

# Department of Oral and Cranio-Maxillofacial Surgery

## Chair of Dental, Oral, and Maxillofacial Medicine – especially Oral and Maxillofacial Surgery

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### Director

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### Research focus

- Tumor research
- Regeneration processes in inflamed and weakly replaced tissue
- Oral medicine
- Biomedical technology

### Structure of the Department

Professorships: 2  
Personnel: 100  
• Doctors (of Medicine): 18  
• Scientist: 1  
• Graduate students: 20

### Clinical focus areas

- Tumor surgery and reconstructive surgery of the oral cavity and the face
- Traumatology of the facial skull
- Surgery of facial skull deformities and orthognathic surgery
- TMJ surgery
- Dentoalveolar surgery

### Research

The scientific focus of the Department of Oral and Cranio-Maxillofacial Surgery relies on tumor research and the further development of reconstructive surgery. Oral manifestations as expressions of general diseases are investigated as a bridge between Dentistry and Medicine. Another research focus is dedicated to digitalization projects in research and teaching. In addition, biomedical research is an established scientific aspect of the Department.

### Tumor research

- Reconstruction and regeneration of weak tissues

In 3-20% of cases, postoperative thromboembolic complications and wound healing disorders

occur during oral and maxillofacial reconstruction in pre-irradiated tissue using microvascular anastomosed grafts. Pathomorphologically, media fibrosis and endothelial damage as well as overexpression of proliferative cytokines are found in the transition area between graft and storage. Since current fibrosis models describe this as a misguided recourse to embryonic tissue regeneration, this research focus consists in the analysis of highly conserved transcription factors of fibrogenesis in pre-irradiated tissue.

#### • Tumor immunology

Carcinogenesis and tumor progression can be understood as immunologically mediated processes in the sense of tolerance induction towards the tumor. We were able to show that there is a correlation between increased tumor malignancy and increased M2 macrophage polarization. In addition, regulatory mechanisms of macrophage polarization are currently analyzed. An additional focus lies on the investigation of the prognostic and pathophysiological significance of checkpoint expression; this is investigated within the framework of a DFG-funded project. Here, an increased expression of the immune checkpoints PD-L1 and PD-L2 in oral cavity carcinomas as well as an association between tumor progression and checkpoint mediated systemic immune tolerance could already be shown.

In a project supported by the Förderverein of the Tumorzentrum Erlangen, the expression of immune checkpoints in tissue samples and peripheral blood of patients with oral cavity carcinoma is investigated by means of NanoString analyses.

In addition, we are working on the establishment of an immunoscore for an improved prognostic assessment of oral cavity carcinomas and neoplasias of the facial skin. Within the framework of this project, a Next-Generation Tissue Microarray will be created. The aim is to supplement the TNM score with immunological parameters and to identify patient subgroups that might benefit particularly from adjuvant immunotherapy.

In the future, it will be investigated whether a „liquid-immuno-biopsy“ of tumor-specific miRNA in peripheral blood is suitable as a diagnostic marker for tumor recurrences and as a predictive marker for the response to tumor therapy with checkpoint inhibitors. The long-term vision is to evaluate neoadjuvant low-dose radioimmunotherapy as induction therapy prior to definitive surgical tumor therapy in a prospective therapy study for patients with oral cavity carcinoma.

We are also working on the development of a multiple marker system for early diagnosis and the malign transformation potential of oral leukoplakia. Next generation sequencing will be used to identify genes and miRNAs that are directly involved in the malignant transformation of leukoplakia. In retrospective studies, it has already been shown that the detection of MAGE-A expression in leukoplakia is a highly specific indication of a timely malignant transformation.

### Regeneration processes in inflamed and weakly replaced tissue

Since teeth and parts of the jawbone are derivatives of the neuroectoderm (cranial neural crest), osteoblast progenitors of this region have specific cellular properties, e.g. a special plasticity. Based on the model disease MRONJ, osteobiological and osteoimmunological characteristics and underlying signaling pathways are compared with extracranial tissues in order to understand the exclusivity of these diseases in the jaw and facial region and to use the special cellular plasticity for regenerative medical approaches.

### Oral medicine

Chronic inflammatory diseases, such as inflammatory bowel disease, scleroderma or multiple sclerosis, are associated with a disturbed immune reaction. Due to the increasing incidence of the diseases, their examination is becoming increasingly important, especially with regard to interdisciplinary cooperation. Current scientific studies show a clear association between chronic inflammatory diseases and the presence of periodontitis. However, their mutual influence with a possible correlation of disease relapses to specific germ expressions has scarcely been studied. In the future, characteristic inflammatory mediators will be investigated to demonstrate a possible link between the oral biofilm and the inflammatory responses of systemic diseases.

### Biomedical technology

The research area biomedical technology comprises research projects on hard and soft tissue regeneration, healing processes of dental implants, and laser applications.

One research focus is on the modulation and optimization of peri-implant tissue in the context of chewing functional rehabilitation using implant-supported dentures. This refers to the preclinical and clinical investigation of new techniques and materials for the regeneration of jaw defects and the long-term stability of hard and soft tissue after jaw augmentation as

well as the regeneration of peri-implant soft tissue and its influence on the health of peri-implant structures. The use of pluripotent stem cells from umbilical cord tissue in combination with tMP to optimize the supply of peri-implant hard tissue is currently being evaluated in a third-party funded study.

Furthermore, we investigate the temporal course of reperfusion and vascularization of free mucosal grafts and collagen matrices in the context of guided soft tissue regeneration.

In cooperation with the Bavarian Laser Center (BLC), tissue-specific laser surgery is also being investigated. The focus here is on the protection of specific tissue through non-contact tissue differentiation in soft and hard tissue surgery. In cooperation with the BLC, we are working on the design of a sensor and process control concept that regulates laser ablation tissue-selectively.

## Teaching

The Department of Oral and Cranio-Maxillofacial Surgery participates in the curricular teaching of Medicine and Dentistry with compulsory and optional subjects. A two-day extracurricular elective „Implantology 1lect“ was developed for dentistry students. Here it is possible to implant plastic models and pig jaws freehand and navigated. In addition, sinus lift techniques and peri-implantitis therapies are implemented.

The optional subject „Skills Lab Facial Surgery“ was designed for students of medicine. In this course, students learn the basics of local flaps on a pig model. In addition, theoretical and practical knowledge of microsurgical techniques is imparted.

The (post-) curricular teaching of dentistry also includes digital courses, which were conceived in cooperation with the Department of Hand Plastic Surgery and the Department of Oral and Maxillofacial Surgery of the Klinikum rechts der Isar in Munich. The course „eReconstruction“, sponsored by the Virtual University of Bavaria (VHB), enables interested participants to learn aspects of plastic-reconstructive surgery free of charge. In cooperation with other (dental) medical disciplines of UK Erlangen and the Ludwig-Maximilians-University in Munich, the VHB has approved an extension of the range of services to include radiological and oral surgical curricula. For students of medicine, there is also the possibility of taking clinical traineeships as well as the elective subject „Oral and Maxillofacial Surgery“ in the practical year.

Furthermore, (dental) medical and scientific doctorates are supervised.

## Selected publications

Kesting MR, Koerdt S, Rommel N, Mücke T, Wolff KD, Nobis CP, Ringel F, Frohwitter G. Classification of orbital exenteration and reconstruction. *J Craniomaxillofac Surg*, 2017. 45(4): 467-473

Weber M, Wehrhan F, Baran C, Agaimy A, Büttner-Herold M, Preidl R, Neukam FW, Ries J. PD-L1 expression in tumor tissue and peripheral blood of patients with oral squamous cell carcinoma. *Oncotarget*, 2017. 8(68): 112584-112597

Buchbender M, Neukam FW, Lutz R, Schmitt CM. Treatment of enucleated odontogenic jaw cysts: a systematic review. *Oral Surg Oral Med Oral Pathol Oral Radiol*. 2018. 125(5): 399-406

Frohwitter G, Rau A, Kesting MR, Fichter A. Microvascular reconstruction in the vessel depleted neck - A systematic review. *J Craniomaxillofac Surg*, 2018. 46(9): 1652-1658

Lutz R, Schmitt CM, Buchbender M, Neukam FW. Diagnosis, avoidance and management of complications of implant-based treatments. *Eur J Oral Implantol*, 2018. 11: S21-S25

Wehrhan F, Büttner-Herold M, Distel L, Ries J, Moebius P, Preidl R, Geppert C, Neukam FW, Kesting MR, Weber M. Galectin 3 expression in regional lymph nodes and lymph node metastases of oral squamous cell carcinomas. *BMC Cancer*, 2018. 18(1): 823

## International cooperations

Dr. E. Felszeghy, EARC (kft), Semmelweis University, Budapest: Hungary

Prof. Dr. Dr. E. Nkenke, Medical University, Vienna: Austria