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LETTER FROM THE SECRETARY

BSCR - A network of friends?

Last week I had my first enquiry from a member for seeking information regarding possible collaborations with other members. As it happens, it was easy for me to steer the enquirer in the right direction and I could even point to a forthcoming meeting of the Society which covered the area and would provide a forum for making contacts. Full marks for the BSCR!

The Secretary has, of course, always held a file of 'research interests' dating back to the foundation of the Cardiac Muscle Research Group. The file has been conscientiously added to, but is grossly out of date, and it is impossible to retrieve the information it contains. What we need, you are saying to yourself, is an updatable computer file - and so we shall have with your cooperation. Our target date for establishing our own computerised mailing list and database is January 1st 1991. Starting this year, we will be sending out an annual reminder for subscriptions, which will give your details as they appear on the mailing list. There will also be an opportunity for you to update your research interests, which should only take a minute of your time!

Keeping such a database would be pointless, of course, unless it were put to good use - for example, targeted mailing for meetings or finding where to ask advice. I am sure members would welcome such uses, and requests from members for complete lists or lists by research interest will therefore be provided at cost (approximately 5p/A4 sheet). The database might also be made available to other learned societies, to publishers or even, dare I mention it, to insurance companies, financial consultants and time-share salesmen! Any decision on this would have to take account of Members' wishes and so if you feel strongly please write to me or to the Bulletin with your views.

In my article on the future of cardiovascular research in Britain, I suggested that more cooperation was needed to get the best from scarce resources. Our new database will be one way to catalyse such cooperation. I hope you will give it, and the underlying concept of the BSCR as a network of friends, your wholehearted support.

BSCR Committee Elections 1900 - Results:

The postal votes which reached the Secretary with a postmark before September 30th 1990 were counted as follows:

Gianni Angelini 42
Trevor Powell 42
Derek Yellon 65

Derek Yellon was therefore elected outright. In view of the tie, the Chairman decided to use his powers under the rules of the Society to coopt both Gianni Angelini and Trevor Powell to the committee. I am sure you will all agree that this is the fairest interpretation of the Members' wishes as expressed in the voting. The new committee members will take up office from 1st January 1991.

Andrew Newby
LABORATORY PROFILE

Molecular Cardiology Research Group, University of Birmingham

From left to right: Bernadette Cummins, Derek Chilton, Sarah Constantine, Terry Jones, Winny Ainsworth, Peter Cummins.

The Molecular Cardiology Research Group was formed in 1982 by Peter Cummins, Senior Lecturer in the University Medical School. The Group has recently moved into purpose-built laboratories in the Department of Physiology, has core-funding from the British Heart Foundation, and is one of the official BHF Research Groups.

The major focus of the Group's research activities stemmed initially from Dr Cummins' interest in the relationship between structure and function of the contractile and regulatory proteins of the cardiac myofibril. Throughout the history of the Group there has always been a heavy commitment to relating findings in experimental animals to the clinical situation. This has led to pioneering studies on transitions in contractile protein isoforms in the human myocardium in response to stress and the use of cardiac-specific proteins as diagnostic aids in detecting myocardial damage. Subsequently, the Group's activities have expanded to the study of the protein factors regulating growth of the myocardium both in the normal and abnormal situation.

Dr Bernadette Cummins, Bhaloo Desai, Sarah Constantine and Geoffrey Russell have established the use of poly- and monoclonal antibodies to the cardiac-specific isoform of
troponin-I for in vivo detection of myocardial necrosis by gamma scintigraphic imaging. This has involved the bulk production and purification of monoclonal antibodies to produce Fab fragments while retaining as much of the immunochemical reactivity as possible. Antibodies have been labelled with a variety of radioisotopes including iodine-131, indium-111 and technetium-99m. Selection of suitable monoclonal antibodies capable of binding to intracellular sites has been conducted by fluorescence activated cell sorting of isolated myocytes and immunofluorescence microscopy. Antibody uptake has been shown to be preferentially located inside necrotic cells in animal models with external imaging potential.

These 'applied' studies go hand in hand with more fundamental research into the role of troponin-I in inhibiting the cardiac actomyosin ATPase. Dr B. Cummins has investigated how these antibodies may interfere with this inhibition with particular emphasis on the role of phosphorylation. The cardiac isoform of troponin-I has two unique phosphorylation sites at the N-terminus which, when phosphorylated, decrease the calcium sensitivity of the force and ATPase response curve. One of our antibodies is directed at or near this site and distinguishes the phosphorylated from non-phosphorylated form. This is proving to be a valuable and much sought-after probe of this important site.

The role of myosin isoenzymes in the development of cardiac hypertrophy has been the subject of studies by several members of the Group. While the adult human ventricle fails to display adaptive transitions in isoforms which are characteristic of experimental small animal models, these have been demonstrated in the developing human ventricle, adult atria and in congenital cardiac conditions. As the response of the adult myocardium to stress is limited to hypertrophy of existing myocytes, attention is now being focused on the developmental stage at which the hyperplastic growth of the heart ceases immediately after birth. To this end, Terry Jones, Sarah Constantine and Bernadette Cummins are engaged in projects to investigate the role peptide growth factors in the development of the heart with colleagues in the Departments of Biochemistry and Medicine. Attention is currently focusing on the role of transforming growth factor-β and the acidic and basic fibroblast growth factors at both the mRNA and protein levels. Studies are being conducted both in whole myocardium and cultured adult cardiac myocytes. We have recently developed immunoassays which suggest that the levels of some growth factors in the heart have been underestimated. The cellular signalling factors involved in the switch between hyperplasia and hypertrophy is being investigated in collaboration with Drs Metin Avkiran and Hiroshi Yamamoto at St Thomas' Hospital, London, using aortic banding of neonatal rats.

On the commercial scene, Derek Chilton is developing a commercial prototype immunoassay kit for detection of cardiac troponin-I as an in vitro diagnostic tool. This research, which is being conducted jointly with a major multinational biotechnology company, is nearing completion and has resulted in the production of a 90 minute assay from an original 2 day prototype. It is hoped that this will be ready for large scale clinical trials in the near future.

The Group is also engaged in a number of international collaborations which bode well for the future.

Peter Cummins

Please remember...

BSCR membership subscriptions are due in January 1991. Please be kind to our Treasurer and ensure prompt payment of your subscription.

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Winter Meeting

PHYSIOLOGY AND PATHOPHYSIOLOGY OF E-C COUPLING

Thursday 6th - Friday 7th December 1990

Royal Pharmaceutical Society of Great Britain
London

Co-organisers: Dr Michael Shattock, Dr Alan Williams, Dr Peter Collins

SPEAKERS AND PROGRAMME:

Normal physiology of E-C coupling in the heart:

Prof. D. Noble, Oxford
Dr J.H.B. Bridge, Utah, U.S.A.
Prof. D.A. Eisner, Liverpool
Dr D.J. Miller, Glasgow

The relation between calcium current and calcium release
The role of the Na/Ca exchange
The role of the sarcoplasmic reticulum
Regulation of contraction by the myofilaments

Pathophysiology of E-C Coupling in the heart:

Dr J.P. Morgan, Boston, U.S.A.
Dr E.G. Lakatta, Baltimore, U.S.A.
Dr R. Altschuld, Columbus, U.S.A.
Dr M.J. Shattock, London

E-C coupling in hypertrophy
E-C coupling in ischaemia, hypoxia and reoxygenation
Heart failure and E-C coupling
Reperfusion arrhythmias: free radicals and ion movements

E-C coupling in smooth muscle:

Dr A.J. Williams, London
Prof. T.B. Bolton, London
Prof. A.H. Henderson, Cardiff
Dr P. Collins, London

Mechanisms of Ca release in cardiac and smooth muscle SR
Regulation of E-C Coupling in smooth muscle
Endothelial control of smooth muscle
Clinical aspects of smooth muscle regulation by endothelium

REGISTRATION: There are a limited number of places still available. Contact Dr Michael Shattock (Tel. 071-928 9292 ext 3376, Fax 071-928 0658) before the meeting or contact the registration desk at the meeting for on-site registration. Registration is free to BSCR members and £25 to non-members.

IF YOU WISH TO ORGANISE A MEETING OR WORKSHOP, PLEASE CONTACT THE SECRETARY OF THE BSCR, DR ANDREW NEWBY (ADDRESS ON PAGE 2 OF BULLETIN).
Spring Meeting

ENDOTHELIUM AND ATHEROGENESIS

Wednesday 10th - Thursday 11th April 1991

University of Wales College of Medicine
Cardiff

Organiser: Dr Andrew Newby

SPEAKERS AND PROGRAMME:

Dame Honor B. Fell Memorial Lecture:

Prof. R. Ross, Seattle, U.S.A.  
Endothelial function and atherogenesis

Dr R.F.G. Booth, Welwyn  
Endothelium-leukocyte interactions

Dr J.D. Pearson, London  
Secretory pathways in endothelium

Dr M. Radomski, Beckenham  
Platelet-endothelium interactions

Dr D. Bowyer, Cambridge  
Endothelium-monocyte-smooth muscle interactions

Dr A.A. Soyombo, Cardiff  
Endothelial control of smooth muscle proliferation

Dr P.L. Weissberg, Cambridge  
Effects of endothelin on smooth muscle proliferation

Dr P.D. Weinberg, London  
Local variation in trans-endothelial mass transport

Dr A.G. Herman, Antwerp, Belgium  
Endothelial function in atherosclerotic arteries

Dr D.S. Leake, Reading  
Mechanisms of lipoprotein modification by vascular cells

Dr M. Jacobs, London  
Endothelium-derived vasoactive factors and lipoproteins

Prof. D. de Bono, Leicester  
Endothelium in clinically-encountered atherosclerosis

Mr G.D. Angelini, Sheffield  
Endothelium in cardiac surgery

POSTERS: Members of the Society are invited to submit abstracts (on any topic) for poster presentation. In accordance with BSCR policy, these abstracts will not be published but will be printed in the BSCR Bulletin.

REGISTRATION: Free to members; £25 to non-members. Registration and abstract forms are included with this issue of the Bulletin. Further copies are available from:

Dr Andrew C. Newby,  
Department of Cardiology,  
University of Wales College of Medicine,  
Heath Park,  
Cardiff CF4 4XN  
Tel. 0222-742 338
BSCR WORKSHOP ANNOUNCEMENT

Spring Workshop

CORONARY SURGERY: CLINICAL AND BASIC PERSPECTIVES

Friday, 17th May 1991

The University of Sheffield

Organiser: Mr Gianni Angelini


The full programme and registration forms are included with this issue of the Bulletin. For further details, contact:

Mr Gianni Angelini
Department of Cardiac Surgery
Northern General Hospital
Herries Road
Sheffield S5 7AU
Tel. 0742-434 343

BSCR WORKSHOP REPORT
GROWTH FACTORS AND THE CARDIOVASCULAR SYSTEM
Birmingham, 31st May 1990

The Spring 1990 Workshop on 'Growth Factors and the Cardiovascular System', organised by Dr Peter Cummins, was held at the Postgraduate Medical Centre, Queen Elizabeth Hospital and University of Birmingham.

As this was a relatively new topic for discussion in the Society, the first session was devoted to an update on the general role of growth factors, without specific reference to the cardiovascular system, from experts in the field.

Dr Clive Dickson (Imperial Cancer Research Fund, London) discussed the role of the fibroblast growth factor family in growth and development. The 7 members of the family, which include interleukin-2, were compared structurally. A notable feature which raised questions as to the cellular role of the FGF's was the lack of a signalling sequence in the acidic and basic FGF's. The role of FGF's in mitogenesis, angiogenesis, mesoderm induction, transformation, tumorigenesis and cell motility was discussed. The Int-2 gene was then used as an example of an FGF expressed during embryogenesis with inappropriate expression causing tumorigenesis. Localisation of protein expression did not necessarily correlate with mRNA expression, a feature which surfaced later in the meeting.

The role of the LIF/DIA growth factor in mouse embryogenesis was discussed by Dr Peter Rathjen (Biochemistry, Oxford). He explained how growth factors were used for different
temporal and spatial purposes during differentiation and how tight control was exerted over which cells were affected by different factors. The effects of transforming growth factor-β and basic FGF on LIF/DIA expression in human fibroblast cells was highlighted.

Dr John Woodget (Ludwig Institute for Cancer Research, London) gave an overview of early gene induction by growth factors. The proto-oncogene transcription factors c-jun and c-fos were used as examples of genes turned on by extracellular stimulation. He indicated that initial induction of gene transcription did not require new protein synthesis but was more likely to be via post-translational modification of pre-existing proteins. The temporal programme of gene induction elicited upon stimulation by growth factors was discussed together with a fascinating insight into the regulation of transcription factor activity by protein phosphorylation at sites close to the DNA binding domain.

Dr A.J. Strain (Liver Research Group, Birmingham) introduced the transforming growth factor family, with particular emphasis on TGF-β. These were transcribed as latent high molecular weight precursors. The role of TGF-β as both a stimulatory and inhibitory growth factor was discussed, with special emphasis on hepatocyte proliferation.

The afternoon session on the cardiovascular system was introduced by Dr P. Cummins (Physiology, Birmingham) who reviewed the evidence for the presence of growth factors, in particular TGF-β and acidic and basic FGF's, in the myocardium. The methods for identifying whether growth factors were expressed in cardiac myocytes were discussed together with an analysis of protein levels. Discrepancies between the intracellular locations of growth factor mRNA's and protein, and the effects of TGF-β and FGF's on expression of contractile proteins and proliferative potential of isolated foetal myocytes were outlined.

The switch from hyperplastic to hypertrophic growth in the developing human heart was the subject of a presentation from Dr R. Wyse (Institute of Child Health, London). The comparison between skeletal and cardiac differentiation together with the expression of H-ras and IGF-2 mRNA's in foetal and adult cardiac muscle was presented. This area of research, which is now stimulated by long term aims of cardiac regeneration, was further examined in terms of the possible constraints on myocyte cytokinesis.

Dr C. Goddard (Institute of Animal Physiology and Genetics Research, Edinburgh) considered the role of insulin-like growth factors in the development of skeletal muscle. While these were highly conserved at the protein level, the genes were less well conserved. IGF-1 and 2 levels in developing skeletal and cardiac muscle were contrasted together with their role in the transformation of uncommitted stem cell to committed myoblast.

The factors controlling proliferation of vascular smooth muscle cells were discussed in the last session by Dr P. Weissberg (Clinical Pharmacology Unit, Cambridge). He compared the effects of growth factors and vasoconstrictors on cultured smooth muscle cells. Vasoconstrictors were shown to be able to potentiate proliferation only in the presence of growth factors but possibly to play a role in cell hypertrophy.

The latter part of the meeting was devoted to the potential role of growth factors in angiogenesis. Dr J. Weiss (Wolfson Angiogenesis Unit, Manchester) examined the role of endothelial cell angiogenesis factor (ECAF) in the proliferation of capillary cell endothelium using the chorio-allantoic yolk cell membrane model. This was followed by the presentation by Professor O. Hudlicka (Physiology, Birmingham) on the use of bradycardial pacing in the induction of angiogenesis in a number of different models.

Overall, the meeting was a great success, heavily oversubscribed and well supported by generous sponsorship from the British Heart Foundation, Amersham International and the British Society for Cardiovascular Research.

Peter Cummins
BHF Molecular Cardiology Research Group
Department of Physiology
University of Birmingham
Pharmacological inhibition of the uptake of atherogenic plasma proteins by arterial walls.

The effects of chloride ion substitution on the electromechanical properties of cardiac muscle.

The role of endogenous mediators, intracellular signalling and intercellular communication in endothelial cell injury.

Morphological and histological studies of atrial isomerism in the human foetus as compared with a murine model.

Regulation of smooth muscle myosin heavy chain gene expression by thyroxine and during hypertension.

Multidisciplinary studies into the role of enteroviruses in the pathogenesis of dilated cardiomyopathy.

Neonatal hypoxia and subsequent vasoconstrictive pulmonary vascular disease.

Do nitrovasodilator drugs inhibit platelet deposition and vascular smooth muscle proliferation following angioplasty?

The peptidergic influence of paraventriculo-spinal neurones.

Studies on the pathogenesis of systemic capillary leak syndrome.

Studies into the mechanisms of insulin resistance due to high fat feeding.

Role of pyruvate dehydrogenase kinase in the longer term regulation of myocardial glucose oxidation.

An investigation of the role of intracellular taurine in the regulation of intracellular sodium.

Comparison of LDL apheresis plus simvastatin versus cholestyramine plus simvastatin.

Regulation of the sodium-dependent potassium channel in the cardiac muscle cell membrane.

A genetic study of chromosome 22 deletions in children with outflow tract defects of the heart.

Measurement of [Ca], and action potential in trabeculae and single cells of mammalian hearts: regional differences.

The role of 11 beta-hydroxysteroid dehydrogenase in vascular tissue.

Structure-function relationships in endothelial plasminogen activator inhibitor (PAI-1).

Studies of insulin resistance and its relationship to risk factors for coronary heart disease.

The role of caldesmon in regulating vascular smooth muscle contractility.
Prof DJ Sheridan et al  
St Mary’s Hospital, London  
The effects of myocardial hypertrophy on cardiac cellular electrophysiology.  
75,418

Drs JI Gillespie & JR Greenwell  
University of Newcastle upon Tyne  
Complex mobilisation of cytoplasmic calcium in single activated endothelial cells.  
75,565

Drs PN Durrington & MI Mackness  
University of Manchester  
The role of high-density lipoprotein paraoxonase in the protection of apolipoprotein-B against oxidative damage.  
69,457

Dr DV Parums  
John Radcliffe Hospital, Oxford  
Studies on inflammation in atherosclerosis using in vitro cell culture techniques.  
42,232

Drs JE Bishop & GJ Laurent  
National Heart & Lung Inst, London  
The role of fibrinogen and its cleavage products in pulmonary vascular remodelling.  
54,819

Prof A Steptoe  
St George’s Hospital, London  
Stress controllability, age and sex: a psychophysiological study of cardiovascular disease risk.  
126,723

Drs ML Rose & S Harding  
National Heart & Lung Inst, London  
Analysis of the immunological mechanisms of damage to the heart in transplant rejection and inflammatory heart disease.  
114,045

Drs MJ Dunn & ML Rose  
National Heart & Lung Inst, London  
Anti-heart antibodies as mediators of damage in the diseased and transplanted heart.  
81,870

Drs J Metcalfe & P Weissberg  
University of Cambridge  
Regulation of gene expression for myosin heavy chain isoforms in vascular smooth muscle cells.  
91,925

Dr DJ Chambers  
St Thomas’ Hospital, London  
Surgical myocardial protection: the development of a crystalloid reperfusion solution to attenuate reperfusion injury.  
49,897

Dr CA Clelland  
Northern General Hospital, Sheffield  
Quantitative analysis of allograft lymphocytes and myocardial fibre function in heart transplant patients.  
6,262

Drs AC Newby & M Davies  
University of Wales College of Medicine  
Interaction of mitogens and matrix degrading metalloproteinases in vascular smooth muscle proliferation.  
49,794

Dr MJO Wakelam  
University of Glasgow  
The mechanism of coupling of the endothelial receptor to second messenger generation.  
8,566

Dr PR Richards et al  
University of Surrey  
The influence of pre-operative storage regimes on the mechanical properties of human aortic allograft valves.  
55,011

Prof SG Haworth  
Institute of Child Health, London  
Modelling ischaemia-reperfusion injury and repair in cultured pulmonary arterial smooth muscle cells.  
66,813

Dr RA Mayou et al  
John Radcliffe Hospital, Oxford  
A controlled trial of treatment of non-cardiac chest pain.  
78,872

Dr CJ Packard et al  
Royal Infirmary, Glasgow  
Influence of genetics on apolipoprotein B and apolipoprotein A synthesis rates.  
91,901

Dr TW Meade  
Northwick Park Hospital, Harrow  
Population-based study of protein C.  
38,206

Dr E Rosenthal  
Guy’s Hospital, London  
Preservation of ductus arteriosus patency to avoid neonatal systemic to pulmonary artery shunting procedures.  
102,860

Dr H Thurston & Mr RD Sayers  
Leicester Royal Infirmary  
Effect of chronic ischaemia on the microvasculature of the lower limb.  
51,029

Drs P Taggart & P Sutton  
Middlesex Hospital, London  
Contraction-excitation feedback in man: a possible link between abnormal ventricular wall motion and arrhythmia.  
16,230

42 AWARDS TOTALLING: 2,385,735
# BSCR Calendar of Events

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<th>Year</th>
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<tr>
<td>1990</td>
<td>6-7 December</td>
<td>Autumn Meeting: &quot;Physiology and Pathophysiology of E-C Coupling&quot;</td>
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<td>7 December</td>
<td>Annual General Meeting.</td>
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<td>1991</td>
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<td>17 May</td>
<td>Spring Workshop: &quot;Coronary Surgery: Clinical and Basic Perspectives&quot;</td>
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# 1991 Meetings Calendar

**April 22-25.** *Fourth International Symposium on Cardiovascular Pharmacotherapy. Geneva, Switzerland.*
Information: Administrative Secretariat ISCP 91, AKM Congress Service, Clarastrasse 57, P.O. Box 6, CH-4005 Basel, Switzerland.

**May 1-3.** *British Cardiac Society Annual Meeting. Glasgow, Scotland.*
Information: British Cardiac Society, 7 St Andrew's Place, Regents Park, London NW1 4LD, UK.

**May 29-June 2.** *International Society for Heart Research (North American Section) Annual Meeting. Cincinnati, USA.*
Information: ISHR-1991 Conference Office, Department of Physiology and Biophysics, University of Cincinnati Medical Center, 231 Bethesda Avenue, Cincinnati, Ohio 45267-0576, USA.

**August 18-12.** *XIII Congress of the European Society of Cardiology. Amsterdam, The Netherlands.*
Information: ECCO, 22 rue Juste Olivier, PO Box 299, CH-1260 Nyon, Switzerland.

**September 9-10.** *Third International Symposium on Lipid Metabolism in the Normoxic and Ischemic Heart. Rotterdam, The Netherlands.*
Information: Hans C.G. Stam, Board of Governors, Erasmus University Rotterdam, PO Box 1738, 3000 DR Rotterdam, The Netherlands.

**September 11-14.** *International Society for Heart Research (European Section) Annual Meeting. Leuven, Belgium.*