UNIVERSITY HOSPITAL

Department of Urology and Paediatric Urology

Chair of Urology

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Structure of the Department

Professorships: 2
Personnel: 49

- Doctors (of Medicine): 19
- Scientists: 4 (thereof funded externally: 0)
- Graduate students: 1 (Dr. rer. nat.), 14 (Dr. med.)

Clinical focus of care

- University outpatient clinic of Urology and Paediatric Urology at the Universitätsklinikum Erlangen (DIN EN ISO 9001-certified)
- Minimal invasive urology including robotics (DIN EN ISO 9001-certified)
- Kidney transplantation unit; Certified Transplant Center Erlangen-Nürnberg at the Universitätsklinikum Erlangen (DIN EN ISO 9001-certified)
- Kidney transplantation unit focused on children; Certified Paediatric Kidney Center (DIN EN ISO 9001-certified)
- Ambulant Uro-Oncologic Therapy Unit Erlangen (AURONTE)
- Adult's urologic ward, therapy center for private insurance patients at the Malteser Waldkrankenhaus St. Marien
- Trial documentation center at the Malteser Waldkrankenhaus St. Marien
- Certified Urologic Oncology Center (certified by the German Cancer Society)
- Part of the Oncolocy Center (certified by the German Cancer Society) at the Universitätsklinikum Erlangen
- Part of the Comprehensive Cancer Center (CCC) Erlangen-EMN
- Certified Continence and Pelvic Floor Center
- Training Program Center and Supervisor in Sexual Medicine (TPSM)
- EBPU board-certified Paediatric Urology training progamme

Research

The research topics in the Department of Urology and Pediatric Urology cover the areas of basic as well as translational urologic research, also with a particular focus on high-quality statistical assessment. Substantial parts of our research rely on a well-maintained, high quality repository of tissue sample and other biosamples that allows the active participation even in European, multicenter, EU-funded studies in patients with urologic tumors.

Continuous extension of an annotated tumor tissue repository containing urologic tumors
Project manager: Prof. Dr. B. Wullich
New insights into the occurrence of malignant tumors and the identification of new and reliable prognostic biomarkers depend upon the molecular characterization of rather large cohorts of tissue samples since the currently used morphologic criteria only poorly reflect the progression behavior of one patient's specific tumor. To facilitate this research, the collection of tissue samples originating from tumors and corresponding non-tumor tissue as well as blood, serum, and various body fluids, e.g. urine, is of vital importance for translational research projects. A high quality tissue sample repository demands a standardized logistics for the sample transportation from the operating theater to the Institute of Pathology, as well as the careful and standardized preparation of the sample carried out by an experienced pathologist. In close cooperation with the Institute of Pathology, a repository of urologic tissue samples has been established in which tissue samples of all surgically treated malignant urologic tumors are introduced. This tissue repository is part of the CCC biobank. For the application of the required Standard Operating Procedures (SOP), we have established a close cooperation with the German Prostate Carcinoma Consortium (DPKK) e.V. and could furthermore introduce a web-based tissue database system that relies on the established clinical information system within the Department of Urology. All incorporated procedures are consistent with the legal, ethical, technical, and organizational regulations of tissue repositories and databases (patients' informed consent, data security, SOPs, and quality management). In order to meet future challenges of biobanking, we actively support the establishment of a general biobank infrastructure, Central Biobank Erlangen (CeBE). By introducing a broad consent document in conjunction with a digital consent management system, hosted by the Institute for Medical Informatics (MIK), a listing in the German Biobank Registry and a membership in the German Biobank Node, the CeBE will be established as a recognized biobank.

Biomarker patterns from the plasma of prostate cancer patients
Project manager: Prof. Dr. B. Wullich
As co-applicant of the BMBF-Project „Diagnostik mit Biomarker Mustern aus Plasma extra-zellulären Vesikeln (pEV) mit Methoden der künstlichen Intelligenz (KI)" (KI-VesD; PI Prof. A. Baur), we contribute with our clinical study center to the analysis of plasma samples of prostate cancer patients from our Department of Urology and Paediatric Urology. Extra-cellular vesicles that may originate as well from the tumor as from the host immune system, transport nucleic acids and proteins, that are specific for the tumor-host-tumor response. The aim of this project is to detect protein patterns by artificial intelligence techniques (Prof. J. Vera) that can be used in diagnostics and possibly also in prediction of therapy response.

Systemic tumor therapy, clinical trials
Project manager: Prof. Dr. P. J. Goebell
The medical care and treatment of patients with uro-oncologic diseases represents an integral part of our urologic expertise. Systemic therapy forms, besides the provision of surgical treatment, are among the fundamental sources of competence in urology. For this purpose, the outpatient center for uro-oncologic diseases (AURONTE) was founded together with the Department of Medicine 5 to draw therapeutic decisions based on a common interdisciplinary conference.
Thus, it can be assured that all currently activated and planned clinical trials are open to all common patients. Currently open clinical trials mainly focus on new therapeutic options for patients with bladder or prostate cancer. An overview of all currently active clinical trials can be found at: http://www.urologie.uk-erlangen.de/universitaetsmedizin/studienzentrale/aktuelle-studien/

- Sunniforcast: papillary and chromophob renal cell carcinoma: Nivolumab + Ipilimumab vs. Sunitinib
- Cabopoint (F-FR-60000-023): Renal cell carcinoma: Cabozantinib after immunotherapy
- CARAT: Epidemiologisches Register zur Darstellung der Behandlungsrealität und der Therapiemodalitäten beim behandlungsbedürftigen metastasierten oder lokal fortgeschrittenen Nierenzellkarzinom
- PCO: Prostate cancer: all patients with prostatectomy + active surveillance
- RhoVac-002: Prostate cancer: biochemical relapse without metastases after local curative therapy, rPE or RT.
- Talapro-2: Metastasized castration resistent prostate carcinoma (mCRPC): Talazoparib and Enzalutamid.
- Keynote 010: Metastasized castration resistent prostate carcinoma (mCRPC): Pembrolizumab + Olaparib after Docetaxel and AR-targeted therapy
- ARASENS: Metastatic Hormone Sensitive prostate Cancer (mHSPC): A randomized, double-blind, placebo-controlled Phase III study of ODM-201 vs. placebo in addition to standard androgen deprivation therapy and docetaxel.
- Keynote 866: Muscle-invasive bladder cancer patients: perioperative Pembrolizumab + neoadjuvant chemotherapy vs. Placebo + neoadjuvant chemotherapy
- CA 045-009: Muscle-invasive bladder cancer

patients: neoadjuvant and adjuvant Nivolumab + NKTR-214 vs. Nivolumab alone vs. Standard of care
- Niagara: Muscle-invasive bladder cancer patients: Durvalumab + Gemcitabine/Cisplatin neoadjuvant followed by Darvalumab adjuvant
- Titan: Muscle-invasive bladder cancer patients: after platinum-based chemotherapy Nivolumab with possible Ipilimumab Boost.
- Thor: Muscle-invasive bladder cancer patients: after platinum-based chemotherapy Erdafitinib vs. Vinflunin or Docetaxel or Pembrolizumab at detection of a FGFR gene mutation.
- Keynote 361: A Phase III Randomized, Controlled Clinical Trial of Pembrolizumab with or without Platinum-Based Combination Chemotherapy vs. Chemotherapy in Subjects with Advanced or Metastatic Urothelial Carcinoma
- STRONG: An Open-Label, Multi-Centre, Safety Study of Fixed-Dose Durvalumab + Tremelimumab Combination Therapy or Durvalumab Monotherapy in Advanced Solid Malignancies
- UroFollow: Marker-based follow-up care of patients with non muscle-invasive low//intermediate-risk bladder cancer

Evidence-based medicine
Project manager: PD Dr. F. Kunath
Evidence-based medicine is the focus of the research projects. It is the aim to use the current best evidence from clinical research to the care of individual patients. There is a close cooperation with the UroEvidence Group of the German Society of Urology and Cochrane Urology of the Cochrane Collaboration to develop high-quality systematic reviews and German language summaries.

Tumor genetic research with focus on identification of biomarkers
Project manager: PD Dr. S. Wach
The identification and characterization of specific biological properties of the prostate carcinoma as well as other malignant tumors, like kidney carcinoma, is the main focus of the research projects. By extensive research using primary tissue samples retrieved from the CCC Biobank, we were able to identify a collection of proteins and RNAs that have the potential for being valuable clinical biomarkers. This knowledge is now being transferred to an experimental diagnostic setting. This will be combined with the advantages of non-invasive biomaterial sampling by investigating protein- and RNA-based biomarkers in blood serum. Besides open surgery, all prostate cancer patients that are eligible for a curative prostatectomy are being offered to be treated by robot-assisted surgery using the da Vinci® surgical system. Here, patient's treatment is supported and supplemented by experimental therapy monitoring. Tumor-associated biomarkers are assessed prior to surgery as well as during the regular follow-up examinations in blood serum. A few selected biomarkers were already successfully validated as targets in experimental therapeutic trials in animal models.

Multifactorial models in uro-tumorpathology
Project manager: Prof. Dr. H. Taubert
In cooperation with the Institute of Pathology and the Tumor Center at the FAU, we collect and assign different clinico-pathological (e.g. TNM-stage, age, gender), tumor biological (e.g. hypoxia, cell lineage) and molecular parameters on RNA and protein level (e.g. stem cell-associated factors, new biomarkers) and analyze them in multifactorial models for their relevance in tumorigenesis, disease progress and survival of the urological tumor patients. We aim at supporting our physicians in identifying urological tumor patients and finding the right therapy stratification and therapy monitoring and in further expanding the basic, molecular knowledge for urological cancers.

Micro-RNA associated regulation of gene expressions in urologic cancers
Project manager: Prof. Dr. H. Taubert
In our ongoing DFG-Project „MicroRNA mediated regulation of key components of the Mediator Complex (MED) and its functional role in CRPC" (TA 145/17-1) we analyze, which microRNAs affect the transcriptional regulation through the Mediator Complex (MED) and which functional role these microRNAs play in castration resistant prostate cancer (CRPC). This is a DFG-cooperation project with partners from the University of Leipzig (Prof. A. Aigner) and the University of Innsbruck (Prof. Z. Culig). In *in vitro* (cell lines) and *in vivo* experiments (mouse and PDX-models) the identified microRNAs will be studied for their effect on tumor(cell)growth and the sensitization for anti-androgen therapies. Furthermore, in cooperation with the Institute of Pathology Erlangen (Prof. A. Hartmann/Dr. M. Eckstein) at applying immunohistochemistry, the clinical relevance of the microRNAs and the components of the MED complex will be determined for prognosis of prostate cancer patients.

Teaching

Medical students are taught in the lecture series of emergency medicine and in general and specialized urological lectures. Students also conduct a block practical in the Department of Urology or one of the associated teaching hospitals. The Department also allows additional education for achievement of the title medical specialist for urology. Additionally, specialized training courses are offered for Systemic Drug Tumor Therapy and the qualification 'Urologic Diagnostic Radiology'. For acquisition and improvement of specialized surgical techniques, the Department of Urology uses patient simulators. These include models for practicing sterile placement of catheters or laparoscopic methods including a simulator at the da Vinci® robotic surgery system for minimally invasive surgery. In addition, practical trainings for basic and advanced techniques in molecular urology are offered.

Selected Publications

Wach S, Taubert H, Cronauer M. Role of androgen receptor splice variants, their clinical relevance and treatment options. World J Urol. 2020 Mar;38(3):647-656.

König P, Eckstein M, Jung R, Abdulrahman A, Guzman J, Weigelt K, Serrero G, Hayashi J, Geppert C, Stöhr R, Hartmann A, Wullich B, Wach S, Taubert H, Lieb V. Expression of AR-V7 (Androgen Receptor Variant 7) Protein in Granular Cytoplasmic Structures Is an Independent Prognostic Factor in Prostate Cancer Patients. Cancers. 2020 Sep 16;12(9):2639.

Wach S, Brandl M, Borchardt H, Weigelt K, Lukat S, Nolte E, Al-Janabi O, Hart M, Graesser F, Giedl J, Jung R, Stoehr R, Hartmann A, Lieb V, Hoebel S, Peters A, Staeubert C, Wullich B, Taubert H, Aigner A. Exploring the MIR143-UPAR Axis for the Inhibition of Human Prostate Cancer Cells In Vitro and In Vivo
Mol. Ther. Nucl. Acids. 2019 Jun 7;16: 272-283

Goebell PJ, Ivanyi P, Bedke J, Bergmann L, Berthold D, Boegemann M, Busch J, Doehn C, Krege S, Retz M, Amsberg GV, Grimm MO, Gruenwald V. Consensus paper: current state of first- and second-line therapy in advanced clear-cell renal cell carcinoma. Future Oncol. 2020 Oct;16(29):2307-2328.

Kahlmeyer A, Stöhr CG, Hartmann A, Goebell PJ, Wullich B, Wach S, Taubert H, Erlmeier F. Expression of PD-1 and CTLA-4 Are Negative Prognostic Markers in Renal Cell Carcinoma. J Clin Med. 2019 May 24;8(5):743.

Sathianathen NJ, Oestreich MC, Brown SJ, Gupta S, Konety BR, Dahm P, Kunath F. Abiraterone acetate in combination with androgen deprivation therapy compared to androgen deprivation therapy only for metastatic hormone-sensitive prostate cancer. Cochrane Database Syst Rev. 2020 Dec 12;12:CD013245.

Kunath F, Jensen K, Pinart M, Kahlmeyer A, Schmidt S, Price CL, Lieb V, Dahm P. Early versus deferred standard androgen suppression therapy for advanced hormone-sensitive prostate cancer. Cochrane Database Syst Rev. 2019 Jun 11;6(6):CD003506.

Sikic D, Eckstein M, Wirtz RM, Jarczyk J, Worst TS, Porubsky S, Keck B, Kunath F, Weyerer V, Breyer J, Otto W, Rinaldetti S, Bolenz C, Hartmann A, Wullich B, Erben P. FOXA1 Gene Expression for Defining Molecular Subtypes of Muscle-Invasive Bladder Cancer after Radical Cystectomy. J Clin Med. 2020 Apr 2;9(4):994.

International Cooperations
Prof. Dr. Henrik Grönberg, Department of Medical Epidemiology and Biostatistics, Karolinska Institute, Stockholm, Sweden,

Prof. Dr. Lars Dyrskjot, Department of Molecular Medicine, Århus University Hospital, Århus, Denmark,

Dr. Boje Nielsen, Molecular Histology, Bioneer A/S, Hørsholm, Denmark,

Prof. Dr. Zoran Culig, Universitätsklinik für Urologie, Medizinische Universität Innsbruck, Innsbruck, Austria