Was ist Lungenfibrose:
Grundlagen und Krankheitsbild

1. Expertenforum des Lungeninformationsdienstes (LID)

Prof. Dr. med. Oliver Eickelberg
Comprehensive Pneumology Center (CPC)
Helmholtz Zentrum München and
Ludwig-Maximilians-Universität München

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LMU KLINIKUM ASKLEPIOS Gemeinsam für Gesundheit HelmholtzZentrum münchen German Research Center for Environmental Health

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Pirfenidone in patients with idiopathic pulmonary fibrosis (CAPACITY): two randomised trials

Paul W Noble, Carlo Albera, Williamson Z Bradford, Ulrich Costabel, Marilyn K Glassberg, David Kardatzke, Talmadge E King Jr, Lisa Lancaster, Steven A Sahn, Javier Szwarcberg, Dominique Valeyre, Roland M du Bois, for the CAPACITY Study Group

Lancet 2011; 377: 1760–69
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Summary

Background Idiopathic pulmonary fibrosis is a progressive and fatal lung disease with inevitable loss of lung function. The CAPACITY programme (studies 004 and 006) was designed to confirm the results of a phase 2 study that suggested that pirfenidone, a novel antifibrotic and anti-inflammatory drug, reduces deterioration in lung function in patients with idiopathic pulmonary fibrosis.

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Lancet. 2011 May 21;377(9779):1760-9

The NEW ENGLAND JOURNAL of MEDICINE

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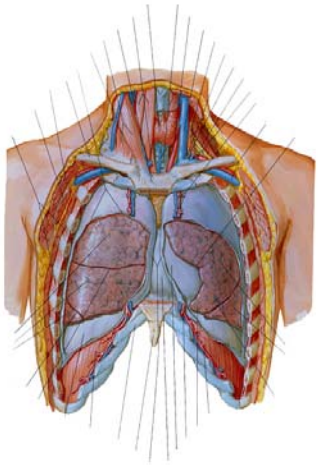
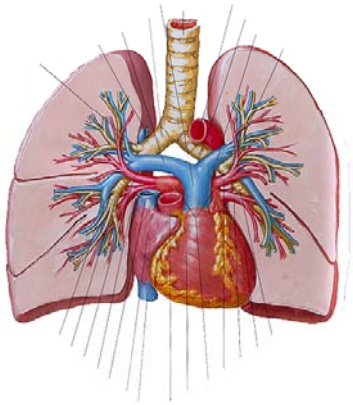
Efficacy of a Tyrosine Kinase Inhibitor in Idiopathic Pulmonary Fibrosis

Luca Richeldi, M.D., Ph.D., Ulrich Costabel, M.D., Moises Selman, M.D., Dong Soon Kim, M.D., David M. Hansell, M.D., Andrew G. Nicholson, D.M., Kevin K. Brown, M.D., Kevin R. Flaherty, M.D., Paul W. Noble, M.D., Ganesh Raghu, M.D., Michèle Brun, M.Sc., Abhya Gupta, M.D., Nolwenn Juhel, M.Sc., Matthias Klüglich, M.D., and Roland M. du Bois, M.D.

N Engl J Med 2011; 365:1079-1087

Unser Atmungsorgan: Die Lunge





Netter Atlas (www.netterimages.com)

Die Lunge

⇒ Ständiger Kontakt zur Aussenwelt!

⇒ Abwehr von Bakterien, Pollen, Abgasen, Rauch, Staub

⇒ Lebenswichtiger Gasaustausch: Sauerstoffaufnahme und Kohlendioxidabgabe

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Chronische Lungenerkrankungen

⇒ Chronische Lungenerkrankungen sind die 2. häufigste Todesursache weltweit

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⇒ 20% aller Todesfälle sind auf die Folgen einer chronischen Lungenerkrankung zurückzuführen

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⇒ Hoffnungsvolle Therapieansätze sind Mangelware

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LEADING CAUSES OF DEATH, 2004 AND 2030 COMPARED

2004 Disease or injury	Deaths (%)	Rank	Rank	Deaths (%)	2030 Disease or injury
Ischaemic heart disease	12.2	1	1	14.2	Ischaemic heart disease
Cerebrovascular disease	9.7	2	2	12.1	Cerebrovascular disease
Lower respiratory infections	7.0	3	3	8.6	Chronic obstructive pulmonary disease
Chronic obstructive pulmonary disease	5.1	4	4	3.8	Lower respiratory infections
Diarrhoeal diseases	3.6	5	5	3.6	Road traffic accidents
HIV/AIDS	3.5	6	6	3.4	Trachea, bronchus, lung cancers
Tuberculosis	2.5	7	7	3.3	Diabetes mellitus
Trachea, bronchus, lung cancers	2.3	8	8	2.1	Hypertensive heart disease
Road traffic accidents	2.2	9	9	1.9	Stomach cancer
Prematurity and low birth weight	2.0	10	10	1.8	HIV/AIDS
Neonatal infections and other*	1.9	11	11	1.6	Nephritis and nephrosis
Diabetes mellitus	1.9	12	12	1.5	Self-inflicted injuries
Malaria	1.7	13	13	1.4	Liver cancer
Hypertensive heart disease	1.7	14	14	1.4	Colon and rectum cancers
Birth asphyxia and birth trauma	1.5	15	15	1.3	Oesophagus cancer
Self-inflicted injuries	1.4	16	16	1.2	Violence
Stomach cancer	1.4	17	17	1.2	Alzheimer and other dementias
Cirrhosis of the liver	1.3	18	18	1.2	Cirrhosis of the liver
Nephritis and nephrosis	1.3	19	19	1.1	Breast cancer
Colon and rectum cancers	1.1	20	20	1.0	Tuberculosis
Violence	1.0	22	21	1.0	Neonatal infections and other*
Breast cancer	0.9	23	22	0.9	Prematurity and low birth weight
Oesophagus cancer	0.9	24	23	0.9	Diarrhoeal diseases
Alzheimer and other dementias	0.8	25	29	0.7	Birth asphyxia and birth trauma
			41	0.4	Malaria

* Comprises severe neonatal infections and other, noninfectious causes arising in the perinatal period.

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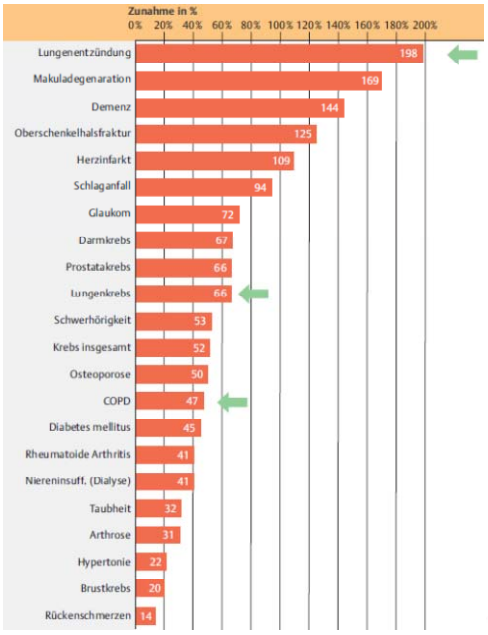

Morbititätsprognose 2050

Pneumologie 2010; 64: 143 – 148

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Erkrankungsschwerpunkte im CPC - Chronische Lungenerkrankungen

1. Chronisch obstruktive Lungenerkrankungen (COPD)
2. Interstitielle Lungenerkrankungen (IPF)
3. Lungenkrebs
4. Abstossung/Versagen bei Lungentransplantation
5. Asthma

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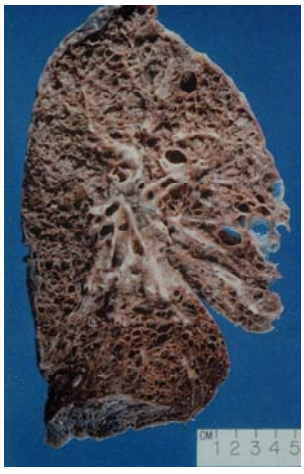
Idiopatische Lungenfibrose (Idiopathic Pulmonary Fibrosis - IPF)



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Dept. Pathology UCSF

Symptome bei IPF

- Progressive Dyspnoe (Atembeschwerden) bei Ruhe oder Anstrengung
- Chronischer, nicht-produktiver Husten
- Restriktive Veränderung der Lungenfunktion
- Röntgen/HRCT mit Befund einer fibrotischen Veränderung

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ATS/ERS Kriterien: Diagnose der IPF (2000)

Major Criteria:

1. **Exclusion of other known causes of ILD**
2. **Abnormal PFT that include evidence of restriction and impaired gas exchange**
3. **Bibasal reticular abnormalities with minimal ground glass opacities on HRCT**
4. **Transbronchial lung biopsy or BAL showing no features to support alternative diagnosis**

Minor Criteria:

1. **Age > 50**
2. **Insidious onset of otherwise unexplained dyspnea on exertion**
3. **Duration of illness greater than 3 months**
4. **Bibasilar inspiratory crackles (dry or "Velcro" -type in quality)**

ALL of the major criteria plus at least THREE minor criteria

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ATS/ERS Kriterien: Diagnose der IPF (2011)

The diagnosis of IPF requires the following:

1. **Exclusion of other known causes of ILD**
2. **The presence of a UIP pattern on HRCT in patients not subjected to a surgical lung biopsy**
3. **Specific combination of HRCT and surgical lung biopsy pattern in patients subjected to surgical lung biopsy.**

The diagnosis of IPF is enhanced by a multidisciplinary discussion

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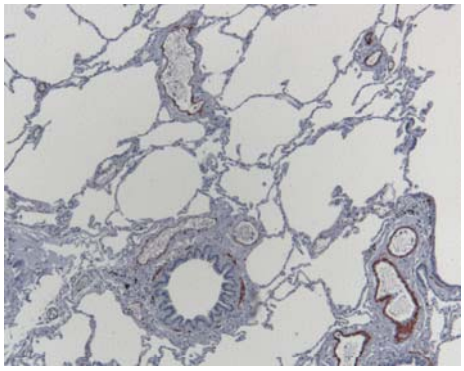
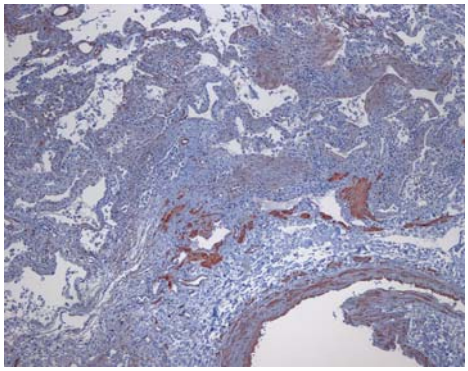
Idiopatische Lungenfibrose (Idiopathic Pulmonary Fibrosis - IPF)



- **small alveolar septae, little ECM deposition**
- **smooth muscle actin expression restricted to the circumference of airways and vessels**



- ***inhomogeneous* picture**
- **small alveolar septae next to massively thickened septae**
- **interstitial ECM deposition**
- **non-restricted smooth muscle actin expression**

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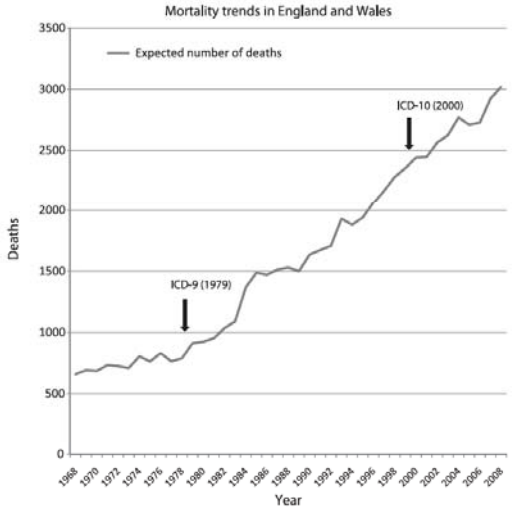

Figure 1 Estimated number of deaths from idiopathic pulmonary fibrosis clinical syndrome, age standardised to the 2008 population of England and Wales. ICD, International Classification of Diseases.

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Thorax. 2011 Jun;66(6):462-7

Idiopatische Lungenfibrose (Idiopathic Pulmonary Fibrosis - IPF)

35%	Sarkoidosis
32%	Idiopathic Interstitial Pneumonia (ca. 30 000 betroffene Patienten in Deutschland
11%	Hypersensitivity Pneumonitis
6,8%	Bronchiolitis oblit. organ. pneumonia = BOOP
5,1%	Postinflammatory Fibrosis (e.g. ARDS)
2,6%	Drugs / Radiation
2,6%	Occupational
2,1%	ILD with Collagen Diseases
0,8%	ILD with Vascular Diseases

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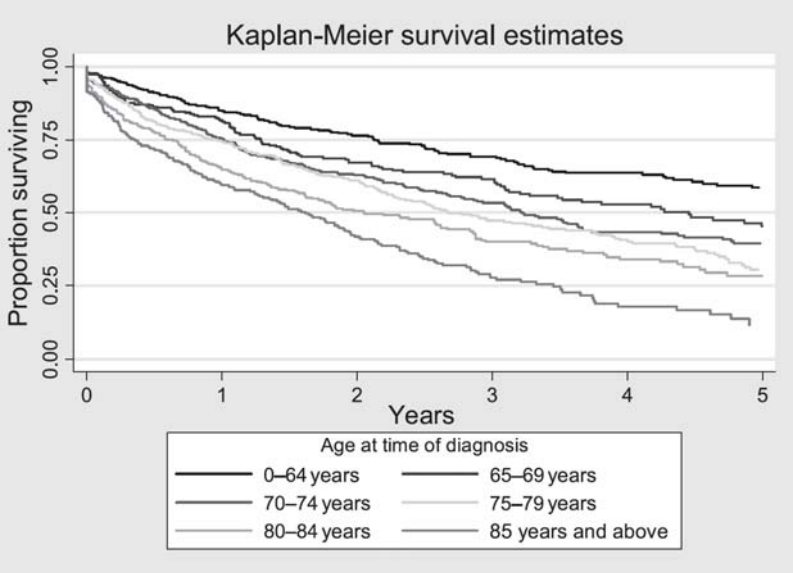

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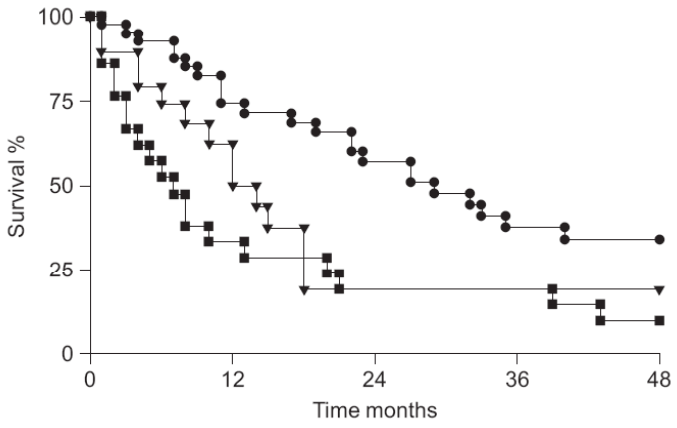
Lungenfunktion in IPF

4-year-survival of 84 SLB proven IPF patients

- stable disease at 6 months (n=38)
- ▼ marginal decline of FVC (5-10 %) at 6 months (n=23)
- ■ significant decline of FVC (>10%) at 6 months (n=23)

p<0.005



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Zappala et al., Eur Respir J, 2010; 35:830-835

AJRCCM Articles in Press. Published on September 22, 2011 as doi:10.1164/rccm.201105-0840OC

Forced Vital Capacity in Patients with Idiopathic Pulmonary Fibrosis: Test Properties and Minimal Clinically Important Difference

Roland M. du Bois, M.D.[1], Derek Weycker, Ph.D.[2], Carlo Albera, M.D.[3], Williamson Z. Bradford, M.D., Ph.D[4], Ulrich Costabel, M.D.[5], Alex Kartashov, Ph.D.[2], Talmadge E. King, Jr., M.D.[6], Lisa Lancaster, M.D.[7], Paul W. Noble, M.D.[8], Steven A. Sahn, M.D.[9], Michiel Thomeer, M.D.[10], Dominique Valeyre, M.D.[11], Athol U. Wells, M.D.[12]

Measurements and Main Results: Correlation of percent predicted FVC between measurements (mean interval, 18 days) was high (r=0.93; p<0.001). Correlations between FVC and other parameters were generally weak, with the strongest observed correlation between FVC and DL_{CO} (r=0.38, p<0.001). Correlations between change in FVC and changes in other parameters were slightly stronger (range, r=0.16 to 0.37, p<0.001). Importantly, one-year risk of death was more than 2-fold higher (p<0.001) in patients with a 24-week decline in FVC between 5-10%. The estimated MCID was 2-6%.

Conclusions: FVC is a reliable, valid, and responsive measure of clinical status in patients with IPF, and a decline of 2-6%, although small, represents a clinically important difference.

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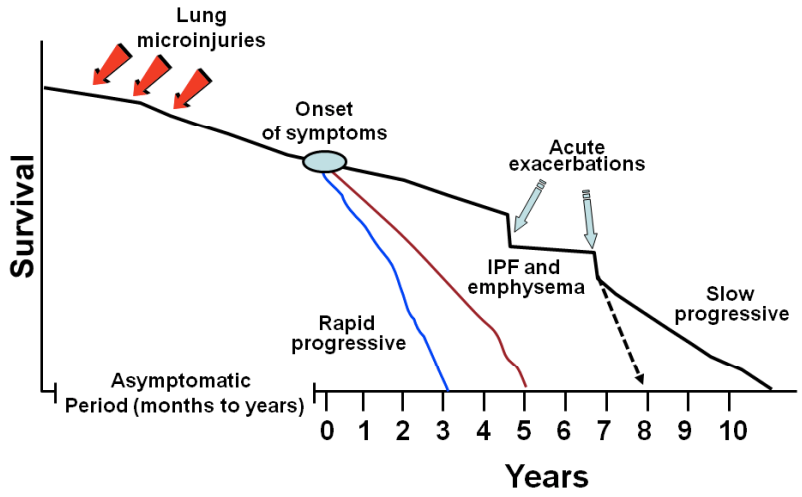
Idiopatische Lungenfibrose (Idiopathic Pulmonary Fibrosis - IPF)



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Courtesy of Moises Selman

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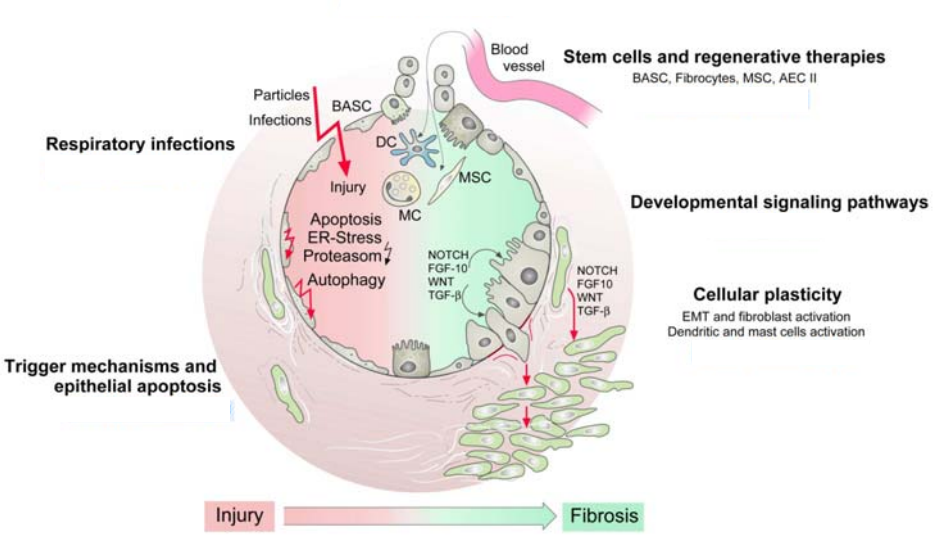

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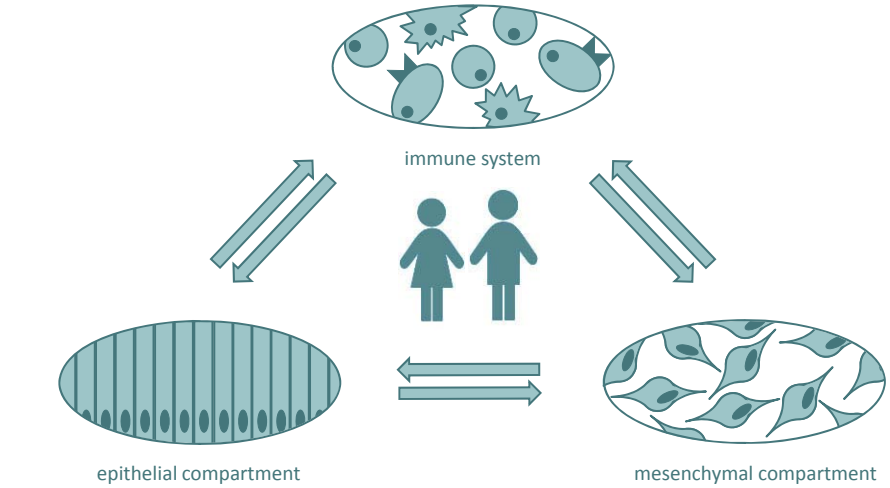
Interstitial lung disease



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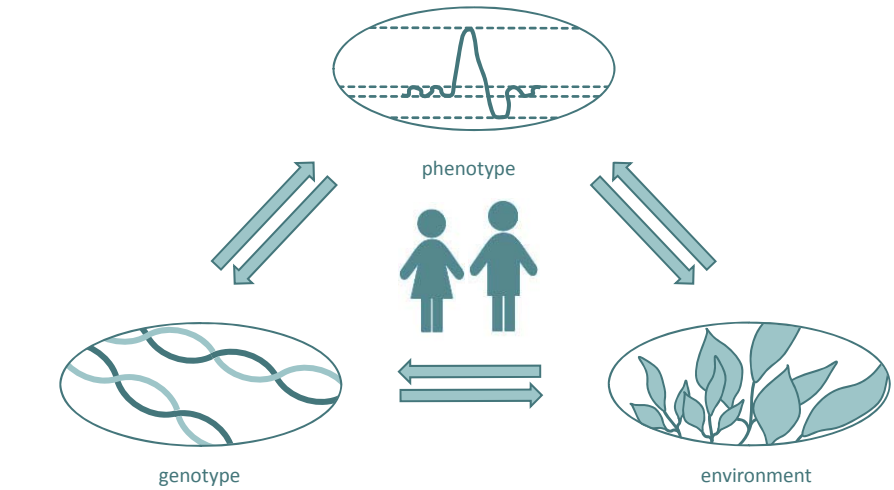

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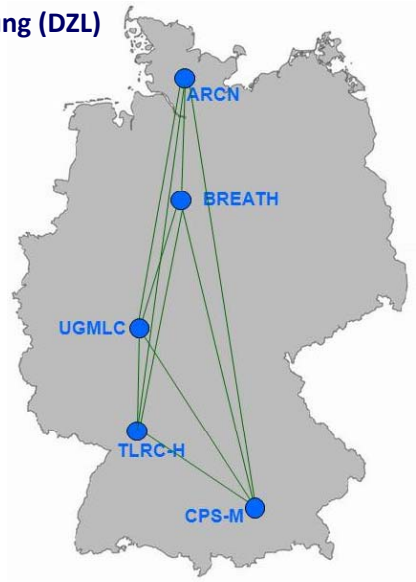
Das Deutsche Zentrum für Lungenforschung (DZL)



Translational Research
to Combat Widespread Lung Diseases

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Erkrankungen im DZL

- **Asthma und Allergie (AA)**
- **Chronisch Obstruktive Lungenerkrankung/Emphysem (COPD)**
- **Zystische Fibrose (CF)**
- **Pneumonie und Akute Lungenschädigung (ALI)**
- **Diffus Parenchymatöse Lungenerkrankung (DPDL - IPF)**
- **Pulmonale Hypertonie (PH)**
- **Endstage Lung Disease / Transplantation (ELD)**
- **Lungenkrebs (LC)**

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Vielen Dank für Ihre Aufmerksamkeit

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