Institute of Experimental and Clinical Pharmacology and Toxicology
Chair of Clinical Pharmacology and Clinical Toxicology

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Research focus
- Molecular characterization of drug transporters and transporter-mediated drug-drug interactions
- Molecular and clinical characterization of new cardiovascular risk factors and risk markers
- Quantification of drugs and endogenous substances including metabolomics
- Medication safety

Structure of the Chair
Professorships: 2
Personnel: 25
- Doctors (of Medicine): 3
- Scientists: 7 (thereof funded externally: 3)
- Graduate students: 8

Special structural feature
The position of the executive director of the Institute rotates between the Chair of Pharmacology and Toxicology and the Chair of Clinical Pharmacology and Clinical Toxicology on a two-year basis.

Clinical focus areas
- Drug analysis
- Clinical trial unit
- Drug information service for physicians

Research
The groups at the Chair of Clinical Pharmacology and Clinical Toxicology investigate mechanisms underlying interindividual differences in drug effects (pharmacogenomics), cardiovascular pharmacology and risk factors, alterations of the L-arginine-NO-metabolism, and medication safety.

Molecular characterization of transporters and transporter mediated drug-drug interactions
PI: Prof. Dr. J. König, Prof. Dr. M.F. Fromm
Transport proteins located in distinct membrane domains are important for the uptake, distribution, and excretion of drugs and drug metabolites. Simultaneously administered drugs or food constituents can modify transporter-mediated uptake or elimination of victim drugs. This leads to altered plasma concentrations and drug effects of the victim drug and possibly an increased risk of adverse drug reactions. For example, we identified using in vitro models the importance of the export transporter MATE1, which is localized in the luminal membrane of renal proximal tubular cells, for the renal secretion of drugs (e.g. memantine, metformin) and endogenous biomarkers (trimethylamine-N-oxide). Moreover, we investigated the functional relevance of transporters for endogenous substances. For example, functional consequences of mutations in the SLC13A5 gene, which encodes for the uptake transporter NaCT (sodium-coupled citrate transporter), were investigated. This transporter plays an essential role in cellular energy metabolism and in brain development. Alterations in function of NaCT are associated with epileptic encephalopathy.

Molecular and clinical characterization of new cardiovascular risk factors and risk markers
PI: Prof. Dr. R. Maas
A major focus of the group is the experimental and clinical characterization of new cardiovascular risk markers and risk factors as potential targets for therapeutic intervention. Currently the group investigates transport and metabolism of homoarginine, l-aminosobutyrate, nitrate and the methylenarginines ADMA and SDMA. The investigations were conducted in long standing cooperation with the Department of Medicine 4, the Universities of Dresden and Kiel and the Framingham Heart Study (USA). In the reporting period we identified an independent association of the risk markers ADMA, SDMA, and homoarginine with the intake of several drugs. Furthermore, we could provide direct evidence that the protective risk marker homoarginine is a substrate of the cationic amino acid transporters CAT1, CAT2A, and CAT2B.

Analysis of drugs and endogenous substances including metabolomics
PI: Dr. A. Gessner, Dr. V. Taudte
The mass spectrometry unit uses samples from both, cell culture experiments and clinical and large epidemiological trials (GCGD study, pop-gen). Analytical methods (mostly LC/MS/MS) are developed, optimized, and validated in our laboratory. The spectrum of the analytes ranges from various drugs, such as pravastatin, etoposide, metformin, clopidogrel, and trimethoprim, to endogenous substances, such as derivatives of arginine, N-methyl-L-arginine, trimethylamine-N-oxide (TMAO), and l-aminosuberic acid. In 2018, the methodological spectrum was broadened to targeted and untargeted metabolomics due to a new mass spectrometer (Q Exactive Focus with U-HPLC) funded by the DFG. The available technologies can be used for cooperations within the Faculty and FAU as well as for external cooperations.

Medication safety
PI: Prof. Dr. R. Maas, Prof. Dr. M.F. Fromm
A project funded by the German Cancer Aid was conducted with a focus on dose adjustment in oncological patients with renal insufficiency (co-operation with Prof. Dr. F. Dörje, pharmacy of UK Erlangen). Moreover, an innovative, three year clinical study is conducted in patients treated with new oral antitumor therapeutics in collabo-
ration with the pharmacy of UK Erlangen, the Comprehensive Cancer Center Erlangen-EMN (CCC), and collaborating private practices, which is also funded by the German Cancer Aid. This prospective, randomized trial is currently testing the hypothesis whether clinical pharmacological/clinical pharmaceutical support improves patient safety, convenience and knowledge in patients newly treated with new oral antitumor therapeutics (AMBORA study).

In addition, problems of medication safety in elderly patients (e.g. anticholinergic burden and cognitive function in elderly patients) are in the focus of collaborative projects with the Geriatrie in Bayern-Database (GiB-DAT). Moreover, in a BMG-funded collaborative project, we evaluated the new nationwide medication plan in clinical praxis (MMP16).

The Chair coordinates the community of practice “Medication Safety” of the Medical Valley EMN e.V. In addition, the Chair participates in a continuing medical education program in Good Clinical Practice for physicians, as required for clinical trials of medicines, and medicinal products.

**Selected publications**

- Selch S, Chafai A, Sticht H, Birkenfeld AL, Fromm MF, König J. Analysis of naturally occurring mutations in the human uptake transporter NaCT important for bone and brain development and energy metabolism. Sci Rep, 2018, 8: 11330

**International cooperations**

- Prof. L. Gustafsson, Karolinska Institutet, Stockholm: Sweden
- Prof. J. Backman, Prof. M. Niemi, University of Helsinki, Helsinki: Finland
- Prof. R. Vasan, Framingham Heart Study, Framingham: USA
- Prof. R. Masereeuw, Utrecht University, Utrecht: The Netherlands
- Prof. A. Sparreboom, Ohio State University, Columbus, OH: USA

**Teaching**

The Chair of Clinical Pharmacology and Clinical Toxicology coordinates the interdisciplinary lecture series and seminar clinical pharmacology/pharmacotherapy for medical students applying problem-based learning. In addition, we teach students of the degree programs Dentistry, Molecular Medicine, pharmacy, and Medical Process Management. In a cooperation project with the Technical University of Munich, we established two online teaching modules for drug therapy of common diseases. Students of pharmacy and medicine are welcome to work with us during their final year.

The Chair of Clinical Pharmacology and Clinical Toxicology offers supervision of Bachelor’s and Master’s theses as well as of MD and PhD theses.