LUDWIG BOLTZMANN INSTITUTE
Lung Vascular Research

ANNUAL REPORT
2020

Content

Contact

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Team

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Partners

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

Ludwig Boltzmann Gesellschaft

(Website: 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 interdisciplinarity 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

(Website: 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

(Website: 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. Caroline Schober



Mag. Caroline Schober, Medical University of Graz

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

Dr. Heidrun Dorsch, Bayer AG

http://pharma.bayer.com/

Dr. Peter Mayrhofer, Ludwig Boltzmann Gesellschaft

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

1 The Institute in Overview

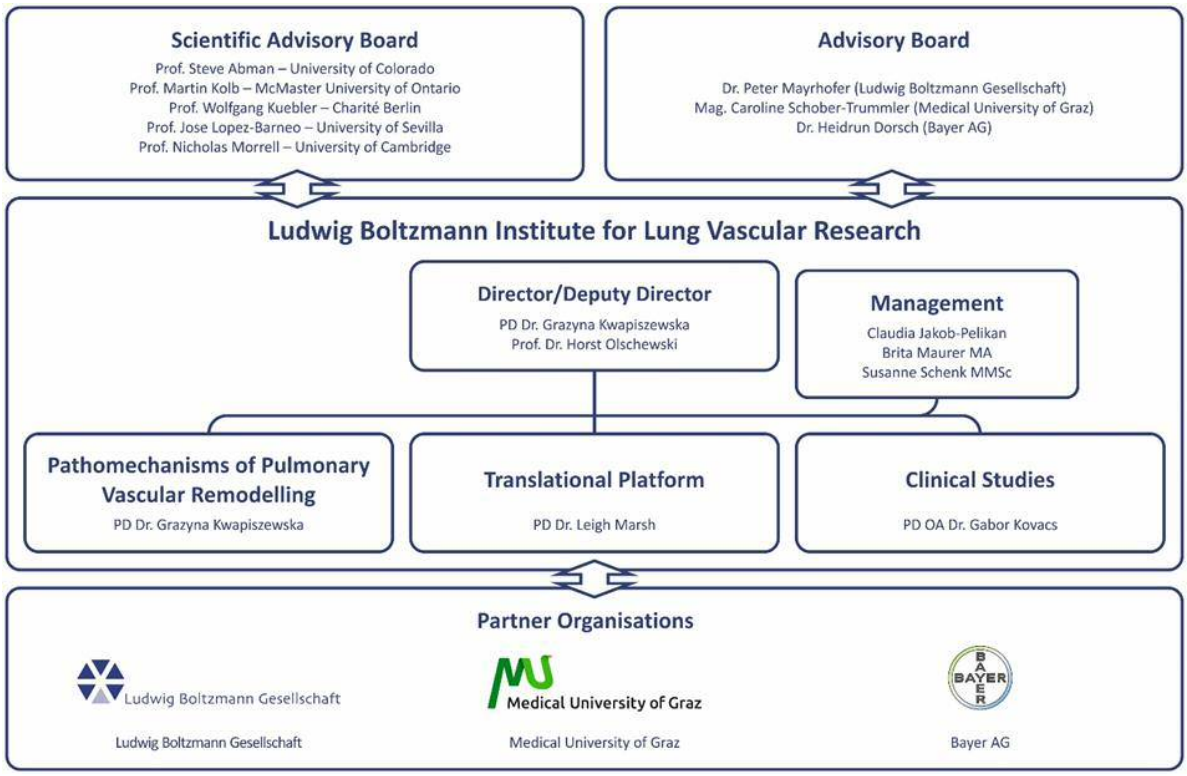
The Ludwig Boltzmann Institute for Lung Vascular Research (LBI-LVR) is a non-profit research institute founded in July 2010 by the Ludwig Boltzmann Gesellschaft (LBG). LBG founded institutes conduct research in the fields of Medicine & Life Sciences or Humanities. The LBI-LVR was established after a 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 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 2020. 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 for Lung Vascular Research has substantial expertise in the basic mechanisms of pulmonary vascular constriction 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.

1.3.2 Graduations of the LBI-LVR Staff in 2020

In 2020, two of our colleagues had their graduation.

MARSH Leigh (Habilitation)
Habilitation in Physiology "The immunophysiology of chronic lung diseases; how the immune system alters lung physiology", Key Researcher at LBI LVR

DOUSCHAN Philipp (Doctor of Medical science)
Dissertation topic: "Clinical relevance of mildly elevated pulmonary arterial pressure", Division of Pulmonology, Medical University of Graz, Austria
and Researcher at LBI LVR

1.3.3 MUG career steps

In 2020, three of our colleagues were taken over by the Medical University of Graz or had important career steps.

CRNKOVIC Slaven
Scientific professorship, Department of Physiology
Medical University of Graz, Austria and Researcher at LBI LVR

KOVACS Gabor
§99(5) professorship, Division of Pulmonology
Medical University of Graz, Austria and Key Researcher at LBI LVR

KWAPISZEWSKA Grazyna
§99(5) professorship, endowed professorship, Department of Physiology
Medical University of Graz, Austria, Director and Key Researcher at LBI LVR

1.3.4 Awards and prizes

Name	Awards 2020
BIRNHUBER Anna	René Baumgart Research Prize, Leipzig, Germany
SHARMA Neha	2nd prize, poster awards at the Annual meeting of the Austrian Society of Pneumology 2020, Vienna, Austria

Name	Travel Awards/Fellowships 2020
DOUSCHAN Philipp	European Respiratory Society Clinical Training Fellowship, Giessen Germany, open due to Covid-19
NAGARAJ Chandran	European Respiratory Society Long-Term Research Fellowship, Budapest, Hungary / open due to Covid-19

1.3.5 Conferences and Meetings of the LBI-LVR Staff

Presentations at national and international conferences: Oral Communications

Pienn M. Quantitative Analyse der Lungengefäßmorphologie - Potential für die Diagnostik der pulmonalen Hypertonie, des Lungenemphysems und der Lungenfibrose. Update RSNA 2019 – Thorax, JAN 10-11, 2020, Cologne, Germany

Sharma N. Neutrophil recruitment in the acute inflammatory phase of interstitial lung disease is determined by RGS5; ÖGP | OGTC annual meeting 2020, OCT 14-16, 2020, Vienna, Austria (virtual) (Nomination for poster prize and Oral Poster Presentation)

Presentations at national and international conferences: Posters

Biasin V, PDGFRα and αSMA mark two distinct mesenchymal cell populations involved in parenchymal and vascular remodeling in pulmonary fibrosis; ERS international congress, September 2020 (virtual)

Biasin V, Steroid hormones influence systemic sclerosis prevalence; eECE (European Congress of Endocrinology), September 2020 (virtual)

Birnhuber A, The CDK4/6 inhibitor, palbociclib intensifies pulmonary inflammation in bleomycin-induced lung fibrosis; ERS international congress, September 2020 (virtual)

Birnhuber A, Pirfenidone exacerbates inflammatory influx to the lung in a mouse model of systemic sclerosis; ÖGP | OGTC annual meeting 2020, OCT 14-16, 2020, Vienna, Austria (virtual)

Jandl K, Basement membrane, a specialized extracellular matrix, shapes endothelial function in IPAH; ERS International Congress 2020, SEP 6-9, 2020 (virtual)

Mutgan A, Pentastatin, a matrikine of type IV collagen, as a potent regulator of endothelial dysfunction in pulmonary hypertension; MolMed Day, MedUniGraz, DEZ 04, 2020, Graz, Austria (virtual)

Nagy B, No indication of insulin resistance in idiopathic PAH with preserved physical activity; ERS International Congress 2020, SEP 6-9, 2020 (virtual)

Pienn, M., Fero, T., Kovacs, G., Olschewski, H., Biederer, J., Jobst B., COSYCONET study group: Lung vessel morphology changes with airway obstruction; ERS International Congress 2020, SEP 6-9, 2020 (virtual)

Schnögl D, Disturbed Innate Lymphoid Cell Function in a Mouse Model of Systemic Sclerosis; ÖGP | OGTC annual meeting, OCT 14-16, 2020, Vienna, Austria (virtual)

1.3.6 Patents of the LBI-LVR

Patents	Inventors
Biomarker for the diagnosis of pulmonary hypertension (PH) Patent No. 16159415.5	H. Olschewski (LBI-LVR), A. Olschewski (LBI-LVR), C. 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. Method for processing images of the pulmonary circulation and apparatus for carrying out this method. Patent No. A 50719/2016.	M. Pienn (LBI-LVR), H. Olschewski (LBI-LVR), G. Kovacs (LBI-LVR) and Z. Bálint (LBI-LVR)
Method and apparatus for processing impedance cardiograms for the assessment of the presence of pulmonary hypertension of a Patient and impedance cardiograph with such a device Patent No. 518396/2017	M. Pienn (LBI-LVR), H. Olschewski (LBI-LVR), G. Kovacs G., Z. Bálint.(LBI-LVR)
Modulation of the calcium-activated chloride channel including TMEM16A represent a novel therapy for pulmonary hypertension (PH) Sold to Bayer AG	A. Olschewski (LBI-LVR), B. Nagy (LBI-LVR), C. Nagaraj (LBI-LVR), R. Papp (LBI-LVR)

1.4 Highlights 2020

1.4.1 Evaluation

The Ludwig Boltzmann Gesellschaft (LBG) invited an international team of experts in order to evaluate the Ludwig Boltzmann Institute for Lung Vascular Research on 9th and 10th of November 2020. This evaluation was a regular procedure within the statutes of the LBG. Independent external experts were invited to evaluate the results of the past period and to give recommendations for the future development.

The meetings of the review panel were chaired by Professor Lucie Clapp and were held online. The panel members submitted independent evaluations based on questions of the LBG before the meeting. During the online-evaluation, the panel had the opportunity to set its own priorities and to adapt the composition of the interviewed groups. The review panel declares that it had full access to the relevant information and was free to ask any questions. The LBG head office accompanied and supported the panel without any influence on the evaluation process or result.

Panel Members

- **Lucie Clapp**, Professor of Vascular Physiology, Deputy Director Institute of Cardiovascular Science, University College London, London, UK
  Clapp, Lucie | FLARRE - UCL – University College London
- **George Giannakoulas**, Associate Professor in Cardiology, Aristotle University of Thessaloniki, AHEPA Hospital, Cardiology Department, Thessaloniki, Greece
  George Giannakoulas (escardio.org)
- **Adam Torbicki**, Department of Pulmonary Hypertension, Thromboembolic Diseases and Cardiology, Centre of Postgraduate Medical Education, Otwock, Poland
  Adam Torbicki - ECZ Otwock (ecz-otwock.pl)
- **Christine Petry**, Programme Director, Deutsche Forschungsgemeinschaft, Bonn, Germany
  DFG Head Office: Christine Petry

Outcome

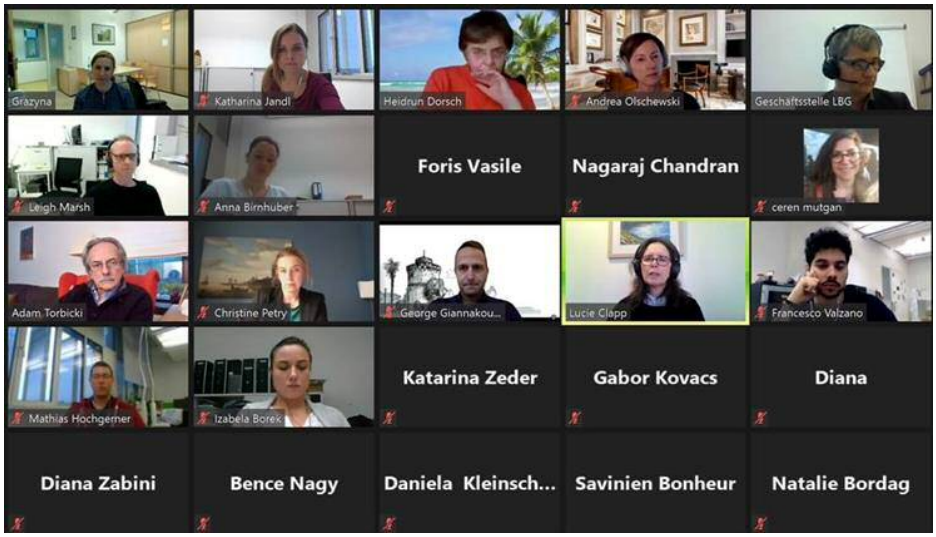
The evaluation was very positive for our Institute. We are pleased to present you the four main messages of the evaluation report:

- Overall, the panel was very pleased with the development of all three programme lines. **The growth of the institute in terms of science as well as in terms of staff development is impressive.** Important progress has been made since the last evaluation with regard to publications and patents as well as third party funding.

- **The Ludwig Boltzmann Institute for Lung Vascular Research has established itself as an institution with a significant international profile.** This international profile is in part related to the **synergy between the three programme lines and the unique setup both in terms of experimental tools (clinical and basic science) and the ability to interrogate research questions "from bench to bedside".**

- This could be even further improved by a more critical evaluation of how results in animal models and patients will actually translate into better healthcare management or knowledge about mechanism of novel drug therapies. **The LBI for Lung Vascular Research offers an excellent environment for young researchers.**

- The panel was especially pleased to see that young researchers identify themselves with and want to work in the LBI: **They see it as a strong functioning unit with a high research output, good training and career opportunities, and a general environment of openness and mutual respect, where they are allowed to flourish**.



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1.4.2 Awards

René Baumgart Research Prize 2020

Anna Birnhuber, PhD was awarded the René Baumgart Foundation Research Prize 2020 for her work "IL-1 receptor blockade shifts inflammation towards Th2 in a mouse model of systemic sclerosis".

Awards at the ÖGP Annual Conference 2020 for the LBI-LVR

Our PhD student Neha Sharma received the 2nd Poster Prize of the Austrian Society of Pneumology. She was awarded for her study on the RGS5 molecule, which plays an important role in acute lung failure.

1.4.3 Fellowships

European Respiratory Society Long-Term Research Fellowship

Chandran Nagaraj was awarded with the European Respiratory Society Long-Term Research Fellowship, Budapest, Hungary.

European Respiratory Society Clinical Training Fellowship

Philipp Douschan was awarded with the European Respiratory Society Clinical Training Fellowship, Giessen Germany.

1.4.4 Grants

FWF Grant for Slaven Crnkovic

Slaven Crnkovic, PhD, has received the ERA CVD JTC Grant for his project "IMPHLeXIONS" in 2019. This is a FWF grant for Transnational Cardiovascular Research Projects driven by Early Career Scientists.

Start of the project: May 2020

IMPHLeXIONS: Inflammation and Metabolism in Pulmonary Hypertension are linked to skewed chromosome X inactivation

Pulmonary arterial hypertension is a rare, but progressive fatal disease of the pulmonary circulation affecting primarily females. The INPHLeXIONS project consortium will investigate the underlying

molecular mechanisms that lead to the observed gender bias in this disease. Research groups from Austria, Germany and Canada will apply newly developed technologies to characterize aberrant inactivation of X chromosome-linked genes involved in inflammatory and metabolic processes. Gained insights will be used to develop and validate novel therapeutic options for pulmonary arterial hypertension.

Project partners: Konda Babu Kurakula (Max-Planck-Institute for Heart and Lung Research, Germany) and Roxane Paulin (Universite Laval, Canada)

FWF KLIF grant for Leigh Marsh (KLI 844-B)

Leigh Marsh, has received a FWF KLIF grant (Programme Clinical Research) for his project "Inflammatory profiling in chronic lung disease"

Start of the project: January 2021

"Inflammatory profiling in chronic lung disease"

Inflammation plays an important role in mediating vascular remodeling in the idiopathic form of pulmonary hypertension (PH). In this context, the accumulation of inflammatory cells in and around the vessel wall correlates with the degree of vascular remodeling. However, very little is known about the role of inflammation in PH in the context of chronic lung disease. In this study, we will determine whether an underlying inflammatory cell profile exists in all forms of PH and how these cells regulate vascular remodeling processes.

FFG grant for Leigh Marsh

Leigh Marsh, was awarded with an FFG grant (Programme Industrial Dissertation) for the project "Involvement of the pulmonary vasculature in the development of pulmonary fibrosis"

Start of the project: July 2020

"Involvement of the pulmonary vasculature in the development of pulmonary fibrosis"

Pulmonary fibrosis is a central and serious problem in various diseases with pulmonary involvement. The pathogenesis of PF depends on the interaction of different pulmonary cell types, ultimately leading to destruction of lung architecture and respiratory deficits. Because the vascular compartment is severely affected, an important role of endothelial cells in disease pathogenesis is suggested. Therefore, we will systematically investigate the mechanisms of vascular maintenance and EC behavior during fibrosis initiation and progression.

1.4.5 Events

SAB Retreat Hotel Loisium, Ehrenhausen, Styria 2020

From September 17th to 18th, 2020, the annual retreat of the LBI LVR took place at the Hotel Loisium in Ehrenhausen, Styria, in compliance with the COVID 19 regulations prescribed by the authorities. Our young colleagues presented their current projects and results. Afterwards, stimulating discussions on the presented topics took place among the participants.

On a common hike along the wine trail, these discussions could be deepened even after the end of the seminar.

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Annual meeting of the Austrian Society of Pneumology

The annual meeting of the Austrian Society of Pneumology was supposed to take place in Graz this year, but had to be held online due to the SARS CoV-2 pandemic. Nevertheless, pneumologists, respiratory physiotherapists, nurses, scientists and students with an interest in pneumology not only registered in large numbers, but actually actively participated between October 14 and 16 to contribute to each other. The more than 1000 participants made the success of the meeting in the new format possible.

One of the main topics - also in these lectures - was COVID-19, with experts from Germany and Austria presenting the current situation of the pandemic and the latest study results. In this regard, a position paper has already been published by the Austrian Society of Pneumology in Wiener Klinische Wochenschrift and serves as a guide for pulmonologists working in Austria.

On the first day, an interesting session on pulmonary hypertension and associated diseases took place. In addition, interstitial lung disease, eosinophilic asthma, and small cell lung carcinoma, among others, were discussed. At the end of the day, the classic "case of the year" session took place, with challenging patient cases brought by the Austrian lung centers. The second day of the congress had an intensive program, discussing topics such as rehabilitation, smoking and vaping, bronchoscopy, and pneumonia. Abstracts and oral poster presentations were also presented, as well as free papers from the Austrian Society of Thoracic Surgery. The last day of the congress was dedicated to interdisciplinarity with numerous updates on COPD, Cystic Fibrosis, Allergology and Pneumologic Oncology being presented.

During the meeting of the Pulmonary Circulation Working Group, **Gabor Kovacs** announced that he would be stepping down from the chairmanship of the Working Group next year due to his concurrent role as Vice President of the Society. Judith Löffler-Ragg from the University Hospital Innsbruck was elected as the new head of the working group. **Philipp Douschan** was elected as the new deputy head.

1.5 Public Relations

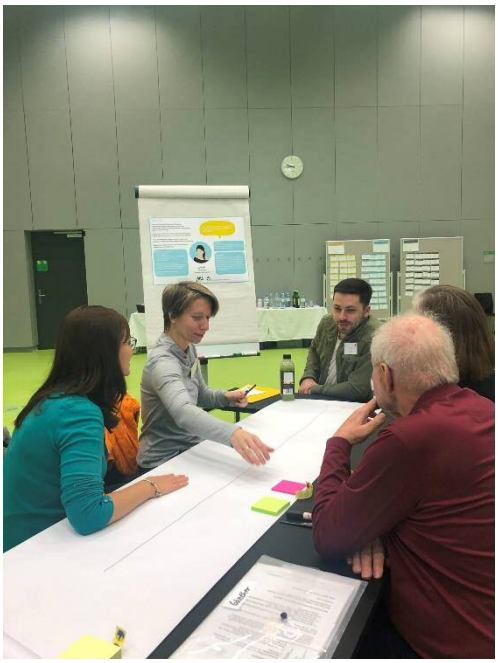
Update from CONNECT - European Researchers Night

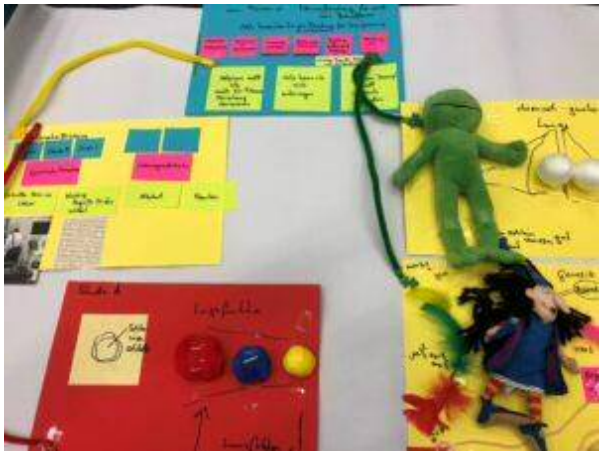
The CONNECT project took part in the European Researchers Night on November 27, 2020 under the title:

„PatientInnen Involvierung in der Lungengefäßforschung".

The project deals with the participation of different user groups in research on fibrosis, with a focus on pulmonary fibrosis. Fibrosis is characterized by a pathological proliferation of connective tissue, which leads to scarring. In addition, the different types of fibrosis are to be networked in this context. The involvement of the user groups takes place through co-creation workshops. According to the Open Innovation in Science process, patients, relatives, therapists and caregivers will be involved in this project to enable an optimal comprehensibility of the current research results.

The implementation of the presentation of such research results is done by special videos, in which the researchers present their current results in a simple way and in German language. The aim of the project is to disseminate comprehensible research results concerning fibrosis on a platform and thus to identify user groups that actively participate in research projects.





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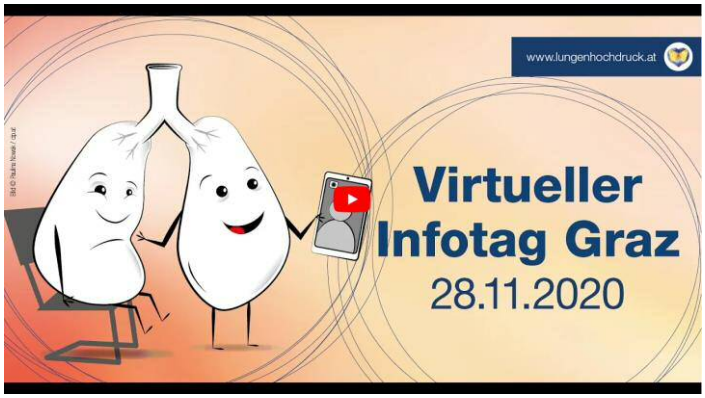
Virtual Patient Meeting on November 28th, 2020 - A Joint information day for patients with pulmonary fibrosis and / or pulmonary hypertension and relatives

On November 28th, 2020, the virtual patient meeting was held. The topic was the COVID-19 pandemic and its impact on patients with pulmonary hypertension. During the information day, Horst Olschewski gave a lecture in which he presented the most important facts about the virus and the disease. He also presented the case of a patient who was treated at our clinic. Although he had suffered severe complications, he was finally able to leave the hospital healthy. At the end of the lecture, practical questions that concern our patients the most were discussed together.

You can find the recording of the virtual info day in Graz with our colleagues Horst Olschewski and Gabor Kovacs, Eva Otter and Monika Tschida, (both PH Austria) here:

PH Austria Infotag Graz am 28.11.2020 - YouTube



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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

Med Uni Graz

Newsletter

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

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9 Im Focus: Philipp Douschan
10 Connect: komplexerte Studien einfach erklärt
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13 Pflegegeld
15 Quiz
16 Spenden für Lungengefäß-forschung
16 Korrespondenz, Rückmeldung, An- und Abmeldung, Impressum

Klinische Programmlinie des Ludwig Boltzmann Institutes für Lungengefäßforschung
V.l.n.r. hinten: Savinien Bonheur, Piet Rostenstock, Teresa Sassmann, Antonia Eger, Philipp Douschan, Vasile Foris, Michael Pienn
Vorne: Daniela Kleinschek, Gabor Kovacs, Horst Olschewski
Nicht am Bild: Katarina Zeder

Ausgabe 13/2020
Jahrgang 7
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Ludwig Boltzmann Institut Lungengefäßforschung

Med Uni Graz

Newsletter

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

In diesem Newsletter

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COVID-19 und PH: ein Bericht über das virtuelle PatientInnentreffen
6 2020 – ein Jubiläumsjahr für das Ludwig Boltzmann Institut für Lungengefäßforschung
7 Highlights der Programmlinie „Pathomechanismen des Lungengefäßumbaus"
8 Highlights der Translationalen Plattform
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14 Konferenzen im Herbst 2020
15 Quiz
16 Spenden für Lungengefäßforschung
16 Korrespondenz, Rückmeldung, An- und Abmeldung

CELEBRATE
2010
2020
LUDWIG BOLTZMANN INSTITUT

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Press Appearances

The LBI for Lung Vascular Research has received several invitations to present their research work and aims to the broad public. A short overview of the **press appearances in 2020** is given here:

- „PhD Positions in biomedical research at the Medical University of Graz" – career.duth.gr, 11.02.2020
- „Forschungspreis 2020 der René Baumgart-Stiftung" – klamm.de/gesundheitsjournal24.de/ lifepr.de/ it-it-prof.de/immittelstand.de/mynewschannel.net, 08.10.2020

2 Research Program 2020

2.1 Pathomechanisms of Pulmonary Vascular Remodelling

In 2020, several crucial studies from our group contributed to the understanding of mechanisms underlying vascular remodeling in the diverse forms of pulmonary hypertension. Our studies could potentially help shape the directions where new therapeutic options could be developed.

Endothelial Dysfunction Following Enhanced TMEM16A Activity in Human Pulmonary Arteries

Endothelial cells form a barrier, effectively separating the luminal from the abluminal side of the vessels and responding to a variety of cues coming from continuous intercellular communication, both locally and systemically. They also function as an endocrine organ, releasing a diverse array of compounds affecting vasoactive, immune, growth and coagulation processes. This makes the endothelium a perfectly positioned critical source of mediators promoting vascular remodeling. Endothelial dysfunction is one of the key players in the development of pulmonary arterial hypertension (PAH), a

multifactorial disorder characterized by a progressive rise in vascular resistance. Ion channels dysfunction in PAH has been traditionally structured around the effect of K+ and Ca2+ channel alterations on the phenotype of pulmonary arterial smooth muscle cells (PASMCs). The focus has recently been extended towards Ca2+-activated Cl− channels, demonstrating their importance in cell physiology and we have just reported the contribution of the Cl− channel TMEM16A in the maintenance of PASMC membrane potential for the first time. In contrast, our knowledge about aberrations in ion channel function in endothelial cells of pulmonary arteries (PAECs) is limited.

In our recent study, we show the pathological consequences of increased TMEM16A activity in primary human PAECs and introduce TMEM16A as a player responsible for pathological changes in idiopathic form of PAH PAECs (Skofic Maurer et al., Cells. 2020 doi: 10.3390/cells9091984).

First, we verified the presence of TMEM16A in von Willebrand Factor positive (vWF+) cells from healthy donors and IPAH patients employing immunofluorescence staining in 3D precision-cut lung slices (PCLS), as well as lung sections and PAECs (Figure 1). We next sought to verify Ca2+-activated Cl− current in IPAH PAECs employing state-of-the art electrophysiology of the cells, the whole-cell patch-clamp recordings. Our results showed significantly increased TMEM16A-sensitive current in IPAH PAECs in comparison to donor PAECs.

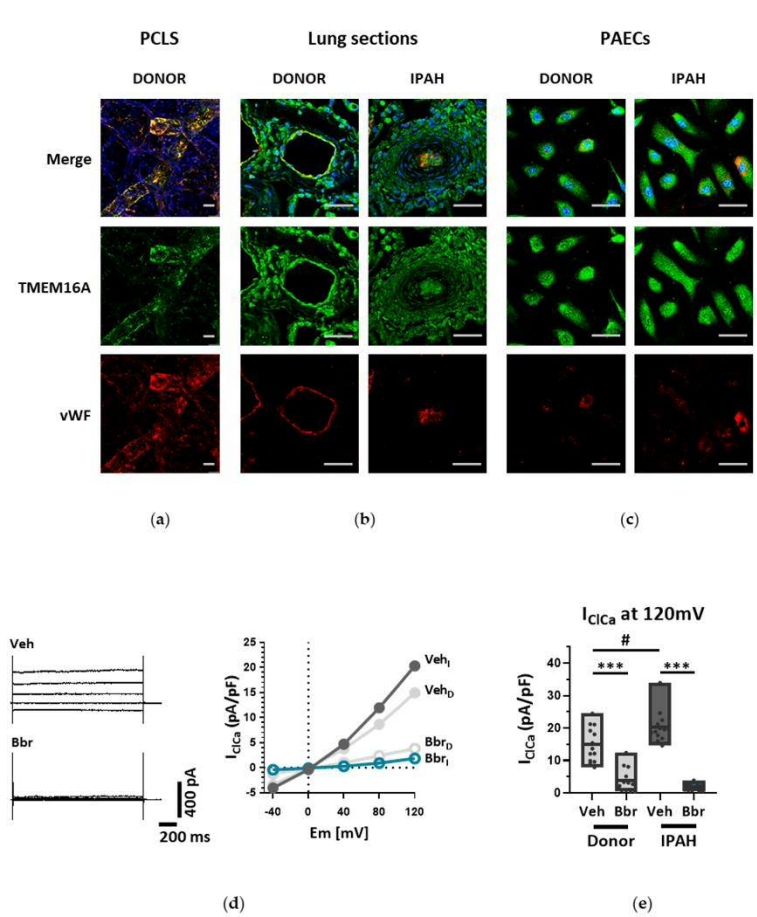

Figure 1: TMEM16A accounts for increased Ca2+-activated Cl− current in IPAH PAECs. Immunofluorescence staining of (a) 3D precision cut lung slices (PCLS), (b) lung sections and (c) PAECs obtained from healthy donor lungs and patients suffering from IPAH. (d) The effect of TMEM16A inhibitor Bbr on representative whole-cell IClCa traces (left) and normalized current-voltage relationships (right) measured with voltage clamp in donor and IPAH PAECs (e) Comparison of the Ca2+-activated Cl− current density of donor and IPAH PAECs. (Source: Skofic Maurer et al., Cells 2020 https://doi.org/10.3390/cells9091984)

One of the fundamental capabilities of endothelial cells is formation into more organized structures. Since enhanced activity of TMEM16A reduced proliferation with cells favoring oxidative, instead of angiogenesis-supporting glycolytic metabolism, we looked further into their angiogenic potential. We found that healthy primary human PAECs form a network of tubular structures whereas TMEM16A-overexpressing PAECs showed reduced spreading potential and tube-formation capabilities, indicating that these cells have a deficiency in new vessel formation.

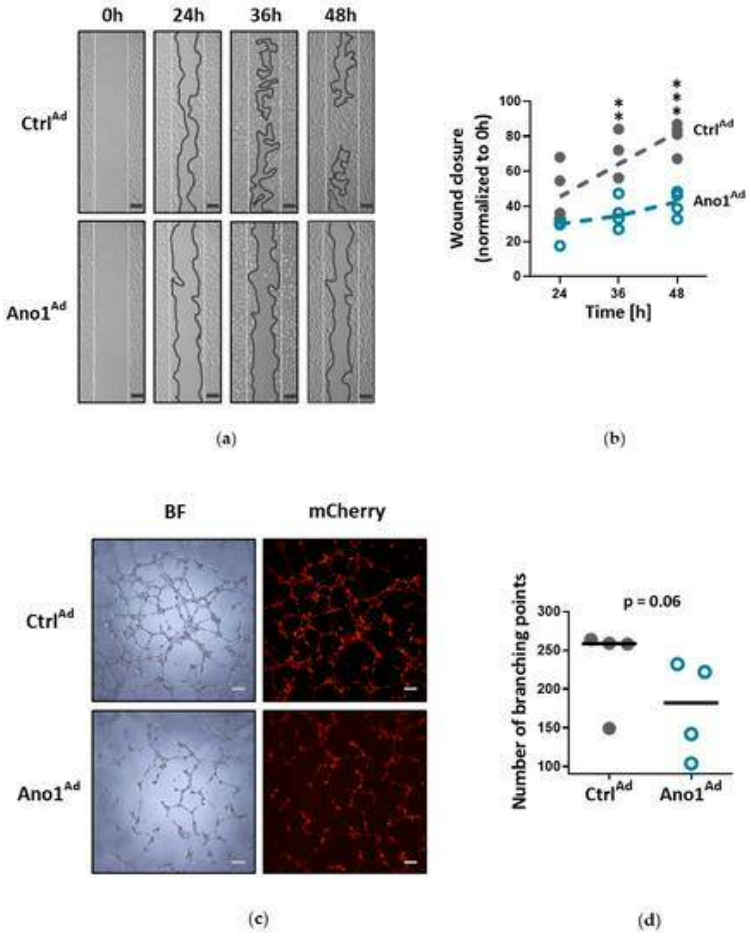

Figure 2: Increased TMEM16A activity causes angiogenic dysfunction. (a) Representative pictures of PAECs wound healing assay, overexpressing TMEM16A using an arteficial adenovirus-system (AnoAd1). (b) Quantification of the wound healing assay. (c) Matrigel tube-formation assay with representative bright-field (BF) and fluorescence pictures of Ano1Ad or control PAECs (CtrlAd). (d) Quantification showing the number of branching points in comparison to CtrlAd. (Source: Skofic Maurer et al., Cells 2020 https://doi.org/10.3390/cells9091984)

Within the scope of our work we were able to extend the pathological footprint of TMEM16A beyond its effect on smooth muscle cell physiology and show its role in the fundamental disruption of downstream signalling pathways otherwise essential to the identity of an endothelial cell. Increased Ca2+ levels of PAECs showed increased proliferation, angiogenesis and nitric oxide production and increased TMEM16A activity weakened the Ca2+ responsiveness of these processes. We traced these detrimental effects at pathways essentially interconnected with all the crucial endothelial-defining processes. As a result, we have established that disease-associated TMEM16A activity pathologically primes healthy pulmonary arteries and ultimately causes severe deficiencies resembling of that found in PAH.

PDGFRα and αSMA mark two distinct mesenchymal cell populations involved in parenchymal and vascular remodeling in pulmonary fibrosis

Lung fibrosis is a severe disease characterized by epithelial cell injury, inflammation and extracellular matrix (ECM) accumulation leading to progressive remodeling and stiffening of the lung which ultimately induce lung functional impairment and death. Remodeling in both the parenchymal and vascular compartments is characterized by aberrant fibroblasts cellular proliferation and enhanced collagen deposition. To date, expansion of α-smooth muscle actin (αSMA)-expressing cells, termed myofibroblasts, is thought to be the major pathomechanism responsible for vascular and parenchymal remodeling. However, recent studies have showed that αSMA positive cells are not the only and main source of collagen production. In our recent study we could show that two different populations of fibroblasts contribute to lung fibrosis: the αSMA-expressing cells and the PDGFRα-expressing cells (Figure 1A). Importantly, analysis of an independent scRNA-Seq data set (GSE122960) analyzing human IPF and donor lungs revealed that (αSMA)-expressing cells and the PDGFRα-expressing cells delineate two distinct sub-clusters of fibroblasts with minimal overlap (Figure 1B).

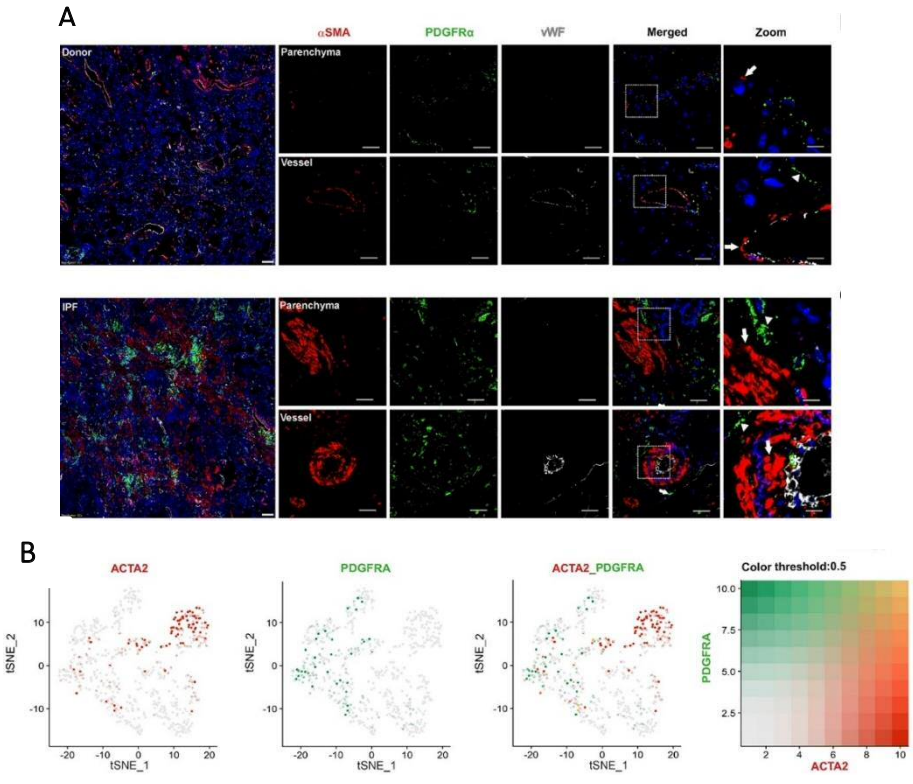

Figure 1: A) immunofluorescence staining of human donor and IPF sections for αSMA, PDGFRα, and von Willebrand factor (vWF). Parenchymal and vascular regions are shown. Scale bar: overview 200 µm; single staining and merged 50 µm; zoomed merged 12.5 µm. Arrows: single αSMA-positive cells; arrowheads: single PDGFRα-positive cells; asterisk: double αSMA/PDGFRα-positive cells. B) t-distributed stochastic neighbor embedding (tSNE) plots showing expression of ACTA2 and PDGFRA expression on the fibroblasts cluster. Data from Reyfman et al. data set (GSE122960). Adapted from Biasin et al AJPLung 2020

To trace lineage hierarchy and possible transdifferentiation between αSMA- and PDGFRα-expressing cells we used a binary fate mapping approach in two different lung fibrosis mouse model. Similar to the human data, we observed that double positive αSMA- and PDGFRα-expressing cells were only a minimal percentage of cells, again corroborating that these two population are independent and separate.

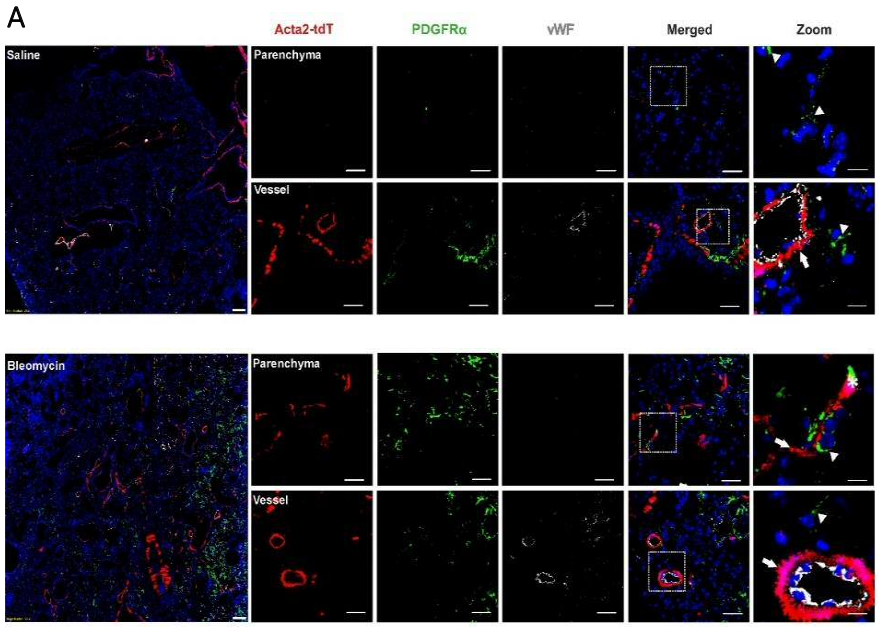

Figure 2: A) Lineage tracing of αSMA-positive cells (Acta2-tdT) and immunofluorescence staining for platelet-derived growth factor receptor-α (PDGFRα) and von Willebrand factor (vWF) was performed in saline- and bleomycin-treated mice. Parenchymal and vascular regions are shown. Scale bar: overview 200 µm; single staining and merged 50 µm; zoomed merged 12.5 µm. Arrows: single Acta-tdT-positive cells; arrowheads: single PDGFRα-positive cells; asterisk: double Acta-tdT/PDGFRα-positive cells. Adapted from Biasin et al AJPLung 2020

To corroborate whether myofibroblasts are really the major contributor to collagen production, we assessed the capability of producing collagen in both αSMA-expressing cells and the PDGFRα-expressing cells. In both human lungs and in mouse model of lung fibrosis, both populations of fibroblasts were responsible for collagen production, suggesting that αSMA-expressing cells are not the only cell type causing lung fibrosis (Figure 3A and 3B).

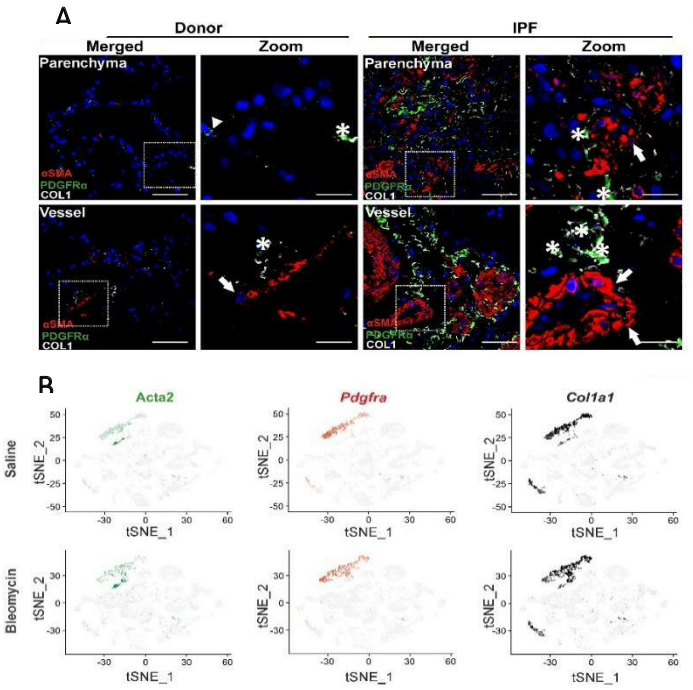

Figure 3: A) Multicolor immunofluorescence staining of human donor and IPF sections for αSMA, PDGFRα, and collagen 1 (COL1). Parenchymal and vascular regions are shown. Scale bar: merged 50 µm; zoomed 12.5 µm. Arrows: single αSMA-positive cells; arrowheads: single PDGFRα-positive cells; asterisk: double αSMA/COL1 or PDGFRα/COL1-positive cells. B) t-distributed stochastic neighbor embedding (tSNE) plots showing expression of Acta2, Pdgfra, Col1a1, and Des on the fibroblasts cluster upon saline and bleomycin treatment. Data from the Peyser et al. data set (GSE129605)

A key conclusion from the present study is that the biology not only of αSMA+ cells, but also that of PDGFRα+ cells should be incorporated into studies focusing on lung fibrosis and on drug development.

The basement membrane – a specialized extracellular matrix – shape endothelial cell function in pulmonary arterial hypertension

Pulmonary arterial hypertension is a severe disease of the pulmonary vasculature, in which progressive remodelling leads to thickening of the pulmonary arterial wall, vessel lumen obstruction. Clinically this leads to increased pulmonary arterial pressure, and a burden on the right heart. Although patients ultimately die of right heart failure, PAH is a disease of the vasculature in the lung due to vessel remodelling. In PAH, vessel remodelling is observed both on cellular level (dysfunctional cellular behavior) and on the extracellular level (increased deposition of extracellular matrix proteins). In this study, we aimed to connect both abnormalities and investigated how the basement membrane, a specialized subset of extracellular matrix proteins, is changed in PAH and how this affects endothelial cell behavior.

First, we aimed to see whether we could observe structural differences in the BM composition in PAH vessel. Using electron microscopy, we detected several ultrastructural changes in the BM ranging from thickening, pronounced deposition of partially degraded BM-like material underlying the intact BM layer, and occasional multiple-layered BM sections (see Figure 1A). Next, we performed a transcriptomic analysis of BM components to see whether changes in gene expression underlay the ultrastructural alterations. For this we used isolated larger and smaller arteries (via laser capture microdissection), and identified that generally, IPAH skewed BM genes toward increased expression. Interestingly, expression changes were dependent on the vessel size. In smaller vessels, mostly BM collagens, such as type IV collagen (COL4A5), and in larger vessels, mostly BM glycoproteins, such as laminin (LAMC1), were increased in PAH (Figure 1B).

We next tested whether different BM components such as laminins or type IV collagens would affect endothelial cell function differently. For this, we seeded human pulmonary arterial endothelial cells (hPAECs) on type IV collagen or laminin and investigated its barrier properties by real-time measurements of endothelial cell resistance (using the electrical cell substrate impedance sensing method) or via visualization of junctional proteins Ve-Cadherin and the localization of mechanosensitive protein YAP. Interestingly, culture of hPAEC on laminin or type IV collagen increased the maximum endothelial cell resistance compared to coating on gelatine, suggesting a tighter endothelial barrier. This was observed for hPAECs from donor and IPAH patients (Figure 1C). The transcriptional coactivator of the hippo pathway YAP is often engaged in ECM signaling and mechanosensing and connected to the formation of tight junctions and VE-Cadherin turnover. Interestingly, culture on type IV collagen, but not laminin, induced YAP nuclear translocation in both donor and IPAH hPAECs. Culture on laminin

however, lead to cytoplasmic retention of YAP, which was visible only in IPAH hPAECs, as they already started with a bigger fraction of nuclear YAP then donor hPAECs (Figure 1D).

Taken together our results suggest that the basement membrane undergoes structural and compositional changes, which ultimately affect the function of endothelial cells. Furthermore, its functional effects can also be determined by inherent differences of endothelial cells determined by disease status. This study was published in the American Journal of Respiratory Cell Molecular Biology. (Jandl et al. Am J Respir Cell Mol Biol. 2020 Jul;63(1):104-117)

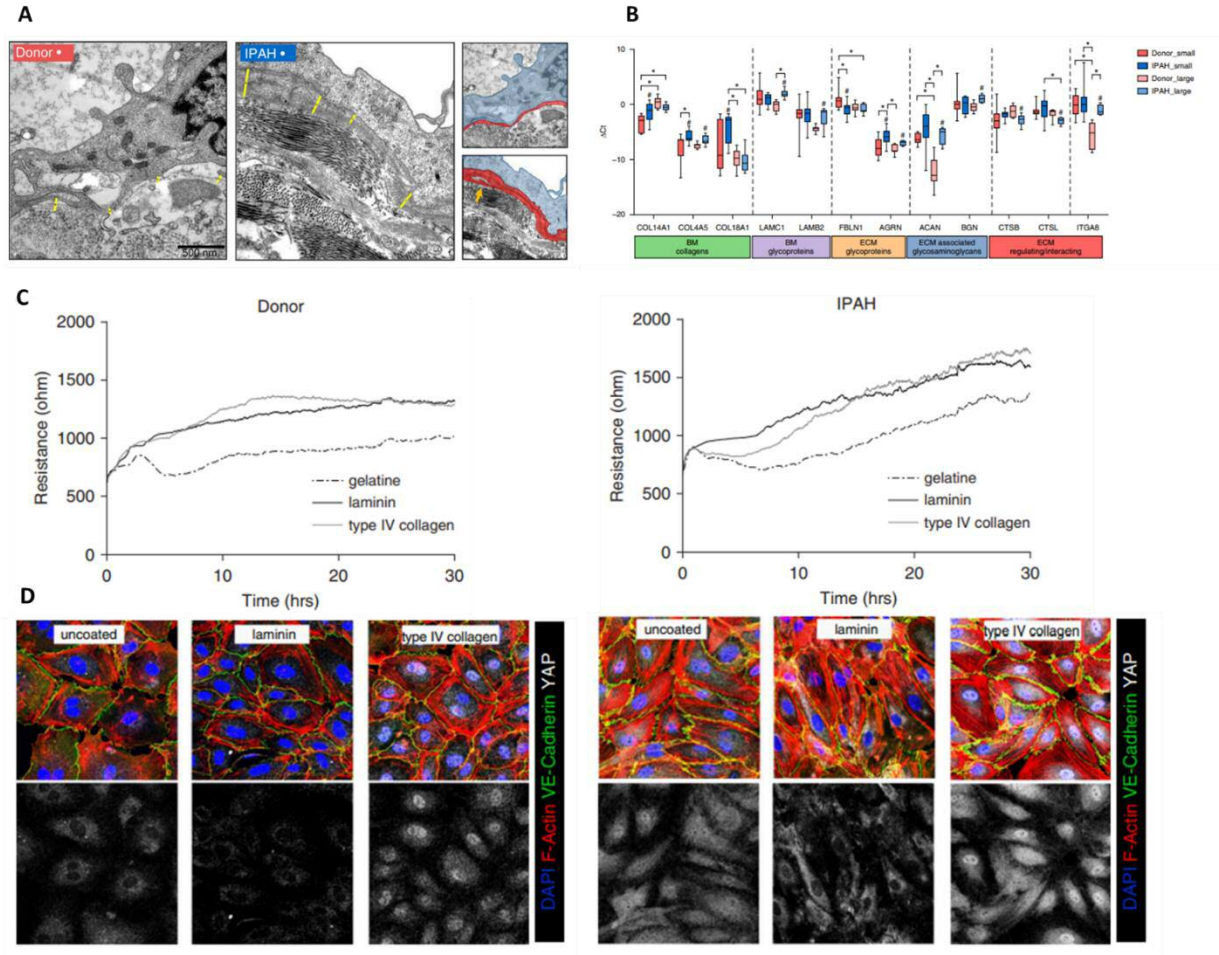

Figure 1: A) Electron-micrograph of pulmonary arteries of Donor and IPAH patients; scale bar: 500 nm. B) ΔCT values of significantly regulated genes in small and large PAs according to extracellular matrix (ECM) class and subclass analyzed. *P<0.05 as determined by two-way ANOVA with interaction and Tukey's multiple comparison test. #P<0.05 as determined by comparison of donor versus IPAH by nonparametric Wilcoxon-Mann-Whitney test. C) Representative ECIS recordings of donor, and IPAH hPAECs. D) Representative immunofluorescence pictures of hPAEC from donor and IPAH coated on the respective matrix.

Scientific Cooperations

ALLANORE Yannick M.D., Cochin Hospital, Paris, France
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2.2 Translational Platform of the LBI-LVR

Two thousand and twenty continued the upward trend for the Translational Platform, we not only again expanded our team, gained extramural funding, but also published several collaborative and group-lead manuscripts.

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Two successful grant applications were among the highlights for the Translational Platform. The first from the Austrian Research Promotion Agency (FFG) industrial dissertation programme, allows us to further our investigations into how the pulmonary vasculature contributes to the development of the severe and deadly disease, pulmonary fibrosis.

From our successful Austrian Science Fund Clinical Research programme (FWF-KLIF) grant application, we were able to expand our staff. The person will support our post-doctoral scientist, Natalie Bordag in determining how inflammatory cells contribute to chronic lung diseases such as pulmonary fibrosis and chronic obstructive lung disease.

We also welcomed Mathias Hochgerner to our group. Mathias joined straight from his PhD at the Institute of Cancer Research in Vienna. His background in cancer immunology further enhances our competence in immunology, specifically immune/stroma-interactions. Based on his input, we have modified our standing protocols for lung processing to include isolation and banking of immune cells both from blood and lung tissue of patients for use in future projects.

To further strengthen scientific exchange, our PhD Student Diana Schnögl, spent two day at Veronika Sexl/Dagmar Gotthardt's research group at the Institute of Pharmacology and Toxicology at University of Veterinary Medicine of Vienna, to learn natural killer cell isolation, cultivation and functional assays and to establish these methods in our laboratory. Data obtained from these techniques was incorporated into two online conference presentations at the doctoral day at the medical university of

Graz and the annual meeting of the Austrian society of pulmonology and at the doctoral day at the Medical University of Graz.

Machine Learning Analysis of the Bleomycin Mouse Model Reveals the Compartmental and Temporal Inflammatory Pulmonary Fingerprint

Idiopathic pulmonary fibrosis (IPF) is a severe, rapidly progressing interstitial lung disease with high mortality rates and short median survival times. We were able to answer fundamental questions about inflammatory kinetics and model robustness by applying recently established as well as newly added machine learning methods. These techniques allowed us to combine existing pre-clinical data from more than a dozen different experiments to conclusively show that pulmonary inflammation is observed at all stages of bleomycin-induced fibrosis. Yet individual populations display distinct kinetics. Cells from the innate immune system characterized the initial inflammatory response, while cells from the adaptive immune system increased over time and strongly associated with advanced pulmonary remodelling. Our data serves as a reference point for future studies investigating the specific role of individual inflammatory populations in pulmonary fibrosis. This study was published in iScience, by Bordag *et al*. with the tile "*Machine Learning Analysis of the Bleomycin Mouse Model Reveals the Compartmental and Temporal Inflammatory Pulmonary Fingerprint".* This data was also presented at the 2020 International Conference of the American-Thoracic-Society.

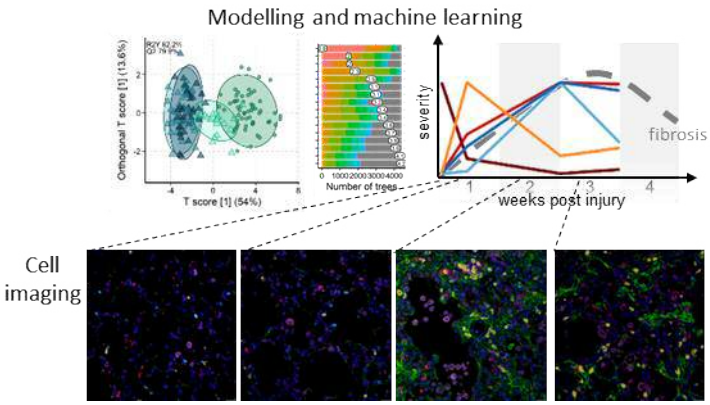

Figure 1: Overview of our iScience publication Application of machine learning methods on an extensive flow cytometry dataset to reveal the kinetics of pulmonary inflammation following bleomycin application (Top). Visualisation of inflammatory cells via cell imaging (Bottom). Reproduced from Bordag et al., iScience 2020. https://doi.org/10.1016/j.isci.2020.101819

In 2019, the Food and Drug Administration (FDA) released a warning that CDK4/6 inhibitors used to treat patients with advanced breast cancers may cause rare but severe pulmonary inflammation. In our 2020 publication "*CDK4/6 inhibition enhances pulmonary inflammatory infiltration in bleomycin-induced lung fibrosis*", we provided experimental evidence for this warning. In a pre-clinical model of pulmonary

fibrosis, CDK4/6 inhibition provided some benefit in reducing collagen deposition (the main cause for scar formation in fibrotic lungs), but also augmented inflammatory cell recruitment into the alveolar compartment. Our data emphasizes the risk of severe inflammatory adverse effects in the lung, especially in patients with known pulmonary risk factors and highlights the necessity to carefully monitor all patients treated with CDK4/6 inhibitors for signs of lung inflammation. This data was published in Respiratory Research by Birnhuber et al. Furthermore, our group contributed expertise to both internal and external collaborators, resulting in three collaborative peer reviewed manuscripts and one preprint.

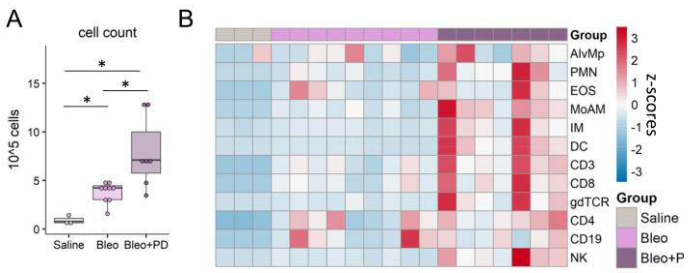

Figure 2: Overview of our Respiratory Research paper
Inflammatory cell changes in the bleomycin fibrosis model with and without CDK4/6 inhibition (+PD). A) Total cell count in the bronchoalveolar lavage and B) heatmap representation of different inflammatory cells, red indicates higher abundance.
Reproduced from Birnhuber et al., Resp Res 2020, https://doi.org/10.1186/s12931-020-01433-w

FFG Forschung wirkt.
FWF Der Wissenschaftsfonds.

Scientific Cooperations

GARN, Holger Prof, Philipps University of Marburg, Marburg, Germany
GOTTHARDT Dagmar Dr, University of Veterinary Medicine, Vienna, Austria
GRILLARI Johannes Prof, Ludwig Boltzmann Institute for Experimental and Clinical Traumatology
GRUNIG Gabriele Dr, New York University School of Medicine, New York, USA
HEINEMANN Akos Prof, Otto Loewi Research Centre, Medical University of Graz, Austria
OGRODNIK, Mikolaj Dr, Ludwig Boltzmann Research Group SHoW - Senescence and Healing of Wounds, Vienna, Austria
STROBL Herbert Prof, Otto Loewi Research Centre, Medical University of Graz, Austria

2.3 Clinical Studies

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The main aim of the clinical arm of the LBI is to promote the early diagnosis of chronic pulmonary vascular diseases. In recent years, we increasingly focused on two clinical research areas: pulmonary hemodynamics during exercise and pulmonary vascular disease in patients with chronic lung diseases. Of course, we aimed to work on these questions in a comprehensive manner and by building on previous results of the Institute.

Pulmonary hemodynamics during exercise

In a European Respiratory Society (ERS) Task Force we recently developed an expert statement on pulmonary haemodynamics during exercise and identified the most important actual research questions. In accordance with this, we aim to investigate the prognostic relevance of pulmonary haemodynamics during exercise by using a multi-center approach and to identify independent predictors of adverse events. In order to achieve this goal, we established an ERS supported Clinical Research Collaboration led by our Institute and a central web based database. We expect that this study may even provide a basis for the planning of therapeutic trials in exercise PH. By now, 40 expert centres from 15 countries have joined this Clinical Research Collaboration and over 1300 patients have already been included into the database. An editorial was published summarizing the main goals of the project (Kovacs et al. ERJ 2019). Based on the achievements of the first three years, the ERS prolonged its

support for PEX-NET until 2024. In 2020, the retrospective part of the database was closed and the first comprehensive analyses is currently being performed.

In addition to this international effort, we aimed to analyse specific questions on the prognostic relevance of exercise haemodynamics based on data from our own patients undergoing comprehensive clinical characterization. We found that pulmonary vascular resistance (PVR) at maximal exercise were significantly associated with age-adjusted long-term mortality in patients with systemic sclerosis and may provide additional prognostic information as compared to resting pulmonary haemodynamics (Zeder et al. Chest 2020).

Pulmonary vascular phenotype in patients with chronic lung diseases

The goal of our projects was to identify criteria and provide characteristics for a “pulmonary vascular phenotype” in chronic lung diseases. In order to investigate these questions, we identified n=142 COPD patients undergoing right heart catheterization (52% of the patients showing severe PH) and complete clinical work-up (including imaging data and blood samples in our biobank) with available follow-up and mortality data (median follow-up time 6 years) in our centre. In addition, there are n=80 explanted lung samples and corresponding blood samples in our tissue bank available from COPD patients undergoing lung transplantation. These patient data and materials form the basis of the continuously developing GRAPHIC registry (Graz Pulmonary Hypertension in COPD). The first analyses of this registry revealed that PVR > 5 WU is the strongest independent hemodynamic predictor of mortality in patients with COPD. A PVR > 5 WU suggests the presence of severe pulmonary vascular disease and this was associated with less severe airflow obstruction and a relatively low pulmonary venous pressure, which is consistent with a pulmonary vascular phenotype of COPD.

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
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LANGE Tobias Dr. University Clinic Regensburg, Germany
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MOAZEDI-Fürst Florentine, Dr. Medical University Graz, Austria
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MÜLLER Veronika, Prof. Semmelweis University Budapest, Hungary
NAEIJE Robert, Prof. Free University of Brussels, Belgium
OCCIPINTI Mariaelena, Dr. University of Florence, Italy
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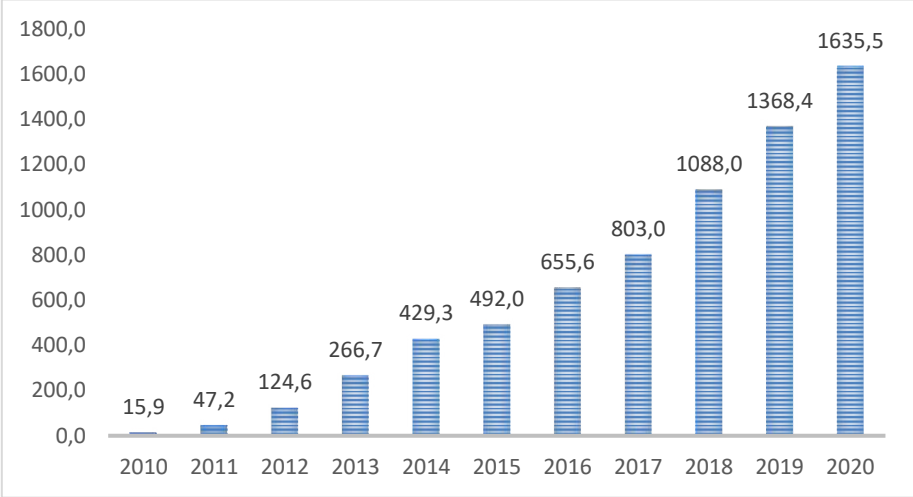
RAGGAM Reinhard, Dr. Medical University of Graz, Austria
REITER Ursula, Dr. Medical University of Graz, Austria
SCHLENKE Peter Prof. Medical University of Graz, Austria
STAUBER Rudolf, Prof. Medical University of Graz, Austria
STOLLBERGER Rudolf, Prof. University of Technology Graz, Austria
TORNYOS Adrienn, 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 2020

The cumulative impact factor, an indicator for the quality of our scientific publications with LBI-LVR affiliation, reached the remarkable value of 1635 by the end of the year 2020.



2.4.1 Top five publications 2020 (in alphabetical order)

(*young scientists of the LBI LVR are underlined)

Biasin V, Crnkovic S, Sahu-Osen A, Birnhuber A, El Agha E, Sinn K, Klepetko W, **Olschewski A,** Bellusci S, **Marsh LM, Kwapiszewska G.** PDGFRα and αSMA mark two distinct mesenchymal cell populations involved in parenchymal and vascular remodeling in pulmonary fibrosis. Am J Physiol Lung Cell Mol Physiol. 2020 Apr 1;318(4):L684-L697. doi: 10.1152/ajplung.00128.2019. Epub 2020 Feb 5. PMID: 32023084, IF 4.406

Bordag N, Biasin V, Schnoegl D, Valzano F, Jandl K, Nagy BM, Sharma N, Wygrecka M, **Kwapiszewska G, Marsh LM**. Machine Learning Analysis of the Bleomycin Mouse Model Reveals the Compartmental and Temporal Inflammatory Pulmonary Fingerprint. iScience. 2020 Nov 18;23(12):101819. doi: 10.1016/j.isci.2020.101819. eCollection 2020 Dec 18. PMID: 33319168, IF 4.447

Jandl K, **Marsh LM,** Hoffmann J, Mutgan AC, Baum O, Bloch W, Thekkekara-Puthenparampil H, Kolb D, Sinn K, Klepetko W, Heinemann A, **Olschewski A, Olschewski H, Kwapiszewska G.** Basement Membrane Remodelling Controls Endothelial Function in IPAH. Am J Respir Cell Mol Biol. 2020 Mar 11. doi: 10.1165/rcmb.2019-0303OC. [Epub ahead of print] PMID: 32160015, IF 5.373

Nagy BM, **Kovacs G,** Tornyos A, Svehlikova E, Foris V, Nagaraj C, **Kwapiszewska G**, Pieber TR, **Olschewski A, Olschewski H.** No indication of insulin resistance in idiopathic PAH with preserved physical activity. Eur Respir J. 2020 Mar 26. pii: 1901228. doi: 10.1183/13993003.01228-2019. [Epub ahead of print] No abstract available. PMID: 32217652, IF 12.339

Zeder K, Avian A, Bachmaier G, Douschan P, Foris V, Sassmann T, Moazedi-Fuerst FC, Graninger WB, Hafner F, Brodmann M, Salmhofer W, **Olschewski H, Kovacs G**. Exercise Pulmonary Resistances Predict Long-Term Survival in Systemic Sclerosis. Chest. 2020 Sep 12:S0012-3692(20)34485-8. doi: 10.1016/j.chest.2020.08.2110. Online ahead of print. PMID: 32931822, IF 8.308

2.4.1 Scientific publications 2020

(*young scientists of the LBI LVR are underlined)

Bauer PK, Flicker M, Fabian E, Flick H, **Brcic L**, Liegl-Atzwanger B, Janisch M, Fuchsjäger M, **Olschewski H**, Krejs GJ. Clinical-Pathological Conference Series from the Medical University of Graz: Case No 170: A 33-year-old psychologist with severe dyspnea and right-sided chylothorax. Wien Klin Wochenschr. 2020 Oct 29. doi: 10.1007/s00508-020-01753-3. Online ahead of print. PMID: 33119872, IF 1.150

Biasin V, Crnkovic S, Sahu-Osen A, Birnhuber A, El Agha E, **Sinn K**, Klepetko W, **Olschewski A,** Bellusci S, **Marsh LM, Kwapiszewska G.** PDGFRα and αSMA mark two distinct mesenchymal cell populations involved in parenchymal and vascular remodeling in pulmonary fibrosis. Am J Physiol Lung Cell Mol Physiol. 2020 Apr 1;318(4):L684-L697. doi: 10.1152/ajplung.00128.2019. Epub 2020 Feb 5. PMID: 32023084, IF 4.406

Birnhuber A, Egemnazarov B, Biasin V, Bonyadi Rad E, Wygrecka M, **Olschewski H, Kwapiszewska G, Marsh** LM. CDK4/6 inhibition enhances pulmonary inflammatory infiltration in bleomycin-induced lung fibrosis. Respir Res. 2020 Jul 2;21(1):167. doi: 10.1186/s12931-020-01433-w. PMID: 32616042, IF 3.924

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3 LBI Inside

For this year's annual report, we would like to give you an insight into the work areas of our management team. In particular, we would like to introduce you to the LBI-LVR Office Team with its different tasks.

3.1 Inside LBI-LVR: Claudia Jakob-Pelikan

I started working at the Institute in December 2012. I am responsible for general secretarial tasks at the institute, with many different things to do every day, such as making appointments, personnel matters, forwarding contracts of employment, interface with the LBG personnel office, organising e-mail addresses, general mail handling. I see myself as a contact point for all kinds of issues.

Another important part of my job is ordering requirements for the laboratory, communication with pharmacy on site of the Klinikum Kages as well as with distributors of laboratory supplies.

In addition, I am responsible for the travel management of the LBI team and of our guests, including hotel bookings, flights and taxi bookings.

3.2 Inside LBI-LVR: Sarah Bundschuh

Since February 2020, I have been employed as project manager for the CONNECT project. CONNECT is a cooperation between the Copenhagen Business School (Marion Poetz), Med Uni Graz (Selma Mautner) and the Ludwig Boltzmann Institute for Lung Vascular Research and I as project manager and Valentina Biasin as a scientific coordinator are involved in its implementation. The aim of CONNECT is to identify and involve those users (e.g. patients) who want to share their knowledge and participate in research. In addition, CONNECT aims to establish a new process where interested users are equally involved in an open research process. The project also contributes to narrowing the gap between science and society. In order to address a broad spectrum of users, we have chosen fibrosis as a topic. I really enjoy working with everyone involved in the dissemination of the project and we are well on our way to creating a very interesting open research platform.

3.3 Inside LBI-LVR: Brita Maurer

In February 2019, I joined the LBI-LVR and started my work in the field of research management. My main area of responsibility is to support the institute's management in all submissions of project proposals, e.g. to the EU, FWF and FFG. Subsequently, my work also includes project coordination and accounting for approved, ongoing projects of the institute.

Another part of my work is the maintenance of public relations. Here, my tasks include maintaining the homepage, sending out press releases and preparing the annual report.

In addition, I support the office team in organizational matters, especially in the planning and execution of the annual retreat, the SAB meetings and the preparation of the biannual board meetings.

Another large part of my work area is the responsibility for the entire sample collection of the Biobank in particular the maintenance of the associated data. I manage the distribution of biological material for all Institute staff. Furthermore, I am the responsible contact person for the cooperation and coordination with the transplantation team of the Medical University of Vienna.

What I appreciate most about my work at the LBI LVR is the opportunity to gain experience in the field of research in a motivated international team. On the one hand, I gain insights in the coordinative and administrative area (project coordination and submissions) and on the other hand into the scientific area of research (biobank). This mixture of science and administration makes my job so interesting and I feel I am making an important contribution to our research.

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 were visited in 2020:

Name	Location	Title of the Lecture/ Workshop
BIRNHUBER Anna	Medical University of Graz, Austria	Project Management (Rainer Svacinka)
BIRNHUBER Anna	LBG Career Center, Vienna, Austria	Career Chat
BIASIN Valentina	Medical University of Graz, Austria	Basic Module Teaching: Testing - did the knowledge transfer take place appropriately? - Overview of examination formats
BIASIN Valentina	LBI Lung Vascular Research, Austria	Scientific writing 2 (Katherine Tiede)
BONYADIRAD Ehsan	LBI Lung Vascular Research, Austria	Scientific writing 1 (Katherine Tiede)
BONHEUR Savinien	LBI Lung Vascular Research, Austria	Scientific writing 1 (Katherine Tiede)
BORDAG Natalie	LBI Lung Vascular Research, Austria	Scientific writing 1 (Katherine Tiede)
BORDAG Natalie	Medical University of Graz, Austria	Basismodul Lehre: Urheberrecht und Datenschutz
BORDAG Natalie	Medical University of Graz, Austria	Basismodul Lehre: Prüfen - erfolgte der Wissenstransfer zweckmäßig? (1) - Überblick Prüfungsformate
BORDAG Natalie	Medical University of Graz, Austria	Betreuung von Abschlussarbeiten – von der Idee zur Realisierung
BORDAG Natalie	Medical University of Graz, Austria	Beurteilung von Abschlussarbeiten
BORDAG Natalie	Medical University of Graz, Austria	Basismodul Lehre: OSCE 1 + 2
BORDAG Natalie	Medical University of Graz, Austria	Evaluierung - Wir wollen besser werden
BORDAG Natalie	Medical University of Graz, Austria	Hochschuldidaktik – Lehr- und Lernmethoden
BORDAG Natalie	Medical University of Graz, Austria	Patientinnen und Patienten stehen im Mittelpunkt der Lehre
BORDAG Natalie	Medical University of Graz, Austria	Pipettieren und Lehre im Labor
BORDAG Natalie	Medical University of Graz, Austria	Einführung in die Hochschuldidaktik
BRCIC Luca	Medical University of Graz, Austria	ICH Good Clinical Practice E6 (R2) training course
BRCIC Luca	Medical University of Graz, Austria	Aufbaumodul Forschung: Statistik 1
CRNKOVIC Slaven	LBI Lung Vascular Research, Austria	Scientific writing 2 (Katherine Tiede)
FLIESSER Elisabeth	BMF Graz, Austria	BMF Graz FELASA B Kurs

FLIESSER Elisabeth	Medical University of Graz, Austria	Einführung in die Hochschuldidaktik
FORIS Vasile	Medical University of Graz, Austria	Master of Science Biobanking (2018-2020), master program
FUCHS Thomas	Medical University of Graz / TecTrain, Austria	MS Excel Basics / Refresher
HALSEGGER Sabine	Medical University of Graz / TecTrain, Austria	MS Excel Basics / Refresher
HOCHGERNER Mathias	LBI Lung Vascular Research, Austria	Scientific writing 1 (Katherine Tiede)
JANDL Katharina	LBI Lung Vascular Research, Austria	Scientific writing 2 (Katherine Tiede)
JANDL Katharina	Medical University of Graz, Austria	Supervision of Doctoral and PhD Candidates
MARSH Leigh	Medical University of Graz, Austria	Supervision of Doctoral and PhD Candidates
MARSH Leigh	Medical University of Graz, Austria	Data protection instruction and IT security
MUTGAN Ayse Ceren	LBI Lung Vascular Research, Austria	Scientific writing 1 (Katherine Tiede)
MUTGAN Ayse Ceren	Medical University of Graz, Austria	Scientific Writing (Eva Müller)
NAGARAJ Chandran	LBI Lung Vascular Research, Austria	Scientific writing 2 (Katherine Tiede)
NAGY Bence	LBI Lung Vascular Research, Austria	Scientific writing 2 (Katherine Tiede)
PIENN Michael	University of Köln, Germany	Update RSNA – Fortbildung in radiologischer Diagnostik
SASSMANN Teresa	Medical University of Graz, Austria	Dissertationsseminar - Diabetes Technology (DS Sustainable Health Research)
SASSMANN Teresa	Medical University of Graz, Austria	Dissertationsseminar - Molecular Mechanisms in Autoimmunity (PhD Molecular Medicine)
SASSMANN Teresa	Medical University of Graz, Austria	Dissertationsseminar - Role of Eosionophils in Obstructive Airway Disease (PhD Molecular Medicine)
SASSMANN Teresa	Medical University of Graz, Austria	Literaturclubs, Projektpräsentationen und Gastvorträge, Cardiovascular JC (TMCB)
SHARMA Neha	LBI Lung Vascular Research, Austria	Scientific writing 1 (Katherine Tiede)
SCHNÖGL Diana	LBI Lung Vascular Research, Austria	Scientific writing 1 (Katherine Tiede)
VALZANO Francesco	LBI Lung Vascular Research, Austria	Scientific writing 1 (Katherine Tiede)
ZABINI Diana	LBI Lung Vascular Research, Austria	Scientific writing 2 (Katherine Tiede)
ZABINI Diana	Medical University of Graz, Austria	Basismodul Lehre: Pipettieren, Messen, Protokollieren - Lehre im Labor
ZABINI Diana	Medical University of Graz, Austria	Aufbaumodul Lehre: Der VMC
ZEDER Katarina	LBI Lung Vascular Research, Austria	Scientific writing 1 (Katherine Tiede)

4.1.2 Invited Speakers 2020

LAMBRECHT Bernd, PhD	Johannes Kepler University, Kepler University Hospital, Linz, Austria	07 JAN 20	**Various aspects of COPD Epidemiology**
RHODES J Christopher, PhD	Faculty of Medicine, National Heart & Lung Institute, Imperial College London, Great Britain	14 JAN 20	**Application of metabolomics and proteomics to Identify Unique Clinical Phenotypes in PAH**
MITTERHAUSER Markus, MD	Ludwig Boltzmann Institute Applied Diagnostics, Vienna, Austria	18 JAN 20	**Applied Diagnostics: you see what you treat, you treat what you see?**
SIBILIA Maria, PhD	Institute for Cancer Research, Department of Medicine, Medical University of Vienna, Austria	09 JUN 20	**Microenvironmental Drivers of Inflammation and Tumorigenesis**
REDL Heinz, MD	Ludwig Boltzmann Institute Experimental and Clinical Traumatology, Vienna, Austria	20 JUL 20	**Diagnostic based acute- and regenerative therapy approaches in LBI Trauma/Austrian Cluster for Tissue Regeneration**
GOTTHARDT Dagmar, PhD	Institute for Pharmacology and Toxicology, University of Veterinary Medicine, Vienna, Austria	16 SEP 20	**Natural Killer cells and their role in the surveillance and immune evasion of cancer**