Pulmonary Circulation Assembly Newsletter

Edited by David B. Badesch, MD, Assembly Chair

American Thoracic Society

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Inside this issue:

Message From the Assembly Chair

David B. Badesch, MD

It has been an exciting year in the field of pulmonary vascular disease. This newsletter provides summaries of a few of the highlights for the Pulmonary Circulation Assembly – I am sure that there are many others not mentioned here. Paul Hassoun organized a highly successful ERS-ATS Joint Conference on the Pulmonary Circulation, Karen Fagan has prepared an outstanding program for the 2006 Grover Conference, consensus statements on genetic testing and counseling for patients with idiopathic and familial pulmonary arterial hypertension have been developed, the ATS (and PC Assembly) websites have been updated, and Troy Stevens and the PC Program Committee have developed a terrific program for the ATS meetings in May. The Pulmonary Hypertension Association (PHA) continues its amazing growth as a patient-driven organization with a strong scientific component. The PHA International Conference will be held in Minneapolis in June, and Greg Elliott has organized a world class scientific session to kick off that meeting. The PHA plays an active role on the ATS Public Advisory Roundtable (PAR), with Judy Simpson currently serving as chair of that group. Basic research findings continue to be translated into new therapies through the conduct of numerous multicenter clinical trials, and the NIH is enhancing its support of pulmonary vascular research through the SCCOR and other mechanisms. It is truly an exciting time to be a part of pulmonary vascular research and patient care!

Looking forward to a fantastic ATS International Conference in San Diego!

Best regards,
Dave Badesh

Jack Reeves Memorial Lecture Fully Endowed

As many of you know, Jack Reeves, MD was an international leader in pulmonary vascular physiologic research, a mentor to many current investigators working around the world, and a humanitarium. Wiltz Wagner has coordinated an effort to honor Jack with a Memorial Lectureship at the biannual Grover Conference. Through kind and generous donations from Jack's family, friends, and colleagues, the Lectureship is now fully endowed in the amount of $10,000. Many thanks to Wiltz, and all who contributed to this very appropriate recognition for Jack.

The 2005 ERS-ATS Joint Conference on the Pulmonary Circulation

Paul M. Hassoun, MD

The first joint ERS-ATS Joint Conference on the Pulmonary Circulation was held in Paris, France in December, 2005, and was entitled "Molecular Determinants of Pulmonary Vascular Remodeling." The conference drew experts from around the world, and focused on the mechanisms underlying the pulmonary vascular remodeling that characterizes pulmonary

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The 2005 ERS-ATS Joint Conference on the Pulmonary Circulation cont'd

Paul M. Hassoun, MD

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arterial hypertension, which is a complex disease involving changes affecting all three layers of the pulmonary vessels (intima, media, and adventitia). It was recognized that there is growing evidence that the matrix and several enzymes (e.g., matrix metalloproteinases) are actively involved in vessel wall restructuring (i.e., remodeling) thus contributing to the narrowing of the vascular lumen. While no effective treatment was available two decades ago for this disease (which carries a 50% survival of 2.5 years when untreated), better understanding of pulmonary vascular physiology (e.g., EC-SMC interaction and regulation) and the intricate balance between mitogens and inhibitors of cell growth, has led to the development of improved therapy such as the use of prostacyclin analogs and endothelin receptor receptor antagonists. These agents have greatly enhanced the functional status of patients with PH and significantly impacted on the survival of these patients, often obviating the need for the more drastic lung transplantation option. The recent discovery of mutations in the Bone Morphogenesis Protein Receptor-2 (BMPR II), a member of the TGF-β superfamily, and identification of polymorhisms of other genes such as activin-receptor-like kinase I (ALKI), another member of the TGF-β superfamily, have shed more light into signaling pathways involved in the pathogenesis of this disease, and represent potential new therapeutic targets. In parallel, the use of transgenic mouse systems, in which expression of specific candidate genes can be modified, have helped determine the specific roles of these genes in altering the course of the vascular remodeling. Finally, the emergence of experimental therapy, such as stem cell transfusion with and without overexpression of specific genes (e.g., endothelial nitric oxide synthase), have raised new promises for the future clinical management of these patients. Based on progress made in the past few years, it is now clear that future therapy for this devastating disease will continue to emerge from a better understanding of genetic and molecular pathways.

It is hoped that a conference summary will be published in the ATS Proceedings, and that a joint ERS-ATS Conference on the Pulmonary Circulation will become a regular event, perhaps being held every two years in an alternating manner with the Grover Conference.

The 2006 Grover Conference on the Pulmonary Circulation

Karen A. Fagan, MD

The 2006 Grover Conference on the Pulmonary Circulation will be entitled "Rho Family GTPases in Pulmonary Vascular Pathophysiology," and will be held at the Lost Valley Ranch in Deckers, Colorado. The goal is to explore the mechanisms by which Rho family GTPases contribute to pulmonary vascular function in both health and disease, and how this knowledge may lead to novel interventions in lung dysplasia, pulmonary edema, lung injury (ARDS), and pulmonary and systemic hypertension. The ultimate goal is to identify new mechanisms of disease, as well as new therapeutic targets for pulmonary vascular-related diseases. We expect that an additional outcome will be enhanced understanding of the role of these signaling molecules in lung airway as well as systemic vascular pathophysiology, since the conference will include researchers and clinicians with interests in airway smooth muscle cell and both the pulmonary and systemic circulations.

The learning objectives of the conference are:

- Describe the cell biology of Rho family GTPases including activation, signaling, etc.
- Describe regulation of pulmonary vascular function through Rho family GTPase signaling, i.e., calcium sensitization and smooth muscle contraction, vascular cell proliferation and migration, endothelial permeability, recruitment and activation of inflammatory cells to areas of injury, etc.
- Consider Rho family GTPases and/or downstream effectors as therapeutic targets in pulmonary vascular-related lung diseases.

As always, it is expected that the Grover conference will involve a broadly representative international group of scientific experts, in an environment that will engender lively discussion and debate.

The PHA Consensus Statement on Genetic Testing and Counseling for Idiopathic and Familial PAH

James E. Loyd, MD

The Pulmonary Hypertension Association (PHA) is a rapidly growing, patient-driven organization, with an active medical/scientific arm known as the Scientific Leadership Council (SLC). The SLC is currently chaired by Dr. Robyn Barst, and has a number of active committees (research, education, journal, and conference). Interactions between the PHA and the ATS are

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The PHA Consensus Statement on Genetic Testing and Counseling for Idiopathic and Familial PAH cont'd

James E. Loyd, MD

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strong and growing. The PHA and ATS will be partnering to jointly sponsor research grants for young investigators working in pulmonary vascular disease.

Among its many activities, the PHA SLC recently supported the development of a "Consensus Statement on Genetic Testing and Counseling for Idiopathic and Familial PAH." In most families, familial pulmonary arterial hypertension (FPAH) is caused by mutation in bone morphogenetic protein receptor 2 (BMPR2). BMPR2 helps regulate the growth of cells in the walls of the small pulmonary arteries. Other factors, probably genetic or environmental, are also needed to produce disease because only about 20% of individuals with a BMPR2 mutation ever develop idiopathic PAH (IPAH). Some individuals in families with a different genetic condition called Hereditary Hemorrhagic Telangiectasia (HHT) may also develop IPAH, due to a mutation in a different gene, called ALK1. Knowledge about genes that cause IPAH is still growing, so it is possible that other genes may contribute and will be discovered in the future.

The Consensus Statement goes on to discuss, in lay language understandable to patients and their families, the likelihood that a family member might have of inheriting the mutated gene for BMPR2, and the subsequent likelihood of contracting PAH. It goes on to discuss the availability and limitations of genetic testing, and the necessity of associated genetic counseling. This is currently an active area of research at three pulmonary hypertension centers: Columbia University, LDS Hospital / University of Utah, and Vanderbilt University.

PC Assembly Website Update

William A. Altemeier, MD

Our website remains a source for members to find information about the PC assembly, including mission statement, officers, awards, projects, and past assembly news letters. Additionally, our website continues to maintain an active web-based journal club reviewing recent articles pertaining to the diseases and pathophysiology of the pulmonary circulation. Currently, our journal club is seeking a new editor responsible for reviews on the topic of leukocyte adhesion/migration. Any suggestions for potential editors would be welcome.

Current efforts ongoing for our website include updating the Welcome page and updating the Links to Web pages of interest to our assembly members. The PC Assembly website's purpose is to facilitate communication between members of the assembly. Any suggestions as to how the website can be improved to better meet this goal are welcome. Please send your comments to our web director, Bill Altemeier (billa@u.washington.edu) for consideration and discussion at the upcoming Assembly meeting in San Diego. Finally, after three years, it is time to select a new Web Director for the PC assembly. Nominations should be sent to pc@thoracic.org.

ATS 2006 – SAN DIEGO
Session Sponsored by the Assembly on Pulmonary Circulation

POSTGRADUATE COURSE			
Friday, May 19			
PG9	Cellular Biology Of Hypoxia	8:00 am	4:10 pm
SCIENTIFIC SYMPOSIA			
Sunday, May 21			
A10	Findings From Recent Clinical Studies On The Prevention, Diagnosis And Risk Stratification Of Venous Thromboembolism	8:15 am	11:00 am
A75	Regenerating The Lung Circulation In Pulmonary Arterial Hypertension: More Than A Pipe Dream	1:30 pm	4:15 pm

ATS 2006 – SAN DIEGO
Session Sponsored by the Assembly on Pulmonary Circulation cont'd

SCIENTIFIC SYMPOSIA			
Tuesday, May 23			
C78	Endothelial Stress Phenotypes In Acute Lung Injury	1:30 pm	4:15 pm
Wednesday, May 24			
D75	Taking The Next Step: Improving Outcomes In Pulmonary Arterial Hypertension	1:30 pm	4:15 pm
EVENING POSTGRADUATE SEMINARS			
Sunday, May 21			
E1	The Current Understanding Of The Pathogenesis And Management Of PAH	7:00 pm	9:00 pm
Monday, May 22			
E6	Treatment Of Pulmonary Hypertension: Who, When, Where, What, Why And How?	7:00 pm	9:00 pm
Tuesday, May 23			
E11	Clinical Crossfire: Current Controversies In Pulmonary Arterial Hypertension (PAH)	7:00 pm	9:00 pm
MEET THE PROFESSOR SEMINARS			
Sunday, May 21			
MP417	Pulmonary And Bronchial Circulation In Health And Disease	12:00 pm	1:00 pm
Monday, May 22			
MP515	Pulmonary Arterial Hypertension (PAH) Associated With Connective Tissue Disease (CTD): What Works? What Doesn't?	12:00 pm	1:00 pm
Tuesday, May 23			
MP617	Clinical Management Of Special Patient Populations In PAH: Case Presentation	12:00 pm	1:00 pm
SUNRISE SEMINARS			
Monday, May 22			
SS116	Chronic Thromboembolic Pulmonary Hypertension	7:00 am	8:00 am
Tuesday, May 23			
SS217	Pulmonary Hypertension In Parenchymal Lung Disease: Current Evidence And Future Directions	7:00 am	8:00 am
Wednesday, May 24			
SS316	Pulmonary Arterial Hypertension: Genotype-Phenotype Correlations	7:00 am	8:00 am
MINI SYMPOSIA			
Monday, May 22			
B18	Molecular Mechanisms Of Pulmonary Vascular Remodeling	8:15 am	11:00 am
B88	Pulmonary Vascular Permeability: Cellular And Molecular Mechanisms	1:30 pm	4:15 pm

ATS 2006 – SAN DIEGO
Session Sponsored by the Assembly on Pulmonary Circulation cont'd

MINI SYMPOSIA			
Tuesday, May 23			
C18	Pathogenic Mechanisms Of Pulmonary Hypertension: New Findings	8:15 am	11:00 am
C85	Clinical Management And Therapy Of Pulmonary Hypertension	1:30 pm	4:15 pm
Wednesday, May 24			
D15	Pulmonary Embolism And Thromboembolic Pulmonary Hypertension	8:15 am	11:00 am
POSTER DISCUSSION SESSIONS			
Sunday, May 21			
A28	Diagnosis And Treatment Of Pulmonary Hypertension	8:15 am	11:00 am
Monday, May 22			
B26	Physiology And Pathophysiology Of Pulmonary Vascular Endothelium	8:15 am	11:00 am
B98	Pathogenesis Of Pulmonary Hypertension	1:30 pm	4:15 pm
Tuesday, May 23			
C96	Hypoxic Regulation Of Pulmonary Vascular Contractility And Remodeling	1:30 pm	4:15 pm
Wednesday, May 24			
D95	Pulmonary Vascular Smooth Muscle Cell Proliferation, Migration And Apoptosis	1:30 pm	4:15 pm
THEMATIC POSTER SESSIONS			
Sunday, May 21			
A132	Pulmonary Embolism And Thromboembolic Pulmonary Hypertension	8:15 am	4:15 pm
A133	Chronic Lung Disease Associated With Pulmonary Hypertension: Cellular And Molecular Mechanisms	8:15 am	4:15 pm
Monday, May 22			
B122	Pulmonary Hypertension: Diagnosis, Treatment And Pathogenesis	8:15 am	4:15 pm
Tuesday, May 23			
C139	Function Of Pulmonary Vascular Endothelial Cells	8:15 am	4:15 pm
C140	Pulmonary Vascular Cell Signaling	8:15 am	4:15 pm

Please Consider Submitting an Assembly/Committee Project Application for Funding in FY2007

For your information, the FY2007 (January 1-December 31, 2007) project application forms for Assembly/Committee projects will be available on the ATS website in April 2006 at: http://www.thoracic.org/assemblies/projectform.asp.

Please consider submitting an application for an Assembly/Committee project. If you have an idea for a project application and you need assistance, please contact your Assembly Planning Com

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Please Consider Submitting an Assembly/Committee Project Application for Funding in FY2007 cont'd

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mittee chair Jason Xiao-Jian Yuan at xiyuan@ucsd.edu.

The timeline for the application and review process follows:

April 2006: FY2007 forms are available.

July 25, 2006: Assembly/ Committee project applications are due to the ATS office. Late submissions will not be accepted.

Early-mid August 2006: abridged versions of the proposals will be posted on the ATS site and emails will be sent to ATS Leadership, Assembly Planning Committee Chairs, Assembly Chairs, ATS Committee Chairs, appropriate ATS staff and the PRS committee, to notify them that the current, unreviewed proposals are available. This will give everyone an opportunity to touch base with any of the applicants if they would like to get involved with a project before it goes to the PRS for review.

August 1-18, 2006: Assembly Planning Committees will meet via conference call to review appropriate proposals. Any proposal that has indicated on the form that a specific ATS committee may want to become involved will be sent to the ATS committee chair and to the appropriate staff member. Committees are encouraged to work with appropriate ATS staff and review any proposals and to send recommendations to the applicant and to the PRS.

September 6, 2006: Revised proposals and all reviews from Assemblies and Committees are due to ATS office. This includes any proposal that has revisions based on a review by an Assembly Planning Committee or an ATS Committee.

Early October 2006: Program Review Sub-Committee (PRS) meeting

Early November 2006: Program & Budget Committee (P&B) meeting. Recommendations from the PRS will be provided to the P&B Committee. At the discretion of the P&B Committee, specific projects will be added to the FY2007 budget as new items.

December 2006: ATS Board reviews FY 2007 Budget.

Please contact Elisha Malanga with any questions at tel: 212/315-8693 or email: emalanga@thoracic.org .

Patients to Speak At Sixteen Designated ATS International Conference Symposia

The ATS Public Advisory Roundtable (ATS PAR) has selected patients to provide a patient perspective at sixteen of the 2006 ATS International Conference Symposia. This concept has worked exceptionally well within the format of the PAR Symposia for the last four years and at over 25 ATS symposia at the 2004 and 2005 International Conferences.

This is the third year that patient speakers will participate within the Assemblies' Symposia. The patients will make a five-minute presentation at the symposia to offer insight into their personal journeys; to address their diagnosis, treatment, and how the disease has dramatically altered their lifestyles, family, career and relationships. They will share their insight into what patients would like physicians and researchers to know about physician/patient relationships; and the importance and relevance of the work in which investigators and researchers are engaged.

The symposia at which a patient-perspective will be presented are listed below:

Assembly	Session Code	Title	Date/Time
All	B7	Genotypic and Phenotypic Predictors of Response to Asthma Therapy: What do NHLBI Clinical Research Studies Tell Us?	Monday, May 22 8:15-11:00 am
BS	A7	Respiratory Lung Health and the Family: The Influence of Family on Adherence, Disease Management, and Health Outcomes	Sunday, May 21 8:15-11:00 am
BS	D9	Community Involvement in Pulmonary and Critical Care Research: What, Why and How?	Wednesday, May 24 8:15-11:00 am
CP	A2	Novel Outcomes for Novel Therapies in COPD	Sunday, May 21 8:15-11:00 am
CP	D2	Update in the Diagnosis and Management of Pulmonary Vasculitis	Wednesday, May 24 8:15-11:00 am
CC	B74	Genetic Influences on the Susceptibility To and Outcome of Critical Illness	Monday, May 22 1:30-4:15 pm

Patients to Speak At Sixteen Designated ATS International Conference Symposia

Assembly	Session Code	Title	Date/Time
CC	C7	Clinical Studies in the Pediatric ICU: Update From the Pediatric Acute Lung Injury and Sepsis Investigator's (PALISI) Network	Tuesday, May 23 8:15-11:00 am
MTPI	C6	Diagnosis and Management of Nontuberculous Mycobacterial Infections – The New ATS Guidelines	Tuesday, May 23 8:15-11:00 am
NRSG	A8	Critical Care of the Geriatric Patient	Sunday, May 21 8:15-11:00 am
NRSG	B6	Biobehavioral Considerations in Prolonged Mechanical Ventilation	Monday, May 22 8:15-11:00 am
PED	A9	Primary Ciliary Dyskinesia: Not Just the Other Inherited Lung Disease	Sunday, May 21 8:15-11:00 am
PC	D75	Taking the Next Step, Improving Outcomes in Pulmonary Arterial Hypertension	Wednesday, May 24 1:30-4:15 pm
RCMB	B77	Evolving Concepts of Stem Cells and Lung Repair	Monday, May 22 1:30-4:15 pm
RCMB	D7	New Deve-lopments in the Genetics of Respiratory Disorders	Wednesday, May 24 8:15-11:00 am
RNS	D76	Sleep, Breathing and Metabolic Function	Wednesday, May 24 1:30-4:15 pm
RSF	A79	Impact of Smoking on Lung Function: Therapeutic Implications and Biological Mechanisms	Sunday, May 21 1:30-4:15 pm

ATS Public Advisory Roundtable (PAR) Symposium and Poster Session

ATS PAR Symposium

The ATS Public Advisory Roundtable (PAR) is pleased to announce the fifth ATS PAR Symposium to be presented at the ATS International Conference in San Diego on Monday, May 22nd from 8:15-11:00 a.m. The topic will be "COPD and Comorbidities: Treating the Whole Patient" chaired by Sharon I. S. Rounds, M.D and John W. Walsh. The program includes the following:

- COPD As A Systemic Condition - S. I. S. Rounds, M.D., Providence, RI
- Panel: Experience of Patients With COPD And Co-Morbidities - J. W. Walsh, Miami, FL
- COPD and Cardiovascular Disease - D. D. Sin, M.D., Vancouver, BC, Canada
- Obesity, Wasting and BODE Index - B. R. Celli, M.D., Boston, MA
- Skeletal Muscle Function in COPD - P. D. Wagner, M.D., La Jolla, CA
- COPD and Endocrine Issues: Diabetes - E. N. Schachter, M.D., New York, NY
- Depression and Anxiety In COPD Patients - J.R. Curtis, M.D., M.P.H., Seattle, WA
- Session Summary - S. I. Rennard, M.D., Omaha, NE

ATS PAR Poster Session

The ATS PAR Annual Poster Session will be open from Sunday, May 21 until Wednesday, May 24, 2006 at the Center Terrace of the San Diego Convention Center. Public Interest Organizations (PIO's) concerned with lung and sleep disorders will present information about their organizations. A representative from each organization will be present at the poster session to provide additional information.

Documents Forum at 2006 International Conference

On Sunday, May 21 from 7-9 PM, the Documents Editor, Holger Schunemann, MD and Documents Staff Judy Corn will lead a forum on Official Documents: what they are, how they're developed, and how they're peer reviewed, approved and disseminated. New Board-approved policy guidelines for document development and their impact on the Society will also be addressed. All Assembly leadership, current writing committee members, as well as individuals interested in serving on writing committees in the future are urged to attend this informative session. Participants will receive a packet of highly cited ATS documents and procedural guidelines.

ATS Documents Forum
Sunday, May 21, from 7-9 PM
Randle Ballroom A/B,
Manchester Grand Hyatt

Pulmonary Circulation Assembly Membership Meeting

Monday May 22nd 4:30-6:30 PM
Manchester Grand Hyatt
Edward A-D (Level 2)

Refreshments will be provided