

Plastic Surgery

Division Details

RESEARCH AND TRAINING DETAILS

Faculty	10
Joint Appointment Faculty	1
Research Fellows and Post Docs	2
Research Graduate Students	2
Total Annual Grant Award Dollars	\$553,677

CLINICAL ACTIVITIES AND TRAINING

Staff Physicians	5
Clinical Fellows	1
Inpatient Encounters	283
Outpatient Encounters	6,411



Row 1: R Jiang, Y Lan, D Jones, A Schwentker, S Brugmann

Row 2: T Sitzman, R Hathaway, J van Aalst, H Elhadi Babiker, B Pan

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Division Highlights

John van Aalst, MD

Dr. John van Aalst, MD, in collaboration with Dr. Dorothy Supp, PhD, received a [CTST PCS pilot grant](#) entitled "Correction of Epidermolysis Bullosa (EB) Via Genome Editing and Tissue Engineering." The long-term goal of this project is to solve the genetic problem that causes chronic, debilitating epidermal blistering in children with EB.

He is also actively involved with a multi-disciplinary group focused on tissue engineering tracheas for children with chronic, long-segment tracheal stenosis. Dr. van Aalst, and this team, including researchers from Cincinnati Children's Hospital Medical Center, Drs. Alessandro DaAlarcon, MD; [Rob Fleck, MD](#); Alister Bates, PhD; [Donna Jones, PhD](#); and Montserrat Caballero, PhD, along with [UC](#) researchers, Drs. [GR Liu, PhD](#), and [James Lin, PhD](#), are using a juvenile pig model to study strategies for combining 3D printed materials with decellularized tracheas to provide engineered solutions for these difficult-to-treat children.

[Dr. van Aalst's lab](#) is also focused on engineered solutions to treat craniofacial bone defects. His lab uses a pig model of a maxillary cleft defect, and has successfully treated this defect with mesenchymal stem cells harvest from the umbilical cord on nanoscaffolds.1,2.

His clinical research focuses on outcome studies of children with congenital anomalies, principally cleft lip and palate. In collaboration with researchers at [Bethlehem University](#) and the [University of Washington](#) in Seattle, this partnership received an R56 entitled "Oral-facial Clefts: Discovery and Characterization of New Genes" to study novel alleles that cause clefting among Palestinians. Tracking the demographic characteristics of these patients and families happens through the Congenial Anomalies Database, a 700-question survey administered to over 600 patient families.

Caballero M, Morse JC, Halevi AE, Emodi O, Wood JS, van Aalst JA. [Juvenile Swine Surgical Alveolar Cleft Model to Test Novel Autologous Stem Cell Therapies](#). *Tissue Eng Part C Methods*. 2015 Sep;21(9):898-908.

Caballero M, Jones DC, Shan Z, Soleimani S, van Aalst JA. **Tissue Engineering Strategies to Improve Osteogenesis in the Juvenile Swine Alveolar Cleft Model**. *Tissue Eng Part C Methods*. 2017 Aug 31. [Epub ahead of print.]

Yu Lan, PhD

Dr. Lan's lab recently discovered that the Golgi-associated protein Golgb1 plays crucial roles in palate development by using a combination of chemical mutagenesis in mice, exome sequencing, and CRISPR/Cas9-mediated genome editing (Lan et al. **Golgb1 regulates protein glycosylation and is crucial for mammalian palate development**. *Development*. 2016 Jul 1;143(13):2344-55). Since Golgb1 is ubiquitously expressed in all cell types, it is puzzling that mice lacking Golgb1 exhibit tissue-specific developmental defects in craniofacial development while many other tissues develop normally. Golgb1 is structurally most similar to another member of the Golgin family, Golga5, with both sharing a similar transmembrane domain and location of localization in the Golgi network. To further investigate the roles of Golgb1 in mammalian organogenesis, the Lan lab generated mice lacking Golga5 using CRISPR/Cas9-mediated genome editing and analyzed developmental phenotypes of Golga5^{-/-} mutants as well as of Golga5^{-/-}Golgb1^{-/-} double mutants. Summarized results are in a new publication (McGee et al. **Golga5 is dispensable for mouse embryonic development and postnatal survival**. *Genesis*. Jul;55(7)). In addition to her independent research projects, Dr. Lan continues productive collaborations with Dr. Rulang Jiang, PhD, in the **Division of Developmental Biology**. They received a new 5-year research grant from **Shriners Hospitals for Children** for the project, "Molecular Regulation of Palate Development" (funded from January 1, 2017 through December 31, 2021). Moreover, they received a new 5-year R01 grant from **NIH/NIDCR** for the project, "Mandible Development" (funded from July 10, 2017 through June 30, 2022).

Li C, Lan Y, Jiang R. **Molecular and Cellular Mechanisms of Palate Development**. *J Dent Res*. 2017 Oct;96(11):1184-1191.

Brian Pan, MD

Dr. Brian Pan, MD, continues to use his robust data set to answer questions related to improving the safety and outcomes of neonates with tongue-based airway obstruction. A **Shriners Hospital for Children—Cincinnati** Hardisty grant partially funded this research. This work led to an accepted publication in the past year, and the submission of three additional publications, with other collaborating authors, that are currently under review. He also partnered with **NYU** to assess the mandibular anatomy of these patients using CT scans to improve the safety of neonatal distraction.

Papers accepted/submitted/in press:

- Runyan CM, Rivera AU, Tork S, Shikary TA, Ehsan Z, Weaver KN, Hossain MM, Gordon CB, Pan BS. **Management of airway obstruction in infants with Pierre Robin sequence**. Submitted for publication.
- Ehsan Z, Weaver KN, Pan BS, MD, Hossain MM, Huang G, Simakajornboon N. **Sleep Abnormalities in Neonates with Pierre Robin Sequence Undergoing Mandibular Distraction: A Longitudinal Analysis**. Submitted for publication.
- Geddam LM, Mahmoud MA, Pan BS, Stevenson CB, Kandil AI. **Airway Management in a 5kg Infant with a Frontoethmoidal Encephalocele**. Submitted for publication.
- Biskup N, Elhadi-Babikar H, Hathaway R, Pan B, van Aalst J, Gordon C. **Decannulation and Airway Outcomes with Maxillomandibular Distraction in Treacher Collins Syndrome: A 25 Patient Experience**. *J Craniofac Surg*. Submitted for publication.
- Biskup N, Altman A, Gendron C, Runyan C, Pan B. **Neonatal Mandibular Distraction without a Consolidation Period: Is It Safe? Is it Effective?** *J Craniofac Surg*. 2017 Sep 21. [Epub ahead of print]
- Pan BS, Vu AT, Saenger NJ, Rapp SJ. **Reconstruction of the Isolated Columellar Defect: A Novel Two- Stage Technique and Review of the Literature**. *J Oral Maxillofac Surg*. 2017 Apr;75(4):822-827.
- Sharp PA, Pan BS, Yakuboff KP, Rothchild D. **Development of a Best Evidence Statement for the Use of Pressure Therapy for Management of Hypertrophic Scarring**. *J Burn Care Res*. 2016 Jul-Aug;37(4):255-64.

Donna Jones, PhD

The lab of Dr. Donna Jones, PhD, pursues the following research:

- Development of a swine alveolar cleft model, performing tridimensional reconstruction from the CT scans of the swine alveolar cleft model. In addition, she has performed morphometric analysis on the reconstruction for asymmetry assessment. She is a co-author for three publications for this project; one accepted for publication in the *Journal of Tissue Engineering and Regenerative Medicine*. She also advises and supports the design of experiments to establish a model of growth restriction (swine alveolar cleft model).
- Experimental mice skulls 3D reconstructions.
- Dr. Jones also contributes to the research surrounding the interplay of muscular and bony features of mandibular hypoplasia

Ronald Hathaway, DDS, MS, MS

Dr. Ronald Hathaway, DDS, MS, MS pursues the following research:

- Primary research interests involve clinical audits and outcome studies of various treatment protocols for cleft lip and palate and craniofacial teams.
- Co-investigator for the Americleft Project, a North American cohort study for evaluating cleft protocols and outcomes through inter-center comparison (four related publications in 2016).
- With Americleft research colleagues, won the 2016 Berkowitz Study Award for the best scientific investigation with long-term outcomes published in the *Cleft Palate-Craniofacial Journal* in July 2016.
- Dr. Hathaway has also pioneered a patient, and family-reported, outcomes study for those affected by Treacher Collins syndrome.

Samantha Brugmann, PhD

The [Brugmann Lab](#) focuses on craniofacial development and a class of disorders that affect the craniofacial complex called ciliopathies. Ciliopathies are a class of diseases caused by the loss of a ubiquitous, microtubule-based organelle called a primary cilium. Ciliopathies commonly result in defective development of the craniofacial complex, causing midfacial defects, craniosynostosis, micrognathia and aglossia. This year, the lab made significant progress by publishing seven manuscripts dedicated to understanding how primary cilia impact craniofacial development. Two of those studies have made the interesting observation that while the loss of cilia in the frontonasal prominence of the developing face causes a gain-of-HH function phenotype (midfacial widening), the loss of cilia in the mandibular prominence causes a loss-of-HH function phenotype (micrognathia/aglossia). The lab determined that impaired processing of the GLI transcription factors dictated how the cells in each facial prominence would interpret the loss of cilia. Together, our data suggested that the developing facial prominences are unique developmental fields that will interpret a genetic insult differently.

Division Publications

1. Workman MJ; Mahe MM; Trisno S; Poling HM; Watson CL; Sundaram N; Chang CF; Schiesser J; Aubert P; Stanley EG. **Engineered human pluripotent-stem-cell-derived intestinal tissues with a functional enteric nervous system.** *Nature Medicine*. 2017; 23:49-59.
2. Chang CF; Chang YT; Millington G; Brugmann SA. **Craniofacial Ciliopathies Reveal Specific Requirements for GLI Proteins during Development of the Facial Midline.** *PLoS genetics*. 2016; 12:e1006351.
3. Lan Y; Zhang N; Liu H; Xu J; Jiang R. **Golgb1 regulates protein glycosylation and is crucial for mammalian palate development.** *Development (Cambridge)*. 2016; 143:2344-2355.
4. Chang YT; Chaturvedi P; Schock EN; Brugmann SA. **Understanding Mechanisms of GLI-Mediated Transcription during Craniofacial Development and Disease Using the Ciliopathic Mutant, talpid(2).** *Frontiers in Physiology*. 2016; 7:468.

5. Millington G; Elliott KH; Chang YT; Chang CF; Dlugosz A; Brugmann SA. **Cilia-dependent GLI processing in neural crest cells is required for tongue development.** *Developmental Biology*. 2017; 424:124-137.
6. Jia S; Kwon HJE; Lan Y; Zhou J; Liu H; Jiang R. **Bmp4-Msx1 signaling and Osr2 control tooth organogenesis through antagonistic regulation of secreted Wnt antagonists.** *Developmental Biology*. 2016; 420:110-119.
7. Schock EN; Chang CF; Youngworth IA; Davey MG; Delany ME; Brugmann SA. **Utilizing the chicken as an animal model for human craniofacial ciliopathies.** *Developmental Biology*. 2016; 415:326-337.
8. Schock EN; Struve JN; Chang CF; Williams TJ; Snedeker J; Attia AC; Stottmann RW; Brugmann SA. **A tissue-specific role for intraflagellar transport genes during craniofacial development.** *PloS one*. 2017; 12:e0174206.
9. Snedeker J; Schock EN; Struve JN; Chang CF; Cionni M; Tran PV; Brugmann SA; Stottmann RW. **Unique spatiotemporal requirements for intraflagellar transport genes during forebrain development.** *PloS one*. 2017; 12:e0173258.
10. Xu J; Liu H; Chai OH; Lan Y; Jiang R. **Osr1 Interacts Synergistically with Wt1 to Regulate Kidney Organogenesis.** *PloS one*. 2016; 11:e0159597.
11. Knorr JM; Jackson J; Batie MR; Narmoneva DA; Jones DC. **Application of strain and calibration of Forster Resonance Energy Transfer (FRET) emission for in vitro live cell response to cytoskeletal deformation.** *Journal of Biomechanics*. 2016; 49:3334-3339.
12. Pan BS; Vu AT; Rapp SJ; Saenger NJ. **Reconstruction of the Isolated Columellar Defect: A Novel 2-Stage Technique and Review of the Literature.** *Journal of Oral and Maxillofacial Surgery*. 2017; 75:822-827.
13. Barbosa GLDR; Emodi O; Pretti H; van Aalst JA; de Almeidas SM; Tyndall DA; Pimenta LA. **GAND classification and volumetric assessment of unilateral cleft lip and palate malformations using cone beam computed tomography.** *International Journal of Oral and Maxillofacial Surgery*. 2016; 45:1333-1340.
14. Sharp PA; Pan B; Yakuboff KP; Rothchild D. **Development of a Best Evidence Statement for the Use of Pressure Therapy for Management of Hypertrophic Scarring.** *Journal of Burn Care and Research*. 2016; 37:255-264.
15. Thompson JA; Heaton PC; Kelton CML; Sitzman TJ. **National Estimates of and Risk Factors for Inpatient Revision Surgeries for Orofacial Clefts.** *The Cleft palate-craniofacial journal : official publication of the American Cleft Palate-Craniofacial Association*. 2017; 54:60-69.
16. Ruppel JK; Long RE; Oliver DR; Semb G; Russell KA; Mercado AM; Daskalogiannakis J; Hathaway RR. **The Americleft Project: A Comparison of Short- and Longer-Term Secondary Alveolar Bone Graft Outcomes in Two Centers Using the Standardized Way to Assess Grafts Scale.** *The Cleft palate-craniofacial journal : official publication of the American Cleft Palate-Craniofacial Association*. 2016; 53:508-515.
17. Sitzman TJ; Coyne SM; Britto MT. **The Burden of Care for Children With Unilateral Cleft Lip: A Systematic Review of Revision Surgery.** *The Cleft palate-craniofacial journal : official publication of the American Cleft Palate-Craniofacial Association*. 2016; 53:e84-e94.
18. Gendron C; Schwentker A; van Aalst JA. **Genetic Advances in the Understanding of Microtia..** *Journal of Pediatric Genetics*. 2016; 5:189-197.

Grants, Contracts, and Industry Agreements

Annual Grant Award Dollars

Investigator	Title	Sponsor	ID	Dates	Amount
Samantha Brugmann, PhD	The Role of Primary Cilia in Murine Craniofacial	National Institutes of Health	R01 DE023804	12/13/2013 -	\$390,000

	Development			11/30/2019	
Betsy Schock	The Role of Ectodermal Primary Cilia in Murine Orofacial Development	National Institutes of Health	F31 DE025537	07/01/2015 -	\$37,976
				06/30/2018	
Thomas James Sitzman, MD	Understanding and Reducing Variation in Outcomes of Cleft Lip and Palate Surgery	National Institutes of Health	K23 DE025023	04/01/2016 -	\$125,701
				03/31/2021	
Total Annual Grant Award Dollars					\$553,677
