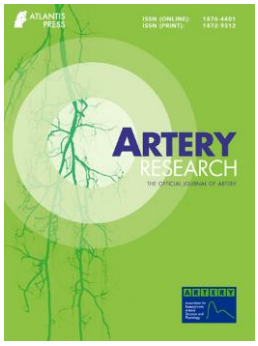

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REMODELLING SMALL ARTERIES AND PHD TRAINING: A JOURNEY

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ARTERY Conference 16 — Speaker

Opening Lecture
REMODELLING SMALL ARTERIES AND PHD TRAINING: A JOURNEY

Michael J. Mulvany, Professor
Professor emeritus, Department of Biomedicine, Aarhus University, Denmark Aarhus University, Aarhus, Denmark

Abstract
Biomedical research is increasingly based on the efforts of PhD students. This talk will trace the development of the author's research, and show how this experience can be used to optimize PhD training. The basis of the research has been that essential hypertension is associated with increased peripheral resistance due to narrowing of the small arteries and arterioles. The author's PhD training ended in 1978 with development of a technique that enabled accurate measurement of the structure and function of small arteries. The technique was adopted by many laboratories world-wide, and also formed the basis for the author to establish a research group (with 22 PhD students over the years) that elucidated excitation-contraction properties and the morphology of small arteries, and how these were altered in essential hypertension. Vessels showed increased media:lumen ratio with inward eutrophic remodelling and limited functional changes. The remodelling was found to have prognostic consequences. The inward remodelling was found to be due to the vasoconstriction itself, mediated through multiple cellular pathways. The remodelling can be prevented by vasodilators and the results have had clinical effect. While this career path points to some success, it would unlikely happen in today's academic environment in that the author's PhD training took about 10 years. Through being head of the faculty graduate school and vice-president of the organization ORPHEUS (Organization for PhD education in Biomedicine and Health Sciences in the European System), the author has sought to establish procedures to ensure that today's PhD students are able to prepare for successful careers — within or outside of academia — even within the normal 3-4 year time constraints.

Special Guest Lecture
STEM CELL THERAPY FOR CARDIOVASCULAR DISEASES

Jean Sebastien Silvestre, Professor
INSERM UMRS 970, Paris Cardiovascular Research Center, Université Paris Descartes, Sorbonne Paris Cité, Paris, France

Abstract
Stem cell-based therapies for vascular regeneration in patients with cardiovascular ischemic diseases initially relied on a very simple concept: therapeutic stem/progenitor cells might differentiate into vascular cells, mainly of endothelial phenotype, increasing new vessel formation and tissue perfusion in the ischemic milieu. This exciting notion challenged the scientific community to start the quest for the Holy Grail in vascular regenerative medicine: the search for the ideal source of endothelial stem/progenitor cells. This concept leads to the development of salutary approaches based on the use of therapeutic autologous adult stem cells thought to contain such bona-fide endothelial progenitor cells such as bone marrow- or peripheral blood-derived mononuclear cells. Beside the classical technical caveats including modalities of cell transfer and optimization of cell engraftment, the negative impact of cardiovascular risk factors as well as the low rate of incorporation of adult stem cells in the targeted vasculature likely explain the mixed results obtained in numerous phase I-II clinical trials incorporating patients with peripheral artery or cardiac diseases. Hence, alternative sources of stem cells have been considered to leverage their intrinsic pluripotentiality and drive them towards a vascular lineage. Both embryonic stem cells and induced pluripotent stem cells have then been tested in various experimental models of post-ischemic vascularization. However, as for their adult counterpart, these "embryonic" cells do not structurally integrate within the recipient vascular network but likely release biomolecules that fine-tune endogenous repair processes. A precise characterization of the cell-released factors purportedly accounting for their benefits still remains elusive. However, there are mounting evidences to suggest that stem cells can release extracellular membrane vesicles that may contain vascular regenerative entities. Hence, the natural evolution of the stem cell theory for vascular regeneration may end with the development of cell-free strategies with multiple cellular targets including vascular cells but also other infiltrating or resident cells.

Invited Lecture
ARTERIAL PROTEOMICS: LESSONS IN RELATION TO STIFFNESS, ANEURYSMS, DIABETES AND OTHER CONDITIONS

Lars Melholt Rasmussen, Professor
Clinical Biochemistry, Odense University Hospital, Odense, Denmark

Abstract
Proteins are the main molecular components of the arterial wall. Alterations in the amounts of specific proteins in both the extracellular matrix and in vascular cells are believed to be associated with different arterial pathologies, however only sparse data is currently available, particularly in relation to human arteries.
Proteome analysis is large scale analysis of the quantity of many proteins in a single analytical run from biological samples. Combining "state of the art" proteome analysis by LC-MS (liquid chromatography-mass spectrometry) with access to samples from a large human artery biobank, we have obtained knowledge about protein changes in arteries from patients with various cardiovascular conditions. Specific alterations in matrix proteins are for example present in relation to increased arterial stiffness and to diabetes, whereas alterations in non-matrix proteins are associated with the growth rate of aortic aneurysms.
Such new knowledge about changes of arterial proteins in specific vascular conditions can direct our attention towards pathophysiological understandings and display routes to new potential treatment targets and novel biomarkers for arterial diseases.

Career Development Lecture
WAVE POTENTIAL: A UNIFIED MODEL OF ARTERIAL WAVES, RESERVOIR PHENOMENA AND THEIR INTERACTION

Jonathan P. Mynard, Joseph J. Smolich
Heart Research, Clinical Sciences, Murdoch Childrens Research Institute, Department of Paediatrics, University of Melbourne, Australia

Abstract
Models of haemodynamics play a central role in current research directed to understanding and addressing cardiovascular disease. Although