UNIVERSITY HOSPITAL

# Department of Orthodontics and Orofacial Orthopedics

## Chair of Dental, Oral, and Maxillofacial Medicine – especially Orofacial Orthopedics


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**Research focus**
- Influence of different regulators on orofacial cleft development
- Identification of genetic risk variants by molecular genetics
- Oral symbiosis and dysbiosis
- Histological and histomorphometric investigation of the midpalatal suture
- MRI for cephalometric analysis in orthodonic diagnosis
- In vitro simulation of orthodontic processes
- Material scientific examinations of orthodontic materials

### Structure of the Department

Professorship: 1
Personnel: 23
- Doctors (of Medicine): 10
- Scientist: 1
- Graduate students: 11

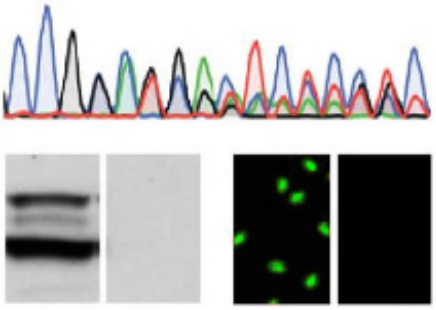
**Clinical focus areas**
- Treatment of newborn babies with cleft lip and/or palate
- Orthodontic treatment of cleft lip and/or palate
- Orthodontic treatment of dysgnathia / malformations of the upper and/or lower jaw
- Orthodontic treatment of craniofacial anomalies and syndromes
- Orthodontic treatment of tooth displacement
- Orthodontic treatment of tooth agenesis (hypo- or oligodontia)
- Evidence-based orthodontics
- Adult orthodontic treatment

## Research

Research of the Department of Orthodontics and Orofacial Orthopedics addresses molecular causes for many of our patients' conditions: cleft lip and/or palate (CL/P), craniofacial dysgnathia, tooth agenesis (hypo- or oligodontia) as well as molar incisor hypomineralization and periodontitis. Other research areas are the composition of the oral microbiome, the histomorphometric analysis of the *Sutura palatina*, the implementation of three-dimensional diagnosis in orthodontics, *in vitro* analyses of molecular processes during orthodontic treatment and material scientific examinations of orthodontic materials.

**Influence of different regulators on orofacial cleft development**

Cleft lip and/or palate are frequent congenital malformations. Etiology is complex, poorly understood and involves environmental and genetic factors. In order to achieve a better understanding of genetic causes for CL/P we analyze the function of several regulators of palate development in a joint IZKF-funded project with the Chair of Biochemistry and Pathobiochemistry.



*Analysis of a gene knockout via DNA sequencing (upper row), western blot (lower left) and immunocytochemistry (lower right)*

**Identification of genetic risk variants by molecular genetics**

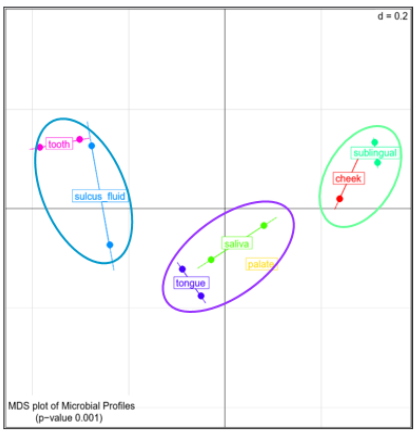
In order to identify risk factors for CL/P, we examine DNA samples from a broad range of patients and, if applicable, their relatives and compare them to data from control groups. In cooperation with the Institutes of Human Genetics of the university hospital of Bonn and of UK Erlangen, we perform next generation sequencing analyses enabling us to analyze large regions of DNA up to whole genomes. Our aim is always to pinpoint (possibly inherited) changes in the patient's DNA sequence that lead to the manifestation of the disease. Chromosomal regions identified in this way serve to find and characterize responsible genes. Those genes are examined in detail with regard to their biological function and how it might cause the cleft. Using the described molecular genetic methods, we also seek to identify relevant genetic loci for craniofacial dysgnathia, tooth agenesis (hypo- or oligodontia).

In further molecular genetic analyses, we seekto identify gene variants contributing to formation and progression of periodontitis. Although the impact of a genetic component is estimably 33 – 50 %, only a few risk variants have been identified up to now. In order to identify unknown genetic variants causing a higher risk for periodontitis, we perform expression quantitative trait locus (eQTL) analyses. By this innovative method, we can identify changes in the transcriptome of immune cells stimulated with periodontal virulence factors and attribute them to certain gene variants. With the same technique, we investigate on genetic factors influencing atherosclerosis and allergies against metals. For these comprehensive analyses, we cooperate with the Institute of Human Genetics and the Institute of Medical Microbiology, Immunology and Parasitology of the university hospital of Bonn and with the Department of Cardiology, Angiology and Pneumonology of the university hospital of Heidelberg and Center of Human Genetics of the university hospital of Marburg.

At best, our molecular genetic analyses lead to new diagnostic possibilities that could direct appropriate therapeutic measures in the sense of personalized medicine. The acquired knowledge might also help to develop new medication and preventive measures.

**Oral symbiosis and dysbiosis**

In order to identify patients at risk and to define prognostic factors for oral dysbiosis and disease, we analyze the oral microbiome and local cytokine concentrations in cooperation with the Institute of Clinical Microbiology, Immunology and Hygiene using 16S rDNA sequencing and multiplex immuno assay in different patient cohorts. Thereby, we analyze microbiome composition and cytokine concentrations in specific oral niches (palate, tongue, cheek, sublingual, plaque, sulcus fluid and saliva).



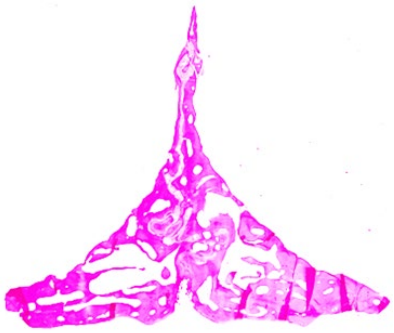

*MDS plot to depict microbial diversity within specific oral niches of two different probands.*

**Histological and histomorphometric investigation of the midpalatal suture**

The hard palate and the mid-palatal suture are of pivotal importance in orthodontics. By

means of palatal expansion in cases of transverse maxillary deficiency, the upper jaw can be widened while simultaneously improving nasal breathing, which is also of general medical relevance. Depending on patients´ age, different orthodontic appliances are employed from ordinary braces to surgical assisted procedures, which involve a subtotal Le Fort I osteotomy in adults.

The aim of the present study, which is conducted in collaboration with the Institute of Functional and Clinical Anatomy, is to gain further insight into the morphology and metabolism of the midpalatal suture in different age groups. Histologic and histomorphometric analysis are employed to enhance the understanding of the midpalatal suture.



*HE-staining of the mid-palatal suture*

**MRI for cephalometric analysis in orthodontic diagnosis**

For several years, our department has examined the potential and possibilities of three-dimensional imaging for different orthodontic questions. Currently, lateral cephalometric radiographs (LCR) are still routinely used for cephalometric analysis in regards to orthodontic diagnosis and treatment planning. However, this two-dimensional method has several disadvantages such as structure impositions, the dependence of the correct head positioning and last but not least the radiation exposure. Therefore, we are working on using magnetic resonance imaging (MRI) for three-dimensional cephalometric analysis in order to overcome these limitations. However, this technology was originally introduced for soft tissue imaging. In recent years, the representation of hard tissue became more and more popular by new developments. In collaboration with the Fraunhofer Institute for Integrated Circuits IIS in Würzburg and the Institute of Radiology of UK Erlangen, we developed special MRI sequences with ultra-short echo times in order to enable hard tissue imaging (as teeth and bone) according to our requirements. Following, we established a reliable method for implementation of cephalometric analysis in the three-dimensional MRI dataset. With a series of studies, we want to proof the clinical comparability of the MRI and LCR-based cephalometric results. The long-term aim of our project series is to introduce MRI-based cephalometric analysis as an available diagnostic tool in orthodontics and as consequence to reduce radiation exposure especially of children and adolescents caused by orthodontic reasons.

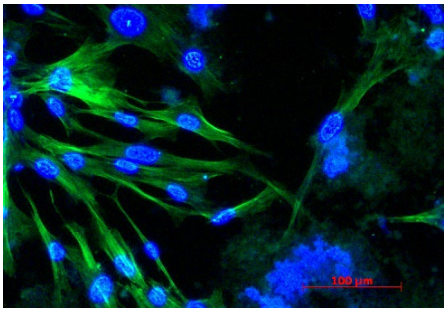
***In vitro* simulation of orthodontic processes**

During orthodontic treatment, tensile strain and pressure load lead to formation and degradation of alveolar bone, respectively. We want to shed light on the molecular processes during these processes and to improve our understanding of bone remodeling. To this aim, we use different cell culture-based *in vitro* models such as the simulation of orthodontic pressure load by applying glass disks of defined weight onto human periodontal ligament fibroblasts.

**Material scientific examinations of orthodontic material**

Further research fields are material scientific examinations of orthodontic materials and the development of antibacterial material for orthodontic applications. For instance, by using these materials as bonding material for brackets in the long term, we want to reduce number and size of demineralized areas after removal of fixed multibracket appliances, thus minimizing risk of caries for patients.

Additionally, investigations concerning the biocompatibility as well as cyto- and genotoxicity of orthodontic materials are conducted in our department. By means of the γH2AX assay, the genotoxic potential of e.g. orthodontic meth-acrylate-based adhesives is investigated *in vitro*. Moreover, EC-50 curves of clinical relevance are established.




*Calcein-staining (green) and DAPI counterstain (blue) of human gingival fibroblasts in order to detect living cells*

## Teaching

The Chair of Dental, Oral, and Maxillofacial Medicine – especially Orofacial Orthopedics is engaged in dental medicine. Within the scope of orthodontic analysis and treatment, the curriculum comprises comprehensive clinically based material. Skills lab work enables the students to collect and evaluate diagnostic data and to control the clinical application of orthodontic devices.

In addition, MD and PhD theses are supervised, and residents are further trained to become specialized orthodontists according to the Bavarian Curriculum.

**Selected recent publications**

Safi S, Frommholz D, Reimann S, Götz W, Bourauel C, Neumann AL, Hoerauf A, Ilges H, Safi AF, Jäger A, Hübner MP, Gölz L (2019) Comparative study on serum-induced arthritis in the temporomandibular and limb joint of mice. Int J Rheum Dis DOI 10.1111/1756-185x.13486

Buerfent BC, Gölz L, Hofmann A, Ruhl H, Stamminger W, Fricker N, Hess T, Oldenburg J, Nöthen MM, Schumacher J, Hübner MP, Hoerauf A (2019) Transcriptome-wide analysis of filarial extract-primed human monocytes reveal changes in LPS-induced PTX3 expression levels. Sci Rep 9(1):2562. DOI 10.1038/s41598-019-38985-x

Taubmann A, Willershausen I, Walter C, Al-Maawi S, Kaina B, Gölz L (2020) Genotoxic and cytotoxic potential of methacrylate-based orthodontic adhesives. Clinical Oral Investigations DOI 10.1007/s00784-020-03569-x

Weider M, Schröder A, Docheva D, Rodrian G, Enderle I, Seidel CL, Andreev D, Wegner M, Bozec A, Deschner J, Kirschneck C, Proff P, Gölz L (2020) A Human Periodontal Ligament Fibroblast Cell Line as a New Model to Study Periodontal Stress. International journal of molecular sciences 21(21) DOI 10.3390/ijms21217961

Seidel CL, Gerlach RG, Wiedemann P, Weider M, Rodrian G, Hader M, Frey B, Gaipl US, Bozec A, Cieplik F, Kirschneck C, Bogdan C, Gölz L (2020) Defining Metaniches in the Oral Cavity According to Their Microbial Composition and Cytokine Profile. International journal of molecular sciences 21(21) DOI 10.3390/ijms21218218

Seidel A*, Seidel CL*, Weider M, Junker R, Gölz L, Schmetzer H (2020) Influence of Natural Killer Cells and Natural Killer T Cells on Periodontal Disease: A Systematic Review of the Current Literature. International journal of molecular sciences 21(24) DOI 10.3390/ijms21249766; *contributed equally