Department of Surgery

Chair of Surgery

Address
Krankenhausstraße 12
91054 Erlangen
Phone: +49 9131 8533201
Fax: +49 9131 8536595
www.chirurgie.uk-erlangen.de

Director
Prof. Dr. med. Robert Grützmann, MBA

Contact
Prof. Dr. med. Robert Grützmann, MBA
Phone: +49 9131 8533201
Fax: +49 9131 8536595
chir-direktion@uk-erlangen.de

Research focus
- Evaluation of prognosis of gastrointestinal tumors
- Randomized trials for gastrointestinal tumors
- Outcomes research of complex surgery with hospital discharge data
- Pathophysiologic role of vascular effects of IFN-γ in gastrointestinal diseases
- Tumor-micromilieu induced plasticity of tumor endothelial cells in colorectal carcinoma
- Genome editing of pancreatic tumor models
- Organoid models in pancreatic cancer
- Immunepathophysiology of acute (sepsis) and chronic (colitis) inflammation
- Immunephenotyping and liquid biopsy analysis of gastrointestinal tumors

Structure of the Chair

Professorships: 4
Personnel: 308
- Doctors (of Medicine): 38
- Scientists: 10 (thereof funded externally: 6)
- Graduate students: 44

Clinical focus areas
- Oncological surgery
- Surgery of the gastrointestinal tract
- Metabolic and bariatric surgery
- Endocrinological surgery
- Minimally invasive surgery
- Transplantation
- Outpatient surgery
- Surgical emergency

Research

Clinical research at the Department of Surgery mainly consists of the clinical cancer registry, randomized trials of gastrointestinal tumors and evaluation of nationwide hospital discharge data. The translational research is focused on colorectal cancers/inflammatory bowel diseases and pancreatic cancer. Groups of investigators focusing on tumor micromilieu and sepsis are connecting the main research topics.

Evaluation of prognosis of gastrointestinal tumors

PI: Prof. Dr. R. Grützmann, Prof. Dr. S. Merkel
Since 1978, a clinical cancer registry has been prospectively maintained for organ specific tumor documentation. At present, more than 30,000 patients are registered. Main foci are on colorectal cancer with over 13,000 and pancreatic cancer with over 2,700 documented cases. Patients are followed for life with only 1% of patients lost to follow-up. The scientific evaluation of this data focuses on health services research, quality management, the improvement of tumor classification, the identification of prognostic factors, the definition of quality indicators, and quality of life research. The documentation of specific diagnostics and multimodal treatment strategies results from an interdisciplinary cooperation of numerous departments and institutes at the Faculty of Medicine.

Randomized trials for gastrointestinal tumors

PI: Prof. Dr. R. Grützmann, Dr. H. Golcher
The Department of Surgery respectively the interdisciplinary Colorectal Cancer Center/ Modul Pancreas Cancer took part in different multicenter trials about gastrointestinal tumors, inter alia " Pancreatoduodenectomy with or without prophylactic Ligamentum teres hepatis wrap around the gastroduodenal artery stump for prevention of pancreatectomy hemorrhage" or "International Prospective Observational Cohort Study for Optimal Bowel Resection Extent and Central Radicality for Colon Cancer (T-REX)". Patients were screened during the interdisciplinary tumor board for gastrointestinal tumors, assigned to the studies and further attended. The surgical second opinion ("panel of surgeons") for the CONKO-007-trial (patients with non resectable pancreatic carcinoma) is organized by the study team, too, and evaluation takes place in the daily tumor conference.

Outcomes research of complex surgery with hospital discharge data

PI: Dr. C. Krautz
A variety of surgical procedures in general surgery are associated with varying perioperative outcomes due to their complexity. Analyses of nationwide hospital discharge data provide the possibility to examine the underlying causes. Currently, we are assessing the effects of volume-based referral on perioperative outcomes in complex surgery in order to give recommendations for the future hospital market structure in Germany.

The interferon-γ pathway in the immune escape of colorectal cancer

PI: PD Dr. N. Britzen-Laurent, Prof. Dr. Dr. M. Stürzl
The presence of an interferon-γ-dominated Th1 immune response in colorectal cancer (CRC) has been associated with improved clinical outcome. Several CRC cell lines are resistant to IFN-γ action. In these cell lines, the loss of IFN-γ-responsiveness correlated with the down-regulation or with the presence of a mis-glycosylated form of the IFN-γ receptor alpha chain (IFNγ Rα). A knock-out of the IFN-γ receptor in intestinal epithelial cells of mice fostered tumor growth. In accord with this decreased expression of IFN γ Rα in human CRC correlated with reduced cancer-related survival and increased metastasis. Our data suggest that the loss of IFN-γ responsiveness is a common escape mechanism of CRC tumor cells against the antitumorigenic effects of IFN-γ.
Funding: IZKF, DFG

Angiocrine mechanisms of tumor suppression in colorectal cancer

PI: PD Dr. E. Naschberger, Prof. Dr. Dr. M. Stürzl
Investigation of cellular memory processes in human tumor endothelial cells allowed the identification of SPARCL1 as angiocrine mediator in CRC. SPARCL1 is specifically expressed and released by tumor vessel cells in tumors with a Th1 tumor microenvironment (TME). It inhibits proliferation and migration of CRC tumor vessel and tumor cells. In accord with this SPARCL1 expression in human CRC tissues and mouse models is associated with reduced angiogenic activity and improved prognosis of the patients. SPARCL1 is a vessel-derived tumor suppressor in CRC actively contributing to the favorable prognosis associated with a Th1-TME.
Funding: IZKF, DFG

Genome editing of pancreatic tumor models

PI: Prof. Dr. C. Pilarsky
Pancreatic cancer is the fourth most frequent cause of cancer in the western world with a five year survival rate of 8%. This is caused by chemoresistance of the tumor. In this project we are trying to understand more precisely which mechanisms influence such a chemoresistance.

Based on the well-known changes in the tumor genome, we are targeting specific genes, especially gene involved in DNA repair, with CRISPR/Cas9 technology and are testing whether our tumor models become more sensitive to the application of chemotherapeutic agents. This allows an adaptation of chemotherapeutic regimens to the mutation pattern of the individual tumor within the framework of modern precision medicine.

Organoid models in pancreatic cancer

PI: Prof. Dr. C. Pilarsky

In this project we will test the influence of the culture conditions on the chemosensitivity of pancreatic carcinomas. For this purpose, pancreas tumor cells are grown as a special tissue culture, the organoid culture, and treated with chemotherapeutic agents. This allows us to examine how the individual models can be treated in a tissue. This allows a better understanding of the necessary dosage of chemotherapeutic agents and a possible better preclinical testing of new chemotherapies.

Immunepathophysiology of acute (sepsis) and chronic (colitis) inflammation

PI: PD Dr. G. Weber

The immune system consists of innate and adaptive components that operate in close proximity to protect the host against infections. During infection the host can be at risk due to imbalanced immune responses. A major therapeutic goal, then, is to establish an equilibrium between controlling infection and controlling inflammation. One promising strategy is to harness the endogenous immune system to augment processes that are beneficial and curb processes that cause harm. Such strategies, however, require understanding of the diseases pathophysiology. Currently, we are focusing on the role of interleukin-3 as central regulator for acute and chronic inflammation.

Immunephenotyping and liquid biopsy analysis of gastrointestinal tumors

PI: PD Dr. G. Weber

Successful treatment of cancer disease is based on the in-depth understanding of the involved mechanisms leading to cancer development and progression. Thus, precise knowledge of the immunogenicity of the individual tumor as well as early and precise diagnosis is required. Within this project, we will develop non-invasive alternative techniques – so called liquid biopsies - to diagnose cancer disease, predict and monitor disease progression, and finally to improve patient selection for established treatment strategies. In addition, we are immunologically phenotyping the individual cancer disease to evaluate immune therapeutic strategies.

Teaching

The Department of Surgery is offering courses for students of Medicine, Dentistry, Molecular Medicine, and biology. The Dr. House colloquium is an interdisciplinary lecture with the internal medicine. By the implementation of a surgical skills lab, surgical residents as well as medical students benefit from learning different surgical approaches and may acquire basic surgical skills using modern laparoscopic simulators.
MD and PhD theses are supervised.

Selected publications

Lehmann B, Biburger M, Brückner C, Ipsen-Escobedo A, Gordan S, Lehmann C, Voehringer D, Winkler T, Schaft N, Dudziak D, Sirbu H, Weber GF, Nimmerjahn F. Tumor location determines tissue-specific recruitment of tumor-associated macrophages and antibody-dependent immunotherapy response. Sci Immunol. 2017 Jan 6;2(7). pii: eaah6413

Naschberger E, Geißdörfer W, Bogdan C, Tripal P, Kremmer E, Stürzl M, Britzen-Laurent N. Processing and secretion of guanylate binding protein-1 depend on inflammatory caspase activity. J Cell Mol Med. 2017 Sep;21(9):1954-1966

Liu B, Yang H, Taher L, Denz A, Grützmann R, Pilarsky C, Weber GF. Identification of Prognostic Biomarkers by Combined mRNA and miRNA Expression Microarray Analysis in Pancreatic Cancer. Transl Oncol. 2018 11:700-714

Krautz C, Nimptsch U, Weber GF, Mansky T, Grützmann R. Effect of Hospital Volume on In-hospital Morbidity and Mortality Following Pancreatic Surgery in Germany. Ann Surg. 2018 267:411-417

Merkel S, Schellerer VS, Wein A, Semrau S, Geppert C, Göhl J, Hohenberger W, Weber K, Grützmann R. The influence of tumour site on prognosis in metastatic colorectal carcinomas with primary tumour resection. Int J Colorectal Dis. 2018 33:1215-1223

Unterer B, Wiesmann V, Gunasekaran M, Sticht H, Tenkerian C, Behrens J, Leone M, Engel FB, Britzen-Laurent N, Naschberger E, Wittenberg T, Stürzl M. IFN-γ-response mediator GBP-1 represses human cell proliferation by inhibiting the Hippo signaling transcription factor TEAD. Biochem J. 2018 475:2955-2967

International cooperations

Prof. M. Gack, Department of Microbiology, The University of Chicago, Chicago: USA

Prof. R.D. Kamm, Massachusetts Institutes of Technology - MIT, Cambridge: USA

Prof. M. Kelly/Prof. D.C. Winter, Department of Surgery, St. Vincent's University Hospital Dublin, Dublin: Ireland

Prof. F.K. Swirski, Center for Systems Biology, Massachusetts General Hospital, Harvard Medical School, Boston: USA

Prof. D. Tuveson, Cold Spring Harbor Laboratory, Cold Spring Harbor: USA