Institute of Pathology
Chair of General Pathology and Pathological Anatomy

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Research Focus
- Diagnostic molecular pathology
- Experimental tumor pathology – gastrointestinal tumors
- Breast and gynecological tumors
- Tumors of the head and neck region
- Clinical and predictive molecular pathology of urogenital tumors
- Pathology of immune and inflammatory reactions in carcinogenesis

Structure of the Chair
Professorships: 3
Personnel: 45
- Doctors (of Medicine): 14
- Scientists: 4 (thereof funded externally: 1)

Clinical focus areas
Histopathology with specific expertise in
- Breast pathology
- Gynecological pathology
- Urogenital pathology
- Head and neck pathology
- Soft tissue pathology
- Molecular pathology

Research
The main research focus of the Institute of Pathology is the identification of molecular alterations in different malignant tumors. In different research groups gastrointestinal tumors, breast cancer, gynecological tumors, tumors of the head and neck region, urological tumors and sarcomas are investigated for both, diagnostic markers and new therapeutic targets. The aim is the integration of the identified molecular alterations into diagnostic molecular pathology. An additional focus is the characterization of immune and inflammatory cell infiltration in tumors and the importance of this immune response for tumor development and response prediction to immunotherapy.

Diagnostic molecular pathology
PI: Prof. Dr. F. Haller, Dr. E.A. Moskalev
The aim of the group is the development and functional validation of novel molecular markers with diagnostic, prognostic, or predictive impact in solid tumors. Next-generation sequencing is a modern technology that has been successfully established in the group during the last five years and enabled the identification of novel key molecular events in different rare soft tissue neoplasms. Whole genome sequencing identified oncogenic mutations of the CTNNB1 gene in sinonasal hemangiopericytoma as well as aberrant hypermethylation of the SDHC gene locus in pediatric gastrointestinal stromal tumors as probable tumor-initiating events on a genetic and epigenetic level, respectively. Another focus is the massive parallel sequencing of multi-gene panels in lung cancer and cancer of the urogenital tract and head and neck cancer to correlate the presence of mutations among distinct genetic pathways with specific histomorphological subtypes, clinical behavior, and therapy response. The functional characterization of novel genetic or epigenetic aberrations in cell culture systems is another aim to develop the basis for future therapeutic options. In the last year, the interdisciplinary molecular tumor board has been successfully installed which aims to detect genetic aberrations in patients with advanced cancer that can be used as therapeutic targets.

Experimental tumor pathology – gastrointestinal tumors
PI: Prof. Dr. R. Schneider-Stock, Dr. K. Erlenbach-Wünsch, Dr. M. Eckstein, Dr. C. Geppert, Prof. Dr. A. Hartmann, Prof. Dr. A. Agaimy
The main focus of our group is the molecular and biochemical characterization of genetic and epigenetic alterations in tumors and preneoplasias of the gastrointestinal tract. Research projects on initiation and progression of colorectal tumors and their molecular subtypes are in focus. We aim at identifying novel valid biomarkers for tumor transformation in colorectal cancerogenesis that could be of potential therapeutic interest. We are interested in tumor invasion front and thus in regulation of EMT and stemness to drive invasion and metastasis. A broad spectrum of 2D and 3D models, co-culture models, and CRISPR-knock out cell lines is established. We are especially interested in three proteins: DAPK-kinase, ATF2, and EZH2, that have dual function in tumors and can act as tumor suppressor or oncogene. To investigate these genes, novel experimental conditional ko mice were designed. Since many years we have been studying successfully the anti-cancer effects of plant-derived drugs for colorectal tumor cells.

Breast and gynecological tumors
PI: Prof. Dr. A. Hartmann, Prof. Dr. A. Agaimy, PD Dr. D. Wächter, Dr. J. Strehi, Dr. K. Brunner, Dr. R. Erber
This group focuses in cooperation with the Department of Obstetrics and Gynecology on the discovery of genetic and epigenetic changes in breast cancer and ovarian carcinomas. The objective of our research is to discover molecular prognostic markers and to identify molecular markers that could be used in the clinical-pathological differential diagnosis and therapeutic stratification of breast and ovarian cancer.

Tumors of the head and neck region
PI: Prof. Dr. A. Agaimy, Prof. Dr. A. Hartmann, Prof. Dr. F. Haller, Dr. K. Brunner, Prof. Dr. R. Rieker
We investigate the molecular changes in tumors of the head and neck region in cooperation with the Departments of Otorhinolaryngology – Head and Neck Surgery and of Oral and Cranio-Maxillofacial Surgery. This research project has two objectives: One is to compile a molecular-pathological and histopathological classification of salivary gland tumors with low and high risk of relapse and progression, the second is to...
identify early molecular markers to identify dysplastic changes as tumor precursors in the mucosa of the head and neck region.

Clinical and predictive molecular pathology of urogenital carcinomas
Pt: Prof. Dr. A. Hartmann, PD Dr. R. Stöhr, Dr. C. Stöhr, Dr. J. Giedl, Dr. S. Bertz, Dr. M. Eckstein, I. Polifka

The group investigates the basic molecular principles of the development, progression and subtyping of urothelial carcinoma of the urinary bladder, prostate cancer, squamous cell carcinoma of the penis and renal cell carcinoma. There is a close cooperation with the Department of Urology, the Institute of Clinical and Molecular Virology and with numerous national and international cooperation partners. The objective is the identification of genomic and epigenetic changes in urothelial carcinomas of the urinary bladder and kidney tumors to identify new markers for early diagnosis and new therapeutic target molecules. In addition, gene expression analyses are used to establish a risk stratification of the tumors that should support the finding of the ideal treatment option for a patient in daily clinical routine. Another focus of the groups' work is the molecular investigation of patients with early-onset disease. These analyses should clarify if tumors in young patients have distinct molecular developmental pathways as compared with tumors from aged patients. Moreover, molecular investigation of tumors from patients with early-onset disease could allow the identification of predisposing factors and disease-initiating events helping to define individuals with high disease risk.

Pathology of Immune and Inflammatory Reactions in Tumor Development
Pt: PD Dr. M. Büttner-Herold, Prof. Dr. A. Hartmann, Dr. C. Geppert

This project examines the interaction between infection and B-cell differentiation in primary and persistent EBV infection and the mechanisms and interactions between the immune system and tumor cells in different tumor types (colorectal cancer, prostate carcinoma, renal cell carcinoma, Hodgkin lymphoma). The objective is the identification of mechanisms through which the tumor cells could escape the immune response of the organism and the characterization of the intratumoral inflammatory cell infiltrate for prognosis and therapy response prediction.

Teaching

The Institute of Pathology is involved in the compulsory and elective curricular teaching of human and dental medicine and of the degree programs Molecular Medicine and Medical Process Management. Particularly noteworthy is the interdisciplinary teaching in the context of cross-cutting subjects Q5 and Q6 together with the Departments of Obstetrics and Gynecology, Medicine 1, Urology, Surgery, Nuclear Medicine and the Institute of Radiology. Bachelor’s and Master’s theses as well as MD and PhD theses are looked after.

Selected Publications


International Cooperation

Prof. H. Gali-Muhetas, Department of Biology, American University of Beirut, Beirut: Lebanon

Prof. F. Amm, Department of Pathology and Genetics, University of Gothenburg, Gothenburg: Sweden

Prof. M. Galovas Jasulionis, Ontogeny and Epigenetic Laboratory, Universidade Federal de São Paulo (UNIFESP), São Paulo: Brazil

Prof. T. Dale, Cardiff Cancer Stem Cell Research Institute, Cardiff University, Cardiff: UK

Prof. F. Real, Spanish National Cancer Research Centre, Madrid: Spain

Squamous cell carcinoma of the penis (usual type) TERT promoter mutations are significantly associated with HPV negativity and no expression of p16. Therefore, TERT promoter mutations might act as a new molecular marker for biologically aggressive penis carcinomas.