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Contents

Editorial

Welcome to the October 2007 issue of *The* Bulletin!

Our review for this issue has been witten by Professor Nadia Rosenthal and colleagues at the National Heart and Lung Institute on one of the most exciting and controversial areas in cardiovascular research today: cardiac regeneration. This fascinating article addresses the challenges, advances and future directions in the search for the 'Holy Grail' of cardiology, a means to repair the injured heart.

After six years as Secretary of the BSCR, Professor Barbara McDermott writes her final column for *The* Bulletin. On behalf of our readers, we would like to thank Barbara for her entertaining and informative contributions to *The* Bulletin as well as her tireless, enthusiastic work for the Committee and the Society over the years. We wish Barbara and all other retiring Committee members well for the future.

Dr Katrina Bicknell provides an account of proceedings at the highly successful Spring BSCR meeting held at Reading University on 'Therapeutic Targets and Novel Technologies for the Treatment of Cardiovascular Disease'.

Bulletin readers who attended the ISHR World Congress in June will no doubt enjoy reminiscing about warm Bologna evenings, melting ice creams and a never-ending variety of pasta dishes while reading a report of the meeting written by Catherine Stables.

Helen Maddock and Nicola Smart

Regenerative Medicine in Cardiovascular Research: Of Molecules, Cells and Scaffolds

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The goal of regenerative medicine is to restore tissues and organs that are lost or damaged by disease, injury and aging. A clear understanding of embryonic development, tissue turnover and stem cell biology is essential and could provide resourceful knowledge in complex organ regeneration. In recent years cardiovascular research benefited from innovative results from studies where implantation of stem cells to build lost tissues, or stimulation of endogenous signalling to replace missing structures improved cardiac tissue regeneration and functional repair. Here we describe the remarkable discoveries that led to major refinements in cardiac regenerative medicine, envisioning achievable therapeutic goals in the near future.

Introduction

Myocardial infarction occurs when cardiac ischemia exceeds a critical threshold, and overwhelms the cellular repair mechanisms, designed to maintain tissue homeostasis. Because of the limited potential of the myocardium for self-repair and renewal, a significant proportion of cardiac muscle loses its ability to perform work, resulting in heart pump failure. Injured myocardial tissue normally heals through a series of complex events that include acute inflammation, formation of granulation tissue and eventual scar[1-3]. The resultant fibrosis produces altered myocardial stiffness and arrhythmogenesis. Until recently, reperfusion of the ischemic myocardium was the only intervention available to restore the various cellular functions affected, including preventing cell death by necrosis or apoptosis. Unfortunately, reperfusion may itself result in extensive myocardial damage and the functional recovery may appear only after several days. Therefore, replacement and regeneration of functional cardiac muscle and the surrounding vasculature is an important therapeutic goal and conceptually fascinating biological study.

Organ Regeneration: The Common Molecular Fingerprints

Interestingly, the regeneration of organs and appendages after injury occurs in diverse animal groups, such as the urodele amphibians and the teleost fishes. Urodele amphibians are unusual among adult vertebrates in their ability to regenerate an entire limb as well as tail, upper and lower jaws, ocular tissues and small sections of the heart[4, 5]. Regeneration in lower vertebrates proceeds through a series of cellular events that are elusive in mammalian cells. An example is limb regeneration, where formation of proliferating cells covering the stump area (blastema) and re-specification of differentiated cells to biochemically- and morphologically-structured progenitor cells lead to proper limb reconstruction[6]. Another example is the remarkable healing process observed in zebrafish heart after ventricular amputation. Regeneration proceeds through two coordinated steps, involving localization of undifferentiated progenitor cells that display an embryonic expression profile to the apical edge of the existing myocardium, and migration of the epicardial cells to cover the injured myocardium[7]. The epicardial cells will subsequently generate new vasculature by invading the myocardium and undergoing epithelial-mesenchymal transition (EMT)[7].

These two modes of organ regeneration appear remote from each other, as limb regeneration is determined by cell de-differentiation and re-specification, whereas zebrafish heart regeneration is mostly mediated by cardiac progenitor cells supposed to originate primarily from an existing or injury-activated reserve[7]. Nonetheless, common principles in their molecular regulation can be identified. Functionally, the

signalling pathways that have definitively been shown to be required for both processes in vivo are the fibroblast growth factor (FGF) and bone morphogenetic protein (BMP) pathways. When the FGF pathway was blocked by expression of a dominant-negative FGF receptor in transgenic fish, epicardial EMT and coronary neovascularisation failed, halting regeneration prematurely[7]. Studies in the chick, in which amputation of the limb bud fails to regenerate, have shown that treatment of the amputation surface with FGF2 or FGF4 induces a regenerative response[9]. Using a stable transgenic line of Xenopus in which expression of the soluble BMP inhibitor noggin is under the control of a heat shock-inducible promoter, Beck et al. showed that BMP signalling is required for blastema formation, msx1 and fgf8 expression, and proliferation of cells in the epidermis as well as the blastema[10].

In all vertebrates, activation of the innate immune system is an early reaction to injury. Consequently, signals regulating the immune response are also good candidates for regenerative processes. Indeed, both in skeletal muscle and liver regeneration, the immune system provides important signals during early phases of the regenerative processes. Similar cytokines, including IL-6 and ligands of the TNF receptor, secreted by cells of the immune system, are implicated in activation of cell proliferation. In particular, the cytokine TWEAK has been shown to be required for progenitor cell proliferation in regenerating liver and muscle. The complement components C3 and C5, which are implicated as triggers of liver regeneration, have been shown to be expressed in specific domains during newt limb and lens regeneration[11], but their functional involvement has not been tested. If specific cytokines activated during the immune response (innate and adaptive) to tissue damage or disease could play an important role in determining the onset of regeneration, the overall impact of adaptive immune response could be deleterious for initiating and/or completing the regenerative pathways. Harty and colleagues hypothesized that the regenerative capacity of lower vertebrates resides in their unspecialized immunological systems[12]. Regenerating urodeles appear to be immunodeficient compared to anurans, which have lost the capacity to regenerate. Although urodeles possess T and B lymphocytes and a diverse repertoire of Ig and T-cell antigen receptor genes, humoral immunity is mediated only by IgM and is apparently amnestic[12]. A correlation between the changes in regenerative capacity, immune system, and scarless wound healing in Xenopus development also supports this view. So far it has been concluded that the components of adaptive immunity that emerge during vertebrate development are likely to account for scar formation and missing regenerative processes after injury[12]. Although not sufficient to explain the signalling and cellular properties acquired during regenerative processes, the importance of immunodeficiency in urodeles is a tempting hypothesis to be experimentally analyzed in higher vertebrates.

Interestingly, newts appear to have adopted the blood-clotting factor thrombin as an essential signal regulating dedifferentiation and proliferation of cells during muscle and lens regeneration. Thrombin induces cell cycle re-entry of cultured newt myotubes and is activated selectively on the dorsal margin of the iris, which after injury of the lens can dedifferentiate and replace the lens[13, 14]. If thrombin activity in the eye is blocked, lens regeneration is impaired. Similarly, muscle dedifferentiation, in which thrombin appears to be involved, might be quite an exceptional feat, only found in urodele amphibians. Therefore, it will be very interesting to test whether the employment of thrombin in regulation of regeneration is a specialized adaptation of newts or important in other organisms and regenerating systems as well.

In summary, while our knowledge of the signalling pathways controlling different regenerative processes is still in progress, it is already clear that there is significant overlap in the pathways involved. Future research will undoubtedly increase the list of common players, but will also reveal differences in their function in different systems.

Cardiac Regeneration: The Cutting Edge

Several strategies in mammalian tissues can be predicted to potentially support regeneration, which include supplementing of cyto-protective growth factors that function to inhibit pro-death pathways, and improvement of cell sources and their delivery into the injured myocardium to reconstitute the lost vasculature and musculature of the heart.

One of the major problems with mammalian tissue regeneration is the inability of the damaged tissue to support cell survival and proliferation. After injury inflammation and apoptosis occurs as an early patho-physiological response to damage[15]. Inflammatory responses leading to fibrous tissue formation and production of oxidative stress species generate a non-permissive environment for cell migration and proliferation/differentiation, considerably reducing the

possibility of cardiac stem cell progenitors, as well as circulating stem cells, properly benefiting the injured organ. A fascinating strategy to create a friendly environment and space for implanted or migrated cells is in situ tissue engineering. To accelerate angiogenesis and engraftment, implanted scaffolds may be impregnated with bioactive molecules that enhance stem cell homing and self-repair[16]. It has recently been shown in different laboratories that the insulin-like growth factor 1, IGF-1, ameliorate cardiac function when bound to nanofiber peptides and injected into the heart of infarcted mice[17]. We recently published that the local isoform of IGF-1, mIGF-1, induce cardiac recovery with decreased scar formation (**Figure 1A**) and lowered inflammatory response (**Figure 1B**) after myocardial infarction[18]. We also found that mIGF-1 induced a gene expression profile related to decreased oxidative stress (increase of UCP1 and methallothionein 2 transcripts) and increase of cardiac-specific protective molecules, such as adiponectin[18]. Furthermore, in regenerating transgenic mouse muscle expressing the mIGF-1 isoform under muscle-specific post-mitotic control, myogenic progenitors were enhanced, maintaining tissue integrity during exercise and aging, countering muscle decline in degenerative disease and cachexia, and enhancing healing following injury[19]. Interestingly, our preliminary data showed that cardiac restricted expression of mIGF-1 increased the side-population (SP) of positive endothelial- and hematopoietic-CD34 precursor cells in the heart, compared to wild-type hearts. Furthermore, cardiotoxin (CTX)-induced cardiac injury increased the number of proliferating cells around the vessels of mIGF1 transgenic hearts compared to wild-type hearts[18]. These results to date demonstrate that tissue-specific supplementary mIGF-1 expression is an effective and potentially powerful approach to counter a number of prevalent and life-threatening cardiovascular pathologies. However, direct gene therapy has yet to provide viable clinical solutions in the heart, due to relatively inefficient delivery and harmful ectopic expression of the genes. We envisage that mIGF-1 delivery by cell therapy could be of extreme importance to re-direct and control the usage of specific genes in therapeutic trials.

Cell Sources and Route of Application: Towards Myocardial Tissue Engineering

The choice of cells that are needed to repopulate the scarred heart with new contracting cardiomyocytes and new vessels to supply oxygen and nutrients to the newly forming tissue remain s a challenge. Although several candidate cell types have been proposed for myocardial repair, the ideal donor cell should probably exhibit electrophysiological, structural and contractile properties of cardiomyocytes and should be able to integrate structurally and functionally with host tissue. It has to have acquired or inherent properties that may improve colonization of the scar tissue, by resistance to an apoptotic and ischemic environment and potentially by retaining an initial high proliferative capacity[20]. In addition, the optimal cell should be of autologous origin and be readily available in large quantity for cell transplantation.

The first clinically relevant cells proposed as a surrogate of cardiomyocytes were skeletal muscle myoblasts[21-23]. Experimentally and for clinical use, skeletal muscle are easy to obtain from autologous skeletal muscle biopsies, rapidly expandable in vitro and injectable directly into the ventricular wall[24, 25]. A limitation of myoblasts is their inability to transdifferentiate into cardiomyocytes or endothelial cells, which causes severe and often life-threatening cardiac arrhythmias[16, 26]. A further step has been taken by the implantation of bone marrow-purified cells[27-32]. Initial results from clinical trials I and II showed a modest effect on the total beneficial improvement of heart functionality (increase in left ventricular ejection fraction (LVEF) by 2.9 percentage points). Moreover, recent report from the Bone Marrow Transfer to Enhance ST-Elevation Infarct Regeneration (BOOST) trial observed that the relative improvement in LVEF after infusion of BMC at 6 months, as compared with no infusion, was no longer significant at 18 months, suggesting that the main effect was an acceleration of recovery[32]. Furthermore, subsequent work in animals has questioned the ability of bone marrow cells (BMC) to effectively generate cardiomyocytes[33, 34] and clinical studies have suggested that only 1.3 to 2.6% of infused BMC are retained in the heart[35]. Indeed, functional benefits may be mediated through paracrine secretion of growth factors or cytokines, which could indirectly promote survival of cardiomyocytes, mobilization of endogenous progenitor cells, or neovascularization.

Embryonic stem cells (ESC) present a clear advantage in myocardial reconstitution. They contain the correct genetic programming to create all body tissues, and they readily adopt the cardiomyocyte phenotype[36]. Transplantation of embryonic stem cell-derived cardiomyocytes into rodent[37, 38], sheep[39], and

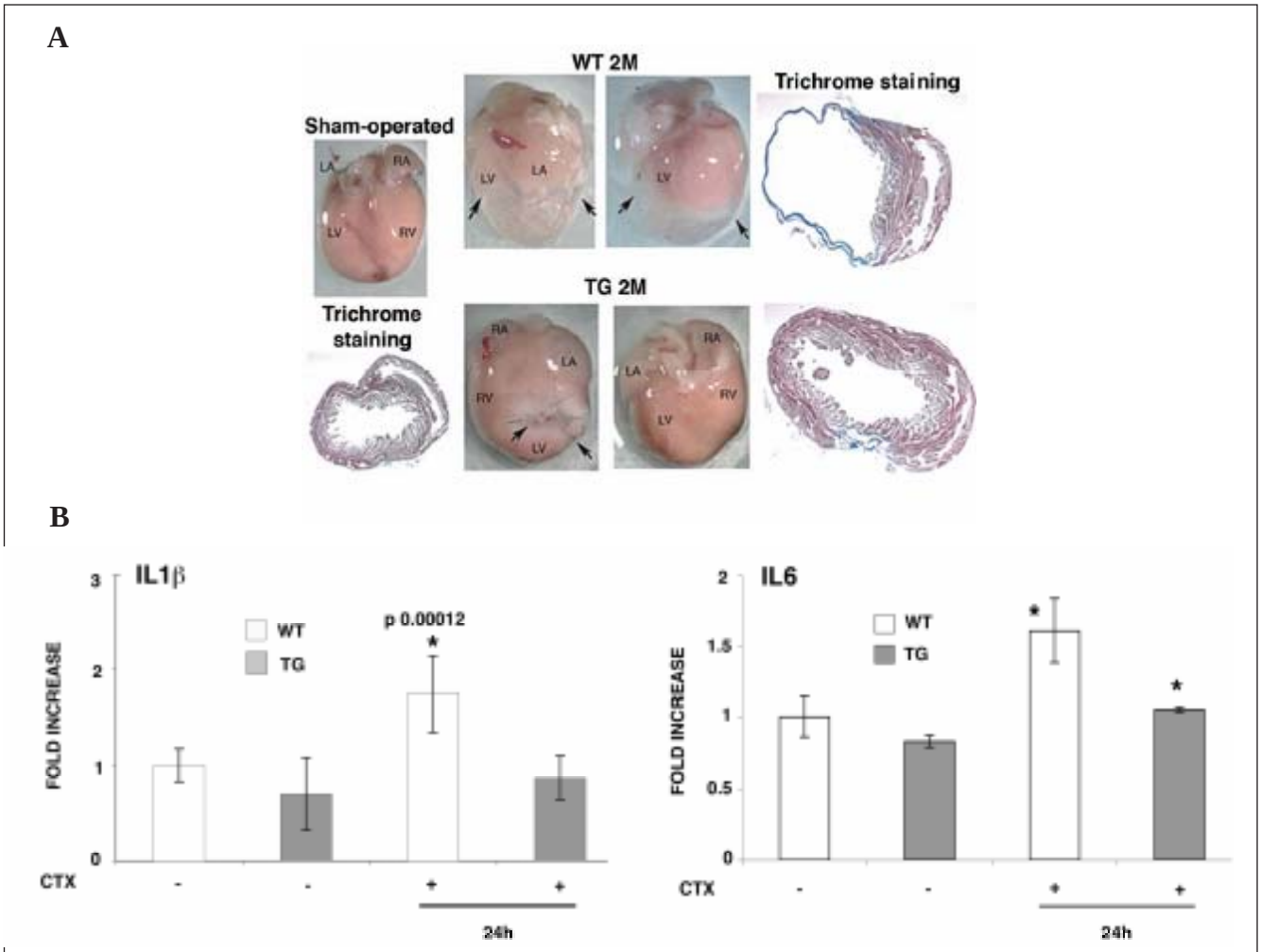

Figure 1: (**A**) Whole mount and histological analysis of sham-operated control (WT) heart (left) and LCA WT and TG hearts (right) 2 months after operation. Hearts were photographed with a Leica MZ12 stereo microscope. Arrows indicate fibrotic tissue. LA, left atrium; LV, left ventricle; RA, right atrium; RV, right ventricle. Histological analysis by trichrome staining is shown for each treatment. (**B**) Real Time PCR analysis of inflammatory interleukins IL6 and IL1b 24 hours after CTX injection in WT and TG hearts. PCR was normalized by GAPDH content in each sample. Asterisks (*) indicate significant increasing values ($p<0.05$) compared to uninjured hearts.

pig[40] models of myocardial damage improved ventricular function and achieved the primary research goal of creating new myocardial tissue. hESC-derived cardiomyocytes integrated functionally and structurally with the host myocardium, and survived following transplantation[41, 42]. However, embryonic stem cells derived-cardiomyocytes also present several disadvantages, which include their allogenic source and carcinogenic nature if not completely purified from residual undifferentiated embryonic stem cells. Moreover, the usage of human embryonic stem cells in therapeutic cloning remains surrounded by ethical concerns in many countries. Although embryonic stem cells partly lack the major histocompatibility complex class 1 expression and survive after transplantation without the need of immunosuppression, differentiation compromises this immune privilege, as more cell surface epitopes are acquired[43]. However, the use of differentiated cells is a necessary step as undifferentiated embryonic stem cells can form teratomas after injection in a variety of organs, including the heart[43]. Interestingly, murine cardiomyocytes derived from embryonic stem cells represent an ideal compromise, since their transplantation into sheep hearts after myocardial infarction did not induce tumor formation and did not require a coadjuvant immunosuppressive treatment[39]. These results are promising but require a more detailed analysis before theses studies can be extended into clinical trials using human cells.

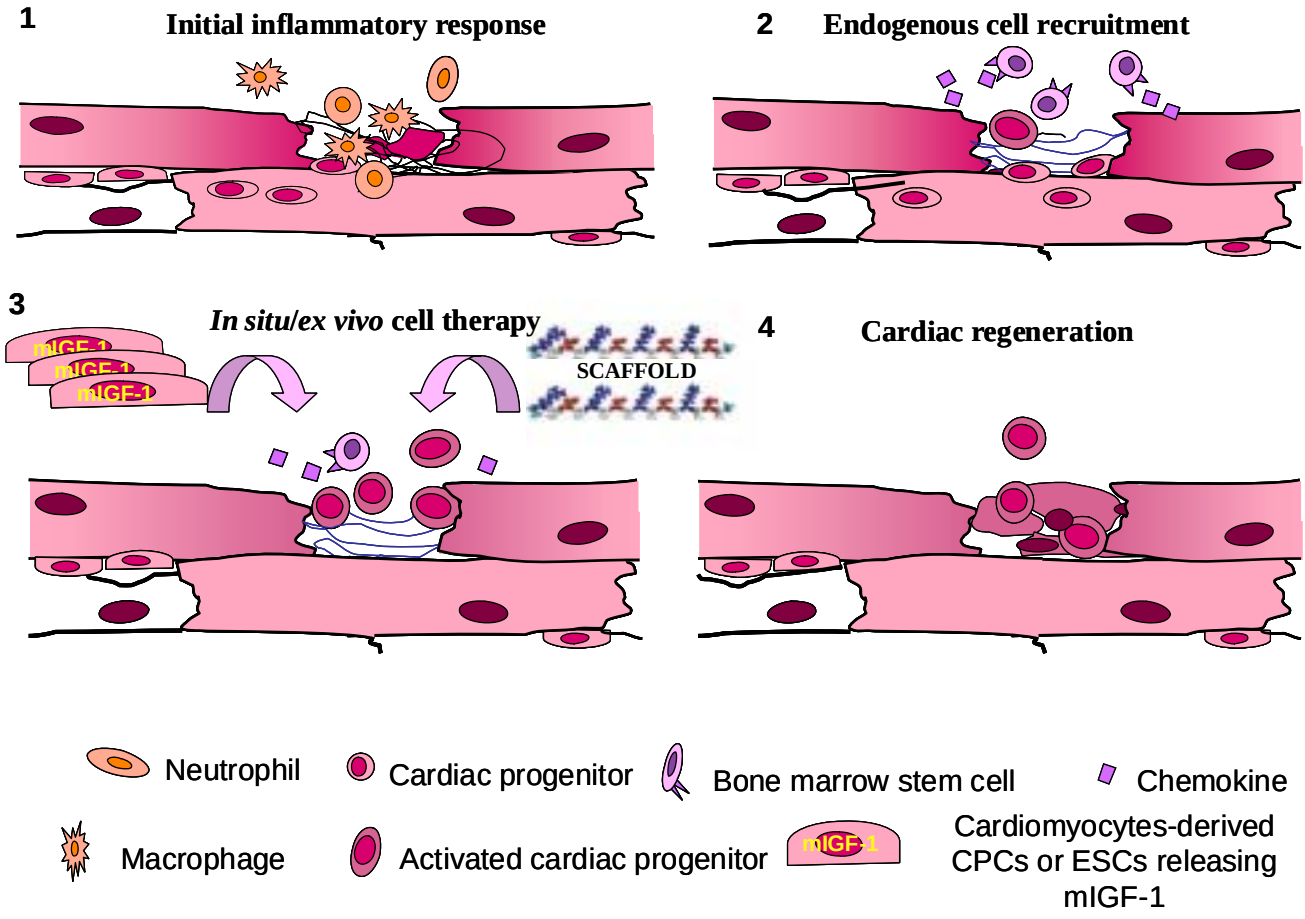

Figure 2: Cell therapy for cardiac regeneration. After myocardial infarct initial inflammatory response triggered by neutrophils and macrophages (1) induces a modest recruitment of circulatory bone marrow stem cells and release of cytokines and chemokines (2) that activate endogenous cardiac progenitor cells (CPCs). To overcome the limited capacity of mammalian heart to regenerate lost tissues (cardiac muscle and vasculature), cardiomyocytes-derived CPCs or embryonic stem cells (ESC) expressing drug-controlled gene cassette carrying specific survival factors, such mIGF-1, could be injected simultaneously with recruiters of endothelial cells, like nanofibers (ex vivo cell therapy), (3) at the site of injury to promote further vasculogenesis and new myocardium formation (in situ cell therapy) (4).

Alternative strategies have been employed in the lasts years that may overcome the ethical problems surrounding therapeutic cloning, such as the use of single blastomeres to create new cell lines without affecting embryo growth and development[44], and the derivation of embryonic stem cells from developing arrested embryos[45]. Indeed, the potential rising from embryonic stem cells capacity to form new myocardium is worthy of further exploration for cardiac regeneration studies.

In this scenario, the most promising autologous cell source for cardiac repair is the resident cardiac progenitor cell (CPC), programmed to form new myocardium. Several groups identified independently different cell populations within the heart with the capacity to self-renew, to differentiate in vitro in cardiomyocytes, endothelial cells and smooth muscle cells, and to ameliorate cardiac function after injection into the infarcted myocardium[46-49]. Hitherto the majority of CPCs have been found in fetal and neonatal mammalian hearts, but their number declines with age, and in patients with cardiac infarct it is not known whether their functional capacity for proliferation and repair remains[43]. Interestingly, a recent study showed that a subpopulation of self-renewing cells, called cardiospheres, exists in the adult heart, with the potential to proliferate in vitro and repopulate the infarcted heart with new cardiomyocytes after transplantation[49]. If endomyocardial biopsies in human patients affected by cardiac pathologies can ensure derivation and expansion of these cells, the beneficial effect of CPCs could leading the field of cardiac regeneration.

An important clinical consideration is the way in

which the chosen cells should be delivered. Progenitor cells for cardiac repair have been delivered in two ways: via an intracoronary arterial route or by injection into the ventricular wall via an endocardial or surgical epicardial approach. The advantage of intracoronary infusion is that cells can travel directly into myocardial regions in which nutrients, blood flow and oxygen supply are preserved, but homing of intra-arterially applied progenitor cells requires migration out of the vessel into the surrounding tissue. Bone marrow-derived and blood-derived progenitor cells are known to extravasate and migrate to ischemic areas[50] whereas skeletal myoblasts or other cell types do not and furthermore may even obstruct the microcirculation after intra-arterial administration, leading to embolic myocardial damage[51]. By contrast, direct delivery of progenitor cells into scar tissue by direct injection during open-heart surgery are not limited by cell uptake from the circulation or by embolic risk. Nevertheless, progenitor cells injected into uniformly necrotic tissue, which lacks the syncytium of live muscle cells that may furnish instructive signals, and overall lacks blood flow for the delivery of oxygen and nutrients,would be unlikely to receive the necessary cues and environment to engraft and differentiate. Thus, given such variations in the underlying clinical context, it is not yet possible to assert an optimal mode of delivery.

An alternative strategy is the ex vivo creation of myocardial tissue, for surgical attachment to the damaged heart. This field of cardiac tissue engineering is advancing rapidly, with cells seeded upon either artificial or biosynthetic three-dimensional matrices.

Pillars of Tissue Bioengineering

Tissue engineering (TE) is the application of knowledge and expertise from a multidisciplinary field to develop and manufacture therapeutic products that utilize the combination of matrix scaffolds and viable cell system for regeneration of cells or tissues damaged by injury, disease or congenital defects[52]. Three dimensional cardiac tissue constructs that express structural and physiological features of native cardiac muscle have been engineered using fetal or neonatal rat cardiac myocytes in collagen gels with mechanical stimulation[53, 54], or on polyglycolic acids and porous collagen scaffolds[55-58]. However, in vivo studies using these scaffolds uncovered limiting factors that reduce their feasibility for therapeutic use. Cardiac implantation did not favour endothelial cell recruitment, it increased inflammatory response and did not produce physiological cardiac muscle contractility[59]. Interestingly nanofibers, a recent addition to tissue engineering materials, offer several advantageous qualities for TE systems. Their porous structure favours cell adhesion, proliferation and differentiation[60], and facilitates efficient exchange of nutrient and metabolic waste, mimicking the architecture and feasibility of physiological extra-cellular matrix[60]. Interestingly, self-assembly peptide nanofibers (RADA16-II) have been injected into the hearts of healthy mice, creating microenvironments that increased endothelial cell precursors and smooth muscle cells migration[61]. The peptide induced the formation of vascular structures and increased the number of cardiomyocytes surrounding the newly formed vessels[61]. Furthermore, RADA16-II did not produce an inflammatory reaction and injection with exogenous neonatal cardiomyocytes increased their survival rate[61]. Another study showed that modification of the peptide with addition of collagen or bone marrow-homing motifs increased neuronal stem cell mobilization and differentiation[60]. However, several problems need to be overcome to biologically mimic the aspects of myocardial tissue.Although, more recently, clinically sized (6x8x2 mm thick), compact cardiac constructs with physiological cell densities were engineered in vitro by mimicking various aspects of the in vivo environment in native myocardium, including oxygen supply, by perfusion of culture medium supplemented with oxygen carriers[62, 63] and the induction of contractions by electrical pacing signals[64], the most advanced existing bioreactors can provide either local micro-environmental control of oxygen and pH (via medium perfusion), or the application of physical stimuli (via electrical stimulation), but are unable to simultaneously deliver both factors. Moreover, a major challenge to be addressed is to extent the application of the same methods and principles to the cultivation of functional cardiac grafts based on human cells.

Future Directions

The regenerative potential of the mammalian heart is a rapidly evolving concept. In the near future, cardiac repair is likely to be augmented through a number of avenues. The dramatic improvements that exogenously administered progenitor cells can affect in both animal and human myocardial repair underscore their therapeutic potential. Although resident cardiac progenitor cell populations have now been identified, the insufficiencies of endogenous stem cells to alleviate acute and chronic damage to mammalian cardiac tissue

remain to be overcome. We think that a combination of ex vivo and in situ cell therapy strategies could be extremely beneficial for cardiac regeneration. Alternatively to gene therapy, we think that preliminary steps should take into consideration a controlled delivery by drug-induced expression of growth factors, such as mIGF-1, to infarcted heart tissue by cardiomyocyte-derived progenitor cells, such as ESCs or CPCs (ex vivo cell therapy; **Figure 2**). Moreover, the possibility of promoting endogenous cell recruitment of endothelial progenitor cells by specific scaffolds, increases the potential to drive the right component to the injured hearts (**Figure 2**). Enhancing the functional regeneration of this most obdurate of organs raises the exciting prospect that regenerative processes in other tissues of the adult mammalian soma might be similarly harnessed to fend off the ravages of aging and disease in a new paradigm of self-renewal.

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BSCR Autumn Meeting 2007

THE QT INTERVAL AND DRUG-INDUCED TORSADES DE POINTES

24th-25th September, 2007 Governors' Hall, St Thomas' Hospital, London, UK

Young Investigator Prizes

The Clinical Science Young Investigator Prize was won by Miss Georghia Michael for her poster:

E-4031-induced Torsades de Pointes is potentiated by HMR1556 or ATX-II but is not predicted by action potential short-term variability or triangulation.

G. Michael, K.A. Kane & S.J. Coker.
Strathclyde Institute of Pharmacy and Biomedical Sciences, University of Strathclyde, Glasgow G4 0NR

The BSCR Prize was awarded to Ian Sabir for his poster:

Effects of hypokalaemia on restitution, alternans and arrhythmogenicity in Langendorff-perfused murine hearts.

I.N. Sabir[1], L.M. Li[1], A.A. Grace[2] & C.L.-H. Huang[1]
[1] Physiological Laboratory, University of Cambridge, Downing Street, Cambridge CB2 4EG
[2] Department of Biochemistry, University of Cambridge, Tennis Court Road, Cambridge CB2 1QW

Secretary's Column

The BSCR met in London again recently for the autumn scientific meeting, which was organized by our current Treasurer, Michael Curtis, at St Thomas' Hospital. It was a particularly focused meeting, on 'The QT interval and drug-induced Torsades de Pointes', which attracted a dedicated audience of about 100 delegates from both university groupings and commercial organizations interested in safety pharmacology. The vitality of the meeting was set at the very beginning when a moderated debate led by a panel of experts on 'QT prolongation - arrhythmogenic or antiarrhythmic?' resulted in a lengthy and animated discussion. There is a proposal to distill all the ideas and information in a document for publication.

The BSCR Committee met earlier for its second meeting of this year and the main item of business was to develop plans for the next scientific meeting that will take place for the first time alongside the annual meeting of the British Cardiovascular Society. The BSCR meeting will take place on the first two days (2-3 June) of the BCS meeting, which will then run until 5 June at Manchester Central (formerly G-Mex Convention Centre). As usual there are no registration fees for BSCR members to attend the BSCR meeting and, to encourage members to stay on for the BCS meeting, there will be no fee to attend the extra days when early registration is made. This is a good idea since a number of the symposia being organized by other of the affiliate groups will involve the BSCR and have a significant basic science component. A first announcement of the BSCR programme can be found on the back page of this issue of the Bulletin and fuller details will be posted on the website (www.bscr.org) within the next few weeks.

The London meeting also provided the opportunity of taking forward the business of the BSCR at the AGM. In the Chairman's report, David Eisner mentioned another highly successful meeting which took place in Spring 2007, in Reading, and gave notice of the future main meetings to be held in Manchester (Spring/Summer 2008) and London (Autumn 2008). A BSCR symposium on 'Vascular calcification' was held at the 2007 BCS meeting in Glasgow. Finally, the Chairman touched on the problem of securing core sponsorship, something that we have enjoyed for a number of years up to the present. The Society remains, however, in a financially secure position, at least in the short term, as long as the income / expenditure for meeting costs is reasonably balanced. This was highlighted in a report provided by the Treasurer, which showed 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 2007. I previously announced that Chris Jackson had been elected by the committee to take over as Secretary in January 2008. This proposal was put to the Society membership present at the AGM and approved. Three ordinary members of the Committee would also finish their terms of office, namely Andy Baker, Katrina Bicknell and Gillian Gray. So with a total of four vacant positions to be filled, a postal ballot of the membership was held in August. Katrina Bicknell was re-elected and others elected were Yvonne Alexander (Manchester), Alison Cave (London) and David Grieve (Belfast), and approval was obtained from the membership at the AGM. Retiring and continuing members were thanked for their contribution to the ongoing business of the BSCR, and particularly for the organization of excellent scientific meetings.

This is my last column and I would like to finish by saying how much I have enjoyed my time as a Committee member and officer of the BSCR. During a six year tenure as Secretary, I have survived two Chairmen, Metin Avkiran, Mike Marber and nearly a third, each with their own very professional approach and great panache. Mike Curtis has been a constant source of wisdom and enduring wit. Nicola Smart with an amazing calm has allowed me huge latitude with publication deadlines. I wish them and other Committee members every success for the future.

Barbara McDermott

Spring 2007 BSCR Meeting: Emerging Therapeutic Targets and Novel Technologies for the Treatment of Cardiovascular Disease.

University of Reading, 29-30th March

A report by Dr Katrina Bicknell, University of Reading

Held on the 130 hectare Whiteknights campus of the University of Reading, the Spring 2007 BSCR meeting was attended by nearly 90 delegates from across the UK, Ireland, Germany, Canada, Brunei and India. The one-and-a-half day programme was designed by organisers Gavin Brooks and Katrina Bicknell to reflect the broad research interests of the Cardiovascular Research Groups within the Schools of Pharmacy and Biological Sciences at the University of Reading, as well as appealing to the wider interests of the BSCR membership. Thus, the programme highlighted cutting edge research aimed at identifying new therapeutic options for the treatment of cardiovascular disease.

The opening session of the meeting focussed on the processes involved in the identification of novel drug targets and the subsequent development of these "drugs" for the treatment of cardiovascular disease. Professor Michael Dunn (Dublin) opened the session with an informative presentation illustrating the advantages and challenges encountered when using proteomics-based approaches to identify novel biomarkers and drug targets. Dr Manuel Mayr (Kings College London) then introduced how his group have combined proteomics and metabolomics to understand the multifactorial processes involved in many cardiovascular diseases. He convincingly emphasised the benefits of determining global changes in protein expressions, post-translational modifications and metabolites to uncover novel molecular and cellular mechanisms involved in cardiovascular disease processes. The next speaker in the session, Dr Clive Long (Organon) then gave an intriguing insight into how pharmaceutical companies approach drug discovery and development. The closing talk of the session was presented by Professor Steve Humphries (University College London), who gave an excellent talk highlighting the impact that an individual's genetic background can have on the effectiveness of certain drug treatments.

The first keynote presentation of the meeting was given by Professor Rüdiger von Harsdorf (Toronto, Canada). He gave an eloquent overview of current therapeutic strategies being investigated worldwide to improve cardiac repair following injury, such as the use of endogenous and exogenous stem cells and pharmacological-based therapies. He then focused on the putative targets that his group have identified in the process of dissecting the molecular mechanisms that limit myocardial repair in the heart. He described how cyclin-dependent kinase inhibitor p21 exerts cell cycle-independent functions that include the modulation of the cardioprotective actions of statins, prevention of cardiac hypertrophy and enhancement of cardiomyocyte survival.

The keynote session was followed by an excellent poster session and wine reception. The poster session provided delegates with the opportunity to discuss their own research interests in poster presentations encompassing a diverse range of topics from both basic science and clinical perspectives. Topics covered included the regulation of platelet function, cardiac development, myocardial regeneration and remodelling, control of heart rate and arrhythmia and atherosclerosis. The poster session was well attended and many discussions were stimulated that, I am sure, were continued at the conference dinner.

The conference dinner that evening was held in the atmospheric grand dining hall in Wantage Hall, the oldest college at the University of Reading, which dates back to 1908. After much good food, wine and company, many of the delegates retired downstairs to

Delegates discussed common research interests during the poster session or refreshment breaks

the "Baa", the bar named in honour of a Hall tradition that started when, in 1928, students released a flock of sheep into the quadrangle to protest against the warden's decision to impose a midnight curfew. Fortunately, forward thinking had ensured that we had extended the Baa's opening hours, so the only protests that arose were over a broken pool table and the rules of tabletop football!

The "early" Friday morning session focussed on the development of novel therapies and delivery methods to target the vasculature. The first speaker of the session was Professor Jon Gibbins (Reading), who critically evaluated current anti-thrombotic drug treatments and highlighted how his group are working to uncover the "Holy Grail" in thrombosis research, the discovery of a drug target that prevents pathological thrombi and not haemostasis. Professor Andrew Baker (Glasgow) then gave an excellent talk on the potential of viral-mediated vascular gene delivery, describing how certain viral pseudotypes or re-engineered viruses can be used to efficiently target specific cell types and improve the safety of viral gene delivery to the vasculature. Dr Martin Oberhoff (Bristol) then discussed the use of drug-eluting stents to prevent in-stent restenosis, a major clinical problem following percutaneous coronary interventions. After weighing up the therapeutic promise of currently-available drug-eluting stents with the associated complications, such as increased risk of stent thrombosis in certain patients, he went on to discuss the development of biodegradable stent materials and new stent coatings. The final presentation in the session was presented by Dr Chris Jackson (Bristol) who gave an entertaining and informative talk in which he challenged the current thinking as to "why atherosclerotic plaques rupture?". He described how his group have shown that vessel expansion and remodelling processes underlie plaque instability.

The second session of the day consisted of four free communications that were selected from submitted abstracts for oral presentation. In the first talk of the session, Ms Catherine Stables (KCL) described the development of a new, robust model of ischaemia-induced ventricular fibrillation using isolated murine hearts. Dr David Ribé (Surrey) then discussed his work investigating the role of NADPH oxidase and reactive oxygen species in adenosine A_2A receptor signalling in murine hearts. The third free communication was presented by Dr Salman Rahman (KCL) who described an essential role for ADAM15 (metagidin) in regulating angiogenesis via a mechanism involving proteolytic processing of urokinase-type plasminogen activator receptor. In the final presentation of this

session, Dr Skakil Ahmad (Birmingham) presented evidence that heme-oxygenase-1 negatively regulates levels of soluble FMS-like tyrosine kinase-1 (sFlt-1) and endoglin, factors that are associated with the clinical symptoms of preeclampsia.

After lunch, the topic of discussion turned to novel therapies for the treatment of the diseased heart. The first speaker in this session was Dr Andrew Trafford (Manchester) who gave a thorough overview of the role of sarcoplasmic reticulum (SR) in modulating contractile function in normal and failing hearts. He described how the distinct roles of sarcoplasmic reticulum calcium content and calcium release by ryanodine receptors in arrhythmogenesis can be dissected and discussed the therapeutic potential of targeting the SR in heart failure. Dr Pat Taylor (National Heart and Lung Institute, London) then presented the impressive advances that her group have made to move towards realising their objective to produce replacement heart valves by tissue engineering. In the final talk of the session, Dr Hüseyin Ince (Rostock, Germany), critically evaluated experimental and clinical evidence addressing the effectiveness and safety of granulocyte-colony stimulating factor (G-CSF) for stem cell mobilisation and/or enhancement of myocardial repair following myocardial infarction. Outlining reasons behind conflicting results from high-profile clinical trials, including patient age, timing of G-CSF treatment and inadequate sample sizes, he concluded that the promise of cytokine therapy to improve myocardial repair warranted further investigation.

The concluding session of the meeting was the second and final keynote presentation, given by Dr Felix Engel (Max Planck Institute, Germany). He described his recent work that has identified p38 MAP kinase as a potential target for improving cardiac repair following injury. He presented evidence to suggest that local delivery of factors that can promote cardiomyocyte proliferation and angiogenesis, p38 MAPK inhibitor SB203580 and fibroblast growth factor, improves heart function, cardiomyocyte survival and angiogenesis following a myocardial infarction. He postulated that this novel pharmacological combination therapy might be employed in the future to enhance cardiac regeneration following myocardial injury.

The meeting was concluded with the announcement of the winners of the Young Investigator Awards for best Poster or Oral presentation, proudly sponsored by the BSCR and Clinical Science Journal. Dr Mehregan Movassagh (Cambridge) was awarded the BSCR Young Investigator Prize for his poster, entitled "Cardiac differentiation in xenopus requires the CDK-inhibitor, p27Xic1". Dr Vinoj George (Surrey), who presented the poster entitled "The role of reactive oxygen species and NADPH oxidase in endothelial cell cycle regulation", was awarded the Clinical Science Young Investigator Prize.

Clinical Science Young Investigator, Dr Vinoj George (Surrey) and BSCR Young Investigator, Dr Mehregan Movassagh (Cambridge).

The BSCR Spring meeting 2007, hosted at Reading, provided a friendly and open forum for BSCR members and non-members with common interests in the treatment of cardiovascular disease, to come together to discuss the current knowledge and approaches being undertaken to develop novel cardiovascular treatments. I would like to take the opportunity to thank the speakers, for their excellent contributions to our programme, the session chairs, BSCR Committee members, past and present, for their support during the meeting, and Sue Aldridge and Tony Cavalheiro, for their administrative support. Special thanks also must go to Fleur Moseley, Andrew Bicknell, Sean Lynch, Andrew Gerry, Liz Williamson, Godfrina McKoy, Christine Williams, and finally, Elaine Nicol and John Pagent at Wantage Hall, as their help and support were invaluable to me and ensured the smooth running of the meeting. Lastly, but certainly not least, this meeting would not have been possible without generous sponsorship from the following organisations, to whom the organisers and the BSCR are very grateful: The British Heart Foundation, The Wellcome Trust, ADInstruments Ltd, BD Biosciences Ltd and Cambridge Bioscience.

Travel report: International Society for Heart Research, Italy, June 2007

By Catherine Stables, Cardiovascular Division, King's College London

ISHR European Section Meeting, Padova-Abano, June 20-22 2007

A summer meeting in Italy was an inspired idea, especially as Britain was experiencing its typical summer weather: it was raining. Lots. So to be wandering through the lovely pedestrianised areas of Padova-Abano on a hot summer's day on the way to the 17th meeting of the European section of the ISHR was very nice indeed.

Though most of the meeting was to be based at the congress centre in Abano, for the opening ceremony we were driven into the centre of Padova to a beautiful old university building. The ceremony started with a lecture on the history of cardiology in Italy, focussing on Padova. It was quite astonishing to hear about the early ideas of the heart as an organ where the "vital spirit" was created, and that for a long time it was thought that the heart had two chambers: one pumping blood, and the other pumping air! Next was a very interesting and comprehensive keynote lecture from Derek Yellon covering a broad range of data on pre- and post-conditioning, from single cells to clinical cases. Roberto Ferrari introduced Professor Tom Ruigrok as winner of the Medal of Merit with a rather unusual, but highly entertaining talk about his "double life", but the theme of the opening ceremony seemed to be of the speakers showing photos of fellow ISHR council members in their younger years (some may now be regretting their choice of hairstyles…). After the lectures there was a reception in an adjacent room. The Italians are certainly experts in hospitality: the buffet was plentiful and delicious, and there was even a choice of wines (and not just 'red' or 'white'!). The evening ended with grappa outside in the courtyard at dusk, surrounded by ancient plaques and statues.

The next morning we were up bright and early for the first full day of the meeting. I was extremely nervous, as I was speaking in one of the first sessions: "Arrhythmias, mechanisms and targets", my first talk at an international conference. Despite the nerves, I really enjoyed the session. It was very well attended, the talks by Karin Sipido, David Eisner and Sylvain Richard were all excellent, and there was some very interesting discussion. As I mentioned, I was very nervous about speaking in front of so many experts in the arrhythmia field, but the atmosphere was quite informal and relaxed, I was asked some good, challenging questions after my talk, and I actually quite enjoyed myself. One of the highlights of the meeting for me was chatting to several people who had attended the session afterwards over coffee, and finding out more about related work they are doing.

Delegates gather in the Congress Centre in Padova-Abano

With another three sessions, and a choice of three parallel symposia in each, the scientific program was excellent. I don't pretend to have understood half of what was discussed in most of the sessions I attended, but I did learn a lot. I hadn't realised, for example, that compartmentalisation of cyclic nucleotides by phosphodiesterases was so important! I particularly enjoyed the session on gender and cardiovascular

disease, as I hadn't even considered the role of gender previously (apparently it is quite a significant factor!), and it was really interesting to hear about the different techniques being used to try and understand the role of sex hormones in various aspects of disease. I hope that gradually I'll expand my knowledge over the next few years to really get to grips with some of the subtleties of these diverse fields.

Overall I thought the meeting was excellent - the science was engaging, with a great range of symposia, the food was delicious (which I think is very important at these things), and the organisation was superb - there always seemed to be a lady from Garden Travel to help you. Would the world congress, with over double the number of delegates, be as good? We would soon find out…

ISHR XIX World Congress, Bologna, 22-25 June 2007

As we strolled in the balmy evening through the beautiful old arcades of Bologna, I had a feeling that I was going to enjoy the World Congress just as much as the European Section meeting. We had already listened to some excellent scientific lectures in the first session of the meeting. David Hearse's lecture on his work on ischaemia/reperfusion injury was diverse and engaging, both in the scientific content and in the style of presentation: I particularly liked his use of a James Bond clip to illustrate the importance of free radicals! After the first of many sessions with a choice of six parallel symposia, followed by a short bus ride into the city centre, we were now heading for the official opening ceremony in the Santa Lucia hall. The venue was a beautiful old church, and a lovely setting for the welcome address by Roberto Ferrari. As they'd promised us, being in Italy, there was a slight air of chaos with microphone problems and one of the speakers delayed due to a train strike, but this didn't affect the quality of the lectures, with an excellent lecture on NO signalling by Nobel Laureate Louis Ignarro. After the session it was a relief to emerge from the rather hot hall out onto the street, to be greeted, in true Italian style, with a huge pasta party. After feasting on a variety of pasta dishes and enjoying a few glasses of the local wine we were treated to another Italian speciality: ice cream. It seemed the perfect way to end the event in the warm evening air, but I felt sorry for the poor waiters who were desperately trying to get us to eat the rapidly melting ice creams!

A view of Bologna

The opening ceremony of the World Congress

The next morning we were up bright and early for the first session of the day, a plenary session on the complexity of the heart beat (focusing on the pacemaker currents). I particularly enjoyed Mike Shattock's back-to-basics lecture on the SA node, though I did feel sorry for the poor lobster. The scientific programme as a whole seemed to cover all aspects of cardiovascular research, and all of the talks were of an extremely high standard. The only complaint was that it was often very difficult to decide which of the parallel symposia to attend! With so many sessions, many with six or more parallel symposia, I can't begin to go into detail about all of the talks I attended, but once again I learnt a lot, and also realised how much more there is to learn! The atmosphere was generally both friendly and exciting: with so many people from all over the world, there was

Bologna's famous arcades

a great buzz. Many of the basic science sessions, such as those on p38 MAPK and other protein kinases were so popular that people were sitting and standing wherever they could fit. The lunchtime sessions were also very successful - the session on the role of the late sodium current was very well attended. The young investigators' symposium on career development was another highlight of the conference for me. There was a range of speakers talking about their own careers and giving advice to those just starting out. Most of the advice was as you would expect - common sense really - but there were some issues raised that left us with things to think about, and it was really nice to have so many young scientists together in one place and to know that we're all in similar situations with some big, and often difficult decisions to make.

I was presenting a poster on the Saturday, and as my first poster presentation at an international meeting I was a little nervous about what to expect. I needn't have worried, however, as it was all very well organised. The posters were in two large marquees, with plenty of room for people to wander around. The lunch (again, lovely Italian food) was also served in the marquees, which almost certainly encouraged people to spend more time looking at the posters than they would have otherwise, and I was very pleased to have 7 or 8 people approaching me to discuss my work.

On the final evening the organisers had arranged for several of the city's most impressive palaces, museums and churches to be opened up, in some cases especially for the congress delegates, on a "white night". Wandering through the town visiting a beautiful old church, a museum with a very impressive statue of Neptune and an ancient palace, all before dinner, was really lovely. The palace, part of the university, was particularly impressive: the dissection room had a marble slab in the centre, and it was incredible to imagine students gathered on the tiered benches around the edge of the room, looking down at a body as the professor read from his anatomy books and directed the dissection.

Inside a University Palace

The dissection room

And so the meeting ended and we headed back to the rainy UK. I'd like to extend my thanks to Fabio Di Lisa and Roberto Ferrari, as well as everyone else who helped to organise these two excellent meetings. I really enjoyed the whole experience, learnt a lot, and am looking forward to the next ISHR world congress in Kyoto in 2010…

Cardiovascular Meetings

Keystone Symposium: Pathological and Physiological Regulation of Cardiac Hypertrophy (A4) Organizers: Leslie A. Leinwand and Eric N. Olson. January 13 - 18, 2008, Copper Mountain Resort, Copper Mountain, Colorado. For further details, please contact:Keystone Symposia, 221 Summit Place #272, PO Box 1630, Silverthorne, CO 80498; www.keystonesymposia.org

Keystone Symposium: Molecular Mechanisms of Angiogenesis in Development and Disease (J5) Organizers: Mark Majesky, Peter Carmeliet and Luisa Iruela-Arispe. January 15-20, 2008. Fairmont Hotel Vancouver, British Columbia. For further details, please contact:Keystone Symposia, 221 Summit Place #272, PO Box 1630, Silverthorne, CO 80498; www.keystonesymposia.org

American Heart Association International Stroke Conference 2008 to be held at Ernest N. Morial Convention Center - New Orleans, LA, USA on Feb 20-22, 2008. For further information, please refer to the meeting website: http://strokeconference.americanheart.org/portal/strokeconference/sc/

AHA Arteriosclerosis, Thrombosis and Vascular Biology Annual Conference 2008 will be held at Omni Hotel at CNN Center - Atlanta, GA on Apr 16-18, 2008. Contact: E-mail: scientificconferences@heart.org; Phone: (888) 242-2453 or (214) 570-5935

XXVIII European Section Meeting of the ISHR will be held on 28-31 May 2008, Athens, Greece. Further information can be obtained from www.ishr-greece2008.gr. Panos Travel Ltd -Attn: ISHR 2008 Phone: +30/2109962500; Fax: +30/2109969245 E-mail: ishr2008@panos-travel.gr

Heart Failure 2008 Congress, 14 June 2008 - 17 June 2008 Milano Convention Centre, Milan, Italy Further Information is available from: Heart Failure 2008 Secretariat, ESC - European Heart House, 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

XXX Annual Meeting of the North American Section of the ISHR. Hilton Cincinnati, Netherlands Plaza, Cincinnati, OH. June 17-20, 2008. Enquiries: Dr Litsa Kranias, litsa.kranias@uc.edu; Dr Jeffrey Robbins, jeff.robbins@cchmc.org

AHA Basic Cardiovascular Sciences Conference 2008 - Heart Failure: Molecular Mechanisms and Therapeutic Targets will be held at Keystone Conference Center - Keystone, CO on 28-31 July, 2008. For further information: E-mail: scientificconferences@heart.org; Phone: (888) 242-2453 or (214) 570-5935

ESC Congress 2008, 30 August 2008 - 03 September 2008 Messe München, Germany. Further information, when available can be found at: http://www.escardio.org/

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 cardiovascular-related meeting and would like to write a report for the Bulletin, please contact the editors. A bursary of **£300** is available towards the cost of your visit, and this will be provided on receipt of the report. *Bon voyage!*

British Heart Foundation Grants

CHAIRS AND PROGRAMME GRANTS COMMITTEE MAY 2007

Special Project Grants

Professor N Chaturvedi et al, Imperial College London. "Ethinic differences in risks and outcomes of the cardiometabolic syndrome: Southall and Brent revisited: SABRE" 5 years (joint award with The Wellcome Trust) £1,000,000

Programme Grants

Professor J Emsley et al, University of Nottingham. "Structure of coagulation factors from the intrinsic pathway: design and development of novel anticoagulants targeting the apple domain" 5 years £759,423

Professor K M Channon, University of Oxford. "Mechanistic importance of tetrahydrobiopterin-dependent eNOS regulation in vascular disease" 5 years £1,261,342

PROJECT GRANTS COMMITTEE MAY 2007

DEFERRED APPLICATIONS AWARDED

Dr P Syrris & Prof W J McKenna, University College London. "Mutations in desmosomal genes as a cause of dominant dilated cardiomyopathy" (1 year) £89,366

Dr S P Hoppler, University of Aberdeen. "Regulation of vertebrate heart muscle differentiation: GATA transcription factors and Wnt signalling interact in a gene regulatory network" (3 years) £166,285

Dr J T B Crawley & Prof D A Lane, Imperial College London. "Characterisation of the molecular interactions between TFPI and protein S" (2 years) £41,245

Prof S Bhattacharya et al, University of Oxford. "GO-CHD: Genetic Origins of Congenital Heart Disease" (3 years) £198,581

Dr R Ascione et al, University of Bristol. "Transplantation of enriched autologous bone-marrow derived CD 133+ cells in patients having coronary surgery after STEMI: a double blind placebo-controlled trial (TransACT)" (3 years) £210,276

NEW APPLICATIONS AWARDED

Prof D M Yellon & Dr D J Hausenloy, University College London. "A study investigating the cardioprotective potential of the novel adipocytokine visfatin" (3 years) £153,536

Prof G D O Lowe et al, University of Glasgow. "Proinflammatory cytokines and cardiovascular risk in later life: British Regional Heart Study and British Women's Heart and Health Study" (1.5 years) £74,037

Dr M Mayr & Prof Q Xu, King's College London. "Proteomic analysis of endothelial progenitor cells" (3 years) £180,878

Prof M T Kearney et al, University of Leeds. "3-hydroxy-3 methylglutaryl-coenzyme A reductase inhibitors, endothelial and endothelial progenitor cell function in Asian men" (3 years) £162,300

Prof C C Lang et al, University of Dundee. "The APEX Trial: Effects of Allopurinol on coronary and Peripheral Endothelial function dysfunction in patients with cardiac syndrome X" (2 years) £120,450

Dr A E Canfield & Dr G A Wallis, University of Manchester. "Determination of the mechanism by which HtrA1 regulates vascular calcification" (3 years) £181,331

Prof C S Peers & Dr J Scragg, University of Leeds. "Regulation of L-type Ca2+ channels by carbon monoxide" (3 years) £140,570

Dr L Venetucci et al, University of Manchester. "The effects on mutations in the ryanodine receptor and removal of FKBP12.6 on Ca release: interactions with β-adrenergic stimulation" (3 years) £178,772

Dr X Wang et al, University of Manchester. "The signalling regulation of cardiac hypertrophy in mice with a cardiomyocyte-specific deletion of ERK5" (3 years) £153,596

Prof M Avkiran & Prof J C Kentish, King's College London. "The role of site-specific cardiac troponin I phosphorylation in PKD-mediated regulation of contraction: an integrated study in murine and human myocardium" (3 years) £158,708

Dr C P Gale et al, University of Leeds. "Characterising hospital performance for acute coronary syndromes using the Myocardial Infarction National Audit Project

(MINAP) Database: data incompleteness, multiple imputation and development of performance indicators" (3 years) £139,271

Prof A M L Lever et al, University of Cambridge. "Lentiviral-mediated gene delivery for attenuating innate and adaptive immune responses to allografts" (3 years) £191,262

Prof K Clarke et al, University of Oxford. "Cardiomyogenesis from cardiac-derived stem-progenitor cells: cell therapy for myocardial infarction and heart failure" (3 years) £299,970

Prof P H Sugden & Dr A Clerk, Imperial College London. "Regulation of nuclear Dbf2-related (NDR)/ Stk38 kinases in the heart and the consequences of their activation" (3 years) £166,245

Dr M Peckham et al, University of Leeds. "How do mutations in the filament-forming region of beta-cardiac myosin cause heart disease?" (3 years) £165,913

Dr A J Jovanovic, University of Dundee. "Overexpression of SUR2A as a strategy to counteract ageing-induced increase in myocardial susceptibility to ischaemia?" (3 years) £136,679

Dr C P D Wheeler-Jones & Dr E M Paleolog, University of London."Prostanoids as key regulators of protease-activated receptor (PAR)-induced endothelial cell activation: autocrine mediators of proliferation, migration and angiogenesis?" (3 years) £177,861

Dr C A O'Callaghan, University of Oxford. "Identification of ligand that activates platelets through CLEC-2 and structural studies of the ligand" (2 years) £112,499

Submission Deadlines for *The* Bulletin:

Volume	*Date*	*Deadline*
21 (1)	***January 2008***	*1st December*
21 (2)	***April 2008***	*1st March*
21 (3)	***July 2008***	*1st June*
21 (4)	***October 2008***	*1st September*

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)

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- Information on forthcoming meetings, workshops and symposia
- All the latest BSCR News
- Job and Study Opportunities
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- Contact details and profiles of BSCR Committee Members

Cardiovascular Related Wellcome Trust Grants

May to August 2007

Programme Grants

Professor Timothy D Spector, St Thomas Hospital, London. Twin research and genetic epidemiology, genetics of ageing: The genetic and environmental determinants of ageing in women. 60 Months £1,856,531

Professor Jonathan R Seckl, Centre for Cardiovascular Science, Queen's Medical Research Institute, University of Edinburgh. 11beta Hydroxysteroid Dehydrogenase Type 1 and atherosclerosis risk. 60 Months £1,529,245

Professor Nishi Chaturvedi, Department of Clinical Pharmacology, National Heart and Lung Institute, Imperial College London at St Mary's. Ethnic differences in risks and outcomes of the Cardiometabolic Syndrome: Southall and Brent revisited: Sabre' 60 Months £17,157

Professor Dermot M F Cooper, Department of Pharmacology, University of Cambridge. Calcium-Sensitive Adenylyl Cyclases and cAMP compartmentation. 60 Months £1,019,885

Senior Research Fellowship

Professor Liam Smeeth, Department of Epidemiology and Pop Health, London School of Hygiene and Tropical Medicine. Making better use of computerised clinical data for epidemiological research. 60 Months £1,206,724

Research Career Development Fellowship

Dr Blanca Rodriguez, Oxford University Computing Laboratory, Wolfson Building. Integrative computational and experimental investigation of the mechanisms of cardiac arrhythmias and defibrillation in acute myocardial ischemia. 60 Months £491,310

Project Grants

Dr Alexandra Gampel, Department of Biochemistry, School of Medical Sciences, University of Bristol. Apical membrane biogenesis and the control of endothelial cell tube formation. 36 Months £254,968

Dr Ming Lei, Core Technologies Facility, School of Medicine, University of Manchester. Electrophysiological and molecular characterization of cardiac conduction system in murine models of Scn5a sodium channel diseases. 36 Months £372,044

Dr P Madeddu, Bristol Heart Institute, University of Bristol. Diabetes-induced bone marrow microangiopathy: a novel target to combat ischaemic complications. 36 Months £218,207

Dr D A Terrar, Department of Pharmacology, University of Oxford. Novel effects of ATP on pacemaker activity of guinea-pig sino-atrial node cells: actions via purinoceptors in the presence and absence of co-activation of other receptor pathways. 36 Months £268,726

Dr Jonathan M Gibbins, School of Animal and Microbial Science, University of Reading. The regulation of platelet signalling and function by integrin-linked kinase. 36 Months £331,896

Dr Mark A Slevin, Department of Biological Sciences, Manchester Metropolitan University. Role of cyclin-dependent kinase-5 in vascularization after ischaemic stroke. 48 Months £321,964

Professor Caroline Fall, MRC Environmental Epidemiology Unit, Southampton General Hospital, University of Southampton. The Cohorts - Consortium of Health Outcome Research in Transitional Societies - Brazil, Guatemala, India, Philippines, South Africa. 24 Months £93,511

Dr Clare V H Baker, Department of Anatomy, University of Cambridge. The role of cell-cell interactions in determining fate choice in sensory ganglia . 36 Months £152,289

Dr Willem H Ouwehand, Division of Transfusion Medicine, East Anglian Blood Transfusion Centre, University of Cambridge. Screening and characterisation of novel platelet candidate genes derived from genome-wide association studies for function in relation to haemostasis and thrombosis in the model organism Danio rerio. 36 Months £223,296

Sir Henry Wellcome Postdoctoral Fellowship

Dr Shane P Herbert, Department of Biochemistry and Molecular Biology, University of Leeds. Molecular genetics of vascular tube and lumen formation in development and disease. 48 Months £250,000

Strategic Translation Awards

Professor Mark B Pepys, Department of Medicine, Royal Free and University College, Medical School, London. Transthyretin depletion for treatment of hereditary systemic and senile cardiac amyloidosis. 36 Months £931,387

Professor Sir A Darzi, Academic Surgical Unit, St Mary's Hospital Medical School, Imperial College School of Medicine, London. I-Snake Surgical Robot (Imaging-Sensing Navigated And Kinematically Enhanced Surgical Robot). 48 Months £2,040,818

FIRST ANNOUNCEMENT - LATE SPRING MEETING 2008

A joint meeting with the

British Cardiovascular Society

"CAUSES AND CONSEQUENCES OF MYOCARDIAL INFARCTION: NEW CONCEPTS"

DATES: Monday 2nd and Tuesday 3rd June, 2008

VENUE: Manchester Central Convention Centre

STRUCTURE: The BSCR Spring Meeting will tale place over 1½ days in parallel with sessions held as part of the BCS Annual Scientific Meeting (2nd - 5th June). The BSCR dinner will be held on the evening of 2nd June.

PROGRAMME: The programme will consist of state-of-the-art presentations by leaders in the field and will include a keynote lecture and four symposia:

Unstable plaque: to inflammation and beyond

Targeting acute and chronic remodelling post-myocardial infarction

Electrophysiological consequences of myocardial ischaemia and remodelling

Novel developments in gene and cell therapy

Free Communications: Part of the programme will be devoted to oral presentation of selected abstracts and others will be presented in a poster exhibition. Submission of abstracts in any area of cardiovascular science is welcomed. There are two prizes of £250 each: the Clinical Science Early Investigator Award and the BSCR Early Investigator Award.

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

Programme details, abstract pro-forma / guidelines, submission deadlines and registration / accommodation arrangements will be available for downloading from the BSCR website by the end of October 2007.

Further Information: Professor Barbara McDermott, BSCR Secretary: Email - b.mcdermott@qub.ac.uk; Phone - 02890 972242 / 975770;

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