The Journal
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Information for Authors
There are no page charges for submission to the journal. All manuscripts are solicited by the Editorial Board, but submissions may also be made to Executive Editor Nikki Krol at nkrol@pvri.info or to Editor in Chief Dr. Sachindra Joshi at sachindraraj_joshi@nymc.edu

Subscription Information
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# PVRI CHRONICLE

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**January- June 2014**

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PVRI Chronicle: an evolved platform for the PVRI communication

The Chinese philosopher Lao Tzu famously said that a thousand mile journey begins with one step. Although the earliest reliable historic reference to the philosopher dates from 100 BCE, his saying still holds true today, as the Pulmonary Vascular Research Institute (PVRI) moves one step ahead in its 8 year journey to increase the awareness and knowledge of pulmonary vascular diseases (PVD).

Its founders foresaw an open and non-hierarchical idea exchange within the field of PVDs, unlimited by the censorship of accepted consensus. As the PVRI grew and evolved, its mission became more defined, and soon the Pulmonary Vascular Research Institute was established as a medical educational centre concerned with the research, education and awareness of PVDs worldwide, with a specific focus on the underserved regions of the world. This identity still holds true today, although admittedly, the PVRI has changed face–most notably in the introduction of this very journal. Following the successful PVRI Review (for details, please see the Annual Report on p.65 and Prof. Harikrishnan’s Guest Editorial on pp. 2-4), the PVRI Chronicle is a natural progression in the PVRI Publications initiative. The journal is divided into sections to fit the articles from a wide range of areas and perspectives, in order to form a truly inclusive view of the state of pulmonary vascular diseases and the actions of the PVRI and its members.

Recent advances in communication technology, the growing popularity of online publication and the increasing use of hand held electronic devices to access news and articles online have swiftly changed the nature and presentation of publications, journals, and even books. For a young institution like PVRI, adaptation to these developments is vital.

So, reflecting the zeitgeist, the new journal is non-peer reviewed, bi-annual, available online and open access, with a likely print on demand feature. Additionally, PVRI Chronicle will expand its communication potential into tablets and smartphones in the form of an app later this year.

Presided over by the PVRI Young Council, the journal is homemade in every way, meaning it is formatted, edited and published entirely by the Institute. This provides flexibility regarding adaptation and saves valuable time and costs. Additionally, this ‘at home’ approach to the formatting, as well as the technological advances, allow far more possibilities than any paper journal. The PVRI App can feature advanced versions of the PVRI Chronicle which could include videos, slideshows, animated figures, image magnification, hyperlinks, and feedback options.

It goes without saying that your support is invaluable. By reading this first issue of the PVRI Chronicle, and sending in submissions for upcoming volumes, you are an asset to the Journal and a major part of its success. The comments and feedback from the readership will help this very new editorial team create an effective platform of communication. Therefore, on behalf of the editorial board of PVRI Chronicle and the members of PVRI Young Council, I urge the senior fellows of PVRI to help us grow by stimulating your junior physicians, medical students, graduate students and post doctoral fellows to contribute articles to the PVRI Chronicle. After all, in the words of Henry Ford, if “coming together is a beginning; keeping together is progress; working together is success”, let us work together to make PVRI Chronicle a success.

Dr. Sachindra Joshi
FPVRI
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I attended the first official formative meeting of PVRI India on June 30th, 2008. The meeting was attended by Prof. Sheila Haworth and Prof. Ghazwan Butrous, as well as a number of PVRI Fellows from India. During the meeting, Ghazwan described the plans and future direction of the PVRI, and it was here that the idea of a PVRI journal was first introduced. Ghazwan told us that he has searched all over before choosing a publisher named Medknow in Mumbai, India, with whom he had previously interacted. The publisher was headed by a pediatrician, Dr. DK Sahu, and published some 70+ journals at the time. Ghazwan enquired whether I would be willing to help him in the venture of a PVRI journal. To this day, I am still not sure why he asked me!

Since it was an opportunity to interact with pioneers in the field of pulmonary hypertension and provided the chance of getting acquainted with the processes of editing and publishing, I accepted the responsibility. The proposed name of the Journal was “Pulmonary Circulation” and Ghazwan had already registered the domain name for PVRI. He wanted the journal to start publishing its first issue in January 2009.

Ghazwan, as per his wonderfully productive character, started bombarding me with mails regarding the progress of the journal. With the deadline for first publication a mere 5 months away, Ghazwan wanted the journal published in multiple languages! He wrote, “I still like to consider the translation issue in advance, for the reason that one of the main missions of the PVRI as a global institute is to have multi-language educational material”. I replied that I fully agreed that the multi-language journal was an excellent idea, but that I was worried about the logistics. This was further confirmed when we got an email from the published Dr DK Sahu on July 25th 2008, reminding us that ‘We need to get started soon if we wish to launch the journal in Jan 2009’.

With the pressure on, our first step was via the medical illustration department in my hospital, which developed a model for the cover page and sent it for feedback to all the editorial board members on July 30th.

On August 4th 2008, there was a meeting of the PVRI Board of Directors, which altered the intended course of the Journal (“all positives, but new ideas” – as per Ghazwan).

The final decision came about two weeks later, and changed the name of the journal to ‘PVRI Bulletin’. This would be the official name until we were established as a journal, at which point the name would be converted to Pulmonary Circulation. By then it was already August 15th and we were nowhere and had nothing, except a draft of the cover page!

On 20th of August 2008, PVRI and Medknow signed an agreement to publish a Quarterly Journal, of which the name had by then evolved to “PVRI Review”. The intention was to publish it as an educational journal which would also reflect the PVRI activities. It was to be printed in English, but with simultaneous issues in other languages like Portuguese, Spanish, and Chinese.

At this point, I was nominated officially as the Editor-in-Chief of the journal with the concurrence of the PVRI India taskforce.
Ghazwan wanted the Journal to be showcased in the Mexico meeting of PVRI in January 2009. So now the deadline was set in stone, Ghazwan was on our case, and we had only the name, publisher, official Editor-in-Chief and cover page of the journal in place. It was time to get moving!

Our next step was an Editorial board – emails started flowing, and before long we formed a good editorial board. As a team, we developed instructions to authors and started creating a workflow for the journal. At this point we had only few review articles, mostly collected through the efforts of Ghazwan. We started sending emails to friends and colleagues in the field soliciting articles, but the tight deadline proved an issue for many of them. In response, we started working with whatever material we had. Ghazwan gave me the additional task of preparing a review article on Rheumatic Heart Disease and Pulmonary Hypertension, which added to my worries. To further complicate the situation, I unfortunately had a health problem and was forced to take rest for a period of 2 months in November 2008. On the upside, this meant I could devote more time to the journal! By then, Medknow Publications also geared up in the form of a devoted team for the PVRI Review. It was on! As we continued to solicit articles, we also searched various options for translation of the journal to other languages like Portuguese, Spanish and Chinese. We explored the options of google translate as well as individual translators, and received a number of proposals. With time quickly running out, we nonetheless decided to translate a few articles to Spanish, Arabic and Portuguese and publish it in the first issue.

Many processes were new to me and the PVRI, and journal publication means a lot of hard work and repetition. The copy-editing, proof-reading, re-sending to the authors, re-proofing is a cycle which involves two or three go-arounds before an article is ready, and as we planned to include the annual reports from various PVRI task forces, we had the additional task of chasing taskforces for reports and photographs. One common problem we faced was the low resolution or ppi of many of the pictures and figures which we received. These figures may look good on the computer screen, but prove very fuzzy in print. It was a little difficult to convince the authors to resend high-quality pictures, but on most occasions they came through and we could manage. Finally, by December 7, 2008, we had collected all the articles and, after proofreading, sent them to Medknow, the publisher. December was hectic, filled with proof reading, finalizing the format of each section, ensuring consistency and quality, etc, etc. Luckily December is not Holiday season in India, meaning Medknow could work in the Christmas week also. On December 27, we sent the final version to all editorial board members for their approval. Our aim to make it online on the first day of 2009 was unsuccessful due to technical issues, but the Journal was published online on 3/01/2009. And so, with much work and a steep learning curve, a new journal was born! The print copies were ready to be shipped to Mexico and reached their destination on time for the meeting. Due to my ill-health I could not attend the Mexico Conference, but Ghazwan show-cased the Journal and let me know it was well appreciated.

We published four issues in that inaugural year. Dr. Maria Virginia Tavares Santana, our colleague from Brazil, did an excellent job in bringing out a Portuguese edition of the journal in 2009. We continued to publish on a quarterly basis in 2010, and by that time we had developed a well-working system in the PVRI for running a journal. So PVRI reinitiated the plan for Pulmonary Circulation, which was to become a peer-reviewed quarterly journal with a focus on original research. The gang of four – Ghazwan, Harikrishnan, Jason Yuan and Nick Morrell started working on it according to
the same lines as we established with the PVRI Review. Our efforts proved successful, and the first issue of *Pulmonary Circulation* (PC) became available online on March 16, 2011. *Pulmonary Circulation* was indexed in PubMed within the publication of just two issues, a remarkable achievement of the PVRI.

Around this same time we started scaling down on PVRI Review. The Journal had a ‘new role’ after the establishment of *Pulmonary Circulation*, and PVRI Review was redesigned as a PVRI newsletter and a medium to publish views and opinions of PVRI members in relation to pulmonary vascular diseases. We had two issues in 2011 as well as a Portuguese supplement.

By then, I was working with *Pulmonary Circulation* and PVRI Review and also took on the additional responsibility of heading the PVRI India task force. PVRI was kind to me in accepting my request to relieve me of the duties related to PVRI Review. Dr. Sachindra Joshi, a very active young researcher within the PVRI, took over as the Editor-in-Chief with the support of a new, young editorial board. Subsequently two issues were published, one each in 2012 and 2013. Post PC, its content was markedly different from previous years, and met with appreciation from its readers.

Now PVRI had made the decision to retire PVRI Review this year and proceed with an online journal named PVRI Chronicle. So PVRI Review is going to be part of history.

I want to take this opportunity to profusely thank the PVRI and its fellows and office bearers for giving me this wonderful opportunity to work as Chief Editor of the PVRI Review. My sincere thanks are to Prof. Ghazwan Butrous, without whom this journal would not have seen the light of day. His dedication and vision were the main force behind PVRI Review and *Pulmonary Circulation*. My thanks are also due to Prof. Stuart Rich and Prof. Martin Wilkins for their support. Similarly, Prof. Sheila Haworth was always a support for me, whilst Ms. Nikki Krol, the PVRI administrator, proved a person to rely on when you have a problem. The publisher Medknow was remarkable and flexible even though we had some issues initially, and my thanks goes to the whole PVRI Review publishing team in Medknow, with special thanks to Dr DK Sahu, who was the CEO of Medknow publications at that time.

I feel I am lucky to be associated with such an endeavor. During my time as Editor-in-Chief, I was able to establish contacts with many researchers in the field of PVD, and learned a lot about the field of medical editing and publishing. For all this, and for their support and their enthusiasm, their articles and their readership, their feedback and their contributions, I thank the PVRI and all its members and Fellows.

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Email: drharikrishnan@outlook.com
The 8th PVRI AGM
& the 7th Workshops and Debates

and

the Joint Symposium PVRI/ECCPS 2014
Giessen/Bad Nauheim 27-31 January 2014

Monday, January 27, 2014

13:00 - 18:00 Board of Directors and Advisors Meeting
(invitation only)
09:00 – 10:30 I Lung vascular compliance and recruitment  
Chair: David Badesch, Anna Hemnes

09:00 Right heart afterload at rest and exercise  
Robert Naeije, Bruxelles

09:20 Discussion

09:30 PA stiffness and right ventricular-PA coupling  
Rebecca Vanderpool, Pittsburgh

09:50 Discussion

10:00 Detection and evaluation of the potential for lung microvascular recruitment in PAH  
David Langleben, Montreal

10:20 Discussion

10:30 – 11:00 Coffee break

11:00 - 12:30 II Anticoagulants and angioplasty in PH  
Chair: Paul Corris, Harrison Farber

11:00 Pro and con of anticoagulants in PAH  
Paul Hassoun, Baltimore

11:20 Discussion

11:30 Role of novel anticoagulants in CTEPH  
Irene Lang, Vienna

11:50 Discussion

12:00 Angioplasty for CTEPH – pro and con

12:00 Pro Hiromi Matsubara, Okayama

12:15 Con Eckhard Mayer, Bad Nauheim

12:30 – 13:30 Lunch
13:30 – 15:00 III Pulmonary hypertension in children
Chair: Glennis Haworth, Maria Jesus del Cerro

13:30 The lung vasculature in bronchopulmonary dysplasia
Dick Tibboel, Rotterdam

13:50 Discussion

14:00 PH classification in children post Panama and Nice
Maurice Beghetti, Geneva

14:20 Discussion

14:30 Current and future therapy of PH in children
Steven Abman, Aurora

14:50 Discussion

15:00 – 15:45 Peter Raymond memorial lecture
Chair: Martin Wilkins, Ghazwan Butrous

Adaptation to high altitude living
Cynthia Beall, Cleveland

15:45 – 16:15 Coffee Break

16:15 – 18:30 Annual General PVRI Meeting

19:30 Dinner
Joint Symposium PVRI-ECCPS

08:55 Welcome

09:00 - 10:45 I Infection, inflammation and pulmonary vascular disease
Chair: Serge Adnot; Friedrich Grimminger

09:00 The Immunesystem component in pulmonary hypertension
Norbert Voelkel, Richmond

09:20 Discussion

09:30 Pulmonary hypertension due to schistosomiasis
Brian Graham, Denver

09:50 Discussion

10:00 HIV associated pulmonary hypertension
Marc Gladwin, Pittsburgh

10:20 Discussion

10:30 Best Abstract selected for oral presentation
to be announced

10:40 Discussion

PVRI Breakout Symposia

08:55 Welcome

09:00 - 10:45 I Technology progress in cardiopulmonary disease – ECCPS platforms
Chair: Thomas Braun, Ralf Brandes

09:00 Genomics, proteomics and bioinformatics
Thomas Braun, Bad Nauheim

09:20 Discussion

09:30 Small animal imaging
Ralf Schermuly, Giessen

09:50 Discussion

10:00 Molecular analysis and high resolution imaging
Ralf Brandes, Frankfurt

10:20 Discussion

10:30 Best technology focused abstract selected for oral presentation
to be announced

10:40 Discussion

10:45 – 11:15 Coffee break
**Combined ECCPS-PVRI session**

**11:15 – 13:00 II Stem cells in heart and lung (re)-generation**  
*Chair: Norbert Voelkel; Thomas Braun*

11:15 Co-development of the lung vasculature and right ventricle  
*Ed Morrisey, Philadelphia*

11:35 Discussion

11:45 Postnatal cardiac regenerative potential: implication for novel therapies?  
*Hesham Sadek, Dallas*

12:05 Discussion

12:15 Cellular plasticity in lung morphogenesis and regeneration  
*Jeffrey Whitsett, Cincinnati*

12:35 Discussion

12:45 Best Abstract selected for oral presentation  
to be announced

12:55 Discussion

**11:15 – 13:00 II Pregnancy and pulmonary hypertension**  
*Chair: Anna Hemnes; Tim Lahm.*

11:15 Genetics and pathophysiology of PH during pregnancy  
*Barbara Cockrill; Boston*

11:35 Discussion

11:45 Management of PH in pregnancy in PH centers  
*Zeenat Safdar, Houston*

12:05 Discussion

12:15 Management of PH in pregnancy in the developing world  
*Manal Al Hazimi, Riyadh*

12:35 Discussion

12:45 Best Abstract selected for oral presentation  
to be announced

12:55 Discussion

**Combined ECCPS-PVRI session**

**15:00 – 16:45 III Genetics and personalized medicine in cardio-pulmonary diseases**  
*Chair: John Newman; Ralph Schermuly*

15:00 Genetics underlying signaling in PAH  
*Jim Loyd, Nashville*

15:20 Discussion

15:00 – 16:45 III Post-IMPRESS – What is the future of TKI in pulmonary hypertension therapy?  
*Chair: Mark Gladwin, Werner Seeger*

15:00 The historical background  
*Ardeschir Ghofrani, Giessen*

15:20 Discussion
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<th>Speaker/Institution</th>
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<td>Heribert Schunkert, München</td>
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<td>Discussion</td>
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<td>16:00</td>
<td>iPSCs and personalized medicine</td>
<td>Marlene Rabinovitch, Stanford</td>
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<td>16:20</td>
<td>Discussion</td>
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<td>16:40</td>
<td>Discussion</td>
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<td>15:30</td>
<td>The FDA’s view</td>
<td>Stuart Rich, Chicago</td>
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<td>15:50</td>
<td>Discussion</td>
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<td>16:00</td>
<td>The EMA’s view</td>
<td>Amany Elgazayerly, EMA</td>
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<td>16:20</td>
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<td>16:30</td>
<td>A clinician’s view</td>
<td>Paul Corris, Newcastle</td>
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<td>16:40</td>
<td>Discussion</td>
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<td>16:45 – 17:15</td>
<td>Coffee break</td>
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<tr>
<td>17:15 – 19:00</td>
<td>IV Left and right heart hypertrophy and maladaptation</td>
<td>Chair: Stephan Rosenkranz; Ardi Ghofrani</td>
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<td>17:15</td>
<td>The left heart</td>
<td>Georg Ertl, Würzburg</td>
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<td>Discussion</td>
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<td>17:45</td>
<td>The right heart</td>
<td>Paul Hassoun, Baltimore</td>
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<td>18:05</td>
<td>Discussion</td>
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<td>18:15</td>
<td>Diagnosis &amp; management of PH &amp; right heart failure due to left heart disease</td>
<td>Marco Guazzi, Milan</td>
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<td>18:35</td>
<td>Discussion</td>
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<td>18:55</td>
<td>Discussion</td>
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<td>17:15 – 19:00</td>
<td>IV PH in chronic lung disease</td>
<td>Chair: Joan A Barbera; Andreas Guenther</td>
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<td>17:15</td>
<td>PH concomitant with or due to COPD</td>
<td>Yochai Adir. Haifa</td>
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<td>17:35</td>
<td>Discussion</td>
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<td>17:45</td>
<td>PH concomitant with or due to ILD</td>
<td>Martin Kolb, Hamilton</td>
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<td>18:15</td>
<td>PH in CPFE &amp; advanced sarcoidosis</td>
<td>Vincent Cottin, Lyon</td>
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<td>Discussion</td>
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<td>Discussion</td>
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<td>19:00</td>
<td>Hot wine punch reception and dinner at the Dolce Hotel</td>
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**Wednesday January 29 2014**

**PVRI Chronicle: Volume 1 Issue 1, January - June 2014**
THURSDAY JANUARY 30 2014

PARALLEL SESSIONS

09:00 – 10:45 V Epigenetics of heart and lung disease
Chair: Jim Loyd; Stefanie Dimmeler

09:00 MicroRNA control of the pulmonary hypertensive vasculature
Kevin White, Glasgow

09:20 Discussion

09:30 HDACs in pulmonary vascular diseases
Kurt Stenmark, Denver

09:50 Discussion

10:00 microRNAs for reprogramming in cardio-pulmonary diseases
Thomas Thum, Hannover

10:20 Discussion

10:30 Best Abstract selected for oral presentation
to be announced

10:35 Discussion

09:00 – 10:45 V Novel technologies for healthcare in the developing world
Chair: Jason Yuan; Julio Sandoval

09:00 The challenges for clinical trials in PH in the developing world
Majdy Idrees, Riyadh

09:20 Discussion

9:35 Recife experience
Angela Bandeira, Recife

9:55 Discussion

10:10 PVRI programs to promote pulmonary vascular disease management in the developing world
Glennis Haworth, London

10:30 Discussion

10:45 – 12:30 Coffee break + Poster Session II

12:30 - 13:30 Lunch
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<tr>
<th>Time</th>
<th>Event</th>
<th>Speaker(s)</th>
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<tr>
<td>13:30</td>
<td>VI Hypoxia and high altitude disease</td>
<td>Chair: Andrew Peacock, Ralf Brandes</td>
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<tr>
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<td>oxygen sensing and HIF regulation</td>
<td>Larissa Shimoda, Baltimore</td>
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<tr>
<td>13:50</td>
<td>Discussion</td>
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<td>14:00</td>
<td>Redox regulation in cardiopulmonary physiology and pathology</td>
<td>Philipp Eaton, London</td>
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<td>14:20</td>
<td>Discussion</td>
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<td>14:30</td>
<td>High altitude pulmonary vascular disease</td>
<td>Erik Swenson, Seattle</td>
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<td>14:50</td>
<td>Discussion</td>
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<tr>
<td>15:10</td>
<td>Discussion</td>
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<tr>
<td>15:15</td>
<td>Coffee break + Poster Session III</td>
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<tr>
<td>17:00</td>
<td>Highlight Lecture “The Robyn Barst Memorial Lecture”</td>
<td>Chair: David Langleben</td>
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<td></td>
<td>Pulmonary vascular abnormalities in lung disease from a global perspective</td>
<td>Nicholas Hill, Boston</td>
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<tr>
<td>18:15</td>
<td>Departure for Dinner by bus</td>
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<tr>
<td>19:00</td>
<td>Reception + Dinner Castle “Burg Gleiberg”</td>
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</table>
**Friday January 31 2014**

**Parallel Sessions**

<table>
<thead>
<tr>
<th>Time</th>
<th>Session</th>
<th>Chair</th>
<th>Speaker/Location</th>
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<tbody>
<tr>
<td>09:00</td>
<td><strong>VII Adaptive and maladaptive angiogenesis</strong></td>
<td>Duncan Stewart; Ingrid Fleming</td>
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<tr>
<td>09:00</td>
<td>Vascular niche and organ function</td>
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<td>Eli Keshet, Jerusalem</td>
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<tr>
<td>09:20</td>
<td>Discussion</td>
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<tr>
<td>09:30</td>
<td>Angiogenesis in lung morphogenesis and repair</td>
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<td>Bernard Thebaud, Ottawa</td>
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<tr>
<td>09:50</td>
<td>Discussion</td>
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<tr>
<td>10:00</td>
<td>Direct reprogramming for therapeutic vasculogenesis?</td>
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<td>John Cooke, Stanford</td>
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<td>10:20</td>
<td>Discussion</td>
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<tr>
<td>10:30</td>
<td>Best Abstract selected for oral presentation</td>
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<td>to be announced</td>
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<tr>
<td>10:40</td>
<td>Discussion</td>
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<tr>
<td>09:00</td>
<td><strong>High altitude medicine</strong></td>
<td>Norbert Weissmann; Almaz Aldashev</td>
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<td>09:00</td>
<td>Hxpoxia sensing</td>
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<td>Paul Schumacker, Chicago</td>
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<tr>
<td>09:20</td>
<td>Discussion</td>
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<tr>
<td>09:30</td>
<td>HIF and erythropoietin: functions in the cardio-pulmonary system</td>
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<td>H.Franklin Bunn, Boston</td>
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<td>09:50</td>
<td>Discussion</td>
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<tr>
<td>10:00</td>
<td>Chronic mountain sickness</td>
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<td>Aaron Waxman, Boston</td>
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<td>Discussion</td>
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**Friday January 31 2014**

10:45 – 11:00 Poster Price Awards

11:00 – 11:30 Coffee break
<table>
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| 11:30 | VIII Molecular imaging in heart and lung disease  
  *Chair: Paul Hassoun; Andreas Zeiher*  
  **11:30** Lessons from patient-specific induced pluripotent stem cells  
  *Joseph Wu, Stanford*  
  **11:50** Discussion  
  **12:00** Imaging of cardiac function and failure  
  *Frank Bengel, Hannover*  
  **12:20** Discussion  
  **12:30** PET in cardio-pulmonary disease  
  *David Newby, Edinburgh*  
  **12:50** Discussion  
  **13:00** Best Abstract selected for oral presentation  
  *to be announced*  
  **13:10** Discussion  
  **11:30 – 12:45** Hot topic session  
  Emerging issues of paediatric pulmonary hypertension  
  *Usha Raj, Chicago*  
  **12:45 – 13:00** Paediatric Taskforce Discussion  
  **13:15 END OF SYMPOSIUM** |
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<tr>
<th>Room 1: Parksaal</th>
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<tr>
<td><strong>MON 27/01</strong></td>
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<tr>
<td>AM &amp; lunchtime</td>
<td>Young Council Meeting 9:00 - 12:00</td>
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<td>PM</td>
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<tr>
<td><strong>TUE 28/01</strong></td>
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<tr>
<td>AM &amp; lunchtime</td>
<td>PVRI Chronicle Lunchtime meeting</td>
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<tr>
<td>PM</td>
<td>Pulmonary Circulation Lunchtime meeting</td>
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<tr>
<td>PM</td>
<td>Women’s Health Taskforce 14:00 - 17:00</td>
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<td><strong>WED 29/01</strong></td>
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<tr>
<td>AM &amp; lunchtime</td>
<td>Paediatric &amp; CHD Taskforces 13:00-15:00 and 17:00-19:00</td>
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<tr>
<td>PM</td>
<td>Women’s Health Taskforce 14:00 - 17:00</td>
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<td><strong>THU 30/01</strong></td>
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<td>AM &amp; lunchtime</td>
<td>Central Asia potential Taskforce 11:00 - 13:00</td>
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<td>High Altitude Taskforce 8:30 - 11:30</td>
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<td>AM &amp; lunchtime</td>
<td>Paediatric &amp; CHD Taskforce 11:00-13:00</td>
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### Schedule abstract, interview and lecture recordings. Please fill as appropriate

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<td>Abstract presentation</td>
<td>Lecture recordings</td>
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<td>Pfizer Board meeting</td>
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<td>Bayer Board meeting</td>
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<td>14:00 - 18:00</td>
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<td>TUE 28/01</td>
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</table>
1. Assessment of Right Ventricular Dysfunction in Pulmonary Hypertension: Which Echocardiographic Parameter is Best?  
Tunthong R & Kane GC  
*Mayo Clinic, Rochester, MN, USA*

2. Clinically measured Pulmonary Vascular Impedance  
Vanderpool, RR1 & Champion HC1, 2  
*University of Pittsburgh, PA, USA*

3. Estimates of end-systolic pressure in clinical pressure-volume loops to assess right ventricular function  
Vanderpool RR, Simon MA, & Champion HC  
*University of Pittsburgh, PA, USA*

4. Heart rate corrected pulmonary artery acceleration time correlates with mean pulmonary artery pressure in children with idiopathic pulmonary artery hypertension: A simultaneous echocardiographic and cardiac catheterization study  
Jain S, Bobhate P, Guo L, Colen T, Trines J, Khoo NS, Kaneko S, & Adatia I.  
*Children's Hospital, Mazankowski Heart Institute, University of Alberta, Edmonton, Alberta, Canada*

5. Indication determines choice of potency assay for intracoronary bone marrow-derived mononuclear cell therapy in ischemic heart disease  
Luu B, Leistner DM, Honold J, Seeger FH, Fichtlscherer S, Dimmeler S, Zeiher AM, & Assmus B  
J. W. Goethe University, Frankfurt, Germany

6. Nucleofection is a highly efficient transfection technique for primary alveolar epithelial cells  
Buchbinder BA*, Vohwinkel CU*, Herold S, Seeger W, & Vadász I  
*Justus Liebig University, Universities of Giessen and Marburg Lung Center, Member of the German Center for Lung Research, Giessen, Germany*

7. Right ventricular Telemetry Measurements in the rodent hypoxia- and sugen hypoxia- pulmonary hypertension model  
de Raaf MA, Schalij J, Westerhof N, & Bogaard HJ  
*VU University Medical Center, Amsterdam, The Netherlands*

8. Time-domain analysis of heart sounds in children with and without pulmonary artery hypertension  
University of Alberta, Mazankowski Alberta Heart Institute, Canada*

9. Validation of Cyclic Hydroxylamines for Quantitative Measurement of Reactive Oxygen Species in Pulmonary System by EPR  
Scheibe Si, Veit Fi, Ghofrani HA1, Seeger W1,2, Grimminger Fi, Schermuly RT1,2 & Weissmann Ni  
1University of Giessen Lung Center (UGLC), Excellence Cluster Cardiopulmonary System (ECCPS), 2Max-Planck-Institute for Heart and Lung Research, Bad Nauheim, Germany  
*STAT5 underlies the sexual dimorphism in pulmonary arterial hypertension*  
Yang YM, Yuan H, & Sehgal PB  
*New York Medical College, Valhalla, USA*

**NOTES**
Pulmonary Hypertension in Chronic Lung Disease

1. Comparison of functional capacity, pulmonary functions, respiratory and peripheral muscle strength, quality of life and depression with disease severity in pulmonary arterial hypertension patients
Demir R, Özyılmaz S, Canbolat UP, Sinan ÜY, & Küçükoğlu MS
Istanbul University Institute of Cardiology, Istanbul, Turkey

2. Hypercapnia impairs cell junction formation by promoting TRAF2-mediated ubiquitination and endocytosis of the Na,K-ATPase β-subunit in alveolar epithelial cells
Gabrielli NM1, Mazzocchi LC1, Dada LA2, Seeger W1, Szajder J2, & Vadász I1
1 Justus Liebig University, Universities of Giessen and Marburg Lung Center, Giessen, Germany, 2Division of Pulmonary and Critical Care Medicine, Feinberg School of Medicine, Northwestern University, Chicago, IL, USA

3. NPY/NPY1R mediated vasoconstrictory and proliferative effects in pulmonary hypertension
Ludwig Boltzmann Institute for Lung Vascular Research, Graz, Austria, Medical University of Graz, Graz, Austria, Excellence Cluster Cardio-Pulmonary System (ECCPS), University of Giessen and Marburg Lung Center (UGMLC), Justus-Liebig-University, Giessen, Germany, Medical University of Vienna, Vienna, Austria

4. Prevention of Cigarette Smoke-induced Emphysema and Pulmonary Hypertension (PH) by the Phosphodiesterase Inhibitors Tadalafil and Picamilast
Parajuli N*, Seimetz M*, Pichl A, Schermuly RT, Grimminger F, Seeger W, Ghofrani HA, & Weissmann N
Universities of Giessen and Marburg Lung Center (UGMLC), ECCPS, Member of the DZL, Dept. of Internal Medicine, Medical Clinic II/V, Giessen, Germany

5. Regulation of macroautophagy in amiodarone induced pulmonary fibrosis
Universities of Giessen and Marburg Lung Center (UGMLC), Justus-Liebig-University Giessen, Giessen, Germany, Agaplesion lung clinic Waldhof Elgerhausen, Greif- enstein, Germany,
Institute for functional and applied anatomy, Hannover Medical School, Hannover, Germany, Institute of Clinical Chemistry and Laboratory Medicine, University of Regensburg, Regensburg, Germany, University College London, Rayne Institute, UK, University of Catania, Catania, Italy

6. Sestrin-2, a repressor of PDGFRβ signalling, promotes cigarette-smoke-induced pulmonary emphysema in mice and is upregulated in individuals with COPD
Heidler J2,* Fysikopoulos A1,* Wempe F2,* Seimetz M, Bangsow T2, Tomasovic A2, Veit F1, Scheibe S1, Pichl A, Weisel F1, Kent Lloyd KC3, Jaksch P4, Klepetko W4, Weissmann N1, & von Melchner H2
1Excellence Cluster Cardiopulmonary System (ECCPS), Justus-Liebig-University Giessen, Universities of Giessen and Marburg Lung Centre (UGMLC), Giessen, Germany, 2Goethe University Medical School, Frankfurt am Main, Germany, 3Mouse Biology Program, University of California Davis, Davis, USA 4Department of Thoracic Surgery, University Hospital of Vienna, Austria

7. Stimulation of Soluble Guanylate Cyclase by Riociguat prevents Tobacco smoke-induced Emphysema and Pulmonary Hypertension in mice
1Pichl A*, 1Parajuli N*, 2Seimetz M, 2Stasch JP, 2Frey R, 1Grimminger J, 1Schermuly RT, 3Klepetko W, 3Jaksch P, 1Seeger W, 1Grimminger F, 1Ghofrani HA & 1Weissmann N
1Universities of Giessen and Marburg Lung Center (UGMLC), ECCPS, Medical Clinic II/V, Giessen, Germany 2Bayer HealthCare, Wuppertal, Germany 3University Hospital of Vienna, Austria

8. The Role of FoxO3 in Idiopathic Pulmonary Fibrosis
1Al-Tamari HM, 1SchmallA, 1Sarvari P, 1Dabral S, 1Eschenhagen M, 1Savai R, 1,2Seeger W, & 1,2Pullamsetti SS
1Max-Planck Institute for Heart and Lung Research, Bad Nauheim, Germany, 2Universities of Giessen and Marburg Lung Center (UGMLC), Giessen, Germany

NOTES
1. A study on the involvement of Poly (ADP Ribose) Polymerase-1 (PARP-1) in pulmonary hypertension
Kaur G, Singh N, & Hanif K
CSIR-Central Drug Research Institute, Uttar Pradesh, India

2. Augmented expression of α-defensin in the pathology of pulmonary hypertension
Kosanovic D, Schneider JN, Bieniek E, Dahal BK, Ghofrani HA, Weissmann N, Grimminger F, Seeger W, & Schermuly RT
Universities of Giessen and Marburg Lung Center (UGMLC), Giessen, Germany, Max-Planck-Institute for Heart and Lung Research, Bad Nauheim, Germany

3. Beriberi presenting as Pulmonary Artery Hypertension
Sastry BKS
CARE Hospital, Nampally, Hyderabad, Andhra Pradesh, India

4. Caveolin-1 levels influence the expression of PPARγ in pulmonary hypertension
Mathew R, Huang J, & Gewitz MH
Maria Fareri Children's Hospital, New York Medical College, Valhalla, NY USA

5. Chloride intercellular channel-4 and endothelial inflammatory responses in pulmonary arterial hypertension
Abdul-Salam VB, Edwards RJ, Gierula M, Wilkins MR & Wojciak-Stothard B
Imperial College London, London, UK

6. Contribution of the JAK-STAT Signaling Pathway to the Pathogenesis of Idiopathic Pulmonary Fibrosis
Universities of Giessen and Marburg Lung Centre (UGMLC), Giessen, Germany

7. Deficiency of the mitochondrial uncoupling protein 2 (UCP2) causes pulmonary vascular remodeling
Excellence Cluster Cardio-Pulmonary System (ECCPS), University of Giessen and Marburg Lung Center (UGMLC), Justus-Liebig-University, Giessen, Germany

8. Endothelial-monocyte-activating polypeptide II (EMAPII) is involved in experimental pulmonary hypertension
Indiana University School of Medicine, Indianapolis, Indiana, USA, Max-Planck-Institute for Heart and Lung Research, Bad Nauheim, Germany, Universities of Giessen and Marburg Lung Center, Giessen, Germany

9. Myocardial inflammation in experimental acute right ventricular failure – Effects of prostacyclin therapy
Université Libre de Bruxelles, Belgium, Erasmus University Hospital, Brussels, Belgium, La Timone University Hospital, Marseille, France

10. PAR-2 inhibition reverses experimental pulmonary hypertension
1Wygrecka M, 1Markart P, 1Dahal B, 1Kojonazarov B, 2Marsh LM, 1Schermuly RT, 3Taube C, 1Meinhardt A, 1Ghofrani HA, 4Steinhoff M, 1Seeger W, 1Preissner KT, 2Olschewski A, 1Weissmann N, & 1,2Kwapiszewska G
1University of Giessen Lung Centre, Giessen, Germany, 2Ludwig Boltzmann Institute for Lung Vascular Research, Graz, Austria, 3Leiden University Medical Center, Leiden, The Netherlands, 4University of California San Francisco, UCSF, San Francisco, CA

11. The polarity protein Scribble is a positive regulator of inflammatory response in endothelial cells
Kruse C, Wandzioch K, Brandes RP, & Michaelis UR
Goethe University, Frankfurt, Germany

NOTES
Stem Cells in Heart and Lung (Re)-Generation

1. Attenuation of Bone Morphogenetic Protein Receptor Expression and downstream signaling axis during HIV-1 and Cocaine-mediated Pulmonary Smooth Muscle Hyperplasia: Implications for HRP AH
Dalvi P, O’Brien-Ladner A, & Dhillon NK
University of Kansas Medical Center, Kansas City, Kansas, USA

2. BMPR-II deficiency leads to an increase in egg deposition and cytokine release in the lungs of mice chronically infected with schistosomiasis
University of Cambridge School of Clinical Medicine, Addenbrooke’s Hospital, Cambridge, UK, University of Cambridge, UK, Papworth Hospital, Cambridge, UK, University of Rochester, New York, USA

3. Epigenetic control of cardiac differentiation in mouse embryonic stem cells: Role of thyroid hormone in pacemaker cell commitment
Institute of Cellular Biology and Neurobiology, National Research Council, Rome, Italy, Institute of Medical Pathology, Catholic University, Rome, Italy, University of Milan, Milan, Italy, University of Messina, Messina, Italy, Goethe University, Frankfurt am Main, Germany

4. Fgf10 overexpression after hyperoxic injury triggers de novo alveologenesis in a mouse model of bronchopulmonary dysplasia
Chao CM, Tiozzo C, Ehrhardt H, Zimmer KP, & Bellusci S
University Children’s Hospital, Giessen, Germany, Saban Research Institute of Children’s Hospital Los Angeles, Los Angeles, USA, Excellence Cluster Cardio-Pulmonary System (ECCPS), Giessen, Germany

5. Fgf10-positive cells represent a progenitor cell population during lung development and postnatally

6. Genetic targeting of organ resident bronchioalveolar stem cells in vivo
Salwig I, Szibor M, & Braun T
Max-Planck-Institute for Heart and Lung Research, Bad Nauheim, Germany, University of Helsinki, Helsinki, Finland

7. Hybrid 574: a chemical approach to human cardiac mesenchymal cell reprogramming
Spallotta F, Cencioni C, Atlante S, Zeiher AM, & Gaetano C
Goethe University, Frankfurt am Main, Germany

8. Identification of alveolar PDGFRα* fibroblast subset-specific miRNA and mRNA expression profiles in postnatal lung development
Max Planck Institute for Heart and Lung Research, Bad Nauheim, Germany, University Hospital Giessen, Giessen, Germany, Philippus University of Marburg, Marburg, Germany

9. Identification of molecular signatures of Lung Bronchioalveolar Stem Cell
Qi H, Yuan XJ, Zhou YG, & Braun T
Max-Planck-Institute for Heart and Lung Research, Bad Nauheim, Germany

10. Influence of Early Growth Response 1 (Egr1) and Tenascin C (Tnc) on compensatory lung growth
University of Giessen Lung Center, Justus-Liebig-University, Giessen, Germany, Excellence Cluster Cardio-Pulmonary System (ECCPS), Giessen, Germany

11. Influenza virus (IV) impairs fibroblast growth factor receptor 2b (FGFR2b) dependent epithelial regeneration from a distal epithelial progenitor pool
University of Giessen Lung Center, Justus-Liebig-University, Giessen, Germany, Excellence Cluster Cardio-Pulmonary System (ECCPS), Giessen, Germany

12. Intermedin promotes phosphorylation and subsequent exocytosis of the Na,K ATPase in the alveolar epithelium in a protein kinase A dependent manner
Mazzocchi LC, Gabrielli NM, Rühl R, Seeger W, Kummer W, Pfeil U, & Vadász I
Justus Liebig University, Universities of Giessen and Marburg Lung Center, Giessen, Germany

13. Lineage differentiation of pulmonary alveolar fibroblasts
Klein F, Seeger W, Roska B, Miescher F, Richardson W D, & Voswinckel R
Max-Planck-Institute for Heart and Lung Research, Bad Nauheim, Germany, University of Helsinki, Helsinki, Finland
14. **Proteomic characterization of lung stem cells**  
Hoelper S, Salwig I, Braun T, & Krueger M  
*Max-Planck-Institute for Heart and Lung Research, Bad Nauheim, Germany*

15. **Role of Bcl-xL in hepatocyte growth factor elicited epithelial protection in idiopathic lung fibrosis**  
Skwarna S, Henneke I, Seeger W, Guenther A, & Ruppert C  
*Universities of Giessen and Marburg Lung Center (UGMLC), Giessen, Germany, German Center for Lung Research (DZL), Giessen, Germany, Lung Clinic Waldhof-Elgershausen, Greifenstein, Germany*

16. **Role of long non-coding RNAs and zinc finger E-box binding homeobox factor 1 and 2 (Zeb1, Zeb2) in stemness maintenance of mouse embryonic stem cells**  
Cencioni C, Spallotta F, Uchida S, Zeiher AM, & Gaetano C  
*Goethe University, Frankfurt, Germany*

17. **Role of Notch signaling pathway in epithelial progenitor cell proliferation in the fibrotic lung**  
Piskulak K, Henneke I, Wilhelm J, Bellusci S, 1,2Seeger W, 1,2,Günther A, & Ruppert C.  
1Universities of Giessen and Marburg Lung Center (UGMLC), Justus-Liebig-University Giessen, Giessen, Germany  
2Agaplesion Lung Clinic Waldhof Elgershausen, Greifenstein, Germany

18. **The impact of cardiotrophin-1 (CT-1) nuclear translocation for cardiomyogenesis of mouse embryonic stem cells**  
Mascheck L, Sharifpanah Fi, Tsang SY, Wartenberg M, & Sauer H  
1Justus Liebig University Giessen, Giessen, Germany,  
2School of Life Sciences, The Chinese University of Hong Kong, Hong Kong, China,  
3Clinic of Internal Medicine I, Friedrich Schiller University Jena, Germany

19. **The nuclear envelope protein emerin regulates cardiac Wnt/β-catenin signalling**  
Stubenvoll A, Wheeler M, & Braun T  
*Max-Planck-Institute for Heart and Lung Research, Bad Nauheim, Germany*

20. **The role of Shh in postnatal mouse lung development**  
Yin M, Ahlbrecht K, Seeger W, & Voswinckel R

21. **The role of WNT/b-catenin signaling in smooth muscle cells during lung development and repair**  
*Excellence Cluster Cardio Pulmonary System (EC-CPS), Justus-Liebig-University Giessen, Germany*

22. **Towards the elucidation of FGF10 mechanisms of action during early lung development**  
Dilai S, El Agha E, Mackenzie B, Moiseenko A, Chao CM, Shrestha A, Carraro G, Goth K, & Bellusci S  
*Excellence Cluster Cardio Pulmonary System (EC-CPS), Justus-Liebig-University Giessen, Germany*

**NOTES**
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<th>1.</th>
<th>Developmental studies for therapeutic approaches using endothelial cells derived from mouse embryonic stem cells</th>
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<td>Golec A, Becker S, Raissi M, Seeger W, &amp; Voswinckel R</td>
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<td>Max Planck Institute for Heart and Lung Research, Bad Nauheim, Germany, University Hospital Giessen, Giessen, Germany</td>
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<th>Endothelin-1 induced downregulation of BMPR-2 signaling contributes to pulmonary artery smooth muscle cell hyperplasia</th>
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<td>Maruyama H, Dewachter C, Belhaj A, Rondelet B, Remmelink M, Vachiéry JL, Naeije R, &amp; Dewachter L</td>
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<td>Laboratory of Physiology and Physiopathology, Université Libre de Bruxelles, Brussels, Belgium, Erasmus University Hospital, Brussels, Belgium</td>
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<th>Increasing BMPR2 signaling with FK506 prevents endothelial mesenchymal transition in coronary artery endothelial cells</th>
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<td>Tian X, Kuang J, Sudheendra D, Reddy S, Zhao M, Bernstein D, &amp; Spiekercottor E</td>
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<td>Stanford University, Stanford, CA, USA</td>
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<th>Quantifying the Variability in Practice Patterns for the Diagnosis and Management of Pulmonary Arterial Hypertension in an International Cohort of Specialists</th>
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<tr>
<td>Ryan JJ, Butrous G, &amp; Maron BA</td>
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<tr>
<td>University of Utah Health Science Center, Salt Lake City, UT, USA, University of Kent, Kent, UK, Brigham and Women’s Hospital, Boston, MA, USA</td>
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<th>Therapeutic approaches to correct BMP signaling in Heritable Pulmonary Arterial Hypertension</th>
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<tr>
<td>Drake KM, Dunmore BJ, McNelly LN, Morrell NW, &amp; Aldred MA</td>
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<td>Genomic Medicine Institute, Cleveland Clinic, Cleveland OH, USA, University of Cambridge, Cambridge, UK</td>
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<th>6.</th>
<th>A major role of Bone Morphogenetic Proteins 9 and 10 in postnatal cardiovascular development and remodelling</th>
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<td>Rice M, Wheeler M &amp; Braun T</td>
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<td>Max-Planck-Institute for Heart and Lung Research, Bad Nauheim, Germany</td>
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<th>7.</th>
<th>Chemical Activation of Lysine Acetylation Rescues Proliferation and Differentiation in Human Cardiac Mesenchymal Cells of Type 2 Diabetic Patients</th>
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<td>Spallotta F, Vecellio M, Colussi C, Nanni S, Farsetti A, Zeiher A, &amp; Gaetano C</td>
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<td>Goethe University, Frankfurt am Main, Germany, Consiglio Nazionale delle Ricerche, IBCM, Roma, Italy</td>
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<th>8.</th>
<th>Evidence of Impaired Autophagic Flux in Right Ventricular Failure (RVF)</th>
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<tr>
<td>Indiana University School of Medicine, Indianapolis, IN, USA</td>
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<th>9.</th>
<th>Involvement of circulating fibrocytes in the progression of adenocarcinomas by modulating the tumor microenvironment</th>
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<td>1Asafova A, 1Nikam V, 1Schmall A, 2Weigert A, 1Voswinckel R, 1Seeger W, &amp; 1Savai R</td>
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<td>1Max-Planck-Institute for Heart and Lung Research, Bad Nauheim, Germany, 2Institute of Biochemistry I, Goethe-University Frankfurt, Frankfurt, Germany</td>
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<th>10.</th>
<th>Involvement of endothelial TRPV4 in alterations of calcium dynamics in a murine model of group 2 pulmonary hypertension</th>
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<tr>
<td>Daya N, Safar S, Gillis M.A, Ledoux J, &amp; Dupuis J</td>
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<td>Montreal Heart Institute, University of Montreal, Montreal, Qc, Canada</td>
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<th>11.</th>
<th>Is it possible to render children with congenital heart disease and pulmonary hypertension better surgical candidates?</th>
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<tr>
<td>Thomaz AM, Zorzaneli L, Gonçalves RC, Kajita LJ, Hironaka JF, Rabinovitch M, &amp; Lopes AA.</td>
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<tr>
<td>University of São Paulo School of Medicine, São Paulo, Brazil, Stanford University School of Medicine, California, USA</td>
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<th>12.</th>
<th>Mena/VASP and cII-Spectrin complexes regulate cytoplasmic actin networks in cardiomyocytes and protect from conduction abnormalities and dilated cardiomyopathy</th>
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<tr>
<td>Benz PM, Unger A, Linke WA, Frantz S, Fleming I, &amp; Schuh K.</td>
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<td>Goethe-University, Frankfurt, Germany, University of Würzburg, Germany, Ruhr University Bochum, Germany, University of Würzburg, Germany</td>
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<th>13.</th>
<th>Report of two pediatric patients with pulmonary vein abnormalities and pulmonary artery hypertensive vascular disease</th>
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<td>1Juaneda E, 2Saellio I, &amp; 3Alday LE.</td>
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<td>1Servicio de Cardiología, Sanatorio Allende, 2CETES- Instituto Oulton, 3Servicio Cardiología Sanatorio Allende. Catholic University, Córdoba, Argentina</td>
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<th>14.</th>
<th>Right heart adaptation to left ventricular STEMI in rats</th>
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15. Riociguat and sildenafil attenuate secondary pulmonary hypertension in a model of left heart failure
University of Giessen & Marburg Lung Center (UGM-LC), Justus Liebig University of Giessen, Giessen, Germany, Bayer HealthCare, Wuppertal, Germany

16. The transpulmonary gradient (TPG) but not the systolic or mean pulmonary arterial pressure (mPAP) correlates with the thickness of peripheral pulmonary arteries and veins in patients with chronic heart failure
Campos PR, Issa V, Honorato R, Fiorelli AI, Bocchi EA, & Aiello VD
University Medical School, Sao Paulo, Brazil

17. Ventricular-ventricular-interactions: a potential target for the treatment of right ventricular failure?
Apitz C, Friedberg M, Schranz D, & Redington AN
University of Giessen, Giessen, Germany
University of Toronto, Toronto, Canada

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1. Alterations in metabolism of bone marrow-derived mononuclear cells of patients with CAD: implications for cell functionality
   Derlet A, Rasper T, Zeiher AM, Dimmelser S, & Seeger FH
   Center for Molecular Medicine, Frankfurt, Germany, University of Frankfurt, Frankfurt, Germany

2. Androgen Receptor Interaction With WN/Tβ-Catenin Pathway As A Novel Signaling Hub At The Blood-Brain Barrier
   Devraj K, Ziegler N, Harter P, Sonja T, Czupalla C, Butcher E, & Liebner S
   Goethe University, Frankfurt, Germany
   Stanford University School of Medicine, Stanford, USA

3. Angiopoietin-2 links angiogenesis and inflammation in human and experimental glioma
   Scholz A, Cremer S, Harter PN, Mittelbronn M, van Slyke P, Dumont DJ, Plate KH, & Reiss Y
   Goethe University, Frankfurt, Germany, University of Toronto, Toronto, Canada

4. Biological role of the proapoptotic transcription factor C/EBP homologous protein (CHOP) in Idiopathic Pulmonary Fibrosis (IPF)
   Klymenko O, Henneke I, Ruppert C, Seeger W, Guenther A, & Korfei M
   Universities of Giessen and Marburg Lung Center (UGMLC), Justus-Liebig-University Giessen, Giessen, Germany
   Agaplesion Lung Clinic Waldhof Elgershausen, Greifenstein, Germany

5. Cardiac mass and bronchiolitis obliterans syndrome (BOS) in patients after double lung transplantation
   Hannover Medical School, Hannover, Germany

6. Characterization of pulmonary hypertension in lung cancer
   Storn S, Pullamsetti SS, Kojonazarov B, Schermuly RT, Grimminger F, Rapp UR, Seeger W, & Savai R
   Max Planck Institute for Heart and Lung Research, Bad Nauheim, Germany, Internal Medicine, University of Giessen Lung Center, Giessen, Germany

7. Contribution of Stromal Lymphocytes to Lung Cancer Metastasis: Role in Epithelial Mesenchymal Transition
   Salazar Y, Schmall A, Grimminger F, Seeger W, Pullamsetti SS, & Savai R

8. Defective autophagy in Hermansky-Pudlak syndrome associated interstitial pneumonia (HPSIP)
   Universities of Giessen and Marburg Lung Center (UGMLC), Justus-Liebig University Giessen, Giessen, Germany,
   Agaplesion lung clinic Waldhof Elgerhausen, Greifenstein, Germany,
   Hannover Medical School, Hannover, Germany,
   NHGRI - National Institute of Health, Bethesda, DC, USA

9. Differentially expressed miRNAs after Legionella pneumophila infection of human macrophages
   Herkt C, Marsico A, Bertrams W, Chen W, Schulz C, Vingron M, Schmeck B, & Sittka A
   Philipps University Marburg, Germany, Max Planck Institute for Molecular Genetics, Berlin, Germany,
   Max Delbrück Center for Molecular Medicine (MDC), Berlin, Germany

10. Echocardiographic Analysis of Right Ventricular Myocardial Texture in Patients with Pulmonary Hypertension
    Tufekcioglu O
    Yuksek Ihtisas Hospital, Ankara, Turkey

11. Experience with subcutaneous treprostinil in children with pulmonary hypertension and inadequate response to combination oral therapies
    Bobhate P, Jain S, Guo L, & Adatia I
    Stollery Children's Hospital and Mazankowski Alberta Heart Institute, University of Alberta, Edmonton, Canada

12. GFL-dependent regulation of TRPA1 and TRPV1 in C-fiber neurons and their role in allergic asthma
    Nandigama R, Weske A, Wiegand S, Kummer W, & Nassenstein C
    Justus-Liebig-University, Universities of Giessen and Marburg Lung (UGMLC)
    German Center for Lung Research (DZL), Giessen, Germany

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Kazimli AV, Ryzhkov A, Goncharova N, Naymushin A, & Moiseeva O
Almazov’s Federal Heart, Blood and Endocrinology Centre, Saint-Petersburg, Russia

2. **Development of bioinformatics tool to analyze RNA editing events**
John D, Ponomareva Y, Dimmeler S, & Uchida S
Institute of Cardiovascular Regeneration, Centre for Molecular Medicine, Goethe-University Frankfurt, Germany

3. **Microvascular (endothelial) dysfunction in congenital heart defects with distinct pulmonary hemodynamics**
Maeda NY, Soares RPS, Mesquita SMF, Siqueira AW, Costa HG, Miura N, & Lopes AA
Pro-Sangue Foundation, São Paulo, Brazil, Heart Institute (InCor), University of São Paulo School of Medicine, São Paulo, Brazil

4. **Plasma Sphingosine 1 Phosphate is elevated in idiopathic pulmonary arterial hypertension**
1Gairhe S, 2Kharel Y, 2,3Lynch KR, 1Fagan K, & 1McMurtry IF
1College of Medicine, University of South Alabama, Mobile, AL, USA,
2University of Virginia, Virginia, USA,
3SphynKx Therapeutics, LLC, Charlottesville, VA, USA

5. **Protein analysis in pediatric patients with congenital systemic-to-pulmonary shunts: Proinflammatory mediators in distinct hemodynamic conditions**
Zorzaneli L, Thomaz AM, Maeda NY, Soares RPS, Bastos ENM, Rabinovitch M, & Lopes AA
Heart Institute (InCor), University of São Paulo School of Medicine, São Paulo, Brazil,
Pro-Sangue Foundation, São Paulo, Brazil,
Stanford University School of Medicine, California, USA

6. **Alternative and classic activation of primary macrophages – a systems biology approach**
1,2Bertrams W, 3Marsico A, 1,2Schulz C, 1,2Sittka A, 1,2Du Bois I, 3Vinigrion M, 4Suttrop N, 4Hippenstiel S, & 1,2Schmeck B
1FORSYS Partner Research Group “Systems Biology of Lung Inflammation”,
2iLung - Institute for Lung Research, Philipps University Marburg, Germany,
3Max Planck Institute for Molecular Genetics, Berlin, Germany,
4Medizinische Klinik m.S. Infektiologie und Pneumologie, Charité – Universitätsmedizin Berlin, Germany

7. **mRNA stability regulation by TTP (tristetraproline) regulates cathepsin B expression under chronic hypoxia**
1Fuhrmann D, 1Tausendschön M, 2Wittig I, 2Heide H, 1Schmid T, 1Brüne B, & 1Dehne N
1Institute of Biochemistry I/ZAFES, Goethe-University Frankfurt, Frankfurt, Germany
2Functional Proteomics, Goethe-University Frankfurt, Frankfurt, Germany

8. **Structural and functional prevention of hypoxia-induced pulmonary hypertension by individualized exercise training in mice**
Excellence Cluster Cardio-Pulmonary System (ECCPS), Universities of Giessen and Marburg Lung Center (UGMLC), Member of the German Center for Lung Research (DZL), Giessen, Germany, Justus Liebig-University Giessen, Giessen, Germany, Charité - Universitätsmedizin Berlin Medical Clinic, Division of Infectiology and Pneumology, Berlin, Germany, Max-Planck-Institute for Heart- and Lung Research, Bad Nauheim, Germany

9. **The role of NADPH oxidase 2 in a mouse model of sleep apnea**
Universities of Giessen and Marburg Lung Center (UGMLC), Excellence Cluster Cardio-Pulmonary System (ECCPS), Member of the German Lung Research Center (DZL), Justus-Liebig-University Giessen, Giessen, Germany, Charité-Universitätsmedizin Berlin, Berlin, Germany, Department of Lung Development and Remodeling, Max-Planck-Institute for Heart and Lung Research, Bad Nauheim, Germany

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Epigenetics of Heart and Lung Disease

1. Characterization of histone-bound IncRNAs in murine ES cells
   Ponomareva Y, John D, Gellert P, Dimmeler S, & Uchida S
   Institute of Cardiovascular Regeneration, Centre for Molecular Medicine, Goethe-University Frankfurt, Frankfurt, Germany
   Physiological Genomics and Medicine Group, MRC Clinical Sciences Centre, Imperial College London, London, UK

2. Deregulation of class I HDAC isoforms in human pulmonary arterial hypertension
   Max-Planck Institute for Heart and Lung Research, Bad Nauheim, Germany,
   Universities of Giessen and Marburg Lung Center (UGMLC), Member of the German Center for Lung Research (DZL), Giessen, Germany,
   Institute of Molecular Biology and Tumor Research, Marburg, Germany

3. Downregulation of the angiomiR-126 contributes to the failing right ventricle in human pulmonary arterial hypertension
   Potus F, Paulin R, Breuils Bonnet S, Michelakis E, Provencher S, & Bonnet S

4. Endothelial angiotensin converting enzyme (ACE) levels decrease in response to activation of the AMP-activated protein kinase (AMPK) via p53 and microRNA(miR)-143/145
   Kohlstedt K, Trouvain C, Böttger T, Fißlthaler, Shi L, & Fleming I
   Institute for Vascular Signalling, Centre for Molecular Medicine, Goethe-Universität, Frankfurt am Main, Germany,
   Max-Planck-Institut für Herz- und Lungenforschung, Bad Nauheim, Germany

5. Hypoxia induced epigenetic regulation in pulmonary hypertension
   Muecke C, Dabral S, Seeger W, & Pullamsetti SS
   Max-Planck Institute for Heart and Lung Research, Bad Nauheim, Germany,
   Universities of Giessen and Marburg Lung Center (UGMLC), Member of the German Center for Lung Research (DZL), Giessen, Germany

6. Identification of laminar flow regulated non-coding RNAs in endothelial cells
   Michalik KM, You X, Doddaballapur A, Jaé N, John D, Chen W, Uchida S, Boon RA, & Dimmeler S
   Institute for Cardiovascular Regeneration, Universi-ty Frankfurt, Frankfurt, Germany,
   Max-Delbrück-Centrum für Molekulare Medizin (MDC), Berlin-Buch, Germany,
   Deutsches Zentrum für Herz-Kreislaufforschung (DZHK), Germany

7. Identification of positionally-conserved lincRNAs between human and mouse
   Militello G, Ponomareva Y, John D, Dimmeler S, & Uchida S
   Institute of Cardiovascular Regeneration, Centre for Molecular Medicine, Goethe-University Frankfurt, Germany

8. Inhibition of the microRNA let-7 enhances epithelial-mesenchymal transition and recruitment of epicardial cells after acute myocardial infarction
   Seeger T, Xu Q, Muhly-Reinholz M, Fischer A, Zeiher AM & Dimmeler S
   Institute for Cardiovascular Regeneration, Center of Molecular Medicine, Frankfurt University, Frankfurt, Germany,
   Internal Medicine III, Frankfurt University, Frankfurt, Germany,
   German Center for Cardiovascular Research (DZHK), Germany

9. MicroRNA-223 regulates platelet function by targeting β1 integrin and coagulation factor XIII A
   Elghazawy A, Randriamboavonjy V, & Fleming I
   Institute for Vascular Signalling, Centre for Molecular Medicine, Goethe-University, Frankfurt am Main, Germany

    Demolli S, Doebel C, Kaluza D, Dimmeler S, & Boon RA
    Institute for Cardiovascular Regeneration, Centre of Molecular Medicine, Goethe-University, Frankfurt am Main, Germany

11. Role of Class IIa Histone Deacetylases in the pathogenesis of pulmonary hypertension
    Gamen E, Chelladurai P, Grimminger F, Seeger W, & Pullamsetti SS
    Max-Planck Institute for Heart and Lung Research, Bad Nauheim, Germany,
    Universities of Giessen and Marburg Lung Center (UGMLC), Member of the German Center for Lung Research (DZL), Giessen, Germany

12. Role of miR-9 in the regulation of PDGFβ signaling in pulmonary arterial hypertension
13. **Systematic screening of chromatin-associated lncRNAs coupled with bioinformatics analysis**
Institute of Cardiovascular Regeneration, Centre for Molecular Medicine, Goethe-University Frankfurt, Frankfurt, Germany, Physiological Genomics and Medicine Group, MRC Clinical Sciences Centre, Imperial College London, London, UK, Institute of Laboratory Medicine and Pathobiology, Molecular Diagnostics, Philipps University Marburg, Marburg, Germany, Department of Internal Medicine, University of Texas Southwestern Medical Center, Dallas, Texas, USA School of Biomedical Sciences, The University of Queensland, Brisbane, Australia, Heart Research Center Göttingen, University Medical Center Göttingen, Georg-August-University, Göttingen, Germany

14. **The apoptosis associated tyrosine kinase gene is frequently hypermethylated in lung cancer and regulated by epigenetic mechanisms**
Haag T, Herkt C & Dammann RH
Institute for Genetics, Giessen, Germany, Justus-Liebig-University, Giessen, Germany, Universities of Giessen and Marburg Lung Center, Giessen, Germany

15. **The LncRNA h342419 (Mantis) is involved in the homeostasis of the vascular system**
Leisegang MS, Fork C, Miller MJ, Ponomareva Y, Uchida S, & Brandes RP
Institute for Cardiovascular Physiology, Goethe-University, Frankfurt, Germany, Institute for Cardiovascular Regeneration, Goethe-University, Frankfurt, Germany

16. **The role of miR-143 in pulmonary arterial hypertension**
Deng L, White K, Stevens HC, Bradshaw AC, MacLean MR, & Baker AH
British Heart Foundation Glasgow Cardiovascular Research Centre, Institute of Cardiovascular and Medical Sciences, University of Glasgow, Glasgow, UK

17. **The role of RNF20 in heart development**
Chichelnitskiy E, Meneceur S, & Dobreva G.
Max Planck Institute for Heart and Lung Research, Bad Nauheim, Germany

18. **Transcriptional regulation of microRNAs 424 and 503 by HDACs and MEF2 in the endothelium: Role in pathogenesis of pulmonary arterial hypertension**
Kim J, Hwangbo C, Comhair S, Erzurum S, & Chun HJ
Yale Cardiovascular Research Center, Yale University School of Medicine, New Haven, CT, USA The Lerner Institute, The Cleveland Clinic, Cleveland, OH, USA

19. **miR-92a controls metabolism and obesity**
Penzkofer D, Seeger T, Bonauer A, Fischer A, Zeiher AM, & Dimmeler S
Institute of Cardiovascular Regeneration, Goethe University Frankfurt, Germany, Internal Medicine III, Cardiology, Goethe University Frankfurt, Germany

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Veith C, Dahal BK, Bálint Z, Murmann K, Seeger W, Schermuly RT, Weissmann N, & Kwapiszewski G
Universities of Giessen and Marburg Lung Center (UGMLC), Member of the German Center for Lung Research (DZL), Giessen, Germany, Ludwig Boltzmann Institute for Lung Vascular Research, Graz, Austria

2. Metabolic control of PHD function and the hypoxic response by isocitrate dehydrogenase (IDH)
Bögürcü N, Garvalov BK & Acker T
Institute of Neuropathology, Justus Liebig University, Giessen, Germany

3. Oncogenic role of Ras association domain-containing protein 1 (RASSF1A) in pulmonary hypertension - regulation of HIF signaling
Dabral S, Muecke C, Savai R, Dammann R, Seeger W & Pullamsetti SS
Max-Planck Institute for Heart and Lung Research, Bad Nauheim, Germany, Universities of Giessen and Marburg Lung Center (UGMLC), Member of the German Center for Lung Research (DZL), Giessen, Germany, Institute for Genetics, Justus-Liebig University, Giessen, Germany

4. Role of classical transient receptor potential channel 1 in hypoxia-induced pulmonary hypertension
Universities of Giessen and Marburg Lung Center (UGMLC), Member of the German Center for Lung Research (DZL), Giessen, Germany, Charité - Universitätsmedizin Berlin, Berlin, Germany, Max-Planck Institute for Heart and Lung Research, Bad Nauheim, Germany, Walther-Straub-Institute for Pharmacology and Toxicology, Ludwig-Maximilians University Munich, Munich, Germany

5. Alteration of microRNA processing during acute respiratory distress
Schlappkohl M, Seay U, Seeger W, & Mayer K
Universities of Giessen and Marburg Lung Center (UGMLC), Giessen, Germany

6. Cytochrome P4502S1 a novel monocyte/macrophage fatty acid epoxygenase
Institute for Vascular Signalling, Centre for Molecular Medicine, Goethe University, Frankfurt am Main, Germany, King’s British Heart Foundation Centre, King’s College London, London, UK, Bristol Heart Institute, University of Bristol, Bristol Royal Infirmary, Bristol, UK, Institute of Pathology, Goethe-University, Frankfurt am Main, Germany

7. In vivo tracing of fluorescently tagged cell types in lung
Kuse N, Nikam VS, Szibor M, Braun B, Seeger W, Voswinckel R, & Morty R
Max-Planck-Institute for Heart and Lung Research, Member of the German Center for Lung Research (DZL), Bad Nauheim, Germany, Universities of Giessen and Marburg Lung Center (UGMLC), Member of the German Center for Lung Research (DZL), Giessen, Germany

8. Spatial Distribution of the Metabolically Active Pulmonary Circulation in Humans
Montreal Heart Institute Research Center, Montreal, Canada, INRS-Armand Frappier Institute, Laval, Canada

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Adaptive and Maladaptive Angiogenesis

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1Goethe University Frankfurt, Frankfurt, Germany, 2Institute of Cardiovascular Regeneration, Goethe University Frankfurt, Frankfurt, Germany, 3Center for Biomolecular Magnetic Resonance, Goethe University Frankfurt am Main, Frankfurt am Main, Germany

4Center for Organic Chemistry and Chemical Biology, Center for Biomolecular Magnetic Resonance, Goethe University Frankfurt am Main, Frankfurt am Main, Germany

5Scientific Genomics Group, Max Delbrück Center for Molecular Medicine Berlin-Buch, Berlin, Germany

2. Chloride intracellular channel 4 and endothelial dysfunction in pulmonary arterial hypertension

1Wojciak-Stothard B, 1Abdul-Salam VB, Lao KH, 1Tsang H, 1Irwin DC, 2Lisk C, 2Loomis Z, 2Stenmark KR, 3Edwards JC, 4Yuspa SH, 5Howard LS, 1Wharton J, 1Zhao L, & 1Wilkins MR

1Centre for Pharmacology and Therapeutics, Department of Medicine, Imperial College London, London, UK, 2Cardiovascular Pulmonary Research Group, University Colorado Denver Anschutz Medical Campus, Aurora, USA, 3Division of Nephrology and Hypertension, Department of Medicine, University of North Carolina, UNC Kidney Center, North Carolina, USA, 4Laboratory of Cancer Biology & Genetics, Centre for Cancer Research, Bethesda, USA, 5National Pulmonary Hypertension Service, Imperial College Healthcare NHS Trust, London, UK

3. Control of endothelial cell posttranscriptional regulation of gene expression and angiogenesis by RNA editing

1,2Stellos K, 1Boon RA, 1Gatsiou K, 1Amrhein C, 1John D, 3Fürtig B, 1Boeckel JN, 1Michalik K, 4You X, 1Uchida S, 4Chen W, 3Schwalbe H, 2Zeicher A, & 1Dimmeler S

1Institute of Cardiovascular Regeneration, Center of Molecular Medicine, Goethe University Frankfurt am Main, Frankfurt am Main, Germany

2Center of Internal Medicine, Goethe University Frankfurt am Main, Frankfurt am Main, Germany

3Institute for Organic Chemistry and Chemical Biology, Center for Biomolecular Magnetic Resonance, Goethe University Frankfurt am Main, Frankfurt am Main, Germany

8. Methylene blue modulates transendothelial migration of peripheral blood cells

1Kanzler I, 1Guo F, 1Bogert NV, 1Stocker UA, 2Mebohm P, 1Moritz A, & 1Beiras-Fernandez A

1Goethe University Hospital, Frankfurt, Germany, 2Clinic of Anesthesiology, Intensive Care Medicine, University of Frankfurt, Germany
9. **Modulation of Calpain 1 and 2 and local inflammation in aortic aneurysms**
   Goethe University, Frankfurt, Germany

10. **Nox4 promotes exercise-induced angiogenesis in murine skeletal muscle**
    Vogel J & Schröder K
    Goethe University, Frankfurt, Germany

11. **Secreted modular calcium binding protein 1 (SMOC-1) promotes angiogenesis by modulating transforming growth factor-regulated gene expression**
    Awwad K, Fisslthaler B, Pfeilschifter J & Fleming I
    Institute for Vascular Signalling, Centre for Molecular Medicine, Goethe University, Frankfurt, Germany

12. **Spingosine-1-phosphate receptor 1 on macrophages is required for tumor-associated lymphangiogenesis**
    Institute of Biochemistry I, Goethe-University, Frankfurt, Germany

13. **Stimulation of vasculogenesis and leukopoiesis of embryonic stem cells by extracellular RNA**
    Sharifpanah F, Jayarathne SWG, 1Preissner KT, 2Wartenberg M, & 1Sauer H
    1Justus Liebig University Giessen, Giessen, Germany, 2Clinic of Internal Medicine I, Cardiology Division, Friedrich Schiller University Jena, Jena, Germany

14. **The AMPKα2 subunit is crucial for myeloid cell-mediated post-ischemic revascularization**
    Institute for Vascular Signalling, Centre for Molecular Medicine, Goethe University, Frankfurt, Germany

15. **The biological actions of R/S 11,12-epoxyeisatrienoic acid in endothelial cells are Gas dependent**
    1Ding Y, 1Frömel T, 2Offermanns S, & 1Fleming S
    1Institute for Vascular Signalling, Centre for Molecular Medicine, Goethe University, Frankfurt, Germany, 2Max-Planck-Institute for Heart and Lung Research, Bad Nauheim, Germany

16. **The NADPH Oxidase Nox4 is a novel target for anti-angiogenic therapy**
    Weinberger V, Henke N, Brandes RP, & Schröder K
    Institute for Cardiovascular Physiology, Goethe University, Frankfurt, Germany

17. **The soluble epoxide hydrolase regulates angiogenesis by modulating Notch signalling in the retina**
    Institute for Vascular Signalling, Centre for Molecular Medicine, Goethe University, Frankfurt, Germany, Max-Planck-Institute for Molecular Biomedicine, Bad Nauheim, Germany, University of Münster, Faculty of Medicine, Münster, Germany

18. **Transforming growth factor-β-activated kinase 1 regulates angiogenesis via AMP-activated protein kinase α1 in endothelial cells**
    1Fisslthaler B, 1Zippel N, 1Abdel Malik R, 1Frömel T, 1Popp R, 1Bess E, 2Strilic B, 2Wettscurek N & 1Fleming I
    1Institute for Vascular Signalling, Centre for Molecular Medicine, Goethe University, Frankfurt, Germany, 2Department of Pharmacology, Max-Planck-Institute for Heart and Lung Research, Bad Nauheim, Germany

19. **Vascular remodeling and reverse remodeling in hypoxia-induced pulmonary hypertension**
    Excellence Cluster Cardio-Pulmonary System, Universities of Giessen and Marburg Lung Center, Justus-Liebig-University Giessen, Giessen, Germany, Northwestern University, Chicago, Illinois, USA, Graduate School of Pharmaceutical Sciences, Chiba University, Chiba, Japan, University of Hamburg, Hamburg, Germany, University Hospital of Vienna, Vienna, Austria, Max-Planck-Institute for Heart and Lung Research, Bad Nauheim, Germany, Ludwig Boltzmann Institute for Lung Vascular Research, Graz, Austria

**NOTES**

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1. Impact of influenza virus infection on alveolar epithelial cell Na,K-ATPase expression and localization
Universities of Giessen and Marburg Lung Center (UGMLC), Giessen, Germany, Northwestern University Feinberg School of Medicine, Chicago, Illinois, Robert Koch-Institute, Berlin, Germany, Max-Planck-Institute for Heart and Lung Research, Bad Nauheim, Germany

2. Involvement of inflammasome activation and IL18 secretion in the pathogenesis of experimental bronchiolitis obliterans syndrome (BOS)
Zakrzewicz A, Rabin L, Fischer A, Padberg W, & Grau V
Justus-Liebig-University Giessen, Giessen, Germany

3. Lung Cancer Epigenetics: Lessons from the mouse embryo to develop novel approaches for early diagnosis and therapy of lung cancer
Mehta A, Dobersch S, Romero-Olmedo AJ, Singh I, Guzmán-Díaz E, Savai R, Böttger T, Bellusci S, Savai R, Szibor M, Böttger T, Bellusci S, Bad Nauheim, Germany, Max Planck Institute for Heart and Lung Research, Bad Nauheim, Germany, Max Planck Institute for Heart and Lung Research, Bad Nauheim, Germany, University of Oaxaca, Mexico, University of Oaxaca (HRAEO), Mexico, Lung Matrix Remodeling, University Justus Liebig, Giessen, Germany, Excellence Cluster Cardio Pulmonary System, Institute for Genetics, University Justus Liebig, Giessen, Germany, Department of Microbiology, Kazan Federal University, Russia, Russian Federation, University of Giessen & Marburg Lung Center (UGMLC), Giessen, Germany

4. Metformin treatment decreases Drp-1 phosphorylation and improves mitochondrial function in platelets from patients with polycystic ovary syndrome
Randriamboavonjy V, Mann A, Elghenzawy A, Dröse S, & Fleming I
Institute for Vascular Signalling, Centre for Molecular Medicine, Goethe University, Frankfurt, Germany, Klinik für Anästhesiologie, Intensivmedizin und Schmerztherapie, Goethe University, Frankfurt, Germany

5. Mitochondrial autophagy in the development of amiodarone induced pulmonary fibrosis
Venkatesan S, Chilappagari S, Henneke I, Seeger W, Günther A & Mahavadi P
Universities of Giessen and Marburg Lung Center (UGMLC), Justus-Liebig University Giessen, Giessen, Germany, Agaplesion lung clinic Waldhof Elgerhausen, Greifenstein, Germany, Philipps University Marburg, Marburg, Germany

6. Modulation of respiratory dendritic cells during Klebsiella pneumoniae infection
Institute for Clinical Immunology and Transfusion Medicine, Justus-Liebig-University Giessen, Giessen, Germany, Freie Universität Berlin, Berlin, Germany, University Hospitals Giessen and Marburg (UKGM), Giessen, Germany

7. Morphological findings in pulmonary vessels from 56 autopsies of sickle cell disease in Brazil
São Paulo, Brazil, Puerto Montt, Chile

8. PHD3 controls an EMT phenotype and therapeutic resistance in lung cancer through TGFα
Dopeso H, Henze AT, Cuesta A, Acker-Palmer A, Garvalov BK & Acker T
Institute of Neuropathology, Justus Liebig University Giessen, Germany, Institute of Cell Biology and Neuroscience and Buchmann Institute for Molecular Life Sciences (BMLS), University of Frankfurt, Frankfurt, Germany, Focus Program Translational Neurosciences (FTN), University of Mainz, Mainz Germany

Idrees MM, Al-Najashi K, Khan A, Al-Dammas S, Al-Awwad H, Batubara E, Al Otai A, Abdulhameed J, & Kashour T
Saudi Association Pulmonary Hypertension (SAPH) Registry Taskforce, Saudi Arabia

Idrees MM, Banana M, & Kashour T
Saudi Association Pulmonary Hypertension (SAPH) Registry Taskforce, Saudi Arabia
11. Role of Fibroblast growth factor signaling pathway in white adipose tissue development and homeostasis
Shrestha A, El Agha E, Carraro G, Mackenzie B, Chao CM, Mooi senko A, Dilai S, & Bellusci S

12. Stromal-cell interaction causes up-regulation of heme oxygenase-1 and protects against chemotherapy induced cell death in HL-60 cells
1Henkenius K, 1Pali M, 1Kaiser T, 1Greif L, 2Stiewe T, 1Neubauer A, & 1Brendel C
1University Hospital of the Philipps-University Marburg, Marburg, Germany
2Institute of Molecular Biology and Tumor Research, Philipps-University Marburg, Marburg, Germany

13. The bidirectional crosstalk between macrophages and cancer cells induce CX3CR1 and CCR2 chemokines: fundamental for lung cancer growth and metastasis
1Schmall A, 1Al-Tamari HM, 2Herold S, 3Kamp schulte M, 4Weigert A, 1Wietelmann A, 1Vipotnik N, 3Grimminger F, 1,2Seeger W, 1,2Pullamsetti SS, & 1,2,3Savai R
1Max-Planck-Institute for Heart and Lung Research, Bad Nauheim, Germany,
2University of Giessen Lung Center, Giessen, Germany,
3Justus-Liebig-University, Giessen, Germany,
4Institute of Biochemistry I/ZAFES, Goethe-University Frankfurt, Frankfurt, Germany

14. The matrix component biglycan triggers the crosstalk between macrophages and podocytes during renal inflammation
1Nastase MV, 1Lazaroski S, 2Heide H, 2Wittig I, 3Young MF, & 1Schaef er L
1Institute of Pharmacology, Goethe-University, Frankfurt, Germany,
2Molecular Bioenergetics Group, Center of Biological Chemistry, Goethe University, Frankfurt, Germany
3NIDR, NIH, Bethesda, Maryland, USA

15. The NADPH Oxidase Nox4 exists in macromolecular complexes within the cell
Prior KK, Wittig I, Heide H, & Brandes RP
Goethe-University Frankfurt am Main, Germany

16. The role of NF-kB/IKK2 pathway in the pathogenesis of lung cancer
El-Nikhely N, Ceteci F, Seeger W, Rapp UR, & Savai R
Max-Planck-Institute for Heart and Lung Research, Bad Nauheim, Germany

17. The Role of the proresolving Chemerin-Receptor 23 in Acute Respiratory Distress Syndrome
1Reichert M, 2Hiesgen C, 2Ott J, 2Buchbinder A, 2Hecker M, 2Fuchs JN, 2Herold S, 2Vadasz I, 2Morty RE, 2Seeger W, 3Barnes M, & 2Mayer K
1University Hospital of Giessen, Giessen, Germany,
2University of Giessen and Marburg Lung Center (UGMLC), Justus-Liebig-University of Giessen, Giessen, Germany,
3Takeda Cambridge Ltd., Cambridge, UK

18. Vascular endothelial growth factor Expression during Acute Respiratory Distress Syndrome (ARDS)
Buchbinder A, Mohr A, Seeger W, & Mayer K
Universities of Giessen and Marburg Lung Center, Giessen, Germany

19. Wnt/β-catenin signaling reduces tumor growth and proliferation in Hedgehog-driven medulloblastoma
1Zinke J, 2Schneider J, 1Momma S, 1Plate K, & 1Lieb ner S
1Neurologic Institute (Edinger Institute) University Hospital Goethe University, Frankfurt, Germany,
2Karolinska Institutet Department of Biosciences and Nutrition, Stockholm, Sweden

20. β-Catenin mediates regulation of CYP1B1 in endothelial cells of the blood-brain barrier
1Ziegler N, 2Fisslthaler B, 1Czupalla CJ, 3Dejana E, 2Fleming I, 1Plate KH, & 1Liebner S
1Institute of Neurology (Edinger-Institute), Goethe University, Frankfurt, Germany,
2Institute for Vascular Signaling, Goethe University, Frankfurt, Germany
3IFOM- The FIRC Institute of Molecular Oncology, Milan, Italy

21. Endogenous FGFR2b ligands, FGF7 and FGF10, are dispensable for fibrosis formation and resolution in bleomycin-treated mice
1MacKenzie B, 2Al Alam D, 1Henneke I, 1El Agha E, Quantius J, 1Chao CM, 1Wilhelm J, 3Königshoff M, 1Seeger W, 1,2Günter A & 1,2Bellusci S
1Universities of Giessen and Marburg Lung Center, Giessen, Hessen, Germany,
2Saban Research Institute of Children’s Hospital Los Angeles, University of Southern California Keck School of Medicine, Los Angeles, CA, California,
3Comprehensive Pneumology Center, Ludwig Maximilians University, University Hospital Grosshadern, and Helmholtz Zentrum München, Munich, Bavaria, Germany,
4AGAPLESION Lung Clinic Waldhof-Elgershausen, Greifenstein, Germany

NOTES
Abstract Presentations

1. Acquired and genetic alterations of the miR-210-ISCU axis promote iron-sulfur cluster deficiency and pulmonary hypertension
Brigham and Women’s Hospital, Harvard Medical School, Boston, MA, USA, Regulus Therapeutics, San Diego, CA, USA, National Human Genome Research Institute, National Institutes of Health, Bethesda, MD, USA, Boston Children’s Hospital, Harvard Medical School, Boston, MA, USA, Ohio State University, Columbus, OH, USA, Egen, Inc., Huntsville, AL, USA, University of Bergen, Haukeland University Hospital, Bergen, Norway

2. Can pulmonary hypertension, by 2D- Transthoracic Echocardiography (TTE) predict the outcomes in patients with the diagnosis of peripartum cardiomyopathy (PPCM)?
Matshela MR
University of Kwa-Zulu-Natal, KZN, South Africa

3. Comparison of dynamic contrast-enhanced (DCE) magnetic resonance (MR) perfusion imaging and magnetic resonance Fourier decomposition (FD) with single-photon emission computed tomography (SPECT) as clinical reference standard for lung perfusion in patients with suspected chronic thromboembolic pulmonary hypertension (CTEPH)
Hannover Medical School (MHH), Hannover, Germany

4. Contribution of association and whole-exome sequencing studies to decipher the genetic architecture of pulmonary hypertension
Soubrier F, Eyries M, Coulet F, Germain M, & Trégouët DA
Hôpital Pitié-Salpêtrière, AP-HP, Paris, France Institute for Cardiometabolism and Nutrition (ICAN), Paris, France UMR_S 937, UPMC, INSERM, Paris, France

5. Effects of a chronic deficiency in nitric oxide on the structural and functional remodeling of the left and right ventricle
Schreckenberg R, da Costa Rebolo RM & Schlüter KD
Physiologisches Institut, Justus-Liebig University Giessen, Germany

6. HMGA1 may contribute to development of vascular lesions in pulmonary arterial hypertension by promoting endothelial to mesenchymal transition
Hopper RK, Rhodes CJ, Tojais NF, & Rabinovitch M
The Vera Moulton Wall Center for Pulmonary Vascular Disease, Stanford University School of Medicine, Stanford, CA, USA

7. HRQoL and collagen biomarkers in pulmonary arterial hypertension
Safdar Z, Tamez E, Guffey D, Minard CG, & Entman M
Baylor College of Medicine, Houston, Texas, USA
2Houston Methodist Hospital, Houston, Texas, USA

8. iNOS and EMAPII induction are part of a feed forward loop to promote lung emphysema
Clauss M, Green L, Seimetz M, & Weismann N
Indiana University School of Medicine, Indianapolis, Indiana, USA, University of Giessen, Giessen, Germany

9. Oxygen uptake efficiency slope is a valid submaximal measure of exercise performance in precapillary pulmonary hypertension
Thomson SD, Peacock AJ, & Johnson MK
Scottish Pulmonary Vascular Unit, Glasgow, United Kingdom

10. Pro-proliferative and inflammatory signaling converge on FoxO1 transcription factor in pulmonary hypertension—a new therapeutic approach
1,2Savai R, 3Sedding D, 1Al-Tamari HM, 2Kojonazarov B, 3Leske R, 4Capecchi MR, 2Weissmann N, 2Grimminger F, 1,2Seeger W, 2Schermuly RT, & 1,2Pullamsetti SS
1Max-Planck-Institute for Heart and Lung Research, Department of Lung Development and Remodeling, Bad Nauheim, Germany, 2Universities of Giessen and Marburg Lung Center (UGMLC), Justus-Liebig University, Giessen, Germany, 3University Clinic of Giessen and Marburg, Giessen, Germany, 4University of Utah School of Medicine, Salt Lake City, Utah, USA

11. Shear stress-regulated miR-27a/b controls pericyte recruitment: implications for vessel maturation
Demolli S, 4Stark K, 1Doddaballapur A, 1Boon RA, 1Doebele C, 4Eckart A, 2Korff T, 2,3Hecker M, 4Massberg S, 1Kaluza D, & 1,3Dimmeler S
1Institute for Cardiovascular Regeneration, Centre of Molecular Medicine, University of Frankfurt, Frankfurt, Germany, 2Institute of Physiology and Pathophysiology, Di-
12. The role of the Isl1-Ldb1 transcriptional complex in heart development
Max Planck Institute for Heart and Lung Research, Bad Nauheim, Germany, Erasmus Medical Center, Rotterdam, The Netherlands

13. The β3-integrin binding protein β3-endonexin is a novel negative regulator of hypoxia-inducible factor-1 (HIF-1)
Kračun D, Riess F, Kanchev I, Gawaz M, & Görlach A
1German Heart Center Munich at the Technical University Munich, Munich, Germany, 2Medizinische Klinik III, University of Tübingen, Tübingen, Germany, 3German Centre for Cardiovascular Research (DZHK), partner site Munich Heart Alliance, Munich, Germany

NOTES
The Board of Directors and Advisors meeting January 21st, 2013, took place in the Ritz Carlton hotel in Istanbul, Turkey. Scheduled one day before the AGM meeting, the Board discussed the progress of the Pulmonary Vascular Research Institute in the last year and since its inception, and proposed changes to the management structure. An important topic was how to generate revenue to allow the PVRI sustainability in future. To this end, the Board invited consultants from management consulting and strategic analytics firm 20/20 to speak during the meeting and present options for the PVRI's sustainability. Also discussed was the lack of annual dues payment in 2012, and options to increase compliance in 2013. Dr. Waxman presented his thoughts on the Right Heart Failure Foundation initiative, later echoed in the scientific workshops, and the progress of the Pulmonary Circulation journal was included in the topics of discussion. Board and BODA members present included Bert van den Bergh, Antonio Lopez, Martin Wilkins, Ghazwan Butrous, Declan Doogan, Sheila G. Haworth, Stuart Rich, Ahvie Herskowitz, Magdi Yacoub, Simon Campbell, as well as Special Member Aaron Waxman and PVRI Executive admin Nikki Krol. The Board decided to meet again in 2013 to see the progress of proposed plans and initiatives.
The meeting began by reviewing the business plan that was developed with the PVRI and 20/20 that began last year. It was reiterated that the PVRI will remain an independent physician/scientists organization, serving as the voice for academia and patients with pulmonary vascular diseases worldwide. The Board reviewed all of the activities of the PVRI in the past and the planned activities for the future. These included:

- the annual scientific meeting of the Fellows
- the continued support of the Pulmonary Circulation Journal
- further development of the host repository of educational material on the PVRI website
- promoting the PVRI’s role as an advisory body to champion the development of and access to new therapies
- establishing a critical focus on increasing membership
- the hiring of an executive director

The meeting was attended by Ghazwan Butrous, Declan Doogan, Ahvie Herskowitz, Bert van den Bergh, Stuart Rich, and Martin Wilkins.

The 7th PVRI AGM and 6th Scientific Workshops and Debates were held in Istanbul, Turkey. Spanning five full days, with nearly 200 attendees, the meeting is considered the largest conference on PVD issues ever held. The discussion-based meeting included topics as diverse as global clinical trials, paediatric pulmonary hypertension, new molecular targets for pharmacotherapy, exercise testing in PVD, the role of inflammation, and region-specific issues, targets and goals. As all delegates were considered both speaker and attendee, they were heavily encouraged to share data, experiences and thoughts both in and out of the meeting room, and many brought slides or prepared poster presentations. Similarly, a number of attendees prepared a secondary lecture, presentation, or interview, to be recorded by the PVRI Young Council for the population of the PVRI Educational Website. Over the course of 5 days, 71 conference talks and abstract presentations were recorded, and are now available on the PVRI educational website.

Full length social and scientific reports are also featured online at http://tinyurl.com/pjil88g.

A captive audience during the PVRI Istanbul Science Sessions

Ghazwan Butrous (left) and Maha al Dabbagh (centre) show off their PVRI shirts, with Manal Alhazmi (right)
Clockwise from top left: Aaron Waxman, Ghazwan Butrous and Victor Tapson smile at the Istanbul meeting; Prof. Xiansheng Cheng accepts the first PVRI Lifetime Achievement Award from President Martin Wilkins; Brian Graham (right), recipient of the 2013 PVRI Certificate of Excellence, smiles with Angela Bandeira; Fellows dance at the Gala Dinner; attendees in the scientific sessions; PVRI 7 year birthday cake; PVRI Fellows smile together; the ECCPS Giessen group receives the PVRI Achievement Award 2013

PVRI Chronicle: Volume 1 Issue 1, January - June 2014
On May 20th, 2013, the PVRI held a Get-Together at the American Thoracic Society meeting in Philadelphia from 9-11pm. The PVRI global family met up again with characteristic enthusiasm, to bring together the pulmonary scientists under one umbrella and spread the mission of PVRI to “increase the awareness and knowledge of pulmonary vascular diseases, and to facilitate advances in the treatment of affected people worldwide”. The event was held minutes away from the Pennsylvania Convention Center, at the Four Points by Sheraton Hotel. Coffee and an array of desserts were available at the social event, though alcohol was not served- which led to some grumblings. Naturally, names will not be named, but it was suggested that a full day of travel and meetings warranted a beer, at least for certain Germans- and PVRI will certainly be consider this feedback for the next Get Together.

Dr. Michael Yeager did an excellent job regarding the organization of the Get Together, and welcomed all the guests and PVRI members. He further initiated the social gathering by asking Prof. Werner Seeger to speak on behalf of PVRI. Prof. Seeger highlighted the recent updates on the PVRI website and mentioned its user-friendly nature and social media-type applications. Similar to Facebook, one can manage their profile online, and post blogs, images and more. He also applauded the “buddy system”, which allows members and Fellows to make donations to cover the costs of membership for those physicians and clinicians living in less affluent areas.

Dr. Seeger also commended the PVRI educational website, and touched specifically on features such as the Atlas, Conference Talks, Interviews, and Lectures. Many of these are open access whilst others are restricted to PVRI members, and their usefulness in terms of education and access cannot be disputed. Prof. Seeger also introduced the newly formed PVRI Young Council led by Dr. Zeenat Safdar and Dr. Stylianos Orfanos, and spoke briefly of their importance to the PVRI. In essence, the Young Council are an imperative part of the PVRI’s future, and aid in populating the educational website, the PVRI Journals, and in organizing recordings at the annual meeting.

These annual meetings and PVRI international conferences are held in different parts of the globe, Prof. Seeger continued, such South America, South Africa and more recently in Turkey, in order to fairly deliver the message of PVRI to a global audience. Continuing the
theme, Prof. Werner Seeger invited all attendees to the next PVRI Annual General Meeting and Scientific Workshops in Giessen, Germany. He mentioned that Giessen may not be the world’s warmest place in January, but that this should be seen as an advantage - after all, when outside is sludge, the meeting rooms and the science becomes all that much more appealing. Prof. Seeger followed this announcement with an acknowledgement of Pulmonary Circulation’s recent accomplishment of being indexed in PubMed, and encouraged applause for Dr. Jason Yuan, Prof. Nicholas Morrell and the Pulmonary Circulation family for its success. He further emphasized the need to promote the Journal by submitting articles and citing it in new work in order to increase the impact factor. Finally, Prof. Seeger thanked everyone who attended the Get Together, and wished everyone an enjoyable evening, with or without beer.

Following his welcome talk, a productive social chat went on for the rest of evening. There were over 40 people in the room actively networking with global partners, hatching new ideas and forging new collaborations. This vibrant and energetic social event fit right into the PVRI tradition, and plans are in place for the next get-together at ATS 2014 in San Diego.

Meeting Report: Regional SAPH meeting, Jeddah, Saudi Arabia, April 2013

Author: Maha Al-Dabbagh, Conference Head, SAPH 2013 Regional Head, Pediatric and CHD Task Force, SAPH

The Regional SAPH 2013 meeting took place in Jeddah, Saudi Arabia, April 24-26th 2013. This year, there were 237 participants. This is a 32% increase in the number of attendees compared to the previous regional conference held in 2011. 2 years ago, there were only 2 International speakers, while this year the SAPH succeeded in inviting 7 international speakers. The total number of regional speakers was 9. During the meeting, SAPH signed a “Memo-
The PVRI China Taskforce organized the 6th National Congress on Pulmonary Embolism and Pulmonary Vascular Diseases and the 4th International Symposium on Pulmonary Circulation disorders in collaboration with PVRI China Centre.

The meeting took place from the 19th to the 21st of July 2013, in the Tianlai International Conference Hall. The PVRI Section contained lectures from PVRI Fellows Martin Wilkins, London, UK; Ghazwan Butrous Canterbury, UK; and Lan Zhao, London, UK.

Below several scenes from the meeting, clockwise from top left: Martin Wilkins, Xiansheng Cheng and Cheng Wang; Ghazwan Butrous and Xiansheng Cheng in PVRI shirts; panellists; listening delegates, Xiansheng Cheng with Lan Zhao; and the view from the audience.
The Pulmonary Vascular Diseases Forum is a product of a longstanding collaboration between the PVRI China Taskforce and Fu Wai Hospital. An annual event, this year's meeting took place August 9-10 2013 in Beijing, China, and featured talks from renowned experts such as Zhihong Liu, Lan Zhao FPVRI, Jianguo He FPVRI, Nazzareno Galie, and Xiansheng Cheng FPVRI.

Fu Wai hospital is the largest hospital in China that specialises in treatment, prevention and research in cardiovascular diseases, hypertension, and their complications. Since its founding in 1956, 6 million outpatients from 32 different provinces in the nation, as well as 6 countries worldwide, have received care in Fu Wai hospital.

Grover Conference, September 4-8, 2013

In 2013, the PVRI co-sponsored the American Thoracic Society 2013 Grover conference held in Sedalia, Colorado, in conjunction with the American Thoracic Society (primary sponsor), the Cardiovascular Medical Research and Education Fund, and co-sponsor, the CPR Council of the American Heart Association. There was also strong support from industry, Actelion Pharmaceuticals US, Inc., Bayer HealthCare Pharmaceuticals, Lung LLC, and the United Therapeutics Corporation. Nearly 80 pulmo-
nary hypertension specialists gathered for four days at the scenic and tranquil Lost Valley Conference Center in September to discuss pulmonary vascular disease and right ventricular dysfunction. The Grover Conference is the ATS Assembly on Pulmonary Circulation’s longest running meeting and featured debates and scientific presentations on ventricular-vascular coupling, right ventricular fetal signaling, stem cell therapy, and metabolism of the RV-PA unit. Conference eponym Robert F. Grover, MD, PhD, also presented his work on high altitude pulmonary hypertension in residents of Leadville and Brisket Disease, which he performed with the late Dr. Jack Reeves and others. The conference talk was recorded, and is available on the PVRI website here: http://pvri.info/content/robert-grover-presentation-grover-conference-2013-0
The 7th Congress of Euro-Asian Respiratory Society and IV Congress of Kyrgyz Thoracic Society was held in Bishkek, Kyrgyzstan, November 7th to 9th 2013. Respiratory colleagues from various Central-Asian countries attended the meeting, including the Russian Federation, as well as delegates from all over the globe. Rich with science and discussion, the meeting was an opportunity for members of the PVRI to interact and innovate with colleagues from Central Asian countries. Martin Wilkins FPVRI, Lan Zhao FPVRI, Jean-Paul Richalet FPVRI, Ralph Schermuly FPVRI, Takeshi Ishizaki FPVRI and Baktybek Kojonazarov FPVRI were amongst those present and active in the meeting. The Congress was opened by Minister of Health Dinara Sagynbaev and President of The Congress Prof. Almaz Aldashev FPVRI.

In the opening ceremony, Prof. Butrous presented a talk on the global impact of pulmonary vascular diseases, which was followed by a number of lectures on sleep disorders at high altitude, chaired by Konrad E. Bloch and M. Mirrakhimov FPVRI, and featuring lectures by Talant Sooronbaev FPVRI, Tsogyal Latshang FPVRI, Konrad E. Bloch and Michael Furian.

During the Hypoxia meeting, Prof Martin Wilkins FPVRI, President of the PVRI, was elected an honorary member (academician) of the National Academy of Sciences of Kyrgyz Republic. This honour was presented by Prof. Erkebaev, the President of the National Academy of Sciences of the Kyrgyz Republic, on 8 November. In his speech, Prof. Erkebaev recognised the contributions of Prof. Wilkins to scientific research in the Kyrgyz Republic, as a result of a longstanding and ongoing collaboration with Prof Aldashev. Prof Wilkins received a diploma and the traditional Kyrgyz gown - the ceremonial Ak-Kalpak and Chepken.
The International Symposium Hypoxic Pulmonary Hypertension and Problems of Mountain Medicine followed the Respiratory Conference in Bishkek, Kyrgyz Republic, and took place in the same location November 8-9th 2013.

During the hypoxia meeting, the PVRI honoured two young investigators for their work and research. Their names are Batyr Osmonov and Diana Asambaeva, and they were presented with a certificate by the Vice-President of the National Academy of Sciences of Kyrgyz Republic, Prof. Almaz Aldashev, PVRI President Prof. Martin Wilkins, and PVRI Managing Director Ghazwan Butrous (all FPVRI). These two young people have shown themselves to be exceptional within their field and have since been made Fellows of the Pulmonary Vascular Research Institute.

Batyr Osmonov is a physician in the Pulmonology and Allergology Department of the National Center of Cardiology and Internal Medicine in Bishkek, Kyrgyz Republic. Currently he holds a residency on the Internal Diseases Department at the Kyrgyz State Medical Institute, and in 2012 he became a member of the Kyrgyz Thoracic Society. His main interests lay in sleep apnea, high altitude pulmonary hypertension and Chronic Obstructive Pulmonary Disease.

Diana Asambaeva is a Junior Researcher at the Research Institute of Molecular Biology and Medicine at the National Center of Cardiology and Therapy in Bishkek, Kyrgyz Republic. Her interests include the study of genetic markers in patients with metabolic syndrome in the Kyrgyz population, the study of the role of polymorphisms in the development of high-altitude pulmonary hypertension in the Kyrgyz highlanders by PCR, and real-time PCR.

Prof. Almaz Aldashev organised a special PVRI session on November 8th and 9th at the National Academy of Sciences of Kyrgyz Republic, with a focus on sleep disorders at high altitude, the role of Rho-kinase and NO in hypoxic pulmonary hypertension, and the problems of mountain medicine. Ralph Schermuly, Norbert Weissmann, Lan Zhao, Almaz Aldashev, Baktybek Kojonazarov, Djuro Kosanovic, Martin Wilkins, Takeshi Ishizaki, and Jean-Paul Richardet were amongst the PVRI Fellows and members presenting at the meeting.
PVRI Taskforces

PVRI Pulmonary Hypertension associated with HIV Taskforce

**Taskforce Leaders**
- Sharilyn Almodovar, USA
- Nicola Petrosillo, Italy
- Sonia C. Flores, USA

**Taskforce Members**
- Rosie Burton, South Africa
- Friedrich Thienemann, South Africa
- Okechukwu Ogah, Nigeria
- Anastase Dzudie, Cameroon
- Jürgen Rockstroh, Bonn, Germany
- Amam Mbakwem, Nigeria
- Mahmoud Sanim, Nigeria
- Harrison Farber, USA

**Educational Events/Meetings**

**November 2012**
Dr. Sharilyn Almodovar was accepted to the Keystone Symposia Fellows Program (Class 2013), which is a research-driven, diversity-centered program that allows early-career scientists to interact with high caliber national and international scientists and provides insights regarding the development of high-powered research meetings. This will represent a significant expansion in the networks of the PVRI members.

**September 2013**
Dr. Nicola Petrosillo attended the “53rd Interscience Conference on Antimicrobial Agents and Chemotherapy” (ICAAC 2013) meeting in Denver, Colorado, USA. This meeting provided Drs. Petrosillo, Almodovar and Flores an opportunity to meet in Denver and discuss their current research endeavors and future plans for the HIV-PH taskforce.

**Publications**

Current research initiatives
Clinical and basic laboratory evidence indicates that HIV proteins are associated with the pathogenesis of vascular remodeling PAH-HIV. Our group found amino acid substitutions in the Nef protein statistically associated with the PAH phenotype; these substitutions clustered around Nef functional domains that may confer the Nef with novel molecular adaptor functions. Drs. Sonia C. Flores and Todd Bull have been recently funded by the National Institutes of Health/ National Lung and Blood Institute with a multi-institutional cooperative grant (U01) to study the mechanisms of HIV-related lung disease. Specifically, the new studies will examine the functional properties of nef alleles containing these amino acid substitutions from PAH-HIV individuals.

Goal Summary 2014
• The HIV-PH taskforce would like to propose the following goals for 2014:
  • To continue increasing the awareness of PH among the HIV Specialists by educational meetings and collaborative projects.
  • To develop new, multi-institutional mechanistic studies using the samples deposited in the Pan African Pulmonary Hypertension Cohort Study (PAPUCO)
  • To engage early career investigators into PVRI Taskforces, in order to foster their development as potential future leaders.

PVRI Pulmonary Hypertension Associated With Congenital Heart Disease Taskforce

Taskforce Leaders
Antonio Augusto Lopes, Brazil
Marlene Rabinovitch, USA

Taskforce members
Adbullah Alkhorayyef, Canada
Maria Virginia T. Santana, Brazil
Ana Maria Thomaz, Brazil
Nair Yukie Maeda, Brazil
Ana Olga Mocumbi, Mozambique
Omar Al-Tamini, Saudi Arabia
Hanaa Banjar, Saudi Arabia
Patricia Cortez, Ecuador
Ian Adatia, Canada
Vera D. Aiello, Brazil
Khalid Alnajashi, Saudi Arabia
Sheila G. Haworth, UK
Leína Zorzanelli, Brazil
Tarek Kashour, Saudi Arabia
Maha Al Dabbagh, Saudi Arabia
Tilman Humpl, Canada
Maria Angélica Binotto, Brazil
Maria Jesus Del Cerro, Spain

Educational events
1. As a result of the kind collaboration of Attitude Studios in São Paulo, Brazil, all of the internet videoconferences included in the PAH Forum Program were kept on site throughout the year of 2013 (www.pahforum.com). The access is completely free, and more than one thousand colleagues (graph) from more than fifty different countries (table) have watched the conferences over the last years.

  • Videoconference 1 - PAH – Congenital heart disease: to operate or not to operate: that the question.
  • Videoconference 2: PAH – Congenital heart disease: from diagnosis to outcome
  • Videoconference 3: Pulmonary hypertension with chronic obstructive pulmonary disease (COPD)
  • Videoconference 4: Congenital heart disease and PAH in high altitudes
  • Videoconference 5: Pulmonary hypertension associated with Schistosomiasis
  • Videoconference 6: The Right ventricle in...
pulmonary hypertension
- Videoconference 7: Pulmonary Vascular Diseases in Rheumatic and Congenital Heart Diseases
- Videoconference 8: Pathology of pulmonary vascular disease
- Videoconference 9: Oxygen sensing in the ductus arteriosus and the pulmonary circulation
- Videoconference 10: Pulmonary arterial hypertension associated with HIV infection
- Videoconference 11: Combined clinical and surgical approaches to congenital heart diseases associated with pulmonary arterial hypertension.
- Videoconference 12: Exercise-induced pulmonary hypertension.

2. The Congenital Heart Disease Taskforce and the Pediatric Taskforce got together in a work session of the PVRI that was held on the 23rd of January, 2013, during the Annual General Meeting (Istanbul, Turkey). The objective was to define the “Minimal Requirements for Safely Assigning Children with Congenital Heart Disease and PAH to Surgery”. Thirty one colleagues (doctors and professors) from 13 different countries gave important ideas and suggestions. The discussion is central in the management of children with congenital heart disease and PAH, as there are no specific guidelines on the subject. The final text has been prepared, and will be submitted for publication.

Publications
Prepared and submitted for presentation in the next PVRI Annual Meeting, Giessen, Germany, January 2014:
- Microvascular (endothelial) dysfunction in congenital heart defects with distinct pulmonary hemodynamics. Maeda NY, Soares RPS, Mesquita SMF, Siqueira AW, Costa HG, Miura N, Lopes AA.
- Is it possible to render children with congenital heart disease and pulmonary hypertension better surgical candidates? Thomaz AM, Zorzanelli L, Gonçalves RC, Kajita LJ, Hironaka JF, Rabinovitch M, Lopes AA.
- Proteome analysis in pediatric patients with congenital systemic-to-pulmonary shunts: proinflammatory mediators in distinct hemodynamic conditions. Zorzanelli L, Thomaz AM, Maeda NY, Soares RPS, Bastos ENM, Rabinovitch M, Lopes AA.

Accepted for presentation in the Scientific Sessions of the American Heart Association, Dallas, USA, November 2013:
- Flow-dependent cardiac dysfunction and pressure-dependent endothelial activation in patients with atrial septal defect. Maeda NY, Costa HG, Siqueira AWS, Soares RPS, Mesquita SMF, Bydlowski SP, Miura N, Lopes AA.

Article
Current research
This is an on-going research project.

1. Title: Drug Therapy and Surgery in Congenital heart Disease with Pulmonary Hypertension
The main focus of the study is to investigate whether pediatric patients with congenital cardiac septal defects (or communications between the great arteries) presenting with clinical features suggestive of elevated pulmonary vascular resistance can be rendered better surgical candidates by means of preoperative (and postoperative) pulmonary vasodilator therapy, and become free of severe pulmonary vasculopathy late after surgery. This is not to say that inoperable patients (severe pulmonary hypertension) can be changed into operable. Actually, the concept of “borderline” is clearly established in the definition of patient population. The idea is to reduce the prevalence of severe immediate postoperative complications (right ventricular failure and death) and late persistence of pulmonary hypertension to less than 10%. The study also includes proteomic and genomic analyses. Patients are from the Heart Institute (InCor) – University of São Paulo, Brazil. The study design has been constructed in the Congenital Heart Disease Taskforce – PVRI.

Advisors: Antonio A. Lopes and Marlene Rabinovitch

Characteristic: open prospective study
Grant: FAPESP, #2011/09341-0 (US$ 30,000)
Clinical Trials registration: NCT 01548950

Workforce of the Research project: “Drug Therapy and Surgery in Congenital Heart Disease with Pulmonary Hypertension” (Clinical Trials NCT15048950).

Goal Summary 2014
• Publication of the consensus “Minimal Requirements for Safely Assigning Children with Congenital Heart Disease and PAH to Surgery”.
• Preliminary publication of “Drug Therapy and Surgery in Congenital Heart Disease with Pulmonary Hypertension”.
• A clinical study is being designed to test the efficacy and safety of a new modality of therapy for patients with advanced pulmonary arterial hypertension. The first step will be a pilot study in patients with Eisenmenger syndrome at end stage of pulmonary vasculopathy. The study design will be discussed within the PVRI for approval and sponsorship.

From right to left, and top to bottom: Ana Maria Thomaz and Leína Zorzaneli, pediatric cardiologists; Vera D. Aiello and Nair Y. Maeda, respectively, pathologist and pharmacist (proteomic analysis); Antonio Lopes and Marlene Rabinovitch, advisors. All doctors are members of the PVRI Congenital Heart Disease Taskforce.
PVRI Paediatric Taskforce

Taskforce Leaders
Ian Adatia, Canada
Maria Jesus del Cerro, Spain

Taskforce Members
Sheila G. Haworth, UK
Gabriel Diaz, Colombia
Julio Sandoval, Mexico
Antonio Augusto Lopes, Brazil
Liliana Moreno, USA

Initiatives
Following the success of the Paediatric PH Classification first presented in Panama City, the Paediatric Taskforce is collaborating with the PVRI Congenital Heart Disease taskforce on guidelines for operability of shunt lesions with PAH.

Educational Events/Meetings
1. Special combined with CHD taskforce evening symposium on CHD and PAH Istanbul 2013
2. Collaboration with 6th International Conference on Neonatal and Childhood Pulmonary Vascular Disease, San Francisco June 2013

Publications
Cardiac catheterization in children with PAH (in preparation)

Goal Summary 2014
• To publish cardiac catheterization guidelines for pediatric PH
• Continue work on operability with CHD taskforce
• Taskforce meeting with the CHD during the PVRI Giessen Conference, Jan 2014
• Collaboration with 1st Latin American Pediatric PH meeting in Cartagena, Feb 2014

Pulmonary Hypertension Associated With High Altitude and Hypoxia Taskforce

Taskforce Leaders
Qadar Pasha, India
Max Gassmann, Switzerland

Taskforce Members
Alexandra Heath, Bolivia
E. Kenneth Weir, USA
Nanduri Prabhakar, USA
Almaz Aldashev, Kyrgyzstan
Inder Anand, USA
Serge Adnot, France
Friedrich Grimminger, Germany
Robert Naeije, Belgium
John Newman, USA
Kurt Stenmark, USA
Louise Ostergaard, Switzerland
Katia Stewart, USA
Ioana Preston, USA
Patricia Thistlethwaite, USA
Norbert Weissmann, Germany
Jun Wang, China
Ishizaki Takeshi, Japan
Jason Yuan, USA
Stuart Rich, USA
Martin Wilkins, UK
Ghazwan Butrous, UK
Sheila G. Haworth, UK
Ghulam Mohammad, India

Research activities
1. A research proposal entitled ‘Responses of EGLN1/VHL and HIF1AN/CBP: The factual oxygen sensor molecules at high-altitude’ has been sanctioned by CMREF to Dr Qadar Pasha. The duration of the project is two years and it will be initiated from November 2013.

2. A project entitled ‘Telomeres in Adaptation and Maladaptation Under Hypobaric Hypoxia’ was initiated by Dr Qadar Pasha at CSIR-IGIB, Delhi, with partial funding support from PVRI. Project summary:
   Inside the nucleus of a cell lies the basic unit of life i.e. DNA, molded into a scaffold called chromosomes. At the ends of these chromosomes are specific stretches of DNA called telomeres. Telomeres are known to protect our genetic data, and make it possible for cells to divide and proliferate. Telomere length is not only related to the basic biology as a trigger of cellular senescence but it seems the same also acts as a mirror of an index of oxidative stress. Hence because of its significance, it was decid-
ed to investigate the telomeres under the harsh environmental conditions of high-altitude (3500m); especially with respect to adaptation in natives and maladaptation in sojourners, healthy or HAPE susceptible. Relative telomere length was determined using a real-time quantitative PCR by calculating the relative ratio of telomere (T) and single copy gene (S) PCR products and is expressed as T/S ratio. All the p-values were adjusted with age and gender. The findings on the length of telomere were significant. The HAPE patients revealed significantly low T/S at a scale of 1 compared to the healthy controls (P<0.05); whereas, the natives had the length near equal to the length of the same controls (P>0.05). In addition, several variants of genes that associate with telomere length were screened and few highly associating genes were could be identified.

Other initiatives
A GSK post doctoral fellow was funded through PVRI under this project.

Collaborations
• Prof. Max Gassmann, who is faculty member at both the Vetsuisse Faculty in Zurich, Switzerland, and the Universidad Peruana Cayetano Heredia (UPCH), Lima, Peru, has undertaken larger efforts to establish a long-lasting collaborative effort with the Es Salud Hospital located in Puno, Peru, a larger city located at the Titicaca Lake (4000 m a.s.l.). The main goal is to establish a research exchange between the scientists and medical staff in Peru and Europe. The Erasmus University (Neonatology) is involved in this endeavor, too. A Memorandum of Understanding is in preparation.
• The Department of Pediatric Cardiology, Kardiozentrum, Fundacion Cardi infantil, LaPaz, Bolivia in collaboration with Dr Qadar Pasha, CSIR-IGIB has agreed to work on HA diseases, especially HAPE.

Conferences/symposiums organized
Leh Symposium 2013: A National Leh symposium is being conducted at Leh, Ladakh scheduled for November 25 & 26, 2013. This symposium will be organized by Dr Ghulam Mohammad with full support from Dr Qadar Pasha. This year’s theme is ‘Ladakh’s contribution in understanding high-altitude diseases’. The symposium will focus on bringing together in-house researchers and clinicians for an effective synchronization in the working of the two.

Conferences and presentations
• Qadar Pasha. 6th Pulmonary Vascular Research Institute (PVRI) Scientific Workshops & Debates, Istanbul, January 21-25 2013

Publications

Goal Summary 2014
• Leh Symposium 2014: The 3rd International Leh symposium is scheduled for September 19-23, 2014. Prof Robert Naeije, Belgium will be the front organizer of this symposium. The other active co-organizers will be Profs Max Gassmann, Norbert Weissmann, Ghazwan Butrous and Qadar Pasha.
**Taskforce Members**
Anna Hemnes, USA  
Karen Sliwa, South Africa  
Ioana Preston, USA  
Barbara Cockrill, USA  
Manal Alhazmi, Saudi Arabia  
Tim Lahm, USA  
Zeenat Safdar, USA  
Ghazwan Butrous, UK

**Initiatives**
We have formed a new working group with a focus on women's health and pregnancy in pulmonary hypertension. This is a multidisciplinary collaborative effort to address issues important to women's health in the context of pulmonary vascular disease including:

1. State of knowledge of the effects of female sex hormones on pulmonary vascular disease  
2. Challenges of pregnancy in pulmonary hypertension  
3. Options and recommendations for contraception and sterilization in pulmonary hypertension  
4. The potential implications of hormone replacement therapy

**Goal Summary 2014**
We are currently planning to add specialists in obstetrics and psychology to complement our group's expertise. Our short term goals are to produce a statement regarding the state of women's health issues in pulmonary hypertension and to answer the pressing need for recommendations surrounding pregnancy in pulmonary hypertension. We will address all WHO groups of pulmonary hypertension in this statement.
The PVRI Journal Editorial Board
Run by Teamleader Sachindra Joshi
• Content for the Journal
• Quality assurance
• Lay out, content and style of the Journal

The Educational Website Board
Run by Teamleader Djuro Kosanovic
• Content
• Quality assurance
• Regular checks to ensure content is correctly linked

The Infography Board
Run by Teamleader Rebecca Vanderpool
• Restructures articles (for infography purposes)
• Publishes on the Elearning Website and in PVRI Journals

The Social Board
Run by Teamleader Ewa Kolosionek
• Organises the PVRI Get Togethers
• Assists in the organisation of the Annual Meeting
• Organises the recordings in the Annual Meeting together with the Managing Director Ghazwan Butrous

Educational Initiatives:
Throughout 2013, the Young Council recorded and produced a number of educational materials. These included lectures, abstracts and interviews. An overview is provided below:

Lectures:
Small Animal Imaging: New Possibilities in Cardiovascular and Respiratory Research
A lecture by Baktybek Kojonazarov MD, PhD, FPVRI, at Justus-Liebig University in Giessen, Germany, produced by Djuro Kosanovic PhD, FPVRI, at Justus-Liebig University in Giessen, Germany.

5. Targeting Cyclic Nucleotide Phosphodiesterases for the Treatment of Pulmonary Vascular Diseases
A lecture by Dr. S. Pullamsetti FPVRI, Max Planck Institute for Heart and Lung Research, Bad Nauheim, Germany

6. MicroRNA in the Pathogenesis of Pulmonary Hypertension
A lecture by Dr. S. Pullamsetti FPVRI, Max Planck Institute for Heart and Lung Research, Bad Nauheim, Germany

7. Role of Rho-Kinase in Hypoxic Pulmonary Hypertension: New Insights
A lecture by Djuro Kosanovic FPVRI, PhD at Justus-Liebig University and ECCPS in Giessen, Germany

8. Western Blot and its Application in Pulmonary Vascular Research
A lecture by Dr. Soni S. Pullamsetti, FPVRI, Max-Planck-Institute for Heart and Lung Research Bad Nauheim, Germany

9. Human Respiratory and Cardiovascular Systems in Extreme Environments
A lecture by Djuro Kosanovic, PhD, FPVRI, and Oleg Pak, MD, both at Justus-Liebig University, Giessen, Germany

10. Cardiovascular Phenotyping: Hemodynamic Measurements in Mice
A lecture by Akylbek Sydykov, M.D., PhD, FPVRI, at the University of Giessen and Marburg Lung Center (UGMLC), Member of German Lung Center (DZL), Justus Liebig University of Giessen, Giessen, Germany.
11. Acute and Chronic PE: Initial Management
A lecture by Dr Hunter Champion, FPVRI
Associate Professor of Medicine, Pulmonary Vascular Disease Center, University of Pittsburgh, USA, recorded by Young Council Member Rebecca Vanderpool FPVRI of the same institution.

Abstracts:
1. A comparison of clinical features of adult patients with different classifications of pulmonary hypertension - G. Chen, China
2. BMPR-II deficiency leads to an increase in egg deposition and cytokine release in the lungs of mice chronically infected with schistosomiasis - A. Crosby, UK
3. Cardiac Catheterization in Children with Pulmonary Hypertensive Vascular Disease - P. Bobhate, Canada
4. Case report: Improvement of severe Pulmonary Arterial Hypertension by inhalation of Vasoactive Intestinal Peptide (Aviptadil) - D. Bevec, Germany
5. Deficiency of Tie2, an endothelial survival pathway, acts as a “second hit” leading to a severe pulmonary arterial hypertension phenotype when combined with VEGFR2 inhibition and chronic hypoxia in mice - M. Taha, Canada
6. Electrocardiographic features of sickle cell disease patients with pulmonary hypertension - A. Mbakwem, Nigeria
7. Importance of pulmonary arterial hypertension measurement in high altitude pulmonary edema at high altitude - G. Mohamed, India
8. Inflammation, caveolin-1 expression and pulmonary hypertension - R. Mathew, USA
9. Non-invasive RV-PA modeling to aid in hemodynamic differentiation in a referral pulmonary hypertension cohort - M. Velez-Martinez, USA
10. Non-invasive measurement of right ventricular-arterial coupling - R. Vanderpool, USA
11. Proposal of a database for scientific and clinical purposes - R. Badagliacca, Italy
12. The prevalence and prognostic implications of pulmonary hypertension in pregnancy - M. Matshela, USA
13. The soluble guanylate cyclase stimulator riociguat prevents from tobacco smoke-induced pulmonary hypertension and emphysema - M. Seimetz, Germany

Goal summary 2014
The Young Council will again be active in the PVRI Conference. This includes the following:
• Recording individual lectures
• Recording individual interviews
• Recording abstract presentations
Additionally, this year the council will also be expected to:
• Record the conference sessions
• Format and publish the PVRI Chronicle twice in 2014 online and in App format
• Organise the PVRI Get Together in May 2014
• Continue to populate the PVRI Educational Website

PVRI Schistosomiasis Taskforce

Taskforce Leaders
Ghazwan Butrous, UK
Nick Morrell, UK

Taskforce Members
Brian Graham, USA
Rubin Tuder, USA
David Dunne, USA
Allan Fennick, UK
Russel Stothard, UK
David Rollison, UK
Ewa Kolosionek, Sweden
Alexi Crosby, UK
Angela Bandeira, Brazil
Ana Lucia Coutinho, Brazil
Rita Ferreira, Brazil
Vera Aiello, Brazil
Roberto Lambertuccia, Brazil
Flavio Gapiassu, Brazil

Initiatives
This year the Taskforce has been trying to discern whether mice that have a heterozygous null mutation in BMPR-II have an exaggerated pulmonary vascular response to S. mansoni infection in our chronic schistosomiasis model. The data suggests that they do not develop more pulmonary arterial hypertension but that
they are more susceptible to the deposition of eggs in the lungs and develop more pulmonary vascular remodelling than wild-type mice.

**Educational events/meetings**
The work described above was presented at the PVRI General Meeting in Istanbul and at the ATS this year.

**Current research**
The taskforce is also investigating the role of bone-marrow derived progenitor cells in pulmonary vascular remodelling in schistosomiasis, in particular the role of the CXCR4 axis. Wild-type C57/BL6 mice underwent a bone-marrow transplant with GFP-expressing bone-marrow cells and were then infected with schistosomiasis for 12 weeks. Mice were then either given a CXCR4 antagonist or a vehicle control for 21 days. Appropriate controls have also been performed. We are measuring haemodynamics, pulmonary vascular remodelling and circulating bone marrow derived cells. This work is currently on-going.

**Goal Summary 2014**
- To further investigate the role of bone-marrow derived progenitor cells in pulmonary vascular remodelling in schistosomiasis, in particular the role of the CXCR4 axis.
- To publish and present findings in assorted PVD and schistosomiasis journals and meetings throughout the year.

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**ANNOUNCING THE PVRI TASKFORCE ON EXERCISE IN PH**

**Taskforce Members**
- Bart Boerrigter, The Netherlands
- Robert Naeije, Belgium
- Bradley A. Maron, USA
- Aaron Waxman, USA
- Marco Guazzi, Italy
- David Systrom, USA
- Ron Oudiz, USA
- Jonathan Myers, USA
- Ross Arena, USA
- Abraham Samuel Babu, India
- Aaron Waxman, USA

**Initiatives**
The taskforce plans to introduce itself and hold its first taskforce meeting during the 7th Annual Joint Symposium ECCPS/PVRI 2014-Molecular Mechanisms and Treatment of Heart and Lung Disease, in Giessen, Germany, January 27-31, 2014.

**1. Agenda:**
Initiate a strategy for the completion of an expert consensus document establishing the definition, diagnosis, and standardized approach to treatment of exercise-induced pulmonary hypertension (PH) along with establishing recommendations for exercise testing and training.

**2. Need for the statements:**
Universally accepted methods for the assessment of exercise capacity in individuals with PH at rest or provoked by exercise are lacking. As a consequence, there is substantial variability in the characterization of the exercise-induced PH pathophenotype in clinical research and in “real world” practice. In addition, increasing reports are available characterizing the consequences of routine exercise on the trajectory of pulmonary vascular disease. Taken together, the development of contemporary recommendations for the safety and potential benefits of therapeutic exercise in pulmonary vascular disease is timely.

**3. Plan:**
- This PVRI taskforce proposes to develop three separate guidelines on the following topics:
  - Laboratory-based methods to identify and evaluate maladaptive changes to cardiopulmonary hemodynamics and right ventricular function provoked by exercise: From experimental animal models to clinical studies of exercise-induced PH patients. (Chairs: Brad & Aaron. Writing group: Abraham, David, Jon, Marco, Padmakumar, Ron, Ross)
  - Recommendations for the standardized approach to evaluating exercise capacity in PH (Chairs: Abraham, Brad, Jon. Writing group: Aaron, Arun, David, Marco, Padmakumar, Ron, Ross)
  - Recommendations for the safety and potential benefits of exercise training, physical
activity, and participation in organized athletics in PH (Chairs: Abraham, Brad, Ross. Writing committee: Aaron, Arun, David, Jon, Marco, Padmakumar, Ron)

4. Outcome of these Guidelines:
These Guidelines will be published in Pulmonary Circulation, which is the official record of academic reports for the PVRI. Endorsement from other key agencies will also be pursued to increase the visibility and strength of these recommendations.

5. Guideline team:
Abraham Samuel Babu, MPT and Bradley A. Maron, M.D. will serve as the Committee Co-chairs of the Guideline documents, which will be written in conjunction with key experts in the field of pulmonary vascular diseases, including Aaron B. Waxman, M.D., Ph.D., Arun G. Maiya, Ph.D., David M. Systrom, M.D, Jonathan Myers, Ph.D., Marco Guazzi, M.D., Ph.D., R. Padmakumar, M.D., D.M., Ronald Oudiz, M.D., and Ross Arena, Ph.D. Other experts may be invited to participate on the specific guidelines.

6. Time plan:
December 2013:
• Finalize the titles of the Guidelines and the involvement of members
January 2014:
• Develop a rough outline for the Guidelines
• Web conference with the taskforce in Germany during the PVRI meeting to finalize the outline and discuss any conflicts in ideas that exist from prior emails
• Allot roles and responsibilities for team members
February 2014:
• Begin writing of the Guidelines

7. Estimated time to completion of all Guidelines – 1 year:
Key project milestones include the PVRI 2015 conference for release of the Guidelines and Guideline publication in Pulmonary Circulation and the annuals PVRI Review (2015). Aim to distribute the Executive Summaries of the Guidelines for consideration for publication in material sponsored by the: Pulmonary Hypertension Association (PHA), American Thoracic Society (ATS), and European Respiratory Society (ERS), and, if permitted, in the Advances in Pulmonary hypertension, American Journal of Respiratory and Critical Care Medicine, and European Respiratory Journal.

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PVRI Regional Taskforces

PVRI Sub-Saharan Africa Taskforce

Taskforce leaders
Karen Sliwa, South Africa
Ana Mocumbi, Mozambique

Taskforce members
Friedrich Thienemann, South Africa
Kemi Tibazarwa, Tanzania
Taiwo Obiabisi Olungu, Nigeria
Gerald Maarman, South Africa
Sandra Pretorius, South Africa
Kamilu Karaye, Nigeria
Sani Mahmoud, Nigeria
Ogah Okechukwu, Nigeria
Dike Ojji, Nigeria
Patience Udo, Nigeria
Amam Mbakwem, Nigeria
Moshood Abiodun Adebayo
Albertino Damasceno, Mozambique
Elijah Ogola, Kenya
Jean-Baptiste Anzouan-Kacou, Ivory Coast
Isaac Kofi Owusu, Ghana
Bertrand Ellenga Mbolla, Congo
Anastase Dzudie, Cameroon
Marie Ntep Gweth, Cameroon

Initiatives
The Pan African Pulmonary Hypertension Cohort Study (PAPUCO) was established in 2011 to describe the epidemiology and characteristics of pulmonary hypertension in Sub-Saharan Africa. Participants are drawn from 10 cardiovascular specialist centres in 9 African countries, namely Cameroon (1), Kenya (1), Mozambique (2), Nigeria (7), South Africa (2), Sudan (1), Tanzania (1), and Uganda (1); Ethiopia (1). To date 216 patients have been enrolled.
One of the aims of the cohort study is to encourage individual physicians and cardiologists who are interested in investing time and effort to do research relevant to Africa. Based on their research activities linked to pulmonary hypertension, 2 African cardiologists, namely Dr Dike Ojji (Nigeria), and Dr Kemi Tibazarwa (Tanzania) will be awarded their PhD's in December 2013. Dr Friedrich Thienemann (South Africa) has received his Master’s degree. Dr Anastase Dzudie (Cameroon), Dr Ogah Okechukwu (Nigeria) and Mr Gerald Maarman (South Africa) are currently registered for PhDs linked to this project.

**Educational meetings**
The Pan African Society of Cardiology (PASCAR)–Senegalese Society of Cardiology, 4th All African Conference on Heart Disease, Diabetes and Stroke. This meeting took place on 16th -20th May 2013, in Dakar, Senegal. As several PAPUCO participants attended this important PASCAR meeting, a PAPUCO satellite meeting was held.

Members who presented/participated at the meeting
- Prof Karen Sliwa gave an overview of the epidemiology on cardiovascular disease in Africa and the 4 colliding large health care problems including non-communicable diseases, HIV/AIDS, maternal health and violence.
- Prof Ana Mocumbi (Mozambique) spoke about the medical and surgical management of cardiomyopathies in Africa and discussed whether we have reached our limit. Cardiovascular disease is highly prevalent in Africa, with 13% of cases per 250. Cardiomyopathies are classed in three classes based on morphology including dilated, hypertrophic and restrictive cardiomyopathies. In Nigeria, 33.7% of cardiomyopathies occur in patients between the ages 18 months and 12 years old. Prof Mocumbi then discussed the various management strategies for cardiomyopathy which include diuretics, ACE inhibitors, nitrates, beta blockers, anticoagulants and antiarrhythmic drugs. Surgery is often used for palliative and corrective purposes, together
with heart transplantation and valvular repair. Prof Mocumbi concluded that there is a need for treatment regimens and guidelines, tailored specifically for Africa, and for educational programmes and training of general practitioners to do echocardiography in order to diagnose heart disease early. She also mentioned that telemedicine is now becoming a common practise, as this gives the physician cardiologist vital information of patients when they are not able to attend the hospital due financial restraint or transport problems.

• Dr Friederich Thienemann presented preliminary data (after one year of patient recruitment) from the hypertension cohort study (PAPUCO). He concluded that left heart disease, HIV, chronic lung disease and congenital heart disease are common contributors to pulmonary hypertension in Africa.

• Dr Friederich Thienemann presented preliminary data (after one year of patient recruitment) from the hypertension cohort study (PAPUCO). He concluded that left heart disease, HIV, chronic lung disease and congenital heart disease are common contributors to pulmonary hypertension in Africa.

Current research initiatives
The Taskforce has now commenced an official collaboration between South Africa and Mozambique, which is mainly facilitated by the PVRI. This collaboration started from the 1st June 2013 and will run until the 31st May 2015 and pertains to the PAPUCO continental registry.

Other initiatives
• Mr Gerald Maarman, a PhD student under the supervision of Prof Karen Sliwa, visited the Excellence Cluster Cardiopulmonary System (ECCPS) translational research centre in Giessen Germany, under the leadership of Prof. Ralph Schermuly (1 – 31 August 2013) – see pictures below. This visit was made possible with financial support from the PVRI (details on p.69). He also attended the European Society of Cardiology (ESC) meeting in Amsterdam, Netherlands.
• Mr Gerald Maarman investigates novel cardioprotective therapies in pulmonary arterial hypertension. During Gerald's visit he learnt the pulmonary artery banding model of right ventricular hypertrophy, state-of-the-art immunohistochemical staining methods and right heart catheterisation. He is currently establishing these techniques in South Africa.

Following his visit to Giessen, he attended the ESC annual congress in Amsterdam, the Netherlands, (31 August to 5 September 2013), where he presented a poster showing his latest data of the cardioprotective effects of melatonin in pulmonary arterial hypertension.

• Prof Mocumbi participated at the Grover Conference on Pulmonary Hypertension, in October 4-7 presenting the talk "Right ventricular endomyocardial fibrosis – Pathophysiology of Pulmonary Hypertension".

Goal Summary 2014

• To publish the data collected from a total of 216 patients in our PAPUCO registry.
• To publish results from our basic research project which investigate the cardioprotective effects of melatonin in pulmonary arterial hypertension.
• To publish data from Dr. Anatase Dzudie's PhD project, which will help us to understand clinical features of group-2 pulmonary hypertension patients in Cameroon, provide information on the outcome of these patients and identify possible predictors of outcome.
• To publish work by Dr. Friedrich Thiemann investigating the overall one-year mortality and predictors of mortality of patients with cardiopulmonary disease in a high HIV/TB prevalence setting.

Saudi Association for Pulmonary Hypertension (SAPH) & The Eastern Mediterranean Region (EMR) Taskforce

Taskforce Leaders
Paul Hassoun, USA
Majdy Idrees, KSA

Taskforce Members
Adriano Mario Francisco Tivane, Mozambique
Albertino Damasceno, Mozambique
Janet Ajuluchukwu, Nigeria
Karen Sliwa, South Africa
Ana Olga H Mocumbi, Mozambique
Maha Al-Dabbagh, Saudi Arabia
Okechukwu S. Ogah, Nigeria
Gulnaze Mahomed Arif, Mozambique
Rosie Burton, South Africa

Initiatives
SAPH has continued to expand its activities quite rapidly. It is now recognized regionally and somewhat internationally for its services in the field of PH. The number of active members has also risen steadily during the last 2 years, reflecting the success of SAPH in building more awareness and creating a positive environment between physicians and healthcare providers interested in the field.

Interestingly, more nurses, paramedics, and patients are now involved in different SAPH activities. The total number of local/regional members has reached 111 in year 2013. This is a 25% increase compared to 2012, reflecting the increased awareness of local health care providers in the region about the disease.

Educational Events/Meetings:
Two main scientific events were held in 2013.
• The first was the PVRI general annual meeting (hosted by SAPH/EMR). This meeting was held in Istanbul, Turkey during the period between 21 and 25 January.
• The second event (SAPH 2013 regional) was held in Jeddah, KSA during the period between 24 and 26 April. (Please find more information about SAPH 2013 Regional in the conference summary).

The Scientific Agenda 2013 was as follows:
• SAPH 2013 International (SAPH/PVRI), Istanbul, Turkey, 21-25 January 2013
• 7th SAPH Master Class - Pediatric, Riyadh, KSA, 11-12 February 2013
• 5th World Symposium on PH, Nice, France, 27 Febr - 1 March 2013
• Pulmonary Hypertension Awareness Day, Qassim, KSA, 6 March 2013
• SAPH 2013 Regional: PH in the Young, Jed-dah, KSA, 24-26 April 2013
• Pulmonary Hypertension Awareness Day, Abha, KSA, 8 May 2013
• Regional Pulmonary Hypertension Awareness Day, Dubai, UAE, 12 September 2013
• 8th SAPH Master Class - Adult, Riyadh, KSA, 23-24 September 2013
• Pulmonary Hypertension Awareness Day, Dammam, KSA, 17 December 2013

Publications
Both The Updated Saudi Guidelines on the Treatment and Management of Pulmonary Hypertension and the early data of Pulmonary Arterial Hypertension Registry in Saudi Arabia (PATENTS) are expected to be published by December 2013.


Current research initiatives
Current research initiatives are:

• Participation in COMPASS II study, which is an international, multi-center, randomized, event-driven, placebo controlled study funded by Actelion. The study was completed in June 2013, and the results are expected to be released by mid 2014.
• Survey on the behavior of Pulmonary Hypertension Treating Physician in the EMR region.
• The prevalence of PH in Sickle-cell disease in the Eastern Provence in Saudi Arabia
• Inhaled Iloprost in severe pulmonary hypertension in COPD patients.
• Genetic studies in Saudi patients with congenital heart disease
• Bronchiectasis & PH in Saudi patients

Other Initiatives
• SAPH has signed a collaboration agreement with the American Pulmonary Hypertension Association (PHA). This should further enrich SAPH by benefiting from the long-standing experience of PHA in helping PH patients.
• To hold a patient-oriented PH seminar for the first time in November 2013.

Scientific & Educational Activities 2014
• Joint Symposium ECCPS/PVRI 2014, Molecular Mechanisms and Treatment of Heart and Lung Disease Bad Nauheim, Germany, 27-30 January 2014
• Joint Symposium SAPH/SSIM/ECS 2014 Pulmonary Hypertension for Internist, Jeddah, KSA, 27 February 2014
• SAPH Executive Annual Meeting, Dubai, UAE, 13 March 2014
• Gulf Thoracic Annual Conference, Dubai, UAE, 13-15 March 2014
• 8th SAPH Master Class Riyadh, KSA, 18-19 March 2014
• Pulmonary Hypertension Awareness Day, Jeddah, KSA, 17 April 2014
• Joint Symposium SAPH/PVRI (Eastern Mediterranean Region) SAPH 2014: The 7th Annual Joint PH Meeting, Muscat, Oman, 1-3 May 2014
• International Pulmonary Hypertension Day, Riyadh & Jeddah, KSA, 5 May 2014
• Pulmonary Hypertension Awareness Day, Abha, KSA, 15 May 2014
• PHA International PH Conference & Scientific Sessions, Indianapolis, Ind., USA, 20-22 June 2014

PVRI Chronicle: Volume 1 Issue 1, January - June 2014
PVRI China Taskforce

Taskforce Leaders
Chen Wang, China
Martin Wilkins, UK

Taskforce Members
Zhenguo Zhai, China
Lan Zhao, UK

Initiatives
The PVRI China Taskforce continues its active participation in organizing national pulmonary vascular meetings and educational courses in China. During the last year, a number of meetings were held for Chinese physicians and scientists on the pathology, clinical presentation and management of PE and PH. Every opportunity was made to engage external speakers and create future international collaboration opportunities. Members of PVRI-China Taskforce with the help of Chinese Medical Society (CMA) and the Chinese Thoracic Society (CTS) enabled the following activities.

Educational Meetings
1. World Pulmonary Hypertension Day, May 5th –7th, 2013. A series of educational activities for pulmonary hypertension were held in Beijing, Shanghai, Tianjin, Shenyang, Chengdu, Dalian, Xi’an and Shenyang with the support of the I-seek pulmonary hypertension advisory group. More than 100 multidisciplinary physicians participated in the activities, to discuss the issues of pulmonary hypertension health education and standardize treatment for Chinese patients.

2. Chongqing July 19th–21st 2013: The 6th National Conference on pulmonary vascular disease and the 4th international workshop on pulmonary circulation diseases was held in Chongqing. This was followed by the National Pulmonary Embolism-Deep Venous Thrombosis Prevention working group meeting and National Pulmonary Vascular Diseases group meeting. Nearly 500 experts from home and abroad attended the meeting and conducted a series of academic and interdisciplinary collaborations and communications. This meeting provided a communication stage that would ensure further progress in the epidemiology, diagnosis and treatment of pulmonary vascular disease for physicians, scientists and other health care providers in China. The meeting summarized the work of the preceding year and also made a plan for the next year.

3. China Heart Congress, Beijing August 2013. The one and a half day pulmonary vascular disease session was attended mostly by cardiology physicians. Professors Xiansheng Cheng, Jianguo He, Changming Xiong, and Lan Zhao gave lectures in the meeting, covering topics on the advances in IPAH, as well as in congenital heart disease and chronic thromboembolism, with specific attention to RV performance.

Educational Courses
• An educational course on standardizing the diagnosis and treatment of pulmonary embolism and pulmonary hypertension was organized in May 12th-14th and August 29th-31st 2013. These courses provid-
ed updates on several important aspects including the hazards of acute pulmonary embolism and pulmonary hypertension, diagnosis technology, and standard thrombolytic and anticoagulant therapy, and clarified a standardized operational procedure for imaging pulmonary hypertension. The course provided an excellent learning and communication platform for physicians.

**Other Initiatives**

- Expert seminars: PVRI China Center held pulmonary vascular expert seminars in Beijing October and November 2012. These meetings discussed on new guidelines on principles and quality control of standardized treatment of pulmonary embolism and pulmonary hypertension.

- Clinical trials: 2013 saw the publication of two important clinical trials with riociguat in the NEJM, for which recruitment in China was a major factor in reaching study conclusion. In addition, several clinical trials of new anticoagulant drugs and goal oriented drugs for pulmonary hypertension have been carried out and completed by the experts from PVRI China Center.

- In April and July 2013, PVRI China Center organized two specific publications in the Chinese Medical Journal (CMI) and Chinese Journal of Practical Internal Medicine. More than 10 multidisciplinary physicians jointly explored and distributed some special points on the clinical practice of evaluation and management of pulmonary embolism and pulmonary hypertension.

- Dr. Michael Madani visited ChaoYang Hospital, Beijing Institute of Respiratory Medicine in May 24th -30th May 2013, to perform surgery for 2 chronic thromboembolic pulmonary hypertension (CTEPH) patients. A whole day symposium on CTEPH and PAH was held in Beijing Hospital. Prof Michael Madani and his assistant gave talks covering the diagnosis, image evaluation, medical and surgical management of CTEPH, intensive care of the patients after surgery, and future prospects for treatment.

**Publications**


PVRI India Taskforce

Taskforce leaders
Prof. Harikrishnan S., India
Prof. Sheila G. Haworth, UK

Initiatives
PVRI India continued its educational and research activities in 2013 as in the previous years. The four research projects supported by GSK and PVRI are progressing as follows:

Project 1 : Title: Genetic insights of idiopathic pulmonary arterial hypertension.
Investigators - Professor Pratibha Nallari (Osmania University) and Dr. BKS Sastry (Care Hospital), Hyderabad
This study was an attempt to profile the genetic and phenotypic basis of this disease in the Indian cohort. PCR SSCP analysis of the Bone morphogenetic protein receptor II (BMPR II), a member of the TGF-β super family, showed a single band pattern variation in exon 3. It has been found that the C123S substitution in exon 3 is associated with right ventricular (RV) dysfunction and severe PAH, though the frequency of the mutation is very low, i.e. 9.25% in comparison with other populations. There was no significant difference in the distribution of VNTR alleles in the IPAH group observed in this study, suggesting that this polymorphism may not play any role in reduced expression and levels of PGI2 in IPAH. The frequency of the VNTR promoter polymorphism is known to be influenced by ethnicity and hence could account for contrasting results obtained in Indian and Caucasian IPAH patients. A novel non-synonymous polymorphism was observed in the study cohort that results in substitution of Arginine with Leucine (R275L) in exon 6 of PGIS. Difference in the presentation of symptoms of angina and pre-syncope were observed in patients based on this polymorphism.

Project II : Title: Does non-regression of pulmonary hypertension following balloon mitral valvotomy correlate with BMPRII mutations?
Dr Harikrishnan S., Mukund A Prabhu, Renuka Nair, Sree Chitra Tirunal Institute for Medical Sciences and Technology, Trivandrum.
The sample collection of 100 subjects, (50 cases and 50 controls) has been completed and DNA separation has been done. Subsequent genetic
analysis was done in few samples in CMC Vel-lore (Salsa M PLA KITS – BMPR II and HHT1 mutations) and the process is being standard-ized. We hope that we will be able to complete the genetic analysis in the coming months.

Project III: Title: Telomeres in adaptation and maladaptation under hypobaric hypoxia
Professor Qadar Pasha, Dr Rahul Kumar and Manjari Rain. CSIR-Institute of Genomics and Integrative Biology, Delhi.

Inside the nucleus of a cell lies the basic unit of life i.e. DNA, moulded into a scaffold called chromosomes. At the ends of these chromosomes are specific stretches of DNA called telomeres. Telomeres are known to protect our genetic data, and make it possible for cells to divide and proliferate. Telomere length is not only related to the basic biology as a trigger of cellular senescence but it seems the same also acts as a mirror of an index of oxidative stress. Considering its significance, it was decided to investigate the telomeres under the harsh environmental conditions of high-altitude (~3500m), especially with respect to adaptation in natives and maladaptation in sojourners, healthy or high-altitude pulmonary edema (HAPE) susceptible.

Relative telomere length was determined using a real-time quantitative PCR by calculating the relative ratio of telomere (T) and single copy gene (S) PCR products and is expressed as T/S ratio. All the p-values were adjusted with age and gender. The findings on the length of telomere were significant. The HAPE patients revealed significantly low T/S at a scale of 1 compared to the healthy controls (P<0.05); whereas the natives had the length near equal to the length of the same controls (P>0.05). We have also measured telomerase activity and plasma level of 8-isoprostaglandin, a marker for oxidative stress. The detailed biostatistical analyses continue.

Project IV: Title: Molecular mechanisms of pulmonary micro-vascular endothelial dysfunction under fluid shear stress
Professor C. C. Kartha, Binil Raj SS Rajiv Gandhi Centre for Biotechnology, Trivandrum.

The study showed that pulmonary microvascular endothelial cell (PMVECs) exposed to disturbed flow results in endothelial dysfunction.

Goal Summary 2014
• The Leh meeting 2013 will be held at Leh, Ladakh in Oct 25-26. A host of national faculty will be participating.
• The third “International Leh Symposium 2014” will be held on September 19-23, 2014 at Leh, Ladakh, J&K, India. The theme of the meeting is “The lung at high altitude: from cellular acclimatization to clinical disease”. The details can be obtained at www.lehsymposium.com.
• Prof. G D Puri is planning to conduct a meeting of PVRI India in mid-March 2013. PVRI India members are actively participating in the National Cardiological society of India meeting and the Pediatric Cardiac Society of India meeting.
Editors-in-Chief
Jason Yuan, USA
Nicholas Morrell, UK
Harikrishnan S., India

Executive Editor
Christina Holt, USA

Initiatives
The most important change to Pulmonary Circulation (PC) in 2013 was the acquisition of a new publisher, the University of Chicago Press (UCP). UCP has been around for more than 120 years and has recently established a Medical Journals division, which we are honored to join. UCP publishes 50 journals per year on average, allowing for specialized and focused attention to each individual journal. The Pulmonary Circulation Editors believe UCP will help to heighten PC’s visibility, increase the efficiency of article publication, and improve the overall quality of the Journal. The Press’ production and editorial teams consist of experienced and professional individuals who are committed to PC’s future success.

The acquisition of the new publisher also brings two new websites to Pulmonary Circulation. The submission website, in particular, is highly efficient and user-friendly and will allow for a smoother and more satisfactory experience for authors submitting to the Journal. The system is efficient, user-friendly, and includes several new functions.

Throughout this year, Pulmonary Circulation published two non-regular series: a six-paper series of articles outlining the newly established Pulmonary Hypertension Academic Research Consortium; and a 10-paper series of articles from the 2012 Thomas L. Petty Aspen Lung Conference.

Progress
To date, Pulmonary Circulation articles have been accessed online over 335,000 times. All 179 published articles have been downloaded as PDFs over 53,000 times. Original research articles continue to be the most commonly article type published in the Journal.

In 2013, Pulmonary Circulation continues to see a proportionate rise in both quantity and quality of submissions to the editorial office.

Promotion
Pulmonary Circulation also continues to heighten promotion of the Journal through various email blasts, including Editors’ Highlights emails, Table of Contents distribution, and Call for Papers announcements. Additionally, Pulmonary Circulation continued to promote the journal at various international conferences, including the American Thoracic Society International Conference 2013, the American Heart Association Scientific Sessions 2013, The Grover Conference, and the 6th Pulmonary Vascular Research Institute Scientific Workshops and Debates.

Most Downloaded Articles Published in 2013:
- Roberto Sessa, Akiko Hata. *Role of microRNAs in lung development and pulmonary diseases*
- Eric D Austin, Tim Lahm, James West, Stevan P Tofovic, Anne Katrine Johansen, Margaret R MacLean, Abdallah Alzoubi, Masahiko Oka. *Signal transduction in the development of pulmonary arterial hypertension*  
  *Gender, sex hormones and pulmonary hypertension*
- Leslie A Hargett, Natalie N Bauer. *On the origin of microparticles: From “platelet dust” to mediators of intercellular...*
communication

- Savas Ozsu, Halit Cinarka
  *Chronic thromboembolic pulmonary hypertension: Medical treatment*

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**Goal Summary 2014**

- Publish online only. By January 2014, Pulmonary Circulation will be published online only. This decision was made in an effort to cut costs and provide a higher quality, more efficiently published journal. A small number of copies of each issue will still be printed and distributed to select institutions and individuals. All issues will have the option for print-on-demand.
- Increase citations made to the Journal. In an effort to ensure an acceptable impact factor for Pulmonary Circulation, one of our main goals is to increase citations made to the journal through promotion and visibility.
- Articles posted online immediately after acceptance. With Pulmonary Circulation’s new publisher, we now have the option to post articles online immediately after acceptance for viewing by the general audience.
- Quicker acceptance to publication date. Our acceptance to publication date goal for 2014 is eight weeks from acceptance of the manuscript to Ahead of Print publication of the final article.

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**PVRI Review**

**Editor in Chief**
Harikrishnan S. 2009-2012
Sachindra Joshi 2012-2013

**Senior Editor**
Ghazwan Butrous 2009-2013

**Executive Editor**
Nikki Krol 2011-2013

The PVRI Review was founded in 2009 as the first journal of the Pulmonary Vascular Research Institute. Originating as an educational journal, it aimed to function as a non-peer reviewed publication in which colleagues could freely express their views and ideas outside of editorial scrutiny. It was concocted in response to requests from PVRI Fellows, at a time when printed unconventional thought was not widely available in the scientific publication community. Progressive perspectives and ideas have since become more widespread with the advent of the internet, and PVRI Review adapted in response to become a repository of PVRI activity.

The PVRI Review was edited by the able hand of Dr. Harikrishnan S., who managed it from the start and ensured its timely publication and quality as Editor in Chief. Its immediate success, and translation into Portuguese and Chinese versions, prompted the PVRI to think seriously about publishing a peer-reviewed journal. In 2011, this thought materialised in the form of Pulmonary Circulation.

Mid-2012, Chief Editor Dr Harikrishnan S. and Senior Editor Ghazwan Butrous concluded that the PVRI Review had achieved its mission. At the end of 2012 and throughout 2013, the PVRI Young Council, mentored by Dr Harikrishnan, slowly took over the reigns of the PVRI Review. Under Young Council member Dr Sachindra Joshi as Editor-in-Chief, PVRI Review Vol 5: Issue 1&2 was published as the journal’s final issue. In the wake of its achievements, the time to establish a new venture had come, and to encourage the forthcoming leaders in the field...
of pulmonary vascular diseases to establish their own publication. As of 2014, the PVRI Chronicle (see below) will be the new non-peer reviewed Journal for the Pulmonary Vascular Research Institute. All of us at PVRI would like to take this opportunity to thank Dr. Harikrishnan S. for leading the PVRI Review initiative with such quality and excellence over the last five years, resulting in a breakthrough journal, multiple translations, a successful transition to Pulmonary Circulation, and now the PVRI Chronicle.

**PVRI Chronicle**

**Editor in Chief**
Sachindra Joshi, USA

**Executive Editor**
Nikki Krol, UK

**Background**
The PVRI Chronicle is the new PVRI Journal, produced entirely by the PVRI Young Council and published by the Pulmonary Vascular Research Institute. The non-peer reviewed bi-annual publication debuted in January 2014, and aims to be a fresh voice within the PVRI. Edited, formatted and published by the Young Council, the journal functions as a unique reflection of the younger generation and beyond-contents focus both on radical new ideas and case studies, and aim for a stronger voice detailing patients’ perspectives, as well as clinician, research and academician points of view. With its new contents, the PVRI Chronicle also has increased its abilities compared to more traditional journals: published online, the PDF can contain active links, whilst plans are in the works to incorporate the journal as an app. The latter will open up the possibilities of embedding videos, slideshows, hyperlinks, and other interactive features which will encourage readers to become more involved with the Journal, the Institute, and its mission. The PVRI Chronicle Editorial Board is also heavily involved in the PVRI Educational website, so frequent cross-references such as a featured lectures, interviews or Atlas images will be found in the journal in link, jpg or mp4 format. Overall, the PVRI Chronicle means to be the brand ambassador of PVRI in upholding the Institute’s mission statement by focusing on the traditional triad of research, education, and clinical care, in activity and report alike. Submissions are encouraged and welcomed.

**Structure**
- **PVRI News & Activities**- A platform that includes an overview of PVRI news, activities, announcements, highlights of the scientific meetings in PVD, and interviews.
- **Journal Club**- A platform for fellows, graduate students, postdocs, junior and senior faculties to send articles 1) commenting on the published articles, books/book chapters in PVD domain, 2) controversial issues criticizing the status quo.
- **Art Club**- A platform that includes 1) cartoons, 2) puzzles, 3) crosswords, 3) selected images from PVD atlas and 4) infographics regarding PVRI Educational Website, PC and other PVD article content.
- **Learners Corner**- A platform for educational activities where fellows, graduate students, postdocs, junior and senior faculties can send 1) a review on PVDs, 2) Did you know articles. A summary on the selected educational lecture as a highlight of the issue will be published with hyperlink.
- **Patients Corner**- A platform where clinical and biomedical scientists can send 1) Case Studies, 2) Patient’s perspectives, 3) Clinician’s perspectives, 4) articles on current advancements in clinical care and basic biomedical research leading to translational goals, 5) articles on management of PVD such as hospital setups, research, availability of drugs, diagnostic tools etc. We encourage articles in this category to be centered on the developing world.

**Goal Summary 2014**
- Online publication Jan and June 2014
- Publish at least one issue in app format for iPad, iPhone, and potentially Android devices
- Include multimedia in publications
- Provide print on demand by Vol 1: issue 2
- Encourage submissions within PVRI
In 2013, PVRI received unrestricted grants and support from the following companies:

- Bayer
- Gilead
- GlaxoSmithKline
- Novartis

All four renewed their Roundtable membership with the PVRI, which holds a number of benefits including free registration to the PVRI annual conference for up to 5 delegates, access to the PVRI Educational website, a monthly newsletter, and free subscription to the PVRI publications. The Institute is grateful to their contributions and support.

Additionally, the PVRI also received the Cardiovascular Medical Research and Education Fund (CMREF) grant this year. Received in July 2013, the $1,000,000.00 USD grant will help fund the Institute for a period of five years.

The above funds have been used for some of the initiatives below, as well as funding travel grants for young investigators, the publications of the PVRI Journal, the modifications and improvements to the PVRI Educational website, and more.

**List of meetings 2013:**

1. Board of Directors and Advisors Meeting in Istanbul, Turkey, January 20th 2013
2. 7th PVRI Annual General Meeting and 6th Scientific Workshops and Debates, Istanbul, Turkey, January 21st -25th 2013
3. SAPH 2013 International (SAPH/PVRI), Istanbul, Turkey, 21-25 January 2013
4. 7th SAPH Master Class- Pediatric, Riyadh, KSA, 11-12 February 2013
5. 5th World Symposium on PH, Nice, France, 27 February – 1 March 2013
6. Pulmonary Hypertension Awareness Day, Qassim, KSA, 6 March 2013
7. SAPH 2013 Regional: PH in the Young, Jeddah, KSA, 24-26 April 2013
8. Pulmonary Hypertension Awareness Day, Abha, KSA, 8 May 2013
10. Board of Directors and Advisors Meeting, Chicago, USA, June 22nd
11. The 6th National Congress on Pulmonary Embolism and Pulmonary Vascular Diseases, Chongqing, China, 19-21 July 2013
12. 4th International Symposium on Pulmonary Circulation Disorders, Chongqing, China, 19-21 July 2013
13. Grover Conference, Colorado, USA, 4-8 September 2013
14. Regional Pulmonary Hypertension Awareness Day, Dubai, UAE, 12 September 2013
15. 8th SAPH Master Class- Adult, Riyadh, KSA, 23-24 September 2013
16. Right Heart Failure Foundation, Boston, USA, 4-5 October 2013
17. International symposium Hypoxic Pulmonary Hypertension, Bishkek, Kyrgyzstan, 7-9 November 2013
18. VIII Congress of Euro-Asian Respiratory Society International Symposium, Bishkek, Kyrgyzstan, 8-9 November 2013
19. Pulmonary Hypertension Awareness Day, Dammam, KSA, 17 December 2013

**List of upcoming meetings 2014:**

1. Annual PVRI Meeting and Workshops in Giessen/Bad Nauheim, January 2014, Germany.
2. The first Latin American meeting on Pulmonary Hypertension in Children. Spanning February 21-22 2014, in Cartagena de Indias,
4. SAPH Executive Annual Meeting, Dubai, UAE, 13 March 2014
5. Gulf Thoracic Annual Conference, Dubai, UAE, 13-15 March 2014
6. 8th SAPH Master Class, Riyadh, KSA, 18-19 March 2014
7. Pulmonary Hypertension Awareness Day, Jeddah, KSA, 17 April 2014
12. 1st Annual Symposium, FDA/PVRI Drug Discovery and Development for Pulmonary Hypertension, Bethesda, USA, 14-15 July 2013.
13. Pulmonary Hypertension in the Gulf, Manama, Bahrain, 11 September 2014.
14. The bi-annual high altitude symposium will take place again in Leh, Ladakh. 14th Sept 2014.
15. Echocardiography and Hemodynamics in PH, Riyadh, KSA, 6 November 2014.

On December 18th 2013, the PVRI consisted of 701 Fellows and members. Of these, 404 paid their annual dues for 2013. In early January 2013, the PVRI implemented the Buddy System which allows members to contribute extra to cover the costs of membership for colleagues.

1. Paying fellows and members will remain part of the PVRI community and are therefore exempt of registration fees for the Annual Conference. They also have access to discussions, forms and various taskforce initiatives worldwide at no extra cost.
2. The membership allows PVRI to send fellows and members the PVRI publications in a printed format free of charge. This includes the PVRI Chronicle (twice yearly) and the renowned peer-reviewed journal Pulmonary Circulation (four times yearly).
3. Fellows and members will receive a monthly newsletter via email, which includes updates on PVRI activity and the PVD community in general.
4. Fellows and members have unrestricted access to the benefits of the wealth of educational materials in the PVRI main and educational website. Most of these advantages are only available to registered fellows as of the second quarter of 2012, and include:
   • recent PVD bibliography
   • PVD atlas
   • online lectures
   • abstract presentations
   • e-books
   • interview
   • conferences presentations and slides
   • commentaries -and much more
5. Fellows and members will be able to participate actively in various initiatives and activities of the taskforces, for example clinical trial initiatives.
6. Fellows and members may benefit from various travelling, research and educational grants provided by the PVRI.

PVRI has maintained a tolerant attitude to dues payments as a significant percentage of the membership resides in the developing world. However, in 2012 membership payment was made mandatory in order to ensure the financial health of the Institute.

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A visit to Prof. Schermuly’s Lab

Gerald J. Maarman FPVRI visits Prof. Schermuly’s lab in Germany

Gerald J. Maarman¹

¹Department of Medicine, Hatter Institute for Cardiovascular Research in Africa (HICRA), Cape Town, South Africa

DATE: 1st of August till the 31st of August 2013
LABORATORY VISITED: Excellence Cluster CardioPulmonary System (ECCPS) in Giessen, Germany
DIRECTOR: Prof. Ralph Schermuly, FPVRI

OVERVIEW OF VISIT, GENERAL CONTRIBUTION AND TECHNIQUES LEARNT

My PhD project investigates the cardioprotective effects of a natural product called melatonin in rat model of monocrotaline induced pulmonary arterial hypertension (PAH). This model develops PAH as an underlying cause which leads to cardiac hypertrophy. My PhD assesses the effects of melatonin on cardiac hypertrophy, but as melatonin may reverse/improve the underlying PAH it will also reverse the cardiac hypertrophy, leaving no opportunity for me to study the molecular processes of this hypertrophic process. For this reason, I will need to test melatonin in a model that does in fact develop cardiac hypertrophy without PAH. Such a model is the rat model of pulmonary artery banding during which these animals develop pressure overload induced cardiac hypertrophy, or more specifically, right ventricular hypertrophy. Unfortunately this model is not available in South Africa (SA) but has already been established at the ECCPS in Germany by our colleagues. They kindly gave me the opportunity to investigate this model at their laboratory. During my time in Germany, I learned how to perform the surgical procedure to induce right ventricular hypertrophy in rats. I also studied how to perform specialized histological staining to assess pulmonary muscularisation, medial thickening and cardiomyocyte size. Furthermore, I learned how to perform right heart catheterisation for the measurement of cardiac hemodynamic parameters. I accomplished the latter with Millar catheter or custom made fluid filled catheter. None of the above techniques were available at the Hatter Institute in South Africa, so upon my return I started the process to establish them there. All of us at the Hatter Institute in South Africa are very pleased that Prof. Ralph Schermuly and his group are willing to start an official collaboration in 2014. Prof. Schermuly has suggested a visit to our laboratory in South Africa, together with two of his postdoctoral fellows. They will then further assist me in finetuning the techniques I established here and help bring it up to standard. Prof. Schermuly suggested that we could also collect some heart and lung samples in South Africa and ship them to Germany which will allow him and his team of experts to do various analyses. Another possible arm of this collaborative effort would be to investigate a population of patients in Cape Town diagnosed with pulmonary hypertension due to various underlying pathologies. We are very excited to start this collaboration in early 2014. I would like to thank the PVRI for their contribution, as without their support, none of the exciting developments would have been possible.

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Gerald Maarman, image courtesy of Stellenbosch University website
Pulmonary vascular remodeling plays a critical role in many cardio-pulmonary disorders such as pulmonary hypertension (PH) and chronic obstructive pulmonary disease (COPD) (often accompanied by PH). The process of remodeling and the associated pathobiology can be quite manifold and even different in the respective diseases. The origin of the narrowing of the respective vessels is still a controversial topic. The present interactive discussion describes briefly the current understanding of the vascular remodeling process in COPD-PH and shows that the origin of remodeling in COPD is not limited to the intima, as often described in the literature. The involvement of the media does not seem to be a rare event in COPD, at least in end-stage. This controversial discussion should animate experts in the field to comment this topic, either by agreeing or disagreeing with our conclusions/hypotheses. The readers are invited to present arguments either pro or contra regarding intima and/or media involvement in vascular remodeling occurring in COPD.

COPD is a collective term for chronic bronchitis and pulmonary emphysema and characterized by progressive, poorly reversible airflow limitation associated with an abnormal chronic inflammatory response in the lung. Exposure to biomass smoke, especially during cooking, is most relevant trigger for the development of COPD in developing countries, whereas in industrialized countries, tobacco smoke (80-90%) and air pollution are the most relevant causes. COPD is not only limited to the lung, but also viewed as a systemic disease which includes skeletal muscle wasting, diaphragmatic dysfunction, and systemic inflammation. There is increasing evidence suggesting involvement of pulmonary vascular pathology for COPD development. Cigarette smoke may directly affect the pulmonary vasculature leading to vascular remodeling, pulmonary hypertension and finally to cor pulmonale. PH developing in COPD condition is classified in the group 3, according to the current clinical classification of PH from Dana Point in 2008. The mean pulmonary artery pressure (mPAP) in PH related to COPD usually ranges between 25 and 35 mmHg with nearly normal cardiac output. However, in patients with advanced COPD, mPAPs higher than 40 mmHg are quite common, especially after at least one previous incident of acute respiratory failure. Furthermore, the presence of PH increases mortality. Importantly, PH is relevant for prognosis in COPD. The role of PH for the pathobiology of COPD is still not fully resolved. PH can be common complication in advanced COPD and can be a consequence of the hypoxia occurring after severe destruction of gas exchange surface. However, several publications during the last decade showed that pulmonary vascular alterations can even precede alveolar destruction indicating that cor pulmonale and late-stage PH are not necessarily secondary to hypoxia in patients with COPD. One characteristic feature of pulmonary vascular remodeling is the thickening of the arterial wall by which the vascular lumen and the internal diameter are reduced, ultimately...
leading to increased pulmonary vascular resistance. In hypoxia-induced PH, the thickening of the vessel is a complex process that finally culminates in uncontrolled proliferation of pulmonary artery smooth muscle cells (PASMCs) causing the hypertrophy of the media layer. In particular, hypoxia is often seen as a driving force leading to these vascular media alterations, in which hypoxia inducible factor (HIF)-1α seems to be a major driver. This transcription factor controls a variety of hypoxia-dependent genes which are involved in the pulmonary vascular remodeling process, such as erythropoietin, glucose transporters, vascular endothelial growth factor (VEGF), endothelin-1 and nitric oxide (NO) synthases, and inflammation. In contrast to hypoxia-induced PH, remodeling in COPD is mostly explained by hyperplasia of the intima instead of the media. But, nevertheless, the other vessel wall layers, the media and the adventitia, are also involved. Interestingly, although apparent in vessels of different sizes, small muscular arteries and arterioles are predominantly affected in COPD, PH could not only be seen in patients with mild and severe COPD, but also in heavy smokers with normal lung function demonstrating occurrence of PH at different degrees of disease severity. In part speculatively, the thickening of the intima may be explained by several possible events: 1) proliferation and hypertrophy of existing smooth muscle cells (SMCs), 2) attraction and differentiation of precursor or bone marrow-derived progenitor cells to SMCs, 3) dedifferentiation and migration of SMCs from the media to the intima and/or 4) epithelial-mesenchymal transition (EMT), whereby endothelial cells transdifferentiate into SMCs. The identification of differentiated and non-differentiated SMCs can be seen by the existence of vimentin and desmin. Interestingly, some SMCs in the intima of smokers and patients with mild COPD express vimentin, but not desmin filaments. SMCs positive for vimentin, but not for desmin represent a subpopulation of less differentiated SMCs that may take part in an ongoing process of vascular remodeling. The origin of these SMCs is still not fully resolved and has to be deciphered in future. Potentially, bone marrow-derived progenitor vascular cells might be an explanation. However, such an involvement might have two effects, which could compete: 1) differentiation into endothelial cells contributing to vascular repair or 2) differentiation into SMCs contributing to vessel remodeling. As mentioned above, the remodeling process observed after chronic hypoxia or cigarette smoke exposure seems to be different. For instance, PH induced by chronic hypoxia at high altitudes is primarily associated with medial

![Figure 1. Pulmonary vascular remodeling in COPD patients. Lung tissues from healthy donors and COPD patients were stained with: 1: α-smooth muscle actin and von Willebrand factor antibodies; 2: only α-smooth muscle actin antibody; 3: only von Willebrand factor antibody; 4: Elastica van Gieson, and 5: HE (hematoxylin-eosin). Representative photomicrographs of remodeled pulmonary vessels (left – media hypertrophy and right – complex neo-intima-like lesion) in COPD patients, compared with healthy vessels in donors are shown.](image)
hypertrophy and is completely reversible a few weeks after return to sea level.7 Also a recent study in mice found a differential gene regulation comparing smoke-induced PH and hypoxia-induced PH, although a similar vascular phenotype was observed.13 In contrast to hypoxia-induced PH, PH associated with COPD can involve all vessel layers. Such differences may explain why PH in COPD can often not be reversed, even not by supplemental oxygen, neither acutely nor chronically.32 It is essential to differentiate between pulmonary vascular remodeling during the development of COPD, when airway obstruction and parenchyma destruction has not occurred yet, and established COPD, when patients suffer from hypoxia as a result of airway obstruction, a loss of alveoli and vessels. According to the pioneer work from J. A. Barberà’s group and subsequent studies, there is no doubt that vascular remodeling already occurs in smokers (in human beings and animals) who do not suffer from COPD/emphysema yet.4, 30 It could be nicely demonstrated that human smokers without changes in lung function showed remodeled vessels with predominant intima thickening whereas the media layer did not seem to be involved.30 Along these lines, the literature suggests alterations in the intima layer as the major pulmonary vascular pathological feature in COPD-PH, without significant change in media.4, 22, 25, 33 In contrast Wick et al. demonstrated that pulmonary vascular remodeling in COPD patients was associated with variable intimal and importantly, prominent medial/adventitial thickening.34 Furthermore, a systematic characterization of pulmonary vascular remodeling in COPD revealed a significant increase of media wall thickness of the small vessels in COPD patients compared with donors.35 Interestingly, uncontrolled proliferation of PASMCs represents indeed a major contributor to medial hypertrophy, and it was shown previously that cigarette smoke extract may stimulate the proliferation of these cells.36, 37 As depicted in the Figure 1, the pulmonary vessels of end-stage COPD patients can strongly be remodeled with a clear thickening of the media, additionally to severe intimal remodeling. This raises the question if this media involvement only occurs as a result of hypoxia/hypoxemia after destruction of gas exchange surface and airway obstruction or if this can also take place in an early stage during the development of COPD. Because of the lack of respective extensive studies, it still stays speculative. Interestingly, our group demonstrated recently, that the vascular alterations and the development of PH preceded the emphysema development in mice.13 This is in line with the observations seen in humans and guinea pigs, where vascular remodeling was present after smoke exposure with a lack of emphysema.12, 30 In addition, we could show that the origin of the PH and emphysema development was independent of hypoxia/hypoxemia.13 This suggests a mechanism for triggering vascular remodeling which does not need the hypoxic stimulus.

SUMMARY AND THE QUESTION FOR INTERACTIVE DISCUSSION

Based on the existing controversies regarding the involvement of the media layer in pulmonary vascular remodeling associated with COPD, we would like to postulate the question: Is pulmonary vascular remodeling in COPD just a matter of intima alteration? We invite all experts and persons/scientists interested in this field to reply and express their valuable views on this important scientific and clinical issue, in the next volume of PVRI Chronicle.

ACKNOWLEDGEMENTS

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REFERENCES

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The complexity of pulmonary hypertensive vascular disease in two year old infant with bronchopulmonary dysplasia

REFERENCE:
Pulmonary hypertension (PH) is a grave disease that causes major disability and early mortality. Although it is a rare disease, it affects a large number of populations all around the world. Nepal is a developing country and the patients of pulmonary hypertension are typically brought to a physician's attention during the latter stages of the disease, as they will have likely been previously underdiagnosed. This is further complicated by the fact that there are no proper studies on its prevalence. In comparison to other developing countries, Nepal has high prevalence rates of rheumatic heart disease, chronic obstructive pulmonary disease, smoking and indoor pollution, and therefore a high prevalence of pulmonary hypertension can be expected. Further complexities include late presentation of the disease and low availability of health personnel who can diagnose and manage the condition. While some studies on genetic factors and high altitude pulmonary hypertension have been done in Nepal, much attention should be allocated on epidemiological studies. In this context, the article gives a nutshell view of the challenges of diagnosing pulmonary vascular disease in Nepal.

PATHOGENESIS
Pulmonary hypertension starts with sustained aberrant vasoconstriction and progresses with intimal proliferation, medial hypertrophy and later remodeling of pulmonary arteries leading to an irreversible phase of the disease. Eventual right heart failure with progression of pulmonary hypertension makes this disease a killer among chronic pulmonary diseases. A typical case presentation: A 77 years old male walked in emergency room at Helping Hands Community Hospital on 20/12/2011. Although his friendly smile revealed how happy he was to reach a hospital in the capital, his efforts to breathe signaled the gravity of illness and immediate need for medical attention. After quick vitals and finger tip saturation probe assay, we started him on 100 percentage Oxygen at 2 liters per minute, gave him nebulisation and a shot of hydrocortisone. This patient, a resident of Khadbari, Sankhuwasabha of rural Nepal, is one of the many chronic obstructive pulmonary disease (COPD) patients we see in our hospitals every day. A general hospital in Nepal sees a lot of COPD patients, mostly associated with corpulmonale, on a daily basis. A case like this either gets missed or falls in hands of a traditional religious healer. Many such cases present with chest infection that only exacerbates this disease and leads to untimely death. This particu-
lar person is one among many such late presenters, who gets stuck at home for days before gathering help to reach the nearest medical center, often many miles away, and is then faced with a long uncomfortable ride on the back of a horse to a healthpost where a paramedic suggests the urgency of specialized care. In this case we must give thanks to the paramedic, who gave him a pocketful of diuretics and bronchodilators to ease his final journey to our hospital. On the second day in bi-level positive airway pressure, a joyful face welcomed us. However, naive and illiterate, many of the patients we see become addicted to cigarette smoking during early childhood and continue smoking till the late phase of COPD, with associated complications, and our patient was no exception. His bedside echocardiogram showed pulmonary hypertension secondary to COPD, right ventricular hypertrophy, dilated right atrium, and tricuspid valve regurgitation. The chronic progression of the diseases diagnosed, and the absence of permanent cure, only left him and his family demoralized, as they had tried so hard and travelled so far to get him here. The expenses in the capital Kathmandu only increased his suffocation. Even if he quit smoking, there is a considerable probability that his COPD will increase over next few years because of the indoor pollution from firewood.

Epidemiology
In Nepal, like in any other country in the world, pulmonary hypertension is expected to be distributed across all the age groups. So far the epidemiological studies in pulmonary hypertension are not done in Nepal. Higher incidence compared to other developing countries can be presumed, especially owing to indoor air pollution, a high smoking rate in rural areas, undiagnosed and untreated congenital heart diseases, a high rate of rheumatic heart diseases, rising HIV infection and high incidence and prevalence of pulmonary tuberculosis. Most households in the rural areas of Nepal have indoor pollution due to passive smoking because of traditional firewood kitchen, thereby contributing to development of COPD and associated complications. Women are exposed more to the indoor pollution than males, since in Nepal, most of the household chores are considered the responsibilities of women. Therefore, it can be presumed that most of the pulmonary hypertension arises secondary to chronic obstructive pulmonary disease.

In concordance with rest of the world, in children and adolescents the most common cause of the pulmonary hypertension in Nepal is presumed to be congenital heart disease. Most of these congenital heart diseases causing pulmonary hypertension are diagnosed late because of inadequate accessibility and availability of the medical expertise needed. In adults, besides COPD, pulmonary hypertension can be a consequence of rheumatic heart disease, pulmonary tuberculosis and HIV infection, owing to the high incidence of these diseases. However, schistosomiasis, a major disease of some of the developing countries responsible for PH, is not reported in Nepal.

The data in some studies suggest that Sherpa are genetically protected for PH, but Sherpa represent only a tiny fraction of Nepalese population. In summary, pulmonary hypertension in Nepal is not properly studied and the cases and its fatalities are potentially rising each year.

Discussion
The relative unavailability of Doppler echocardiogram for screening pulmonary hypertension is one of the major challenges in the diagnosis of PH in Nepal. Very few centers in the capital offer catheterization services. Additionally, as suggested in the presented case, the relative lack of expertise to assess pulmonary pressure, unavailability of manpower and equipments in rural areas, low health education about pulmonary hypertension and poor screening of congenital heart diseases make the diagnosis of pulmonary hypertension a challenge in Nepal. Therefore, only the tip of the iceberg of pulmonary hypertension cases reach tertiary centers, and those cases often come at a late stage with associated with right ventricular failure. Furthermore, most of the early manageable cases of PH are also underdiagnosed.

In Nepal, most of the patients approach traditional healers. The absence of government scrutiny regarding traditional practitioners has resulted in unsystematic and unrecorded numbers of such patients. Lack of proper referral by such healers has hidden a lot of
pulmonary hypertension at early stages, which will eventually be fatal. Moreover, most of the traditional healers refuse to tell the ingredients of their medicines, and almost always declare their products as "adverse affects free", which attracts more patients still. Some of these traditional herb medicines and cough syrups might ease the patients for a short time, but no proper studies have been conducted to prove their efficacy.

The current approved treatment options known to improve survival rate of the disease is not readily available in Nepal. Tertiary centers provide limited medical management to the disease, and they include calcium channel blockers and phosphodiesterase type 5 inhibitors, the latter afforded only by a high socioeconomic class. As a result, excepting a few centers in the capital, the treatment of congenital and rheumatic heart diseases with interventions that would prevent progression of pulmonary hypertension associated with these diseases is simply not possible. Therefore, even with proper diagnosis, PH treatment in tertiary centers is commonly restricted to diuretics, general supportive measures like bed rest, calcium channel blockers and low doses of aspirin with supplemental oxygen therapy. As a result of this variety of factors, pulmonary hypertension poses a great burden for the patient and their family. Although families in a high socioeconomic class can afford the treatment in the tertiary centers, an average family with PH will suffer economically, especially if the bread earner is stricken with the disease. Patients suffer clinical and hemodynamic deterioration sooner than expected due to poor compliance to the medicines, complex treatment protocol and relative inaccessibility of the tertiary health service providers. Congenital heart diseases leading to pulmonary hypertension later in life are hard to screen, especially against the background of a conservative, male predominant, shy Nepalese society. Low literacy rates hinder the proper medical education regarding harmful effects of indoor air pollution and passive and active smoking, meaning that the necessary change of attitudes and practices that prevent non communicable diseases like COPD and PH is extremely slow. Although the government has banned cigarette advertisements in public and has made some efforts to raise awareness of the preventable diseases, recent political turmoil and allegations in the health sector have only augmented the distrust towards the policy makers, further complicating the implementation of plans and policies each year.

**Conclusion**

Although there is considerable progress in diagnosis and management of pulmonary hypertension in developed countries, Nepalese medical practitioners face great challenges regarding diagnosis and proper management of pulmonary hypertension in the country. Early diagnosis and treatment of the pulmonary hypertension is advocated with use of echocardiogram, which serves as a fairly sensitive and specific method for the diagnosis of PH, although a gold standard test requires an organized hospital and catheterization lab set up. Follow up echocardiogram studies in rheumatic heart diseases, pulmonary tuberculosis, HIV/AIDS and connective tissue diseases should be advocated to timely diagnose pulmonary hypertension, educating the patient at the same time. Finally, the availability as well as accessibility of the drugs needed to treat pulmonary hypertension should be increased in Nepal, and the government should implement policies for substantial price reduction in such medicines to improve quality of life of the pulmonary hypertension affected patient.

**Suggestions and Future Directions:**

Needless to say, a substantial proportion of PH results from preventable causes (e.g. COPD) or manageable causes (e.g. rheumatic valvular diseases, connective tissue diseases). However, guidelines are not yet envisioned to address the majority of these cases and therefore, addressing pulmonary hypertension in Nepal is neither easy nor instant. Considering this, a multidimensional approach to the disease from all sectors is needed to early diagnose, treat, and prevent pulmonary hypertension in Nepal.

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DID YOU KNOW... 

... THAT THE PATHO BIOLOGY OF PULMONARY ARTERIAL HYPERTENSION (PAH) HAS NEOPLASTIC FEATURES?

Pulmonary arterial hypertension (PAH) is a disease of the small pulmonary arteries, characterized by vascular narrowing leading to progressive elevations in artery pressures and, ultimately, right heart failure. In 1891, Von Romberg discovered pulmonary vascular lesions, which he named “pulmonary vascular sclerosis”. In PAH, vascular lesions involve a distinct constellation of lesions known clinically, as “plexogenic pulmonary arteriopathy”.

One of them, the plexiform lesion (Figure 1), is considered the histological hallmark of this arteriopathy. However, the etiology of vascular lesion remains controversial. Although vascular lesions involve three components: smooth muscle layer, adventitia and the endothelium, much of the research performed over years focused on the smooth muscle component. This was due to studies with rats exposed to chronic hypoxia or treated with monocrotaline that suggested pulmonary vasoconstriction as the cause of vascular remodeling. Although investigations into this vasoconstrictive theory of PAH have yielded a number of drugs currently used to treat the disease, it has now been shown that less than 10% of PAH patients respond to vasodilators. Thus, the development of new theories has become necessary.

In 1994, Tuder, using immunohistochemistry, described augmented endothelial cell proliferation leading to complicated capillary-like channels (angio-proliferation), as the main component of the plexiform lesion. In 1998, the discovery of endothelial monoclonality in...
plexiform lesions of primary pulmonary hypertension⁴, led Voelkel and collaborators to formulate that year, the neoplastic hypothesis of the disease.⁵ Neoplasia is understood to be an abnormal proliferation of cells that results in tumor formation without metastasis. Two important events occur during tumor formation; uncontrolled angio-proliferation and inhibition of apoptosis.⁵⁷ In the last 15 years of research, several mutations have been linked to both events in endothelial cells from plexiform lesions. For instance, alterations in transforming growth factor-β (TGF-β) receptor II may turn endothelial cell insensitive to the cell growth-controlling effects of TGF-β⁵. Interestingly, mutations in bone morphogenetic protein receptor II (BMPRII), a member of the TGF-β receptor family, are responsible for the familial forms of PAH. Moreover, expression of anti-apoptotic protein survivin which inhibits activation of caspases 3 and 7 has been reported in PAH plexiform lesions.⁴ Consistent with these findings, endothelial cells isolated from pulmonary arteries of patients with PAH are hyperproliferative and apoptosis-resistant.⁵

In addition to mutations effecting apoptosis resistance, tumor cells suppress mitochondrial function which also prevents apoptosis and gives them a proliferative advantage.⁷ As a consequence, a shift from oxidative phosphorylation to aerobic glycolysis occurs, which is known as the Warburg effect.⁸ The Warburg effect, originally described in tumor cells, is characterized by decreased oxygen consumption and increased glucose uptake.⁹ Recently, this phenomenon has been described in pulmonary artery endothelial cells from patients with PAH.⁹ Clinically, the most striking evidence supporting the neoplastic hypothesis and the involvement of the Warburg effect is a study using positron emission tomography scan in PAH patients.¹⁰ This technique is utilized to detect tumors, based on the faculty of tumor cells to actively consume glucose at high rates. Higher fluoro-deoxy-D-glucose (labeled glucose analog) uptake was found in PAH lungs compared with healthy controls indicative of the Warburg effect.

Current therapies used in the treatment of PAH have limited effectiveness and do not prevent mortality. Most of these therapies are targeted against the vasoconstriction component of PAH. Furthermore, diagnosis of the disease requires invasive techniques. Exploration into the neoplastic theory of PAH opens the door to develop new diagnostic techniques and targeted therapies against the vascular remodeling component.

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DID YOU KNOW...

...That tapeworms, which typically reside in canines, could cause lung disease?

The tapeworms, Echinococcus granulosus and E. multilocularis both induce pulmonary hydatid disease in humans when their eggs are accidentally ingested. Once ingested, digestive enzymes disrupt the eggs, allowing embryos to hatch out, penetrate the bowels, and enter the circulatory or lymphatic systems. These embryos migrate to various organs including the lungs, where they form cysts. Pulmonary cysts, which can measure more than 10 cm in diameter, accommodate the larval cestode and progeny that form daughter cysts (Figure 1). Cysts also contain odorless, colorless, sterile fluid with antigenic elements. Over time or if the cyst ruptures, fluid can leak into the bronchi causing suffocation or anaphylactic shock; protoscolices, which can form new cysts, are also released perpetuating the disease state. Although the risk of infection is low in developed countries, hydatid disease is considered an occupational hazard as those most affected are people who work closely with sheep and herding dogs as well as populations in high endemic areas such as southern South America, the Middle East, Australia, and parts of China. In 1950, the debate was settled when it was discovered that E. granulosus and E.multilocularis both induce hydatid disease. Clinical research was advancing at the same time with Barrett’s (1949) development of an operational technique, which enabled physicians to successfully remove an intact pulmonary cyst preventing cyst rupture and re-infection.

Our current understanding of parasitic tapeworms and how they form pulmonary cysts has allowed for better treatment of patients. Pulmonary hydatid disease can go unnoticed for more than 15 years; patients that eventually become symptomatic complain of coughing, shortness of breath, and chest pains. Diagnosis requires imaging, the most common being chest radiographs (Figure 2), and surgery, which is typically followed by chemotherapy, is needed to remove.

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the cyst and prevent re-infection.\textsuperscript{1,2,5,6}
Preventive measures such as improved water sanitation and hygiene, as well as de-worming livestock and dogs, has helped decrease the incidence of pulmonary hydatid disease in endemic areas. So, although common companion animals in certain working conditions can cause the uncommon pulmonary hydatid disease, there are measures available to prevent and treat this disease.

\textbf{References}


Further learning on the subject of hydatid diseases is available on the PVRI Educational Website, in the form of an online lecture entitled ‘Hydatid Disease in Pulmonary Hypertension’ by Dr Bedrettin Yidezeli, FPVRI: http://pvri.info/content/hydatid-disease-pulmonary-hypertension

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...that rapid ascent to high altitude causes pulmonary edema in susceptible individuals?

In 1913, Thomas Ravenhill provided the first clinical description of high-altitude pulmonary edema (HAPE) in his landmark paper Some experiences of mountain sickness in the Andes. While serving as a medical officer in the mines of northern Chile at altitudes of 4,690–4,940 meters, Ravenhill's case reports described the patients as “slack and disinclined for exertion” shortly after arrival at high altitude from sea level, which progressed to cyanosis, acute dyspnea, air hunger and vomiting. He accurately describes “reduplication of the secondary heart sound,” now known as a diagnostic indicator of pulmonary hypertension associated with alveolar hypoxia. When the patients returned to sea level, their condition rapidly resolved.

In the 1930s and ’40s, several reports of HAPE emerged in the Spanish literature from studies in the Peruvian Andes not far from where Ravenhill had worked. HAPE would not be reported in the English literature again until 1960 when Charles Houston, an internist in Aspen, Colorado, reported a case of HAPE in the New England Journal of Medicine. Houston’s most peculiar finding was that the patient’s X-rays originally showed patchy infiltrates throughout the lung fields; however, two days later, the edema had resolved (Figure 1). He excluded pneumonia or cardiovascular disease as the cause of the edema and suggested a sum of three stresses brought on the condition: altitude, cold and heavy exertion. Houston confirmed Ravenhill’s finding that descent promoted dramatic recovery. In the early 1960s, Fred and Hultgren independently performed hemodynamic studies on patients with acute high altitude pulmonary edema. These studies revealed that pulmonary hypertension, which responded to oxygen therapy, was associated with the patchy edema. This non-cardiogenic pulmonary hypertension was initially thought to be due to constriction of the pulmonary veins, but subsequent studies clearly demonstrated the vasoconstriction primarily occurs in pulmonary precapillary vessels in response to low oxygen tensions. Hultgren and Grover proposed HAPE is due to non-uniform precapillary vasoconstriction, which redirects blood to unobstructed vessels. This regional over-perfusion induces high pressures within unobstructed portions of the pulmonary capillary bed, which in turn initiates a patchy hydrostatic edema.

Not everyone who rapidly ascends to high altitude is affected by HAPE. Susceptibility to HAPE is linked to exaggerated hypoxia-induced vasoconstriction of the pulmonary circulation. Decreased bioavailability of vasodilators, such as nitric oxide, as well as an increase in vasoconstrictors, such as sympathetic activity and endothelin-1 release, contribute to the exaggerated hypoxic vasoconstriction. Certain risk factors increase an individual’s susceptibil-
ity to HAPE, such as rapid ascent to an altitude greater than 2,500 meters, cold temperature, strenuous exercise, gender, age, recent or concurrent unrecognized underlying illness, congenital unilateral loss of pulmonary artery, and re-entry to altitude by high-altitude residents following a sojourn at a lower altitude. HAPE can be fatal if left untreated, but may be prevented by slow ascent. Rapid descent is the most important treatment method, while supplemental oxygen and vasodilators, such as nifedipine, may be used for immediate improvement to facilitate descent. Importantly, studies on HAPE have not only provided greater understanding of the disease itself, but have also provided insight into other pulmonary diseases associated with the lung’s response to low oxygen tensions.

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A case of a patient with pulmonary hypertension associated with multiple endocrine dysfunctions and connective tissue disorder

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Abstract
Pulmonary hypertension in association with connective tissue disorders, thyroid dysfunctions and hyperestrogenism has been reported. However, the presence of pulmonary hypertension in multiple endocrine dysfunctions (i.e. pituitary adenoma, endometriosis and ovarian cysts, thyroid dysfunction) with connective tissue disorder has rarely been described. This is a case of the coexistence of pulmonary hypertension in a patient with functional pituitary adenoma, thyroid cysts and goiter with endometriosis and connective tissue disease with a diagnostic difficulty faced in presence of long standing bronchial asthma. The case illustrates the association of pulmonary hypertension in the setting of endocrine dysfunctions and connective tissue disease, and the effect on its course.

The case
This is a case report of 42 year old Hispanic female (Figure 1), who with gradually increasing shortness of breath approached our research team asking for medical help at the Pulmonary Hypertension Association conference in Florida, 2012. Our team’s first impression of this case was a bronchial asthmatic patient who suddenly got dyspneic. Upon further question-
rash on her malar area. She had occasional bones and joint pains too in the past and was investigated for joint disease. She was found rheumatoid factor positive in her 27th year, but no attention was given to her connective tissue disease until her 29th year when her tests for Systemic Lupus Erythematosus (SLE) came out positive. That is when proper treatment of the SLE and joint pain was started. She explains, “My SLE was discovered in 2004. The usual treatment for my SLE was Prednisone tablets and the dosage ranged from 5mg to 80mg or 125mg a day, depending on, whether I have a flare up or not. I used Prednisone 200mg tablets two times a day and the chemo Methotrexate Injections subcutaneous weekly. I also had Rituximab 1,000mg infusions every two to three months for almost 3 years. I stopped the Rituximab infusion treatments and the Methotrexate weekly injections and the Prednisone due to recurrent skin and blood bacterial infections. I did not start them again until my recurrent infections were stable. If I had a flare up, I use the Prednisone treatment.” (Figure 3)

With no remission in the past and after ten years of SLE treatment, she developed progressive worsening of shortness of breath which she had since her childhood. Her chest X-ray showed normal findings. With high suspicion of pulmonary hypertension associated with SLE, an echocardiogram was performed to analyze the condition of her heart. Based on its findings, she was diagnosed with pulmonary hypertension for the first time. When she was 37, anticardiolipin antibodies were sent which came out positive. At 40 years of age, she was diagnosed with having multinodular goiter on basis of her ultra-sonogram of thyroid and thyroid function tests (Figure 4).

In her own words, she says “My PAH was discovered on an echocardiogram on November of 2009, but I started my treatment on January 2010 with the Bosentan 62.5mg, then the dosage changed to 125mg two times a day. On February of 2010, I started the Sildenafil 20mg tablets three times a day. I also used a diuretic Hydrochlorothiazide 50mg daily to manage...”
fluid retention.” The diagnosis of pulmonary hypertension was confirmed by right heart catheterization, with pressure of more than 50mmHg. The bronchoscopy and pulmonary biopsy showed an enlarged carina and inflammation, and her right heart catheterization showed elevated baseline pressure. Pulmonary function tests with measurement of forced vital capacity (FVC) and diffusion capacity of CO (DLCO) were also performed, and showed a ratio of more than 1.6, favoring her dyspnea because of the pulmonary hypertension to the restrictive pathology of her lungs, due to the connective tissue disorder (Figure 5).

“Past medical conditions before my diagnosis of SLE …,” she exhales deep and tells that she had too many surgeries and biopsies since adolescence, including those for ovarian cysts and endometriosis. Except for the maxillofacial surgery for torus mandibularis on both jaws and cordialis surgery when she was 12 years old, tonsillectomy for bilateral recurrent tonsils infection at 6 years old, and admission for supracondylar fracture of the right, her school health was unremarkable and she believed herself to be in a good health. However, when she was 14 year old, she underwent abdominal laparoscopy to remove ovarian cysts, which was unsuccessful for technical reasons (Figure 6). At the age of 22, she was operated for pilonidal cyst and this cyst changed into chronic draining sinus for 6 months. One year later she underwent another surgery for spinal cyst and draining pilonidal sinus. She was also diagnosed with colon polyps and colon hyperplasia by a gastroenterologist at the age of 21, which were successfully removed. When she was 24,
she was diagnosed with endometriosis, and ovarian cyst in the same setting. She had rectal bleeding which was treated with superficial mucosal laser erosion at 29. She developed irregular menstrual bleedings, and underwent dilatation and curettage. The biopsy reports showed dissociation of stromal and glandular elements.

**Discussion**

With the rising incidence of PAH patients and associated debilitation, it is necessary to consider every possible past clinical pathology as a possible trigger for PAH. In every case of dyspnea in connective tissue disease, the probability of pulmonary hypertension should be actively sought as in this case, where proper management could be done in a timely manner. Furthermore, it is absolutely necessary to manage both SLE and bronchial asthma side by side since SLE flares pulmonary hypertension and bronchial asthma would not only hide the progress of pulmonary hypertension, but also make symptoms of the heart failure worse. This case also points to the positivity of rheumatoid factor and anticardiolipin antibodies which served as a guide to investigate pulmonary hypertension associated with SLE, though further studies need to be done on their sensitivity and specificity and thereby relevance of their prognostic use in future. The dyspnea becomes favorable with predominance of pulmonary hypertension, if the ratio of FVC/DLCO is more than 1.6, than with the restrictive pathology because of the connective disease, owing to the fact that the fall in DLCO will be much higher than FVC.

In this case, even in a midst of diagnostic difficulty with symptoms of bronchial asthma, a diagnosis was made. After making a relatively early diagnosis, the case was treated with Bosentan, Sildenafil and Thiazides and her symptoms have decreased to NYHA grade 2 dyspnea. Her pulmonary arterial pressure has decreased from 55mmHg to 36mmHg. Another option available for the management of a case like this is IV prostacyclin, although if prescribed, its potential complications like infection of the central venous site should be properly explained to the patient. In addition, the patient’s ability to store the drug properly in refrigerator and its preparation on a daily basis should be considered. In a case like this, where the symptoms of bronchial asthma hid the early manifestations of pulmonary hypertension, constant vigilance is essential, with proper screening modalities like echocardiogram and six minute walk test. Pulmonary hypertension has been linked with autoimmune thyroid diseases and hyperthyroidism. Nevertheless, as in this case, we might encounter pulmonary hypertension with hypothyroidism. Thus thyroid function tests should be sought, especially if the patient is over sixty years old.

This case may illustrate the issue of the association of pulmonary hypertension with multiple endocrine dysfunctions, which also should not be overlooked. The association of pulmonary hypertension with abnormalities in metabolism of insulin, adipokines, estrogen and lipids have already been suggested by research. For our patient, the presence of pulmonary hypertension with multiple endocrine dysfunctions is highlighted. The association of high incidence of pulmonary hypertension in females had been previously attributed to the presence of estrogen, especially if it is in high levels with early and long term exposure. The rare associations of pituitary adenoma, polycystic ovarian syndrome, endometriosis and multinodular goiter in a same case suggest pulmonary hypertension might have precipitated and/or aggravated multiple endocrine dysfunctions, which is particularly important in current research of pulmonary hypertension as hormones such as estrogen, progesterone and thyroid have been linked to the disease’s course.
**Summary:**
In this case study, an association of pulmonary hypertension with bronchial asthma, systemic lupus erythematosus and multiple endocrine dysfunctions is highlighted. Though systemic lupus erythematosus with high titers of rheumatoid factor and anticardiolipin factor have been associated with pulmonary hypertension, its association with other endocrine syndromes in concert suggests it could be a part of multiple endocrine dysfunctions as well, including dysfunctions of the pituitary gland.

**References:**

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