Ludwig Demling Center for Molecular Imaging

Speaker
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Aims and structure

The aim of the project „Molecular endoscopic imaging at interfaces in inflammatory and neoplastic diseases", initially funded by the Emerging Fields Initiative (EFI), is to improve the detection of disease-specific changes in the tissue of patients with inflammatory or neoplastic disease entities.
Innovative imaging techniques will enable a more precise assessment of the mucosa. The techniques used include multispectral optoacoustic tomography (MSOT), functional magnetic resonance imaging (fMRI), the latest generation of endoscopic devices, and in particular endoscopic detection of the cellular molecular signature of the examined tissue. The improved detection of tissue alterations by means of identification and visualization of molecular target structures represents a pioneering field of medicine. By using interdisciplinary synergetic effects between different departments of UK Erlangen as well as theoretical and basic scientific institutes, innovative methods for molecular endoscopic imaging of inflammatory or neoplastic diseases have been established. In the process, findings from basic research regarding the immunopathogenesis of disease entities were incorporated and the resulting molecular signature of the cells was clinically used for the *in vivo* imaging of disease-specific changes. In memory of Prof. Dr. Ludwig Demling, former holder of the Chair of Internal Medicine and Director of the Department of Medicine, the corresponding clinical studies have been carried out mainly at the „Ludwig Demling Center for Molecular Imaging", named after him.
The aim of the Center is to clinically translate innovative translational research approaches into molecular imaging procedures and thereby create improved diagnostic and therapeutic algorithms for the lasting benefit of the patient.

Research

An improved detection of lesions by means of identification and visualization of molecular target structures represents a future-oriented field within medicine. This structure-building approach has already been successfully implemented in a phase I study in Crohn's disease patients. A GMP-compliant, fluorescence-labelled anti-TNF antibody (in cooperation with the GMP-unit of the hospital pharmacy at UK Erlangen) was locally applied to the intestinal mucosa of the patients in order to enable detection and quantification of membrane TNF (mTNF)-positive mucosal cells *in vivo* by means of endoscopic confocal laser endomicroscopy (CLE). The subsequent data evaluation showed a significant correlation between the clinical efficacy of subsequent anti-TNF therapy in Crohn's disease patients and the number of mTNF-positive intestinal cells detected by CLE. Subsequently, for the first time an approval was obtained to conduct a clinical study of molecular imaging with fluorescence-labelled anti-TNF antibodies in ulcerative colitis patients. Within the ongoing study, the expression of the molecular target structure mTNF in mucosal cells before and during anti-TNF therapy will be investigated endoscopically *in vivo*. To our knowledge, there is worldwide no ongoing comparable study on the prediction of response to therapy by molecular imaging. This approach could enable a novel, personalized therapeutic approach.
Patients with intestinal inflammation require optimized endoscopic care to determine the severity and extent of inflammation. In this context, the Ludwig Demling Center is conducting numerous studies with the latest generation of endoscopes. In addition to the endoscopic procedures mentioned above, sonography represents another important examination procedure for determining disease activity in patients with inflammatory bowel disease (IBD). For the first time, a new method was established for IBD patients. MSOT is the basis of this new and promising procedure for the non-invasive diagnosis of gastrointestinal diseases. The technique is based on the observation that the absorption of light leads to thermoelastic expansions of excited molecules, which can be registered as ultrasonic waves (photoacoustic effect). In addition, the use of excitation light with different wavelengths allows a targeted excitation and detection of certain molecules with characteristic absorption spectra (e.g. hemoglobin, melanin, etc.) and thus molecular imaging in biological tissue without additional staining methods. In current studies, experience with the use of MSOT for the assessment of gastrointestinal inflammation has been gained for the first time and a connection with endoscopic inflammatory activity has been demonstrated. In addition to these studies, pain perception before and after biological therapy is investigated by functional magnetic resonance imaging (fMRI) of the brain in cooperation with the Institute of Experimental and Clinical Pharmacology and Toxicology and the Divsion of Neuroradiology. The application of the blood-oxygen level-dependent (BOLD) fMRI study allows the visualization of pain perception in different brain areas after abdominal compression of the patients.

Teaching

A further objective of the Ludwig Demling Center for Molecular Imaging is to disseminate the contents of this technology in courses. Furthermore, the endoscopic application of this procedure in the relevant endoscopic departments is passed on to medical staff by experienced endoscopists in practical HandsOn courses.
The L. Demling Center for Molecular Imaging has been organizing an international congress every two years since 2014 and awards a „Ludwig Demling Medal" for outstanding endoscopic achievements in memory of Prof. Dr. Ludwig Demling. In the meantime, this event has established itself as a high-quality continuing medical education event that is well recognized by national and international endoscopic experts.

Presentation of the Ludwig Demling Medal 2018 (from left to right): Prof. Dr. J. Siebler, Prof. Dr. M. Götz (University Hospital Tübingen), Prof. Dr. A. Dechene (Klinikum Nuremberg), Prof. Dr. C. Ell (Sana Klinikum Offenbach), Prof. J. Bergmann (university of Amsterdam; awardee 2018), Prof. Dr. M.F Neurath*, Prof. Dr. R. Atreya*. (Photo: UK Erlangen; *Department of Medicine 1)*