

# Department of Urology and Pediatric Urology

## Chair of Urology

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### Director

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### Research focus

- Continuous extension of an annotated tumor tissue repository containing urologic tumors
- Systemic tumor therapy, clinical trials
- Tumor genetic research with focus on identification of biomarkers
- Biomarker-supported MRI-TRUS-fusion guided biopsies for the diagnosis of prostate cancer
- Multifactorial models in uro-tumorpathology

### Structure of the Department

Professorships: 2

Personnel: 46

- Doctors (of Medicine): 20
- Scientist: 1 (thereof funded externally: 0)
- Graduate students: 12

### Clinical focus areas

- Urologic polyclinic and children's urology ward
- Minimal invasive urology including robotics
- Kidney transplantation unit
- Kidney transplantation unit focused on children
- Ambulant uro-oncologic therapy center (AURONTE)
- Certified center for prostate cancer with kidney- and bladder cancer
- Certified continence and pelvic floor center
- Adult's urologic ward, therapy center for private insurance patients within Malteser Waldkrankenhaus St. Marien
- Trial documentation center within Malteser Waldkrankenhaus St. Marien

### Research

The research topics in the Department of Urology and Pediatric Urology cover the areas of basic as well as translational urologic research,

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 biomaterials 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

PI: 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. 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 Comprehensive Cancer Center (CCC) biobank. For the application of the required Standard Operating Procedures (SOP), we have established a close cooperation with the German Prostate Carcinoma Consortium 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 and Pediatric 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).

### Systemic tumor therapy, clinical trials

PI: PD 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 on the website of our Department.

### Tumor genetic research with focus on identification of biomarkers

PI: 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.

### Biomarker-supported MRI-TRUS-fusion guided biopsies for the diagnosis of prostate cancer

PI: PD Dr. B. Keck, Dr. A. Kahlmeyer

The MRI-TRUS-fusion guided biopsy of the prostate is the advanced version of the conventional, ultrasound guided biopsy of the prostate. It combines the accuracy of multiparametric MRI imaging with the standardized and easy to perform TRUS-guided biopsy of the prostate which can be further extended by methods, such as elastography or Doppler ultrasound. A highly standardized diagnostic evaluation of the MRI images according to the PIRADS classification system is the basis for the identification of lesions suspicious for harboring prostate cancer. An interdisciplinary cooperation with the Institute of Radiology provides the basis for the successful application of this diagnostic method. Current clinical trials have shown that the application of MRI-TRUS-fusion guided biopsies is able to reduce the diagnosis rate of well-differ-

entiated, clinically insignificant prostate cancers while highly aggressive prostate cancers can be diagnosed with improved sensitivity. Nevertheless, the clinical interpretation of PIRADS class 3 lesions still poses a great challenge because these are not unanimously regarded as suspicious for a tumor. Here, the diagnostic procedure is supported by an experimental diagnostic method. Tumor-specific RNA-based biomarkers are assessed in blood serum. By combining advanced MRI-imaging and biomarker analysis, it could be possible to aid in the clinical decision if patients should undergo prostate biopsy or clinical surveillance.

### **Multifactorial models in uro-tumorpathology**

PI: 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.

### **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 and Pediatric Urology or one of the associated teaching hospitals.

The Department also allows additional education for achievement of the specialization in 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 and Pediatric Urology uses patient simulators. These include models for practicing sterile placement of catheters or laparoscopic methods including a simulator at the da Vinci®-operation system for minimally invasive surgery. In addition, practical trainings for basic and advanced techniques in molecular urology are offered.

We supervise Bachelor's and Master's theses as well as MD and PhD theses.

### **Selected publications**

Sikic D, Keck B, Wach S, Taubert H, Wullich B, Goebell PJ, Kahlmeyer A, Olbert P, Isfort P, Nimphius W, Hartmann A, Giedl J, Bridge Consortium. Immunohistochemical subtyping using CK20 and CK5 can identify urothelial carcinomas of the upper urinary tract with a poor prognosis. *PLoS One*. 2017 Jun 20;12(6):e0179602

Bellut J, Bertz S, Nolte E, Stohr C, Polifka I, Lieb V, Herrmann E, Jung R, Hartmann A, Wullich B, Taubert H, Wach S. Differential prognostic value of MYC immunohistochemistry in subtypes of papillary renal cell carcinoma. *Sci Rep*. 2017 Nov 27;7(1):16424

Kunath F, Schmidt S, Krabbe LM, Miernik A, Dahm P, Cleves A, Walther M, Kroeger N. Partial nephrectomy versus radical nephrectomy for clinical localised renal masses. *Cochrane Database Syst Rev*. 2017 May 9;5:CD012045

Greither T, Fischer K, Theil G, Marcou M, Holzhausen HJ, Weigelt K, Serrero G, Hicks D, Yue BB, Fornara P, Wullich B, Taubert H, Wach S, Lieb V. Expression of GP88 (progranulin) in serum of prostate cancer patients is associated with Gleason scores and overall survival. *Cancer Manag Res*. 2018 Oct 5;10:4173-4180

Narayan V, Kahlmeyer A, Dahm P, Skoetz N, Risk MC, Bongiorno C, Patel N, Hwang EC, Jung JH, Gartlehner G, Kunath F. Pembrolizumab monotherapy versus chemotherapy for treatment of advanced urothelial carcinoma with disease progression during or following platinum-containing chemotherapy. *A Cochrane Rapid Review*. *Cochrane Database Syst Rev*. 2018 Jul 23;7:CD012838

Goebell PJ, Staehler M, Muller L, Nusch A, Scheffler M, Sauer A, von Verschuer U, Tech S, Kruggel L, Janicke M, Marschner N, RCC Registry Grp Tumour Registry. Changes in Treatment Reality and Survival of Patients With Advanced Clear Cell Renal Cell Carcinoma - Analyses From the German Clinical RCC-Registry. *Clin Genitourin Cancer*. 2018 Dec;16(6):e1101-e1115

### **International cooperations**

Prof. Dr. H. Grönberg, Department of Medical Epidemiology and Biostatistics, Karolinska Institutet, Stockholm: Sweden

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

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

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