



2025 Research Aid Award
Gina DeLeonibus, University of Pittsburgh

1. Biography

I am from Cleveland, Ohio, and I am currently a second-year resident in the Department of Orthodontics and Dentofacial Orthopedics Program at the University of Pittsburgh, School of Dental Medicine. I first became interested in orthodontics at my Team Smile Volunteer experience with the Guardians. I looked forward to being in a field where I could provide individuals with renewed self-confidence by improving their smile. I received my dental degree at Case Western Reserve University and I had the opportunity to work on a research project in craniofacial orthodontics as a second-year dental student. I assisted with measuring the cortical bone thickness and bone depths in the maxilla from CBCT data of patients with unilateral cleft lip and/or palate (CLP). Understanding where the most cortical bone depth and thickness were located in CLP patients would allow for more predictable orthodontic treatment for these patients. As a resident, I am continuing to pursue my interest in craniofacial orthodontics and biology as I work with my research mentor, Dr. Alice Goodwin. I aspire to make a difference in the lives of patients with Pierre Robin sequence (PRS) through my research; develop my orthodontic knowledge and skills when working with patients; and educate predoctoral students as they rotate through our orthodontic clinic at Pitt. Outside of residency, I enjoy baking desserts, spending time with my family and my dog, and traveling to new places.

2. Description of My Project

People with PRS have a micrognathic mandible, glossoptosis, and airway obstruction and often present with a cleft palate. PRS varies in severity, and these individuals may be treated with supportive therapies such as prone positioning, or more invasive therapies like tracheostomy, tongue-lip adhesion, or distraction osteogenesis in infancy and childhood. The majority of non-syndromic PRS patients have genetic mutations in regulatory regions of *SOX9* or the gene itself. The Goodwin Lab aims to better understand the genetics and pathogenesis of PRS. Dr. Goodwin developed a novel *Hand2^{Cre}* mouse line that drives Cre recombination in the mandibular mesenchyme and she used this mouse to generate a PRS mouse model with mandibular mesenchyme specific (including the tongue and mandible) deletion of *Sox9*. These *Sox9^{fl/fl};Hand2^{Cre}* mouse embryos developed a hypoplastic and retrognathic mandible and fully penetrant, complete cleft palate. For my research, I am studying the gene, *Six6*, which was identified as a downstream target of *Sox9* in an RNA-sequencing experiment performed in the Goodwin Lab on RNA from the mandible of *Sox9^{fl/fl};Hand2^{Cre}* and control embryos. I will explore what role *Six6* plays in craniofacial development and how this transcription factor may influence other *Six* family members-1, 2, and 4 utilizing a mouse model with *Six6* deleted in the mandibular mesenchyme (*Six6^{fl/fl};Hand2^{Cre}*). H&E staining and skeletal preps will be performed on *Six6^{fl/fl};Hand2^{Cre}* and control embryos to study mandible, palate, and tongue development at critical timepoints. RNAscope and immunohistochemistry will also be used to assess *Six1, 2, and 4* expressions in *Six6^{fl/fl};Hand2^{Cre}* and control embryos at the RNA and protein level, respectively. I expect *Six6* plays an important role in mandible and tongue development by regulating *Six1, 2, and 4*, and loss of *Six6* will result in a PRS phenotype with mandibular retrognathia and cleft palate.

3. How Orthodontic Education will Benefit from My Award

I believe that orthodontic education will benefit from my award because this project will increase our understanding of PRS. More people will be able to learn about PRS on a profound level, understand how the cleft forms in utero, and know how to diagnose and treat these complex cases

in clinic. Furthermore, this work will test *SIX6* as a candidate gene for PRS, adding to the foundation of which improved therapeutics and diagnostics will be developed for PRS patients.

4. Why the Foundation is Important to my Project

I am grateful to have the support of the AAOF for my research project. This award will provide funding to complete the proposed experiments, which will increase our understanding of the role of *SIX6* in craniofacial development and PRS. The funds will also allow me to attend and present at a meeting, which will be a wonderful opportunity for me to develop my presentation skills and interact with other researchers. Presenting at a meeting, utilizing AAOF funds, will also allow me to spread awareness for my research topic. As of now there are only supportive procedures to help these babies with PRS. Hopefully, we can better understand the role of *SIX6* in craniofacial development and how this gene influences other *SIX* family members so we may move closer toward finding better therapies for PRS patients.

5. How is the Foundation Funding Expected to Benefit my Career

The AAOF funding has helped me to develop my research skills by devising a hypothesis and setting objectives to test with experiments when applying for the AAOF research funding. Completing the proposed experiments will hone my critical thinking skills, which I will utilize as an orthodontist. Moreover, I will have the opportunity to meet other researchers and orthodontists at conferences, and I look forward to learning from them, which will benefit me during my time as a resident and as a future orthodontist and mentor for the next generation of individuals.