

Research

UNIVERSITY OF LEICESTER GRANTS FROM EXTERNAL SOURCES

PRESS COVERAGE OF RESEARCH GRANTS

The *Bulletin* is sent to the media as well as other external contacts. As a result, details of grants appearing in this section may stimulate press interest. The Press Office may also actively seek media coverage of particular grants detailed in this section. It is therefore the grantholder's responsibility to request that any grant of a sensitive/confidential nature be excluded from the *Bulletin*.

This can be done by contacting the Research Office, which has responsibility for compiling this Research section (2495).

ARCHAEOLOGY

Prof G Barker, Prof D Mattingly

Archaeology and Desertification in the Wadi Faynan

£16,592 Arts and Humanities Research Board

BIOCHEMISTRY

Dr P C E Moody

PETN Reductase: High Resolution Structures of Enzyme-Ligand Structures

£246 CLRC

Dr A E Willis

The Role of Eukaryotic Internal Ribosome Entry in Regulating Expression of Oncoproteins – Advanced Fellowship

£373,664 BBSRC

BIOCHEMISTRY, CARDIOLOGY WITH IMPERIAL COLLEGE

Dr C A Pritchard, Prof B Williams

Use of Gene Targeting to Define the Invivo Functions of the A-Raf & Raf-1 Protein Kinases

£241,743 Wellcome Trust

BIOCHEMISTRY, CHEMISTRY

Prof N S Scrutton, Dr M Sutcliffe

Elucidating the Mechanism of Enzymatic Hydrogen Tunnelling

Enzymes are biological molecules that accelerate chemical reactions. From the discovery of enzymes just over a century ago, we have witnessed an explosion in our understanding of enzyme catalysis, leading to a more detailed appreciation of how they work. Based on current dogma, the vast majority of studies have concentrated on understanding how enzymes facilitate passage of the reaction over a static potential energy barrier. However, recent studies have revealed that passage through, rather than over, the barrier can occur. These reveal that – contrary to current dogma – quantum mechanical phenomena, driven by protein dynamics that produce a fluctuating potential energy barrier, can play a pivotal role in enzyme action. The wave-particle duality of matter suggests that quantum tunnelling may have a prominent role in enzymatic H-transfer. However, unlike for electron tunnelling, evidence for H-tunnelling in enzyme molecules has been extremely limited. We recently reported the first example of extreme hydrogen tunnelling through a fluctuation potential energy surface

in an enzyme molecule. This dynamic approach to H-tunnelling – termed Vibrationally Enhanced Ground State Tunnelling (VEGST) – has also recently been demonstrated in our laboratory for other enzymes that cleave stable C-H bonds. The theoretical development, and verification by experiment, of a role for protein dynamics in driving enzymatic H-tunnelling is the focus of this grant. This dynamic approach to catalysis points to major flaws in transition state theory for describing enzyme catalysis, and will likely impact on strategies for enzyme design/redesign, the development of active site inhibitors and the isolation of effective catalytic antibodies.

£193,848 BBSRC

BIOLOGY

Dr D M Harper

Analysis of Zooplankton, Norfolk Broads

£9,540(supp) Environment Agency

Dr D Twell

Targeted Genetic Screening and Cloning of Gametophytic Plant Fertility Genes that Function During Programic Development – ROPA Award

Plant fertility and seed production are of vital importance both in the natural environment and for crop plants in agriculture. Our research is aimed at understanding at the molecular and genetic levels the key steps in how plants produce seeds through sexual reproduction. These key steps may be in the development and functioning of the male (pollen) and female (ovule) reproductive structures.

We have designed a genetic screen to identify genes which are required for the production and fertility of pollen (containing the sperm cells) and ovules (containing the eggs) in the model plant species *Arabidopsis thaliana* (thale cress). First, plant genes are mutated by introducing mobile pieces of DNA (termed transposons) into the host plant. We then screen for mutations which lead to defects in pollen or egg production. These mutations resulting from insertions of transposons are said to be 'tagged', which enables the mutated genes to be isolated using standard laboratory techniques. By screening thousands of plants we expect to isolate many genes which are important for plant fertility.

These genes will subsequently be used to precisely understand sexual development in plants. Furthermore, we expect that this information may be used to improve plant breeding strategies to create useful and novel hybrids and to monitor and limit the spread of DNA from transgenic plants into the environment.

£51,728 BBSRC

Prof G C Whitelam

Development of Diagnostic Tests for BSE

£12,500(supp) MAFF via ADAS

CELL PHYSIOLOGY & PHARMACOLOGY

Prof S R Nahorski

Coupling of Human Muscarinic M5 Receptors to Different G-Proteins

£95,538(supp) Roche Bioscience

CHEMISTRY WITH UNIVERSITIES OF EAST ANGLIA, READING, CAMBRIDGE, LEEDS & IMPERIAL COLLEGE

Dr P S Monks

Atmospheric Chemistry and Transport of Ozone in the Upper Troposphere/Lower Stratosphere (ACTO-UTLS)

The work to be undertaken as part of this grant will quantify the budget of ozone in the upper troposphere, assessing the relative importance of in-situ photochemical production and long-range transport. The North Atlantic UTLS region will be studied using a comprehensively instrumented C-130 aircraft and measurements will be interpreted using correlation techniques, calculation of fast in-situ chemical rates and equilibria, and by the use of chemical-transport models when chemical and dynamical timescales are comparable. The strong emphasis on the meteorological and chemical context of the measurements will enable deductions to be made on a wider domain in space and time. Previous measurements from recent and ongoing aircraft programmes will also be analysed as part of the project.

£32,478 NERC

CHILD HEALTH

Dr M McKean

Mechanisms of Lower Airway Narrowing in an Experimental Human Coronavirus (common cold) Infection – Yr 2

£16,703(supp) National Asthma Campaign



ECONOMICS (MANAGEMENT CENTRE)

Dr P Davies

Grant for the Unit for Membership Based Organisations

£23,000 *Barrow Cadbury Trust*

EDUCATION

Mrs T Jarvis

Phase 2 Providers

The AstraZeneca Science Teaching Trust has agreed to a further £78,740 to continue to support science teaching in the first cohort of 16 Leicester City Primary schools plus funding to support an additional 16 schools. The funds will enable teachers to attend a course on 'Developing and Assessing Science Investigations' which includes a visit to a local industry. One class from each of the 32 schools will also be enabled to visit the Challenger Space Centre. Teachers will also be given tutor support and time for school-based work linked to the project.

There has been detailed evaluation of the project to date which is already showing positive outcomes in respect of the children's science learning. The evaluation included the development of four new instruments exploring pupils' and teachers' attitudes and science cognitive development. Research articles on these and the subsequent changes for the two phases of the project are in hand. £78,740(supp) *AstraZeneca Science Teaching Trust*

Prof A Osler

Human Rights and Democracy in Schools – Transfer from Birmingham University

£6,565 *ESRC*

ENGINEERING

Prof N B Jones

Royal Society Royal Fellowships Programme – Dr Xiang Jianping

£4,805 *Royal Society*

Dr T Pearce

An Optical-Based "Electronic Nose" for Broadband Chemical Sensing

Chemical Sensor Array Device (ChemSAD) or 'electronic nose' based instrumentation is currently limited by the sensitivity and the repeatability of its measurements. New applications areas such as environmental and medical monitoring will require far higher levels of chemical sensitivity combined with significant miniaturisation. The aim of this project is to develop a novel prototype electronic nose intended for use in such performance critical applications. The final system will not only demonstrate the feasibility of using a variety of fluorescent indicators deployed on large populations of porous silica microspheres to achieve highly sensitive, lower-power, portable chemical monitoring, it will also provide an ideal-test-rig to conduct pilot studies which will be vital in securing funding to develop the technology. £9,369 *Royal Society*

ENGINEERING, ANAESTHESIA

Prof N B Jones, Dr J C Fothergill, Dr C D Hanning

Propofol Sensor

£58,092 *AstraZeneca*

ENGINEERING (JOINT PROJECT WITH UNIV. OF SHEFFIELD)

Dr S Spurgeon

Recursive Interlacing and Sliding Mode Control of Flat and Non-Flat Nonlinear Systems

In its widest context, this joint study between the Universities of Sheffield and Leicester is concerned with the development of novel nonlinear control approaches which may be applied to nonlinear, complex, uncertain industrial processes which may be 'non-flat'. This is a particularly challenging application area as non-flat systems comprise those systems which cannot be effectively controlled using standard linear and nonlinear techniques. £48,069 *EPSRC*

ENGLISH

Prof G Walker

The Fashioning of Henry VIII – Research Leave Scheme

The aim of this project is to provide a new account of the life and reputation of Henry VIII. Rather than attempting another 'revisionist' biography, however, the intention is to focus more precisely upon the ways in which the king's life and character were themselves carefully fashioned and presented (by Henry himself, his supporters and critics) to a variety of audiences during his lifetime, and also to examine the subsequent attempts to refashion his image, as politicians, scholars and commentators sought to enlist his reputation for contrary confessional, political, and academic causes. The aim is historiographical in its broadest sense, but the study is designed not simply to catalogue previous accounts of the king's life, but to set the whole process of fashioning such representations in a relevant contemporary context. The resulting volume will be a cultural history of the king and his court which draws upon the separate disciplines of political, literary, and art history. £16,241 *Arts and Humanities Research Board*

EPIDEMIOLOGY & PUBLIC HEALTH

Dr W Baird, Dr C McGrother

Development and Evaluation of a Preventive Oral Health Programme for MS Patients: A Randomised Controlled Trial

£104,747 *NHS Executive Trent*

Dr B Sheppardson

Access to Social Care for Older People

Appropriate social support services are essential if vulnerable older people are to maintain their independence and achieve a satisfactory quality of life. However, social care services for older people can be compromised

by the financial difficulties which local authorities are experiencing.

This study intends systematically to assess the effects of cost containment on older people. The aims of the study are to identify the policies and practices which exist in local authorities concerning the allocation of community care services, and to describe the impact of these policies and practices on the lives of older people at home, or in residential or nursing home care. The work will be carried out in eight local authorities in England and Wales.

The study is being undertaken in conjunction with Help the Aged and is funded by the National Lottery Charities Board. £191,688 *National Lottery Charities Board via Help the Aged*

Dr B Young

Vacation Studentship for Michelle Cox

£800 *The Leicester Royal Infirmary NHS Trust*

EPIDEMIOLOGY & PUBLIC HEALTH (UKCCSG)

Prof M Clarke, Dr K Abrams, Prof C R Pinkerton
UKCCSG Administrative Office

The UK Children's Cancer Study Group has just received renewal of its 5 year grant from the Cancer Research Campaign. The grant covers many of the running costs of the Data Centre in Leicester from which all the activities of the group are co-ordinated. For the first time a substantial increase has been awarded including a grant to allow the group to further its work in the area of pharmacology. The main interest of the group is in the co-ordination and running of collaborative clinical trials of childhood cancer, the majority of which are now run on an international basis. £405,215 *Cancer Research Campaign*

GASTROENTEROLOGY

Prof R J Playford

The Use of Colostrum to Repair Gastrointestinal Injury

£1,500 *Leicestershire Health*

GENERAL PRACTICE

Dr R Baker, Dr K Khunti

Evaluation of the Salaried Doctors Scheme in Leicestershire

Most general practitioners are self-employed. They have contracts with the health service to provide general medical services to patients who register with them. In recent years some practices have experienced difficulties in recruiting new general practitioners. At the same time, some general practitioners do not want to be self-employed. For example, some doctors wish to work part-time.

To address this problem, a scheme to employ doctors directly has been introduced by Leicestershire Health Authority. The objective of this salaried doctor scheme is to



develop and improve services for patients. The salaried doctors themselves may also need support to meet their education and training needs. Therefore, the aim of this study is to investigate the extent to which services have been improved, and to check that the salaried doctors have received the required support. If the salaried doctor scheme is successful, it may offer an approach for developing services in other practices.

£6,953 *Leicestershire Health*

Dr F Cheater

Funding for Research Post

£65,000 *Leicestershire & Rutland Healthcare Trust*

Prof R C Fraser

Funding for Clinical Governance R & D Unit

Clinical governance is the framework for monitoring and improving the quality of care throughout the National Health Service. The grant from Leicestershire Health will be used to underwrite the costs of the core staff of the CGRDU which came into existence on 1st April 1999. The CGRDU will build on, and extend, the activities and achievements of the Eli Lilly National Clinical Audit Centre.

The work of the CGRDU will include:

- Research into effective methods of implementing change in the performance of health professionals.
- Determination of methods for the professional development of individuals and teams in the National Health Service.
- Development and evaluation of ways of involving patients in clinical governance.

£111,942 *Leicestershire Health*

GENERAL PRACTICE (WITH IMPERIAL COLLEGE MED SCHOOL)

Dr R H Baker

Should Primary Care Groups Act to Improve Personal Care

General practices are undergoing major changes. Practices must now work together in groups, called "primary care groups". The government is also introducing a 24 hour telephone service for enquiries and advice (NHS Direct) and walk-in centres as an alternative for people who find getting to their doctor difficult. Because of these developments there is a danger that services for patients will become less personal. The aim of this study is to identify the key features of personal care in general practice. It will then be possible to design services to preserve these key features. The study is being undertaken in Leicester, in collaboration with colleagues from Imperial College, London. Patients, general practitioners and nurses will take part in interviews and focus groups. The participants will be identified from different types of practice, and their views on key features of personal care and their importance will be studied in depth.

VALUE REPORTED IN OCTOBER BULLETIN

MATHEMATICS & COMPUTER SCIENCE

Dr N Ghani

Categorical Rewriting: Monads and Modularity

£52,569 *EPSRC*

MEDICINE & THERAPEUTICS

Prof B Williams

Grant in Aid of Research

£21,340 *Merck Sharp & Dohme*

MICROBIOLOGY & IMMUNOLOGY

Prof P Andrew

Grant in Aid of Research

£5,779 *AstraZeneca*

Prof W D Grant

Environmental Gene Screening to Obtain DNA Libraries

£65,000 *Genencor International*

Dr A Lloyd

Grant in Aid of Research

£11,916 *PanTherix Ltd*

Dr K G Nicholson

Clinical Trial – Chiron Influenza H5N3 Vaccine Study

In early summer of 1997, a young boy died from avian influenza in Hong Kong. Later that year a small outbreak involving 17 additional cases that were hospitalized occurred in Hong Kong with 5 additional deaths. This outbreak and the high associated mortality sparked fears that the world was on the brink of a lethal pandemic of influenza. Whilst the authorities in Hong Kong tackled the source of the outbreak by slaughtering the poultry in Hong Kong, public health authorities in the rest of the world revised their pandemic plans for influenza and examined the need to develop new vaccines and test them in man. The work by Dr Nicholson is the first step in an international collaboration between vaccine manufacturers, the UK Department of Health, and Leicester University to better prepare us for the next pandemic.

£24,600 *Chiron SpA*

OBSTETRICS & GYNAECOLOGY

Dr J Konje

Grant in Aid of Research

£69,080 *Schering Health Care Limited*

ONCOLOGY

Dr K J O'Byrne

Phase III Study in Non-Small Cell Lung Cancer AG 3340-0117

£87,147 *Agouron Pharmaceuticals Inc*

A Phase I, Open-Label, Safety and Pharmacokinetic Study of Escalating Doses of Docetaxel when Administered with Valspodar in Patients with Solid Tumours

£55,348 *Novartis Pharma AG*

Prof W Steward

A Phase I Study of the CCK-B Antagonist L-365,260 in Patients with Cancer-Related Opioid-Poorly Responsive Pain

£11,229 *M L Laboratories plc*

A Double-Blinded Placebo Controlled, Minimised Phase III Study Comparing Marimastat to Placebo as Adjuvant Therapy in Patients with Resectable Pancreatic Cancer

£75,000 *British Biotech*

ONCOLOGY, ANAESTHESIA

Prof W Steward, Prof D Rowbotham, Dr G N Rudd

CAPTAIN CONTINUE: CCK Antagonist, Devacade as an Adjunct to Strong Opioids in the Management of Patients with Pain which has a Neuropathic Element

£9,000 *M L Laboratories plc*

PATHOLOGY (CHEMICAL)

Dr W Lawley, Dr K E Herbert

UV-induced Reactive Oxygen Species Production Resulting in Altered Processing of the Ro60 Autoantigen – Oliver Bird Fund 1999

Systemic Lupus Erythematosus (lupus) is an incurable rheumatic disease. Symptoms include sensitivity to sunlight, a severe skin rash, arthritis and fatigue. Lupus occurs when the immune system does not recognise certain proteins as a normal part of the body and instead attacks them.

Ultraviolet light (UV) is one of several environmental triggers known to exacerbate lupus. We are investigating the effect of UV on one model protein known to be involved in lupus. We hypothesise that the shape and structure of this protein may be changed by UV to the extent that the immune system no longer recognises it. We aim to determine how this protein is recognised by cells of the immune system before and after UV treatment; and also to see how this differs between cells isolated from lupus patients and control patients.

£59,237 *Nuffield Foundation*

PHYSICS & ASTRONOMY

Dr C Binns

A Fully Characterised, High Resolution, Polarisation Selectable, Synchrotron Beam Line for VUV Science

£984 *CLRC*

Dr G W Fraser, Dr J E Lees

Bioimaging-Testing of Protein Gels

£83,520 *Bayer via MRC*

PSYCHOLOGY

Dr A North

Music and Employee Productivity

A person's performance on any task is influenced by his/her degree of arousal: people perform best when they are moderately aroused. However, job requirements often push employees towards extremely low or high arousal states. For example, entering a large quantity of data on to a PC produces boredom (i.e. low arousal), whereas working to a tight deadline produces anxiety (i.e. high arousal). Either condition will hamper employee productivity.



Music can influence arousal: up-tempo music can increase arousal, whereas the calming properties of many other musical styles are similarly well-known. This means that music may help to moderate the extreme levels of arousal produced by job requirements, and therefore increase productivity. More specifically, it may be possible to increase the productivity of employees engaged in boring repetitive tasks by playing stimulating music: this would raise their degree of arousal to an optimal moderate level. Similarly, calming music may soothe the nerves of employees working in stressful environments, and therefore improve productivity by lowering arousal to an optimal moderate level.

This basic idea will be tested with participants in a real workplace situation. Those in a low arousal (LA) condition will be asked to e.g. code a large body of meaningless data on to a spreadsheet. Those in a high arousal (HA) condition will be given the same task, but will also be set a difficult target e.g. requiring them to encode a very large amount of data. Whilst carrying out either of these tasks, participants will be required to listen to either stimulating or sedative music. The two principal measures taken will be the amount of e.g. data encoded, and the number of errors made. In the LA condition, participants should be most productive and make fewer errors when they hear stimulating music. In the HA condition, participants should be most productive and make fewer errors when they hear sedative music. A no music condition will allow a test of the potential benefits of playing music in the workplace.

£7,855 *Performing Rights Society Ltd*

RADIOLOGY

Prof G R Cherryman

Funding of Research Nurse

£7,323 *Glenfield Hospital
NHS Trust*

RADIOLOGY, MEDICINE & THERAPEUTICS

Prof G R Cherryman, Dr P R Sensky, Prof N J Samani

Utility of Ultrafast Magnetic Resonance Imaging Techniques in Identifying Hibernating Myocardium and Predicting Left Ventricular Functional Recovery following Coronary Revascularisation – Research Training Fellowship

£104,254 *Wellcome Trust*

SCARMAN CENTRE FOR THE STUDY OF PUBLIC ORDER

C Wilkinson

Under-Age Drinking and Drug Abuse in Clifton, Nottingham

£5,842 *Nottingham Chief Executive's Department*

SCARMAN CENTRE FOR THE STUDY OF PUBLIC ORDER WITH NOTTINGHAM TRENT UNIVERSITY

Dr A Hucklesby

Evaluation of Leicester Bail Support Scheme

£20,000 *Leicester City Council*

SOCIOLOGY (SNCCFR)

Mr J Williams

Asian Football

£3,450 *London Borough of
Newham*

SURGERY

Prof P R F Bell (Supervisor), Mr B Axisa, Mr M M Thompson

The Role of Doxycycline in the Prevention of Acute Stroke – Fellowship Mr B Axisa

A large number of strokes are caused because of disease in the carotid arteries in the neck. These blood vessels become narrowed by the deposition of fatty materials and blood clot. Some of these deposits remain hard and are not thought to be dangerous but others become softened and when they soften they can burst releasing clot and fatty material into the brain causing strokes. The reason why they suddenly burst in this way is not known but one possibility is that chemicals in the body react with tissues in the deposit and break down the protein. These substances are called proteinases and could lead to destabilisation of the deposit leading to its break down in the way described above. Doxycycline is an antibiotic of the tetracycline group and has been used for many years to treat acne. One of its side effects is to inhibit the action of proteinases which cause break down of tissue and the aim of this study is to see if it does that in patients prior to operations on these deposits [carotid endarterectomy]. Patients will be given doxycycline or a placebo drug. The number of emboli caused by pieces of the deposit going to the brain will be measured and also the pathology of the plaque looked at following surgery and its removal. We anticipate that doxycycline will stabilise the plaque and make them harder and less dangerous and therefore less liable to cause strokes.

£29,857 *Royal College of
Surgeons of England*

Mr M Gallinanes

Grant in Aid of Research

£17,400 *Caledonian Medical Ltd*

Mr M Gallinanes, Dr B Matata

By what Mechanism does Exogenous Nitric Oxide Exert a Regulatory Role on Inflammatory Cytokine Production?: The Effect of Diabetes

The Physiological and pathological role of nitric oxide (NO) in the body has attracted the attention of many researchers recently. Several studies have reported that inhaled NO attenuates lung injury and sepsis, and in vitro studies have also shown that NO inhibits the production of inflammatory mediators. Results from our recent study using NO-donors on patients undergoing cardiac surgery indicates a differential regulatory role on inflammatory mediators. The mechanism by which NO exerts its regulatory role on the inflammatory

reaction is unknown. Therefore, the aim of this project is to investigate how NO modulates inflammation and whether it does so by altering cellular responses to injury. We believe that the results from such a study would provide important data both from a clinical and scientific perspective.

£10,000 *Glenfield Hospital
NHS Trust*

Dr R F L James

Assessment of the Role of Anti-Islet Auto-Immunity Induction in Patients Receiving Islet Auto-Transplants

£3,000 *Novo Nordisk UK
Research Foundation*

SURGERY

Prof P R F Bell (Sponsor), Dr N Brindle, Mr P N Morris (Fellow)

Molecular Basis of Venous Malformations, Caused by the Mutation in the Endothelial Receptor Tyrosine Kinase Tie-2-Entry Level Training Fellowship – Mr P N Morris

Venous malformations (VM) are large varicose veins which are present from birth. They can cause symptoms but can also be unsightly as many of them occur on the face causing a deformity as well.

The research in the Department of Surgery will look at the basic genetic reason for the formation of these abnormal blood vessels using modern techniques. It is hoped that this will lead to a more effective treatment of VM at an early stage and provide an insight into the normal development and formation of blood vessels at an early stage in life.

£50,485 *Wellcome Trust*

Dr K E Porter, Mr M M Thompson, Prof N J M London

A Combined Anti-Proliferative and Anti-Migratory Approach to the Amelioration of Intimal Hyperplasia in Vein Grafts

Atherosclerosis can cause progressive narrowing of the arteries in the heart and/or legs with an accompanying reduction in blood flow which presents as angina in the case of the coronary arteries, and critical ischaemia causing rest pain in the lower limbs and possibly gangrene in the feet. Such narrowings can be treated by a bypass operation using vein taken from the patient's leg. One of the problems with these vein bypass operations is that a considerable percentage of such bypass grafts develop tight narrowings known as stenoses. Stenoses result from the migration and proliferation of the smooth muscle cells in the vein graft wall subsequently forming a lesion which compromises blood flow. The purpose of this project is to develop pharmacological strategies to inhibit smooth muscle cell migration and proliferation and thereby improve the outcome of vein bypass grafting.

£64,373 *British Heart Foundation*