Abstracts

11th International Symposium on Resistance Arteries

From Molecular Machinery to Clinical Challenges

(www.karger.com/jvr_51_S2_14)

Banff, Alberta, Canada, September 7–11, 2014

Guest Editors

Maria Sancho, Calgary, Alberta

Donald G. Welsh, Calgary, Alberta

135 abstracts, PDF (811Kb), 2014
Editorial

The eleventh International Symposium on Resistance Arteries (ISRA) was successfully hosted in Banff, Alberta, Canada (September 7-11, 2014) under the subtheme of “from Molecular Machinery to Clinical Challenges”. The Banff Centre, a leader in the development and promotion of creative work in the arts, sciences, business, and the environment and it was an ideal venue to foster interactions, discussions and to exchange ideas. It is the second time that ISRA has been held in Canada and Banff National Park was an ideal although snowy setting. There were 180 attendees from 18 countries and high quality forum on resistance artery research were presented over the 4 day period. These forum consisted of oral presentations designed to provide in-depth analysis on key topics and poster sessions (130 total abstracts) that fully engaged faculty, postdoctoral fellows, graduate and undergraduate students. Thematic symposia highlighted calcium imaging, excitation-contraction coupling, vascular pathology, unique vasculature, ion channels, genetic regulation of the arterial wall, adiposity and vascular control, cell-cell communication and endothelial structure/function. In the overview below, we summarize key highlights of the meeting.

Donald Welsh, Professor of Physiology and Pharmacology (Faculty of Medicine, University of Calgary (Canada)) was the Conference Chairperson and opened the meeting on September 7, 2014. The Plenary Lecture (sponsored by Danish Myo Technology) by Constantino Iadecola (Weill Cornell Medical College, USA) was enlightening and entitled “Neurovascular pathways to cognitive impairment: blood flow and beyond”. This lecture detailed the importance of cerebral blood vessels and how alterations in vascular function can lead to cognitive impairment and neurodegenerative dementia such as Alzheimer’s disease. Dr Iadecola’s presentation began at the integrative level and progressed towards current research highlighting a role for TRP channels in cerebral vascular dysfunction.

The opening oral session on September 8, 2014 centered on calcium imaging and excitation-contraction coupling. In the first presentation, Fernando Santana (University of Washington, USA) discussed how the anchoring protein AKAP150 and protein kinase C (PKC) dynamically regulate transient receptor potential vanilloid 4 (TRPV4) channels in arterial myocytes during angiotensin II (Ang II) signaling. Subsequently, Osama Harraz (University of Calgary, Canada) discussed how Cav3.2 channels drive a local Ca\(^{2+}\)-induced Ca\(^{2+}\) release-like process that restrains arterial constriction through the induction of Ca\(^{2+}\) sparks and the activation of large-conductance Ca\(^{2+}\) activated K\(^{+}\) (BKCa) channels. Matthew Nystoriak (University of California Davis, USA) detailed how diabetes influences cAMP-dependent protein kinase (PKA) contractility via signaling components in microdomains including L-type voltage-dependent Ca\(^{2+}\) channels (LTCCs). This session was closed in a lively manner by Theodor Burdyga (University of Liverpool, UK) who utilizes live confocal imaging of ureteric microvascular network to better detail the structural and signaling properties of myocytes and pericytes and probe the influence of blood flow control in this key vascular bed.
Two related sessions were presented on September 8 and 11, with a focus on **smooth muscle ion channels**. Ryuji Inoue (Fukuoka University, Japan) discussed the post-translational modulation of TRPC6 (a canonical transient receptor potential protein) and its physiological/pathophysiological consequences on vessel function. Pernille Hansen (University of Southern Denmark, Denmark) and Lars Jensen (University of Copenhagen, Denmark) focused the audience’s attention on non L-type Ca\(^{2+}\) channels and how their expression in smooth muscle and potentially endothelial cells influence mechano-sensitive responses. Mohammed Trebak (SUNY CNSE, USA) closed the second session with a presentation on Orai channels and how defined subunits encode for a leukotriene C4-regulated Ca\(^{2+}\) channel that is modulated distinctly from Ca\(^{2+}\) release-activated Ca\(^{2+}\) (CRAC) channel. On September 11, Teresa Perez-Garcia (University of Valladolid, Spain) used a mouse model of genetic hypertension to explore how alterations in K\(^{+}\) and Ca\(^{2+}\) channel activity lead to vascular dysfunction. These intriguing discussions dovetailed nicely into work presented by Thomas Jepps (University of Copenhagen, Denmark) which identified KCNE4 in vascular smooth muscle and demonstrated altered expression with hypertension. The dynamic interplay between nitric oxide and BK channels was described by Rudolf Schubert (Medical Faculty Mannheim, Germany). In the closing presentation, Iain Greenwood (St George’s College, UK) provided a grand overview of KCNQ channel expression and how they impart vasomotor behavior in the mesenteric circulation.

Forty-eight posters were presented during the First Poster Session on September 8, with a focus on offering wider reflection on different aspects of current vascular research. These sessions were designed to encourage knowledge exchange and networking between all the attendees. A number of posters were also presented as part of the oral presentations. The awardees in the first Trainee Poster Competition were: Christopher Moore (University of Arkansas), Ahmed Hashad (University of Calgary), Thomas Jepps (University of Copenhagen), David Rosenegger (University of Calgary), and Matthew Nystoriak (University of California, Davis).

The first day of the meeting ended with a session entitled “**Unique Vasculature**”. David Zawieja (Texas A&M University College of Medicine, USA) characterized the regulation of lymphatic contractile activity and highlighted their unique sensitivity to shear and pressure. Presentations selected from abstracts focused on: 1) the importance of sarcoplasmic reticulum and inositol triphosphate receptors in retinal tone regulation (Olga Kudryavtseva, Aarhus University Hospital, Denmark); and 2) the role of BK channels in enabling pulmonary artery adaptation to high altitude (David Hessinger, Loma Linda University, USA). This session was followed by Michael Walsh’s seminar (University of Calgary, Canada) on afferent renal arteries and mechanisms of dephosphorylation of myosin light chain.

Early mountain snow greeted delegates on the second full day (September 9, 2014). Avril Somlyo (University of Virginia, USA) opened “**Calcium sensitization**” (IUBMB Sponsored session) with a presentation focused on the function of the RhoA GTP exchange factor p63RhoGEF and its role in blood pressure regulation. Postdoctoral trainees from University of Calgary (Ryan Mills) and Toronto (Jeffrey Kroetsch) honed in on specific aspects of Ca\(^{2+}\) sensitization as it related to Pyk2, a tyrosine kinase, and TNF\(\alpha\), an endogenous tumor necrosis factor that can modulated myogenic tone in isolated skeletal muscle resistance arteries. Katsuya
Hirano (Kagawa University, Japan) ended the session with his discussion of Rho-associated coiled-coil protein kinase 2 (ROCK2), and how intrinsic circadian rhythms influence its activity and consequently myofilament Ca\(^{2+}\) sensitivity. Following the morning break, a second session on **Cytoskeletal Dynamics** (IUBMB Sponsored session) began with William Cole (University of Calgary, Canada) who demonstrated the importance of integrin receptors and actin polymerization to the initiation of myogenic constriction of rat cerebral arteries. Khaled Abd-El Rahman, a PhD student with Dr Cole, extended these observations into the Goto-Kakizaki type 2 diabetes rat model, highlighting that the loss of actin polymerization was associated with a reduction of myogenic tone. Building upon the myogenic theme, fluorescence microscopy experiments by Maria Bloksgaard (University of Southern Denmark) showed how intravascular pressure induced microarchitectural changes in the elastin/collagen matrix of porcine pericardial resistance arteries. In closing this session Louis Martinez-Lemus (University of Missouri, USA) discussed the long term remodeling changes with hypertension and their association with cytoskeletal structures.

Great science and ample discussion were again present at the Second Poster Session (48 posters) which provided another opportunity for networking and the exchange of innovative ideas about current vascular research. In this session, Jeffrey Kroetsch (University of Toronto), John Reho (University of Maryland), Ryan Mills (University of Calgary), Sara Turner (University of Calgary), Irene Lopez (University Picardie Jules Verne) and Sevvandi Sendhara (University of Melbourne) were all winners of the Second Trainee Poster Competition. We congratulate all awardees as well as the judges who worked hard during the competition. Conference travel awards were provided to Holger Schneider (Walter Brendel Centre of Experimental Medicine, Ludwig Maximilians University Munich), Maria Jelinic (University of Melbourne), Erik Behringer (University of Missouri), Irene Lopez (University Picardie Jules Verne), Robert Little (University of Manchester), Bjorn Hald (University of Copenhagen), Thomas Lautz (Walter Brendel Centre of Experimental Medicine), Magdalena Sternak (Jagiellonian Centre for Experimental Therapeutics, Poland), Vibeke Secher Dam (Aarhus University), Nuria Villalba (University of Vermont), Christopher Moore (University of Arkansas), Michal Behuliak (Institute of Physiology AS CR) and Jin Quek (Australian School of Advanced Medicine). Trainee travel and poster awards were sponsored by the IUBMB and the University of Calgary (Biochemistry & Molecular Biology, Clinical Neurosciences and Physiology & Pharmacology departments) and Cumming School of Medicine Associate Dean of Research.

The evening session turned towards translational science and focused on **Adiposity and Vascular Control**, Anthony Heagerty (University of Manchester, UK) examined the interaction between perivascular adipocytes, the inflammatory process and arterial function during Type 2 diabetes and hypertension. Building upon this paradigm, Charlotte Bussey from the same institution explored in detail the anti-contractile effects of perivascular adipose tissue on the contractility of mesenteric arteries. Keeping with the mesenteric circulation, Erika Boerman (University of Missouri, USA) showed a decrease in function and density of perivascular sensory nerves with aging and that this change compromised functional vasodilation. Ending this session, Maik Gollasch (Charite University Medicine, Germany) addressed the role of adipose-derived relaxing factor (ADRF) in vascular dysfunction in obesity and hypertension and what role
particular $K^+$ channels play in mediating this response. It was a stimulating session and
discussion continued into the evening at the local pub.

There was no reprieve from the snowy weather on September 10, 2014. The first session
centered on **Endothelial Cell Structure and Function** with Mark Nelson (University of
Vermont, Canada) discussing his recent work on discrete $Ca^{2+}$ signals and the how the PKC-
anchoring protein, AKAP150, at myoendothelial projections is required for Gq-coupled receptor
activation of TRPV4 channels. Calcium imaging by Matthew Socha (University of Missouri,
USA) next demonstrated that intracellular transmission of $Ca^{2+}$ waves along the endothelium of
mouse resistance arteries and that it can be actively modulated by stimulus intensity and
duration. Shaun Sandow (University of the Sunshine Coast, Australia) presented provocative
data to suggest that BK channels are expressed in arterial endothelium following focal cerebral
ischemia and acute hypoxia. Prior to the morning break, Dolly Mehta (University of Illinois,
USA) provided a qualified review on her recent advances in understanding the role of $Ca^{2+}$
permeable TRP channels in increasing endothelial permeability, edema formation and
inflammation.

The second morning session on **Cell-Cell Communication** began with examination of kidney
blood flow and how Neils-Henrick Holstein-Rathlou (University of Copenhagen, Denmark) is
utilized experimental approaches to explore the importance of the vascular conducted responses
(VCR) to the synchronization of regional perfusion responses. Bjørn Hald from the same
laboratory (University of Copenhagen, Denmark) presented computational approaches to explore
the nature of electrical communication in the arterial wall and the minimal number of
myoendothelial gap junctions needed to sustain cell-cell communication and an efficient
conducted response. The second half of this session shifted to neurovascular coupling with David
Rosenegger (University of Calgary, Canada) illustrating that astrocyte activity following brief
stimulation was not required for cerebral arterial dilation to occur. Finally, Anna Devor
(University of California, USA) presented a state-of-the-art review on neurovascular coupling
and how new innovative technologies such as optogenetics allows one to address key unresolved
questions such as how neuronal metabolism is linked to tissue oxygenation and arterial tone
control.

The day continued after lunch with the presentation of late breaking abstract posters (16 posters),
and the afternoon session (**Vascular Pathology: From Cell Physiology to Clinical Practice**)
which initiated an interesting discussion on the clinical diagnosis and management of cerebral
small vessel disease. Eric Smith’s (University of Calgary, Canada) lecture focused on emerging
neuroimaging biomarkers of vascular integrity and vascular function while Jaime Grutzendler
(Yale University, USA) focused his presentation on angiophagy as a ubiquitous mechanism that
could be therapeutically targeted for vascular occlusive disorders. David Liebeskind (UCLA,
USA) highlighted the collateral circulation in the brain and its importance in ameliorating acute
ischemic stroke and intracranial atherosclerotic disease. This session concluded with a talk from
Loch Macdonald (St Michael’s Hospital, Canada) who evaluated the role of TNF in a
subarachnoid hemorrhage and then proposed that anti-TNF and anti-S1P treatment may improve
clinical outcome.
A gala dinner was held in the evening of September 10, 2014. It was an enjoyable event that included entertainment and fortuitously a break in the weather. The sun continued to appear on the final day and the warmer temperatures greeted the participants in the session entitled Genetic Regulation of the Arterial Wall. Joe Milano (University of Rochester, USA) discussed the role of long non-coding RNA genes and a highly permutable transcription factor binding site known as a CArG box in vascular smooth muscle cells. Robert Little (University of Manchester, UK) delved into the regulation of the plasma membrane calcium ATPase isoform 1 (PMCA1) protein with hypertension, concluding that it could be a possibly viewed as a therapeutic target. Next, John Reho (University of Maryland, USA) addressed how sympathetic neural inputs developmentally program mesenteric resistance artery smooth muscle and that stress-induced hyperactivity in a critical window may mis-program tissue and lead to hypertensive diseases in childhood. Finally, Sebastian Albinsson (Lund University, Sweden) discussed his most recent work involving a novel mechanism for regulation of calcium signaling and vascular tone by microRNAs.

In summary, the 11th ISRA successfully provided a dynamic forum for scientific presentations. Ample opportunities were available for delegates to discuss current research on resistance arteries and future collaborative efforts. Presentations were excellent and there was considerable interaction between trainees, junior and senior faculty. The site for the 12th ISRA Symposium in 2017 is England and Anthony Heagerty will lead the organizing efforts.
Acknowledgements

We gratefully acknowledge our platinum sponsor, the Hotchkiss Brain Institute for its substantial support. Additional conference funds were also provided from Heart & Stroke Foundation Alberta, Alberta Innovates-Heath Solutions, Libin Cardiovascular Institute of Alberta, International Union of Biochemistry & Molecular Biology (IUBMB), Danish Myo Technology Inc, Olympus Canada, Nikon Canada, Applied BioPhysics, Living Systems Instrumentation, IonOptix, Department of Clinical Neurosciences (University of Calgary), Department of Biochemistry & Molecular Biology (University of Calgary), Department of Physiology and Pharmacology (University of Calgary). Special thanks to Eric Smith, MD who sponsored ISRA through the Katthy Taylor Chair in Vascular Dementia Program and Andrew Demchuck, MD who sponsored ISRA through the Heart and Stroke Foundation Stroke Research Chair Program.