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The Bulletin

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Contents

Editorial

Happy New Year and Welcome to the January 2009 issue of *The* Bulletin. With the new year comes a new Chairman, new Committee members and a new style Bulletin. We have followed the example of many societies and journals by moving to an environmentally-friendly, online-only format. We hope you will continue to download and enjoy reading your copy of *The* Bulletin.

Our review for this issue has been written by Sarah Withers of the University of Manchester, who was one of the prize winners at the Autumn 2008 BSCR Young Investigators meeting at Bristol. Sarah and colleagues describe their recent studies investigating the effect of perivascular fat on vessel contractility and its modulation by aldosterone. We look forward to publishing the work of many more Young Investigators. Anyone wishing to write either a full review or mini-review is invited to contact us for further information.

Another typically entertaining column from our Secretary Chris Jackson provides an update on the recent goings on of the Society. This is followed by a travel report by Agnieszka Kozak on the ADMA 2008 International Symposium in the beautiful Austrian setting of Bregenz on Lake Constance.

As always, we include details of recently awarded Cardiovascular grants by the British Heart Foundation and Wellcome Trust, and end with a final reminder of our forthcoming meeting, to be held jointly with the British Atherosclerosis Society, in April. Hope to see you there!

Helen Maddock and Nicola Smart

Investigating the effects of Aldosterone on the anti-contractile properties of perivascular fat

by S. Withers, A. Greenstein, R. Aslam, K. Khavandi, K. Sonoyama, A. Price, R.A. Malik and A. M. Heagerty

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With the ever growing incidence of obesity, it is unsurprising that there is increasing interest in fat. Obesity, particularly abdominal adiposity, is associated with an increased risk of a number of co-morbidities including type 2 diabetes, metabolic syndrome and hypertension. Although this link is well established, the mechanisms behind the association are less well understood, and it is this area of adipose research which are of particular interest to our group.

The presence of healthy fat around an artery, or perivascular fat, exerts an anti-contractile effect (**Figure 1**) via production of a releasable factor, which has vasoactive properties (Soltis et al., 1991; Ahima et al., 2000), thus influencing arterial basal tone. With increasing obesity, adipose tissue undergoes a series of changes including adipocyte hyperplasia (Marques et al., 1998) and hypertrophy (Bahceci et al., 2007), increased intracellular lipids, increased inflammatory markers including TNF-α and MCP-1 (Kern 1997; Lyon et al., 2005), and changes in adipokine expression, such as increased leptin (Maffei et al., 1995) and decreased adiponectin (Chandran et al., 2003). We have recently observed that these changes in the perivascular adipose tissue are associated with a loss of anti-contractile function, possibly illuminating a mechanistic relationship between obesity and vascular dysfunction.

Aldosterone is an attractive link in the chain between obesity and subsequent complications. Aside from classical genomic actions (reviewed by Funder 1996) there are also non-genomic effects which are typically faster and thought to involve an, as yet, unidentified receptor, which initiates second messenger pathways, leading to increased intracellular calcium (Losel et al., 2004). In relation to the vasculature, Aldosterone is known to cause (1) effects on the endothelium, which result in increased constriction (Lariviere et al., 1993) and oxidation (Haller 1997), and reduced relaxation (Ahokas et al., 2003) (2) effects on vascular structure resulting in remodelling (Virdis et al., 2002; Sanz-Rosa et al., 2005) and (3) inflammatory effects (Sun et al., 2002; Joffe et al., 2005)

The aim of this current study was to determine whether Aldosterone can influence the anti-contractile effect of perivascular fat, and to understand the mechanisms which may be involved. This was done by comparing the effects of aldosterone using an established model of damage to perivascular adipose function; hypoxic incubation. We also investigated whether any damage was reversible using commercially available antagonists.

Wire myography was used to assess contractility. Arteries from the mesenteric bed of healthy male wistar rats were used with their surrounding fat intact or with the fat entirely removed. Dose response curves to noradrenaline were constructed to compare contractility before and after addition of Aldosterone, Eplerenone and/or hypoxia. Data are expressed

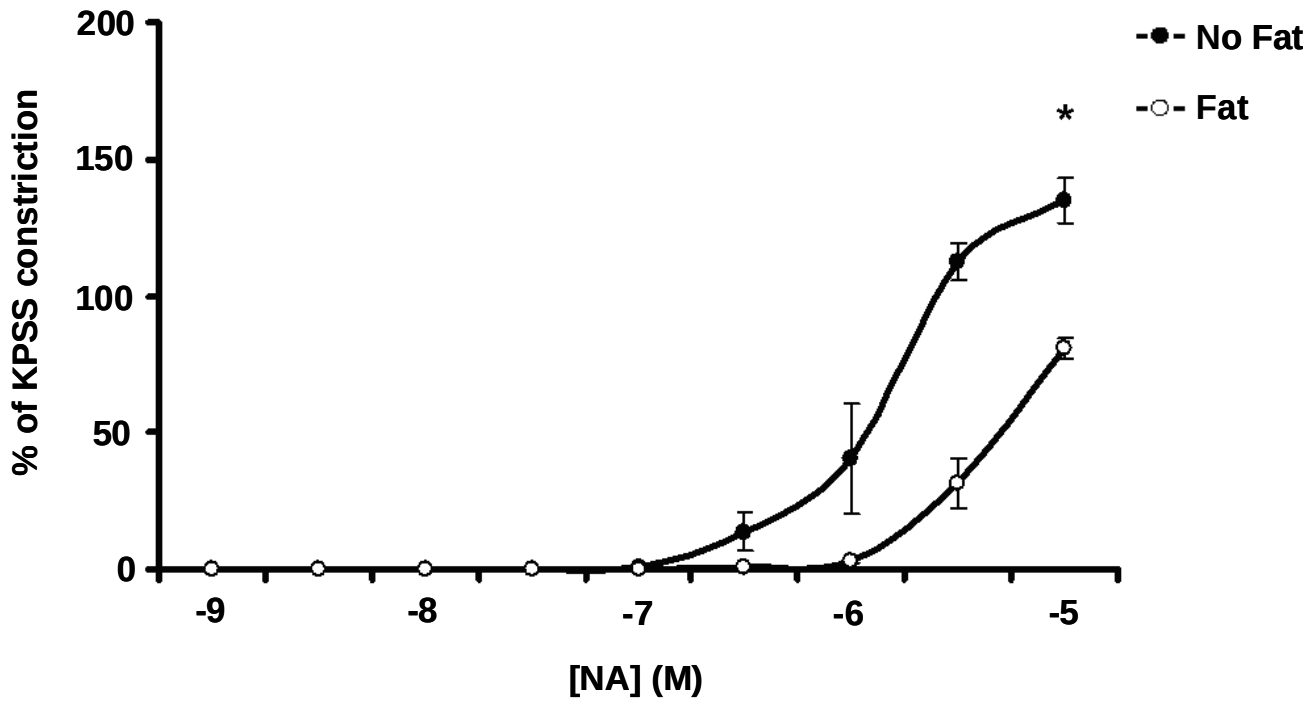

Figure 1. The effect of healthy perivascular fat on contractility. The presence of perivascular fat around the artery causes a significant reduction in contractile response to noradrenaline (*P<0.05, n=21).

as a mean percentage of the arterial response to KPSS, a high potassium solution, ± SEM.

Incubation of arteries surrounded by fat with Aldosterone (5nM) for 10 minutes caused an increase in constriction in response to noradrenaline (Fat: 80.9±4% n=21, Fat + Aldosterone: 123.6±5.5%, n=9, P<0.05), the response was similar to that observed in arteries without fat (No fat: 135±8.2%, n=21), that is, the anti-contractile effect of healthy fat was lost following incubation with Aldosterone. This was presumed to be a non-genomic effect as it occurred in a relatively short incubation period, which precludes the necessary genomic changes required to cause such an effect. This was further supported in that the non-genomic antagonist, Eplerenone (5µM), was able to restore the anti-contractile capacity of the fat (Fat + Aldosterone + Eplerenone: 92.6±3.9%, n=9) (**Figure 2**). The mechanism by which Eplerenone exerts its activity has not yet been fully elucidated, although it is well known that it does not cause antagonism of the genomic effects associated with Aldosterone (Delyani et al., 2001).

Longer incubation of arteries with Aldosterone (3 hours) evoked a further increase in contractility compared to the shorter incubation (Fat + Long Aldosterone: 133.6±4.6%, n=9). This was not fully reversible by Eplerenone (Fat + long Aldosterone + long Eplerenone: 121.6±1.8%, n=9), suggesting that Aldosterone is able to cause non-genomic AND genomic effects on vascular contractility in the presence of perivascular fat (**Figure 2**).

The next question was to address how Aldosterone was able to affect contractility. Previous literature suggested that Aldosterone may share a common pathway with hypoxia and inflammation; for instance both are able to cause the generation of reactive oxygen species via NADPH phosphorylation (Kulisz et al., 2002; Nagata et al., 2006) and eNOS uncoupling (Konduri et al., 2003; Landmesser et al., 2003). We therefore created a hypoxic environment around the arteries using 95%/N_2/5% CO_2 for

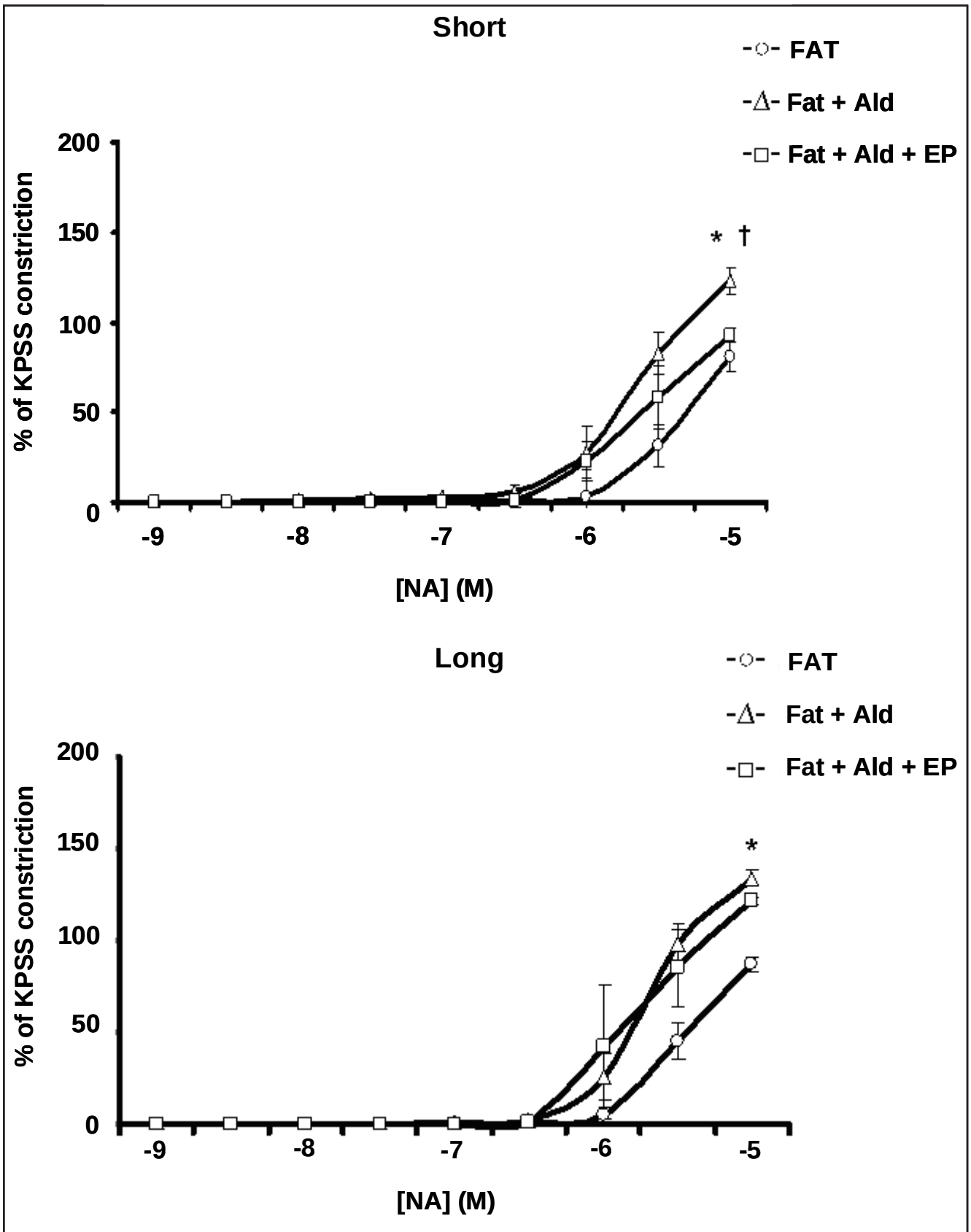

Figure 2. Effects of short and long incubation of Aldosterone on constriction of arteries to a dose response of noradrenaline in the presence of perivascular fat. Arteries were incubated for 10 mins (Short) or 3 hours (Long) with 5nM Aldosterone. Following both incubations, there was an increase in arterial contractility (*P<0.05, n=9), however despite Eplerenone (5μM) being able to significantly reverse this effect following short Aldosterone incubation (†P<0.05, n=9), this was not the case after a 3 hour incubation, suggesting that the increase in contractility was in part due to genomic changes.

3hours, which caused an increase in constriction to a similar level of that observed following treatment with Aldosterone (Fat + Aldosterone: 123.6±5.5%, Fat + Hypoxia: 117.5±11.8%). Of particular interest is that, despite NO Aldosterone being added to the wire myograph bath, the incubation of arteries with Eplerenone during hypoxia was able to restore the anti-contractile effect of the perivascular fat (Fat + Hypoxia + Eplerenone: 84.4±16.5%, n=8) (**Figure 3**), suggesting that hypoxia causes changes in adipose function, following a similar pathway to the non-genomic effects of Aldosterone.

This work has demonstrated that the anti-contractile property of fat is lost upon incubation with Aldosterone, and that changes are associated with both its genomic and non-genomic actions on the vasculature. Eplerenone is in some way able to reverse the non-genomic actions, although is not sufficient following longer incubations. Hypoxia also affects contractility in a similar way to Aldosterone, which we believe may occur via a common pathway, as the effects are fully reversible by incubation with the non-genomic Aldosterone antagonist, Eplerenone.

However, despite this work giving us a small insight into how the function of fat can be altered and restored, it has also generated a whole new series of unanswered questions which we are beginning to explore. Further knowledge is required regarding the pathways involved, identifying the receptors that are involved and the series of changes in the fat tissue which result in changes to the vascular response. Despite all these unknowns, the cardiovascular research community is awakening to the concept that fat plays an important role in vascular tone, and we are only now beginning to appreciate the complex mechanisms behind this.

ACKNOWLEDGEMENTS

This work was generously supported by The Wellcome Trust Research Facility, Manchester.

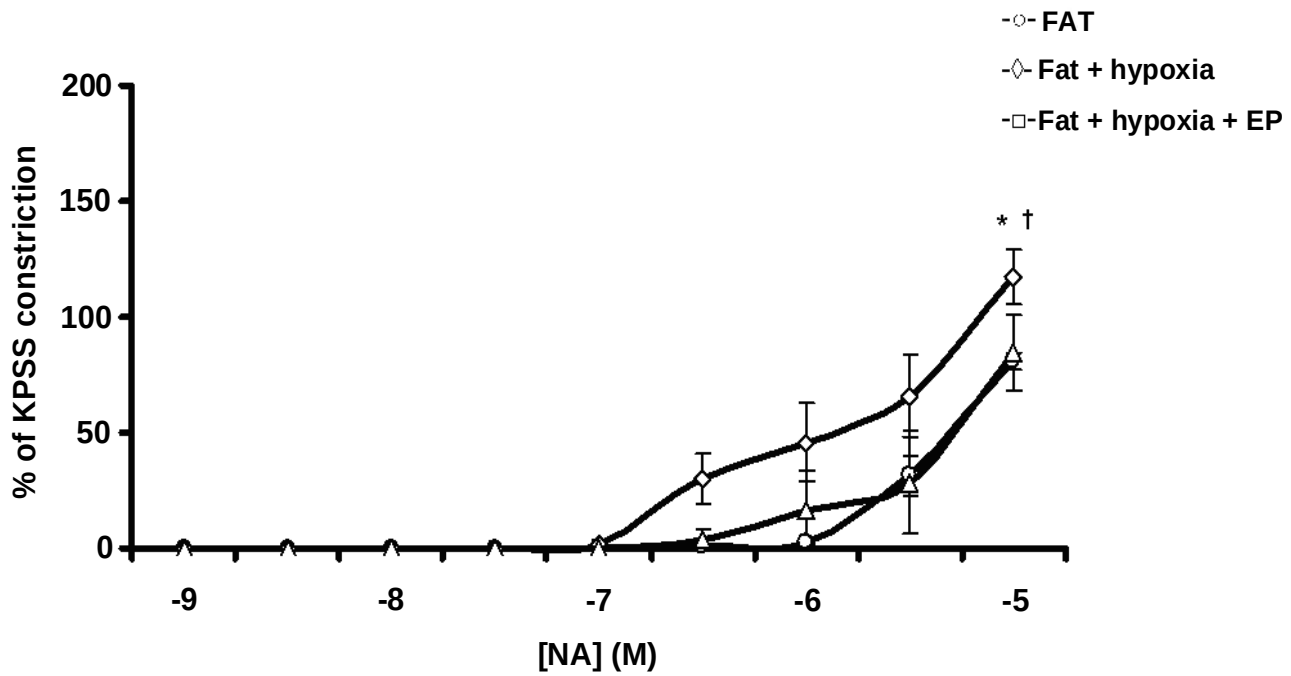

Figure 3. The effect of hypoxia on artery constriction in the presence of perivascular fat. Hypoxia causes a significant increase in constriction in response to noradrenaline (*P<0.05, n=8) which is reversed in the presence of Eplerenone (5μM) (†P<0.05, n=8).

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Sarah Withers was a Young Investigator Prize winner at the Autumn 2008 BSCR Young Investigators meeting in Bristol

Secretary's Column

With the new year comes a new Chair, as Chris Newman takes over from David Eisner in the hot seat. I would like to say what a pleasure it has been to work with David on the BSCR Committee, and that I am looking forward very much to working with Chris.

We also say farewell to our furthest-flung Committee member, Dr Nicola King in Brunei, who has also come to the end of her term of office. I'm sure the whole BSCR will join me in thanking both her and David Eisner for all their hard work on behalf of the Society.

It promises to be a busy year, starting with a joint BSCR/British Atherosclerosis Society workshop on February 5th at the University of Sheffield entitled "Studying Vascular Biology Using the Zebrafish". Tim Chico and Martin Denvir have assembled an excellent programme.

Another joint BSCR/BAS effort follows in April in Oxford with the Spring Meeting on "Atherosclerotic Plaque Rupture". Details of our Autumn Meeting are still being finalised, but it is being organised by Barbara Casadei, Saadeh Suleiman and Kieran Clark and will again be at the University of Oxford. Full details of all meetings and workshops are available on the Society's website (www.bscr.org).

It may be a good idea to store your back issues of the Bulletin carefully as we have now switched to an online-only format. In years to come a complete set of hard copies of the Bulletin in good condition will no doubt fetch premium prices on eBay. However, you should take that advice with a pinch of salt because I decided several years ago to ditch all my old childhood toys but to hang on to my collection of prog rock LPs, with a view to selling them to enthusiastic and stupidly rich collectors. If I had done things the other way round I could have been writing this from a beach on a tropical tax haven, which is pretty much the exact opposite of Bristol Royal Infirmary on a damp January day.

I hope all members enjoyed a peaceful holiday break, and I wish everyone a happy and successful 2009.

P.S. If anyone would like to offer me a small fortune for a slightly scratched copy of the Third Ear Band's "Music from Macbeth" then drop me a line.

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THE BRITISH SOCIETY FOR CARDIOVASCULAR RESEARCH

Joint Spring Meeting 2009: Programme

St. Catherine's College, Oxford

Atherosclerotic Plaque Rupture

Thursday 2nd April

09.00 **Registration** (Medical Sciences Teaching Centre)

09.50 **Introduction and Welcome**

Session 1: Pathology of Atherosclerotic Plaque Rupture

a. Why are only some plaque ruptures lethal?

10:00 What is a Vulnerable Plaque? *Patrick Serruys (Erasmus Medical Center, Rotterdam)*

10:35 Discussion

10:45 How Representative are "Culprit" Plaques? *Allard van der Wal (AMC, Amsterdam)*

11:05 Discussion

b. Do we have an animal model of plaque rupture?

11:15 Spontaneous Plaque Rupture in Mice: Real or Imaginary? *Florian Bea (Heidelberg)*

11:35 Discussion

12:45 Induced Plaque Rupture in Mice: Quick but Dirty? *Erik Biessen (University of Maastricht)*

12:05 Discussion

12:15 **---- Lunch ----**

Session 2: Inside the Unstable Atherosclerotic Plaque

13:15 Inflammation and Instability: Which is Chicken and Which is Egg? *Rob Krams (Imperial College London)*

13:35 Discussion

13:45 Cell Death and Cell Senescence: Root Causes or Collateral Damage? *Martin Bennett (University of Cambridge)*

14:05 Discussion

14:15 Plaque Repair: More Important Than Plaque Rupture? *Allen Burke (CVPath Institute, Maryland)*

14:35 Discussion

14:45 **---- Tea ----**

15:15-16:15

Session 3: Young Investigators: Michael Davies Award and BSCR Award

16:30 **British Atherosclerosis Society John French Lecture**

17:15 **BAS AGM (Medical Sciences Teaching Centre)**

18:30 **Poster Session and Drinks Reception** (St Catherine's College)

19:45 **Conference Dinner and announcement of the winners of the Young Investigator awards**

Friday 3rd April

08:00 **BAS Committee meeting (Medical Sciences Teaching Centre)**

Session 5: Free Communications

09:30 Presentation 1

09:40 Discussion

09:45 Presentation 2

09:55 Discussion

10:00 Presentation 3

10:10 Discussion

10:15 Presentation 4

10:25 Discussion

10:30 Presentation 5

10:40 Discussion

10:45

---- Coffee ----

Session 6: Diagnosis and Treatment of the Vulnerable Plaque

11:15 Imaging the Wall, Not the Lumen *Andreas König (Ludwig-Maximilians-Universität, Munich)*

11:35 Discussion

11:45Do Biomarkers Tell You Any More Than You Already Know? *Juan Carlos Kaski (St Georges, London)*

12:05 Discussion

12:15 Drugs For Primary And Secondary Prevention: From Statins To Beyond *Andrea Mezzetti (University of Chieti)*

12:35 Discussion

12:45 **Presentation of the Clinical Science award for best poster**

12:50 **Concluding remarks**

13:00 **Close of meeting, poster removal, and lunch**

13:00 **BSCR Committee meeting** (Medical Sciences Teaching Centre), over lunch

ADMA 2008 - 4th International Symposium on ADMA

Bregenz, Lake Constance, Austria 28-29th August, 2008

A travel report by Agnieszka Kozak, Centre for Cardiovascular Science, University of Edinburgh, Scotland

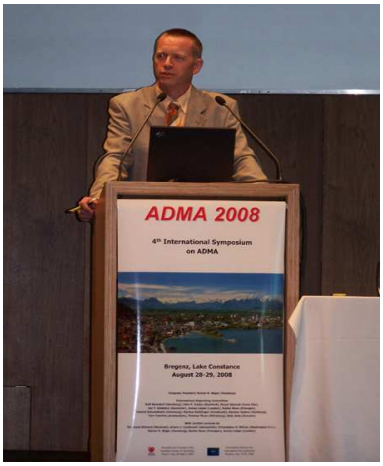
Asymmetric dimethylarginine (ADMA) is an endogenous inhibitor of nitric oxide synthase (NOS) and as such plays an important role in regulation of nitric oxide production. A number of recently published studies indicate the clinical role of ADMA as a mediator of endothelial dysfunction and a marker of cardiovascular risk.

The series of biannual ADMA scientific conferences, initiated in 2002 in Hamburg, Germany, provides an international platform for discussion on the role of ADMA in physiology and pathophysiology. "ADMA 2008" took place in the beautiful city of Bregenz situated on the eastern shores of Europe's third largest lake, Lake Constance. The meeting was held in the Festspielhaus Bregenz, famous for the world's largest floating stage and outstanding open-air opera productions. Unfortunately we had just missed the last of this summer's performances but the conference itself provided plenty of mental stimulation and a taste of Austrian culture.

Festspielhaus Bregenz

The meeting, with fewer than 150 delegates, was relatively small but highly focused, creating a unique opportunity for young investigators to discuss their work with experienced senior researchers. Overall 69 abstracts were presented as oral and poster presentations in 6 sessions spread over 2 days, making this an extremely intense and interesting event.

The symposium began with a warm welcome from Prof Rainer Böger, the meeting organizer, who briefly introduced the program and indicated how the ADMA field had grown in depth and breadth over last decade.



Welcoming Remarks by Professor Rainer Böger

The first session was opened with a keynote lecture from Dr Stephane Richard (McGill University, Montreal, Canada) who provided an excellent overview on ADMA synthesis by protein arginine methylation. Dariusz Zakrzewicz (University of Giessen, Germany) went on to describe how a reduction in activity of protein arginine methyltransferase 1 (PRMT1) in pulmonary artery smooth muscle cells may contribute to proliferation of these cells in patients with pulmonary artery hypertension (PAH). The concentration of ADMA is controlled, not only through synthesis by PRMT, but importantly by ADMA breakdown by the dimethylarginine dimethylaminohydrolases (DDAHs). Dr Roman Rodionov (University of Iowa, USA) introduced an alternative pathway for degradation of ADMA by alanine:glyoxylate aminotransferase 2 (AGXT2); demonstrating that overexpression of AGXT2 results in decrease of ADMA levels *in vivo* and *in vitro*. The poster session that followed included evidence of a regulatory role for ADMA in the evolution of the acute inflammatory response (Dr Scott Blackwell, University of Glasgow, UK). This was reinforced in a later presentation from Dr Karsten Sydow (Hamburg University, Germany) who dem-

onstrated enhanced leukocyte activation by ADMA, resulting in increased degranulation and superoxide production.

Opening the second session with his keynote lecture, Dr Arturo Cardounel (University of Florida, US) presented tantalizing new evidence for ADMA independent regulation of endothelial NO production by the DDAH enzymes. I then had the opportunity to present my own data on the investigation of the DDAH expression and function post-myocardial infarction. Our results so far suggest that expression of both DDAH1 and DDAH2 is increased post-MI, where they may protect NOS enzymes from the increased circulating levels of methylated arginines associated with MI. Worsening of outcome post-MI observed in DDAH1+/- mice supports a protective role for this enzyme.

Agnieszka presents her data to the conference

At the end of this extremely stimulating day the delegates had an opportunity to relax and integrate with each other during an informal welcome reception organised in the "Wirtshaus am See" restaurant positioned beautifully beside the lake. The large bowls of Spätzle (gnocchi-like pasta with cheese and onions), a local speciality, were a source of particular fascination and discussion for the Japanese delegates seated with us, although all enthusiastically participated in degustation.

The second day of the conference began with a review on regulation of ADMA in health and its

'Wirtshaus am See' Restaurant

proposed role in a growing number of diseases (Prof Christopher Wilcox, Georgetown University Hospital, Washington DC, USA). The following presentations described modulation of DDAH activity by overexpression (Dr Dorothee Atzler, University Medical Center Hamburg-Eppendorf, Germany; Dr Belen Torondel, University College London, UK) and siRNA gene silencing (Arthur Pope, University of Florida, USA), concluding that manipulation of DDAH expression or activity may represent a novel therapeutic approach in cardiovascular disease. The subsequent poster session dealt with ADMA and DDAH in pathophysiology. A role for NO deficiency in endothelial dysfunction preceding hypertension was identified by Dr Adrian Doroszko (Wroclaw Medical University, Poland). Dr Arkadiusz Derkacz (Wroclaw Medical University, Poland) demonstrated that elevated pre-procedural ADMA levels were associated with increased risk of restenosis following coronary angioplasty.

Delegates discuss their research during the poster session

Young Investigator Award winners with Professor Böger

The ADMA theme was continued by Prof Rainer Böger (University Medical Center Hamburg-Eppendorf, Germany) in his keynote lecture that provided an extensive insight into a role of ADMA as a marker of cardiovascular risk. Importantly he presented early data from the first large scale clinical study aimed at investigation of whether ADMA is a valid clinical marker of cardiovascular risk. He concluded that ADMA has prospectively been proven as risk marker of cardiovascular events over the whole range of global risks; however its contribution to the individual risk assessment has not become clear yet and requires further investigation.

The next session moved on to genetic manipulation of DDAH. While it was reported that DDAH2 knockout leads to impaired macrophage NO production (Peter Kelly, University College London, UK); overexpression of DDAH1 was found to be protective against vascular dysfunction in hyperhomocysteinemic mice (Dr Roman Rodionov, University of Iowa, USA). Interestingly some novel human gene polymorphisms have now been identified in both DDAH1 (Dr Ben Caplin, University College London, UK) and DDAH2 genes (Dr Nicole Lüneburg, University Medical Center Hamburg-Eppendorf, Germany), being associated with renal dysfunction and PAH respectively.

The final oral presentation session of the meeting dealt with the therapeutic potential of ADMA and DDAH. In his keynote lecture Dr James Leiper (University College London, UK) demonstrated progress in the development of drugs to modify DDAH activity and their potential application. In the same session, Dr Manasi Nandi (University College London, UK) presented her studies of DDAH inhibitors in septic shock, an area in which DDAH inhibition may provide an alternative to NOS inhibition for regulation of blood pressure.

View over Lake Constance and the Pfänder Mountain

ADMA 2008 Conference Delegates

At the end of formal proceedings a wine reception was held in the gardens of the Deuring Schlössle Hotel, a small baroque palais with romantic ambience and magnificent views of Lake Constance. Young Investigator Awards were presented to Dr Roman Rodionov (University of Iowa, USA); Peter Kelly (University College London, UK) and Dr Karsten Sydow (Hamburg University, Germany) for oral presentations. In the category of poster presentations prizes were awarded to Felix Fleissner (Julius-Maximillians University, Würzburg, Germany), Dr Adrian Doroszko (Wroclaw Medical University, Poland); Eva Flick (Otto-von-Guericke University, Magdeburg, Germany) and Dr Joachim Weil (University Hospital Lüberck, Germany). The conference concluded with an official dinner in the Gourmet Restaurant of Deuring Schlössle Hotel. The fantastic, heavenly and delicious 5 course meal served by award winning head chef Heino Huber was an amazing finale to an excellent meeting.

Overall, the "ADMA 2008" conference proved to be highly successful and enabled young investigators as well as senior researchers to share their findings on the subject of ADMA. Prof Rainer Böger and the International Organizing Committee should be congratulated on this undeniable success. I would like to acknowledge British Heart Foundation for their financial support of my PhD and provision of a travel grant which allowed me to attend this conference. My presentation during the meeting provided me with the opportunity to get constructive feedback and advice from the best specialists in the field of ADMA and, as such, was an invaluable experience.

Travel Reports for *The* Bulletin

The Bulletin editors look forward to publishing 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 to travel to a relevant cardiovascular meeting and would like to write a report for *The* Bulletin, please contact the editors beforehand. A bursary of **£300** is available towards the cost of your visit which will be provided on receipt of the report.

Bon voyage!

Cardiovascular Meetings

Keystone Symposium: Dissecting the Vasculature: Function, Molecular Mechanisms and Malfunction. Organizers: Stephanie Wengert Watts, Nancy J. Rusch and William F. Jackson. 24th February - 1st March, 2009 Fairmont Hotel, Vancouver, British Columbia. Further details are available from: info@keystonesymposia.org; Tel: 800-253-0685; http://www.keystonesymposia.org/

Keystone Symposium on Cardiac Disease: Development, Regeneration and Repair, organised by Michael D. Schneider and Nadia A. Rosenthal, will be held at Grove Park Inn, Asheville, NC on 15th - 20th March, 2009. Further details can be found at http://www.keystonesymposia.org/

Keystone Symposium: Common Mechanisms in Arrhythmias and Heart Failure. Organizers: Alfred L. George, Jeffrey A. Towbin and Elizabeth M. McNally. 2nd - 7th April, 2009. Keystone Resort, Colorado. Further details are available from: info@keystonesymposia.org; Tel: 800-253-0685; http://www.keystonesymposia.org/

The 2009 Weinstein Cardiovascular Development Conference will be held at the Hyatt Regency Hotel, San Francisco, California on 7th-9th May, 2009. Further details on registration, abstract submission and accommodation can be obtained from www.weinsteinmeeting.org

7th-9th May 2009, Focused Meeting: New Drugs in Cardiovascular Research. Joint Meeting with the German Societies for Pharmacology & Clinical Pharmacology.Dresden, Germany. Further information regarding the programme, registration and abstract submission can be obtained http://www.bps.ac.uk

ESC 'Heart Failure Congress 2009' joint meeting with XIX Annual Meeting of the ISHR European Section will take place in Palais Acropolis, Nice, France on 30th May - 2nd June, 2009. Further details can be obtained from http://www.escardio.org/congresses/Pages/welcome.aspx

British Cardiovascular Society Annual Conference & Exhibition will be held at ExCeL, London on 1st - 3rd June, 2009. For more information, please visit: http://www.bcs.com/pages/conference.asp

American Heart Association Basic Cardiovascular Sciences Annual Conference 2009 - Molecular Mechanisms of Cardiovascular Disease will take lace at The Ritz Carlton, Lake Las Vegas, Nevada from 20th - 23rd July, 2009. More information is available from http://www.americanheart.org; E-mail: scientificconferences@heart.org; Phone: (888) 242-2453 or (214) 570-5935

European Society of Cardiology Congress 2009 will be held in Barcelona, Spain 29th August - 2nd September 2009. Further details are available at: http://www.escardio.org/congresses/esc-2009/Pages/welcome.aspx; Tel: +33 (0)4 92 94 76 00

Keystone Symposium: Advances in Molecular Mechanisms of Atherosclerosis. Organizers: Russell A. DeBose-Boyd and Christopher K. Glass 12th - 17th February, 2010 Fairmont Banff Springs, Banff, Alberta. Further details are available from: info@keystonesymposia.org; Tel: 800-253-0685 http://www.keystonesymposia.org/

Keystone Joint Symposia: 'Cardiovascular Development and Repair' and 'Angiogenesis in Health and Disease'. Organizers: Doris A. Taylor and Brian Annex. 28th February - 5th March, 2010 Keystone Resort, Colorado. Further details are available from: info@keystonesymposia.org; Tel: 800-253-0685 http://www.keystonesymposia.org/

XX World Congress of the International Society for Heart Research Kyoto 13-16 May 2010. For further details, please visit: http://www.ishrworld.org/

British Heart Foundation Grants

Project Grants Committee July 2008

Prof C H Fry & Prof N S Peters, University of Surrey. "The role of calcineurin in regulating action potential propagation in normal and hypertrophied myocardium through connexin43 dephosphorylation" (2 years) £133,554

Professor J G McCarron et al, University of Strathclyde. "Mitochondrial control of Ca^{2+} signalling in vascular smooth muscle: development and use of caged mitochondrial uncouplers" (3 years) £136,469

Dr P W F Hadoke et al, University of Edinburgh. "Determining the influence of vascular smooth muscle and endothelial cell endothelin B receptors on neointimal proliferation through cell-specific knockout" (3 years) £199,798

Mr G J Pettigrew et al, University of Cambridge. "Humoral alloimmunity and autoimmunity in allograft rejection and tolerance" (3 years) £198,924

Dr D Bishop-Bailey & Dr D Gilroy, Queen Mary, University of London. "Cytochrome P450 2J2 as an endogenous regulator of monocyte- macrophage inflammation and phenotype switch" (2 years) £101,582

Dr S Xu & Professor S L Atkin, University of Hull. "Effect and mechanism of homocysteine on human vascular endothelial cells: role of TRP calcium-permeable channels" (2 years) £125,824

Prof T M Griffith & Dr D H Edwards, Cardiff University. "Interactive roles of hydrogen peroxide and calcium in the endothelial signalling network that underpins the EDHF phenomenon" (3 years) £181,963

Dr D P Ramji, Cardiff University. "Transforming growth factor-β signalling in human macrophages and the control of foam cell formation" (2 years) £98,709

Dr V Budhram-Mahadeo & Dr R Heads, University College London (ICH). "Analysing expression and function of POU4F2/Brn-3b and determining redundancy with POU4F1/Brn-3a in developing heart" (2 years) £111,891

Dr A E Canfield & Dr A P Gilmore, University of Manchester. "AXL signalling - identifying new therapeutic targets for vascular calcification" (3 years) £170,984

Professor M P Frenneaux et al, University of Birmingham. "Epidemiology and diagnosis of heart failure with preserved left ventricular ejection fraction" (3 years) £270,799

Dr C E Gallon & Prof S B Marston, Imperial College London. "Molecular mechanisms of contractile dysfunction in hypertrophic cardiomyopathy: the roles of altered contractile protein, O-glycosylation and oxidative stress" (3 years) £199,358

Professor DA Eisner et al, University of Manchester. "An integrative approach to define the cellular mechanisms underlying the slow changes of QT interval following changes of heart rate" (3 years) £190,327

Dr M P Gordge, University of Westminster. "Redox regulation of platelet cell surface protein disulphide isomerase" (2 years) £111,110

Dr C A Lygate & Prof S Neubauer, University of Oxford. "Malonyl-CoA decarboxylase inhibition as a new therapeutic approach in chronic heart failure" (2.5 years) £130,953

Dr K M O'Shaughnessy, University of Cambridge. "Resolving the molecular genetics of familial hyperaldosteronism type II (FH-II)" (2 years) £96,459

Dr I B Squire et al, University of Leicester. "Plasma matrix metalloproteinase and tissue inhibitor of metalloproteinase after acute myocardial infarction in man: a cardiac magnetic resonance study of left ventricular remodelling" (1 year) £111,148

Professor P M W Bath et al, University of Nottingham. "Safety and tolerability of adding clopidogrel to aspirin and dipyridamole in patients with acute ischaemic stroke or TIA: a randomised trial" (3 years) £233,283

Dr P J R Barton et al, Imperial College London. "Role of follistatin-like genes in the heart and the response to myocardial injury" (3 years) £229,212

Dr G M Ellison et al, Liverpool John Moores University. "Bidirectional interactions between myocytes and resident stem cells in the heart's adaptive response to exercise stress" (2 years) £101,427

Dr K J Buckler, University of Oxford. "Oxygen dependent regulation of background potassium channels in arterial chemoreceptor cells: role of metabolism, other oxygen dependent signalling pathways and TASK1/3" (2 years) £122,537

Prof V A Zammit & Dr A M Dixon, University of Warwick. "The role of structural motifs within the transmembrane domains of cardiac CPT1B in determining its distinctive oligomerisation and kinetic characteristics" (3 years) £162,582

Professor I C Zachary, University College London. "Role of neuropilins and neuropilin-associated proteins in vascular smooth muscle cell (VSMC) function and neointimal VSMC hyperplasia in vivo" (3 years) £174,252

Chairs and Programme Grants Committee August 2008

Infrastructure Grant

Professor S Neubauer et al, University of Oxford. "A new 1.5 Tesla MR Scanner for clinical research in cardiovascular disease" £500,000

Special Project Grants

Professor J N Danesh, University of Cambridge. "Collaborative pooled analysis of data on C-reactive protein gene variants and coronary disease" 3 years £406,334

Dr J R Bradley & Prof M R Bennett, University of Cambridge. "Cambridge Yale collaborative programme in cardiovascular research" 2 years (renewal: years 4-5) £40,000

Dr J M Armitage et al, University of Oxford. "ASCEND: A study of cardiovascular events in diabetes. A randomised study of aspirin and of omega-3 fatty acid supplementation for the primary prevention of cardiovascular events in diabetes" 5 years (renewal: years 6-10) £1,579,519

Programme Grants

Professor M D Schneider, Imperial College London. "Fate-mapping and clonal analysis of cardiac side population cells" 5 years £1,227,453

Professor S E Humphries et al, University College London. "Disecting the molecular genetic architecture of plasma lipid traits: Identifying functional changes and their use in determining CHD causality" 5 years (renewal: years 24-28) £1,297,201

Professor M R Bennett et al, University of Cambridge. "Regulation of vascular smooth muscle cell apoptosis and cell senescence in atherosclerosis" 5 years (renewal: years 11-15) £1,617,732

Professor S B Marston et al, Imperial College London. "Molecular mechanisms of contractile dysfunction in cardiac muscle hypertrophy and failure" 3 years £636,991

Professor A M Shah et al, King's College London. "NADPH oxidases in cardiac hypertrophy and failure" 5 years (renewal: years 11-15) £1,499,347

Professor B D Keavney et al, University of Newcastle. "An investigation of the genetic basis of cardiovascular malformation" 5 years (renewal: years 6-10) £1,639,518

Professor P H Whincup et al, University College London. "British Regional Heart Study: A prospective investigation of the aetiology and prevention of coronary heart disease, stroke and heart failure among older British men" 5 years (renewal: years 25-30) £862,273

Project Grants Committee September 2008

Dr P Eaton, King's College London. "15-Deoxy-prostaglandin J2 and the heart: looking beyond PPARγ and receptor mediated signaling" (2 years) £159,098

Dr P Syrris & Prof W J McKenna, University College London. "Mutation screening of the plectin gene in arrhythmogenic right ventricular cardiomyopathy (AVRC)" (1 year) £83,535

Prof J R Pepper et al, Imperial College London. "Randomised ischaemic mitral evaluation (RIME)" (2 years) £101,538

Dr A Stephanou, University College London (ICH). "Role of p53 and STAT1 in regulating the autophagic pathway in the ischaemic myocardium"

(3 years) £161,591

Dr P Syrris et al, University College London. "Mutations in RAS-MAPK signalling pathway components: a novel cause of non-syndromic left ventricular hypertrophy in children?" (1 year) £79,997

Dr M S Sandhu et al, University of Cambridge. "Genome wide association study of HDL: linking genetic loci for HDL to risk of coronary artery disease" (2 years) £154,266

Dr N L M Cruden et al, University of Edinburgh. "The effects of ischaemia-reperfusion and ischaemic preconditioning on endogenous fibrinolysis in man" (2 years) £188,321

Prof R S Bonser et al, University of Birmingham. "Identification of heart donors using biochemical probes" (3 years) £161,594

Prof S E Harding, Imperial College London. "Signalling pathways of growth in cardiomyocytes derived from human embryonic stem cells" (2 years) £166,303

Dr G C Rodrigo et al, University of Leicester. "Mechanistic insights into the role of calcium loading in cardioprotection: a study using a novel cellular model of ischaemic preconditioning" (3 years) £161,457

Dr S G Wannamethee et al, University College London. "Explaining the association between Type 2 diabetes and coronary heart disease in older men and women using two linked epidemiological studies: the role of novel risk factors" (1.5 years) £84,075

Prof C G Proud & Dr P A Townsend, University of Southampton. "Molecular mechanisms controlling ribosome biogenesis in cardiomyocytes" (3 years) £187,424

Prof J M Gibbins, University of Reading. "Investigation of the role of the receptor tyrosine kinase EphB2 in the regulation of platelet function, haemostasis and thrombosis" (3 years) £199,094

Dr T D Karamitsos et al, University of Oxford. "Myocardial tissue oxygenation in hypertrophy assessed with blood- oxygenation-level-dependent (BOLD) MRI" (2 years) £216,808

Dr D A Middleton, University of Liverpool. "Further studies on the structure and function of phospholemman, a regulator of cardiac ion flux" (1 year) £61,106

Prof A D Hughes et al, Imperial College London. "Southall and Brent revisited (SABRE) - Heart3D" (3 years) £109,566

Prof J C Hancox et al, University of Bristol. "Modulation of the electrophysiology of the atrioventricular node by endothelin-1" (3 years) £242,099

Dr A E Munsterberg, University of East Anglia. "The origin and migration of secondary heart field progenitors" (3 years) £203,607

Prof A J Jovanovic, University of Dundee. "Increased expression of SUR2A as a strategy to counteract ageing- induced decrease in cardiac output and physical endurance" (2 years) £95,646

Prof A H Baker & Prof G Milligan, University of Glasgow. "Interrogation and manipulation of micro RNA during differentiation of human ES cells to cardiomyocyte and vascular lineages" (3 years) £144,514

Dr N J Brand, Imperial College London. "Investigating the mechanism of action of the anti-hypertrophic transcription factor kruppel-like factor 15 (KLF15)" (6 months) £14,002

Dr D S Steele, University of Leeds. "Mechanisms of RYR2 dysfunction underlying myocardial disease" (3 years) £222,174

Dr A C Brewer & Prof A M Shah, King's College London. "Molecular mechanisms underlying NOX4-mediated cardiomyocyte differentiation" (3 years) £189,388

Prof N Rosenthal et al, Imperial College London. "Insulin like-growth 1 and serum glucocorticoid kinases: in concert for cardiac protection and repair" (3 years) £257,456

Chairs and Programme Grants Committee November 2008

Personal Chairs

Professor M Gautel, King's College, University of London. "BHF Chair of Molecular Cardiology" (10 years) £1,421,811

Professor M D Schneider, Imperial College London. "The BHF Simon Marks Chair of Regenerative Cardiology" (10 years) £1,538,239

Strategic Initiatives

Professor A F Dominiczak, University of Glasgow. "A 3Tesla cardiac magnetic resonance imaging facility" (1 year) £1,500,000

Infrastructure Grants

Professor A M Shah, King's College, University of London. "Funding towards core specialist cell biological equipment for the Cardiovascular Division" £100,000

Programme Grants

Professor J N Danesh et al, University of Cambridge. "Systematic approaches to the evaluation of emerging coronary risk markers. Large-scale epidemiological analyses of existing data and stored biological samples" 5 years (renewal: years 6-10) £1,899,999

Professor D M Yellon & Dr D Hausenloy, University College London. "Protection of the ischaemic and reperfused heart: investigation of basic mechanisms and therapeutic potential in animal and human myocardium" 5 years (renewal: years 16-20) £1,238,938

Professor R D Vaughan-Jones, University of Oxford. "Regulation of intracellular pH in ventricular myocardium" 5 years (renewal: years 11-15) £1,221,461

Project Grants Committee November 2008

Prof D J Henderson et al, University of Newcastle (3 years). "Outflow tract development in normal and abnormal human embryos" £153,524

Dr I Hers, University of Bristol. "The role and regulation of phosphodiesterase 3A in human platelet" (2 years) £117,397

Dr D P Francis et al, Imperial College London. "Non-invasive haemodynamics to probe physiology and echocardiographic measurements of dyssynchrony in chronic heart failure" (3 years) £265,093

Dr D P Francis et al, Imperial College London. " 'AQURO', a new, potentially automatable approach for quantifying mitral regurgitation: technology development and validation through collaboration between cardiovascular science and bioengineering" (3 years) £170,127

Prof C L-H Huang & Dr A A Grace, University of Cambridge. "Genetic determinants of triggering and perpetuation of atrial fibrillation" (3 years) £228,253

Prof J T B Crawley et al, Imperial College London. "Characterisation of the molecular basis for activated protein C-mediated vascular endothelial cell cytoprotection" (3 years) £172,150

Prof G J Graham & Prof A Baker, University of Glasgow. "Investigation into the role of the atypical chemokine receptor D6 in atherosclerosis: human and murine studies" (3 years) £194,090

Prof K M Channon et al, University of Oxford. "The BioHAP Study: determining the effect of endogenous tetrahydrobiopterin availability on vascular function through genetic variation in GTP cyclohydrolase 1" (3 years) £197,589

Dr S A Deuchars et al, University of Leeds. "Mechanisms underlying rhythmic sympathetic activity: network, single cell and in vivo approaches" (3 years) £196,290

Prof H C Watkins & Dr H Ashrafian, University of Oxford. "The role of HIF-1α cardiotoxicity in chronic heart failure" (2 years) £160,964

Dr P J Kilner et al, Imperial College London. "Magnetic resonance based numerical modelling of whole heart structural and fluid dynamics" (1 year) £87,766

Dr N P J Brindle, University of Leicester. "Role of the protein kinase Tp12/Cot in control of endothelial function" (2 years) £106,203

Dr D S Gardner & Dr K Sinclair, University of Nottingham. "Cardiovascular health of aged adult offspring derived from mothers deficient in B-vitamins during the periconceptional period" (2 years) £149,092

Dr T M Palmer et al, University of Glasgow. "EPAC1- and ERK-dependent activation of C/EBP transcription factors: a new cyclic AMP-activated anti-inflammatory gene expression module in vascular endothelial cells" (3 years) £198,213

Dr G C Burdge et al, University of Southampton. "Maternal fat intake and vascular function in the offspring" (3 years) £184,912

Prof N A Booth et al, University of Aberdeen. "Spontaneous and endogenous fibrinolysis in human thrombosis" (2 years) £152,784

Prof G B Nash & Dr G E Rainger, University of Birmingham. "Regulation of the adhesive and effector functions of neutrophils as they migrate through endothelium" (3 years) £196,556

Dr M Bond & Prof A C Newby, University of Bristol. "Functional analysis of novel F-box proteins: role of FBXL6 and FBXO10 in smooth muscle cell proliferation and apoptosis" (1 year) £23,794

Cardiovascular Related Wellcome Trust Grants

September to December 2008

Technology Development Grant

Dr Mark Howarth, Dept of Biochemistry, University of Oxford. Development of monovalent streptavidin and monovalent quantum dots, for singlemolecule imaging of receptor trafficking. 36 months £270,401

The Bulletin Book Reviews

We would like to make book reviews a regular feature of The Bulletin. Anyone interested in reviewing the following title should contact the editors. The review author may keep the book afterwards.

'Handbook of Venous Disorders 3ED'

by Hodder Education

HODDER EDUCATION
www.hoddereducation.co.uk

Further details on this title available from http://www.hoddereducation.co.uk/Title/9780340938805/Handbook_of_Venous_Disorders_Guidelines_of_the_American_Venous_Forum_Third_Edition.htm

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*
22 (2)	***April 2009***	*1st March*
22 (3)	***July 2009***	*1st June*
22 (4)	***October 2009***	*1st September*
23 (1)	***January 2010***	*1st December*

Clinical SCIENCE

Spring Meeting 2009

A joint meeting with the British Atherosclerosis Society

Atherosclerotic Plaque Rupture

Dates: Thursday 2nd and Friday 3rd April, 2009

Venue: Medical Sciences Teaching Centre/St Catherine's College, Oxford

Organisers: Martin Bennett, Chris Jackson and Chris Newman

Programme: The programme will consist of state-of-the-art presentations by leaders in the field. Speakers will include: Patrick Serruys (Rotterdam), Allard van der Wal (Amsterdam), Florian Bea (Heidelberg), Erik Biessen (Maastricht), Rob Krams (London), Martin Bennett (Cambridge), Allen Burke (Gaithersburg), Andreas König (Munich), Juan Carlos Kaski (London) and Andrea Mezzetti (Chieti)

Free Communications: A full session will be devoted to oral presentation of selected abstracts. There will also be a Young Investigator Award session, with the Michael Davies and BSCR Prizes to be won. There is also a Clinical Science Early Career Investigator Award for best poster.

Student Bursaries: The BSCR will consider awarding travel grants of up to £200 to BSCR members who are bona fide students. Application forms are available from the BSCR website (www.bscr.org).

Deadlines: **Submission of abstracts** Friday 6th February

Registration Friday 13th March