

# German Center for Lung Research

ANNUAL REPORT



2017

Translational Research to Combat Widespread Lung Diseases

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# Foreword



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The anniversary year 2016 let us gain insights into the great research efforts of the scientists at the partner institutions throughout Germany, whose achievements are already put into practice in numerous occasions for the prevention, diagnosis, and treatment of lung diseases. 2017 lets us now look further ahead, taking a closer look at the promising future of the German Center for Lung Research (DZL).

In summer 2017, the German Centers for Health Research (DZG) received a great accolade from the German Council of Science and Humanities (Wissenschaftsrat) with its "Recommendations for the Further Development of the DZG". According to the Council, the DZG are a model to promote translational research in the areas of disease covered, while they have also earned great visibility and recognition on a global scale. Overall, the Council recommends strengthening the pioneering role of the DZL and its five partner centers and expanding the centers as needed.

And there is a clear need to do so. Every four minutes, a person dies from lung or airway diseases in Germany. This is mostly due to Chronic Obstructive Pulmonary Disease (COPD), pulmonary infections (primarily pneumonia and tuberculosis), and lung cancer. All these diseases are among the 10 most common global causes of death; the World Health Organization (WHO) estimates that they are responsible for almost 16 million deaths each year.

The newly established German government wants to address this challenge. According to the coalition agreement, health research is to be advanced in general, placing the focus on the patients' needs. It is particularly the translation of research results on the major widespread diseases, also expressly referred to as lung research, that the expansion of the DZG seeks to advance.

DZL researchers have earned this recognition themselves with their exceptional commitment towards lung patients. The following pages will provide you with an insight into this research work, and we hope that you will continue to accompany us along our way to the promising future of the DZL.

Giessen/Heidelberg/Grosshansdorf/Munich/Hanover in July 2018

The Board of the German Center for Lung Research



# About the DZL: Science – Translation in the Focus of Research

Founded in late 2011, the German Center for Lung Research (Deutsches Zentrum für Lungenforschung, DZL) is one of six German Centers for Health Research (Deutsche Zentren der Gesundheitsforschung, DZG). The DZL is supported by the German Ministry of Education and Research (Bundesministerium für Bildung und Forschung, BMBF) and the States in which each of the sites are located. Leading scientists and clinicians in the field of pulmonary research work together to develop new and innovative therapies for patients with lung disease.

Currently, over 240 principal investigators and their research groups work together to combat respiratory disease through translational research. Twenty-nine leading German research institutions at five sites cooperate in this work: Airway Research Center North (ARCN, Borstel, Grosshansdorf, Kiel and Lübeck), Biomedical Research in Endstage and Obstructive Lung Disease Hannover (BREATH, Hannover), Comprehensive Pneumology Center Munich (CPC-M, Munich), Translational Lung Research Center Heidelberg (TLRC, Heidelberg), and

the Universities of Giessen and Marburg Lung Center (UGMLC, Giessen, Marburg and Bad Nauheim).

Research efforts in the DZL are focused on eight Disease Areas: Asthma and Allergy, Chronic Obstructive Pulmonary Disease, Cystic Fibrosis, Pneumonia and Acute Lung Injury, Interstitial (Diffuse Parenchymal) Lung Disease, Pulmonary Hypertension, End-Stage Lung Disease, and Lung Cancer. In each of these disease areas, the entire “bench-to-bedside” translational research chain is applied. Basic scientific findings are applied to the design and implementation of clinical trials and patient care, whilst clinical needs become the scientific questions tackled by DZL scientists. The close cooperation of basic scientists and clinicians is integral to the success of the DZL and is facilitated by regular meetings, symposia, and common infrastructures. Furthermore, many investigators belong to more than one Disease Area team, allowing cross-fertilization of ideas and findings across the research areas.





## Asthma and Allergy

Asthma is the most prevalent chronic respiratory disease in children and is also very common in adults. Although the clinical manifestations of asthma in children and adults are rather uniform (e.g. wheezing, shortness of breath, and cough), population-based clinical and genetic studies suggest that asthma is not one but many disease. Thus, a single “one-size-fits-all”

treatment approach is unlikely to work to tackle this important health problem. In order to design personalized treatment approaches for asthma patients, there is urgent need to elucidate the particular molecular mechanisms underlying the various types of asthma. The decoding of such mechanisms and their translation to the individual patient is the aim of the Disease Area Asthma and Allergy of the DZL.

### Goals Achieved in 2017

- ✓ 10 joint publications of several DZL sites (15 achieved)
- ✓ Conduct of a retreat towards focusing translational orientation
- ✓ Two work meetings on the data analysis strategy including discussion of initial evaluations of the ALLIANCE asthma cohort
- ✓ Start of the standardized recruitment process in two new centers of the ALLIANCE asthma cohort

### Goals for 2018

- 15 joint publications of several DZL sites
- Design of a study on specific immunotherapy as a preventative action in early childhood
- 300 additional study visits in the ALLIANCE asthma cohort
- Start of 10 projects for using the biomaterial and accompanying data collected

### Disease Area Leaders

Prof. Dr. Heinz Fehrenbach (ARCN)

Prof. Dr. Erika von Mutius (CPC-M)

### Administrative Coordinator of the Disease Area

Dr. Jörn Bullwinkel (ARCN)

### Participating DZL Partner Sites

all

## Research Highlight 2017

### Antibody therapy as an alternative for treatment with glucocorticoids

Asthma is a chronic inflammatory airway disease that affects 358 million people worldwide. Patients suffering from a severe form of asthma have to inhale high-dose glucocorticoids or bronchodilators regularly. Some patients also have to take cortisone pills in addition to glucocorticoids. Cortisone pills often have side effects that impair the patients' quality of life. Therefore, use in pediatric patients is possible only in exceptional cases.

Glucocorticoids suppress the chronic airway inflammation and ameliorate asthma symptoms. Their mode of action is relatively broad and hence they have a number of side effects. A new approach also tries to counteract inflammation but does so in a much more focused way. In the center of this therapy are eosinophile granulocytes, specialized immune cells that foster inflammation and occur in large numbers in blood and lungs of many asthmatics. The new drug is the antibody benralizumab, which binds and blocks the IL-5 receptor on eosinophile granulocytes. In this scenario, IL-5 can no longer reach the receptor, and the inflammatory action of eosinophiles is suppressed. Moreover, the immune system recognizes, attacks and destroys the complex of benralizumab and eosinophiles. Therefore, the number of these immune cells is reduced.

The key question of the ZONDA study was whether the dose of glucocorticoids can be reduced by an alternative therapy with subcutaneously injected benralizumab. Scientists tested this hypothesis in a collective of 220 asthma patients and found that this is indeed true: the benralizumab-treated patients were able to reduce their glucocorticoid dose by 75 % within six months, a quarter of them by more than 90 %. In a placebo group, the reduction was just 25 %. As expected, the number of eosinophile granulocytes was reduced in both blood and lungs. Patients treated with benralizumab had a reduced risk of suffering from acute worsening of the disease (exacerbation). This also resulted in a reduced number of hospitali-

zations due to asthma. Asthma symptoms were controlled equally or even better. This is remarkable, taking into account that patients had to take a much lower dose of glucocorticoids. The patients' quality of life was slightly improved. Finally, the fraction of patients suffering from side effects was lower in the benralizumab group than in the placebo group.

The ZONDA study was sponsored by AstraZeneca and published in the New England Journal of Medicine.

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#### Further information:

📄 Nair P, Wenzel S, Rabe KF, Bourdin A, Lugogo NL, Kuna P, Barker P, Sproule S, Ponnambal S, Goldman M, Investigators ZT (2017) Oral Glucocorticoid-Sparing Effect of Benralizumab in Severe Asthma. *N Engl J Med* 376: 2448–2458





## Chronic Obstructive Pulmonary Disease (COPD)

Chronic Obstructive Pulmonary Disease (COPD) is characterized by a progressive and largely irreversible restriction of lung function. Shortness of breath, the most often observed symptom of COPD, contributes significantly to the decrease

in the quality of life of many patients. Although COPD can, to a certain extent, be avoided, the disease is the fourth most frequent cause of death worldwide. The main causes of this disease are smoking and air pollution.

### Goals Achieved in 2017

- ✓ 10 joint publications of several DZL sites (12 achieved)
- ✓ Conference calls every two months for the purposes of research coordination
- ✓ Raising of competitive funds from the DZL Clinical Trial Board (one study)
- ✓ Start of two DA-spanning projects (involving the AA/ELD DA)

### Goals for 2018

- Clinical studies on GATA3 and iNOS-EMAPII completed
- 15 joint publications of several DZL sites
- Conference calls every two months for research coordination
- Start of a project on cardiovascular effects with the Hamburg City Health Study
- Start of a project in collaboration with the German Center for Cardiovascular Research (DZHK) on cardiovascular biomarkers in COPD patients

COPD combined with an emphysema is the most frequently occurring destructive lung disease. The loss of structural integrity and the lung's ability to regenerate are critical factors for the course of the disease and therapeutic success; the basic mechanisms are, however, hitherto hardly known. The long-term aim of the DZL research in this area is to translate new therapy concepts based on mechanisms into effective treatment for COPD patients.

### Disease Area Leaders

Prof. Dr. Klaus F. Rabe (ARCN)

Prof. Dr. Claus F. Vogelmeier (UGMLC)

### Administrative Coordinator of the Disease Area

Dr. Jörn Bullwinkel (ARCN)

### Participating DZL Partner Sites

all



## Research Highlight 2017

### COPD and cardiovascular diseases are connected

Among the key research topics of the Disease Area COPD is the elucidation of interactions of COPD and its comorbidities. To this end, DZL has built an associated partnership with the COSYCONET cohort study ('COPD and Systemic Consequences-Comorbidities Network').

Regarding comorbidities it is known that COPD and a number of cardiovascular diseases are closely connected. This is mostly due to the shared risk factor cigarette smoking. However, there is little knowledge on prevalence and clinical relevance of peripheral artery disease (PAD) in COPD. PAD is caused by atherosclerosis and leads to narrowing of the inside of arteries in arms and legs. This can result in insufficient perfusion leading to pain, reduced physical capacity and necrosis. A consequence of necrotic tissue breakdown might be amputation of the affected limb. Moreover, PAD is a risk factor for other cardiovascular diseases.


In order to fill this knowledge gap, an international study group including four DZL sites investigated PAD in COPD patients within the framework of COSYCONET. They found that 8.8% of all COPD patients had measurable PAD – significantly more than in study participants without COPD. Surprisingly, two thirds of these patients had not stated to have PAD in the accompanying questionnaire: They were not aware of their cardiovascular comorbidity. This means that COPD is a risk factor for PAD that is often underestimated. Moreover, COPD patients with PAD had a lower exercise capacity compared to COPD patients without PAD. They also had worse results in the six minute walking test and a worse generic health status.

The conclusion is that physicians should screen their COPD patients for PAD. Doing this, they would get a better picture of the risk of developing a cardiovascular disease and get a more comprehensive understanding of physical limitations. Altogether, this might improve prevalence and mortality rate of the disease.

In this study, scientists analyzed data from almost 3,000 patients of COSYCONET as well as from two epidemiological control groups with more than 4,000 subjects from SHIP (Study on Health in Pomerania). The results were published in the American Journal for Respiratory and Critical Care Medicine.

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#### Further information:

 Houben-Wilke S, Jörres RA, Bals R, Franssen FM, Glaser S, Holle R, Karch A, Koch A, Magnussen H, Obst A, Schulz H, Spruit MA, Wacker ME, Welte T, Wouters EF, Vogelmeier C, Watz H (2017) Peripheral Artery Disease and Its Clinical Relevance in Patients with Chronic Obstructive Pulmonary Disease in the COPD and Systemic Consequences-Comorbidities Network Study. *Am J Respir Crit Care Med* 195: 189-197



## Cystic Fibrosis (Mucoviscidosis)

Cystic Fibrosis (CF) is the most common genetically determined, early onset and still lethal disease. CF affects approximately one in 2,500 newborns in Germany. With improvements

in symptomatic therapies and standardized CF medical care, the median survival age of CF patients in Germany has risen to approximately 40 years. However, despite recent breakthroughs in disease-modifying therapies for a small subgroup of patients with specific CF genotypes, there are currently no therapies available to the majority of patients that target CF lung disease at its root. The overall aim of the DZL CF research program is to advance the current understanding of the pathogenesis of CF lung disease and to use this knowledge to improve CF diagnostics, to develop more sensitive tools for monitoring of disease activity, and novel strategies for the effective prevention and therapy of CF lung disease.

### Goals Achieved in 2017

- ✓ First results of the Orkambifacts® study (mechanism of action of combination therapy) published
- ✓ Potential of the IL-1R pathway as a therapeutic target in CF patients identified
- ✓ Chronic Pseudomonas infection model established
- ✓ New improved diagnostic approach (qPCR test) on Pseudomonas aeruginosa infection established

### Goals for 2018

- Complete Orkambifacts® recruitment
- Record 400 patients in the CF register
- Establish metagenomic pipeline for non-CF diseases
- Create association dataset (airway microbial metagenome/CF disease severity)
- Launch of a clinical investigator initiated trial to study the efficacy of a new antiinflammatory therapy with Anakinra to treat CF
- Launch of the first controlled and randomised clinical trial for the evaluation of the efficacy of the CF modulators Lumacaftor and Ivacaftor in toddlers, in cooperation with Vertex Pharmaceuticals

### Disease Area Leaders

Prof. Dr. Marcus Mall (BIH)

Prof. Dr. Burkhard Tümmler (BREATH)

### Administrative Coordinator of the Disease Area

Dr. Birgit Teucher (TLRC)

### Participating DZL Partner Sites

ARCN, BREATH, TLRC, UGMLC

## Research Highlight 2017

### Advancement of non-invasive diagnosis and therapy monitoring in children with cystic fibrosis

Cystic Fibrosis (CF) is a genetic condition that affects more than 8,000 children, adolescents and adults in Germany. Although it is a multi-organ disease, the irreversible damage to the lungs determines life expectancy and quality of life. Over time, the build-up of sticky mucus in the airways predisposes patients with CF to chronic infections and inflammation, which result in progressively reduced lung function. In general, the lungs of patients with CF are regularly monitored with computed tomography (CT), which is considered an invasive method due to the exposure to radiation. Therefore, it is of utmost importance to advance and improve sensitive non-invasive techniques for the diagnosis and monitoring of CF lung disease, such as magnetic resonance imaging (MRI) of the lung and the measurement of the lung clearance index (LCI) by the multiple breath-washout method. Previously, Heidelberg scientists advanced and optimized both methods with regard to feasibility and efficiency of the detection of early onset lung disease in separate trials.

The earlier targeted therapy for CF lung disease commences, in particular in response to difficult to detect exacerbations, the longer the onset of irreversible lung damage and complications can be delayed. In the most recent trial, the MRI and LCI method were for the first time systematically compared in patients with CF ranging in age from newborns to young adults. For most of the 97 children and young adults investigated, the findings revealed that the changes detected in lung structure and perfusion by MRI corresponded to a higher than usual rate of lung volume turnover, as measured by the clearance of a marker gas from the airways (LCI). It has thus been demonstrated for the first time that the non-invasive and

radiation-free methods MRI and LCI are both equally suitable to detect very small changes in lung function across all age groups, at onset and during the course of disease. Both methods allow distinguishing between patients with mild and severe lung disease as well as their response to antibiotic therapy for acute pulmonary exacerbations. Not only are these results groundbreaking in terms of diagnosis and monitoring of CF lung disease, but they will also enable testing of the efficacy of recently developed novel preventive and therapeutic strategies without placing too high a burden on patients, in particular children.

The trial was published in the American Journal of Critical Care Medicine and is the result of a successful cooperation between the Cystic Fibrosis Center, at the Heidelberg University Medical Center for Children and Adolescents, the Clinic for Diagnostic and Interventional Radiology and the Department of Translational Pulmonology at Heidelberg University Hospital, funded by the German Center for Lung Research (DZL), the Dietmar Hopp Foundation and the German Cystic Fibrosis Foundation (Mukoviszidose e. V.).

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#### Further Information:

✉ Stahl M, Wielputz MO, Graeber SY, Joachim C, Sommerburg O, Kauczor HU, Puderbach M, Eichinger M, Mall MA (2017) Comparison of Lung Clearance Index and Magnetic Resonance Imaging for Assessment of Lung Disease in Children with Cystic Fibrosis. *Am J Respir Crit Care Med* 2017; 195: 349-359



*Magnetic Resonance Imaging (MRI)*





## Pneumonia and Acute Lung Injury

Acute lower respiratory tract infections represent an increasing public health problem worldwide, resulting in a disease burden greater than that of any other infection with mortality rates unchanged over the past 50 years. Likewise, the lack of any

therapeutic treatment for the most devastating clinical course of pulmonary infection, Acute Respiratory Distress Syndrome (ARDS), and an unacceptably high mortality rate, underscore an urgent need for novel, effective therapeutic approaches. Both microbial attack (bacteria, viruses, fungi) and non-microbial inflammatory injury (aspiration, inhalation of toxic gases) may cause Acute Lung Injury (ALI) with severe respiratory failure. The goal of this Disease Area is to decipher the molecular mechanisms underlying the spread of inflammation into the alveoli and to understand the cellular and molecular signaling pathways leading to dissolution of inflammation and repair of the alveolar epithelium integrity. Based on this knowledge, new therapeutic concepts are being developed to attenuate lung tissue damage and promote tissue repair and organ regeneration.

### Goals Achieved in 2017

- ✓ Host-pathogen interactions during colonization and invasion of *S. pneumoniae* in the respiratory tract defined
- ✓ Angiopoietin 2 as a predictive marker for mortality in patients with severe pneumonia identified
- ✓ CIGMA trial finalized and analyzed: adjuvant therapy with Trimodulin significantly improves survival in defined sCAP patients

### Goals for 2018

- Establishment of a bronchoalveolar lung organoid in-vitro model for high-resolution display of infection processes as well as lung damage and repair
- Definition of molecular mechanisms of macrophage-stem cell interaction in pulmonary repair after severe pneumonia for future therapeutic use
- Completion of recruitment for cohort 1 of the GI-HOPE study
- Establishment of a cross-DZG project with the German Center for Infection Research (DZIF)

### Scientific Coordinators of the Disease Area

Prof. Dr. Jürgen Lohmeyer (UGMLC)

Prof. Dr. Tobias Welte (BREATH)

### Administrative Coordinator of the Disease Area

Dr. Sylvia Weißmann (UGMLC)

### Participating DZL Partner Sites

all

## Research Highlight 2017

### Pneumococcal colonization of the nasopharynx protects against pneumococci: role of dendritic cells

*Streptococcus pneumoniae* (pneumococcus) is a colonizing commensal of the human nasopharyngeal compartment that colonizes around 40-70 % of the population in an asymptomatic and transient manner. Colonization of the nasopharyngeal compartment with *S. pneumoniae* is an important precondition for endogenous translocation of the bacteria to distal airways, leading to the development of invasive pneumococcal disease. However, some studies point out that nasopharyngeal colonization with *S. pneumoniae* also mounts protective immune responses against this pathogen, with protective potential against future pneumococcal infections. Overall, cellular and humoral responses of the nasopharyngeal compartment to pneumococcal colonization and their importance for developing adaptive immune responses are poorly defined. Furthermore, it remains unclear what mechanisms are involved to facilitate bacterial decolonization.

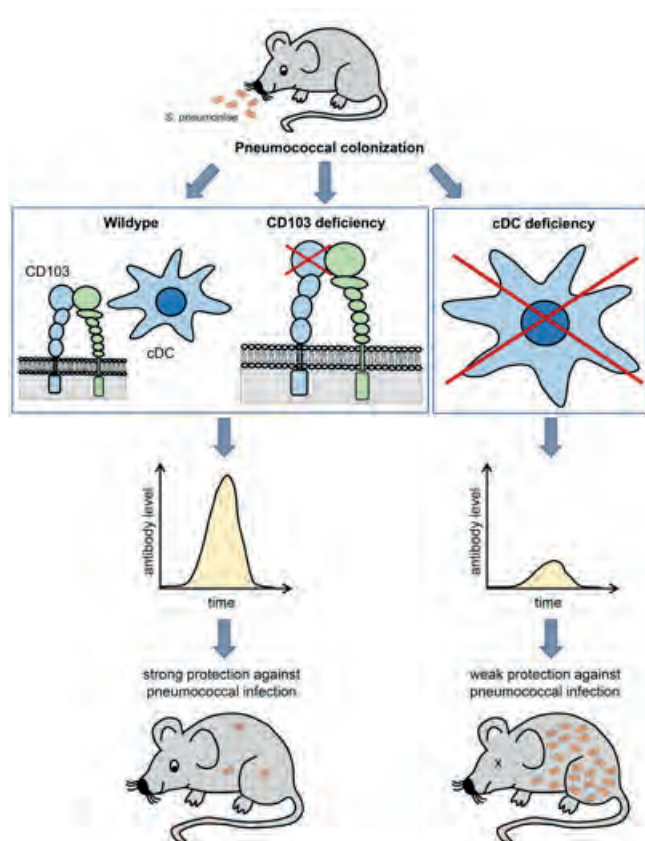
Under the lead of the DZL partner site BREATH investigators have found that nasopharyngeal colonization with pneumococcus led to substantial expansion of dendritic cell subsets (DCs), including classical dendritic cells (cDCs) and so-called

CD103 expressing DCs (CD103 DCs). Using different transgenic mouse models, both depletion of DCs and congenital DC deficiency resulted in significantly diminished antibody responses after colonization with *S. pneumoniae*, along with impaired protective immunity against invasive pneumococcal disease in mice. In contrast, CD103 deficient mice colonized with pneumococci showed a similar nasopharyngeal de-colonization, pneumococcus-specific antibody response and protection against pneumococcal infections as observed in colonized wild-type mice. Therefore, it can be concluded that classical dendritic cells but not CD103 expressing DCs contribute to pneumococcal colonization-induced adaptive immune responses against invasive pneumococcal disease in mice. Collectively, these data improve our understanding of cellular processes in colonization-induced immunity against pneumococcus and may foster the development of future nasopharyngeal vaccination strategies against pneumococcal diseases in humans.

#### Further information:

Dommaschk A, Ding N, Tort Tarres M, Bittersohl LF, Maus R, Stolper J, Jonigk D, Braubach P, Lippmann T, Welte T, Maus UA (2017) Nasopharyngeal colonization with *Streptococcus pneumoniae* triggers dendritic cell dependent antibody responses against invasive disease in mice. *Eur J Immunol* 47:540-551

Dommaschk A, Lang LF, Maus R, Stolper J, Welte T, Maus UA (2018) Colonization-induced protection against invasive pneumococcal disease in mice is independent of CD103 driven adaptive immune responses. *Eur J Immunol* 48:965-974





## Diffuse Parenchymal Lung Disease (DPLD)

Diffuse Parenchymal Lung Disease (DPLD) refers to more than 200 different diseases, which are characterized by progressive scarring of the lung architecture and often result in respiratory failure. DPLDs occur in children and adults secondary to acute or chronic lung injury provoked by the inhalation of toxic gases

or dusts, as part of systemic diseases, or as a result of therapeutic measures. In a considerable part of the cases, however, the cause remains unknown. This is referred to as Idiopathic Interstitial Pneumonia (IIP), which also comprises Idiopathic Pulmonary Fibrosis (IPF). Although different in origin, the course of many DPLDs is similar in terms of progressive severity and poor prognosis. The only curative treatment is lung transplantation. This Disease Area aims to develop new diagnostic strategies and causal treatment options by gaining deeper insights into the underlying disease mechanisms, from the newborn to the elderly patient.

### Goals Achieved in 2017

- ✓ Genetic profiling of neonatal/adult DPLD cohorts
- ✓ Identification and validation of novel molecular and cellular biomarkers in newborns, children, and adults
- ✓ Conduct and re-establishment of clinical studies (RELIEF study) as well as expansion of registers and cohorts across generations
- ✓ Demonstration of the distribution and effect of disease-specific drugs
- ✓ Characterization of epithelial differentiation, regeneration, and fibroproliferation

### Goals for 2018

- New strategies on clinical phenotyping of pediatric and adult DPLD cohorts
- Establishment of new clinical and interventional studies for neonatal and adult patients
- New disease models (in vivo and ex vivo)
- Development of markers and cellular therapies for initial epithelial damage and fibroproliferation (interactome atlas)

### Scientific Coordinators of the Disease Area

Prof. Dr. Andreas Günther (UGMLC)

PD Dr. Anne Hilgendorff (CPC-M)

### Administrative Coordinators of the Disease Area

Franziska Hauptkorn (CPC-M), Dr. Jutta Schlegel (UGMLC)

### Participating DZL Partner Sites

BREATH, CPC-M, TLRC, UGMLC



## Research Highlight 2017

### Early Diagnosis of Lung Disease in Babies

Bronchopulmonary Dysplasia (BPD), a severe disease, most often affects premature infants with a birth weight of not even 1,500 g but may also occur in fully developed newborns suffering from a lung problem after birth.

A team led by neonatologist PD Dr. Anne Hilgendorff, group leader at the Comprehensive Pneumology Center and the Institute of Lung Biology and Disease (ILBD) of the Helmholtz Center in Munich, partner of the German Center for Lung Research (DZL), and leader of the Center for Comprehensive Developmental Care at the Dr. von Hauner Children's Hospital and the Integrated Social-Pediatric Center at the University Hospital of Munich, in significant collaboration with Dr. Kai Martin Förster from the Perinatal Center at the University Hospital of Munich, has now found a method that, for the first time, might allow for early and safe diagnosis of BPD. In a paper published in the *American Journal of Respiratory and Critical Care Medicine*, the scientists identified three proteins that might suggest later development of BPD shortly after birth.

The lungs are among the organs to undergo full maturation at a very late stage. This means that they are not fully developed in premature infants, which makes them susceptible to acute complications such as respiratory distress syndrome and the later development of long-term complications such as the chronic lung disease BPD. At birth, there is a lack of fully developed alveoli and relevant blood vessels to absorb oxygen in these little patients. This leads to an increased oxygen demand and clinically apparent, great breathing efforts.

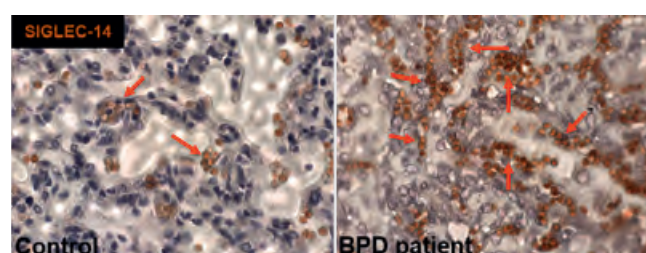
Mechanical ventilation, similar to long-term treatment with oxygen, ensures the children's survival, since it combats their acute shortness of breath. At the same time, however, mechanical ventilation and oxygen supply contribute significantly to the development of chronic long-term consequences.

To date, BPD cannot be detected sufficiently in advance. It is therefore not possible to initiate important therapies right after birth; instead, the child is monitored and treated according to the suspected risk.

However, the researchers from Hilgendorff's work group have now analyzed blood plasma samples of 35 premature infants collected during the first week of life and searched for changes to any detectable proteins in these samples. The test was repeated on the 28th day of life in order to identify permanent changes to these proteins. For the analysis of all data, the

scientists were able to develop a statistical model allowing to determine the proteins that may suggest imminent BPD right after birth.

It was precisely three proteins that were found during the analysis; in fact, not only do these proteins suggest the condition, but they may also contribute to the pathogenesis as a causative factor. They are part of the systems indicating reorganization of the alveoli, status of vascular development, and typical inflammatory response.



*C-14 protein in lung tissue of a BPD patient.*

Additional tests should now follow up on the results. A test is to be developed that allows for the identification of the three “marker proteins” in everyday clinical practice. In a clinical study, the children are then to be treated earlier according to the changes to the three proteins using protective methods that may contribute to the prevention of BPD.

If these methods proved to be useful and feasible in clinical practice, early diagnosis would significantly facilitate early treatment of the little patients and encourage the success of potential treatment options. However, these methods would also allow for studies related to the development of new treatments.

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#### Further Information:

Forster K, Sass S, Ehrhardt H, Mous DS, Rottier RJ, Oak P, Schulze A, Flemmer AW, Gronbach J, Hubener C, Desai T, Eickelberg O, Theis FJ, Hilgendorff A (2017) Early Identification of Bronchopulmonary Dysplasia Using Novel Biomarkers by Proteomic Screening. *Am J Respir Crit Care Med* 197: 1076-1080



## Pulmonary Hypertension

Pulmonary Hypertension (PH) is a disease of the pulmonary vasculature, leading to shortness of breath, dizziness, fainting, and ultimately right heart failure. A total of approximately 100 million people worldwide suffer from one of the forms of Pulmonary Hypertension. Vascular pathology is characterized

by vasoconstriction of the pulmonary vessels and abnormal (pseudomalignant) remodeling processes (thickening) of all vessel layers. Excessive proliferation of the vascular smooth muscle cells (SMC) is a prominent feature in virtually all forms of the disease. These remodeling processes lead to a severe loss of the cross-sectional area of the vessels, vascular pruning, and a concomitant increase in right ventricular afterload. Current PH therapy provides symptomatic relief and improves prognosis but falls short when it comes to recovering structural and functional lung vascular integrity, a prerequisite for symptom-free long-term survival. Restoration of the vascular structure and function (reverse remodeling) is the main goal of the research work carried out by the PH team.

### Goals Achieved in 2017

- ✓ 20 publications across the sites
- ✓ Initial description of PH in lung cancer
- ✓ Publication of the MERIT-1 study for evaluating the effectiveness of macitentan in Chronic Thromboembolic PH (CTEPH)
- ✓ Submission of authorization dossiers of macitentan for the treatment of CTEPH at the US regulatory authority FDA

### Goals for 2018

- Assessment of the applicability of the Heidelberg Gene Panel to estimate the prognosis of patients with Pulmonary Arterial Hypertension (PAH)
- Protein profiling analysis (Sciomics) of PAH patients to identify subgroups with different response to therapy
- Initiation of and recruitment into a proof-of-concept study: inhaled Paclitaxel for the treatment of PAH
- Publication of guidelines as a result of the 6th World Symposium on Pulmonary Hypertension (WHO conference)

### Scientific Coordinators of the Disease Area

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Prof. Dr. Ralph T. Schermuly (UGMLC)

### Administrative Coordinators of the Disease Area

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### Participating DZL Partner Sites

all

## Research Highlight 2017

### Macitentan to significantly reduce vascular resistance in Chronic thromboembolic pulmonary hypertension (CTEPH) patients

Chronic thromboembolic pulmonary hypertension (CTEPH) is characterized by narrowing of the pulmonary arteries. This constriction can be caused by blood clots that attach to the walls of the pulmonary arteries and can also be the result of acute pulmonary embolism. As a consequence, excessive tissue forms around the clot at the inner wall of the vessel building scars within the arterial wall. This causes constriction that restricts blood flow, increases blood pressure in the pulmonary circulation and leads to Pulmonary Hypertension. Consequently, right heart hypertrophy and dysfunction limit the physical capacity of affected patients. Left untreated, patients with CTEPH have a mean life expectancy of less than three years.

The gold standard treatment for CTEPH is pulmonary endarterectomy (PEA), a procedure in which the scar tissue is surgically removed from the pulmonary arteries. This complex procedure can be the cure of the disease, but 30 to 50 percent of patients are inoperable or still have increased resistance in the pulmonary vessels after surgery. Therefore, new drug options are needed to effectively treat this patient population. So far, only the soluble guanylate cyclase stimulator Riociguat has been approved for drug therapy of inoperable CTEPH. The mechanism of action of Macitentan is based on inhibiting the signalling of the hormone Endothelin, a protein with strong vasoconstrictive and growth-promoting properties. Endothelin acts via specific receptors in cells of the vessel wall, which are blocked by the drug Macitentan.

The Phase II clinical trial MERIT-1 demonstrated that the endothelin antagonist Macitentan significantly reduced pulmonary vascular resistance at 16 weeks versus placebo in 80 patients with inoperable CTEPH. The drug also showed significant improvements in the six-minute walking distance, an important performance parameter in patients with severe pulmonary or cardiac diseases.

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#### Further information:

✉ Ghofrani HA, Simonneau G, D'Armini AM, Fedullo P, Howard LS, Jaïs X, Jenkins DP, Jing ZC, Madani MM, Martin N, Mayer E, Papadakis K, Richard D, Kim NH; MERIT study investigators (2017) Macitentan for the treatment of inoperable chronic thromboembolic pulmonary hypertension (MERIT-1): results from the multicentre, phase 2, randomised, double-blind, placebo-controlled study. *Lancet Respir Med*; 5(10): 785-794.





## End-Stage Lung Disease

Various acute and chronic lung disorders may ultimately lead to End-Stage Lung Disease (ELD). Once all options for mechanical ventilation have been exhausted, only two treatment options remain for these patients on the brink of death: extracorporeal membrane oxygenation (ECMO) or lung transplantation. Today, however, ECMO therapy remains restricted to short-term application, primarily as a bridge to transplantation

### Goals Achieved in 2017

- ✓ Increase in human and material resources in the “Stem-Cell Research” flagship project
- ✓ DZL professorship for pulmonary pathology with a focus on end-stage lung disease (has been appointed)
- ✓ DFG (German Research Foundation) priority program funding for the development of implantable, artificial lungs received
- ✓ Funding of the ELD Translational Flagship project requested at the DFG (clinical study)

### Goals for 2018

- Preparation of position papers on organ donation (LTx) and post-Tx donor management
- Establish and pilot a prevention concept for post-Tx patients
- Joint ELD project for ex-vivo evaluation of stem-cell therapies

and as a bridge to recovery in acute pulmonary infections (e.g. H1N1). In chronic lung injury, transplantation remains the only available therapy with the potential of true long-term survival. This treatment option, however, may only be used in a limited number of patients, excluding those with lung tumors, and long-term survival can be severely compromised by chronic rejection. Regenerative therapies that promote endogenous lung repair, cell transplantation, or tissue engineering are currently not available. The research program therefore aims to refine transplantation procedures and further develop preoperative preparation and postoperative care in lung transplantation to minimize acute and chronic rejection. It also aims to optimize ECMO therapy towards fully implantable lung devices and set the stage for regeneration of diseased lung tissue.

### Scientific Coordinators of the Disease Area

Prof. Dr. Axel Haverich (BREATH)

Prof. Dr. Veronika Grau (UGMLC)

### Administrative Coordinators of the Disease Area

Dr. Annegret Zurawski (BREATH)

### Participating DZL Partner Sites

BREATH, CPC-M, UGMLC

## Research Highlight 2017

### New insights into the physiology of chronic lung allograft dysfunction

Clinician scientists from the Comprehensive Pneumology Center Munich (CPC-M) have shed new light on the pathophysiology of chronic rejection following lung transplantation. Chronic lung allograft dysfunction (CLAD) is the main limiting factor for long-term survival after lung transplantation. Early determination of diseases phenotypes could help to identify patients who are at risk of poorer outcome and, as such, are in need of specialized care.

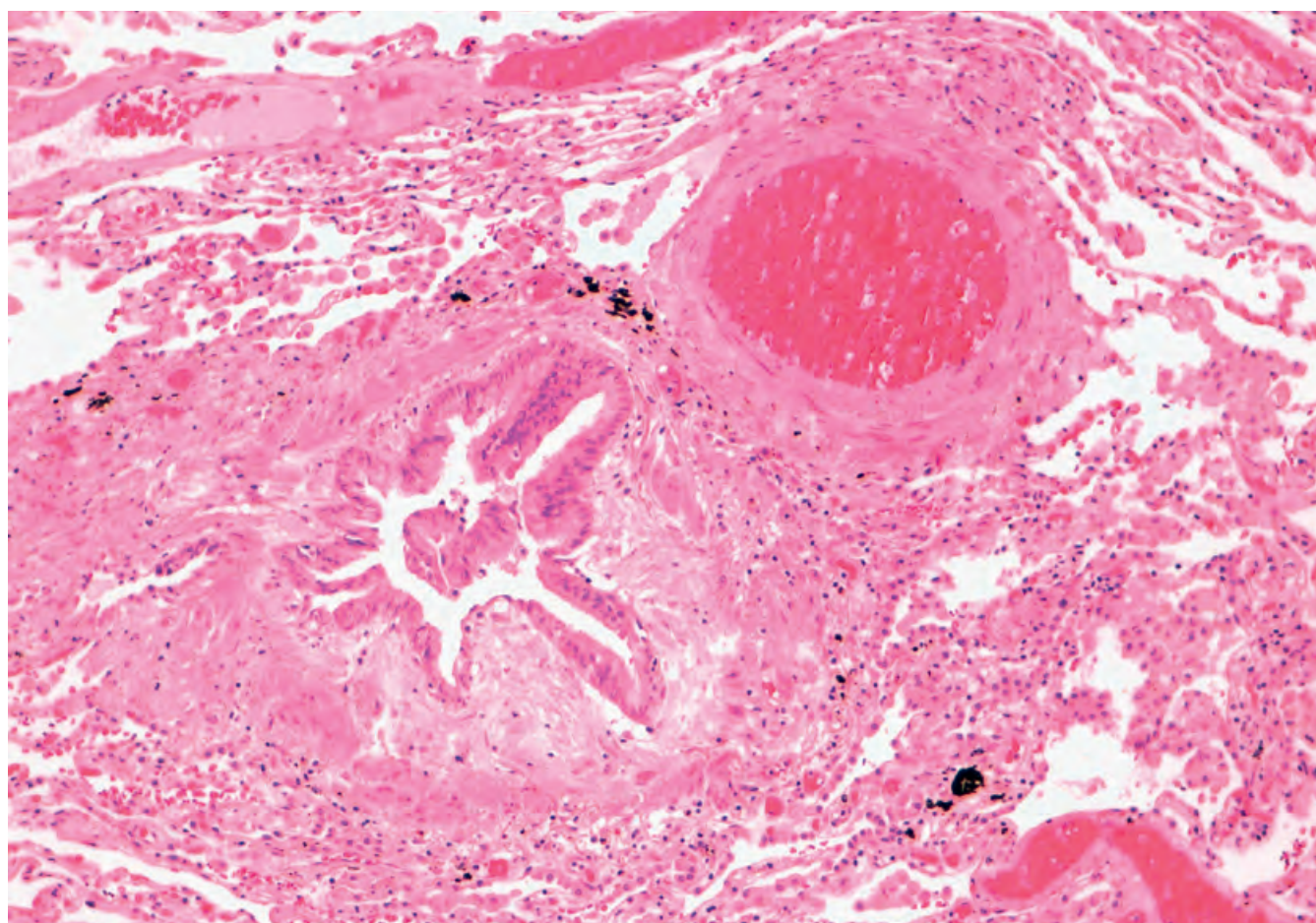
DZL-PI Nikolaus Kneidinger and colleagues investigated the utility of longitudinal lung volume measurements in the surveillance of lung transplant recipients. They demonstrated that comprehensive pulmonary function tests permit the identification of specific physiological phenotypes of CLAD. Both pulmonary restriction and air trapping at the onset of CLAD were associated with poor survival. This finding allows the early identification of patients who are at risk and the possibility of targeted intervention. The results were published in the European Respiratory Journal. An accompanying editorial by

Professor Alan Glanville provides context on the mechanisms of CLAD phenotypes and suggests how the physicians can use these findings for the benefit of their patients.

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#### Further information:

✉ Kneidinger N, Milger K, Janitz S, Ceelen F, Leuschner G, Dinkel J, Königshoff M, Weig T, Schramm R, Winter H, Behr J, Neurohr C (2017) Lung volumes predict survival in patients with chronic lung allograft dysfunction. *Eur Respir J*; 49(4). doi: 10.1183/13993003.01315-2016.



*Constructive bronchiolitis in Bronchiolitis obliterans syndrome following lung transplantation. Atypical lung resection. HE-Staining.*





## Lung Cancer

Lung Cancer is among the most common types of cancer in Germany. The high mortality rate is often due to diagnosis at a late

### Goals Achieved in 2017

- ✓ Establishment of a mass spectrometry approach for absolute quantification of the TGF- $\beta$  receptor
- ✓ Confirmation of p53 mutations promoting the maturation of a fibronectin receptor that stimulates metastasis (integrin alpha-5)
- ✓ Development of a gene panel for early detection of tumor diseases
- ✓ Identification of a critical lung cancer gene leading to pleural effusion
- ✓ Identification of a high-risk factor for metastasis and early treatment failure (ALK gene mutations)

### Goals for 2018

- Evaluation of integrin alpha-5 maturation as a therapeutic target in p53 mutations
- Establishment of a prognostic marker in squamous cell carcinoma for overall survival
- Genotyping of the prospective lung adenocarcinoma cohort
- Characterization of the clinical relevance of important molecular features of ALP patients
- Start of a joint pulmonary fibrosis/lung cancer cohort for multi-omics analysis

stage: 40% of Non-Small Cell Lung Cancer (NSCLC) patients present with metastases at the time of diagnosis. Advances in molecular tumor analysis have led to new opportunities to develop targeted therapies that act on specific molecular targets of the cancer cell. Besides chemotherapy and targeted therapy, immunotherapy has gained significance as the third main pillar of systemic therapy. Immune checkpoint inhibitors unmask the cancer cells and enhance the body's immune response against malignant cells. Today, combined treatment approaches in precision medicine enable the application of the most effective treatment regimen for each patient. However, not all patients respond to targeted therapy or immunotherapy. Therefore, an important research goal is the identification of predictive markers indicating clinical response or potential treatment failure, for example through evidence of genetic tumor material towards biomarker-directed precision medicine.

### Disease Area Leaders

Prof. Dr. Ursula Klingmüller (TLRC)

Prof. Dr. Michael Thomas (TLRC)

### Administrative Coordinator of the Disease Area

Dr. Birgit Teucher (TLRC)

### Beteiligte DZL-Standorte

all



## Research Highlight 2017

### How cancer cells flood the lung

Malignant pulmonary effusion (MPE) frequently occurs in patients with metastatic breast or lung cancer. It involves build-up of excess fluid in the pleural cavity, the area between the lungs and the chest wall, which contains malignant cells. The MPE lung is surrounded by fluid, which can cause shortness of breath and chest pain, for example, and may even prove fatal. The reasons why some patients develop MPE while others do not remain unclear. There are currently no effective therapies for this complication and patients with MPE have a lower life expectancy compared to those without MPE. In the case of large pulmonary effusions with volumes exceeding one liter, symptomatic treatment usually involves aspiration in order to relieve pressure on the lung.

DZL scientists at the Institute for Lung Biology (ILBD) and the Comprehensive Pneumology Center (CPC) at the Helmholtz Zentrum München investigate possible causes and mechanisms of pleural effusion to develop future preventive strategies and treatment options. In a first step, using animal models and cancer cell lines, mutations of the KRAS gene were identified as possible triggers for MPE. In a next step, the scientists were also to isolate mutant KRAS gene in MPE material from lung cancer patients. KRAS is known to play a key role in the growth of various malignant tumors. Further experiments showed that the KRAS mutant cells released a messenger substance into the bloodstream, which in turn attracted immune cells. The messenger substance in question is CCL2 (CC-Chemokine ligand 2), which is often released when inflammation occurs. The immune cells then wander to the pleural cavity via the spleen, where they cause the effusion.

In order to verify whether the newly acquired knowledge could be applied in clinical practice, the scientists tested two active substances that interrupt the mechanism at two different points. In an experimental model, they were able to demonstrate that both the KRAS inhibitor Deltarasin, which prevents the transport of the cancer-causing protein KRAS to the cell membrane, and an antibody against the messenger substance released by the cancer cells prevented pleural effusion.

Lung cancer is one of the most common types of cancer in Germany, and about one third of all MPEs are the result of lung cancer. Considering the still large number of smokers, appropriate treatments are urgently needed. While the search for further mechanisms continues, the results of this study suggest that drugs targeting the mechanism discovered could be

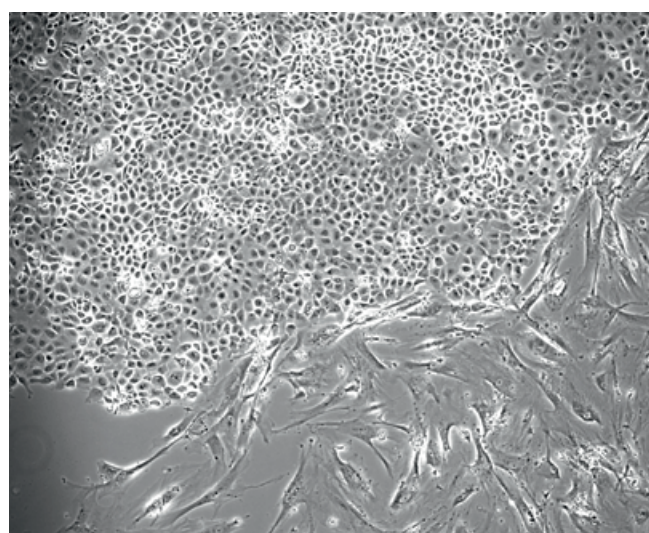
a potential treatment option. Further studies are now needed to confirm that.

Lung cancer expert and principal investigator Georgios Stathopoulos joined the Helmholtz Zentrum München in 2015. He also heads a working group at the Laboratory for Molecular Respiratory Cancerogenesis at the University of Patras in Greece. The study that has now been published was the outcome of a collaboration between the two working groups.

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#### Further information:

✉ Agalioti T, Giannou AD, Krontira AC, Kanellakis NI, Kati D, Vreka M, Pepe M, Spella M, Lilis I, Zazara DE, Nikolouli E, Spiropoulou N, Papadakis A, Papadia K, Voulgaridis A, Harokopos V, Stamou P, Meiners S, Eickelberg O, Snyder LA, Antimisariis SG, Kardamakis D, Psallidas I, Marazioti A, Stathopoulos GT (2017) Mutant KRAS promotes malignant pleural effusion formation. *Nature Communications*, DOI: 10.1038/ncomms15205



*The image shows isolated cells from a pleural effusion. The cancer cells in the lower half of the picture carry mutated KRAS genes.*



## Biobanking & Data Management Platform

### Goals Achieved in 2017

- ✓ Operation of the central DZL data warehouse, integration of initial databases, and periodic updates
- ✓ Creation of teaching videos on how to use the data warehouse
- ✓ Development of a catalog for clinical parameters using the LOINC/SNOMED/SPREC codes and a uniform phenotype and specimen catalog, including the online reference work CoMetaR (Collaborative Metadata Repository)
- ✓ Establishment of the “Omics Platform” DIOP (DZL integrative omics platform)
- ✓ Harmonization and consolidation of the platforms’ internal regulations Biobanking & Data Management and Imaging

### Goals for 2018

- Integration of additional databases into the DZL data warehouse
- Improvement of data quality through data harmonization (annotation, terminology, ontology)
- Creation and implementation of a Broad Informed Consent for children & young people
- Project planning and assignment using the central data warehouse
- Further development of interaction with the DZG centers

The DZL Disease Areas are supported by an extensive network of central infrastructure including the Biobanking Platform. The overall aim of the DZL Biobanking Platform is the collection and storage of biospecimens and associated clinical data of different pulmonary diseases, with the intention of facilitating access for research purposes within and outside the DZL. Ethical and data protection rules apply. All DZL sites contribute to the Biobanking Platform and the focus is on the harmonization of procedures, quality control and data management.

### Scientific Coordinators

Prof. Dr. Andreas Günther (UGMLC)

Dr. Thomas Muley (TLRC)

### Administrative Coordinator

Dr. Jutta Schlegel (UGMLC)

### Central Biobanking Management

Dr. Clemens Ruppert (UGMLC)

### Central Data Management

Raphael Majeed (UGMLC)

### Broad consent for pediatric biobanking – discussing crucial points of a template

The reluctance to conduct pediatric research has long mirrored the general paradigm that children need special protection as a vulnerable group. This has led to a relative lack of research in children. International recommendations now emphasize that “children and adolescents must be included in health-related research unless a good scientific reason justifies their exclusion” (CIOMS/WHO 2002, Revision 2016). Children participation in research must be protected as well as possible.

Including samples of children in biobanks for scientific purposes demands reconsidering central aspects of biobank-governance (Hens et al. 2011). Particularly thorny questions revolve around informed consent/assent of children, for example understanding and decision making in the developing child, or the proper age for assent (e.g. Hunfeld/Passchier 2012; Hens et al. 2013).

One aim of the “All-Age-Asthma-Cohort” (ALLIANCE) is the observation of children with different asthma phenotypes from childhood to adulthood. To enable ethical and effective research, we considered the option of broad consent for pediatric biobanking, with the aim towards developing an ethical framework for pediatric broad consent. To the best of our knowledge, this is the first such attempt for German biobanks.

Whilst working towards the framework, we identified the following pertinent ethical issues we offer for discussion:

- The question of whether the children as well as their parents have a right to withdraw;
- The question of whether the parents could have the right to give their consent for sequencing of the whole genom of the minor for research purposes or whether sequencing of the whole genom could only be carried out after the minor has reached the age of majority and consented himself.
- That parents have no surrogate ‘right not to know’ and that pediatric biobanks should thus have a clear policy about returning clinically actionable information on early onset diseases. Minors should be notified regardless of their parents’ wishes, provided the findings are subject to assessments of clinical validity and utility.
- That each pediatric biobank should develop a policy for how data and samples will be handled once a pediatric

participant has reached the age of majority. Two ways seem acceptable: anonymization of samples and data, or re-contacting.

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#### Further Information:

📄 Hens, K., Lévesque, E. and Dierickx, K (2011) Children and biobanks: a review of the ethical and legal discussion *Human Genetics* 130, 403–413

📄 Hens K, Van El CE, Borry P, et al. (2013) Developing a policy for paediatric biobanks: Principles for good practice. *Eur J Hum Genet* 21:2e7

📄 Hunfeld JA, Passchier J (2012) Participation in medical research; a systematic review of the understanding and experience of children and adolescents. *Patient Educ Couns* 87(3):268–76

📄 Revision of the International Ethical Guidelines for Biomedical Research Involving Human Subjects. Prepared by the Council for International Organizations of Medical Sciences (CIOMS) in collaboration with the World Health Organization (WHO) CIOMS Geneva 2002, 2016





## Imaging Platform

### Goals Achieved in 2017

- ✓ Involvement of all DZL centers in prospective clinical studies with a focus on the development and validation of imaging-based biomarkers
- ✓ Imaging Platform meetings with hands-on workshops in the microscopy and radiology fields
- ✓ Formation of a work group for the creation of reviews on the subject of "Growing and Ageing of Vessels and Airways (GAVA)"
- ✓ Development and implementation of a concept on the production of webcasts for the DZL Online Academy
- ✓ Establishment of a data backup concept for the imaging database

### Goals for 2018

- Continuation of prospective clinical studies
- Writing and submitting the first review paper on "GAVA"
- Formation of a group of microscopy experts for the creation of a lung atlas
- Transformation of the Imaging Platform into a "Science-Driven Reference Network"
- Setup of interfaces to the other Centers for Health Research and consortia of the German Medical Informatics Initiative for exchanging images and associated data

A wide range of innovative imaging approaches in microscopy and radiology is available to scientists to gain improved knowledge of the emergence and development of lung diseases, or to evaluate the effectiveness of drugs and support the drug-discovery processes. The Imaging Platform has been established with the aim to ensure the availability of different imaging technologies within the DZL and facilitate the use of imaging for research. "Imaging" is understood as the interaction of imaging approaches of various modalities and with different resolutions and dimensions in the preclinical, translational, and clinical fields. The Imaging Platform has established itself as a comprehensive methods platform, with a focus in 2017 on the promotion of prospective clinical studies related to the development and validation of imaging biomarkers as well as the implementation of standardized protocols and relevant training of staff.

### Scientific Coordinators

Prof. Dr. Heinz Fehrenbach (ARCN)  
 Prof. Dr. Hans-Ulrich Kauczor (TLRC)  
 Prof. Dr. Matthias Ochs (BREATH)

### Administrative Coordinators

Dr. Birgit Teucher (TLRC)  
 Kerstin Burmester (TLRC)



### Patient-friendly acquisition of regional ventilation and perfusion dynamics in the lung with phase resolved functional lung (PREFUL) MRI

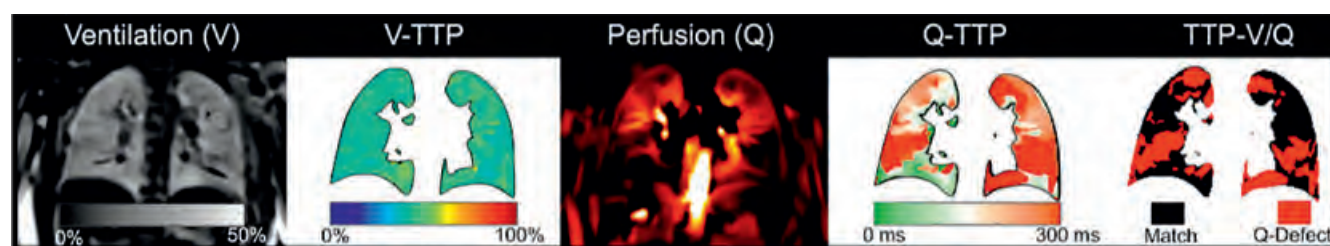


Figure 1. PREFUL MRI depicts the typical V/Q mismatch of a CTEPH patient and shows increased Q-TTP.

Results published in Magnetic Resonance in Medicine confirm the feasibility of phase resolved functional lung (PREFUL) magnetic resonance imaging (MRI), which allows the calculation of new quantitative biomarkers with a high correspondence to computed tomography (CT) and dynamic contrast-enhanced (DCE) MRI in healthy volunteers and patients with lung disease.

This feasibility study was conducted at the Biomedical Research in End-stage and Obstructive Lung Disease Hanover (BREATH) at the Department of Diagnostic and Interventional Radiology at Hannover Medical School (MHH).

Time series of MR images of two healthy volunteers, one patient with chronic thromboembolic hypertension (CTEPH), one patient with cystic fibrosis (CF) and one patient with chronic obstructive pulmonary disease (COPD) were acquired at 1.5 T in free breathing without inhalation or injection of contrast media. After correction for respiratory motion and filtering, a mathematical model to estimate cardiac and respiratory phases was applied. Subsequently, all images were sorted to create one complete cardiac and respiratory cycle with increased temporal resolution. In addition to conventional parameters, new parameters like time to peak (TTP) and regional ventilation flow-volume loops were derived.

Whereas the volunteers showed homogenous distribution and no ventilation or perfusion defects, the CTEPH patient showed increased perfusion TTP (see Figure 1) in hypoperfused regions in visual agreement with DCE MRI. CF and COPD patients showed a pattern of increased ventilation and perfusion TTP in regions of hypoventilation and decreased perfusion. Ventilation flow-volume loops of the COPD patient were smaller in comparison with healthy volunteers (see Figure 2), and showed regional differences in agreement with functional small airways disease and emphysema on CT.

This study successfully adapted the flow-volume concept from spirometry for analysis of phase resolved regional ventilation

data. Given the additional regional information, this method appears to be sensitive to differences even during normal tidal breathing. As the new parameters take into account the whole breathing and cardiac cycle they have the potential to show a higher sensitivity for early lung disease in comparison with conventional parameters.

In contrast to previous studies, which used modified sequences for ultra-fast imaging or self-gating, a simple and robust MR acquisition was used in this study. Therefore, the scan can be performed on every clinical scanner. This patient-friendly MR method has high potential for clinical translation in the near future for improved early disease detection and quantitative monitoring of lung disease.

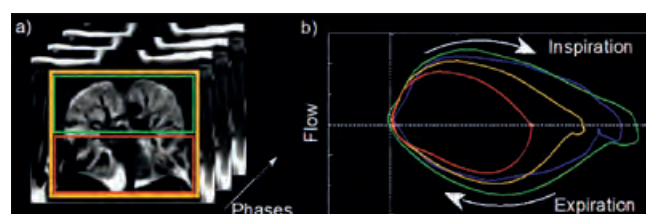


Figure 2. The reconstructed respiratory cycle a) can be used to calculate regional flow-volume loops b). Note the much smaller loop of the COPD patient in the lower lung (red) in comparison to whole lung average (orange), the upper lung (green) and the healthy volunteer (blue).

#### Further information:

✉ Voskrebenezov A, Gutberlet M, Klimes F, Kaireit TF, Schönfeld C, Rotärmel A, Wacker F, Vogel-Claussen J. (2018) Feasibility of quantitative regional ventilation and perfusion mapping with phase-resolved functional lung (PREFUL) MRI in healthy volunteers and COPD, CTEPH, and CF patients. *Magnetic Resonance in Medicine* 79(4):2306-2314

## Research Highlight Microscopy 2017

### 3D insights into the lung's capillary system

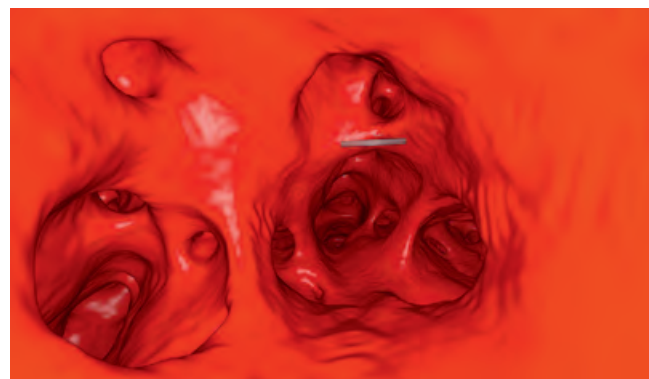
The system that forms the basis of the lung's fine structure is complex and highly branched. At the very end of the respiratory tree, within the alveoli, blood and air are separated by only a few hundred nanometers. To ensure the necessary gas exchange, it is essential that the surface area is very large. In-depth knowledge of these structures is important to better understand mechanisms of vascular development and pathology of the lung.

However, previously available two-dimensional images provide only limited insight into structural properties or changes. Although stereological techniques allow characterization of three-dimensional (3D) attributes as well, these do not provide full 3D representation. By contrast, the spatial interpretation of sections offers a means not only of examining the 3D structure of the airways and blood circulatory system – especially the capillary system – but also of visualizing it. More than 300 serial sections of lung tissue embedded in epoxy resin were aligned to each other in order to create a 3D datasets of a sample with an edge length of about 1 mm. Specially developed computer programs allow to distinguish between airways, tissue and blood vessels, which is not only the basis for a 3D animation.



3D reconstruction (approx. 1 mm x 1 mm x 0.3 mm, at a resolution of approx. 0.3  $\mu$ m) based on histological sections of lung tissue, with cross-sectionally cut blood vessels, airways (bronchus) and alveoli. The arteries are shown in red, the veins in blue, the capillary network in magenta and the surface of air-containing spaces in grey. Partial transparency reveals how the capillary blood vessel system envelopes the alveoli. A schematic representation of the route taken by an oxygen molecule – through the airways, entering an alveolus and then the blood – and the 'return journey' of a carbon dioxide molecule can be viewed in video form at the project's web presence: <http://osf.io/gbsns/>

The result is astonishing: the viewer practically races through the vessels from a blood cell's perspective. This experience is augmented by an oxygen molecule's 'view' as it moves through the airways. The visualization extends from the bronchioles and alveoli to the capillaries of the blood system. The resolution of the data is less than one micrometer. These data clearly show the course taken by both blood flow and airflow, as well



3D view provided by a virtual endoscopy through the network of blood vessels, at the transition point between the arterioles and the capillary vessels (lateral outflows) with a very high branching density and a marked reduction in the vascular cross-sectional area. A video clip showing the virtual endoscopy from the artery, through the capillaries and to the vein, is available at the project's web presence: <http://osf.io/jhsd3/>

as how many alveoli a blood cell passes, which would not be possible with a two-dimensional tissue analysis. The high ratio between sample size and resolution make the result more detailed than other tomographic methods. Moreover, the procedure developed is technically straightforward and relatively cost-effective. Now the aim is to further automate the process and thus obtain an efficient way of answering questions about normal and impaired pulmonary development.

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#### Further Information:

✉ Grothausmann R, Knudsen L, Ochs M, Mühlfeld C (2017) Digital 3D reconstructions using histological serial sections of lung tissue including the alveolar capillary network. *American journal of physiology Lung cellular and molecular physiology* 312(2):L243-L57

# DZL Technology Transfer Consortium

## Chairman

Dr. Christian Stein (MD, Ascenion GmbH)

Dr. Peter Stumpf (MD, TransMIT GmbH)

## Administrative Coordinator

Dr. Annegret Zurawski (BREATH)

## Scientific Adviser

Prof. Dr. Werner Seeger (DZL-Chairman)

Efficient and effective exploitation of research results remains a key priority of the DZL. The DZL Technology Transfer Consortium, founded in 2013, is made up of representatives from the technology transfer organizations of all DZL partners as well as representatives from DZL, among them Prof. Dr. Werner Seeger (Chairman of the DZL), who acts as Scientific Advisor, and Dr. Annegret Zurawski, Manager of BREATH (Hannover).

The Consortium provides key services to DZL members including:

- Abstract screening services for DZL meetings
- Abstract screening "hotline" for DZL scientists on an as-needed basis
- Exploitation contract review
- Counsel regarding preparation for scientific review meetings with BfArM with the aim of minimizing potential procedural errors

The institutions participating in the DZL Technology Transfer Consortium are:



Max-Planck-Innovation







## Clinical Trial Board and Clinical Studies in the DZL

The DZL annually allocates a portion of its budget for innovative clinical trials based on the initiatives of DZL scientists (Investigator-Initiated Trials). These competitively awarded funds allow DZL investigators (DZL-PIs) to respond to new advances in the field and translate those findings as quickly as possible into positive outcomes for patients.

These funds are considered seed money, enabling the rapid transfer of novel findings into “first in human” investigations before external sponsoring is considered or may be achieved. Since 2012, annual calls for proposals have been distributed to DZL-PIs, giving them the opportunity to apply for these funds. The proposals are then reviewed and evaluated by the DZL Clinical Trial Board in a competitive process. Final funding decisions are approved by the DZL Executive Board, based on the recommendations of the Clinical Trial Board.

In the following Table, the clinical studies selected according to this procedure (Investigator-Initiated Trials) and currently running in this reporting year are listed.

DZL investigators are also involved in more than 250 clinical trials, addressing novel diagnostic and therapeutic approaches in lung diseases. Most of these studies are externally sponsored.

In addition, in 2017, for the second time, DZL investigators were able to apply for special funds for the preparation and completion of applications for clinical studies.

These additional funds were provided to encourage investigators to apply for funding for clinical trials not only at DZL, but also from other sponsors, e.g. the DFG or the BMBF.

### Scientific Coordinators

Prof. Dr. Jürgen Behr (CPC-M)

Prof. Dr. Susanne Herold (UGMLC)

Prof. Dr. Norbert Krug (BREATH)

Prof. Dr. Michael Thomas (TLRC)

PD Dr. Henrik Watz (ARCN)

### Administrative Coordinator

Dr. Annegret Zurawski (BREATH)



## Investigator Initiated Trials supported with DZL Funds

Coordinator(s)/ scientist(s)	Disease Area	DZL Partner Site(s) involved	Title
Behr J / Günther A	Diffuse Parenchymal Lung Disease (DPLD)	all	Exploratory efficacy and safety study of oral pirfenidone for progressive, non-IPF lung fibrosis (RELIEF in lung fibrosis)
Griese M	Diffuse Parenchymal Lung Disease (DPLD)	all	Hydroxychloroquine (HCQ) in pediatric ILD (= children's interstitial lung disease; chILD)
Herold S	Pneumonia and Acute Lung Injury	BREATH, UGMLC	GM-CSF Inhalation to improve Host defense and Pulmonary barrier restoration (GI-HOPE)
Herold S / Lohmeyer J / Welte T	Pneumonia and Acute Lung Injury	BREATH, UGMLC	Promotion of host defense and alveolar barrier regeneration by inhaled GM-CSF in patients with pneumonia-associated ARDS
Heußel C	Lung Cancer	BREATH, CPC-M, TLRC, UGMLC	Early response capturing in the treatment of adenocarcinoma
Jobst B	COPD	all	Imaging disease progression in COPD
Kreuter M / Vogelmeier C / Herth F	COPD	TLRC, UGMLC	Exploring efficacy of periodontal treatment on systemic inflammation and for prevention of exacerbations in patients with COPD: A multi-center, prospective, randomized, controlled, parallel-group pilot study
Reck M / Ammerpohl O / Barreto G	Lung Cancer	all	Monitoring of patients with NLCLC – epigenetic analysis of liquid biopsies and RNA-analysis in exhaled breath condensates
Schulz H / Meiners S / Vogelmeier C / Behr J	COPD	CPC-M, UGMLC	Proteasom Function as a Bio-Marker for COPD
Seeger W / Ghofrani A / Gall H	Pulmonary Hypertension	BREATH, UGMLC	Influence of specific PAH medication on right ventricular function in patients with pulmonary arterial hypertension
Tümmler B	Cystic Fibrosis/ Mucoviscidosis	BREATH, TLRC, UGMLC	Orkambifacts – Intestinal current measurements (ICM) to evaluate the activation of mutant CFTR in treated with lumacaftor in combination with ivacaftor.
Vogel-Claussen J	Radiology/Pulmonary Hypertension	BREATH, CPC, UGMLC, TLRC	Change-MRI – Phase III diagnostic trial to demonstrate that functional lung MRI can replace VQ-SPECT in a diagnostic strategy for patients with suspected CTEPH.
Vogelmeier C	COPD	ARCN, BREATH, UGMLC	Clinical study to investigate safety, tolerability, efficacy, pharmacokinetics and pharmacodynamics of multiple doses of the human GATA-3-specific DNAzyme solution SB010 in patients with moderate to severe COPD – A randomised, double-blind, parallel, multicentre, phase IIa pilot study
Zabel P/Herth F/ König I/ Rabe K/ Welte T	COPD	ARCN, BREATH, TLRC	Evaluation of non-invasive pursed-lip breathing ventilation in advanced COPD

# DZL Collaborations, Partnerships, and Networks

In the German Center for Lung Research (DZL), more than 240 scientists and their work groups, currently from a total of 29 university and non-university research institutions as well as clinics at five DZL sites in Germany and other sites of associated partners, all work together. This means that an intensive exchange both between DZL researchers among the sites and of the entire network with external partners is of particular importance, all devoting themselves to one common goal: to research and combat lung disease to the best of their ability. Besides weekly telephone conferences and numerous regular meetings of the work groups, committees, and administrative units, particular attention should be brought to the Annual Meeting, for which all DZL members, including many junior researchers, get together to exchange views on the status of their projects.

With around 470 participating scientists, physicians and junior researchers, the **6th DZL Annual Meeting on January 30 and 31, 2017 in Munich** saw a new record number of participants. With highlight presentations, moderated poster sessions on around 290 submitted poster abstracts, numerous work-group meetings, and the get-together on the first evening, the Annual Meeting provided excellent conditions for a networking scientific exchange. Six members of the Advisory Board strongly supported the Board of Directors with advice on the further development of the Center. On the two days before the start of the Annual Meeting, participants of the **DZL Mentoring Program “Careers in Respiratory Medicine”** were able to take part in an exciting workshop on the subject of “Strategic Career Planning for Junior Researchers”. This opportunity for the promotion of junior researchers with intensive and individual support by experienced mentors attracts wide interest; the aim is to continue and advance this program in the future as an important component of the DZL Academy program (see also “Promotion of Junior Scientists and Equal Opportunities”).

On top of that, numerous other events with DZL involvement took place at the DZL sites. Since its foundation, the German Center for Lung Research has been part of several networks conducting research into various pulmonary diseases, while it is associated with other organizations contributing to the

realization of research projects. The expansion and development of **partnerships in the fields of science and research, promotion of junior scientists, patient information and interests, clinical studies, industry, and educational work** continue to be actively pursued. Numerous **national and international** collaborations strengthen the position of the DZL as an outstanding institution and the largest German research network in the field of pulmonary research.

The DZL cooperates closely with the **Lung Information Service (LIS)** based at the Helmholtz Center in Munich and supports the range of easy-to-understand information from research and clinical practice about pulmonary diseases. The scientists and doctors at the DZL sites take on an advisory role for editorial contributions of the LIS and individual patient inquiries sent to the LIS. In addition to its online platform, the Lung Information Service also organizes events such as patient fora on special subjects. In 2017, patient fora were organized in collaboration with the DZL at various sites of the Center.

For instance, together with the LID and for the first time with the German Lung Day (Deutscher Lungentag), the DZL invited interested patients and their families to the **17th Patient Lung Forum** on the subject of “Clinical Studies in Lung Research” in Stuttgart, immediately followed by the Annual Meeting of the German Respiratory Society (DPG), which took place there as well. The focus of the event was on questions such as how clinical studies are conducted, what benefits and burdens they entail for the patients participating, how science can benefit from these studies, and what kinds of studies there are with regard to major chronic conditions such as asthma, pulmonary fibrosis, and lung cancer. For one afternoon, proven experts outlined the current state of knowledge in short presentations and answered the participants’ personal questions.

Additional patient events with DZL involvement included the **ALPHA-1 Patient Day** on June 2, 2017 at Hannover Medical School (MHH) and the **18th Patient Lung Forum** on the subject of “Medication, Movement, Surgery? – Treatment of Chronic Lung Disease”.



Since September 2016, the DZL and the LIS have also been offering patients, their families, and interested members of the general public an **overview of clinical studies currently carried out by DZL researchers**. The internet-based list on the LIS website sets out the objectives, admission criteria, duration, and investigation/treatment methods of each study in a way that is easily understandable. Using this service, interested patients may contact the study sites directly, which facilitates access to clinical studies. This new list of studies is updated and extended on a regular basis.

Following the request to focus more strongly on patient interests, the DZL invited representatives of **patient organizations** to a **Round Table** for the second time. The event took place on March 24, 2017 in Stuttgart on the margins of the DGP Annual Meeting. Scientists of the different DZL Disease Areas presented recent activities and research results in summary reports. The Round Table offered the option of exchanging information and discussing matters of common interest.

Particularly pleasant and important for strengthening the representation of patient interests within the DZL is the contribution of **Dr. Pippa Powell**, Manager of the European Lung Foundation (ELF), as a member of the Scientific Advisory Board of the DZL. Founded by the European Respiratory Society (ERS), ELF aims to bring together patients, the general public, and pulmonary professionals to make a positive contribution to respiratory medicine.

A success arising directly from this collaboration is the publication of the German translation of the **European Patient Ambassador Programme (EPAP)**. This free online program has been developed for patients, their families, and carers. The course enables them to expand their skills in obtaining information and interacting with medical staff, political decision-makers, researchers, and the media. The program is suitable for patients with any kinds of diseases. It has been developed by ELF; besides English, French, Italian and Dutch, it is now also available in German.

Ever since the foundation of the DZL, there has been a close cooperation with the **COSYCONET (German COPD and Sys-**

**temic consequences – COMorbidities NETwork)** through scientists belonging to both institutions. In the German-wide register for the pulmonary disease COPD, the fourth most common global cause of death, 31 study centers are involved. The cohort study COSYCONET involves long-term observation of more than 2,700 COPD patients. The investigations are to provide new data on the development of the disease, its level of severity, and its comorbidities. COSYCONET has at its disposal a biobank, an image database, and phenotypic data, which serve as a basis for various subprojects. COSYCONET has been integrated into the DZL as an associated partner since 2016.

Since the beginning of 2013, **CAPNETZ (German Competence Network for Community Acquired Pneumonia)** has been an associated partner of the DZL. The Competence Network has set itself the goal of acquiring new information related to the origin and the course of Community-Acquired Pneumonia (CAP), developing improved diagnostic standards and therapies, and strengthening methods of clarification and prevention. CAP is still a potentially life-threatening disease and the sixth most common cause of death in Germany. With the largest Europe-wide comprehensive epidemiological study comprising over 10,000 CAP patients and the most extensive CAP database in the world, the DZL has gained a strong partner in this field. The DZL has also expanded its network even further, increasing its number of scientists and study centers in Europe. For instance, CAPNETZ is involved in PREPARE (Platform foR European Preparedness Against (Re)emerging Epidemics), a program funded by the European Union to carry out research into infectious diseases with epidemic potential.

**Registries and patient cohorts** are of great and increasing importance to translational research carried out by the DZL. Large cohorts and registries are brought into the DZL by associated institutions. For instance, together with CAPNETZ, the DZL has since 2015 been involved in the establishment of the bronchiectasis registry **PROGNOSIS (The Prospective German Non-CF-Bronchiectasis Registry)** and the pediatric CAP cohort **Ped-CAPNETZ**. PROGNOSIS is also part of the EU-funded European registry **EMBARC (European Multicentre Bronchiectasis Audit and Research Collaboration)** and has been an associated partner of the DZL since the turn of



the year 2016/17. DZL scientists are also actively involved in many other registries and cohorts, e.g. in the pulmonary hypertension registry **COMPERA (Prospective Registry of Newly Initiated Therapies for Pulmonary Hypertension)** or in the **German National Cohort (NAKO)**.

Initiated in 2014, the **German National Cohort (NAKO)** is to date the largest German population study to carry out research into widespread diseases. The DZL has been connected with the German National Cohort from the beginning through scientists from its own ranks and has in the meantime established an associated partnership. In this cooperation, projects on the prevalence of pulmonary health and lung disease as well as other research projects are pursued.

The long-standing cooperation of DZL researchers with **PROGRESS (Pneumonia Research Network on Genetic Resistance and Susceptibility for the Evolution of Severe Sepsis)** was formalized at the turn of the year 2016/17 with the admission of the network as an associated partner. Research is carried out on the genetic basis for disease pathogenesis and the resistance to community-acquired pneumonia. The focus of this research is on the question as to what factors influence whether pneumonia will take an uncomplicated or a difficult course, including progression to septic shock.

Since 2015, there has been an associated partnership with the **Pulmonary Research Institute (PRI)** based at the Lungen-Clinic Grosshansdorf. The PRI has at its disposal an extensive range of methods for the investigation of functional alterations and inflammatory processes of the lungs. Cohort projects in the field of COPD and bronchial asthma are carried out, while phase I-IV clinical studies in the field of respiratory medicine with a focus on COPD, bronchial asthma, and other more rare disorders are conducted. The long-standing close cooperation with the LungenClinic Grosshansdorf and the DZL has since then been intensified through this new partnership.

The **Robert Koch Institute (RKI)** is the central facility of the German government in the field of applied and action-oriented biomedical research. It has a unique population-based database for both non-communicable and communicable pul-

monary diseases. An associated partnership with the RKI was finalized in March 2017. This allows strengthening the DZL expertise in the important field of epidemiology. Use of RKI-relevant data will, in particular, contribute to DZL research in the Disease Areas of Asthma and Allergy, COPD, Pneumonia and Acute Lung Injury, and Lung Cancer. On top of that, a cooperation is envisaged in various pilot projects related to infectious diseases.

Furthermore, an associated partnership of the **Berlin Institute of Health (BIH)** was initiated in 2017 and formally agreed upon in March 2018. For instance, this cooperation involves partnership projects on translational lung research in the Cystic Fibrosis Disease Area. Further collaborations are pursued in the Disease Areas of Pulmonary Hypertension, Pneumonia and Acute Lung Injury, and Asthma and Allergy.

From the beginning, the **German Respiratory Society (DGP)** has been an important strategic partner of the DZL. Collaborations, e.g. in the field of promoting young pulmonary scientists and doctors as well as in the exchange with patient organizations, will continue to be strengthened. What is more, the DZL regularly publishes its **“Mitteilungsseiten”** (announcement pages) in **“Pneumologie”**, the official journal of the DGP, the DZL, and the DZK (German Central Committee against Tuberculosis). At the DGP Annual Meeting, the German Center for Lung Research is regularly represented with an information desk and presentations. Members of the DZL Board and DZL scientists have also held and continue to hold significant positions within the DGP, thereby contributing to the promotion of joint activities. For instance, DZL Board member Prof. Dr. Klaus K. Rabe (Grosshansdorf/Kiel) is currently President of the DGP.

The **German Society for Pediatric Pneumology e. V. (GPP)** promotes research, networking, and the exchange of information among scientists and clinicians as well as the dissemination of new findings in the field of pediatric respiratory medicine. Thus, the GPP is an important partner in the field of pediatric pneumology. The GPP organizes scientific symposia and workshops on a regular basis, while integrating research content of the DZL. DZL researchers also hold key positions

within the GPP and are greatly involved in the scientific work groups of the society, thereby promoting the scientific exchange between the GPP and the DZL.

Since 2013, the DZL has been a full member of the **Technology, Methods, and Infrastructure for Networked Medical Research (TMF)**, the umbrella organization for networked medical research in Germany. Particularly in the fields of biobanking and establishing central data management, the DZL cooperates closely with the TMF. Especially the field of biobanking draws on the regular and intensive exchange with biobanking and IT representatives from the German Centers for Health Research and the German Biobank Node (GBN).

The DZL also supports various **anti-smoking campaigns**. One of them is the Education against Tobacco (AGT) initiative, which focuses on young people. Medical students from 30 faculties in Germany, Austria, and Switzerland inform approximately 20,000 students from grades 6 to 8 each year on a voluntary basis about the dangers of smoking tobacco and campaign for smoke-free classes. The project involves not only students but also teachers, doctors, and professors. The DZL Chairman and other DZL researchers are members of the Scientific Advisory Board of the initiative. As in 2014, the campaign was again recognized in 2017 by the German Chancellor within the framework of the “startsocial” competition as one of the seven most outstanding voluntary projects in Germany.

Together with the other **German Centers for Health Research (DZG)**, the DZL is part of a German-wide network in medical research. The DZG benefit from the regular exchange of information on joint strategic, infrastructural, and scientific subjects on many different work levels. For the benefit of the patients, synergistic effects can thus be used and created where, for instance, topics in pulmonary, cancer, infection, or cardiovascular research overlap, as is the case with the Disease Areas of Lung Cancer, COPD, Pneumonia, or Pulmonary Hypertension. A joint objective of the DZG is continuous access to information from decision-makers and the general public. The DZG centers were thus represented for the second time at the Annual **Meeting of the German Society of Internal Medicine (DGIM)** and held another workshop on “New

Structures for Translational Research – Better Ways to Deliver Precision Medicine” at the **World Health Summit** in October 2017. At this event, organized in 2017 in cooperation with the Helmholtz Association, international speakers and members of the audience from industry and science spoke about the challenges regarding new structures for translational research. The DZG were also represented with an individual workshop on “New Career Paths in Clinical-Translational Research” and an information desk at the 17th **GAIN Conference**, which took place in August 2017 in San Francisco, USA. Interested junior researchers working in the United States had the opportunity to gain information on the career paths offered by the DZG and get in touch with relevant DZG stakeholders.

The **European Respiratory Society (ERS)**, one of the largest and most significant societies in the field of respiratory medicine, is an important partner of the DZL. This close association is marked, for example, by the appointment of Prof. Dr. Tobias Welte as President of the ERS for the 2018/19 term of office or the chairing of the ERS International Congress in Munich in 2014 by DZL scientists. The DZL is regularly represented at the Annual Congress of the European Respiratory Society (ERS) with an information desk and presentations by DZL scientists, as was also the case in 2017 in Milan. The ERS Congress is the largest meeting of respiratory researchers and clinicians in the world.

In 2017, the DZL attended numerous other meetings and scientific conferences contributing presentations and scientific expertise, for example at the **Leibniz Symposium on Biomarkers** in November 2017 in Berlin or at the **Gordon Research Conference on Lung Development, Injury, and Repair** in August 2017 in New London, NH, USA.

DZL doctors are committed to finding ideal diagnostic and therapeutic approaches to lung diseases by contributing to keep **treatment guidelines** up to date. In 2017, both the **Guideline for Asthma** and the **Guideline for Tuberculosis in Adulthood** were revised. The first quarter of 2018 also saw the revision of the **Guideline for Nosocomial Pneumonia** and of the **Updated Treatment Recommendation on Metastasized Non-Small Cell Lung Cancer (NSCLC)**. All four papers have

recently been published in the “Pneumologie” journal. On top of that, a publication of the revised guideline on COPD and on **Lung Cancer** is expected in the near future. In this case, too, DZL doctors are involved.

In addition, further numerous strategic partnerships of the individual DZL sites have been set up with **international scientific and economic partners**. The expertise in industrial contacts is strengthened by the contribution of **Prof. Dr. Stephen Rennard**, member of the International Scientific Advisory Board of the DZL.

DZL scientists are currently cooperating with well over 100 international economic partners, especially within the framework of projects on basic research and applied research as well

as in the conduct of clinical studies. These particularly registration-oriented clinical studies are conducted and supported by partners such as AstraZeneca, Bayer, Boehringer Ingelheim, Bristol-Myers Squibb, Eli Lilly and Company, GlaxoSmithKline, Hoffmann-La Roche or Novartis/Novartis Pharmaceuticals.





# Promotion of Junior Scientists and Equal Opportunities

## DZL Academy

Training and enhancing careers of the next generation of lung researchers and doctors has been a top priority of the DZL from the very beginning. The first promotion period of the DZL focused on the scientific involvement of junior researchers in the DZL Annual Meeting and in disease-specific DZL workshops as well as on filling numerous junior group leader positions. What is more, the DZL mentoring program “Careers in Respiratory Medicine” was established successfully. All 25 mentees are supported by an individual mentor. The program is complemented by workshops and soft-skills courses. The be-



### Goals Achieved in 2017

- ✓ Formation of the DZL Academy Board, made up of members of all five DZL sites
- ✓ Increase the visibility of the DZL Academy (i. e. websites, brochures)
- ✓ Initiate joint continuing education courses within the network of the German Centers for Health Research
- ✓ Conclusion of a joint research fellowship agreement with the European Respiratory Society (ERS)  
DZL Fellowship Programme kick-off with 100 new registrations (success to be expected in 2018)

### Goals for 2018

- Create a draft paper on “Career and education in translational research” together with all German Centers for Health Research
- Start 3rd call for application for the DZL Mentoring Programme
- Offer DZL Academy training courses throughout the network of the German Centers for Health Research
- Carry out a survey among the DZL Fellows in order to tailor the DZL Academy Program to their needs
- Elect DZL Fellow Representatives of all DZL sites to the DZL Academy Board

ginning of the second promotion period saw the launch of the DZL Academy in 2017.

The DZL Academy aims to promote career development of students, doctoral candidates, and post-doctoral researches of medicine and the life sciences relating to clinical, translational, and basic scientific lung research. The Academy supports scientifically active physicians within the DZL during training and research. Moreover, it provides attractive offers for excellent, international junior researchers to become involved with the DZL.

The DZL Academy is dedicated to family-friendly career development and the reconciliation of family and research activity.

In addition to the versatile range of offers at the individual DZL sites, the DZL Academy aims to strengthen the junior researchers’ sense of belonging to the DZL and build up an active network across all sites.

## Programs and Promotional Opportunities

- DZL mentoring program
- DZL symposia and regular workshops
- DZG-spanning symposia
- DZL Academy mobility scholarships
- ERS/DZL research fellowships
- DZL poster awards
- DZL Online Academy

## Promotion of Junior Scientists in Site-Specific Programs

All DZL sites offer graduate training or junior researcher promotion programs emphasizing lung research:

*DZL Site Kiel, Lübeck, Grosshansdorf and Borstel (ARCN)*

- Borstel Biomedical Research School (BBRS)
- Clinical Scientist Training at the University of Lübeck
- Graduate Centers at the Universities of Kiel and Lübeck
- Graduate programs resulting from the DFG Excellence Initiative
- Junior Research Cluster “Chronoflammation – Circadian gated neutrophil inflammation” at the University of Lübeck

## DZL Academy Board

The DZL Academy Board is made up of members of all five DZL sites. It is dedicated to conceptual and strategic planning as well as to the implementation of programs and promotional opportunities. It supports the DZL Board in the selection process for all tenders and prepares recommendations on the allocation of funds.



Antje Brand



Jörn Bullwinkel



Doreen Franke



Michael Kreuter



Silke Meiners



Rory E. Morty



Birgit Teucher



Annegret Zurawski

### *DZL Site Hannover (BREATH)*

- Hannover Biomedical Research School (HBRS)
- HBRS Structured Medical Doctors' Program (StrucMed Program)
- Ina Pichlmayer Mentoring Program of Hannover Medical School for young female researchers studying for habilitation
- Lower Saxony International Summer Academy (LISA)
- BREATH quarterly DZL colloquia

### *DZL Site Munich (CPC-M)*

- CPC Research School "Lung Biology and Disease"
- Else Kröner research programs on "Rare Diseases of the Immune System" and "Immunotherapy in the Treatment of Cancer"
- European Respiratory Society (ERS) Summer School
- European network for translational research in children's and adult interstitial lung disease (CA COST Action CA16125)
- Helmholtz Graduate School Environmental Health (HELENA)
- Helmholtz mentoring program "Taking the Lead"
- International doctoral student program "i-Target: Immunotargeting of Cancer"
- Life Science Campus Network Munich
- Master of Business Research (PhD Program), Munich School of Management at Ludwig Maximilian University of Munich (LMU)
- Munich Medical Research School (MMRS)
- Oncology Winter School at LMU
- Doctoral studies "Molecular and Clinical Translational Medicine" (FöFoLe) at the University Hospital of Munich
- Training network IMMUTRAIN (HORIZON 2020 ITN)

### *DZL Site Heidelberg (TLRC)*

- Hartmut Hoffmann-Berling International Graduate School of Molecular and Cellular Biology (HBIGS)
- Research projects in TLRC laboratories
- Monthly TLRC research seminars
- Heidelberg Research Center for Molecular Medicine Fellowships

### *DZL Site Giessen, Marburg, Bad Nauheim (UGMLC)*

- International Max Planck Research School for Heart and Lung Research (IMPRS-HLR)
- Molecular Biology and Medicine of the Lung Program (MBML Program)
- UGMLC School

## Equal Opportunities

Measures to ensure equal opportunities are implemented in close cooperation with the relevant committees at the corresponding institutions of the DZL partner sites. Within the framework of gender-equality programs of the participating university partners, priority is placed on the active recruitment of female scientists at every level, from trainees to Scientific Advisory Board members. Particular focus has been placed on increasing the number of female personnel in the DZL, especially in leadership positions. Ever since the foundation of the DZL, the percentage of female Principal Investigators (PIs) has increased from 14% in 2011 to 23% in 2017, when the percentage of female personnel funded by the DZL had reached 70%.

# The Public Face of the DZL

Informing the general public, decision-makers, patients, and other target groups about pulmonary diseases and lung health is very important to the DZL. Despite increasing morbidity rates, there still tends to be insufficient awareness of pulmonary diseases compared to other widespread diseases.



In the field of public relations, the DZL is involved with its own scientific symposia, its presence at national and international conferences, printed information such as brochures, flyers, and Annual Reports, its web presence ([www.dzl.de](http://www.dzl.de)), a newsletter as well as joint activities with the German Lung Information Service (LIS), including events organized for patients.

The year of 2017 was also marked by the activities organized for the general public on the occasion of the **5th anniversary of the DZL**. From May 5 to July 1, 2017, the five DZL sites attracted great interest of the general public by organizing special events called Lung Action Days. In Hannover, Giessen, Munich, Heidelberg, and Hamburg, doctors, scientists, and employees invited those interested to lung function tests and many other activities to join in (e.g. a lung quiz) at a promo-

tional stand in the city centers, informing the audience on successes and recent research priorities of the DZL in cooperation with the Lung Information Service.

Around 400 citizens took the opportunity to have their lung function tested and analyzed free of charge. On the occasion of its anniversary, the DZL wanted to raise public awareness for lung health and pulmonary diseases with its **Lung Action Days**. With its **special publication** "Forschungswelten: Spitzenforschung" [Research Worlds: Cutting-Edge Research], published on September 7, 2017, the German newspaper **DIE ZEIT** also presented the DZL and its five-year success story. In five individual contributions, highlights of the current state of research were presented. These and other special contributions on practical examples of success can also be retrieved at **ZEIT ONLINE** in a web presence on the DZL (in German). On top of that, the DZL published the special contribution "DZL: 5 Jahre erfolgreiche translationale Forschung im Kampf gegen Lungenerkrankungen" [DZL: 5 Years of Successful Translational Research to Combat Lung Disease] in the April 2017 edition in the German scientific journal **Pneumologie**.

Several times a year, as again in 2017, the DZL also publishes the latest research results, event information, new appointments, and other news about the Center on its "Mitteilungsseiten" (announcement pages) in the scientific journal **Pneumologie**.

With numerous news items about DZL lung research and a great deal of information on the background and the structure of the DZL, the range of information offered in 2017 could again be expanded further on the DZL website. The special homepage section "**New this week in PubMed**" shows the latest publications by DZL researchers on a weekly basis. The research association also introduces itself in a short film portrait, which can be found on the DZL website as well as on YouTube.

In 2017, the comprehensive **DZL Annual Report 2016** was published again in both English and German. Alongside the achievements and highlights of the year 2016, the report presents the numerous successes of the DZL from its first five years of existence. Furthermore, diverse papers by and with DZL researchers were published in specialist journals and press reports.



## Scientific Conferences and DZL Annual Meeting

In 2017, the DZL was represented at many large conferences. With an information desk and numerous award winners and presentations by its own scientists, the DZL played a highly visible role at the **58th Congress of the German Respiratory Society (DGP)** in March 2017 in Stuttgart. The DGP Congress represents the largest scientific forum in the field of respiratory medicine in the German-speaking world. During the Congress, DZL Chair Prof. Dr. K. F. was installed in office as President of the DGP.

The DZL was also represented for the second time at the **Annual Meeting of the German Society of Internal Medicine**

**(DGIM)** in April/Mai 2017 with a joint fair presence of the DZG centers and held another workshop on “New Structures for Translational Research – Better Ways to Deliver Precision Medicine” in cooperation with the Helmholtz Association at the **World Health Summit 2017** in Berlin. At the **17th GAIN Conference**, which took place in August 2017 in San Francisco, USA, interested junior researchers working in the United States had the opportunity to gain information on the career paths offered by the DZG and get in touch with relevant DZG stakeholders in a workshop organized by all DZG centers and at a joint DZG information desk.

At the **ERS (European Respiratory Society) International Congress** in Milan in September 2017, the DZL was also present with award winners, speakers, and session chairs. In the



6<sup>th</sup> DZL Annual Meeting 2017 in Munich

“World Village” Congress Area, together with other professional associations from all over the world, the DZL provided information about its activities and welcomed the ERS (Past) President, Prof. Dr. Guy Joos, to its booth. The DZL’s presence at the largest congress in the world on respiratory medicine with more than 22,000 participants from 130 countries worldwide plays a vital role in making the DZL more visible, both nationally and internationally.

In 2017, the DZL also attended numerous other meetings and scientific conferences contributing presentations and scientific expertise, for example at the **Leibniz Symposium on Biomarkers** in November 2017 in Berlin or at the **Gordon Research Conference on Lung Development, Injury, and Repair** in August 2017 in New London, NH, USA.

Even in times of modern media, the personal exchange between scientists and the numerous DZL partner institutions from different German sites remains essential. The most important and largest meeting is the DZL Annual Meeting, which takes place alternately at all sites of the Center. On January 30 and 31, 2017, more than 470 scientists, clinicians, and junior scientists discussed their project results, strategies and research objectives at the **6th DZL Annual Meeting in Munich**. The work groups of the Disease Areas and Platforms also used the opportunity to exchange opinions and benefit from intensive consultation.

## Focus on Patients

Strategically, the DZL is moving the concerns and interests of the patients increasingly into focus. Ever since the DZL was founded, the **Lung Information Service (LIS)** has been a professional and reliable partner for direct and understandable patient information. During the year, the DZL and the LIS organized four fora specifically for patients and their families at the DZL sites, each with more than 100 participants:

- March 25, 2017 (Stuttgart): 17th Patient Lung Forum on “Clinical Studies in Lung Research” as part of the DGP 2017 Annual Meeting
- April 8, 2017 (Hannover): 3rd patient seminar on “Pulmonary Fibrosis” at Hannover Medical School

- May 13, 2017 (Hannover): 4th patient seminar on “Bronchiectasis” at Hannover Medical School
- November 29, 2017 (Munich): 18th Patient Lung Forum on “Medication, Movement, Surgery? – Treatment of Chronic Lung Disease”

Another important part of the contact established with patients (or representatives) are the **DZL round-table discussions** held since 2016, enabling direct exchange on common concerns in the field of lung research. Furthermore, particularly important for strengthening the representation of patient interests within the DZL is the contribution of **Dr. Pippa Powell**, Manager of the European Lung Foundation (ELF), as a member of the Scientific Advisory Board of the DZL. Ever since the foundation of the European Respiratory Society (ERS), ELF aims to bring together patients, the general public, and pulmonary professionals to make a positive contribution to respiratory medicine. A success arising directly from this collaboration is the publication of the German translation of the **European Patient Ambassador Programme (EPAP)**. This free online program has been developed for patients, their families, and carers. The course enables them to expand their skills in obtaining information and interacting with medical staff, political decision-makers, researchers, and the media. The program is suitable for patients with any kinds of diseases. It has been developed by ELF; besides English, French, Italian and Dutch, it is now also available in German.

## Lung Information Service

The Lung Information Service (LIS), based at the Helmholtz Center in Munich, is an important professional and reliable partner of the DZL to inform patients. It aims to compile scientifically valid information for



patients in an up-to-date, independent and easily understandable manner. Information is provided mainly in three different ways: via a comprehensive online portal, through patient events ("Patient Lung Forum") and by means of publications ("Fact Sheets: The Most Important Information in Brief").

At [www.lungeninformationsdienst.de](http://www.lungeninformationsdienst.de), the LIS provides basic knowledge and new research results to patients, their families, and interested members of the general public in an easily understandable manner. Since September 2016, the LIS has also integrated a platform on current clinical studies into the portal. Those interested can obtain information on the objectives, admission criteria, duration, and investigation/treatment methods of each study, set out in an easy-to-understand way. Using this service, interested patients may contact the study sites directly, which facilitates access to clinical studies. The list is updated and extended on a regular basis. By the end of 2017, 102 studies had already been recorded on the platform.

### Online Portal Key Topics of the Lung Information Service in 2017:

Cystic Fibrosis (January); Motivation, Self-Management, and Mind (February); Pneumonia (March); Oxygen Devices (April); Immunotherapy (May); ACOS (June); Nutrition with Lung Disease (July); Antibiotics (August); Clinical Studies (September); RSV (October); Active Ingredient Research (November); COP (December).

From 2011 to 2017, the Lung Information Service has published more than 700 news articles on its website. The main basis for the news published twice a week are publications on patient-relevant subjects in well-known scientific journals. Alongside these purely scientific contents, the online portal also informs patients on recent topics, such as patient-relevant events, recommendations on recently published patient literature, or announcements of interesting TV or radio reports. The LIS also offers a monthly newsletter.

Since 2016, the Lung Information Service has also been active on social media. It has its own Facebook profile with 1,853 subscribers and publishes new research information several times per week via the news service Twitter, where the LIS now has 278 followers.

In 2017, the Lung Information Service published a new fact sheet on the subject of "Bronchiectasis" and reissued seven fact sheets on the subjects of "Imaging", "Inhalation", "Lung Infection", "Lung Exercise", "COPD", "Breathing Techniques", and "Pulmonary Hypertension". Pieces of information of the Lung Information Service are often picked up on by daily newspapers and other media. In 2017, for example, articles were published in the *Münchner Merkur* ("Munich Mercury"), the *Bremer Nachrichten* ("Bremen News"), and the scientific journal *Arzt und Wirtschaft* ("Physician and Economy").



# Highlights of the Year 2017

More information can be found at [www.dzl.de](http://www.dzl.de)

## JANUARY

### Three new partners support the DZL

At the turn of the year, NAKO, PROG-NOSIS, and PROGRESS become associated partners of the DZL.

### Scientific Advisory Board expanded

Dr. Pippa Powell, Prof. Dr. Hans-Ulrich Prokosch, and Dr. Stephen Rennard support the International Scientific Advisory Board of the DZL with their expertise in the fields of patient interests, bioinformatics, and industrial cooperation.

## FEBRUARY

### Record number of participants at the 6th DZL Annual Meeting in Munich

Around 470 scientists, physicians, and junior researchers get together in Munich for the most important internal exchange of the Center.



### Stage win in the fight against pulmonary fibrosis

The mechanism of action of the medication "pirfenidone" for the treatment of Idiopathic Pulmonary Fibrosis (IPF) is reproduced by a team of DZL researchers. This understanding helps develop even more effective active ingredients.

### Cigarette smoke slows down self-healing process of the lungs

DZL researchers detect a self-healing mechanism of the lungs that is inhibited by cigarette smoke, which is a good starting point for future therapies to treat COPD.

## MARCH

### DZL researcher receives Oskar Medizin Award

DZL scientist Prof. Dr. Marius Hoepfer (Hannover) is honored with the Oskar Medizin Award 2016 for his research achievements in the treatment of pulmonary hypertension.



### DZL Board member becomes new DGP President

At the 58th DGP Annual Meeting in Stuttgart, Prof. Dr. Klaus F. Rabe assumes the office of President of the German Respiratory Society (DGP).



### Robert Koch Institute becomes new partner of the DZL

The RKI joins the DZL with its expertise in the important field of epidemiology and becomes an associated partner.

### 17<sup>th</sup> Patient Lung Forum in Stuttgart

For the first time as part of the DGP Annual Meeting, the DZL successfully offers a patient forum on the subject of "Clinical Studies" in cooperation with the ILS.



## APRIL

### Breath test for early detection of lung cancer

A breath test developed by DZL scientists diagnoses lung cancer more precisely as current X-ray and CT examinations.

## MAY

### DZL researchers receive Paul Martini Prize

For their work on a new drug to treat allergic asthma, the DZL researchers Prof. Dr. Harald Renz and Prof. Dr. Holger Garn from the Philipps University of Marburg are honored with the Paul Martini Prize.



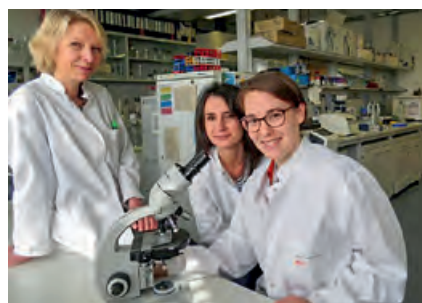
## DZL celebrates its 5th anniversary

With five Lung Action Days, the DZL celebrates its fifth anniversary and reaches many people interested, many of whom have their lung function tested and participate in other activities to join in.



## Molecular switch for the emergence of asthma detected

DZL researchers detect a molecular switch that promotes the development of specific immune cells and is therefore involved in the development of allergic diseases such as asthma.



## New active ingredients for the treatment of pleural effusion associated with lung cancer

DZL researchers detect a mechanism for malignant pleural effusion (the collection of fluid between the lining of the lungs and the pleura) and carry out successful tests of new drugs in an experimental model.

**JUNE**

## Honored by Federal Chancellor

The Education against Tobacco (AGT) initiative is recognized by Federal Chancellor Angela Merkel as part of the

“startsocial” competition as an outstanding volunteering project.



**JULY**

## DZL scientists establish new catheter method for pulmonary hypertension

For the first time, DZL researchers carry out a multicenter study in Germany on the treatment of patients with inoperable Chronic Thromboembolic Pulmonary Hypertension (CTEPH) using Balloon Pulmonary Angioplasty (BPA), a catheter-based procedure.

## Idiopathic pulmonary fibrosis as an autoimmune disease?

DZL scientists show that an autoimmune disease could be involved as a causative factor for certain types of pulmonary fibrosis, whose cause remains undetermined to this day.

## Excellent assessment by the German Council of Science and Humanities

According to the expert opinion of the German Council of Science and Humanities (Wissenschaftsrat), the German Centers for Health Research (DZG) are a suitable model to promote translational research in Germany, which is why the Council recommends their further development.

**AUGUST**

## Cell aging in lung epithelium responsible for pulmonary fibrosis

DZL researchers trace pulmonary fibrosis back to cell-aging processes and are able to counteract with medication in the cell model.

## DZL and DZG at 17th GAIN Conference in San Francisco, USA

For the first time, the DZG centers are represented with an information desk at the GAIN Conference and inform those interested on career paths in clinical-translational research in Germany.



**SEPTEMBER**

## DZL at 27<sup>th</sup> International Congress of the European Respiratory Society (ERS)

The DZL was again present at the ERS International Congress in Milan with more than 22,000 participants from over 130 countries with numerous lecturers, prize winners, and its own information desk.



### Honor for outstanding lifetime achievement for DZL Board member

Within the framework of the ERS International Congress, DZL Board member Prof. Dr. Erika von Mutius is honored with the ERS Assembly Lifetime Achievement Award for her research work in the field of respiratory medicine.



### Erwin Schrödinger Prize for DZL researchers

DZL scientist Prof. Dr. Dr. Fabian Theis (Munich) and his team are awarded the Erwin Schrödinger Prize, the science award of the Donors' association (Stifterverband), for their breakthrough in single-cell data analysis.



## OCTOBER

### Joint workshop of DZG and Helmholtz Association at World Health Summit 2017

The participants of the workshop on "New Structures for Translational Research – Better Ways to Deliver Precision Medicine" held by the DZG and the Helmholtz Association discussed the challenges regarding new structures for translational research.



### Early diagnosis of lung disease in babies

A team of DZL researchers develops a method that, for the first time, might allow for early and safe diagnosis of the severe disease Bronchopulmonary Dysplasia (BPD).



## NOVEMBER

### Lung cancer and pulmonary hypertension

DZL researchers discover immune and inflammatory processes that might result in pulmonary hypertension second-

ary to lung cancer; they intend to take this as a starting point for treatment.

### Endogenous protein reverses scarring in the lungs

DZL scientists discover a new DNA repair mechanism that offers a promising approach to the treatment of pulmonary fibrosis.

## DECEMBER

### Act independently as patients

The DZL makes the ERS European Patient Ambassador Programme (EPAP) available in German. This course helps patients, their families, and carers obtain important skills and background knowledge for competent interaction with medical staff, political decision-makers, researchers, and the media.

### DZL researcher honored with Christiane Herzog Prize 2017

DZL scientist Dr. Mirjam Stahl is awarded the Christiane Herzog research prize 2017 for her outstanding work in the field of cystic fibrosis research.





# The German Centers for Health Research



The main objective of the German government's framework program for health research is to more effectively combat complex common diseases that are becoming increasingly prevalent in the population. To create favorable conditions to achieve this goal, the German Federal Ministry of Education and Research (BMBF) has established the German Centers for Health Research (DZG). These Centers have been set up as long-term, equal partnerships between universities with university hospitals and non-university research institutions.

The German Centers for Health Research leverage existing competencies and thus make a significant contribution to closing gaps in knowledge and to improving prevention, diagnosis and treatment of diseases. The aim is to achieve the highest possible level of therapeutic efficacy for each patient. The Centers' research policy emphasizes the close cooperation between the basic and clinical research of all partners, based on the indications and the needs of the patients. This close networking and expansion of existing research structures allows faster transfer of research findings into clinical practice

(translational research). In the long term, the strategic collaboration of leading scientists in the German Centers for Health Research will make Germany internationally more competitive on the research level and markedly more attractive for young researchers both within Germany and from around the world.

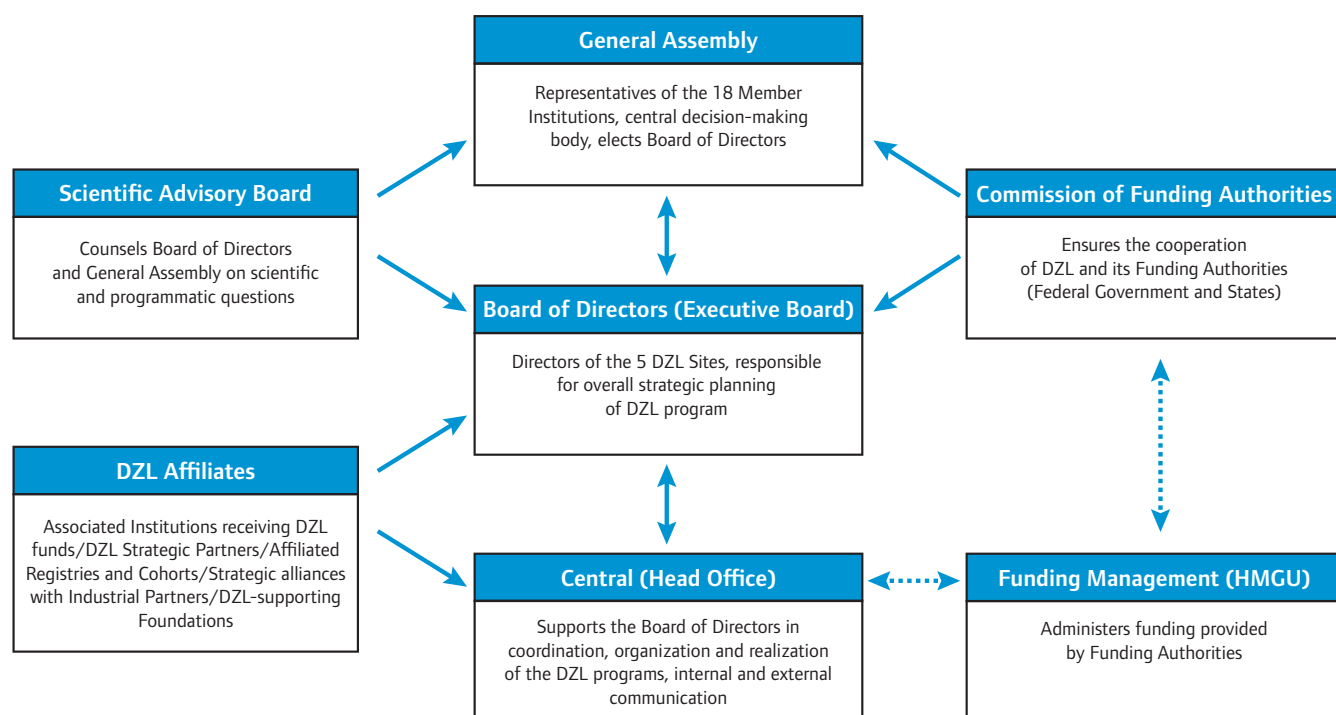
In 2009, the German Center for Neurodegenerative Diseases (DZNE) and the German Center for Diabetes Research (DZD) were founded. In 2011, four additional German Centers for Health Research were established: the German Center for Infection Research (DZIF), the German Center for Cardiovascular Research (DZHK), the German Consortium for Translational Cancer Research (DKTK) and the German Center for Lung Research (DZL).

The six German Centers for Health Research cooperate with one another in order to share their findings, exploit synergies, and promote the mission of the German government's framework health research program.



DZG presence at the German Academic International Network (GAIN) 2017

# DZL Organization



ARCN	BREATH	CPC-M	TLRC	UGMLC	6 further associated partners, nationally organized or based outside the DZL sites
4 Member Institutions + 3 Associated Partners	3 Member Institutions + 1 Associated Partner	3 Member Institutions + 1 Associated Partner	5 Member Institutions	3 Member Institutions	

## DZL Executive Board

- Prof. Dr. Werner Seeger (DZL Chairman and Speaker) – Director of the DZL Site Giessen, Marburg, Bad Nauheim (UGMLC)
- Prof. Dr. Hans-Ulrich Kauczor – Director of the DZL Site Heidelberg (TLRC)
- Prof. Dr. Klaus F. Rabe – Director of the DZL Site Borstel, Grosshansdorf, Kiel, Lübeck, (ARCN)
- Prof. Dr. Erika von Mutius – Director of the DZL Site Munich (CPC-M)
- Prof. Dr. Tobias Welte – Director of the DZL Site Hannover (BREATH)

## DZL Head Office

- Dr. Christian Kalberlah, Managing Director
- Sabine Baumgarten, M. A., Press and Public Relations
- Susanne Klasen, Management Assistant
- Alina Zidaric, Management Assistant

## Scientific Advisory Board

The Scientific Advisory Board of the DZL is made up of internationally acclaimed experts in lung research. The twelve members of the Scientific Advisory Board are:

### **Jacob I. Sznajder**

Chairman of the Scientific Advisory Board  
Chief, Division of Medicine-Pulmonary, Ernest S. Bazley  
Professor of Asthma and Related Disorders, Northwestern  
University Feinberg School of Medicine; USA

### **Peter J. Barnes**

Head of Respiratory Medicine, Imperial College London; UK

### **Rachel Chambers**

Professor of Respiratory Cell and Molecular Biology, Center  
for Respiratory Research, University College London; UK

### **Jeffrey M. Drazen**

Distinguished Parker B. Francis Professor of Medicine,  
Harvard Medical School; Editor-in-Chief, New England Jour-  
nal of Medicine; USA

### **Stuart Elborn**

Professor of Respiratory Medicine, Director Cystic Fibrosis  
Center, Belfast City Hospital, President of the European Cystic  
Fibrosis Society ECFS, Centre for Infection and Immunity,  
Queen's University Belfast; Northern Ireland

### **Mark Gladwin**

Division Chief, Pulmonary, Allergy, and Critical Care Medicine,  
Director Vascular Medicine Institute, University of Pittsburgh  
Medical Center; USA

### **Pippa Powell**

Director of the European Lung Foundation (ELF), Sheffield;  
UK

### **Hans-Ulrich Prokosch**

Holder of the Chair for Medical Informatics, Friedrich-  
Alexander-Universität Erlangen-Nürnberg; Chief Information  
Officer, Universitätsklinikum Erlangen; former Member of the  
Board of the German Society for Medical Informatics, Biom-  
etry and Epidemiology (GMDS); D

### **Marlene Rabinovitch**

Professor of Pediatric Cardiology, Stanford University School  
of Medicine; USA

### **Stephen Rennard**

Larson Professor of Medicine in the Pulmonary and Criti-  
cal Care Medicine Section, and courtesy professor of the  
Department of Pathology and Microbiology and the Depart-  
ment of Genetics, Cell Biology and Anatomy, University of  
Nebraska, AstraZeneca; USA

### **Susan Shurin**

Deputy Director, National Heart, Lung and Blood Institute  
(NHLBI), National Institutes of Health (NIH); USA

### **Peter M. Suter**

Akademien der Wissenschaften Schweiz, Centre Médical Uni-  
versitaire, University of Geneva; CH

## Head of Funding Management

- Dr. Dorothe Burggraf – Finance Department (Commercial  
Funding Management, Helmholtz Zentrum München)

## General Assembly

Currently, 18 member institutions belong to the DZL. In  
addition, the DZL has eleven Associated Partners (as at  
june 2018)

## Commission of Funding Authorities

- German Federal Ministry of Education and Research  
(Bundesministerium für Bildung und Forschung): Chair
- Baden-Württemberg – Ministry of Science, Research and  
the Arts Baden-Württemberg
- Bavaria – Bavarian State Ministry of Science and the Arts
- Hessen – Hessian Ministry for Science and the Arts
- Lower Saxony – Lower Saxony Ministry of Science and  
Cultural Affairs
- Schleswig-Holstein – Ministry of Education, Science and  
Cultural Affairs



# Selected Prizes and Awards

Award Winner	Award
<b>Aufklärung gegen Tabak e. V.</b>	Federal Award as part of the “startsocial” competition for outstanding volunteering projects
<b>Dr. Elie El Agha</b> Giessen	DGP Research Prize 2017 for the best scientific work
<b>Prof. Dr. Holger Garn and Prof. Dr. Harald Renz</b> Marburg	Paul Martini Prize of the Paul Martini Foundation for groundbreaking work on the treatment of allergic asthma
<b>Prof. Dr. Marius Hoeper</b> Hanover	Oskar Medizin Prize of the Oskar-Helene-Heim Foundation for groundbreaking research on pulmonary hypertension
<b>Prof. Dr. Danny Jonigk</b> Hanover	Consolidator Grant of the European Research Council to carry out research into incurable lung disease
<b>Dr. Stefan Karrasch</b> Munich	DGP Research Prize 2017 for the best clinical-therapeutic work (shared prize)
<b>Prof. Dr. Matthias V. Kopp</b> Lübeck	Elected President of the German Society for Pediatric Pneumology (GPP)
<b>PD Dr. Dr. Nikolaus Kneidinger</b> Munich	DGP Research Prize 2017 for the best clinical-therapeutic work (shared prize)
<b>Prof. Dr. Marcus A. Mall</b> Heidelberg	Received the title of Fellow of ERS (FERS)
<b>Dr. Patricia Morán-Losada</b> Hanover	Adolf Windorfer Prize of the Mukoviszidose e. V. (German Cystic Fibrosis Association)
<b>Prof. Dr. Klaus F. Rabe</b> Grosshansdorf	Assumed DGP presidency at the 58th Annual Meeting
<b>Dr. Rajkumar Savai</b> Bad Nauheim	Early Career Achievement Award of the American Thoracic Society in the field of thoracic oncology
<b>Dr. Mirjam Stahl</b> Heidelberg	Research Prize 2017 of the Christiane Herzog Foundation for outstanding research work on careful follow-up and treatment of cystic fibrosis
<b>Prof. Dr. Dr. Fabian Theis and colleagues</b> Munich	Erwin Schrödinger Prize, science award of the Donors’ association (Stifterverband), for research work in the field of cell research
<b>Prof. Dr. Erika von Mutius</b> Munich	ERS Assembly Lifetime Achievement Award for outstanding lifetime achievement in the field of respiratory medicine
<b>Dr. Darcy Wagner</b> Munich	Science and Innovation Center Rising Star of Research Award of the American Thoracic Society
<b>Dr. Benjamin Waschki</b> Grosshansdorf	Appointment as ERS National Delegate for Germany
<b>Prof. Dr. Tobias Welte</b> Hanover	Elected ERS Vice President

Abbreviations: \* DGP – Deutsche Gesellschaft für Pneumologie und Beatmungsmedizin e. V. (German Respiratory Society),

\*\* ERS – European Respiratory Society

# DZL Member Institutions and Sites



## Associated Partners of the DZL

- Asklepios Clinic Munich-Gauting
- Berlin Institute of Health (BIH)
- CAPNETZ STIFTUNG
- COSYCONET (German COPD and Systemic Consequences – Comorbidities Network)
- The German National Cohort (NAKO)
- Pulmonary Research Institute (PRI) at LungenClinic Grosshansdorf
- PROGNOSIS (The Prospective German Non-CF-Bronchiectasis Registry)
- PROGRESS (Pneumonia Research Network on Genetic Resistance and Susceptibility for the Evolution of Severe Sepsis)
- Robert Koch Institute
- University Hospital Schleswig-Holstein, Kiel Campus
- University Hospital Schleswig-Holstein, Lübeck Campus

## DZL Site Borstel, Lübeck, Kiel, Grosshansdorf

### Airway Research Center North (ARCN)

#### Partner Institutions of the Site

- Research Center Borstel – Leibniz-Center for Medicine and Biosciences
- University of Lübeck
- University Medical Center Schleswig-Holstein, Lübeck Campus
- University Medical Center Schleswig-Holstein, Kiel Campus
- Christian-Albrechts-University Kiel
- LungenClinic Grosshansdorf
- Pulmonary Research Institute at the LungenClinic Grosshansdorf

#### Prof. Dr. Klaus F. Rabe



- Director of the DZL Site ARCN
- Medical Director of the LungenClinic Grosshansdorf
- Professor of Pneumology, Christian-Albrechts-University, Kiel
- Chairman of the Institute for Lung Research (ILF)
- President of the European Respiratory Society (ERS) 2011/2012
- Fellow of ERS (FERS)
- President of the German Society for Pneumology and Respiratory Medicine (DGP) 2017–2019

#### Contact

DZL Site Coordinator, ARCN:

Dr. Jörn Bullwinkel

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Tel.: +49 (0)4102 601-2410

#### Research Profile

Scientists and clinicians of the Airway Research Center North (ARCN) focus on research on Chronic Obstructive Pulmonary Disease (COPD) and Lung Cancer as well as Asthma and Allergy. This translational research consortium combines top-level expertise in basic research and medicine in the field of pulmonology in Schleswig-Holstein. As the biggest North German clinic specializing in lung and airway diseases with more than 13,000 patients treated per year, the LungenClinic Grosshansdorf is, together with the University Clinic Schleswig-Holstein (UKSH) and the Medical Clinic Borstel, responsible for clinical and patient-oriented research in the ARCN. The Research Center Borstel focuses on the investigation of infectious as well as non-infectious lung diseases and contributes to the success of ARCN basic research and the development of animal models. Additional partners are researchers at the University of Lübeck and the Christian-Albrechts-University Kiel. These scientists test asthma in animal models, analyze the epigenetic causes of lung diseases and are committed to developing novel imaging techniques. Cohort projects and clinical studies are conducted together with the Pulmonary Research Institute at the Lung-Clinic Grosshansdorf. To strengthen the connection between clinical and basic research, the Biomaterialbank Nord has been set up as a joint central infrastructure. In the field of asthma, our physicians for pediatric and adult lung medicine work closely together for a better understanding of different disease courses. This crosslink between complementary partners in the ARCN is intended to support the collaborative implementation of translational research strategies.



## DZL Site Hanover

### Biomedical Research in Endstage and Obstructive Lung Disease (BREATH)

#### Partner Institutions of the Site

- Hannover Medical School (MHH)
- Fraunhofer Institute for Toxicology and Experimental Medicine (ITEM), Hanover
- Leibniz University Hanover (LUH)
- CAPNETZ Foundation

#### Prof. Dr. Tobias Welte



- Director of the DZL Site BREATH
- Chairman of the German Sepsis Society
- Speaker for the Clinical Study Center Hanover (KS-MHH)
- Member of the Presidium of the German Interdisciplinary Association for Intensive Care and Emergency Medicine (DIVI)
- Chairman of the Board of Trustees of the CAPNETZ Foundation
- Head of the Competence Center for Infectious Diseases
- Director of the Competence Network AsCoNet
- President of the German Society for Pneumology and Respiratory Medicine (DGP) 2013–2015
- Vice-President of the European Respiratory Society (ERS) 2016/2017, ERS President Elect 2017/2018, ERS President 2018/2019
- Fellow of ERS (FERS)

#### Contact

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#### Research Profile

The focus of BREATH is the translation of findings from basic research into clinical practice, with regard to all topics listed below. This includes the execution of clinical studies of all phases relevant for registration and with the opening of the Clinical Research Center Hanover in 2015, a joint initiative of the federal government and the State of Lower Saxony, the last gap in this area was closed successfully. Hanover Medical School is one of the three largest Lung Transplantation Centers in the world, and research in End-Stage Lung Diseases is therefore one of the core areas of BREATH. Other closely connected aspects are research on an artificial lung and stem cell research. Preclinical research is extensively performed in the areas of Infection, Pulmonary Hypertension, Interstitial Lung Diseases as well as Asthma and Allergies. In the area of basic research, BREATH focuses on the pathobiology of bacterial infections of the lung. In cooperation with the Fraunhofer Institute for Toxicology and Experimental Medicine, research is conducted on the pathophysiology of allergic diseases. The Leibniz University adds expertise in health services research and health economic aspects as well as in the area of imaging based on laser techniques. The national research network CAPNETZ aims to improve the patient-centered care for adults and children with Community-Acquired Pneumonia (CAP), and is also involved in the construction of the bronchiectasis registry PROGNOSIS.

## DZL Site Munich

### Comprehensive Pneumology Center Munich (CPC-M)

#### Partner Institutions of the Site

- Helmholtz Zentrum München – German Research Center for Environmental Health
- Ludwig Maximilian University Munich
- Munich University Hospital
- Asklepios Clinic Munich-Gauting

#### Prof. Dr. Dr. h.c. Erika von Mutius



- Director of the DZL Site CPC-M
- Head of the Department Asthma and Allergy at the Dr. von Hauner Children's Hospital of the Ludwig-Maximilians-University Munich
- Member of the Editorial Board of the New England Journal of Medicine (since 2006)
- Recipient of the Gottfried Wilhelm Leibniz Prize from the German Research Foundation
- Holder of the Cross of Merit of the Federal Republic of Germany
- Fellow of ERS (FERS)

#### Contact

DZL Site Coordinator, CPC-M:

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#### Research Profile

At the Comprehensive Pneumology Center Munich (CPC-M), the Helmholtz Zentrum München – German Research Center for Environmental Health, Ludwig-Maximilians-University Munich with its University Hospital and the Asklepios Clinic Munich-Gauting have come together to form one of the largest centers in the world for translational research on chronic lung disease. The Helmholtz Zentrum München is a renowned expert in linking fundamental research and applied medical research. Ludwig-Maximilians-University is one of the top-level universities in the German Excellence Initiative. Its medical faculty is involved in high-level pulmonary research and medical care. The Asklepios Clinic Munich-Gauting is one of the leading hospitals in Germany that specializes in lung diseases. Research at CPC-M is focused on chronic lung diseases. CPC-M scientists integrate state-of-the-art techniques in molecular and cell biology, pharmacology, molecular pathology and clinical medicine in order to develop new diagnostic tools and therapies. In addition to the research program, CPC-M scientists are coordinators for the Disease Areas “Interstitial Lung Disease” and “Asthma and Allergy”. As an important link between clinical and basic research, the CPC-M also runs a research clinic. Here, clinicians and scientists work closely together to connect research results with therapeutic approaches. The CPC-M also operates the Lung Information Service ([www.lungeninformationsdienst.de](http://www.lungeninformationsdienst.de)), which is responsible for effective public and patient education and outreach about lung diseases.

## DZL Site Heidelberg

### Translational Lung Research Center Heidelberg (TLRC)

#### Partner Institutions of the Site

- Heidelberg University Hospital
- Heidelberg University
- Thoraxklinik at Heidelberg University Hospital
- German Cancer Research Center (DKFZ)
- European Molecular Biology Laboratory (EMBL)

#### Prof. Dr. Hans-Ulrich Kauczor



- Director of the TLRC DZL site
- Provisional Director of the Department of Translational Pulmonology at Heidelberg University Hospital
- Medical Director of the Department of Diagnostic and Interventional Radiology at Heidelberg University Hospital Heidelberg

#### Contact

DZL Site Coordinator, TLRC:

Dr. Birgit Teucher

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Phone: +49 (0)6221 56 4296

#### Research Profile

The Heidelberg Translational Lung Research Center (TLRC) is an interdisciplinary center for translational lung research, where physicians and scientists at Heidelberg University Hospital and the Medical Faculty of Heidelberg University, the Thoraxklinik at Heidelberg University Hospital (one of Germany's oldest and largest hospitals specializing in lung disease), and the non-university research centers (the German Center for Cancer Research and the European Molecular Biology Laboratory) all work together to combat lung disease. The common goal is to improve diagnosis and therapy of chronic lung diseases in children and adults by promoting the close collaboration and exchange of expertise between basic research and clinical research. The research focus is on elucidating the mechanisms underlying common genetic and acquired chronic and malignant lung diseases, such as Cystic Fibrosis (CF), COPD, and Lung Cancer. TLRC scientists also contribute to research in the fields of Pulmonary Fibrosis, Pneumonia and Acute Lung Injury, and Pulmonary Hypertension. The scientists' goal is to identify new therapeutic targets to improve diagnostics and develop further curative treatment options. Within the basic research program, cell and animal models are used to investigate molecular causes of chronic airway diseases. Use is made of next-generation sequencing as well as state-of-the-art immunobiology and molecular biology techniques. Current research investigates the mechanisms leading to airway mucus obstruction and chronic inflammation in Cystic Fibrosis and other chronic obstructive pulmonary diseases, such as COPD and Asthma. At the TLRC, systems biology is applied to improve our understanding of the molecular causes of Lung Cancer. The Biobanking and Imaging platforms are crucial to the success of the translational lung research program. Early clinical trials are conducted to make new diagnostic and therapeutic strategies available to patients as early as possible.



## DZL Site Gießen, Marburg, Bad Nauheim

### Universities of Giessen and Marburg Lung Center (UGMLC)

#### Partner Institutions of the Site

- Justus Liebig University Giessen
- Philipps University Marburg
- Max Planck Institute for Heart and Lung Research Bad Nauheim
- German COPD and Systemic Consequences – Comorbidities Network (COSYCONET)

#### Prof. Dr. Werner Seeger



- Chairman and Speaker of the German Center for Lung Research (DZL)
- Director of the DZL site UGMLC
- Director of Medical Clinic and Polyclinic II/Head of the Department of Internal Medicine, Justus Liebig University Giessen
- Director, Department of Lung Development and Remodeling, Max Planck Institute for Heart and Lung Research, Bad Nauheim
- Speaker of the Excellence Cluster “Cardio-Pulmonary System” (ECCPS)
- Fellow of ERS (FERS)

#### Contact

DZL Site Coordinator, UGMLC:  
 Dr. Sylvia Weißmann  
 E-Mail: [sylvia.weissmann@ugmlc.de](mailto:sylvia.weissmann@ugmlc.de)  
 Tel.: +49 (0)641 99-42411

#### Research Profile

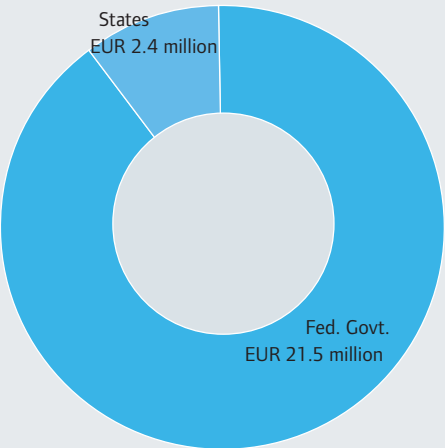
Translational research at the Universities of Giessen and Marburg Lung Center (UGMLC) focuses on lung diseases caused by inflammatory and hyperproliferative processes. This includes research on the antenatal and postnatal impact of environmental factors on the development of Asthma as well as on the development and therapy of Chronic Obstructive Pulmonary Disease (COPD), with particular focus on the alterations of airways and blood vessels. In the Disease Area Pneumonia and Acute Lung Injury (ALI), UGMLC concentrates on the role of innate immunity and inflammatory mechanisms in the acute disease and during resolution and regeneration. Molecular and cellular mechanisms that may help to develop efficient regenerative therapies are studied in the Disease Areas Diffuse Parenchymal Lung Disease (DPLD) and Pulmonary Hypertension (PH). The UGMLC partners complement one another through a close interplay of basic research and clinical research, based on the cooperation of the Max Planck Institute, the universities and the university hospital. Marburg focuses on the areas of Asthma and COPD, Giessen on DPLD and PH, whereby Giessen can be regarded as a national and international center for these diseases. The Max Planck Institute in Bad Nauheim focuses on the fields of stem cell research, developmental biology and cell signaling pathways. Further synergies result from cooperation with the other DZL sites as well as other networks (such as AsCoNet and COSYCONET) and local research consortia like the Excellence Cluster Cardio-Pulmonary System (ECCPS). Within the DZL, UGMLC hosts the DZL Head Office as well as the DZL Biobank and Data Management Platform.

# Finance and Personnel

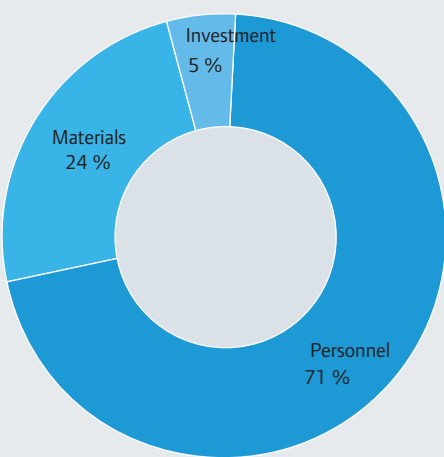
## Total Funding and Cost Breakdown 2017

The total funding for the DZL in 2017 was 23.9 million euros. 90 % was received from the German Ministry of Education and Research (BMBF) and 10 % from the German states with participating DZL centers. Across the eight Disease Areas studied by DZL scientists, around 50 major research projects were supported. Finance is managed by the DZL Funding Management based at the Helmholtz Center in Munich. The Funding Management forwards the project funds to the DZL partner institutions. (As of June 2018)

Total Funding 2017



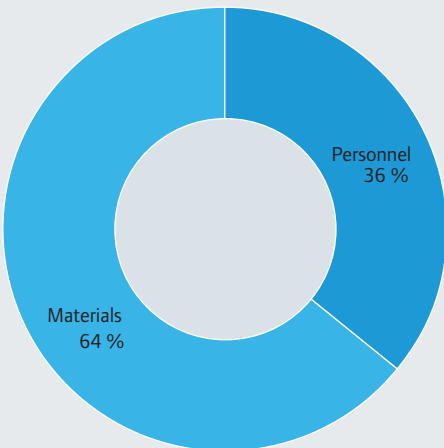
Cost Breakdown: DZL Expenses 2017



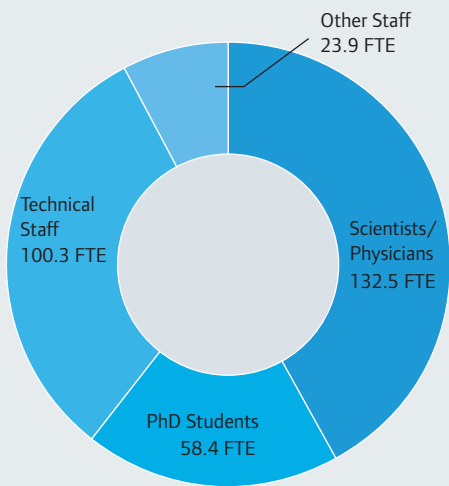
## Cost Breakdown: DZL Expenses 2017

The DZL e. V. is financed through membership fees collected from each member institution as well as from donations. Membership fees amounted to €500,000 in 2017. The 2017 Annual Financial Statement and Year-End Close of the DZL was prepared by the firm Haas & Haas (Giessen)

Cost Breakdown: DZL e. V. Expenses 2017

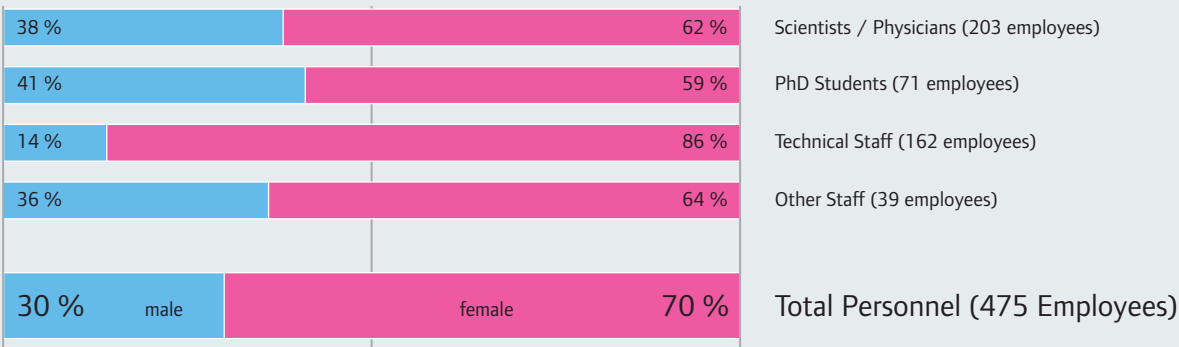


Personnel and Gender Equality 2017

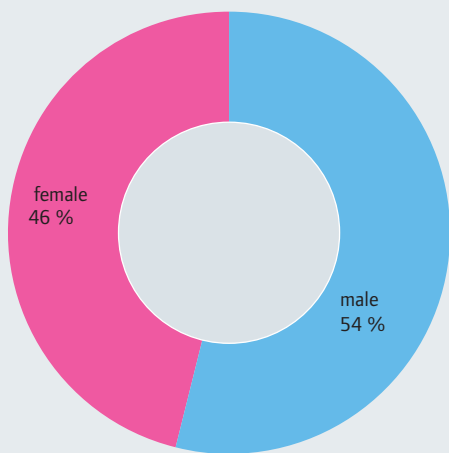


Personnel and Gender Equality 2017

In 2017, 475 employees (315.1 Full-Time Equivalents, FTE) were directly financed with DZL funds across the five partner centers. Of the 475 funded employees, 332 were women (70% of total personnel).



Professorships and Leaders of Junior Research Groups 2017



Professorships and Leaders of Junior Research Groups DZL 2017

In 2017, there were 13 professorships and leaders of junior research groups funded within the DZL, 6 of whom were women (46%).



# Masthead

## Publisher

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## Managing Director

Dr. Christian Kalberlah

## Editors/Authors

Dr. Christian Kalberlah and Prof. Dr. Werner Seeger (Chief Editors), Susanne Klasen, Staff of the Disease Areas and Platforms/Departments incl. Managers and Directors of the DZL sites.

## Project Management/Research

Dr. Christian Kalberlah, Susanne Klasen

## Photos/Graphics

DZL/DZL partners, unless otherwise specified.

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## Editorial Comment

Insofar as the masculine form is used in the contents of this report, it is assumed that this refers to all genders on equal terms.

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