. Structural models of the mutant proteins are also being generated. Several prediction algorithms are used to assess each mutation and whether it is likely to contribute to disease.

Proteins are linked to functional annotation resources and are annotated with structural and functional features. There are also links to the target synopsis in the canSAR database so that possible chemical inhibitors can be directly identified. Protein-protein interactions of mutated proteins can be explored using an interactive program ROCKscape. The data is stored in a MySQL database and the updated website will be launched in 2013.



LEFT: SAAP structural impact prediction data of the EGFR L858R mutation in the active and inactive conformation of the kinase domain.

DR PRITI CHIVERS

Priti Chivers has recently finished her Daphne Jackson fellowship in the Department of Biochemistry & Physiology in the Faculty of Health & Medical Sciences at the University of Surrey.

BELOW: Priti in Kyoto, Japan in June 2010 at the conference dinner if Selenium 2010, the 9th International Symposium on Selenium in Biology and Medicine where she presented her research findings. Priti (2nd from left) with Professor Margaret Rayman, one of her supervisors, an internationally renowned Selenium scientist and herself a past Daphne Jackson Fellow (2nd from right) and two scientists from New Zealand.

Her project has involved a study of the effect of methylation status on the selenium (Se) responsiveness of genes implicated in colorectal cancer (CRC), with a particular focus on the role of selenoproteins.

Since colorectal cancer is the third most common malignant cancer worldwide, even a small improvement in treatment-outcome will have a significant impact on the society.

The aim of Priti's work has been to reveal potential molecular mechanisms for the apparent protective effect of Se in cancer and provide the basis for the development of preventive, diagnostic, prognostic and/or therapeutic strategies that may be useful in a clinical setting. Selenium (Se) is a dietary micronutrient critical for human health that is considered to have cancer-protective properties, probably mediated through selenoproteins. It has been shown that most human selenoproteins have an antioxidant/redox function and interact in many cellular pathways and that the expression of several selenoproteins is significantly reduced in many cancers, including CRC The population in most northern European countries, including the UK, is relatively Se-deficient, whereas optimal intake of Se (by diet or supplement) has been associated with reduced cancer-risk. This may be through the maintenance of 'normal' DNA methylation, and thereby suppression of oncogene expression, or possibly through maximising the expression of protective selenoprotein genes which are hypermethylated and downregulated in cancer.

DNA hypermethylation, a common epigenetic occurrence in cancer, is emerging as a suitable biomarker. (Epigenetics is the study of heritable changes in gene expression, the process by which information from a gene is used in the synthesis of a functional gene product).

Priti's initial hypothesis was that the hypermethylation of selenoprotein genes would affect their expression and responsiveness to Se supplementation in colon cancer. Selenoprotein genes will respond to Se-supplementation once demethylated using decitabine, a cancer drug. This may lead in future to Se-supplementation in cancer patients from low-Se countries like the UK. This may result in activation of beneficial cellular pathways/networks in the patients and may enhance epigenetic CRC treatment with demethylating agents (eg decitabine), and facilitate development of new CRC therapeutic strategies.

Priti has used microarray analysis, quantitative RT-PCR (qPCR) of RNA and pyrosequencing of the DNA to analyse gene expression and correlate with DNA hypermethylation to identify the specific genes regulated by Se and silenced through hypermethylation in colon cancer.

Normal and cancerous human colon/rectum tissue were analysed to assess whether similar findings apply to the real human situation (rather than the cultured cell-lines). Although hampered by the small number of colon cancer tissue samples Priti was able to obtain, her findings have indicated that the Se-inducibility of some selenoprotein genes methylated in colon cancer cell-lines can be reactivated by demethylation and that these genes may be candidates for future use as diagnostic markers if they are found to be methylated in colon cancer tissue.

Priti has been able to conclude from her work that in colon cancer, the selenoprotein genes are differentially regulated by selenium, and the low response of some of the selenoprotein genes to selenium is due to epigenetic changes which could be a future biomarker if also found in colon cancer samples.

She envisages that the project could be extended to consider whether Se-supplementation could improve treatment of colon cancer in conjunction with demethylating agents such as decitabine. She would also like to investigate whether the methylation patterns observed in colon cancer tissue are also present in blood of the same patients, to develop a blood-based methylation biomarker for future clinical use.

Priti is currently continuing on a part-time basis in the Department of Biochemistry & Physiology at Surrey on a project on breast cancer, and is applying some of the techniques and ideas developed during her fellowship to this project.

DR RACHEL WHITE

Dr Rachel White is a Daphne Jackson Fellow who is investigating the role of the sodium/hydrogen exchanger regulatory factors in osteoarthritis.

She is hosted and sponsored by the University of Aberdeen.

Although Osteoarthritis (OA) is the most common musculoskeletal ailment, it is also one of the least understood. It causes untold suffering to individuals and imposes huge costs on the nation in terms of healthcare and days lost from work.

It is estimated that by the age of 75, 85% of people will show either clinical or radiological evidence of OA although only 60% may be symptomatic. There is no established pharmaceutical therapy other than analgesia. In recent years OA has been seen as a degenerative disease of articular cartilage with erosion of this tissue being the main feature. However, tissue growth is a key characteristic but the reason for this is unclear.

Rachel's hypothesis is that there is a fall in the levels of NHERF1 (a member of the sodium regulatory factor protein family) in patients with OA. As NHERF1 is known to play a role in tumour suppression and intracellular pH regulation, she will investigate whether a reduction in NHERF1 could affect the acidity of the cells and cause them to multiply, leading to tissue loss and joint deformity characteristic of the disease. The specific aim of her project is to test this hypothesis using articular cartilage from the hip or knee joint of patients with OA and compare these to controls (patients with osteoporosis or amputees) in the first instance, to show that dysregulated expression of NHERF1 is a key part of the abnormal behaviour of the cartilage cells.

Rachel is in the initial stages of the project based on a pilot study that compared gene expression in tissue samples from patients with OA and osteoporosis. This study demonstrated that a gene (SLC9A3R1) encoding for NHERF1, was differentially expressed. She is now investigating whether a decrease in the NHERF1 protein causes a change in the intracellular pH of the articular cartilage cells.

"The internal acidity of cartilage cells has a large effect on how they behave and controlling it is essential for maintaining a healthy joint", commented Rachel. *"Through combining cutting edge techniques I will be able to ascertain whether a reduction in NHEFRF1 affects the acidity of cells, and open new approaches for therapy."*

She intends to continue with her research by comparing the structure and morphology of cartilage from OA patients using standard histological techniques and methods, and examine the localisation of NHERF1 and β-catenin (another protein) in articular cartilage.

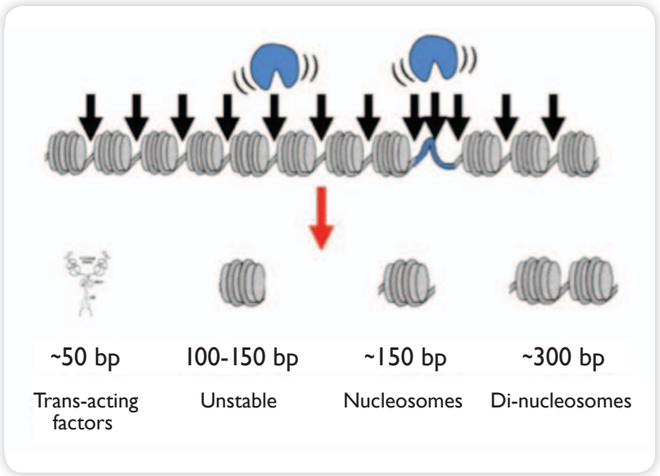
MRS JANET HARWOOD

Mrs Janet Harwood is a Bioinformatician and Daphne Jackson Fellow at the University of Cardiff, funded by the BBSRC.

She is developing computational biology tools for the analysis and visualisation of complex biological data sets generated from next-generation sequencing experiments. From these analyses it is possible to generate genome-wide 'landscape maps' and to study genome-wide changes in chromatin structure. This will provide key detailed information about the three-dimensional organization of DNA in the cell nucleus.

The genome of an organism comprises all of the hereditary information of an organism that is encoded in the DNA. The publication of the sequence of the human genome in 2001 was a key milestone in modern science. Since then, there has been a revolution in sequencing technology which means that it is possible to sequence whole genomes at unprecedented speeds. However, the knowledge of the DNA sequence alone is not sufficient to deduce the mechanisms involved in the control of the use of its code for the execution of the vital processes occurring in a cell. The next challenge in modern biology is the study of epigenetics, which refers to inherited changes in gene expression that arise without alteration of the genetic code (the DNA sequence).

BELOW: Partial digestion of chromatin by Micrococcal nuclease produces a range of particle sizes.



The genomes of higher organisms comprise very large amounts of DNA. If all of the DNA from a human cell nucleus were joined together, it would be approximately two metres long. Packaging this DNA in to the nucleus of a cell is equivalent to bundling 200km of cotton into a basketball. This packaging is achieved by coiling the DNA around proteins, analogous to coiling a hosepipe around a reel and then these coils are further packaged into complex 3D structure. This protein super-structure that packages, protects and manages accessibility to DNA is called chromatin. Understanding chromatin structure is important because the malfunction of some of the proteins involved in its control cause human diseases and many cancers.

Recent developments in 'next-generation sequencing' techniques mean that the analysis of genome-wide chromatin structure is possible. However, the volume and complexity of data generated in these experiments is immense.

"My research addresses the need to develop computational biology tools for the analysis and visualisation of these very large, complex biological data sets so that we can compare chromatin structure at the level of the whole genomes and produce 'genome landscape maps' of the data," says Janet. *"Currently I work on the yeast genome, but we are developing tools so that we will be able to tackle the much larger human genome."*

DR MALARVIZHI RAMESH-JEYASHANKAR

Dr Malarvizhi Ramesh-Jeyashankar is a microbiologist and Daphne Jackson Fellow who is investigating the uptake of iron by the bacteria E. coli.

She is hosted by the University of Reading and sponsored by the Biotechnology and Biological Sciences Research Council.

A major component of our normal immune response to bacterial infections is withdrawal of iron availability – this counters infection by starving the pathogen of iron (an essential nutrient).

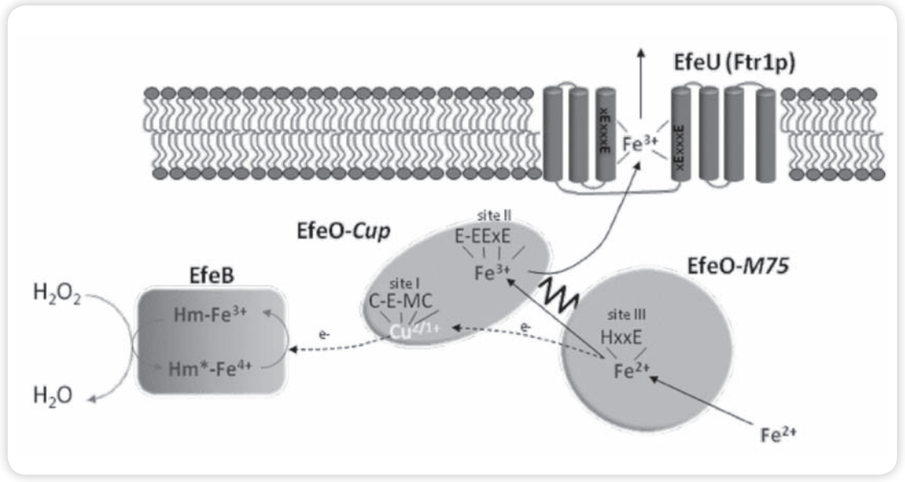
However, pathogens employ counter-measures to wrest iron from the host. This frequently involves the deployment of iron-acquisition systems by bacterial pathogens that target host-iron sources. Such iron uptake systems act as key virulence factors that are critical for infection.

Malarvizhi studies a recently discovered new type of bacterial iron uptake system (EfeUOB) in E. coli, which works aerobically (in the presence of oxygen) under low pH and low iron conditions. However, little is known about EfeUOB, although it is clear that it is very different from all previously recognised iron-uptake pathways. The EfeUOB system (Figure) consists of 3 components all of which are functionally essential: EfeU, an inner-membrane protein; EfeO, a ferrous-iron-binding protein that has the capacity to oxidise the ferrous iron it binds; and EfeB which may play a role in the ferrous oxidation process.

In her project, Malarvizhi primarily focuses on how the M75 domain of the EfeO protein binds metal and oxidises iron. Malarvizhi is a third through her fellowship and has so far focused on protein purification. She explains: *"At present, I have cloned and over expressed the M75 domain of E.coli. Also I have over expressed the 'M75' protein and am currently working towards purification of the protein from the periplasm to carry out further studies."*

Once this is achieved, Malarvizhi plans to investigate the ability of the M75 domain to oxidise ferrous iron into ferric iron and to perform crystallization and structural work on the purified M75 domain.

Finally she hopes to examine the ability of EfeUOB to assist colonisation and its role in bacterial infections.



ABOVE: Proposed EfeUOB mechanism, Fe2+ is initially bound by the M75 domain at the 'HxxE' motif. It is then oxidised and the released electrons are passed on to the H2O2-oxidised haem group of EfeB via the EfeO-Cup domain. The oxidised iron is passed on to EfeU via 'site II' of the EfeO-cupredoxin (Cup) domain. Hydrogen peroxide acts as the ultimate electron acceptor. Energy is provided by the redox reaction.

SARAH GOODING

Sarah Gooding is a microbiologist who is studying the genome sequences of fungi so that better anti-fungal drugs can be developed.

She is a former Daphne Jackson Fellow, who was hosted by Swansea University and sponsored by the BBSRC.

The clinical importance of the ubiquitous fungus *Aspergillus fumigatus* has risen dramatically over the last 20 or 30 years. *A. fumigatus* grows on dead organic matter in the soil and on decaying vegetation, but is also an opportunistic pathogen.

Until recent times it was not considered a severe threat to health; patients being restricted to the farming population who inhale large doses of spores on a daily basis causing an allergic hypersensitive reaction commonly known as 'Farmer's lung'. The rising number of immunocompromised patients, as a result of organ transplants, cancer, stem cell therapy and individuals with genetic immunodeficiency or AIDS, has given *A. fumigatus* the opportunity to adapt to a new ecological niche, the human lung, where it causes the fatal disease invasive aspergillosis (IA). Present anti-fungal compounds have low efficacy against IA with a mortality rate of more than 50% in those infected. A more directed approach to the search for novel therapeutic agents and novel targets is therefore required, which today is feasible thanks to the availability of the complete genome sequences of many micro-organisms.

Sarah uses bioinformatic tools to study the genes responsible for the production of Cytochrome P450s, which are a group of proteins that are involved in important biosynthetic reactions. Inhibitors to various Cytochrome P450s have been developed as commercially important drugs. Looking at genes that are directly involved in cell survival and growth in one organism may lead to the discovery of a potential drug target in another.

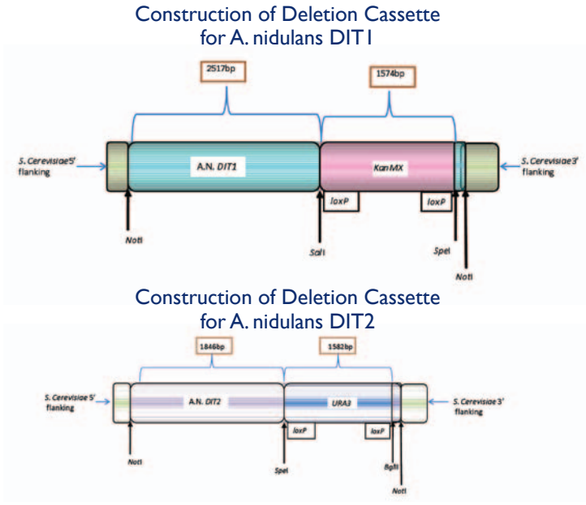
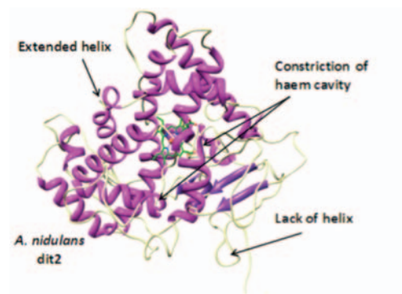
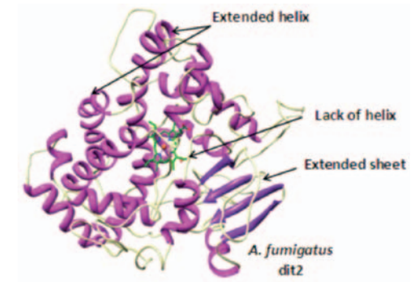


FIGURE: The deletion cassettes for the genes DIT1 and DIT2 in the fungus Aspergillus nidulans



POTENTIAL STRUCTURES OF DIT2P PROTEINS PRODUCED BY PROTEIN MODELLING OF *A. NIDULANS* AND *A. FUMIGATUS*



The major differences between the two Aspergilli dit2p proteins are the reduced size of the haem cavity in A. nidulans (Haem cavity volume = 3447 Å3) compared with A. fumigatus (Haem cavity volume = 6207 Å3) and the presence of an extended β sheet in A. fumigatus. The implications of this dramatic difference in the size of the active site will be interesting to unravel.

In particular, Sarah is focusing on the biosynthesis of dityrosine, which in the yeast *Saccharomyces cerevisiae* stabilises cross-links and is important for the integrity and resistance to environmental stresses of the spore cell wall. Two genes, *DIT1* and *DIT2*, have been identified as a requirement for the biosynthesis of dityrosine in yeasts. Sarah has found that both genes are present in *Aspergillus nidulans*, a close relative to *A. fumigatus*. She has furthermore cloned cDNA of both genes from *A.nidulans* into yeast (see figure), where the native genes have been 'knocked out' in the process; to see if the *A.nidulans* genes perform the same function in the yeast and produce dityrosine.

Finally, Sarah has identified homologous genes to *DIT1* and *DIT2* in *A. fumigatus* with several potential *DIT1* coding sequences. However, only one of these is on the same chromosome as *DIT2*, as in yeast and *A.nidulans*.

Sarah is continuing her research at Swansea University as part of 'Beacon – from Plants to Products' supported by the Welsh Government and ERDF, where she hopes to further elucidate the role of dityrosine biosynthesis in these fungi and its potential as a drug target in *A. fumigatus*.

DR JOANNE TAYLOR

Dr Joanne Taylor is a Daphne Jackson Fellow investigating the fungi associated with the Scots Pine *(Pinus sylvestris)*.

She is working at the Royal Botanic Gardens Edinburgh (RBGE), at the Herarium and is sponsored by NERC.

Fungi are of immense importance to humans, used as food products (mushrooms, Quorn), to produce medicines (penicillin), as biocontrol agents against insects and plants, and enzymes from fungi are used in the production of detergents. However, fungi can also be problematic, causing numerous diseases on crop plants, and infections in animals and humans.

The Scots Pine is an important tree both ecologically and economically. It is very widespread in the northern Europe and Asia. Consequently Scots Pine has been subject to much study in terms of the fungi associated with it and approximately 970 species of fungi have been recorded. The microfungi associated with this host in Britain are well documented but many have not been sequenced and are therefore not available when searching DNA sequence databases such as Genbank. This is particularly problematic when carrying out DNA sequencing studies of uncultured fungi as many can not be identified in this way.

LEFT: Caption text here please

Joanne's current study aims to provide sequences of correctly identified vouchered specimens of commonly encountered pine fungal saprophytes and endophytes for inclusion in Genbank. Furthermore, this will provide a sequence library for a second component of her study which is to compare the endophytes associated with needles of regenerated young pines in Caledonian Pine forests with seedlings grown from seed from different native pine forest provenances but planted in common gardens. This study will provide information on the effect on the endophyte assemblages of planting of trees in plantations remote from other pine forests and also to determine whether seed provenance is influential.

"Working at the Gardens is both a great privilege and amazing opportunity", comments Joanne. *"The resources available are so conducive to my particular field of study. The library is excellent, a complete joy for a mycologist to use with key references available going back to the 1820s! The lab facilities are excellent and are well run and the training I have received has really helped to increase my confidence and skills base. My colleagues have been very helpful and supportive and, of course, I can enjoy my lunch times in the gardens. As well as brushing up on skills I already have, and learning new areas of research such as metagenomics, I am being encouraged to learn about current bioinformatic analyses. This will prove to be quite a challenge to me, but it is where my field is heading and is a great opportunity to learn these techniques."*

Joanne took time away from the Royal Botanic Gardens Edinburgh, during her fellowship, to visit China and work in the Key State Mycology Laboratory of the Chinese Academy of Science in Beijing with Prof Guo Liang-Dong. During her visit, Joanne learnt additional techniques in metagenomics specifically with endophytic fungi. She returned to Europe midway through her visit to attend the 'One Fungus, Which Name' conference in Amsterdam before completing her travels by visiting Thailand and the laboratory of Prof Kevin Hyde, one of the world's leading experts on fungal taxonomy.

DR SARAH BUCKLAND

Dr Sarah Buckland is a Daphne Jackson Fellow at the University of Sheffield, sponsored by NERC.

Species-rich grasslands are important habitats for conservation, agriculture and amenity. It is essential that we protect and manage these grasslands effectively through the potential disruptive impacts of rapid climate change and intensive land-use.

Tapping into the data from a unique field experiment in which climate conditions have been manipulated over a period of 15 years to replicate climate change, her project is to investigate the long-term effects of simulated climate change on species-rich grassland communities.

Sarah investigates how different species respond to the treatments in relation to the variation in soil depth. This will determine the extent to which the constraints imposed by the climate simulations, arising from temporal shifts in the growing season, can be made more by the variation in soil depth present in these limestone grassland communities.

Genetic diversity is also an important feature of these grasslands and is thought to be a critical property that maintains species richness and provides the genetic variation to allow adaptation to anticipated global environmental change. The impacts on clonal diversity of species which grow at different times in the year is being examined in conjunction with measurements of plant traits to characterize the nature of selection that may be developing on these long-term experimental plots.

The results will show the potential of such grasslands to resist the impacts of long-term climate change. They will also show whether genetic diversity and phenotypic variation is important in maintaining species co-existence in these important grassland habitats.

PHENOLOGY is the scientific study of periodic biological changes, such as flowering, breeding, and migration, in relation to climatic conditions.

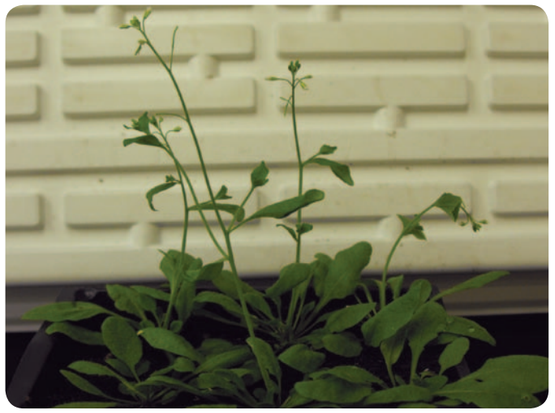
DR. DEBRA FREDERICKSON MATIKA

Debra is sponsored and hosted by the University of Edinburgh, in the School of Biological Sciences.

Her project will provide a greater understanding of the genetic processes underlying disease resistance in plants, leading to more disease-resistant plants in the future.

Plants can be infected by a wide assortment of harmful fungi, bacteria and viruses, and the resulting diseases can cause substantial crop losses. Understanding what happens inside plants when such pathogens enter cells can provide information that can be exploited to make it more difficult for pathogens to attack plants in the first place or to grow and spread once inside.

Recent evidence suggests that the regulation of cellular nitric oxide is crucial for plants to combat disease: if nitric oxide rises, plants are more susceptible. Debra is using a plant called *Arabidopsis*, a member of the cabbage family with a relatively simple genetic system, as a model to investigate what happens to the resistance response if the activity of genes that appear to be associated with changes in nitric oxide levels are 'blocked'. The genes encode regulators, called Zinc finger transcription factors (ZnTF), proteins that switch other genes on and off by binding to DNA. ZnTFs are known to manage nitric oxide stress in animals and Debra is investigation whether they have a similar role in plants.



ABOVE: Arabidopsis being grown in the laboratory. Picture courtesy of D Frederickson Matika.

To do this Debra alters one ZnTF gene at a time, the new plant is grown and Debra attempts to infect it with a pathogen. She then measures the amount of nitric oxide it has in its cells and the amount of disease that results with the purpose of determining the pattern of genes that are functional when *Arabidopsis* is resistant to disease compared to when the plant is susceptible. Modern DNA techniques are used to view all the genes that are active at any one time, a kind of gene 'snapshot' and it is then possible to visualise the ZnTFs binding to the genes that they regulate.

In this way Debra intends to evaluate whether ZnTF activity influences nitric oxide levels and will begin to see the impact upon the pathways used in the disease response. Preliminary data indicates a number of nitric oxide responsive ZnTF in *Arabidopsis*.

DR ALLEN Y. MSWAKA

Dr Allen Mswaka is a Daphne Jackson Fellow at Queen's University Belfast sponsored by the BBSRC.

Microorganisms are involved in many processes that enable the Earth's biosphere to function in a healthy and sustainable way by degrading plant and animal waste materials. Saprotropic microbes, microbes that breakdown organic material, are also used in diverse industrial process such as waste degradation, bioremediation and industrial biocatalysis.

Allen is investigating how microorganisms, such as the fungi and bacteria that exist in nature, can be encouraged to be more efficient in their saprotrophic activities and how solutes intervene in saprophytic processes at both the enzymatic and ecosystem level. For these microbes to function efficiently knowledge of the environment, in particular, the solute concentration they reside and work in is essential

Extensive sampling of microbes from various marine habitats on the Northern Ireland coast has been conducted. Sampling of sites has been replicated in winter, spring and summer seasons to account for seasonal variations in microflora.

A series of experiments are being conducted to quantify the impact of: MgCl2, glycerol, urea, ammonium nitrate, ethanol, phenol, benzene (chaotropes) and NaCl, sucrose, ammonium sulphate, xanthan gum, proline, and trehalose (kosmotropes) on the catalytic activity of enzymes involved in biodegradation of cellulose, lignin, and chitin.

ABOVE: Sampling sites comprising different Coastal Habitats of Northern Ireland.

The specific aim of the work is to gain a better understanding of how chemicals that are present in all natural environments can prevent microbes from growing and degrading material saprotrophically.

The results of this study may lead to enhanced microbial activity in arid regions of the planet and thereby improve soil and plant health, and also agriculture and food supply. It will also have uses in recycling plants and for breakdown toxic substances in the environment such as crude oil and pesticide residues.

SOLVEIGH LASS-EVANS

Dr Solveigh Lass-Evans is a Daphne Jackson Fellow at the British Geological Survey in Edinburgh.

Her research topic is: 'Sediment and water quality and contaminant migration in the River Clyde post-industrial catchment

Potential chemical contamination of the ground and of watercourses is one of the legacies of the UK's past industrialisation. Resulting chemical pollution poses current and future threats, as many substances are toxic in high concentrations, and their occurrence could have long-term implications for ecosystems and human health.

In order to assess sediment and water quality in the post-industrial River Clyde catchment, the British Geological Survey (BGS) collected rural stream sediments across the Clyde basin; stream sediment and water samples from selected urban tributaries draining into the Clyde (Clyde Tributary Geochemical Project) and sediment and water samples in the Clyde estuary.

Solveigh's project integrates and interprets these datasets, to assess urban impacts on environmental quality in the Clyde catchment and to understand the processes that control pollutant migration through the river system.

Geographic Information System (GIS) maps of stream sediment element distributions show elevated concentrations of potentially-harmful metals in the urban area, compared with the rural environment. To assess urban impacts on sediment quality, natural background concentrations were modelled and used to calculate the additional impact of human sources on overall pollutant levels. The results reveal more than ten times the natural background levels for Arsenic, Copper, Lead, Antimony and Tin in central Glasgow stream sediments .

ABOVE: River Clyde, Glasgow © BGS, NERC

Although Glasgow's heavy industry has declined, its legacy of metal-rich waste remains significant and potentially poses long-term environmental issues. Only by fully understanding the problem can effective management of the river system be made possible for the benefit of present and future generations.

DR CHRISTINE ROGERS

Prior to a break of 13 years, Dr Christine Rogers had built up considerable experience in the nuclear industry, drawing on her background as a chemist.

Since completing her Daphne Jackson fellowship in the School of Earth and Environment at the University of Leeds in October 2010, Christine has continued to investigate aspects of her work on the application of green rusts to environmental contamination problems.

The aim of Christine's Daphne Jackson fellowship research project was to study the in-situ remediation of groundwater contamination using permeable reactive barrier (PRB) technology. This is an important field of work which could have tangible benefits for society by finding an effective remediation strategy for the more recalcitrant polluting chemicals typically found in hyperalkaline toxic and radioactive waste streams.

Hyperalkaline wastes (pH >10) are formed during a number of metal extraction and purification processes. Examples include nuclear reprocessing wastes, currently stored at sites in the US and Europe. Hyperalkaline conditions are also predicted to be present in cementitious radioactive waste repositories where cement pore waters will maintain pH>12 for thousands of years. However the most common hyperalkaline waste streams are formed by Cr(VI) rich waters leaching Chromite Ore Processing Residue (COPR). The ore is no longer processed in Britain but there are many abandoned waste sites that are a legacy from our industrial heritage and now exceed environmental limits. Cr(VI) contamination is also a problem for newly industrialised countries such as China and India where COPR waste continues to be produced but is poorly managed. Cr(VI) is an example of a redox active contaminant that can be reductively immobilised using green rust in hyperalkaline solutions. Radioactive contaminants in hyperalkaline waste such as U(VI), Tc(VII) are also redox active and may respond in a similar way to treatment with GR.

Christine's initial work during her fellowship focused on identifying a reactive material for use in the barrier from several candidate green rust (GR) formulations and finding one that successfully immobilised toxic metal, in particular chromium found as Cr(VI), in contaminated waste water at high pH.

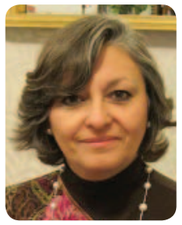
Cr(VI) can be reductively immobilised using material such as zero-valent iron (ZVI). In this process the highly soluble, oxidised form of the contaminant is chemically converted to a reduced form that has lower solubility and mobility, e.g. Cr(VI) Cr(III). However, the most commonly used forms of ZVI, granular and micro, have limited efficiency for reducing contaminants in hyperalkaline conditions. Therefore key to developing a remediation strategy for hyperalkaline wastes and groundwater is the development of materials which can effectively immobilise contaminants at high pH.

Christine tested the hypothesis that green rusts (GRs) are significantly more effective than granular zero valent iron (ZVI) in the reductive removal of Cr(VI) from alkaline solutions. She used batch experiments to compare the rates of Cr(VI) reduction by carbonate green rust (GR-CO3), carbonate green rust containing zinc (GR-Zn-CO3) and granular ZVI, in synthetic alkaline fluids and alkaline waste water.

The results indicated that both of the green rusts reacted in seconds, were unaffected by changes in pH and were up to 200 times faster than with granular ZVI. The rate of reduction of chromate solutions by granular ZVI decreased linearly with increasing pH and became ineffective at hyperalkaline conditions (pH>10).

Speaking of her future research plans, Christine comments, *"I plan to continue my research with green rust at the University of Manchester, where there is interest in the application of green rust materials to radioactive contamination problems. In this work I will be able to combine my newly acquired knowledge and understanding of environmental science with my background in the nuclear industry. Dusting off my PhD thesis that I wrote many years ago on fission product iodine, will help me revise my knowledge of radiochemistry and enable me to come full circle in my research work."*

DR REYNA AL-ASHAAB



Dr Reyna Al-Ashaab commenced her fellowship in May 2010 at Cranfield University, in the Centre for Energy and Resource Technology, sponsored by NERC.

Growing awareness of our well-being and that of our planet has changed the way waste is managed. The escalation in the number of green waste composting sites has significantly reduced the amount of waste sent to landfill, aiming to meet legal obligations outlined in the EU Landfill Directive (1999/31/EC).

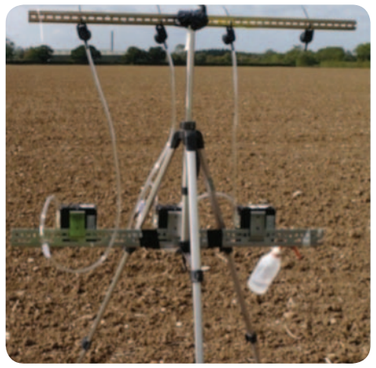
During the composting process large amounts of biological particles (bioaerosols) are released into the air as a consequence of the shredding, turning and screening (sieving) of the green waste being composted. Bioaerosols are everywhere and they are part of our everyday life. However, there is some concern over the amounts emitted as they have the potential to cause respiratory problems to vulnerable individuals.

Reyna's research involves the detection and monitoring of the bioaerosols suspended in the air around open air garden waste composting facilities. She has sampled for bioaerosols at several composting facilities, with measurements being taken close to the source of the emission, upwind and at four points downwind. The data collected includes information about the atmospheric conditions (wind speed, wind direction, humidity and temperature), the source of bioaerosols (type, height, size and concentration) and the terrain (hills, buildings and trees).

The information collected is later used as the input into the Air Modelling Dispersion Model (ADMS 4.2) software in order to produce contour maps and depletion curves. Her results to date highlight the inadequacies in current monitoring and modelling techniques.

Reyna is currently developing her portfolio of bioaerosols dispersion modelling examples from open air green-waste composting facilities. She is also taking the project to the next level by including data from in-vessel (enclosed) composting sites and examining whether there is a correlation between odour levels and the concentration or bioaerosols.

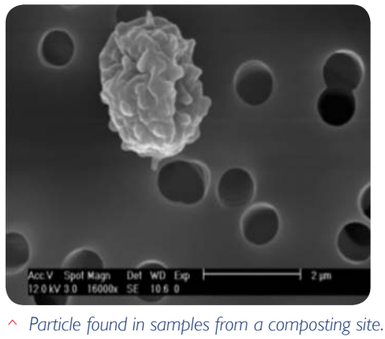
The output of her project could have a significant impact on the composting industry and bioaerosol researchers.



^ *Equipment used to sample for bioaerosols*

^ *Emissions from compost turning*

^ *Emissions from loading a screening machine*



^ *Particle found in samples from a composting site.*

"Going back to work in research part-time has provided me with a new perspective", says Reyna. *"It has brought sanity back into me as I have a more balanced life, with personal aspirations added to those that I have for my family members".*

MRS REBECCA WARD

Using Building Energy Simulation to Assist Retrofit Decision Making for the Glasshouses at the Royal Botanic Gardens, Kew

The requirement for large organisations in the UK to comply with the Carbon Reduction Commitment energy reduction scheme has led many to investigate the potential for energy consumption reduction across their building portfolio. This means that retrofitting strategies have to be examined for a wide range of buildings of different ages, architectural merit and function. Heritage buildings present unique restrictions on appropriate retrofit technology, even more challenging when highly specific climate control conditions are required. In this instance, the use of building simulation tools can play an important part in deciding on the relative merits and cost-effectiveness of different retrofit strategies.

The Royal Botanic Gardens, Kew is an internationally renowned botanical research and education institute as well as a World Heritage Site. In all, there are over 50 buildings within the Kew Gardens complex, many of which are of historic importance, recognized by the English Heritage Grade I and II listing. Finding ways to reduce the carbon foot print of such a varied and historic site is a challenge, but Daphne Jackson Fellow, Rebecca Ward, has taken on the venture. Rebecca is working for the Department of Engineering at the University of Cambridge but using data from the Royal Botanic Gardens, Kew.

She is creating a case study in support of retrofit decisions at the Royal Botanic Gardens, Kew, specifically in relation to the glasshouses, iconic structures which house a wide range of valuable plants under defined climatic control conditions. Within a greenhouse, physical processes occur that are not accounted for in typical building energy simulation programs, especially those involving the interactions between the plants and their environment.

A general one-dimensional greenhouse model, developed specifically for the analysis of a multi-zone ornamental greenhouse, has been used to calculate the heat flows within the glasshouses under normal operational conditions and potential retrofit scenarios. It is a complex model because plants interact with their environment, altering the internal temperature and humidity of the greenhouse and this can have a significant effect on the energy required to maintain the temperature.

"Kew Gardens is an amazing place to work", says Rebecca. *"It's such a great environment, and I feel invigorated every time I cycle through the gardens to the office. There's a great mix of scientific and artistic interests and activities. There's always something happening - a constantly changing programme of events throughout the year. Cambridge University is also a very exciting place to be. There's a good support network for postgraduates and there seem to be lots of opportunities to get involved with activities within the department and through the university. I've found everyone to be very interested in what I'm doing and in the Daphne Jackson Fellowship and people are very supportive."*

Rebecca's project aims to use the simulations to help identify improvements to operation strategies and suggest possible building modifications. It is hoped to harness heat lost from specific locations for use elsewhere, improving efficiency. Finally, her project will look at whether alternative energy generation methods might be sympathetically employed, taking into account the unique heritage of the site.

DR TZANKA KOKALOVA

Dr Tzanka Kokalova is a Nuclear Physicist and Daphne Jackson Fellow who is investigating alpha condensation in nuclear matter.

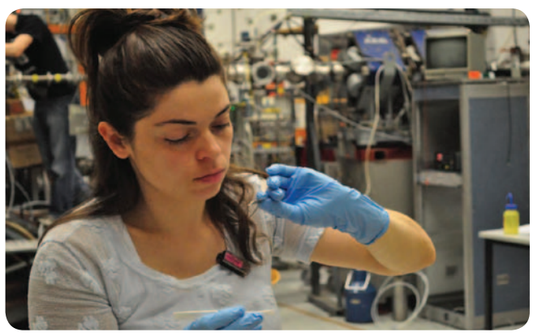
The aim of her project is to investigate a new type of nuclear matter in which the nucleus condenses into alpha particles in one common state.

The well-known picture of an atomic nucleus is that of a spherical bag of protons and neutrons. In the last decade investigations have shown that in special cases nucleons can cluster together into alpha-particles inside the nucleus. Looking closer still there is evidence that the alpha-particles can condense into the same state; all acting together and losing their individual identity (see Figure 1). Such a state is called a Bose-Einstein condensate.

The possible existence of Bose-Einstein condensation in nuclei is fundamental to modern nuclear physics and its discovery would open a whole new area of research and will influence many other fields, such as nuclear astrophysics.

The basic principle behind Tzanka's project is that in a nuclear condensate the constituent alpha particles would share the same state and, therefore, act coherently. Hence during a decay process, the multi-alpha-emission should be simultaneous rather than sequential. This leads to detectable differences, which may be observed using a carefully designed experimental set up. From a theoretical point of view, Carbon-12 is one of the best candidates for a condensate.

Tzanka was able to perform her experiment at the Australian National University's Heavy Ion Accelerator. She spent two weeks at the establishment; the first week setting up the experiment and the second performing the measurements. She measured the reactions: 28Si + 28Si and 28Si + 12C and collected data over six different beam energies: 70, 92, 105, 117, 130 and 144 MeV. A charged-particle silicon-detector array was constructed to record the position, energy and multiplicity information necessary for the identification of the decay particles.



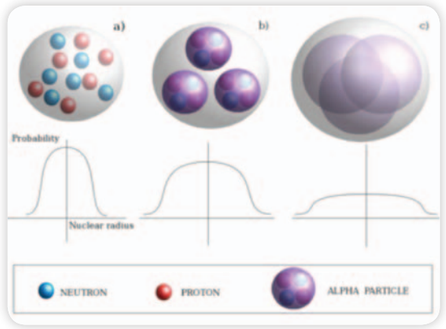


FIGURE 1: Structure of atomic nuclei, shown in this figure for Carbon-12 (6 protons and 6 neutrons). (a) In the ground (lowest energy) state, the protons and neutrons are distributed randomly. (b) In one of the excited states these protons and neutrons cluster together to form three distinct alpha particles. (c) These three alpha-particles can condense into a single state similar to that of an atomic Bose–Einstein condensate. The plots below the nuclei illustrate the corresponding change in the size of the nucleus (from compact in a to dilute in c).

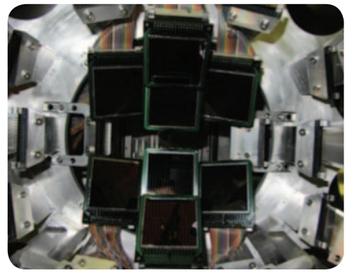


FIGURE 2: Detector set up for Tzanka's experiment in ANU.

"The experiment was a magnificent experience from both a retraining and experimental point of view, since we had to build the electronics from scratch and synchronise everything with the data acquisition system. Furthermore, following the initial test runs we had to carefully consider and optimise the experimental set-up and energies. This taught me a lesson not only in experimental nuclear physics but also taking the right decisions under time pressure," reported Tzanka.

The measurements will enable Tzanka to distinguish between, and compare, condensed (12C(02+)) and 'normal' nuclear matter (12C(3–)) emission. During the on-line analysis she was able to reconstruct the excitation spectra of 8Be and 12C, which on its own is a success, but at this stage it is still early to talk about the primary results of the experiment. This is her next challenge along with examining the emission of higher alpha-particle multiplicities.

Tzanka is based at the University of Birmingham and sponsored by STFC.

DR DAVID AYRE

Following a degree in chemistry and 10 years working in the chemical and power industries, Dr David Ayre completed a PhD at Cranfield University investigating rubber toughening mechanisms in polymers.

This industrially-relevant project led on to further part-time research and consultancy work at Cranfield, which David found he was able to fit successfully around looking after his young family for a period of several years. He applied for a Daphne Jackson fellowship when he felt that he was ready to develop his academic career further and since the end of 2010 David has been working in the Composites Centre at Cranfield, focusing on the effect of nanoparticles in epoxy resins used in aerospace applications.

The aim of David's project, which is sponsored by the EPSRC, is to optimise the dispersion of the nanoparticles in the epoxy polymers and to characterise the mechanical and electrical properties of the resultant thermoset/nanoparticle blends. Nanotechnology is perceived to be able to promote radical improvements in material properties and he hopes to be able to realise some of these changes.

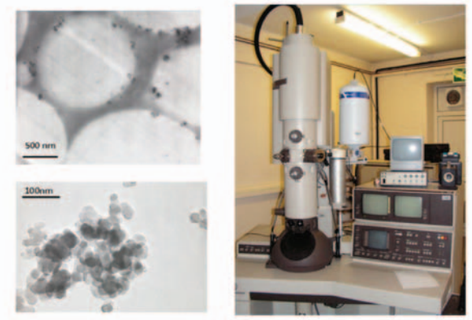
Aerospace and high performance applications for composite materials demand materials capable of withstanding large temperature ranges (-50° to 120°C). The epoxy thermosetting resins capable of withstanding the higher temperatures are generally very brittle materials and are non-conducting. Improved damage tolerance will be realised if the resin system can be toughened. Also there is a requirement for some composite structures to be electrically conductive, providing electrostatic discharge and electromagnetic-radio frequency interference protection. The current nanoparticle dispersion process investigated in this project can be adapted to produce a degree of localised modification in composite structures, possibly providing improved toughness and improved conductivity only in areas of interest.

Although current results demonstrate adequate dispersion of the nanoparticles into the thermosetting resin, the expected improvement in material properties has not been observed. David has worked with carbon black (regular, spherical) nanoparticles in the initial stages of the project and now proposes to investigate whether carbon nanotubes (high aspect ratio) can be dispersed in a similar manner and whether the carbon nanotubes can impart superior mechanical and electrical properties to these blends.

David comments that the Daphne Jackson Fellowship has presented him with challenges and opportunities, providing both valuable experience and recognition within his host institute. He feels that challenges are those associated with managing a research project and always trying to move the project forward in the event of the inevitable disappointing results. Whilst working as a Daphne Jackson Fellow he has had the opportunity to support the teaching of MSc students and is currently completing a PG certificate in teaching, learning and assessment. He also contributes to other projects within the new EPSRC 'Centre for Innovative Manufacture (Composites)' at Cranfield, as well as acting as Health and Safety representative for the Centre.

He has very much appreciated the opportunity to meet with other Daphne Jackson Fellows and share experiences at the informative Daphne Jackson Trust Fellowship training days. As he enters the final year of his fellowship, David is focusing on the important task of securing follow-on funding to enable him to establish a research career within the University sector.

ELECTRON MICROSCOPY



ABOVE: Transmission electron microscopy provides images of any phase separation in polymer blends and can resolve nanoparticles much smaller than the 30nm diameter carbon black particles, illustrated above.