Ludwig Boltzmann Institute
Lung Vascular Research

ANNUAL REPORT

2018

Content

Contact

Zentrum für Medizinische Grundlagenforschung
Stiftingtalstraße 24
8010 Graz, Austria
Tel.: +43 (0)316-385-72057
E-Mail: office@lvr.lbg.ac.at
Website: www.lvr.lbg.ac.at

Team

Director: Grazyna Kwapiszewska
Deputy Director: Horst Olschewski

Employee:

Key Researchers:

Gabor KOVACS
Grazyna KWAPISZEWSKA
Leigh MARSH

Scientific Staff':

Alexander AVIAN assoc. MUG
Valentina BIASIN
Elisabeth BLANZ
Savinien BONHEUR
Ehsan BONYADIRAD assoc. MUG
Natalie BORDAG
Luka BRCIC, assoc. MUG
Visnja BUBALO
Slaven CRNKOVIC
Philipp DOUSCHAN assoc. MUG
Bakytbek EGEMNAZAROV
Vasile FORIS assoc. MUG
Thomas FUCHS assoc. MUG
Nicola GIULIANI
Eva GRASMAN
Anna GUNGL assoc. MUG
Sabine HALSEGGER assoc. MUG
Tatjana HIRSCHMUGL
Andelko HRZENJAK assoc. MUG
Katharina JANDL
Daniela KLEINSCHEK
Ceren MUTGAN, assoc. MUG
Chandran NAGARAJ
Bence NAGY
Lisa OBERREITER (Maternity leave)
Balazs ODLER
Horst OLSCHEWSKI assoc. MUG
Michael PIENN
Daniela RAINER
Piet ROSENSTOCK
Anita SAHU-OSEN
Teresa SASSMANN
Bettina SCHRENK
Davor SKOFIC-MAURER assoc. MUG
Neha SHARMA assoc. MUG
Katharina SINN assoc. MUW
Helene THEKKEKARA PUTHENPARAMPIL
Simone TISCHLER assoc. MUG
Alexandra Nina TREITLER
Diana ZABINI assoc. MUG
Hans Peter ZIEGLER, assoc. MUG

Management:

Claudia JAKOB-PELIKAN
Stefanie KAINZ (Maternity leave)
Angelika SCHEIRING

Partners

We thank our partners, the Ludwig Boltzmann Society, Bayer AG and Medical University of Graz, as well as the Government of Austria for their continuous support.

Ludwig Boltzmann Society (http://www.lbg.ac.at/)

The Ludwig Boltzmann Gesellschaft (LBG) is a non-profit organization establishing non-university research institutes in Austria. It is named after the Austrian physicist, mathematician and philosopher Ludwig Boltzmann, whose broad scientific interests still remain the basis for the interdisciplinary of the Ludwig Boltzmann Gesellschaft today. The LBG, which is financed from public and private resources, manages institutes and clusters and currently employs more than 550 people.

Medical University of Graz (http://www.medunigraz.at/)

Research activities of the Medical University of Graz (MUG) cover a broad range of clinical as well as pre-clinical fields. The MUG applies a pro-active approach in research management to involve and integrate researchers in international research initiatives. The LBI for Lung Vascular Research fits excellently in this concept and will be an important core for promotion of lung vascular research, diagnostic and innovative therapy of lung vascular diseases at the MUG.

Bayer AG (https://www.bayer.de/)

Cardiovascular diseases are in the main focus of Bayer AG (BAG). BAG is currently developing new therapeutic options for the treatment of cardiovascular and lung diseases. The novel treatment for pulmonary hypertension (PH), the soluble guanylate cyclase stimulator Riociguat has recently been launched worldwide for pulmonary arterial hypertension (PAH) and chronic thromboembolic pulmonary hypertension (CTEPH). BAG has a broad experience in pulmonary hypertension associated research and in the transfer of results from “bench to bedside”. The interest of BAG is to further understand the underlying pathophysiology of pulmonary vascular diseases.

Committees

Scientific Advisory Board (SAB) – chaired by Prof. Wolfgang Kübler

Prof. Wolfgang Kübler – Charité - Universitätsmedizin Berlin, DE

https://physiologie-ccm.charite.de/en/

Prof. Steve Abman – University of Colorado, US

http://www.cudoctors.com/Find_A_Doctor/Profile/5902

Prof. Nick Morrell – University of Cambridge, UK

http://www.med.cam.ac.uk/morrell/

Prof. Jose Lopez-Barneo – University of Sevilla, ES

https://www.ibis-sevilla.es/investigacion/neurociencias/neurobiologia-celular-y-biofisica/lopez-barneo-jose.aspx

Prof. Martin Kolb – McMaster University of Ontario, Canada

https://fhs.mcmaster.ca/medicine/respirology/faculty_member_kolb.htm

Advisory Board of the Partners (Board) – chaired by Mag.ª Caroline Schober-Trummler

Mag.ª Caroline Schober-Trummler, Medical University of Graz

http://www.medunigraz.at/rektorat/vizerektorin-fuer-forschung-und-internationales/

Dr. Peter Mayrhofer, Ludwig Boltzmann Gesellschaft

http://www.lbg.ac.at/bereichsleitung

Dr.in Heidrun Dorsch, Bayer AG

http://pharma.bayer.com/

1 The Institute in Overview

The Ludwig Boltzmann Institute for Lung Vascular Research (LBI-LVR) is a non-profit research institute founded in July 2010 by the Ludwig Boltzmann society (LBG). LBG founded institutes conduct research in the fields of Medicine & Life Sciences or Humanities. The LBI-LVR was established after a demanding two-stage evaluation by international peers who strongly recommended the founding of the institute.

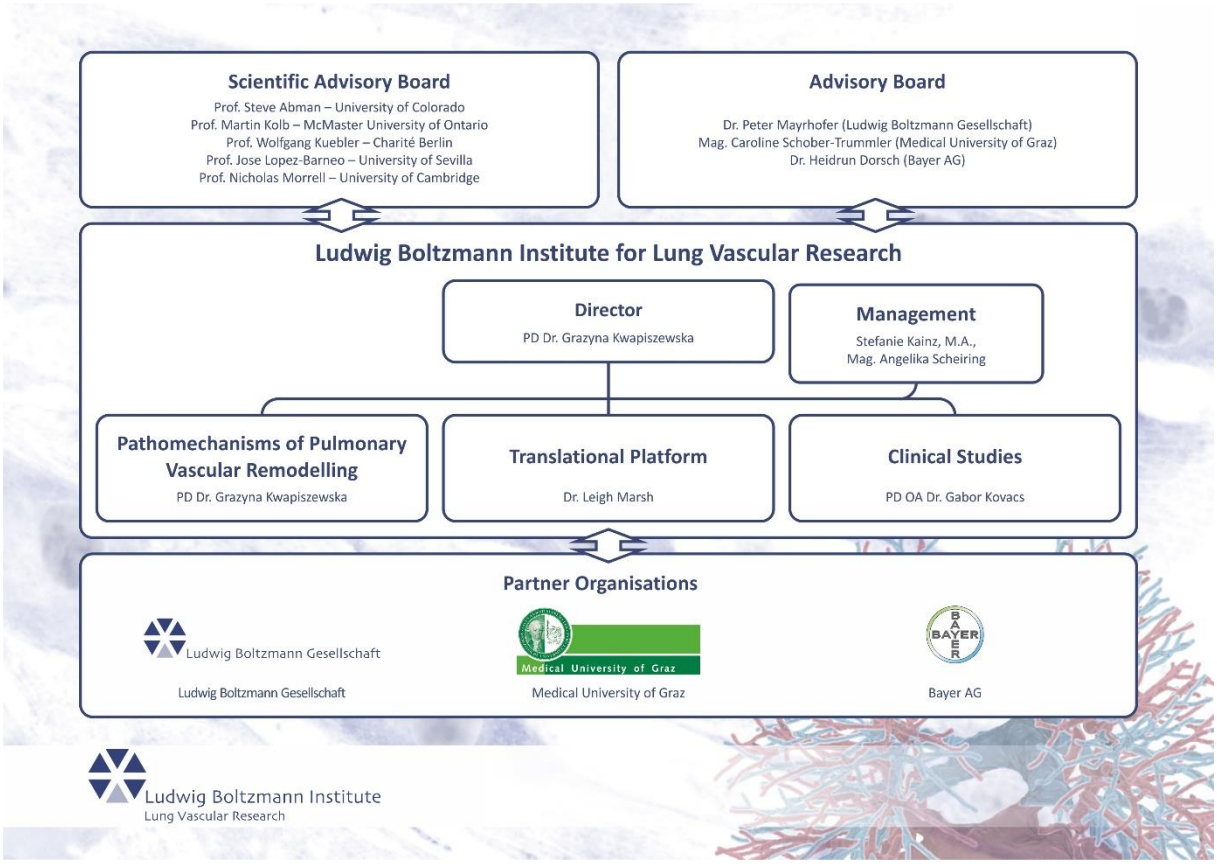
The LBI-LVR, like the other Ludwig Boltzmann Institutes, is established on a partnership between organizations and institutes that traditionally carry out research and organizations that traditionally apply research. The LBI-LVR Consortium currently comprises the Ludwig Boltzmann society as carrier institution in partnership with the Medical University of Graz (MUG) and Bayer AG. The Advisory Board of the LBI-LVR, composed of the representatives of each partner organization (LBG, MUG, and Bayer AG), supervises the progress of the LBI-LVR. The Scientific Advisory Board (SAB) of the LBI-LVR is an independent, world-wide recognized group of experts in pulmonary vascular biology and in pulmonary hypertension and monitors the scientific activities of the institute.

The budget of the institute is approx. 14.9 million Euro cash and in kind for the first seven years. The Ludwig Boltzmann Society covers 56% of the total costs. The remaining 44% of the costs are shared by the consortium of our partners.

The LBI for Lung Vascular Research is predominantly located at the Center for Medical Research (ZMF) at the MUG, which supports the LBI with cutting-edge research facilities guaranteeing high-yield development in this field. The clinical research group is hosted next to the Center for Pulmonary Hypertension of the Division for Pulmonology / Department of Internal Medicine of the MUG.

For contact please visit our website: **http://lvr.lbg.ac.at**

The scheme depicts the structure of our institute



1.1 What you should know about Lung Vascular Diseases: Facts, Diagnostics and Therapy

In recent years, the area of lung vascular diseases has emerged as a leading field of medical research. In particular, the diagnosis and therapy of pulmonary hypertension (PH) has made tremendous progress over the past 25 years. This has started with the first approval of a drug for idiopathic pulmonary arterial hypertension in 1995 and resulted in 14 approvals of different drugs and applications up to the year 2018. All these approvals were based on international pivotal trials providing evidence for efficacy and safety for targeted drugs for PAH or chronic thromboembolic pulmonary hypertension. However, PH remains a notoriously under-diagnosed chronic and fatal disease. Therefore, early recognition of the disease is still crucial. As the diagnosis of PH is performed by invasive right heart catheterisation, the development of reliable non-invasive methods to assess increased pulmonary arterial pressure values may represent a unique selling proposition. An additional urgent challenge is the development of PH in chronic heart and lung diseases: large patient populations with severe left heart disease or chronic obstructive lung disease may develop PH during the course of their disease, but currently no effective

treatment options exist for these conditions. This represents an opportunity to develop novel concepts and therapeutic approaches.

Progressive loss of exercise capacity and worsening dyspnoea represent the most common symptoms of lung diseases, particularly if PH is involved. Clinical care for pulmonary vascular diseases is extremely costly; therefore, this condition poses a large burden on the Austrian as well as on the European healthcare system. Current therapies improve exercise capacity and may prolong survival of the affected individuals, but are far away from curing the disease or providing a substantially prolonged lifespan with a good quality of life. Future development must address these challenges in a multidisciplinary approach combining findings from basic research and clinical research.

1.2 Mission Statement/Aims of the Institute

The LBI-LVR has substantial expertise in the basic mechanisms of pulmonary vasoconstriction and remodelling, combined with a broad and profound clinical background. We aim to provide a significant contribution to early recognition of pulmonary vascular diseases, including pulmonary hypertension, via novel and non-invasive methods and to develop innovative therapeutic strategies for an improved prognosis and better quality of life for the victims of this serious disease. The integrative, multidisciplinary and translational structure of the LBI-LVR allows it to uncover underlying molecular pathways, identify distinct targets for reverse-remodelling therapy, foster drug development based on these targets, and prove these new treatment options in preclinical and clinical proof-of-concept trials.

All our actions, both in research and implementation, will be based on mutual respect and esteem with regard to the patients, our partners, and our staff.

The main objectives of the LBI for Lung Vascular Research are:

- Exploring mechanisms of pulmonary vascular diseases enabling the identification of both novel therapeutic targets and new disease biomarkers that could enable specific diagnosis and therapy monitoring
- Developing new diagnostic tools for non-invasive screening for pulmonary vascular diseases
- Implementing the achieved results into preclinical as well as clinical pilot studies
- Increasing awareness for pulmonary vascular diseases in the society and for healthcare providers

1.3 Personal and Human Resources Development

1.3.1 Development of the LBI-LVR Staff

The LBI-LVR staff consists of the director, the program line leaders, senior and junior researchers (PhD students) and master students, technicians, study nurses and administrative assistants. Every PhD or postdoctoral fellow has an individual project and each group has scientific independence in generating their individual progress. Please refer to table above for an overview about the staff.

1.3.2 Awards and prizes

Name	Awards 2018
BIASIN Valentina	Hertha Firnberg Grant 2018, Vienna, Austria
CRNKOVIC Slaven	European Respiratory Society Long Term Scholarship, Perelman School of Medicine, University of Pennsylvania, Philadelphia, USA Ed Morrisey Lab, Cardiology 2018
DOUSCHAN Philipp	Julius Klob Preis 2018, Deutsche Gesellschaft für Kardiologie, Germany
DOUSCHAN Philipp	Michael Neumann Gedächtnispreis 2018, Österreichische Gesellschaft für Pneumologie, Linz, Austria
JANDL Katharina	ÖGP Posterprize, 2nd place, Österreichische Gesellschaft für Pneumologie, Linz, Austria
JANDL Katharina	ÖGP Wissenschaftsförderung, Österreichische Gesellschaft für Pneumologie, Linz, Austria
NAGY Bence	Wilhelm-Auerswald-Preis 2018, Vienna, Austria
NAGY Bence	Best projects in Basic Research, 1st price, Österreichische Gesellschaft für Pneumologie, Linz, Austria
NAGY Bence	Wilhelm-Auerswald-Preis 2018, Vienna, Austria
SKOFIC-MAURER Davor	Lek Regional BioCamp 2018, 1st place, Category: Best group project, Ljubljana, Slovenia
ZABINI Diana	René Baumgart Research Award 2018, Stuttgart, Germany

Name	Travel Awards/Fellowships 2018
CRNKOVIC Slaven	ERS Long-Term Research Fellowship 2018
GUNGL Anna	ERS Short Term Research Travel Fellowship 2018
SASSMANN Teresa	ERS Abstract Travel Grant, Österreichische Gesellschaft für Pneumologie, Linz, Austria 2018

1.3.3 Conferences and Meetings of the LBI-LVR Staff

- **Presentations at national and international conferences: Oral Communications**

Crnkovic S et.al. Single cell resolution reveals cellular diversity and major heterotypic interactions in pulmonary vasculature. Biomedical Postdoctoral Council Symposium, Perelman School of Medicine, University of Pennsylvania, Philadelphia, USA.

Giuliani N, et.al. Pulmonary Lobe Segmentation in CT Images using Alpha-Expansion. 13th International Joint Conference on Computer Vision, Imaging and Computer Graphics Theory and Applications (VISIGRAPP 2018), Funchal, Madeira, Portugal.

Jandl K et.al. Proteolytic product of BM: endostatin and its role in vascular remodeling. Phaedra Fall Meeting, Amsterdam, Netherlands.

Jandl K et.al. Basement membrane remodelling defines the progression of IPAH: the role of Collagen XVIIIA1. ÖGP Jahrestagung, Linz, Austria.

Marsh, LM et. al. AP-1 Subunit Overexpression Drives a Non-Allergic Asthma Phenotype in Mice. American Journal of Respiratory and Critical Care Medicine ATS, San Diego, USA.

Thekkekara Puthenparampil H et. al. Dysregulated lncRNAs in IPAH: the role of PAXIP1-AS1 on human PASMC. MUG DocDay 2018, Graz, Austria.

Thekkekara Puthenparampil H et. al. Differentially expressed lncRNAs in IPAH: the impact of PAXIP1-AS1 on human PASMC function. DK MOLIN Retreat, Seggau, Austria.

Tornyos A, Pulmonary Hypertension in Hypersensitivity Pneumonitis. 17th International Pulmonary Hypertension Forum, Madrid, Spain.

Puthenparampil H. T et.al. Transcriptomic Profiling Reveals Pivotal Involvement of lncRNAs in the Pathogenesis of IPAH: the Role of PAXIP1-AS1. FEBS ECM Conference, Patras, Greece.

Presentations at national and international conferences: Posters

Gungl A et. al. Eosinophilic inflammation and worsening of lung function upon pirfenidone treatment in the Fra-2 transgenic mouse. ERS International Congress, Paris, France.

Gungl A et.al. Blockade of IL-1 signalling exacerbates Th2 inflammation in the Fra-2 transgenic mouse model of systemic sclerosis. ÖGP Jahrestagung, Linz, Austria.

Jandl K et.al. Role of NKT cells in vascular remodelling in pulmonary fibrosis. ÖGP Jahrestagung, Linz, Austria.

Nagy BM, et.al. Metabolic fingerprinting of pulmonary hypertension; Metabolic fingerprinting of pulmonary hypertension. Keystone Symposia on Molecular and Cellular Biology, Hannover, Germany.

Sharma N. et. al. Role of RGS5 in pulmonary vascular homeostasis. International vascular biology meeting, Helsinki, Finland.

Sharma N et.al. Impact of RGS5 in pulmonary vascular homeostasis. ÖGP Jahrestagung, Linz, Austria.

Skofic Maurer et.al. The role of the Ca2+-activated Cl- channel TMEM16A in the pulmonary vasculature. International vascular biology meeting, Helsinki, Finland.

1.3.4 Patents of the LBI-LVR

Patents	Inventors
Biomarker for the diagnosis of pulmonary hypertension (PH) Patent File No. 16159415.5	H. Olschewski (LBI-LVR), A. Olschewski (LBI-LVR), CH. Magnes (Joanneum Research), N. Bordag, S. Narath (CBmed GmbH), E. Gander (Joanneum Research) and B. Nagy (LBI-LVR)
Method for non-invasive diagnosis of pulmonary hypertension using impedance cardiography Patent File No. is A 50719/2016.	M. Pienn (LBI-LVR), H. Olschewski (LBI-LVR), G. Kovacs (LBI-LVR) and Z. Bálint (LBI-LVR)
Method and Device for Processing Impedance Cardiograms for the Determination of a Presence of Pulmonary Hypertension in a Patient and Impedance Cardiograph with such a Device Patent Nr. 518396; Austrian Patent Office, Vienna, Austria; October 15th, 2017	M. Pienn (LBI-LVR), H. Olschewski (LBI-LVR), G. Kovacs G., Z. Bálint.(LBI-LVR)

1.4 Highlights 2018

1.4.1 Awards

René Baumgart-Stiftung, Research Prize 2018

On 5th of March 2018, for the 15th time the Research Prize of the René Baumgart Foundation for scientific work in the field of pulmonary hypertension was announced. **Diana Zabini** received the prize for her work: „Loss of SMAD3 promotes vascular remodeling in pulmonary arterial hypertension via MRTF disinhibition“.

l.t.r.: Horst Olschewski, Anne-Christin Kopp, Diana Zabini, Hans-Dieter Kulla

©Rene Baumgart Stiftung

Julius Klob Award 2018

Philipp Douschan received the Julius Klob Award at this year's annual congress organized by the German Cardiac Society. This prize represents the highest award of the German Cardiac Society for scientific work in the field of pulmonary hypertension. Title of the paper "Mild Elevation of Pulmonary Arterial Pressure as a Predictor of Mortality." The work makes a significant contribution to the question of how increased pulmonary arterial pressure is associated with mortality.

l.t.r.: Tobias Lange, Philipp Douschan, Horst Olschewski
© 2018 Deutsche Gesellschaft für Kardiologie - Herz- und Kreislaufforschung e.V.

Wilhelm-Auerswald-Prize 2018

The "Wilhelm Auerswald Prize" for the best doctoral thesis at an Austrian Medical University was awarded for the 27th time on 19 June 2018. **Bence Nagy** received the 3rd prize for his work "The role of ABCG2 transporter in Pulmonary Hypertension (PH)".

l.t.r.: Botond Ponner, Bence Nagy, Christine Mannhalter, Helmut Sinzinger
© Stefan Burghart

Symposium of the Austrian Society of Pneumology (ÖGP 2018): Six awards go to our institute!

The Annual Meeting of the Austrian Society of Pneumology, which took place from the 18th till the 20th of October 2018 in Linz, was a very successful event for our institute. Four of our employees were honoured with scientific prizes for basic and clinical research at the Congress. Additionally two travel awards went to our institute.

- NAGY Bence: ÖGP Posterprice, 1st place
- JANDL Katharina: ÖGP Posterprice, 2nd place
- JANDL Katharina: ÖGP Wissenschaftsförderung
- DOUSCHAN Philipp: Michael Neumann Memorial Award
- GUNGL Anna: ERS Short Term Research Travel Fellowship
- SASSMANN Teresa: ERS Abstract Travel Grant

l.t.r.: Katharina Jandl, Bence Nagy

l.t.r.: Teresa Sassmann, Anna Gungl

l.t.r.: Neha Sharma, Bence Nagy, Teresa Sassmann, Philipp Douschan, Tobias Welte, Horst Olschewski, Anna Gungl, Grazyna Kwapiszewska, Katharina Jandl, Andrea Olschewski, Gabor Kovacs;

1.4.2 Fellowships

Slaven Crnkovic awarded the European Respiratory Society Long-Term Fellowship

Slaven Crnkovic, a postdoctoral researcher at LBI for Lung Vascular Research, has been awarded the European Respiratory Society Long-Term Fellowship to support his research stay in the laboratory of Prof. Edward Morrisey at Perelman School of Medicine, University of Pennsylvania. Prof. Morrisey is one of the world's leading pulmonary biologists and at the forefront of using novel research techniques deciphering the mechanisms behind normal and pathological lung development.

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1.4.3 Grants

FWF Grant for Valentina Biasin

Valentina Biasin, has received the Hertha Firnberg Grant for her project "The role of sclerostin in pulmonary arterial hypertension". This is a FWF grant for extremely well qualified female scientists, which aims to support women at the start of their scientific career.

© LBI LVR

ÖGP Wissenschaftsförderung for Katharina Jandl

The Austrian Society of Pneumology promotes the implementation of scientific studies and projects in Austria. At the Annual Meeting in Linz, Katharina Jandl has received a grant called ÖGP Wissenschaftsförderung.

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1.4.4 Events

SAB Retreat St. Gallen, Styria 2018

The SAB-Retreat took place on April 23th - 24th, 2018 in the Schloss Kassegg in Styria, Austria. Our young colleagues presented their current projects and discussed their findings with **Edda Spiekerkoetter** Division of Pulmonary and Critical Care Medicine and with Vera Moulton, Wall Center for Pulmonary Vascular Disease, Stanford University, US.

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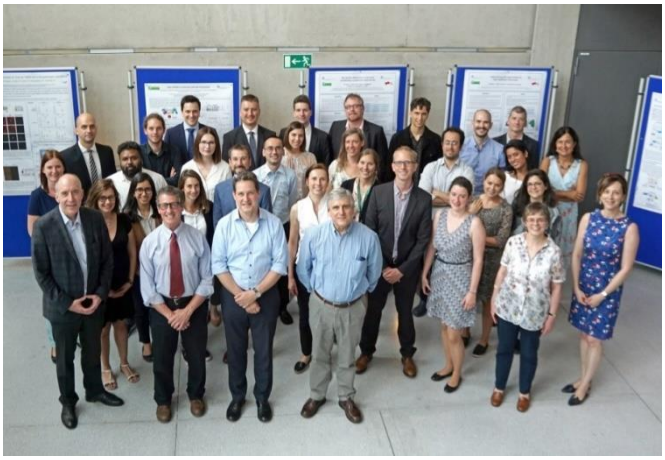
SAB Meeting 2018 in Graz

On 15th of June the 6th Scientific Advisory Board Meeting took place at the Center for Medical Research in Graz. The SAB members **Wolfgang Kuebler** (Charité Berlin), **Jose Lopez-Barneo** (University of Sevilla) and **Steve Abman** (University of Colorado) visited our institute for the annual scientific review of the LBI LVR. The scientific process was presented and it resulted in exciting and stimulating discussions. A great pleasure was the participation of the Board Members **Heidrun Dorsch** (Bayer AG**), Peter Mayrhofer** (Ludwig Boltzmann Gesellschaft) and **Caroline Schober-Trummler** (Medical University of Graz).



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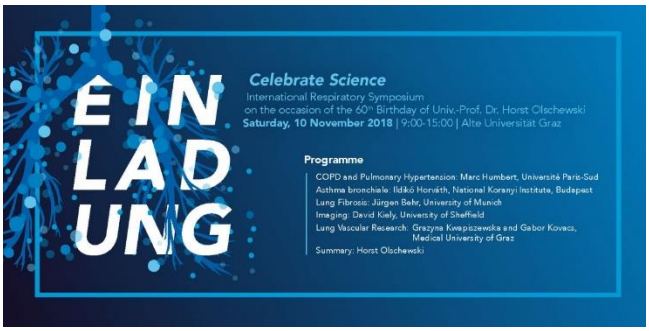
Celerbrate Science 2018

The International Respiratory Symposium "Celebrate Science", which was organized by **Horst Olschewski**, Head of the Clinical Unit for Pulmonology at the Medical University of Graz and the Ludwig Boltzmann Institute for Lung Vascular Research, took place on 9th and 10th November 2018 in Graz.



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Different speakers discussed the following points:

- COPD and Pulmonary Hypertension: **Marc Humbert**, Université Paris-Sud
- Asthma bronchiale: **Ildikó Horváth**, National Koranyi Institute, Budapest
- Lung Fibrosis: **Jürgen Behr**, University of Munich
- Imaging in Pulmonary Hypertension: **David Kiely**, University of Sheffield
- Lung Vascular Research: **Grazyna Kwapiszewska** and **Gabor Kovacs**, Medical University of Graz
- Summary: **Horst Olschewski**

6th World Symposium on Pulmonary Hypertension

The 6th World Symposium on Pulmonary Hypertension from February 27th to March 1st 2018 took place in Nice. Purpose of this Symposium was to foster constructive scientific interactions and collaborations. First a Review of the major advances in pulmonary vascular science in the past 5 years was given. After that, one other objective was to analyze the available evidence in different basic and clinical areas by expert task forces. We are proud that two experts from the LBI LVR were nominated as members of these 13 established taskforces. **Andrea Olschewski** was a member of taskforce 1, called “Pathology & Pathobiology” and **Horst Olschewski**, was a member of taskforce 10, called “PH due to Chronic Lung Diseases”. Discussions of the taskforces documents at the symposium sessions with worldwide experts and with other stakeholders followed there.

1.5 Public Relations

Patient meeting on October 12th, 2018 - A Joint information day for patients with pulmonary fibrosis and / or pulmonary hypertension and relatives

This year the PH patient meeting took place with 90 participants in the lecture hall of the Medical University of Graz. **Eva Otter** from PH Austria Initiative "Lungenhochdruck" welcomed the participants and gave an overview of the activity of their Initiative.

Afterwards, the chairperson of the pulmonary fibrosis forum, **Günther Wanke**, presented the pulmonary fibrosis forum Austria.

Various short lectures by **Gabor Kovacs**, **Philipp Douschan** and **Vasile Foris** and a talk by **Horst Olschewski** completed the program. They reported on the relationship between lung diseases and pulmonary hypertension as well as diagnostic and therapeutic options. **Horst Olschewski** spoke about the role of oxygen therapy in lung diseases. Afterwards there was the possibility to meet each other at a buffet.

© PH Austria Initiative Lungenhochdruck


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Students of the 7th grade of the Gymnasium of the Ursulines in Graz visited the Ludwig Boltzmann Institute for Lung Vascular Research

On June 25, 2018, students of the 7th grade of the Gymnasium of the Ursulinen in Graz visited our institute. Head of the LBI, **Grazyna Kwapiszewska** warmly welcomed the students. They were guided through the laboratories by the staff of the LBI and the everyday life of the researchers was presented. Afterwards, the clinical research laboratories were also presented, the importance of clinical research and the close collaboration between research and clinical medicine discussed. According to the feedback from the students, we have been able to give an insight into the world of research and medicine, and perhaps this visit has helped in choosing a career.

©LBI LVR with kind approval of the Ursulinen, Graz

Newsletter

In addition, the Newsletter of the Pulmo-Outpatient Clinic of the Hospital Graz and the Ludwig Boltzmann Institute for Lung Vascular Research for patients with pulmonary hypertension or a high risk for this disease is available via email by **Daniela Kleinschek**: daniela.kleinschek@lvr.lbg.ac.at or online at the LBI LVR Homepage.


Ludwig Boltzmann Institut Lungengefäßforschung

Medizinische Universität Graz

Newsletter

der Pulmo-Ambulanz des LKH-Universitätsklinikums Graz und des Ludwig Boltzmann Institutes für Lungengefäßforschung

In diesem Newsletter

Frohe Weihnachten und viel Glück, Freude und Gesundheit für das Jahr 2019 wünscht Ihnen und Ihren gesamten Familie herzlichst das Team des Ludwig Boltzmann Institutes für Lungengefäßforschung sowie die Mitarbeiterinnen und Mitarbeiter der Klinischen Abteilung für Lungenkrankheiten des LKH Universitätsklinikum Graz.

Ausgabe 10/2018 Jahrgang 5

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Ludwig Boltzmann Institut Lungengefäßforschung

Medizinische Universität Graz

Informationsheft

der Pulmo-Ambulanz des LKH-Universitätsklinikums Graz und des Ludwig Boltzmann Institutes für Lungengefäßforschung für unsere PatientInnen mit Lungenhochdruck

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Press Appearances

The LBI for Lung Vascular Research has received several invitations to present the research work and aims of the institute to the broad public. A short overview of the **press appearances in 2018** is given here:

- „Medizin braucht Wissenschaft“ – Karriere Medizin am 02.03.2018
- „Neues über die Abklärung der Belastungsdyspnoe“ – Universum Innere Medizin am 14.05.2018
- „Die Effekte der Hypoxie auf die Lungengefäße“ – Universum Innere Medizin am 06.07.2018
- „Lunge unter Druck“ – Kronenzeitung am 17.07.2018
- “Grundlagenforschung Lungenhochdruck“ – ruhig atmen Ausgabe 02/2018 PH Austria
- „Preisregen für Grazer Institut für Lungengefäßforschung“ – AERZTE Steiermark am 13.12.2018

2 Research Program 2018

2.1 Pathomechanisms of Pulmonary Vascular Remodelling

The main goal of this program line is to understand the mechanisms underlying vascular remodeling in the diverse forms of pulmonary hypertension. In the last years, several papers attempted to address the origin and cellular composition of remodeled vessels, implicating different cell types in this process. Given these divergent findings, we investigated the contribution of major resident vascular cell types to the remodeling process using genetic lineage tracing of multiple lung resident cell types and two different murine models of pulmonary vascular remodeling. We showed that the resident, mature lineage-labeled smooth muscle cells (Acta2+, Myh11+) are the ones that proliferate and incorporate into newly muscularized vessels and thus represent the major source of cells in remodeled vessels. We further showed that all other major cell types (endothelial, fibroblast and pericyte) are present in both normal and remodeled vessels, but do not show significant overlap with smooth muscle cell markers. Indeed, our major finding is that expression and localization of major cell type markers (VEcadherin, CD31, NG2, PDGFRα, αSMA, SMMHC) is preserved during pulmonary vascular remodeling process in both animal models and human disease.

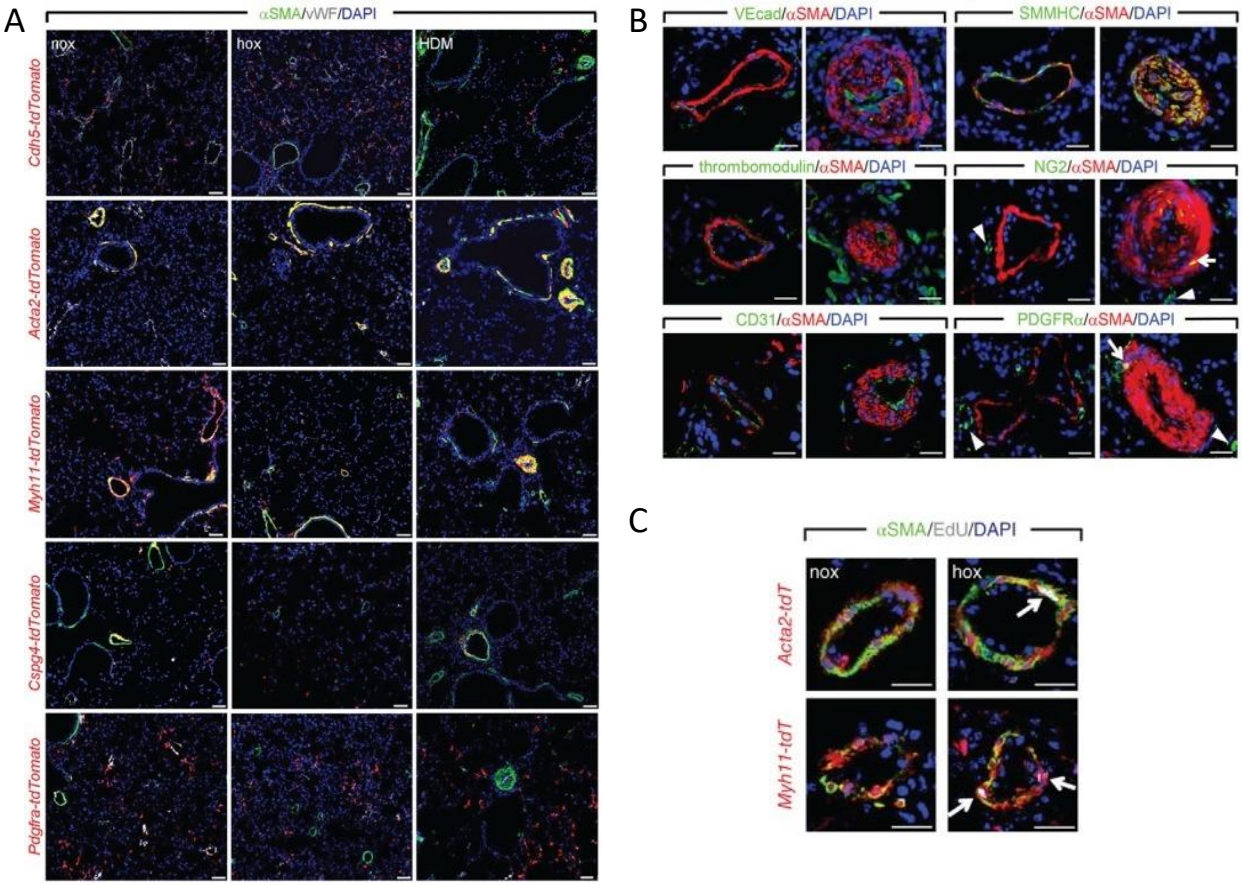


Figure 1. A) A low-magnification overview portion of the lung slide co-stained with alpha smooth muscle actin (αSMA, green), von Willebrand factor (vWF, white), and containing lineage-labeled (red) endothelial cells (Cdh5-tdTomato), smooth muscle cells (Acta2- and Myh11-tdTomato), pericytes (Cspg4-tdTomato), and fibroblasts (Pdgfra-tdTomato) in control (nox), chronic hypoxia (hox), and house dust mite (HDM)-exposed mouse lungs. Scale bar = 50 µm. B) Localization of lineage markers (alpha smooth muscle actin (αSMA), smooth muscle myosin heavy chain (SMMHC), vascular-endothelial cadherin (VEcad), neural/glial antigen 2 (NG2), and platelet-derived growth factor receptor alpha (PDGFRα)) in human pulmonary arteries (donors, IPAH). C) In vivo labeling of proliferating cells using EdU. Representative image showing pulmonary arteries with lineage-labeled smooth muscle cells (Acta2-, Myh11-tdT, red) and co-stained against αSMA (green). Arrows depict SMC with incorporated EdU label (white) within nucleus (DAPI counterstain, blue).

To gain further insight into molecular mechanisms and to identify novel pathways and mechanisms that are perturbed in IPAH, we performed a compartment specific gene analysis on small remodelled vessel of IPAH patients and healthy controls. Our transcriptional profiling of coding genes revealed global perturbations in metabolic, neuronal, proliferative, and immunological processes, thus implying dysfunctional underlying control mechanisms. Recently, lncRNAs have emerged as potent biological regulators. Indeed, in our transcriotional analysis identified an IPAH specific lncRNA expression profile. Furthermore, we identified the lncRNA PAXIP1-AS1 as upregulated in remodelled vessels as wells on IPAH-PASMC. In PASMC, using complementary knockdown models we identified that PAXIP1-AS1

interferes pathways commonly perturbed in IPAH, such as the focal adhesion and ECM-receptor interaction pathways. Acting via its downstream target Paxillin, the lncRNA PAXIP1-AS1 mechanistically interfered with the apoptotic, migratory and proliferative behaviour of the cell – all processes that are part of the IPAH-specific phenotype of PASMCs.

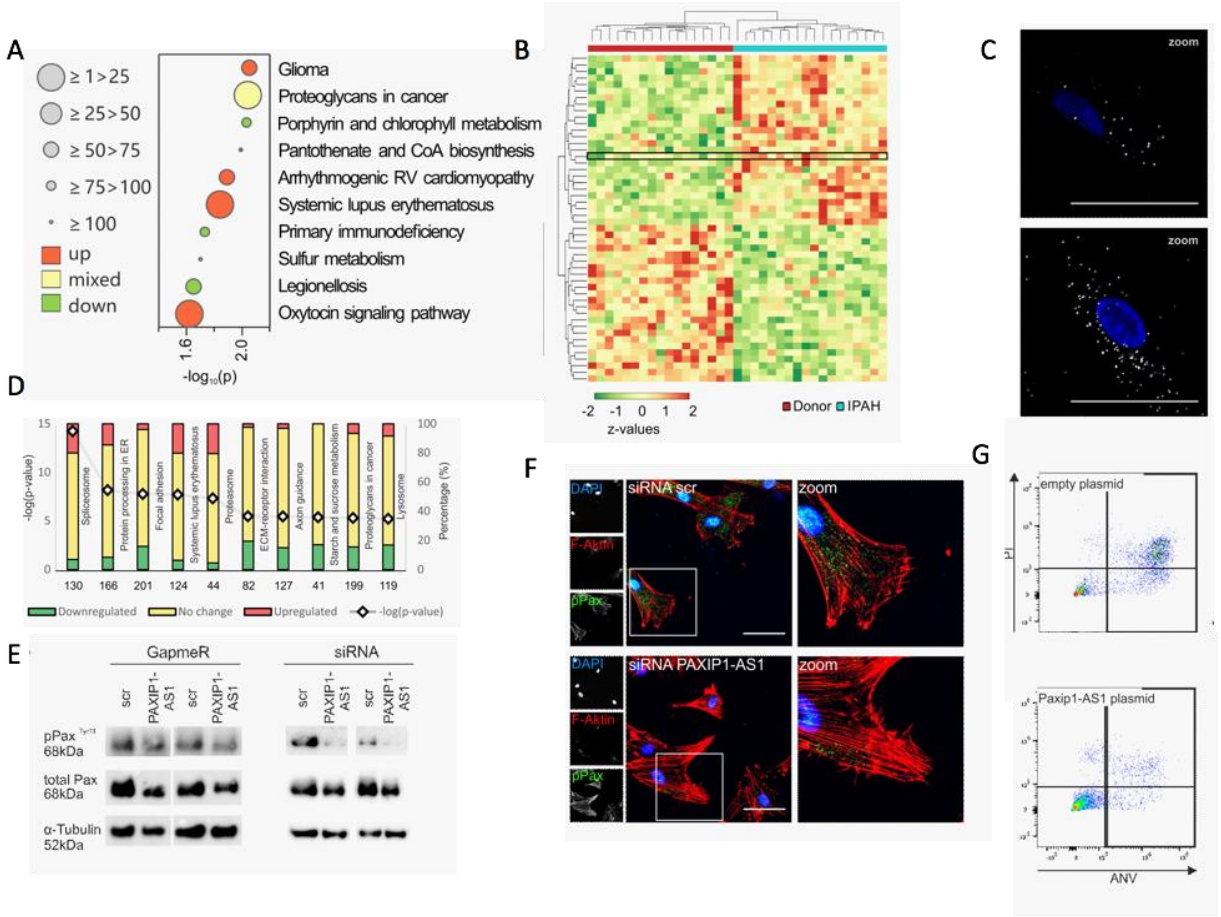


Figure 2 A) Expression profiling of small pulmonary arteries from IPAH and control. Top ten KEGG pathways after gene set enrichment from all detected genes. B) Heatmap representing the expression levels of the 50 most regulated lncRNAs at single patient level. PAXIP1-AS1 is highlighted. C) Fluorescent images of PAXIP1-AS1 (red) RNA in situ hybridisation on PASMCs of IPAH and donors. Scale bar 50 µm. (D) KEGG-pathway analysis of gene set enrichment of all genes in PASMCs after knockdown of PAXIP1-AS1.–log10 P values of the perturbation and the percentages of genes from corresponding KEGG pathway that are down- and up-regulated are depicted. E) p-paxillin (Tyr118) and total paxillin expression relative to α-tubulin 48 h after GapmeR- or siRNA-mediated knockdown of PAXIP1-AS1 in donor PASMCs. F) Immunofluorescence of donor PASMCs 48 h after siRNA-mediated PAXIP1-AS1 knockdown of p-paxillin (green), F-actin (phalloidin, red), and nucleus (DAPI, blue). Scale bar = 50 µm. G) Apoptosis measurements in donor and IPAH PASMCs determined by flow cytometric AnV/PI staining 48 h after transfection with PAXIP1-AS1 overexpression plasmid.

Indirect consequence of remodeling process in the lung vasculature are functional and structural changes in the right ventricle (RV). The proper adaptation of RV towards increased resistance in the pulmonary vascular compartment has long be recognized and confirmed as a key to long term survival of patients with pulmonary hypertension. Expanding our investigations on cellular basis of remodeling process to RV, we investigated the cellular composition, molecular mechanisms and functional consequence of right ventricular fibrosis. We identified that RV fibrosis in animal models and human disease is accompanied by increased expression of galectin-3 and expansion of PDGFRalpha+ fibroblasts While different genetic (galectin-3 knock-outs) and pharmacological treatments (NacLac galectin-3 inhibitor, pirfenidone) diminished developed fibrosis, we found that this amelioration in fibrotic burden was not accompanied with RV functional improvement.

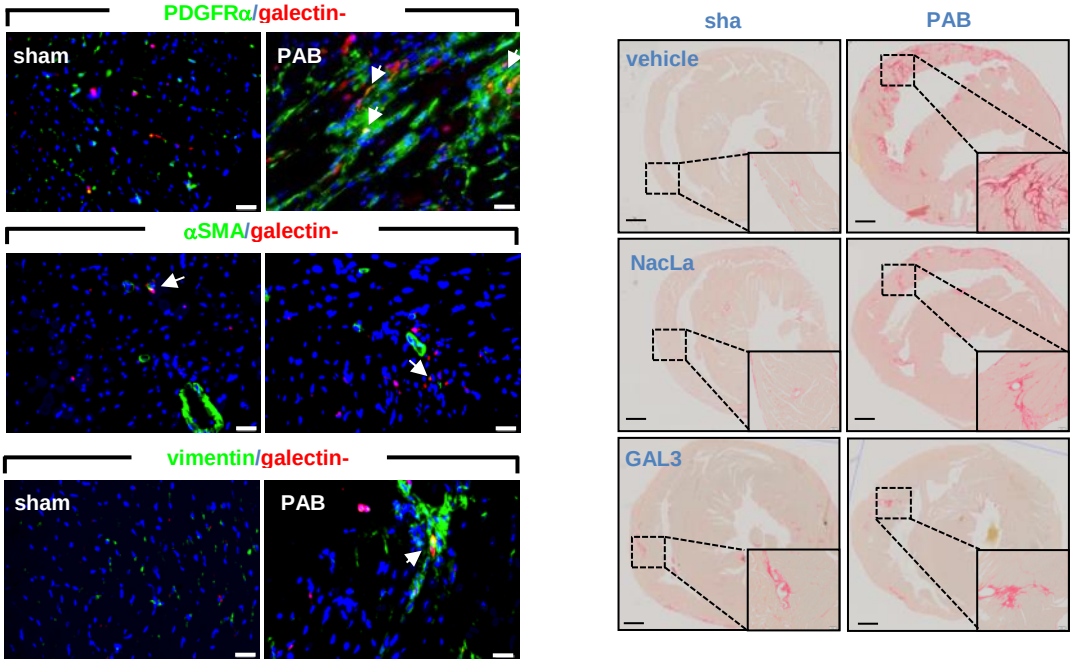


Figure 3. A) Representative immunofluorescent staining of RV fibrotic regions against galectin-3, vimentin, PDGFRα, and αSMA; n=4 mice/group (3 weeks PAB). Scale bar: 20 µm. B) Pharmacological inhibition and genetic deletion of galectin-3 ameliorates the progression of right ventricle (RV) fibrosis. Representative sirius red staining of hearts were collected from inhibitor (NacLac), knockout (GAL3 KO) or vehicle/wild type (WT) treated mice 21 days post randomization and treatment. Scale bar: 500 µm.

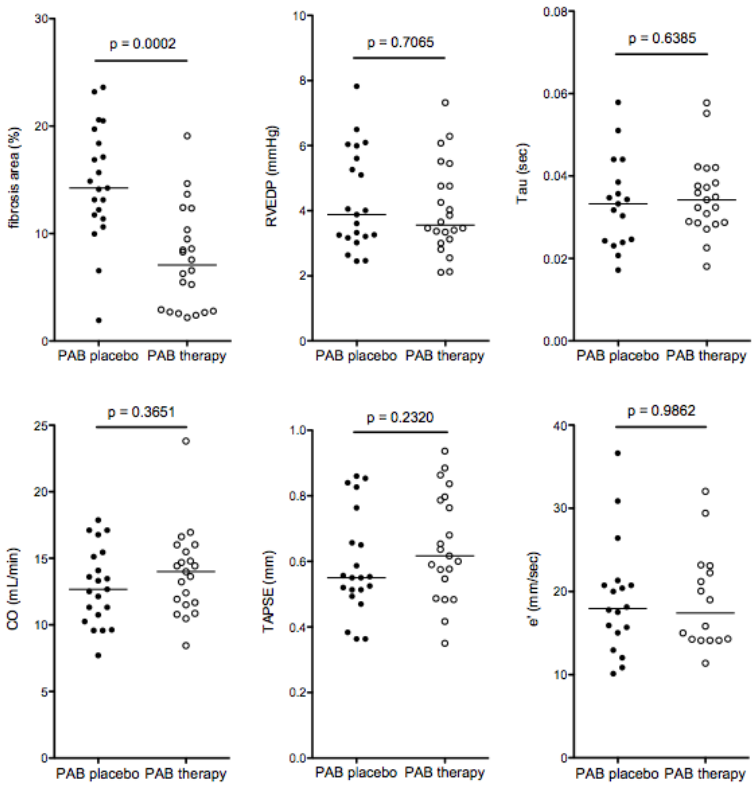


Figure 4. Lack of improvement in RV functional parameters despite effective amelioration of RV fibrosis. Fibrosis was assessed 21 days after pulmonary artery banding operation in controls or treated mice (galectin-3 inhibitor NacLac, galectin-3 knock-out mice, pirfenidone). Pooled measurements of RV fibrosis area, RV end diastolic pressure (RVEDP), tau (time constant of monoexponential curve fitting model of RV diastolic pressure decay), cardiac output (CO), tricuspid annular plane systolic excursion (TAPSE), and RV relaxation velocity (e').

Scientific Cooperations

ALLANORE Yannick M.D., Cochin Hospital, Paris, France
BELLUSCI Saverio, PhD., Justus Liebig University, Giessen, Germany
EFERL Robert Dr., Medical University of Vienna, Austria
HASSOUN Paul M., M.D., Johns Hopkins University, Baltimore, Maryland
HEINEMANN Akos Prof., Medical University of Graz, Austria
HOEFLER Gerald Prof., Medical University of Graz, Austria
KLEPETKO Walter Prof., Medical University of Vienna, Austria
KUEBLER Wolfgang Prof., St. Michael's Hospital, Toronto, Canada
MORRISEY Ed Prof., University of Pennsylvania, Philadelphia, USA
PEREZ Vinicio de Jesus, M.D., Stanford University, Stanford, California
WEIR E. Kenneth Prof., University of Minneapolis, Minnesota, US
WEISSMANN Norbert Prof., ECCPS, University Giessen Lung Centre, Giessen, Germany
WILHELM Jochen Dr., University Giessen Lung Centre, Giessen, Germany
WITZENRATH Martin Prof., Charité –University Medical Department, Berlin, Germany
WYGRECKA Malgorzata Prof., University Giessen Lung Centre, Giessen, Germany

2.2 Translation Platform of the LBI-LVR

The Translational Platform bridges the institute's molecular and clinical arms. By using pre-clinical models, we investigate the role of specific genes and molecules in vivo and determine how they contribute to disease pathogenesis. The Translation platform provides crucial resources, which facilitates the planning, coordination and implementation of in vivo experiments. The use of standard operating procedures ensures all experiments and analyses are performed according to the highest standards. An overview of available techniques and readouts are shown in Figure 1.

During 2018, the team expanded with the inclusion of a part-time bioinformatician, Dr Natalie Bordag. Natalie complements the translational platform with her expertise in metabolomics and data interpretation. Following successful application for FFG funding, Diana Schnögl joined the team as a PhD student.

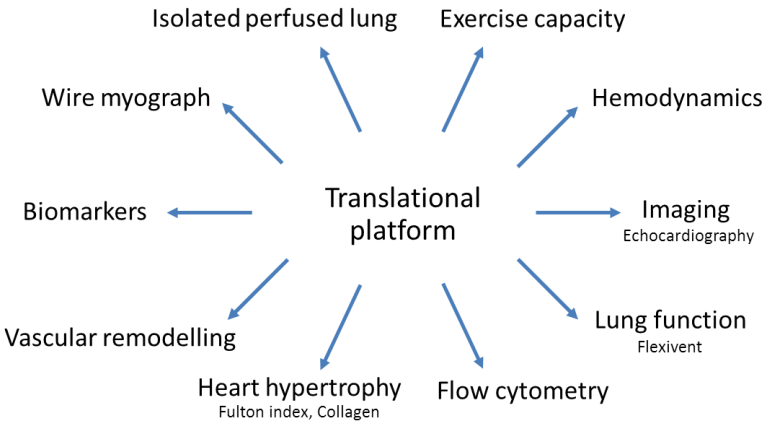


Figure 1. Overview of techniques available in the translation platform

These techniques and readouts contributed to six peer-reviewed articles published by the LBI-LVR during 2018. Highlights of these articles include "*Disconnect between Fibrotic Response and Right Ventricular Dysfunction*" by Slaven Crnkovic et al published in the American Journal of Critical Care Medicine in December 2018, and "*The inflammatory cell landscape in the lungs of patients with idiopathic pulmonary arterial hypertension*" by Leigh Marsh and colleagues in the European Respiratory Journal in Jan 2018. In our paper "*Fra2 Overexpression in Mice Leads to Non-allergic Asthma Development in an IL-13 Dependent Manner*" by Anna Gungl et al., we describe how the overexpression of the AP-1 transcription factor family member Fra2, produces a strong Th2-inflammatory environment and was associated with pronounced airway remodelling and airway hyperactivity. This asthma-like phenotype was induced without the need for additional allergen challenge. Via intervention strategies, we could show that this phenotype could only be partially reversed by treatment with anti-IL-13 antibodies or by inhaled corticosteroids. This data suggests that the morphological and functional changes caused by Fra2 overexpression are due to a combination of direct effect of Fra2 overexpression and activation of the IL-13 pathway.

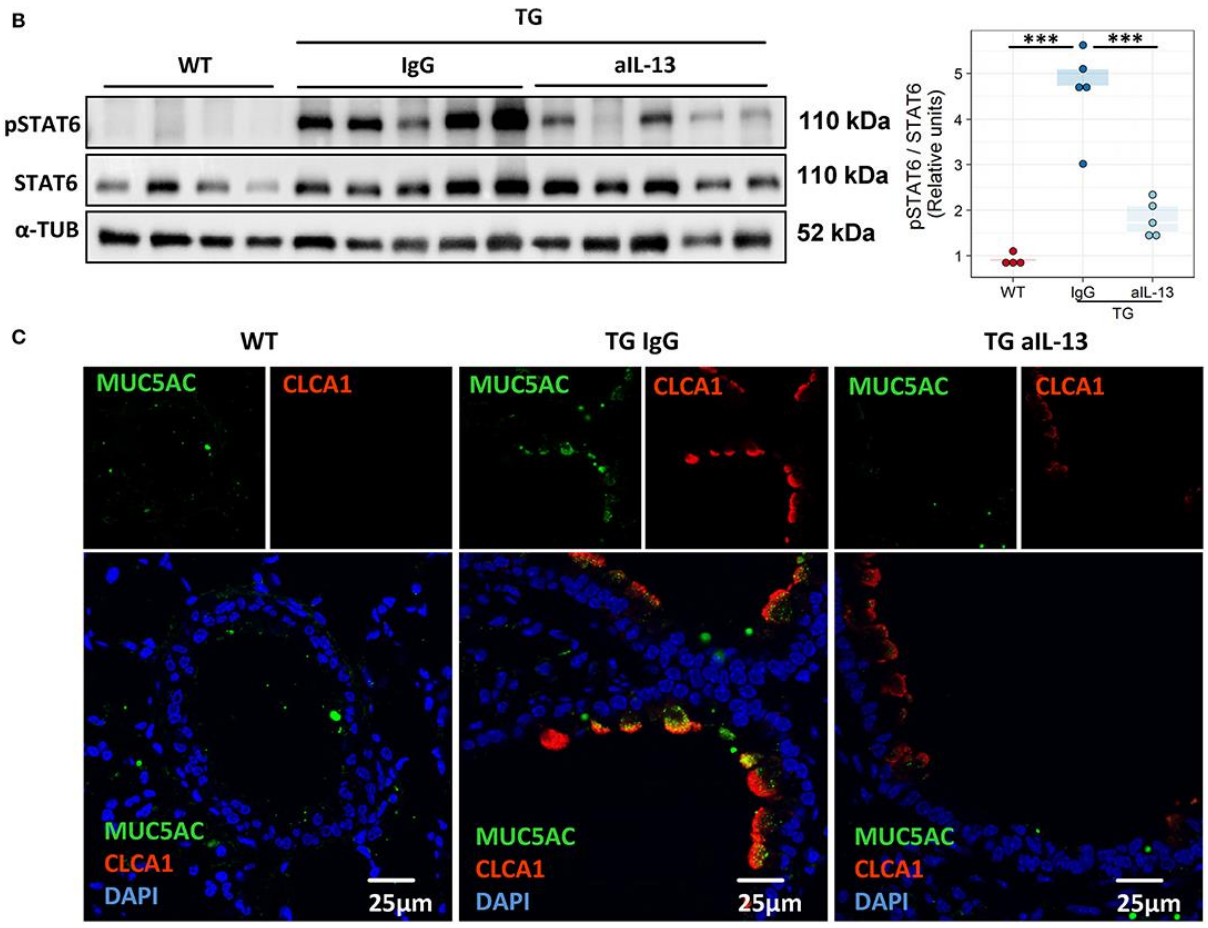


Figure 2. Blocking of IL-13 signaling decreases STAT6 activation and downstream remodelling caused by the overexpression of Fra2. Figure modified from Gungl A et al., Front Immunol. 2018 Sep 5;9:2018.

Scientific Cooperations

GRUNIG Gabriele Dr., New York University School of Medicine, New York, USA
HAITCHI Hans-Micheal Dr., University Hospital Southampton, UK
HEINEMANN Akos Prof. Medical University of Graz, Austria
STROBL Herbert Prof. Medical University of Graz, Austria

2.3 Clinical Studies

Project overview and main research results

The major research interest of the clinical arm of the LBI is the promotion of early diagnosis of pulmonary hypertension (PH), the appropriate integration of innovative non-invasive tools in the management of PH, the understanding of the clinical relevance of pulmonary hemodynamics during exercise and the recognition of a pulmonary vascular component in chronic lung diseases. In 2018, there were three major projects among these which we would like to highlight.

Clinical Research Collaboration - Pulmonary Hemodynamics during Exercise Research Network (PEX-NET)

In subjects with normal pulmonary arterial pressure at rest, an abnormal increase during exercise in relation to the increase in pulmonary arterial blood flow has been proposed as a condition termed “exercise pulmonary hypertension” (exercise PH). Exercise PH may represent an early stage of pulmonary vascular disease and other pathologic mechanisms in the heart and/or in the lungs. All these mechanisms may lead to dyspnoea on exertion which is one of the most worrying symptoms in respiratory medicine. Currently available data support a definition for exercise PH as an increase in the mean PAP > 30 mmHg combined with an increase in total pulmonary resistance > 3 Wood Units during maximal exercise. Probably the most important unanswered clinical question in the field is whether exercise PH is of prognostic relevance. In order to provide solid evidence and to answer this question a multi-centre, long-term registry study was initiated by the Clinical Arm of the LBI. This study is supported by the European Respiratory Society as the “Pulmonary Hemodynamics during Exercise Clinical Research Network (PEX-NET)” and until now 34 international PH expert centres have joined the project. An overview on PEX-NET can be read in an editorial of the European Respiratory Journal by Kovacs et al. in 2019.

The web-based PEX-NET database has been developed in close collaboration with the Institute for Medical Informatics, Statistics and Documentation at the Medical University of Graz. The database has been developed in Clincase®, a web-based, 21 CFR (Code of Federal Regulations) 11-compliant Electronic Data Capture system for multicentre clinical trials. In the retrospective part of the database, prevalent data provided by the centres will be analysed. Data entry began in 2018 and by the end of the year the data of n=77 patients were included. We expect that within the next two years over 1000 patients will be included (all available patients with clinically indicated right heart catheterization with exercise hemodynamics and sufficient follow-up data from the participating centres). Also in the prospective part, the first patients were included in 2018. In these individuals, study end points will be prospectively documented for a planned duration of five years. The planned number of patients in the prospective part is 498. Main elements of a centre specific hemodynamic protocol are shown below.

Highly flexible PEX-NET database for capturing data from different laboratories with diverse devices and protocols (from Kovacs et al. Eur Resp J 2019)

- patient position: supine, semi-supine or upright
- achieved maximal exercise: maximal effort or other
- exercise method: cycle-ergometry or other
- zero reference level: mid thoracic level in the supine patient, the intersection of the frontal plane at the mid thoracic level, the transverse plane at the level of fourth anterior intercostal space, and the midsagittal plane in the semi-supine patient, or other
- determination of cardiac output: direct Fick method or thermodilution
- determination of pressure values: averaged over 3-5 respiratory cycles or other
- transition from rest to exercise: changes in any relevant condition (position, zero level, determination of pressures, breathing maneuvers, cardiac output assessment)?

We are convinced that PEX-NET will provide answers regarding the prognostic relevance of pulmonary hemodynamics during exercise and will stimulate further research on the underlying pathophysiology of exercise PH as well as on the diagnostic and therapeutic options for patients.

Healthy lung vessel morphology

In 2018 we continued our projects on automatic algorithms derived from computed tomography images on the pulmonary vessels. In order to recognize pathologic deviations beyond the normal inter-subject variation, it is of great importance to describe the properties of the healthy lung vasculature. Knowledge of the lung vessel morphology in healthy subjects is also necessary to improve our understanding about the functional network of the lung. In order to determine morphologic readouts from a large number of healthy subjects, computed tomography pulmonary angiography datasets, negative for pulmonary embolism, and other thoracic pathologies, were analyzed using a fully-automatic, in-house developed artery/vein separation algorithm. Validation of the algorithm was performed manually by a radiologist on randomly selected subjects. The algorithm provided reliable measures of pulmonary arteries and veins with respect to age and gender which can be used in order to provide reference values for morphometric analysis of lung vessels. As expected, there was a large variation between subjects in all readouts. No relevant dependence on age, gender, or vessel type was observed. Interestingly, the vessel density was about 15% higher in women than in men.

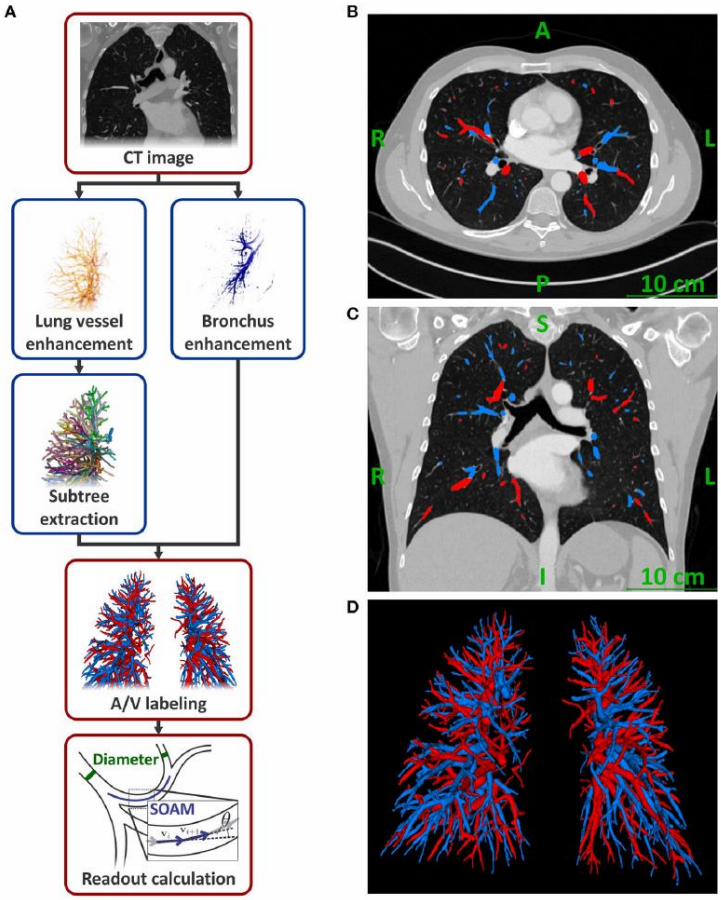


Figure 1. Flowchart of the fully-automatic artery/vein separation algorithm (A). Representative computed tomography pulmonary angiography images in transversal (B) and coronal (C) plane of a male subject with automatically labeled arteries and veins. Representative 3D rendering of the detected vessel trees from the same subject (D). Arteries are colored blue; veins are colored red. (from Pienn et al. Frontiers Physiology 2018)

Pulmonary Vascular Phenotype in chronic obstructive lung disease

In 2018, a very experienced group of world-wide known experts on airway diseases and a similar group on pulmonary vascular diseases formed an expert panel led by the Clinical Arm of the LBI in order to develop a working definition on the Pulmonary Vascular Phenotype in chronic obstructive lung disease (COPD). This represents a new way of thinking and views simultaneously the epithelial and endothelial dysfunction in the lung leading through different pathways and interactions between both systems (Figure 2) to abnormalities of the airways and the vessels. From the clinical point of view, the presence of pulmonary vascular disease in COPD is associated with poor prognosis and frequent exacerbations. In most cases the presenting pulmonary hypertension (PH) is relatively mild, but in a subset of COPD patients, the presence of certain clinical features supports the existence of a “pulmonary vascular phenotype”. Such a phenotype is characterized by severe pre-capillary PH with strongly elevated pulmonary vascular resistance, moderate airflow limitation, severely decreased diffusion capacity for carbon monoxide, normo- or hypocapnia, circulatory exercise limitation and progressive right heart failure. The work of this expert panel prepared the field for studies in clinical and baseline research in order to better understand the pathobiology to improve early recognition and to develop novel therapeutic concepts for the COPD pulmonary vascular phenotype.

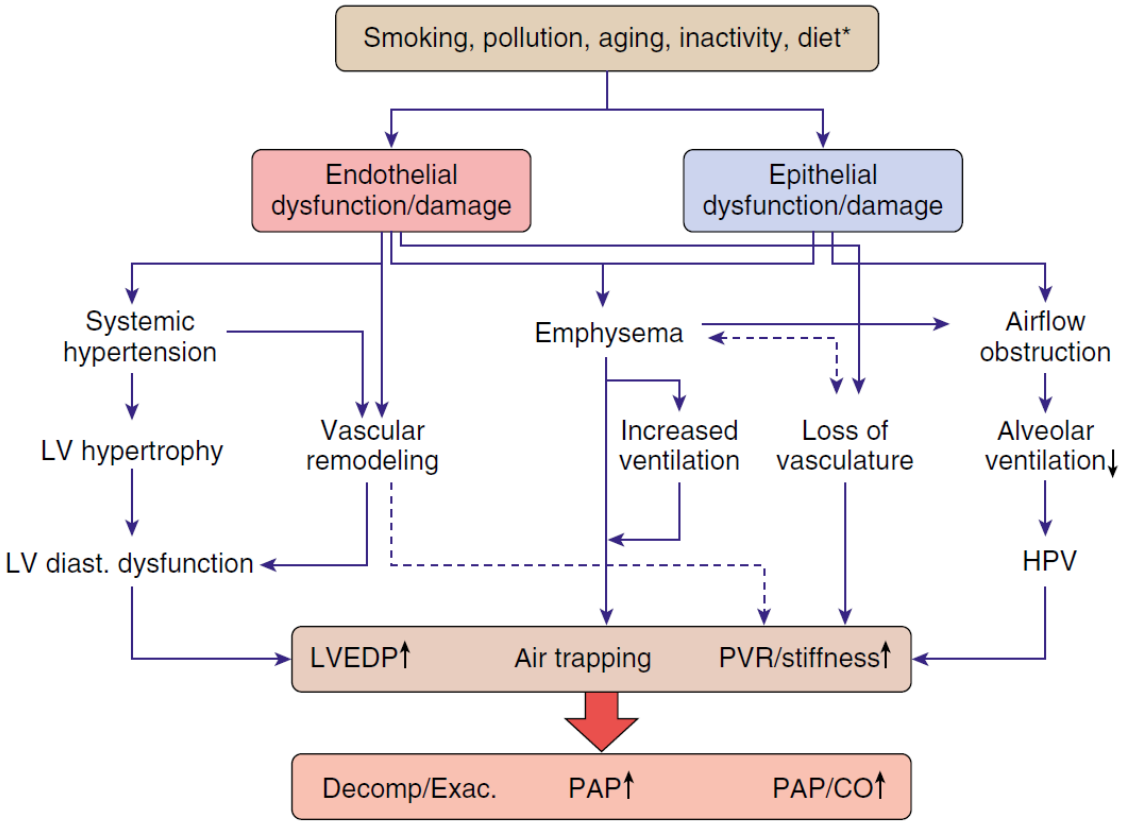


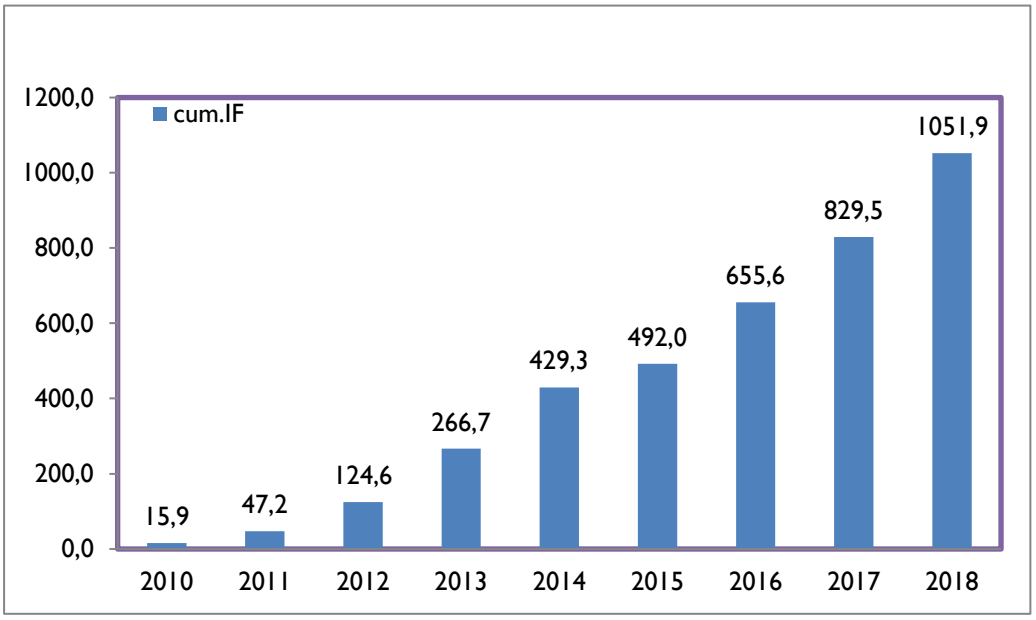
Figure 2. Emergence of epithelial and endothelial dysfunction and interaction of cardiac, thoracic, and pulmonary vascular factors contributing to the development of pulmonary hypertension in COPD. (from Kovacs et al. AJRCCM 2018). CO = cardiac output; HPV = hypoxic pulmonary vasoconstriction; LV = left ventricular; LVEDP = left ventricular end-diastolic pressure; PAP = pulmonary arterial pressure; PVR = pulmonary vascular resistance

Scientific Cooperations

AVIAN Alexander, Mag. Medical University of Graz, Austria
BERGHOLD Andrea, Prof. Medical University of Graz, Austria
BRODMANN Marianne, Prof. Medical University of Graz, Austria
CONDLIFFE Robin, Prof. Sheffield University, England
GRANINGER Winfried, Prof. Medical University of Graz, Austria
D'ALTO Michele, Prof. University of Campania, Neaples, Italy
DUMITRESCU Daniel, Dr. University of Cologne, Germany
FUCHSJÄGER Michael, Prof. Medical University of Graz, Austria
HAFNER Franz, Prof. Medical University of Graz, Austria
HERMANN Josef, Prov.Doc. Medical University of Graz, Austria
HORWARTH-WINTER Jutta, Priv.Doc. Medical University of Graz, Austria
JACOB Joseph, Dr. Royal Brompton Hospital, United Kingdom
JOBST Bertram, Dr. Heidelberg University Hospital, Germany
LANGE Tobias Dr. University Clinic Regensburg, Germany
LAWRIE Allan, Prof. Sheffield University, England
MAIER Robert, Prof Medical University of Graz, Austria
MARON Bradley, Prof. Harvard Medical School, Boston, USA
MOAZEDI-Fürst Florentine, Dr. Medical University Graz, Austria
MORRELL Nicholas, Prof. Cambridge University, Great Britain
MÜLLER Veronika, Prof. Semmelweis University Budapest, Hungary
NAEIJE Robert, Prof. Free University of Brussels, Belgium
OCCIPINTI Mariaelena, Dr. University of Florence, Italy
ODLER Balazs, Dr. Medical University of Graz, Austria
RAGGAM Reinhard, Dr. Medical University of Graz, Austria
REITER Ursula, Dr. Medical University of Graz, Austria
SCHLENKE Peter Prof. Medical University of Graz, Austria
STAUBER Rudolf, Prof. Medical University of Graz, Austria
STOLLBERGER Rudolf, Prof. University of Technology Graz, Austria
TORNYOS Adrienn, Dr. Medical University of Graz, Austria
ULRICH Silvia, Prof. University of Zurich, Switzerland
URSCHLER Martin, Dr. LBI for Clinic Forensic Imaging, Austria

2.4 Publications of the LBI-LVR 2018

Starting in 2010 when our institute was first founded, the cumulative impact factor, an indicator for the quality of our scientific publications with LBI-LVR affiliation, reached the remarkable value of 1052 by the end of the year 2018.



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3 Clinical Research

For this year's annual report, four of our colleagues related to the clinical studies department were available for an interview about "Clinical Research". Exciting answers and insights into their daily work were given to us.

3.1 Interview with Philipp Douschan

What does "clinical research" mean to you?


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Clinical research is patient orientated. It focuses on the development of novel screening tools and algorithms for early detection of diseases on the one hand and it is responsible for high quality studies evaluating the effect of novel drugs aiming to ease suffering and to enhance the quality of patients` life on the other hand.

Why is clinical research exciting / interesting for you?

I believe that observations from clinical routine are the fundament for major developments in medical science. Problems observed during clinical routine may lead to novel concepts in the understanding of diseases.

Can you briefly introduce your field of research?

As physician and clinical scientist, I am sharply focused on the early detection and definition of pulmonary hypertension. In one of my recent projects, I was able to point out that even mild elevations of the mean pulmonary arterial pressure are of prognostic relevance. My special interest lies in non-invasive screening tools, such as echocardiography and exercise echocardiography. I am also focused on subgroups of patients at increased risk of pulmonary vascular disease, such as patients with liver disease and collagen vascular disease.

How did you get into the research? / What motivated you?

During my time as a diploma student, I got in touch with research groups at the Medical University of Graz. Shortly after, I became a research fellow there. I was taught by my supervisors, all of them working as physician-scientists, how to perform clinical science. The possibility to gain new insights into disease mechanisms and to take actively part in the development of new diagnostic- and treatment strategies motivated me to continue with science after medical school.

3.2 Interview with Vasile Foris

What does "clinical research" mean to you?

For me clinical research means collecting and analysing patient associated data and laboratory data from the examinations that we perform in our daily routine. Moreover, we often generate data from extra investigations for research purposes that are not in the routine but as a result of systematic analysis, these investigations may become also part of the routine practice. Additionally blood analysis for yet unknown markers is also an important part of the clinical research. In order to perform high quality clinical research you should always ask a valid research question which has not been answered yet. I strongly believe that every clinician is a somehow a researcher.

Why is clinical research exciting / interesting for you?

The results of clinical research may have an immediate impact on our diagnostic and therapeutic decisions. By performing clinical research, you often have the opportunity to see interesting patient cases, which are atypical, however later they will become typical once we know the undelaying mechanisms, diseases and eventually treatment. The search for “something typical” is the most exciting part.

Can you briefly introduce your field of research?

My aim is to find biomarkers that can be developed into laboratory tests that will help patients with pulmonary hypertension for early diagnosis, as well as treatment decisions. I am basically bridging the laboratory and the clinic.

How did you get into the research? / What motivated you?

I was always wondering how the human body works, what drives different diseases and what can we do in order to avoid diseases as well as to treat them. That is why I decided to study medicine. I also was interested in research so I decided to do my PhD and to work also as a researcher. The exciting part for me is always the challenge to find out the right diagnosis and to tailor treatment in a very personalized way.

3.3 Interview with Piet Rosenstock

What does "clinical research" mean to you?

For me, clinical research means on the one hand the development of modern diagnostics and on the other hand the development of new therapeutic possibilities where patients can be included. That means that patients have the opportunity to get involved in researching their specific diseases.

Why is clinical research exciting / interesting for you?

As a student, it is very interesting to be involved in clinical research and to get the opportunity to work on the research of modern diagnostics. I am particularly excited about participating in clinical trials. Another interesting point of clinical research is to see how a research network works. Different people work together and make progress in research.

Can you briefly introduce your field of research?

First of all, I am responsible for database administration and for data maintenance concerning study purposes. Here I get tasks and support from Gabor Kovacs. In addition to this field of research, I am part of a study, which is called “Non-invasive diagnosis of pulmonary hypertension with impedance-cardiography - a prospective study”.

How did you get into the research? / What motivated you?

During the work for my diploma thesis "Screening and therapy for latent tuberculosis before liver, kidney and heart transplantation at the LKH Graz between 2007 and 2012” I got in contact with the research institute, especially to Gabor Kovacs. Working in a Research institute has always been interesting for me, especially since research is the foundation of modern medicine.

3.4 Interview with Teresa Sassmann

What does "clinical research" mean to you?

For me, clinical research means science directly for people. By performing clinical studies, I am able to understand diseases better. Thus, I gain knowledge in order to offer patients the best available diagnostic tools and therapy at any time.

Why is clinical research exciting / interesting for you?

Being a clinical researcher, I have one finger on the pulse of time. Science allows me to be an active part by influencing the future of standard knowledge. In addition, we are able to suggest, offer, and prove new therapies and diagnostic tools at the very beginning. Placing new ideas in the name of research is my passion.

Can you briefly introduce your field of research?

Patients undergo several diagnostics, such as blood-gas-analysis, lung function test, echocardiography, and sometimes even right heart catheterization, when applied to our clinic. As a medical student, my job is to find and transfer these clinical data to our research database. In this regard, I have to check, whether the data is complete and correct. Moreover, I am also dealing with echocardiography, a non-invasive real-time assessment of the structural and functional heart.

How did you get into the research? / What motivated you?

While working on my diploma thesis about diastolic dysfunction in liver cirrhosis at Department of Pneumology, Gabor Kovacs asked me to become a part of his working group. The opportunity to influence the diagnostic and therapy of my patients is both, exciting and challenging, but also a unique chance for me to push boundaries. My motivation is also a result of those who taught, led, and supervised me. That is why I would like to thank Gabor Kovacs, Philipp Douschan and Horst Olschewski.

4 Teaching and Training Activities of the Institute

4.1 Training in the LBI for Lung Vascular Research

4.1.1 Training of the LBI-LVR Staff

Following advanced trainings and congresses were visited in 2018:

Name	Location	Title of the Lecture/ Workshop/Congress
CRNKOVIC Slaven	University of Philadelphia, USA	Biomedical Postdoctoral Council Symposium
FORIS Vasile	Medical University of Graz, Austria	Master of Science Biobanking (2018-2020), master program
GIULIANI Nikola	Funchal, Madeira, Portugal	13th International Joint Conference on Computer Vision, Imaging and Computer Graphics Theory and Applications (VISIGRAPP 2018),
GUNGL Anna	USA	FASEB scientific research conference
	Linz, Austria	ÖGP Jahrestagung
	Paris, France	ERS International Congress
JANDL Katharina	Amsterdam, Netherlands	Congress
	Linz, Austria	ÖGP Jahrestagung
	Vienna, Austria	LBG / ÖAW Workshop
	Vienna, Austria	FWF Information
KLEINSCHEK Daniela	Hof, Salzburg, Austria	1st PH Nurse Workshop
KOVACS Gabor	Heidelberg, Germany	DACH Symposium
	Innsbruck, Austria	Österreichischer Kollagenosenkongress
	Linz, Austria	ÖGP Jahrestagung
	Köln, Germany	International Congress of spiroergometry
	Lissabon, Portugal	ERS Summer School
	San Diego, USA	American Thoracic Society Congress
	St. Gallen, Suisse	SEP Congress (Schweizer Gesellschaft für Pulmologie)
	Mannheim, Germany	DGIM (Deutsche Gesellschaft für Pulmologie)
	Dresden, Germany	DGP Congress (Deutsche Gesellschaft für Pulmologie)
	Schaffhausen, Suisse	ERS Hermes Comites Sitzung

	Nice, France	6th World Symposium on Pulmonary Hypertension
KWAPSIZEWSKA Grazyna	Heidelberg, Germany	DACH Symposium
	Linz, Austria	ÖGP Jahrestagung
	Amsterdam, Netherlands	Congress
	Vienna, Austria	ÖGTERM
	San Diego, USA	American Thoracic Society Congress
	Bad Aussee, Austria	Pulmonale Circulation
	Munich, Germany	CPC Conference
	Seggau, Austria	MOLIN-DK Retreat
	Nice, France	6th World Symposium on Pulmonary Hypertension
MARSH Leigh	Vienna, Austria	LBG Science Health Meeting
	Vienna, Austria	Cemm RNASg
	Amsterdam, Netherlands	Congress
	San Diego, USA	American Thoracic Society Congress
	Seggau, Austria	MOLIN-DK Retreat
NAGY Bence	Boston, USA	BAYER Workshop
	Hannover, Germany	Keystone Symposia on Molecular and Cellular Biology
	Graz, Austria	Lipotox Symposia
	Vienna, Austria	LBG / ÖAW Workshop
PIENN Michael	Vienna, Austria	LBG Science Health Meeting
THEKKEKARA-PUTHENPARAMPIL Helene	Patras, Greece	FEBS ECM Conference
	Seggau, Austria	MOLIN-DK Retreat
	Graz, Austria	MUG DocDay
TORNYOS Adrienn	Madrid, Spain	17th International Pulmonary Hypertension Forum
TREITLER Nina	Giessen, Germany	Workshop DS-Färbung
SHARMA Neha	Helsinki, Finland	International vascular biology meeting
	Linz, Austria	ÖGP Jahrestagung
SKOFIC MAURER Davor	Helsinki, Finland	International vascular biology meeting

4.1.2 Invited Speakers 2018

LANKEIT Mareike, PD	Department of Internal Medicine and Cardiology, Charité Universitätsmedizin Berlin	23 JAN 18	Risk assessment following acute pulmonary embolism
BELLUSCI Saverio, MD	ECCPS Professor of Lung Matrix Remodelling at the Justus-Liebig University Giessen, Germany	30 JAN 18	Fibroblast growth factor 10, a master regulator of epithelial and mesenchymal alveolar lineage formation during embryonic lung development and beyond
OBERMAYER-PIETSCH Barbara, MD	Division of Endocrinology and Osteology, Medical University of Graz	13 FEB 18	Bone molecules
ARSCHANG Valipour, MD	Otto-Wagner-Spital Sozialmedizinisches Zentrum Baumgartner Höhe, Wien	6 MAR 18	Different COPD Phenotypes - are they important?
ELLER Kathrin, MD	Division of Nephrology, Department of Internal Medicine, Medical University of Graz	13 Mar 18	Unraveling pathomechanisms in glomerulonephritis
MUSSOLINO Claudio, PhD	Institute for Transfusion Medicine and Gene Therapy, University Medical Center Freiburg	20 MAR 18	Genome and Epigenome Editing to tackle immunodeficiences
GRAIER Wolfgang, MD	Gottfried Schatz Research Center for Cell Signaling, Metabolism and Aging, Medical University of Graz	27 MAR 18	Why the „How“ of mitochondrial calcium uptake matters
LAHM Tim, MD	Indiana University School of Medicine, Richard L. Roudebush VA Medical Center, Indianapolis, Indiana	17 APR 18	Sex differences in pulmonary hypertension — have we come closer to solving the estrogen paradox
SCHAEFER Liliana, MD	Goethe University, Frankfurt/Main, Germany	8 MAY 18	Proteoglycan signaling at the crossroads
PROSCH Helmut, MD	Vienna General Hospital, Medical University of Vienna, Dept. of Biomedical Imaging	15 MAY 18	Chest Computed Tomography of interstitial lung disease – the view of the Radiologist

	and Image Guided Interventions		
VOELKEL Norbert, MD	Virginia Commonwealth University	26 JUN 18	Position and Direction of PAH
BAUM Oliver, PD	Insitute of Physiology, Charité Berlin	18 SEP 18	nNOS in the integration of metabolism and capillary density in skeletal muscle
MORIGGL Richard, MD	Ludwig Boltzmann Institute for Cancer Research	16 OCT 18	Driver mutations in the JAK-STAT3/5 pathways in cancer and how to target them