



Dear CAPNETZ community,

We are pleased to bring you the latest news on activities and scientific publications from the CAPNETZ in this newsletter!

Continuing the mission of the two-decade-old CAPNETZ competence network, we seek to expand and strengthen its mission by engaging clinicians and researchers in a spectrum of activities ranging from biomedical and clinical research to practice for the prevention, timely intervention, and reduction of the burden of severe community-acquired pneumonia (CAP) in Germany and beyond.

We look back at some of our scientific activities from the beginning of 2024 and give you a brief overview. Stay also tuned to our website www.capnetz.de for regular updates.

Yours,

Gopinath Krishnamoorthy, Grit Barten-Neiner and
the foundation board of CAPNETZ STIFTUNG

CAPNETZ Clinical studies

Can hypertonic saline solution treatment be used to improve respiratory function in PCD patients?

The interventional study HELP-PCD (CREATING EVIDENCE FOR THE USE OF HYPERTONIC SALINE IN PEOPLE WITH PRIMARY CILIARY DYSKINESIA) (supported by PARI Pharma GmbH), funded by the Deutsches Zentrum für Lungenforschung (DZL), will evaluate the effect of MucoClear® 6% Inhalation Solution in people with PCD (≥ 12 years of age) to aid mucus clearance and potentially improve respiratory outcomes.

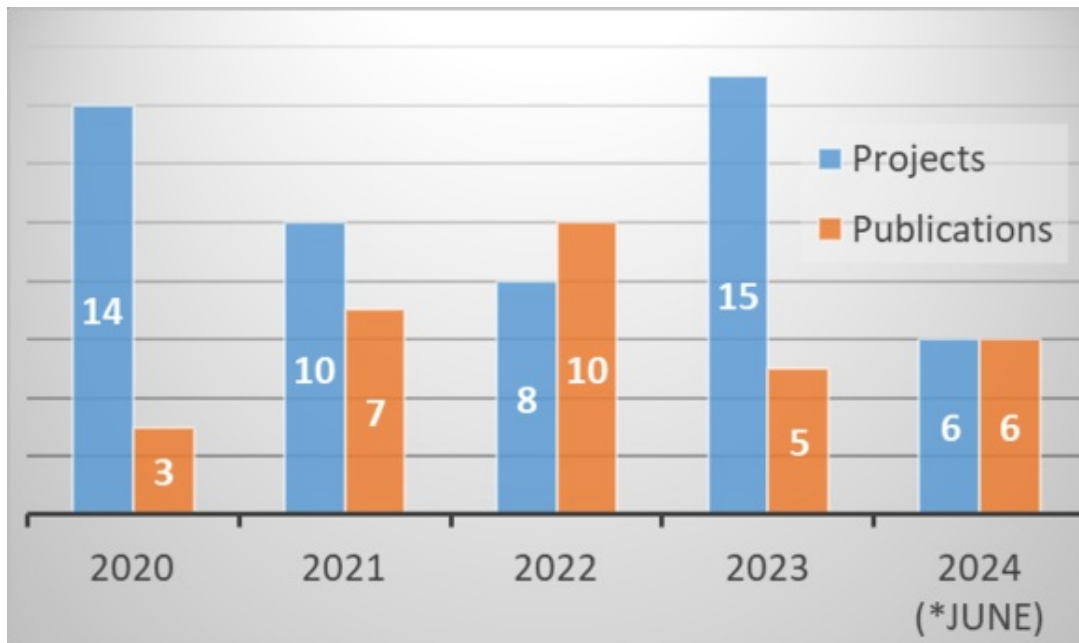
The change in lung clearance index (LCI) at 8 weeks is the primary efficacy endpoint. Assessment of change in global ventilated lung volume by magnetic resonance imaging (MRI) in adults with PCD is an exploratory endpoint. This proof-of-concept study with its innovative primary endpoint LCI and the exploratory MRI sub-study goes beyond the current state-of-the-art and will provide invaluable new resources to the DZL research community as well as external collaborators.

CAPNETZ STIFTUNG is the sponsor. The study will be conducted at several DZL sites and other centers in Germany.

The study will be coordinated by Dr. med. Isabell Pink and Prof. Dr. med. Felix Ringshausen, Medizinische Hochschule Hannover, Klinik für Pneumologie und Infektiologie.

CAPNETZ resources and support

CAPNETZ collects extensive clinical data and biological samples from patients with CAP and systematically stores them in a central database. This centralized approach enables comprehensive and high-quality research aimed at understanding the epidemiology, pathogen types, pathophysiology and clinical management of the disease. Fifty-three research projects are underway using either clinical data or patient-derived samples from the CAPNETZ database and repository, with thirty-two peer-reviewed articles published between 2020 and now.



CAPNETZ-associated research publications

Some of the most recently published research studies are highlighted below.

Clinical epidemiology

How does the pathogen and clinical spectrum of CAP vary in people living with HIV or in hospitalized patients with SARS-CoV2 infection?

Two recent published studies in the scientific journal *Infection* provide evidence that can directly influence how clinicians diagnose, treat, and manage health conditions. First, [Schleenvoigt et al.](#) determined the prevalence of CAP causing pathogens in people living with HIV and emphasized the need for empirical antibiotic treatment covering pneumococci and *Haemophilus influenza*. Second, [Meyer et al.](#) found that more severe clinical progression in COVID-19-CAP compared to patients with non-COVID-19-CAP resulting in extended admission in ICU units with high mortality rate.

What is the impact of COVID-19 associated restriction on CAP causing pathogens?

Comparing the respiratory pathogen frequencies over three consecutive years (July 2020 - May 2023) from 1388 patients in CAPNETZ cohort, a newly published study by [Dähne et al.](#) in *Journal of Clinical Virology* showed that community-acquired viruses that cause have reemerged post-COVID19 pandemic. Note that the more than two thirds of the detected viral infections can be prevented by effective vaccines or treated by drugs.

Mechanisms of treatment response

Why is dexamethasone only effective for some patients?

Despite the proven clinical effectiveness of dexamethasone, a substantial number of patients progress to critical illness and die from COVID-19 with apparently little or no response to dexamethasone treatment. *Knoll, Hellbig et al.* in the journal *Cell* investigated the molecular effects of dexamethasone in patients with severe COVID-19 who responded differently to treatment with the drug. They used a state-of-the-art so-called single-cell transcriptomic analysis of clinical samples from single- and multi-center cohorts (CAPNETZ & PROVID-CAPNETZ). The data obtained showed that the life-saving benefits of dexamethasone are associated with the reversal of monocyte dysregulation. The methods optimized in this study are not only able to predict the therapeutic response in COVID-19, but also potentially be applied to other diseases.

Microbial pathogenesis

What is the role of Activin A in Tuberculosis pathogenesis?

Tuberculosis is responsible for more deaths than any other infection worldwide. Tuberculosis affected approximately 229000 people in the WHO European Region during the year 2022. Understanding the mechanisms of Tuberculosis pathogenesis is therefore key to disease prevention and control.

Nieuwenhuizen et al. in *journal mBio* showed that a protein called activin A was increased in the serum of patients with active tuberculosis (Gambian and German TB Cohorts) and pneumonia (CAPNETZ cohorts). Blocking activin A function reduced pathogen replication in a mouse model, encouraging future studies to explore activin A as a potential host-directed therapeutic target for Tuberculosis and other respiratory infections.

Host-Microbial interaction

Are there immune markers that can distinguish acute from chronic methicillin-resistant *S. aureus* infections?

Methicillin-resistant *S. aureus* can spread in the community and are known to be resistant to many classes of antibiotics. A proof-of-concept study by *Gheitsi et al.* in *Frontiers in Immunology* has identified a specific set of immune markers that can potentially predict the acute to chronic stage of methicillin-resistant *S. aureus* infection. These laboratory findings, however, need to be further validated in preclinical models and clinical trials.

How are innate immune responses, gut microbiota and pneumonia susceptibility linked?

Röwekamp, Maschirow, Rabes et al. in *PNAS* elucidate the mechanism by which IL-33 regulates IL-22 cytokine-dependent antibacterial defenses. However, this effect depends on the modulatory influence of IL-33 on the gut microbiota. Importantly, the authors identified genetic variation in genes involved in IL-33 signaling and its association with bacterial pneumonia in humans using samples provided by the CAPNETZ competence network.

News from the community

A new S2k guideline for the management of bronchiectasis in adults (AWMF Reg.-Nr. 020-030) is available. More details can be found in www.awmf.org/service/awmf-aktuell/management-erwachsener-patienten-mit-bronchiektasen-erkrankung CAPNETZ STIFTUNG and its infrastructure was critical in setting up the PROGNOSIS NON-CF bronchiectasis registry. The results obtained in the PROGNOSIS study also partly informed this new guideline.

New employees at the CAPNETZ headquarters

Since May this year, we have welcomed two colleagues to our team.

Sabine Klingenberg has joined us as a data manager and medical writer to support ongoing clinical studies. She holds a degree in biology and has experience as a clinical research associate, data manager and medical writer.



Gopinath Krishnamoorthy has joined us as a Scientific Officer. He holds a PhD degree in Molecular Microbiology and has several years of research experience. He will oversee the scientific work of the CAPNETZ STIFTUNG, public and community engagement with research, and facilitate interaction among the young clinicians and researchers.

