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Contents

Editorial

Welcome to the October 2004 issue of *The* Bulletin!

This issue includes a review article written by Dr Andrea Münsterberg and colleagues from the School of Biological Sciences at the University of East Anglia. Andrea presents a summary of the signalling pathways that control cardiac cell specification and their migration during the early stages of heart devlopment.

In the Secretary's Column, Dr Barbara McDermott announces the result of the recent ballott of members to serve on the Society's Executive Committee. We would like to thank retiring members for their efforts during their terms of office and particularly, for their cooperation in providing material for *The* Bulletin. We look forward to working with the newly-elected Committee members in the new year.

Following a successful Autumn meeting, plans are now coming together for next year's Spring meeting,which will be organised by Professors Nilesh Samani and Alison Goodall. Details of the meeting can be found on the back page of this issue.Finally, we bring you the latest details of grants awarded to researchers in the Cardiovascular field, by the British Heart Foundation and the Wellcome Trust.

Helen Maddock and Nicola Smart

Bristol - Myers Squibb

BRISTOL-MYERS SQUIBB CARDIOVASCULAR PRIZE FELLOWSHIP AWARDS 2004

Since 1984 the Bristol-Myers Squibb Cardiovascular Prize Fellowship has supported young physicians providing funding for up to three years research in the field of cardiovascular medicine. Fellowships will be awarded each year to physicians – usually at SHO or SpR level who already hold MRCP or equivalent – and are committed to research or academic careers in Cardiovascular Medicine. No restrictions are placed on the type of cardiovascular research carried out – both clinical and laboratory-based projects are eligible for funding.

Applications must be received by October 31st 2004 for awards to commence the following year.

A Selection Committee of distinguished scientists and physicians Chaired by Professor Morris Brown (Cambridge) is responsible for the selection of Fellows. The Committee also includes Professor Keith Fox (Edinburgh), Professor Michael Frenneaux (Cardiff), Professor Hugh Watkins (Oxford) and Professor Anna Dominiczak (Glasgow). The successful candidate will have the opportunity to present data on an annual basis to the Committee, peers and senior academics and receive feedback. The Award will cover annual salary together with up to £15,000 per annum toward research costs and attendance at one international meeting per year. Interviews of short-listed candidates will take place on 8th **December 2004.**

For further information on the application procedure and a brochure detailing the high quality research carried out by previous Fellows, please contact:

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The molecular mechanisms controlling cardiac precursor cell specification and movements

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The cells that will give rise to the heart, the cardiac precursors, become specified very early in developing vertebrate embryos. The origin of cardiac precursors has been mapped in a number of vertebrate model organisms, including chick and frog. Over recent years Wnt signalling has been implicated as one of the mechanisms controlling cardiac cell specification. However, not much is known about how cardiac precursor cells move within the embryo, how this movement is controlled and how the cells are guided to ensure that they arrive at their correct topographical location. In this review, we will summarize what is currently known about the signals controlling specification of cardiac cells and their movement in early development. We then look at recent studies in vertebrate embryos that have uncovered a crucial role for FGF signalling in controlling the movement of early mesodermal cells through the primitive streak during gastrulation and its implications for cardiac precursor cell migration. In addition, we will discuss the role of Wnt signalling in specification of cardiac cell fate and early heart formation. We will report on our own studies in chick and Xenopus embryos, which investigate the migratory routes of future cardiac cells during development. We have developed a method that uses live imaging in chick embryos, which allows us to observe migrating cells *in vivo*.

The origin of cardiac cell in vertebrate embryos

The vertebrate heart is the first organ to form and function during development. In the chick embryo a contractile heart tube is present at Hamburger-Hamilton (HH, Hamburger and Hamilton, 1951) stage 10, about 2 days of incubation. In mice a primitive tubular heart is present at E8 and in Xenopus leavis the heart tube has formed by stage 22 (1 day). The cells that will become the heart, or cardiac progenitors, are among the first cell lineages to be established and among the first mesoderm cells to invaginate through the primitive streak in a process called gastrulation, during which the different germ layers of the embryo are generated. In chick, cardiac progenitors have been mapped in the epiblast of pre-streak embryos (Hatada and Stern, 1994). In the early gastrula (HH stage 3), they are located in the anterior primitive streak, from which they enter the mesoderm bilaterally (Garcia-Martinez and Schoenwolf, 1993; Rosenquist, 1970). Prospective heart cells with a rostral position will form anterior structures of the tubular heart, while more caudally localized cells will form posterior structures (Garcia-Martinez and Schoenwolf, 1993). Due to the lack of genetic markers of heart progenitors as they ingress, it has not been possible to observe their migration route directly. Therefore it is not clear, where the heart cells go after they leave the streak. The current, widely accepted view is that cardiac progenitor cells migrate anterior-laterally, and at HH stage 5 cardiogenic mesoderm can be found in the heart fields on either side of the primitive streak (see schematic in **Figure 1**). The progenitors that will form the atrial and ventricular cell lineages, as well as cells that will form proximal outflow tract and endocardial tissues are present in the heart fields. All cell lineages have already separated at the time the progenitors reside within the primitive streak in the chick and cell fate analysis suggests that atrial precursors are present in the caudal part of the heart field, while future ventricular cells are mainly localised anteriorly (Redkar et al., 2001; Wei and Mikawa,

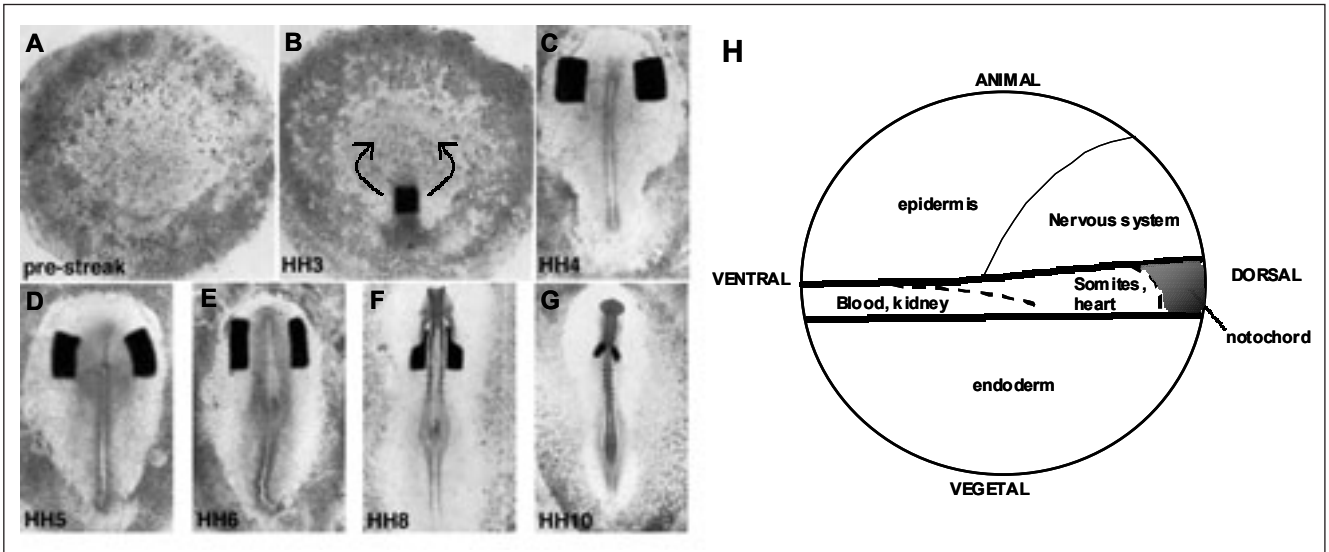

Figure 1: Fate map of prospective cardiac cells in chick and frog. (A-G) Chick embryos of different developmental stages as indicated on each panel. The black shading indicates the location of prospective cardiac cells. (B) At stage HH3, prospective heart cells are located in the primitive streak. The arrows indicate the assumed route of migration anterior laterally from the primitive streak. (C-F) Cardiogenic mesoderm can then be found in lateral regions. (G) At stage 10, a primitive heart tube has formed at the ventral midline. (H) The fate map of a Xenopus laevis blastula stage embryo, with the animal pole at the top, the vegetal pole at the bottom, the future dorsal side to the right and the future ventral side to the left. Signals from the Spemann organizer (grey shaded area) and the endoderm help to determine the fate of mesodermal tissues including the heart.

2000). Eventually, the heart primordia fuse in the ventral midline, to form a beating single heart tube (Brand, 2003; Yutzey and Kirby, 2002). In addition to the control of morphogenetic movements, environmental cues are involved in the progressive specification of cells as they leave the primitive streak. It is unclear to what extent cardiac progenitor cells within epiblast or primitive streak are already specified, and it is possible that they are specified according to the signals they encounter on their migration path. In chick embryos the hypoblast has been implicated as the source of the earliest inductive signals and these can be mimicked by activin or TGFβ (Yatskievych et al., 1997). In mice, explants of cardiogenic mesoderm will differentiate into cardiac muscle in the presence of both visceral endoderm and primitive streak (Arai et al., 1997). In Xenopus, the Speman Organizer and the dorsoanterior endoderm, which underlies the pre-cardiac mesoderm, are both necessary for induction and together are sufficient to induce a beating heart tube in non-cardiogenic mesoderm (**Figure 1H**, Nascone and Mercola, 1995).

Signals involved in cardiac precursor specification

In recent years, signalling pathways that specify cardiac mesoderm have been extensively studied in model organisms. Furthermore, a number of transcription factors that regulate different aspects of cardiac morphogenesis and cyto-differentiation have been identified and characterized. These include regulators of cardiac contractile protein gene expression such as Nkx2.5, GATA4, -5 and -6, and members of the T-box family of transcription factors, Tbx-5 and Tbx-20, (Brand, 2003). In the chick, one of the earliest transcription factors that is expressed in heart precursors is Nkx2.5 (Schultheiss et al., 1995).

Work by a number of laboratories has demonstrated that BMPs, Wnt and FGF signalling all play a role in the specification of cardiac muscle precursors (Marvin et al., 2001; Tzahor and Lassar, 2001; Alsan and Schultheiss, 2002; Lopez-Sanchez et al., 2002). Wnt signaling pathways have been extensively studied in the past several years and a number of different cellular pathways can be triggered by ligand binding to seven-pass trans-membrane receptors of the frizzeld family. Wnt signaling through the canonical or β-catenin dependent pathway is best understood (Peifer and McEwen, 2002). Other pathways include the planar cell polarity (PCP) pathway and the less well characterized Ca^{2+}/Protein Kinase C pathway (**Figure 2**, Veeman et al., 2003). Outside the

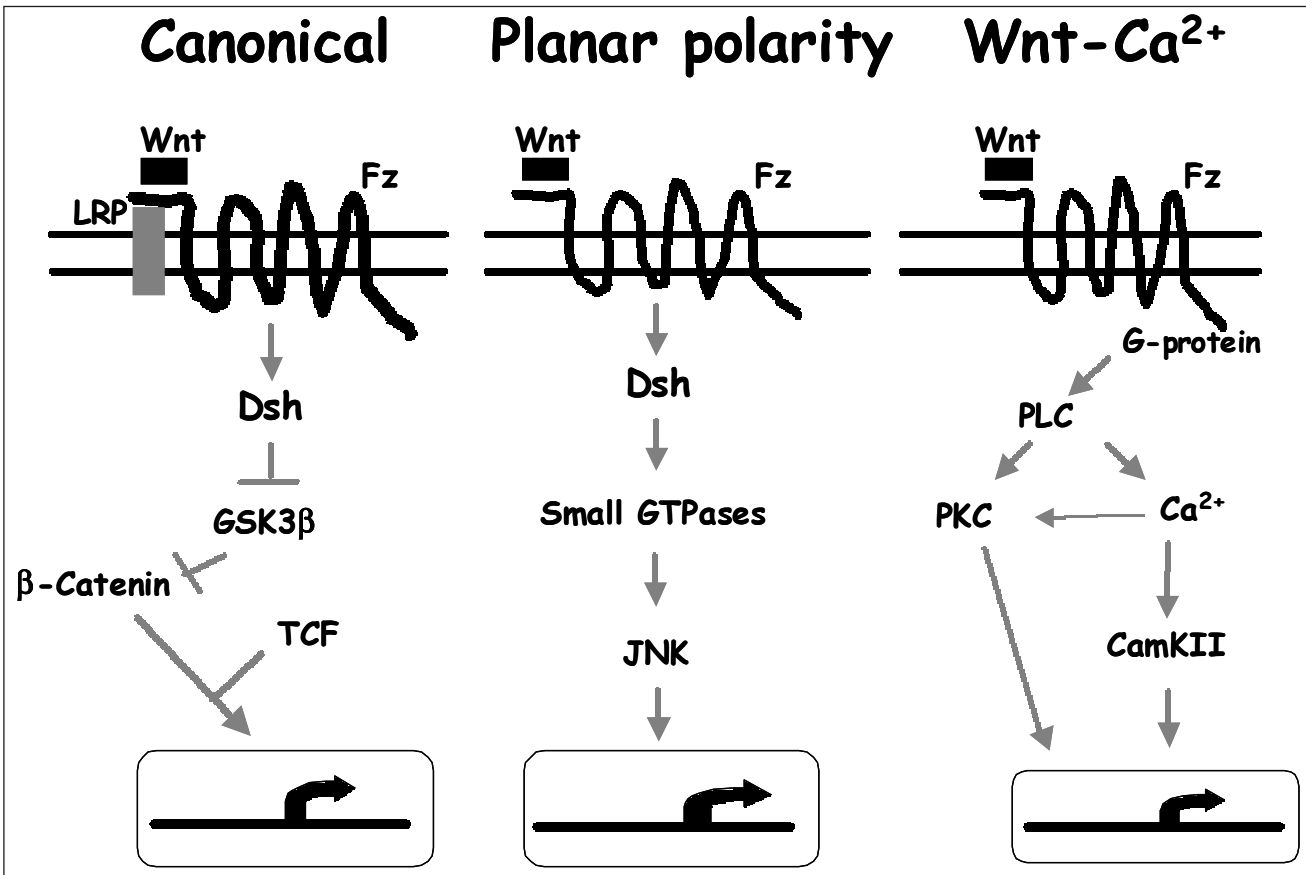

Figure 2: Canonical and non-canonical Wnt signalling pathways. (A) A simplified scheme of the canonical Wnt signalling pathway. In this pathway a Wnt ligand binds to a Frizzled (Fz) receptor and a co-receptor of the low density lipoprotein recptor-related protein (LRP) family. This leads to the inhibition of Glycogen synthase kinase beta (GSK3β by dishevelled. This leads to an accumulation of β-catenin in the cytoplasm. In the absence of Wnt GSK3β phosphoylates β-catenin and thus targets it for degradation. Stabilized β-catenin is able to associate with transcription factors of the ternary complex factor (TCF)/ lymphoid enhancer factor 1 (LEF1) family. (B) Planar polarity involves a non-canonical β-catenin independent Wnt/fz pathway that requires Dsh. Small GTPases of the rho/cdc42 family are also thought to be involved as are Jun kinases (JNK). (C) The Wnt/Ca^{2+} pathway probably signals via hetero-trimeric G-proteins to mobilise intracellular Ca^{2+} and in some contexts, to stimulate protein kinase C (PKC). Whether this pathway requires Dsh remains unclear.

cell, Wnt signaling is modulated by antagonists, which have structural homology with the ligand binding domain of frizzled receptors. They are called secreted frizzled-related proteins (sFRPs). Other classes of extracellular inhibitors have also been identified, including cerberus and dickkopf (Rodriguez-Esteban et al., 1999; Kawano and Kypta, 2003).

Experiments in chick and Xenopus embryos first demonstrated that inhibition of β-catenin mediated canonical signalling led to heart formation (Marvin et al., 2001; Tzahor and Lassar, 2001; Schneider and Mercola, 2001). In addition, it was demonstrated that Wnt-11 signalling through a non-canonical pathway is required for cardiogenesis in Xenopus (Pandur et al., 2002). These results, together with the finding that loss of β-catenin function in mice results in ectopic heart formation, suggest that there may be a competitive interaction between non-canonical and β-catenin dependent pathways for early cardiac fate specification in vertebrates (Lickert et al., 2002). Interestingly, β-catenin function seems to be required for the specification of endocardial cushions slightly later in development (Hurlstone et al., 2003).

As part of our work on skeletal muscle cell specification in response to Wnt, we have isolated a number of chick homologues of components of Wnt signalling pathways and expression studies in chick embyros suggest that Wnt signalling may be important

for the movement of cardiac mesoderm cells (Münsterberg et al., 1995; Schmidt et al., 2000; Schmidt et al., 2004). We are currently investigating the function of Wnt signalling in cardiogenic cells emerging from the primitive streak. We have found that the putative Wnt-11 receptor, frizzled-7, (Fz-7), which signals through disheveled in both a canonical and a non-canonical planar polarity pathway (Medina et al., 2000), is expressed in Koller's sickle at the posterior marginal zone, in the primitive streak and in a fan shaped pattern around the streak of HH2-3 embryos. This suggests a possible role for frizzled-7 signalling in primitive streak cells and cardiogenic mesoderm in chick and is consistent with our finding that Xfz-7 is expressed in cardiogenic mesoderm in Xenopus (Wheeler and Hoppler, 1999). Furthermore, recent experiments have shown that interfering with Xfz-7 function in Xenopus embryos caused heart malformations, in particular cardia bifida, indicating that the cells may be unable to reach their correct position at the ventral midline (MAE and GW unpublished). Frizzled-7 could thus be important for heart morphogenesis and cardiac fate specification.

Imaging the migration of GFP labeled cells in live embryos

In order to study the cell movements involved in forming the heart we need to be able to image individual cells in a live embryo during development. We have recently developed a new method, using long-term video microscopy and extensive image analysis, to monitor the movements of individual GFP labelled cells in live chick embryos. We have employed this technique to investigate cell movement patterns that occur during gastrulation (Yang et al., 2002). We used electroporation to transiently transfect cells with GFP during the early stages (HH2-3) of development (Itasaki et al., 1999; Momose et al., 1999). GFP expression became visible within 2-3 hours. Labelled tissues were grafted into unlabelled host embryos, which allowed us to follow the movement of individual cells emerging at different positions along the primitive streak. Movement tracks were monitored in HH stage 4 embryos (fully extended streak stage) until the embryos reached the 3-6 somite stage (15 hours). These studies showed that at HH stage 4, cells from the anterior and middle primitive streak migrate away from the streak towards

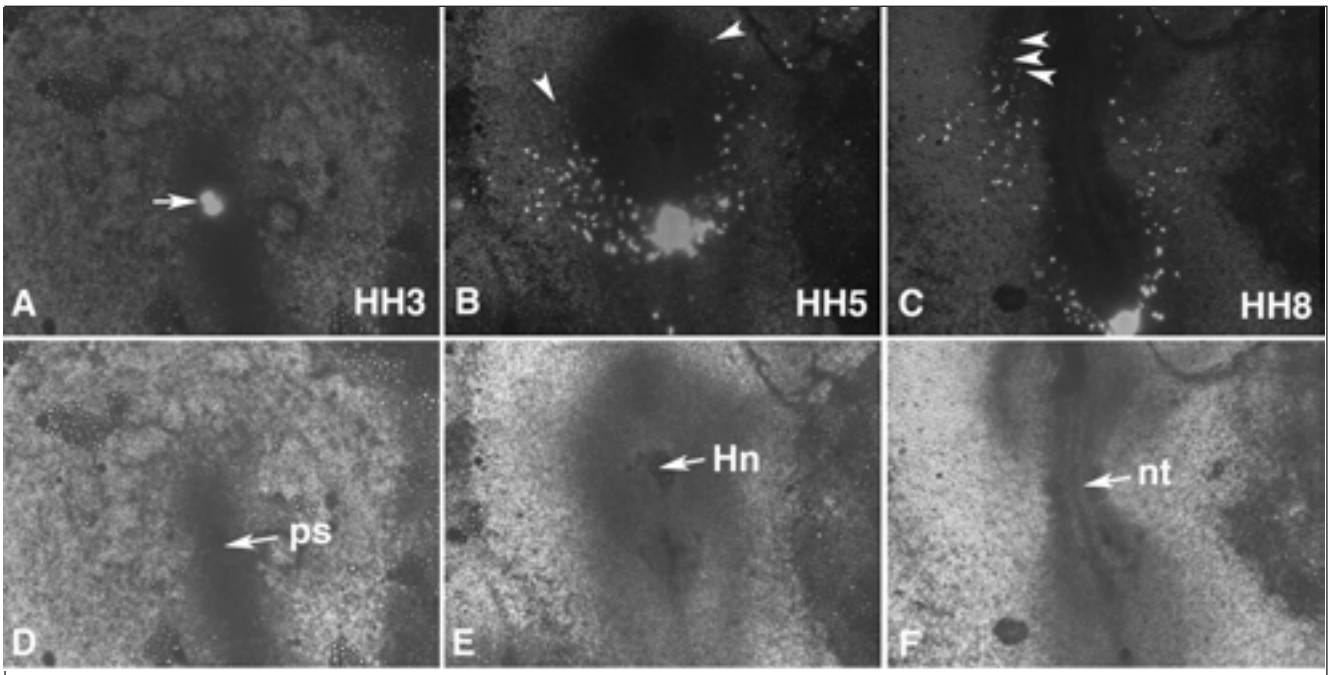

Figure 3: Long-term video microscopy of GFP positive primitive streak cells migrating into the heart. Primitive streak cells of HH3 chick embryos were injected and electroporated with a GFP expression vector. After further incubation, to allow GFP protein to be expressed, positive cells were grafted into a stage matched host embryo. The white arrow in panel (A) marks the graft. Panels (B) and (C) show different frames of the video after 12 and 20 hours approximately. Migrating GFP labelled cells are indicated by white arrowheads. In panel (C) GFP positive cells can be identified in the area of the heart field (white arrows). HH stages are indicated on each panel. Panels (D-F) are bright field images of the embryo corresponding to panels (A-C). ps, primitive streak; Hn, Hensen's node; nt, neural tube

the periphery of the embryo, and once Hensens node has regressed past them, they migrate back towards the midline (Yang et al., 2002).

Experiments with FGF soaked beads, which were used to challenge the movement behaviour of GFP labelled primitive streak explants, or which were grafted into the embryo, provided strong evidence that these movements are controlled by FGF-8 mediated repulsion from the streak and subsequent FGF-4 mediated attraction towards the notochord. This was confirmed by interference with FGF signaling using the FGF receptor inhibitor SU5402, or by electroporation of a dominant negative FGF receptor GFP fusion construct. These results were consistent with phenotypes of homozygous FGF-8 knock-out mice, where mesodermal cells are 'trapped' in the streak (Sun et al., 1999). Experiments in mouse also suggest that FGFR1 signalling is required for streak cells to undergo epithelial to mesenchymal transition by down-regulating E-cadherin expression (Ciruna and Rossant, 2001).

The migration of cardiac progenitor cells in developing embryos

Chick embryos are very similar to human embryos in their early morphogenesis and we are currently using the method described above (Yang et al., 2002) to establish the movement trajectories of cardiac precursors. According to earlier fate mapping studies, these leave the primitive streak at HH3+ (Rosenquist, 1970; Garcia-Martinez and Schoenwolf, 1993). We have begun to label cardiogenic precursors in the primitive streak with GFP by electroporation of DNA expression vectors into gastrula stage embryos in EC culture (Chapman et al., 2001). When GFP is expressed at sufficient levels, the labelled cells from prospective cardiogenic regions are grafted to unlabelled hosts. To identify where and when cardiac precursors emerge from the primitive streak and to characterize their movement trajectories, cell movement is observed for up to 24 hours (HH stage 8/9, **Figure 3**). We are currently employing this experimental system to investigate whether cardiogenic precursor cell movements are also guided by FGF signals in vertebrate embryos. Interestingly, studies of the *Drosophila* FGF receptor mutant, *heartless*, indicate that FGF signalling is required for the migration of cardiac mesoderm. In addition, we will use this system to address how Wnt signalling may influence cardiac cell movement behaviour, by affecting gene expression and/or cell adhesive properties.

Conclusion and outlook

Pluripotent embryonic cells have to receive the correct signals and environmental stimuli to differentiate appropriately. In recent years, much has been learned about this fundamental process from studies in different model organisms. Ongoing studies will elucidate the factors involved in guiding the movements of prospective cardiac cells and will shed light on the question of whether cell fate specification and the control of movement behaviour are linked.

Acknowledgements

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Secretary's Column

The BSCR returned to London, after three and a half years out of town, for the autumn scientific meeting organized by Professor Ajay Shah and Dr Alison Cave on 9-10 September on the Guy's Campus of King's College. The panorama from the top of the Guy's Tower was spectacular, but there was no difficulty in being drawn away to the lecture theatre by the excellent series of symposia on 'Integrative cardiovascular physiology in gene-modified models'. In addition, the work described in just over 40 abstracts was presented, some as themed oral presentations and the others as posters. It seems that the initiative of free membership on top of a generous bursary scheme for students has impacted favourably on meeting attendance. Please remember that undergraduate students also can apply for membership and a bursary, in particular for presenting findings from final year research projects.

The London meeting also provided the opportunity of taking forward the business of the BSCR, firstly with a meeting of the Committee and then later, the AGM. At the AGM, the Chairman reported on a previous also highly successful meeting which took place during 2003/4, in Manchester, and gave notice of future main meetings to be held in Leicester (Spring 2005) and London (Autumn 2005). A BSCR symposium on 'Repairing the broken heart: the promise of stem cells' was held at the 2004 British Cardiac Society meeting in Manchester and a joint one with the British Atherosclerosis Society is scheduled for the BCS meeting in May 2005, also to be held in Manchester. Finally, the continued sponsorship from Aventis was highlighted as a significant contribution to the strength of the Society, along with the support given for invited speakers by the BCS and the National Heart Research Fund. This was taken up in an interim report provided by the Treasurer, which showed that expenditure was covered by income and the total reserves reflected a comfortable position. The Secretary's report concerned mostly a consideration of the current committee membership and the proposals to fill vacancies which would arise in December 2004. My own position as Secretary, having been in office for the past three years, and that of Dr Mike Curtis, who has been the Treasurer for the last six years, would terminate, in the usual order of affairs, at the end of the year. Showing, however, just how much we enjoy and are dedicated to the BSCR, it was put to the Committee that we would each run for another term, that is, unless anyone else wanted to take over. Well, we weren't killed in the rush, so the proposal was put to the Society membership present at the AGM and approved. Four ordinary members of the committee would also finish their terms of office, namely Professor Gavin Brooks, Dr Gillian Gray, Professor Ajay Shah and Dr Saadeh Suleiman. So with four vacant positions to be filled, a postal ballot of the membership was held in August. Dr Gillian Gray was re-elected and others elected were Dr Andrew Baker (Glasgow), Dr Katrina Bicknell (Reading) and Dr Chris Jackson (Bristol), and approval was obtained from the membership at the AGM. Retiring members were thanked for their contribution to the continuing business of the BSCR, which was in addition to having all run excellent scientific meetings within the last few years. The composition of the committee from January 2005 will include three clinical scientists, so meets with the requirement of the constitution. At the end of 2005, however, these three members will have completed terms of three years, so we will be looking particularly for clinicians for the vacant positions to be taken up in January 2006.

Barbara McDermott

Cardiovascular Related Meetings

Scientific Sessions of the American Heart Association. November 7th-10th, 2004. Morial Convention Centre, New Orleans, Louisiana, USA. Enquiries: American Heart Association, Meetings and Councils, 7272 Greenville Avenue, Dallas TX 75231. Tel +1 214 706 1543; Fax +1 214 373 3406; E-mail: scientificconferences@amhrt.org; Website: www.americanheart.org

The Failing Heart under Stress. 24 - 27 November 2004. Amsterdam, Netherlands. For further information, please contact EUROECHO Secretariat: ESC, 2035 route des Colles, Les Templiers - BP 179, 06903 Sophia Antipolis Cedex, France. Tel: +33 (0) 4 92 94 76 00; Fax: +33 (0) 4 92 94 76 01;E-mail:info@failingheart.org; Website: http://www.failingheart.org

EUROECHO 8 Annual Meeting of the European Association of Echocardiography Athens, Greece, 1st-4th December, 2004. For further information, please call EUROECHO Secretariat: ESC, 2035 route des Colles, Les Templiers - BP 179, 06903 Sophia Antipolis Cedex, France. Tel: +33 (0) 4 92 94 76 00; Fax: +33 (0) 4 92 94 76 01; E-mail: euroecho@escardio.org; Website: www.escardio.org.

Winter Meeting of the Working Group on Myocardial Function "Molecular Mechanisms in Heart Failure".13th - 15th January 2005. Isola 2000, France. Further information can be obtained from: EUROECHO Secretariat: ESC, 2035 route des Colles, Les Templiers - BP 179, 06903 Sophia Antipolis Cedex, France. Tel: +33 (0) 4 92 94 76 00; Fax: +33 (0) 4 92 94 76 01; E-mail: hasenfus@med.uni-goettingen.de

The Cellular Biology of Atherosclerosis (A7) Jan 22 - 27, 2005. Keystone, Colorado. For further information: Phone: (800) 253-0685 or (970) 262-1230; Fax: (970) 262-1525; info@keystonesymposia.org; Website:http://www.keystonesymposia.org/

Molecular Biology of Cardiac Diseases and Regeneration (D2) Apr 3 - 8, 2005 Steamboat Springs, Colorado. For further information: Phone: (800) 253-0685 or (970) 262-1230; Fax: (970) 262-1525; info@keystonesymposia.org; Website: http://www.keystonesymposia.org/

Heart Failure 2005. 11th-14th June. Lisbon, Portugal. For further information: EUROECHO Secretariat: ESC, 2035 route des Colles, Les Templiers - BP 179, 06903 Sophia Antipolis Cedex, France. Tel: +33 (0) 4 92 94 76 00; Fax: +33 (0) 4 92 94 76 01;E-mail: HFsecretariat@escardio.org; http://www.escardio.org/congresses/HF2005/general_information/

Travel Reports for *The* Bulletin

The Bulletin editors are happy to publishes travel reports written by BSCR members. These can be on any conference, course or laboratory visit of interest to other members and could perhaps contain photographs. If you are planning on travelling to a cardiovascular-related meeting and would like to write a report for the Bulletin, please contact the editors. A bursary of **£100** is available towards the cost of your visit, and this will be provided on receipt of the report. *Bon voyage!*

XXV European Section Meeting, Intenational Society for Heart Research. 22-26 June, 2005. Tromso, Norway. Enquiries: Dr T. Larsen, Department of Medical Physiology, Faculty of Medicine, University of Tromso, N-9037 Tromso, Norway. Tel: +47 77 644694; Fax: +47 77 645440; E-mail: ishr-tromso2005@fagmed.uit.no; Website: www.fm.uit.no/ishr2005.

International Academy of Cardiology - 12th World Congress on Heart Disease, New Trends in Research, Diagnosis and Treatment. 16 July 2005 - 19 July 2005. Vancouver, Canada. Contact: klimedco@ucla.edu; Website: www.CardiologyOnline.com

European Society of Cardiology Congress 2005. 3rd-7th September, 2005. Stockholm, Sweden. E-mail: congress@cardio.org.

3rd European Meeting on Vascular Biology and Medicine 2005. 28-30 September, 2005. Hamburg, Germany. For further information: Address: M:con, Rosengartenplatz 2, 68161 Mannheim, Germany; Tel: +49 621 4106-137; Fax: +49 621 4106 207; E-mail: daniela.ruckiegel@mcon-mannheim.de; http://www.embvm.org

World Congress of Cardiology 2006: Joint Congress of the European Society of Cardiology and the World Heart Federation. 2nd - 6th September 2006. Barcelona, Spain. Further information can be obtained from: EUROECHO Secretariat: ESC, 2035 route des Colles, Les Templiers - BP 179, 06903 Sophia Antipolis Cedex, France. Tel: +33 (0) 4 92 94 76 00; Fax: +33 (0) 4 92 94 76 01; E-mail:webmaster@escardio.org; Website: www.escardio.org

For up to date information on forthcoming meetings, workshops and symposia, please remember to check the

new BSCR Website:

http://www.bcs.com/affiliates/bscr.html

*** Notice to current student members ***

Membership of the BSCR is now free to all students registered for a higher degree.

If you pay your membership of the BSCR by direct debit, please cancel and make this known to antonio.cavalheiro@kcl.ac.uk

There will continue to be a fee for Joint membership of the BSCR/ ISHR

University of Bristol, UK
17th - 20th July 2005

4th international symposium the mammalian myocardium

http://www.bristol.ac.uk/mm2005/

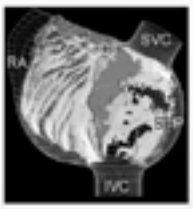
CHANNELS: Trafficking & Biophysics
W. Catterall (USA), I. Cohen (USA), D. Roden (USA),
M. Sanguinetti (USA), D. Yue (USA)

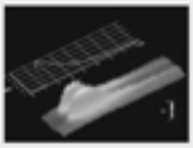
CELL & TISSUE ELECTROPHYSIOLOGY
A. Kleber (Switzerland), D. Paterson (UK),
R. Winslow (USA)

EXCITATION-CONTRACTION COUPLING
H. Cheng (USA), S. Gyorke (USA),
G. Isenberg (Germany), A. Marks (USA),
R. Sitsapesan (UK)

CELL SIGNALLING
R. Fischmeister (France), E. Kranias (USA),
E. Moore (Canada), M. Rosen (USA)

HYPERTROPHY, FAILURE, ARRHYTHMIAS & REMODELLING
G. Hasenfuss (Germany), S. Houser (USA),
J. Molkentian (USA), S. Nattel (Canada),
U. Ravens (Germany), G. Smith (UK)





The Mammalian Myocardium
Bristol 2005

ORGANIZERS:
M.R. Boyett (Leeds, UK)
D.A. Eisner (Manchester, UK)
J.C. Hancox (Bristol, UK)
G. Hart (Liverpool, UK)
C.H.Orchard (Leeds/Bristol, UK)

BRITISH HEART FOUNDATION GRANTS

CHAIRS AND PROGRAMME GRANTS COMMITTEE, MAY 2004

Programme Grants

Prof M Frenneaux et al, University of Wales School of Medicine. "Mechanisms controlling venous tone and preload in CHF" (5 years) £626,902

Dr RW Farndale & Dr W Ouwehand, University of Cambridge. "Platelet receptors for collagen; activatory pathways, their control and inhibition" (5 years, renewal) £821,815

Prof GL Smith & Prof S Cobbe, University of Glasgow. "A longitudinal study of myocardial remodelling following infarction in the rabbit heart" (5 years, renewal) £1,005,488

Basic Science Lectureships

Dr SE Ozanne, Addenbrooke's Hospital, Cambridge. "Molecular mechanisms by which poor early growth links coronary artery disease, insulin resistance and type 2 diabetes" (5 years) £277,198

Dr CH George, University of Wales College of Medicine. "Molecular mechanisms underlying ryanodine receptor dysfunction in stress-induced ventricular tachycardia" (5 years) £243,736

PROJECT GRANTS COMMITTEE, MAY 2004

Professor M J Shattock & Dr W Fuller, St Thomas' Hospital, London. "Electrophysiological characterisation of sodium-potassium pump regulation by phospholemman" (3 years) £160,994

Dr B H Cuthbertson et al, University of Aberdeen. "The use of BNP as a predictor of outcome in coronary artery bypass surgery" (3 years) £127,534

Professor M Galinanes et al, Glenfield Hospital, Leicester. "Efficacy of mode of delivery of autologous bone marrow cells into heart scar muscle for the recovery of contractile function" (3 years) £157,540

Dr I P Salt, University of Glasgow. "Regulation of endothelial nitric oxide synthesis by the AMP- activated protein kinase cascade" (3 years) £119,703

Prof C Kielty & Dr C Shuttleworth, University of Manchester. "Marfan syndrome: fibrillin-1 mutations and disease severity correlations" (3 years) £205,584

Professor G Brooks & Dr K Patel, University of Reading. "The role of myostatin as a cell cycle regulator of cardiomyocyte growth" (3 years) £155,452

Professor M R MacLean, University of Glasgow. "Interactions between serotonin transport inhibitors and 5-HT_{1B} receptors in pulmonary arteries" (3 years) £139,442

Dr L Zhao et al, Hammersmith Hospital, London."The role of tetrahydrobiopterin in the pulmonary circulation" (2 years) £88,578

Professor V R Preedy et al, King's College London. "A proteomic investigation into post-translationally formed protein adducts in alcoholic cardiomyopathy" (3 years) £153,429

Dr J M East & Professor A G Lee, University of Southampton. "Targeting the cardiac calcium pump modulator phospholamban to the sarcoplasmic reticulum: identifying targeting motifs and characterisation of the retention apparatus" (3 years) £126,463

Professor G L Smith, University of Glasgow. "A study of the subcellular actions of sorcin in ventricular cardiac muscle" (3 years) £130,251

Professor C S Peers, University of Leeds. "Is testosterone an endogenous Ca^{2+} channel antagonist?" (2 years) £79,494

Professor M Perretti et al, Queen Mary, University of London."Investigation into the protective role of carbon monoxide (CO) in vascular inflammation using new CO-releasing molecules (CO- RMs)" (2 years) £96,513

Dr K T MacLeod & Prof P Collins, NHLI, London. "The effect of oestrogen-related compounds on L-type Ca current in the heart" (2 years) £104,297

Professor A D Struthers et al, Ninewells Hospital Med Sch, Dundee. "Does aldosterone blockade improve endothelial dysfunction in patients with coronary artery disease but without heart failure?" (2.5 years) £104,071

Dr A Graham, Glasgow Caledonian University. "Mitochondrial sterol 27-hydroxylase and regulation of macrophage cholesterol efflux pathways" (2 years) £80,297

Professor J D Pearson et al, Guy's Hospital, London. "Polymorphonuclear leucocytes, vascular damage and systemic inflammation" (3 years) £99,356

Professor K P Moore, Royal Free Hospital, UCL, London. "Anandamide and cardiac dysfunction in cirrhosis" (3 years) £166,290

Dr S Currie & Professor G L Smith, University of Glasgow. "An integrated biochemical and physiological study of the cardiac ryanodine receptor complex and its regulation by calcium/calmodulin dependent protein kinase II" (3 years) £171,586

Dr R C M Siow, Guy's Hospital, London. "Effects of TGF-β1 on Nrf2 mediated heme oxygenase-1 expression in vascular smooth muscle cells" (2 years) £100,691

FELLOWSHIPS COMMITTEE, JULY 2004

Intermediate Research Fellowships

Dr V Pucovsky, St George's Hospital Medical School, London. "Investigation of non-contractile cells with filopodia resembling interstitial cells of Cajal, freshly isolated from the wall of resistance arteries" (3 years) £166,398

Dr A Snabaitis, St Thomas' Hospital, London. "Novel regulation of the Na^+/H^+ exchanger by protein kinase B in the adult myocardium" (3 years) £170,226

Dr M Mayr, St George's Hospital Medical School, London. "Proteomic analysis of smooth muscle cells in response to mechanical stress" (3 years) £158,861

Junior Research Fellowships

Dr T C Pakrashi, St George's Hospital Medical School, London. "Electrocardiographic assessment of response to cardiac resynchronization therapy" (2 years) £95,522

Dr B J McHugh, University of Edinburgh. "Investigating novel modulators of integrin affinity" (2 years) £77,617

Dr L Howard, Addenbrooke's Hospital, Cambridge. "Mechansims of pulmonary artery smooth muscle cell proliferation and survival in hypoxia: a key role for the phosphoinositide 3-kinase/Akt pathway" (2 years) £109,454

Dr S Muzaffar, Bristol Royal Infirmary. "The pathobiology of reactive oxygen species in vein graft disease" (2 years) £66,953

Dr S M Munir, St Thomas' Hospital, London. "Effects of exercise on pressure wave reflection" (2 years) £106,549

Dr W M Bradlow, Royal Brompton Hospital, London. "Assessment of structure and function of the right ventricle and central pulmonary arteries in pulmonary hypertension using cardiovascular magnetic resonance" (2 years) £97,743

Dr L E Hudsmith, John Radcliffe Hospital, Oxford. "Hypertrophic cardiomyopathy and the myocardial energy depletion paradigm - a cardiac magnetic resonance study in patients with genotyped HCM" (2 years) £97,443

Clinical PhD Studentships

Dr M J Zaman, University College London. "Prognosis of coronary disease in different South Asian populations in Britain" (3 years) £155,624

Dr G Pieles, University of Oxford. "Genetic mechanisms in heart development" (3 years) £112,570

PhD Studentships

Unnamed and Dr A Baker, University of Glasgow. "Targeted gene delivery *in vivo* using a novel adeno-associated virus-2 (AAV-2) virus library" (3 years) £68,208

Miss R David, Hammersmith Hospital, London. "The role of Vav1 in the regulation of T cell recruitment in inflammatory sites" (3 years) £73,500

Mr M Eikebu, University College London. "The role of G-protein coupled receptor dimerisation in cardiac signalling" (3 years) £83,484

Unnamed and Dr P Riley, Institute of Child Health (UCL). "Investigating nucleolar sequestering of Hand1 as a novel mechanism of negatively regulating Hand1 activity in the developing heart" (3 years) £74,214

Ms G Pourmahram, Guy's Hospital, London. "Modulation of hypoxic pulmonary vasoconstriction by luminal flow" (3 years), £74,736

Mr D J Rowlands, Royal Free Campus - (UCL). "Expression of ApoAI-Milano and analogues: towards effective HDL therapy for acute treatment of atherosclerosis" (3 years) £77,710

Unnamed and Dr C Kennedy, University of Strathclyde. "Signalling mechanisms underlying P2Y receptor-mediated vasoconstriction in pulmonary arteries" (3 years) £68,208

Unnamed and Prof D Firmin, Royal Brompton Hospital, London. "Investigating imaging artefacts and improving MRI measurement of myocardial perfusion" (3 years) £63,653

Miss K A King, University of Oxford. "Determination of the functional role of individual domains of cardiac myosin binding protein-C and the effects of cardiomyopathy-causing mutations" (3 years) £80,933

Miss H Mikolajek, University of Southampton. "Structural basis of complement activation by C-reactive protein in atherothrombotic disease" (3 years) £68,208

Miss H Woolson, University of Glasgow. "Suppressor of cytokine signalling-3 (SOCS3) induction as a novel mechanism of A2A adenosine receptor-mediated inhibition of pro-inflammatory cytokine signalling in endothelial cells" (3 years) £68,508

Miss J A Wray, Barts & the London NHS Trust. "Cytochrome P450 2J2 as an endogenous source of PPAR-alpha ligands" (3 years) £73,530

Miss A Asimaki, University College London. "Arrythmogenic right ventricular cardiomyopathy: a disease of the desmosome; genetic and functional studies" (3 years) £73,500

Travelling Fellowship

Dr S Thomas, National Inst for Biological Standards, Herts, "Real-time studies of platelet and aggregation, thrombus formation and coagulation under flow conditions using confocal technology and thrombin generation" (6 months) £6,000

Articles for *The* Bulletin

Would you like to write a Review or Laboratory Profile for the BSCR Bulletin? These articles provide an excellent opportunity to let BSCR members know about your research activities and also provide an insight into your research field.

We are keen to hear from anyone in cardiovascular research who would be willing to write for *The* Bulletin.

If you are interested, please contact the Bulletin editors with your ideas: Helen (h.maddock@coventry.ac.uk) or Nicola (N.Smart@ich.ucl.ac.uk)

Submission Deadlines for *The* Bulletin:

Volume	*Date*	*Deadline*
18 (1)	***January 2005***	*December 1st*
18(2)	***April 2005***	*March 1st*
18 (3)	***July 2005***	*June 1st*
18 (4)	***October 2005***	*September 1st*

Cardiovascular Related Wellcome Trust Grants

June to August 2004

Research Career Develpoment Fellowships in Basic Biomedical Science

Dr Keith Brain, Department of Pharmacology, University of Oxford. The Regulation of Excitatory and Inhibitory Junctional Transmission. 48 Months. £324,808

Dr Eleni Tzima, Wellcome Trust Cent Cell-Matrix Research, School of Biological Sciences, University of Manchester. Role of Cell-Cell Junctions and Integrins in Endothelial Cell Responses to Fluid Shear Stress. 48 Months. £449,340

Clinician Scientist Fellowship

Dr N J Alp, Department of Cardiovascular Medicine, John Radcliffe Hospital, University of Oxford. Tetrahydrobiopterin Regulation of Endothelial Nitric Oxide Synthase in Vascular Disease. 48 Months. £582,546

University Translation Awards

Dr Stephen Lewis Hart, Molecular Immunology Unit, Institute of Child Health, London. Molecular Therapy For Vascular Diseases. 24 Months. £393,029

Advanced Training Fellowship

Dr G D Batty, MRC Social and Public Health Science Unit, Glasgow. Cognition and Health: Analysis of Data from a Series of Population-Based Studies. 12 Months. £1,000

Collaborative Research Initiative Grants

Dr D V Gordienko, Department of Pharmacology and Clinical Pharmacology, Jenner Wing, St George's Hospital Medical School, London. Functional Coupling Between Receptors, Receptor-Operated Channels and Intracellular Ca2+ Homeostasis in Smooth Muscle Cells. 36 Months. £116,084

Professor Nina Japundzic-Zigon, Department of Medicine, Bristol Royal Infirmary, University of Bristol. The Role of Brainstem and Spinal Cord Vasopressin Receptors in the Modulation of Autonomic Cardiovascular Controls. 36 Months. £120,006

Dr Peter Ferdinandy, Department of Veterinary Basic Sciences, Royal Veterinary College, London. Roles of Cgmp/Cgk-I Signalling in Ischaemic Myocardium. 36 Months. £98,882

Training Fellowships for Medical and Dental Graduates

Dr Kelvin Lee, Department of Cardiology, University of Newcastle, Newcastle Upon Tyne. A Genomic Approach to Atherosclerotic Plaque Vunerability. 3 Months. £10,832

Dr Lucinda K Barrett, Wolfson Institute For Biomedical Research, University College London. Mechanism of Vasopressin Hypersensitivity in Septic Shock. 36 Months. £171,705

Project Grants

Dr D Bishop-Bailey, Department of Cardiac, Vasc and Inflammation, William Harvey Research Institute, St Bart's and Royal London Medical School. The Farnesoid X Receptor (Fxr) As a Novel Target in Cardiovascular Disease. 36 Months. £159,686

Dr J G McGeown, School of Medicine, Medical Biology Centre, Queen's University of Belfast, Northern Ireland. Instiation and Intracellular Coupling of Ca2+-Signals in Intact Retinal Arterioles. 36 Months. £306,373

Dr D A Terrar, Department of Pharmacology, University of Oxford. Possible Role of Nicotinic Acid Adenine Dinucleotide Phosphate (Naadp) in the Control of Cytosolic Calcium and Contraction in Cardiac Ventricular Myocytes. 36 Months. £210,006

Dr Mark Wheatley, School of Biosciences, University of Birmingham. the Extracellular Surface of a Peptide Hormone G-Protein-Coupled Receptor Family: Its Role in Hormone Binding, Ligand Selectivity and Receptor Activation. 36 Months. £187,649

Dr Helen M Arthur, Institute of Human Genetics, The International Centre For Life, University Of Newcastle. Cardiovascular Development and Maintenance of Mature Blood Vessels: The Role of Endoglin in vivo. 36 Months. £263,400

Professor Thomas B Bolton, Department of Pharmacology and Clinical Pharmacology, Jenner Wing, St George's Hospital Medical School, London. Functional Role of Non-Contractile Cells (Interstitual Cells) With Processes (Filopodia) Recently Discovered in the Wall of Arteries and Veins. 36 Months. £602,911

HCPC Masters Research Training Fellowship

Dr Felix Kembe Assah, MRC Epidemiology Unit, University of Cambridge. Development and Validation of Feasible Methods For Measuring Physical Activity in Population Studies in Africa. 30 Months. £94,677

Dr Saleem Jessani, Aga Khan University, Karachi, Pakistan. Relationship Between Salt and Blood Pressure in South Asian Population in Pakistan. 30 Months. £41,283

Dr J J Miranda-Montero, Department of Epidemiology and Pop Health, Epidemiology Unit, London School of Hygiene and Tropical Medicine. The Effect on Cardiovascular Risk Factors of Migration to Urban Cities in Peru. 30 Months. £81,327

Wellcome - South African Senior Research Fellowships

Dr Johanna C Moolman-Smook, US/MRC Centre For Mol and Cell Biology, Tygerberg South Africa. Identification of Sarcomere-Associated Modifiers of Cardiac Phenotype in Hypertrophic Cardiomyopathy Families. 60 Months. £450,000

Symposium

Helen Alderson, World Heart Federation, Geneva, Switzerland. 37th 10-Day International Teaching Seminar On Cardiovascular Disease Epidemiology and Prevention. 2 Months. £10,000

THE BRITISH SOCIETY FOR CARDIOVASCULAR RESEARCH

BSCR Spring Meeting 2004

Emerging Concepts in Atherothrombosis

Dates: Thursday 21st and Friday 22nd April, 2005

Venue: Stamford Hall, University of Leicester, Leicester.

Organisers: Professor Nilesh J Samani and Professor Alison H Goodall

Objectives: Atherothrombosis is the underlying mechanism for the majority of clinical cardiovascular events. There is increasing evidence that factors in both the vessel wall and the blood contribute to atherothrombotic risk. This symposium will cover current and emerging concepts regarding the molecular, cellular and genetic mechanisms that underlie atherothrombosis and their potential impact on future therapeutic strategies.

Program: The program will consist of state-of-the-art presentations by leaders in the field. Part of the meeting will be devoted to oral presentation of selected abstracts, and poster presentations. Prizes will be awarded for the best oral and best poster presentations given by young investigators.

Travel & Accommodation: Stamford Hall is located about 2 miles from the Centre of Leicester and the train station, and is easily accessible by bus or taxi. Accommodation will be available at the Hall or in hotels nearby (if required). Logistics for the meeting will be handled by Fiona Legate, Millbrook Medical [fionalegate@millbrookconferences.co.uk]

Registration (excluding accommodation): Free to BSCR members, £40 for non-members.

Bursaries: The Society will consider awarding travel grants of up to £150 to *bona fide* students.

A full programme, the abstract pro-forma and meeting registration / accommodation forms will be available on the BSCR website in December 2004. Forms for application for student bursaries can be downloaded at anytime.

Deadline for submission of abstracts, registration and application for student bursaries: 31st January, 2005.

Further enquiries: Enquiries about the programme should be directed to Professor Nilesh Samani, Cardiology Group, Department of Cardiovascular Sciences, University of Leicester, Clinical Sciences Wing, Glenfield Hospital, Groby Road, Leicester, LE3 9QP, Leicester. Tel: 0116 2563021; Fax: 0116 2875792;
E-mail: njs@le.ac.uk.

Enquiries about registration and accommodation should be directed to Fiona Legate, Millbrook Conferences Ltd, Suite 13, Devonshire House, Bank Street, Lutterworth, Leicestershire LE17 4AG. Tel: 01455 552559; Fax: 01455 550098;
E-mail: fionalegate@millbrookconferences.co.uk