**Dear Member,**

The Annual Scientific Meeting will be held on the 21-23 October 2015 at the Maritime Museum Fremantle. The scientific program and abstract submission deadline will be released very soon but below is a glimpse on the confirmed international and national speakers for 2015.

International speaker:
**Prof. Bart Staels** - Université de Lille, France

National speakers:
**Prof. Leonard Kritharides** - University of Sydney, Australia
**Prof. Karlheinz Peter** - Baker IDI, Melbourne, Australia

Included in this e-News letter:
• Annual Scientific Meeting Information
• Information for SCOLAR 2015 - SCOLAR 2015 is proposed to be held on October 16th 2015 at the Charles Perkins Centre- University of Sydney. Further details and confirmation of this sate and venue will follow in the near future.
• AAS and Social Media (Facebook and Twitter)
• Membership renewals
• AAS Trust Fund Travel Awards Information
• ASMR newsletter
• A Feature article entitled: **"Is it clinically relevant to measure circulating PCSK9 levels?"** from **A/Prof. Gilles Lambert**, Université de Nantes, Nates France

**Fatiha Tabet, Editor**

## AAS Scientific Meeting 2015

**Date:** 21-23 October 2015 at the
**Location:** Maritime Museum Fremantle.

With prizes for Young Investigators and Students, both oral and poster presentations, there is something for everyone to aim for.

Dinner at the ASM will be held in the Mussel Bar, a great waterfront location just a short walk from the meeting venue.The scientific program is still under development and all meetings details including accommodation options can be found on the new secretariat website: Click here to view.

Confirmed International Speaker:

**Prof. Bart Staels - Université de Lille, France**
Prof. Bart Staels' research focuses on molecular pharmacology of cardiovascular and metabolic diseases, including dyslipidemia and type 2 diabetes. He particularly studies the role of nuclear receptors (such as the PPARs, FXR, Rev-erba and RORa) in the control of inflammation, lipid and glucose homeostasis as well as the transcriptional mechanisms involved. Prof. Staels was among the first to identify a crucial role for the nuclear receptor PPARa in the control of lipid and glucose metabolism as well as cardiovascular function in humans. He elucidated the action mechanism of the fibrate class of drugs that are currently used in the treatment of lipid disorders and worked also on the action mechanism of the glitazones, a very recently developed class of anti-diabetic drugs. His work has identified the PPAR transcription factors as potential drug targets for the treatment of diabetes, dyslipidemia and cardiovascular disease, which contributed to the development of several novel therapeutic compounds, one of them is currently in type IIb of clinical development.

Confirmed National Speaker:

**Prof. Leonard Kritharides - University of Sydney**
Professor Len Kritharides is Head of the Department of Cardiology and Director of Echocardiography at Concord Repatriation General Hospital, and Professor in Medicine University of Sydney. He practices as a General and Interventional Cardiologist and undertakes a wide range of clinical and

basic research. Particular clinical interests include the primary prevention of coronary disease, the management of complex hyperlipidemia, cardiac involvement in muscular dystrophy, pulmonary embolism and pulmonary hypertension, and cardiac toxicity after chemotherapy or after psychotropic medications.

**Prof. Karlheinz Peter - Baker IDI Melbourne**
Prof Karlheinz Peter laboratory pursues a broad range of projects that have the common focus on improving diagnosis and therapy of thrombotic and inflammatory diseases such as myocardial infarction and atherosclerosis. A range of biotechnological methods are used in Prof. Peter's Laboratory, including recombinant protein design/production, generation of functionalised nanoparticles/ lipsomes/microbubbles, cell culture, flow cytometry, flow chamber, intravital microscopy, ultrasound, MRI, PET various fluorescence imaging systems and various animal models of thrombosis, atherosclerosis and inflammation. All of these projects have a strong translational orientation.

## SCOLAR 2015

**Date:** 16th October 2015
**Location:** Charles Perkins Centre - University of Sydney

The SCOLAR Program will showcase research in areas relevant to the AAS Annual Scientific Meeting. This year it will be held at the **Charles Perkins Centre - University of Sydney**. A webinar will be available live from the University of Sydney venue.
For SCOLAR Program information please contact Dr. Mary M Kavurma: Mary.Kavurma@hri.org.au

## AAS and Social Media

Information regarding the AAS activities will be posted on Facebook and Twitter. You can now follow us using the links below:

**Facebook Page:**
Click here or search for Aus Atherosclerosis Society

**Twitter Page:**
Click here or search for Athero Aussie

## Membership Renewals

If you have any problems renewing your membership online by following the instructions below, please do not hesitate to contact admin@yoursecretariat.com.au or call 02 4356 0007.

If your email is up to date, you should by now have received an email with instructions to re-set your password and update your details, as the new Secretariat website has now been launched, and you old password for the meetings first membership site **will not work.**

All of your details on file have been uploaded into the new system, however we have noted that there are a number of details which may be out of date, so please, when you change your password, take a moment to update all of your details, to ensure you receive all communications and information.

The new **Secretariat site** allows you to manage all aspects of your membership in one spot including:
- Applying / renewing membership for both AAS and HBPRCA with multi-year options
- Registering for meetings in due course

- Applying for travel grants when they become available
- Find your fellow members though the directory and
- Keep up to date with HBPRCA and AAS twitter feeds

Instructions and a snapshot of the website are provided below:

1. **IMPORTANT:** You will need to set a NEW password to use the new site. Please click on the link in the e mail you received or contact admin@yoursecretariat.com.au if you did not receive it or cannot locate it.
2. Log into the membership site using your email and newly created password.
3. Click on Renew/Apply for membership to check and update your personal details.
4. Please add our email address, admin@yoursecretariat.com.au to your contacts and bookmark the new membership site aashbprca.yoursecretariat.com.au for future reference.

Annual memberships were due for renewal by March 31, so please take the time to renew now if you have not already done so, to ensure you continue to receive the benefits only membership can bring you.

If you have any questions about your membership, please call 02 4356 0007 or email admin@yoursecretariat.com.au

**PLEASE ENSURE YOU ADD admin@yoursecretariat.com.au TO YOUR CONTACTS AND SAVE THE LINK TO YOUR FAVOURITES. If you have any issues at all or did not receive the e mail to reset your password please e mail admin@yoursecretariat.com.au directly – thank you.**

## AAS Trust Fund

The AAS Trust Fund is available to our young investigator members to attend their favorite scientific meeting.
Once confirmation of abstract acceptance to the conference is received, please apply via http://aashbprca.yoursecretariat.com.au/

We have received 3 grant applications, all of which have been approved:

Denuja Karunakaran and Liming Hou are both to attend the ATVB / PVD 2015 meting in San Francisco this month and Vyoma Patel will be attending the ISA in Amsterdam.

We look forward to receiving their report upon their return an hearing about their experiences and details of both meetings are below.

### ISA 2015

An interactive schedule is available: http://www.isa-2015.com/program/interactive-schedule/

### ATVB/PVD 2015

The Arteriosclerosis, Thrombosis and Vascular Biology/ Peripheral Vascular Disease 2015 Scientific Sessions will be held in San Francisco, California USA- May 7-9, 2015.
This meeting will be held in Collaboration with the Council on Functional Genomics and Translational Biology, and the Society for Vascular Surgery's Vascular Research Initiatives Conference. ATVB 2014 Abstracts will be published in the ATVB Journal.

Please visit the meeting website:
http://my.americanheart.org/professional/Sessions/ATVBPVD/ATVB-PVD-Home_UCM_316902_SubHomePage.jsp

If you have any questions regarding the AAS Trust Fund, please contact the secretariat admin@yoursecretariat.com.au

## A message from ASMR

Please click here to view the ASMR's first newsletter for the year. It includes articles covering topics on current state of funding, past-present and future of NHMRC, scientific advocacy, the challenges faced by clinician-scientists, indigenous health and ASMR activities. I would like to take this opportunity to thank ASMR Director Dr Andrew Burgess for producing a great newsletter and also all the contributing authors for providing us with interesting current articles.

ASMR Medical Research Week® is just around the corner (28th May-5th June, 2015). The ASMR MRW® events are a chance for the whole sector to unite and continue to share your breakthroughs in your field with other researchers, the community and politicians. Abstract submissions are open for ASMR state conferences, tickets are available for Gala dinners to meet this years ASMR medallist Prof Ashok Saluja – a champion from bench to bedside. Thank you to all of the hard work of ASMR state committees and ASMR Director Dr Rebecca Patrick for putting together an outstanding program of national events. Behind the scenes of every ASMR event across the country is our extremely hard working Senior Executive Officer Ms Catherine West and our administrative assistant Priscilla Diment – thank you both!

I am very pleased to announce ASMR's 54th National Scientific Conference (15th-18th November, 2015) to be held in Adelaide. The theme of our conference is 'Bugs, Bowels and Beyond: Innovations in Digestive Health and Disease Research'. Read our newsletter for details on invited speakers. I would like to thank ASMR Directors Dr Luke Hesson and Dr Joanne Bowen for organising this event.

Dr Phoebe Phillips

**ASMR President**

## AAS Feature article – A/Prof. Gilles Lambert

**Is it clinically relevant to measure circulating PCSK9 levels?**

Université de Nantes, Faculté de Médecine, Nantes, France

A/Prof. Lambert is a Principal investigator on the Cardiovascular benefits of PCSK9 inhibition at the Faculté de Médecine, Université de Nantes, Nantes, France.
A/Prof Lambert was a professional member of the AAS from 2006 to 2011, while he was performing his research on PCSK9 in the Lipid Group at the Heart Research Institute (Sydney) in collaboration with Prof. Kerry-Anne Rye and Prof. Philip Barter.

"It is well established that PCSK9 acts primarily as a secreted inhibitor of the LDL receptor. The enzymatic activity of PCSK9 allows auto-processing of the PCSK9 precursor within cells [1]. After this initial maturation step, PCSK9 is routed towards the secretory pathway. Following secretion, PCSK9 binds to the LDL receptor at the surface of cells and is internalized together with the receptor by endocytosis [2-5]. The affinity between the LDL receptor and PCSK9 increases as a result of the acidic conditions in endosomes [6-9]. The interaction between PCSK9 and the LDL receptor locks the

receptor in an extended or 'open' conformation. The failure of the receptor to adopt a 'closed' conformation in endosomes precludes normal recycling to the plasma membrane and targets the LDL receptor for lysosomal degradation [10]. The characterization of total and liver-specific PCSK9 knockout mice indicates that hepatocytes are the main source of circulating PCSK9 [11]. It has been proposed that PCSK9 acts on the receptor before it reaches the cell surface of hepatocytes [12], but a series of cellular and in vivo experiments have clearly demonstrated that PCSK9 acts primarily as an extracellular factor [13, 14]. It may then seem relevant to measure circulating levels of PCSK9 from a clinical perspective.

The first reports of PCSK9 measurements in human plasma were published in 2007. What is most striking about these studies is that plasma PCSK9 levels consistently correlated with LDL-cholesterol [15-19], in agreement with the role of PCSK9 as an inhibitor of the LDL receptor. In familial hypercholesterolemia [14], low PCSK9 plasma levels were observed in patients with the milder phenotypes [20]. Positive correlations between LDL cholesterol and PCSK9 were similar in control individuals and untreated FH patients, irrespective of their LDLR genetic defects [20, 21]. PCSK9 levels were the highest in homozygous FH patients and higher in heterozygous FH than in non-FH individuals [20-23], an expected observation since the LDL receptor plays a pivotal role in PCSK9 plasma clearance [21]. In addition, statin treatments consistently increased circulating PCSK9 levels [24-29], in agreement with the activation of PCSK9 gene expression by statins observed in vitro [30, 31]. For instance, in the JUPITER trial, rosuvastatin (20mg/day) was found to increase plasma PCSK9 by 35% in women and 28% in men [32].

The correlations between PCSK9 and LDL cholesterol levels reported in the literature appear surprisingly low (r=0.19-0.58) [15-19, 24-29]. Indeed, the ELISAs developed in research laboratories or commercially available lack the ability to discriminate between the various forms of PCSK9 present in the plasma, such as, (1) the gain of function and loss of function variants [33], (2) the mature form and shorter forms (e.g. furin cleaved) [34, 35], (3) the forms differentially modified post-translationally (e.g. through sulfation or phosphorylation) [34, 36], and (4) the self-associated forms (e.g. monomers vs. dimers) [37] that have all been shown to display variable LDL receptor degrading activities in vitro. Furthermore, >30% of total PCSK9 circulates associated with LDL particles by interacting with apoB100 whereas 70% is free in the plasma [38]. Thus, in patients with severe FH, lipoprotein apheresis removed not only LDL particles (-80%) but also a large proportion of circulating PCSK9 (-50%) [39]. It is not known whether LDL-bound and LDL-free PCSK9 equally inhibit the LDL receptor.

Overall, PCSK9 ELISAs do not account for the various forms of PCSK9 mentioned above., and neither do they account for the presence of natural PCSK9 inhibitors in the plasma (e.g. Annexin A2) [33, 40, 41]. Despite these limitations, measuring PCSK9 plasma concentration with ELISAs has greatly improved our knowledge of this fascinating protein. It is to date the less invasive and most practical method to readily investigate the biology of PCSK9 in humans. Since PCSK9 expression is regulated in part by the nutritional status and displays a diurnal regulatory pattern [42, 43], PCSK9 should be measured in plasma samples drawn ideally around 8AM after an overnight fast [44]."

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Sincerely,

Your Secretariat

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