University of Birmingham

Dr Stuart Egginton BSc PhD DSc FIBiol FHEA

Honorary Reader in Cardiovascular Sciences

Cardiovascular and Respiratory Sciences

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About

Stuart Egginton is a Reader in Cardiovascular Physiology, and Director of the Angiogenesis Research Group.

Stuart has published nearly 200 research papers and reviews in scientific journals as well as book chapters, and has edited 2 books, in the fields of angiogenesis and cardiorespiratory control. His research has been supported by grants from the British Heart Foundation, Biotechnology and Biological Sciences Research Council, Leverhulme Trust, Medical Research Council, Natural Environment Research Council, and Wellcome Trust.

He is an enthusiastic communicator on the theme of biological research, particularly the translational benefits of *in vivo* experimentation, and regularly talks to both local and national groups in various fora. Stuart contributes to local, national & international media on a range of biomedical topics from hypoxia to hypothermia. His work on cardiorespiratory control and hypothermia was featured on the BBC homepage.

Qualifications

- DSc (Bham) 2008
- Fellow, Higher Education Academy 2007
- Fellow, Institute of Biology 2003
- PhD Physiology (St And) 1982
- BSc Hons Zoology (Wales) 1977

Biography

Stuart Egginton qualified with a BSc (Hons) in Zoology from the University of Wales (Bangor) in 1977, with experience working at the Universities of Bristol and Helsinki, before studying for a PhD in Physiology at St Andrews University where he was awarded a Maitland-Ramsay Fellowship. Stuart was awarded a personal Research Fellowship to work in the USA (Maine) before coming to Birmingham to join the Department of Physiology as a Post Doc in 1985. After another personal Fellowship held in School of Biological Sciences, Stuart returned to Physiology as a Lecturer in 1989, and has continued to work there since. He studies the stimuli inducing blood vessel growth (angiogenesis), and the mechanisms underlying cardiorespiratory control, in health and disease.

His contribution to *in vivo* experimental techniques and contributions to biomedical research have been acknowledged with the conferment of a President's Medal by the Society for Experimental Biology (1990), and holding the position of Visiting Professor at the University of Salzburg, Austria (1997-1998), Erskine Fellow at the University of Canterbury, New Zealand (1998-1999), and Honorary Research Fellow in the Nuffield Department of Medicine, University of Oxford (from 2009). Stuart was awarded a DSc in 2008.

He has been a member of grant awarding panels of the Natural Environment Research Council, and is a regular reviewer for BBSRC, BHF, MRC, NSF and Wellcome Trust grants. His scholarship lead has been recognised by appointment as editor for a number of learned journals: Microcirculation (2003-2010), Experimental Physiology (initially 2006-2009, extended to 2012), Frontiers in Vascular Physiology and Frontiers in Aquatic Physiology (both 2010-2013). He has acted as external assessor for various institutes and departments, as well as examining postgraduate degrees, in the UK and abroad.

In the wider academic circles, Stuart has been elected to Councils of the SEB (1996-2003), British Microcirculation Society (1999-2003), The Physiological Society (2009-2012), and was recently elected President of the BMS (2011-2014). He was elected to Fellowship of the Institute for Learning and Teaching in Higher Education in 2002 (later, Fellow of the Higher Education Academy, 2007) in recognition of breadth and innovation in his teaching. Stuart is a committed participant in the Public Understanding of Science initiative, regularly giving talks to schools and community groups, is the College liaison with Understanding Animal Research, and is a STEM Ambassador for Birmingham. He has given invited lectures around the world on his research, which has attracted widespread international publicity *via* print, radio, TV and web reports and interviews.

Teaching

- BMedSc I, BMedSc II lectures/practicals: cardiovascular & respiratory physiology
- BMedSc III: CVS (angiogenesis in health & disease), CVRS research projects
- Small Group Teaching: all aspects of physiology (BDS, BMedSc, GEC, MBChB)
- MBChB Graduate Entry Course: Designated Expert/Lectures/Practicals
- MBChB I: Student Selected Activity
- MBChB I & II: Integrated Problems, Cancer SGTs
- MBChB II, MBChB III: Special Study Modules
- Module co-ordinator: BMedSc II CVRS, MBChB II SP1, MBChB III SP2

- Joint program co-ordinator: MRes Biomedical Research (*in vivo* skills)
- PBL development: BMedSc, GEC, MBChB
- Personal tutor: MBChB
- Host: Summer Research Studentships (A level & undergraduate students)

Postgraduate supervision

- PhD supervision: currently 2 students (12 to date)
- Regular external examiner within the UK, Europe and beyond
- Hosts PhD students from around the world for training
- Director of Postgraduate Education, Department of Physiology (1992-2002)

Stuart is interested in supervising doctoral research students in the following areas:

- Modelling oxygen transport to tissue
- Angiotherapies for muscle ischaemia
- Stem cell support of angiogenesis
- Ameliorating peripheral organ contribution to central morbidities
- Cardiorespiratory control in hypothermia

If you are interesting in studying any of these subject areas please contact Dr Egginton (see details above), or for any general doctoral research enquiries please email: **dr@contacts.bham.ac.uk (mailto:dr@contacts.bham.ac.uk)** or call +44 (0)121 414 5005. For a full list of available Doctoral Research opportunities, please visit our **Doctoral Research programme listings (http://www.bham.findaphd.com/?es=y&apl=y&aplt=&show)**, or search **http://www.findaphd.com/ (http://www.findaphd.com/)**. For details of the MRes opportunities, please email: **s.l.musgreave@bham.ac.uk (mailto:s.l.musgreave@bham.ac.uk)** or browse **www.mds.bham.ac.uk/biomedicalresearch-invivo (http://www.mds.bham.ac.uk/biomedicalresearch-invivo)**. or call +44 (0)121 414 5005.

Research

Stuart's group studies the mechanisms of blood vessel growth, using physiological remodelling to devise targetted therapeutic repair of a pathologically damaged microcirculation, and how interactions between the cardiovascular and respiratory systems are controlled in hypothermia, showing how its deleterious effects may be ameliorated and lead to safe interventions involving therapeutic bradycardia. The multidisciplinary approach ranges from mathematical modelling and bioinformatic network analysis, through cell and molecular assays, to *in vivo* tissue performance and integrative function in a range of animal species and man. These experiments explore the limits to physiological adaptation, and the origins of human morbidity.

1) Angiogenesis

The Angiogenesis Research Group is studying the mechanisms underlying growth of blood vessels in skeletal and cardiac muscle, with a particular emphasis on determining how mechanical factors (i.e. the local physical environment of endothelial cells) may initiate and control the proliferation of capillaries during *in vivo* angiogenesis. Currently under investigation is how increased blood flow (elevated shear stress) and muscle overload (increased longitudinal strain) lead to different patterns of growth originating at the inner (luminal) and outer (abluminal) surfaces, respectively. The combination of local factors invoked during muscle activity is compared with those seen during alterations in the external environment (e.g. hypoxia, hypothermia), including the differential influence of humoral and perivascular signals. These data are essential for the development of angiotherapies to promote regulated vascular growth or controlled vascular rarefaction, as required. This work has widespread implications - some estimates suggest 80% of NHS medical burden could benefit from targetted angiotherapy.

Important developments include the observations that capillary growth can be induced with or without breakage of the basement membrane, endothelial proliferation may precede the formation of sprouts, the lack of involvement of FGF, and that VEGF, NO and metalloproteinases may differentially regulate physiological angiogenesis. These findings do not conform to the patterns established for pathological or *in vitro* models of angiogenesis. Further studies to elucidate this distinction include the role of stromal cells (pericytes, fibroblasts, macrophages) in controlling angiogenesis, and the link between small and large vessel growth. Exciting new avenues for angiotherapy being explored include manipulation of the HIF transcription pathway, the potential role for stem cells in treatment of muscle ischaemia (using endothelial progenitors), and how mobilisation of other blood components (platelets, leukocytes) may affect the angiogenic response to physiological or pathological stimuli.

2) Oxygen transport

The responses to impaired blood flow or increased activity are used to examine how oxygen supply and demand are balanced. Analysis of capillary distribution within heterogeneous tissue (e.g. muscle with different fibre types) utilises morphometric quantification of capillary supply among fibres in terms of 'supply equivalents'. Scaling of capillary supply with respect to fibre size is the usual pattern observed in skeletal muscle of all vertebrates, and this basic growth process may be modified to a limited extent with training or under pathological conditions (see above). This work identifies the need for tight spatial organisation of adaptive angiogenesis. Complimentary to the extracellular diffusion distances described in this manner, changes to intracellular oxygen tension are examined using mathematical models to examine the relative efficiency of different changes in the pathway of oxygen transport to tissue. Bioinformatic analysis of complex diseases, those with central and peripheral components involving impaired oxygen transport, is used to explore the possibility of better targetted treatment for established co-morbidities (e.g. heart failure, respiratory disease).

3) Muscle plasticity

The metabolic and ultrastructural responses of skeletal muscle to chronic reduction in blood flow or increased activity are followed in order to identify the range of strategies available to balance nutrient supply and demand. Work on chronic ischaemia is continuing to examine the apparent dissociation between structural and functional damage to the endothelium, and impairment of vascular reactivity liked with NO production. Glycolytic and oxidative muscles respond differently to similar stimuli, although metabolic and structural indices of aerobic capacity are closely related in most, but not all, cases (e.g. capillary supply and oxidative capacity may be varied independently, and localised interventions may have significant remote effects). Adaptations examined include myopathic and training responses in humans; electrical stimulation and ischaemia in mammals; steroid and overload hypertrophy in mammals; migratory fitness in a range of vertebrate species.

4) Cardiorespiratory control

How well the cardiovascular system copes with reduced core temperature has major implications for survival in all vertebrates, and use of clinically invoked hypothermia. Using a specially designed environmental chamber (photoperiod and temperature control), the strategies adopted by species that adapt to a cold environment are compared with the more limited tolerance of other mammals (including man). The cardiovascular response of hibernators to hypothermia examines angiogenic potential, vascular reactivity and cardiac autonomic control mechanisms; this has required development of new software (for power spectral analysis) and hardware (data loggers for long term storage), with potentially broad application. Ectotherms from polar & tropical environments provide additional insights into the physiological limits to life on the edge from an evolutionary perspective. Identifying the preserved or ancestral mechanisms will define the most robust, and therefore likely profitable, avenues for therapeutic intervention.

Other activities

Non-university activities include helping with an overseas student hospitality scheme, serving on the local PCC, and as Church Warden helped steer a £1.1m rebuild of an Anglican church and community centre.

Publications

Egginton, S., Badr, I., Williams, J., Hauton, D., Baan, G.C., Jaspers, J.T. (2011) Physiological angiogenesis is a graded, not threshold response. **J. Physiol.** 589.1: 195-206.

Ormerod, J.O.M., Ashrafian, H., Maher, A., Arif, S., Steeples, V., Egginton, S., Feelisch, M. Watkins, H., Frenneaux, M.J. (2011) The role of vascular myoglobin in nitrite-mediated blood vessel relaxation. **Cardiovasc. Res.** 89.3: 560-565.

Egginton, S. (2010) Regulation of angiogenesis – may the force be with you! **J. Physiol.** 588.23: 4615-4616.

Egginton, S., Gaffney, E.A. (2010) Tissue capillary supply – it's quality not quantity that counts! **Exp. Physiol.** 95.10: 971-979.

Egginton, S. (2009) Activity-induced angiogenesis. **Pflügers Archiv.** 457: 963–977.

Scott, G., Egginton, S., Richards, J.G., Milsom, W.K. (2009) Evolution of muscle phenotype for extreme high altitude flight in the bar-headed goose. **Proc. Roy. Soc. B** 276: 3645-3653

Campbell, H.A., Fraser, K.P.P., Bishop, C., Peck, L.S., Egginton, S. (2008) Hibernation in an Antarctic fish: On ice for winter. **PLoS ONE** 5;3(3): e1743

Facucho-Oliveira, J., Alderson, J., Spikings, E., Egginton, S., St. John, J. (2007) Mitochondrial DNA replication during differentiation of murine embryonic stem cells. **J. Cell Biol**. 120.22: 4025-4034

Details of further publications can be found **here (http://labs.ukpmc.ac.uk/search/?page=1&query=AUTH:%22Egginton+S%22+SORT_DATE:y&restrict=All+results)** .

Expertise

How blood vessels grow (angiogenesis) to treat pathologies associated with poor oxygen supply (ischaemia, hypoxia), and muscle inactivity or overload; determine origin of cold tolerance in warm-blooded animals (how to avoid hypothermia) and in Antarctic fishes (evolutionary biology); the adaptability of cardiovascular and blood pressure control