

### 13<sup>th</sup> Workshop "Models of Asthma and COPD" at the Fraunhofer ITEM Hannover/Germany, January 24-25, 2014

The 13<sup>th</sup> workshop on "Models of Asthma and COPD", organized by the Fraunhofer ITEM in Hannover in cooperation with the German Center for Lung Research (DZL) and held at the Fraunhofer ITEM on January 24 and 25, 2014, attracted about 90 international participants from academia and industry. They appreciated a well diversified translational program with top-notch speakers giving comprehensive overviews and presenting new exciting data. A poster exhibition and generously timed coffee breaks allowed intensive scientific exchange and networking.



#### Biomarkers of inflammatory lung disease

After a short welcome and introduction by organizer Armin Braun (Fraunhofer ITEM), day one started with a session on biomarkers of inflammatory lung disease, chaired by Jens Hohlfeld (Fraunhofer ITEM). Jan de Backer, CEO of FLUIDDA, introduced functional respiratory imaging (FRI), an innovative CT-based technique capable of analyzing lung function, morphology, perfusion, or drug deposition. This is aiming to be a novel biomarker tool for decision making, phenotyping, or evaluating bioequivalence in the development of drugs for the treatment of respiratory diseases such as asthma and COPD. Olaf Holz (Fraunhofer ITEM) gave a comprehensive overview of the current status of exhaled breath diagnostics, also summarizing technical challenges, device development, and clinical value. Another source of pulmonary biomarkers is bronchoalveolar lavage (BAL), a long-standing research interest of Marek Lommatzsch from the University of Rostock. He gave an overview of the cellular compartment of BAL with a special focus on dendritic cells, demonstrating new data that give further insights into the role of this cell type in the pathology of COPD. Bernd Schmeck from the University of Marburg talked about the potential of systems biology in understanding mechanisms of asthma resulting in a higher success rate of new therapies. He pleaded to combine current bottom-up and top-down approaches and to integrate different 'omics, also referring to ongoing efforts of European consortia such as CASyM, U-BIOPRED, and Airprom. The session was finished by Holger Garn, University of Marburg and co-founder of sterna biologicals, a biopharmaceutical company dedicated to the development of therapeutic DNazymes. Sterna's most developed candidate SB010 antagonizes a transcription factor (GATA-3) that plays a major role in the pathology of allergic diseases like asthma. After substantial preclinical work and phase-I studies, the results of a completed multi-center allergen provocation study in mild to moderate asthmatics are now eagerly awaited.



### **In-vitro and ex-vivo methods to model pulmonary disease**

The second session on day one, chaired by Armin Braun, dealt with in-vitro and ex-vivo models of pulmonary disease. Meike Müller (Fraunhofer ITEM) reported on the development of cellular in-vitro models of allergy to evaluate efficacy and safety of drug candidates. Models were successfully validated for different allergens. The following two talks were about precision-cut lung slices (PLSC). Christian Martin (RWTH Aachen) gave a comprehensive overview of the insights and limitations of this versatile technique allowing functional analysis of lung material from patients with different respiratory diseases. New data demonstrated long-term viability without loss of reactivity. Ongoing work was presented regarding the mechanical properties of lung slices and the role of elastic fibers in the differentiation of disease types. Finally, Katherina Sewald (Fraunhofer ITEM) reported substantial work on the development and standardization of a translational model of PLCS for toxicity and efficacy testing of compounds. New data on nerve fiber-induced bronchoconstriction and cytokine-induced hyperresponsiveness were followed by an outlook on a chronic model including the induction of remodeling.



### **Special lecture provided food for thought**



A special lecture on “Science” by Thomas Hartung (Johns Hopkins University, Baltimore, USA) entertainingly unmasked widespread mistakes and limitations in academic research and preclinical drug development leading to false conclusions and non-reproducibility of results. Possibly as a consequence, 95 percent of drugs that enter clinical trials do not make it to the market. A change was deemed to be desperately needed. This excellent food for thought talk surely inspired several thoughts at food during subsequent dinner.

### **Holistic tools to understand respiratory diseases**

The second day opened with a session on holistic tools to understand respiratory disease, chaired by Thomas Tschernig (Homburg University Hospital). Thomas Illig, who is heading the Hannover Unified Biobank, reported on efforts to combine genomics with metabolomics for the discovery of new therapeutic targets. Recent data from cohort studies revealed highly significant associations that might lead to interesting drug candidates. A novel technique, chip cytometry, was introduced by Christine Happle (Hannover Medical School). Chip cytometry, already commercialized by the spin-off Zellkraftwerk, enables high-content analysis of cells or tissues fixed to a special slide. Furthermore, functional chip cytometry is capable of tracing cells or detecting signal transduction processes on a single-cell level (calcium flux; work in progress). In respiratory investigations, cells from blood and bronchoalveolar lavage as well as human lung samples were successfully analyzed.



## New therapeutic targets and technologies



New therapeutic targets and technologies was the topic of the second and last session of day two, chaired by Norbert Krug (Fraunhofer ITEM). The session started with a novel therapeutic approach presented by Alex Eggel (University of Bern). DARPINs, developed by Molecular Partners, are proteins addressing IgE, an immunoglobulin playing an important role in the pathology of asthma. Structure-activity relationship data were presented, elegantly evaluating the molecular mode of action of DARPINs and omalizumab, a marketed therapeutic antibody with the same target. Mark Kühnel (Hannover Medical School) then introduced SLOT (Scanning Laser Optical Tomography), a novel imaging technique. SLOT is a highly sensitive method to investigate tissue morphology that has been successfully demonstrated for murine and human lung tissue. Kühnel's near-future plan is to correlate aspects of lung architecture measured by SLOT with biological activity and gene expression. Christine Falk (Hannover Medical School) gave a comprehensive overview of natural killer cells that are much more than just killers, but important regulators of immunity. She presented new data regarding the role of donor-derived NK cells in the periphery of lung transplant recipients, implicating an involvement of allograft tolerance. In the workshop's last talk, Matthias Düchs (Boehringer Ingelheim) reported on the development of a novel 12-day in-vivo model of influenza-induced COPD exacerbation in smoke-exposed mice. The combination effect of infection and smoke was more than additive. Effects of the reference compounds fluticasone, tiotropium, and roflumilast were presented. In a next step, it is planned to include chronic aspects and different as well as combined inducing agents.

Taken together, this workshop gave an excellent overview of the development process of respiratory drugs and highlighted the paradigm shift in science that is being induced by upcoming new technology. The next workshop of this series will be held in early 2015.

