Document Synopsis

1. Biography

Alice Goodwin, DDS,PhD, is an assistant professor in the Department of Orofacial Sciences at the UCSF School of Dentistry. She is an ABO certified orthodontist and practices in the Orthodontic Clinic as a faculty provider and attending faculty and provides care for patients with craniofacial difference in the UCSF Craniofacial Center. She also runs her research lab studying the biology underlying craniofacial anomalies using mouse models and mentors students and orthodontic residents.

2. Project Description

Pierre Robin sequence (PRS) is defined as a clinical triad of mandibular hypoplasia, glossoptosis, and airway obstruction. PRS is associated with cleft palate in the majority of cases, and the genetic cause is mutations in enhancers of *SOX9* or the gene itself. It is thought the hypoplastic and retrognathic mandible physically blocks palatogenesis, contributing to cleft palate, however, the mechanisms underlying this process are not fully understood. The aim of this BRA project is to determine the contribution of mandibular dysmorphology to cleft palate in PRS (Aim 1) and analyze the role of *Sox9* in mandibular development (Aim 2) utilizing a newly generated genetic tool (*Hand2*^{Cre}) to delete *Sox9* specifically in the mandible and not surrounding tissue. By completing the proposed experiments, we will further our understanding of the mechanism of palatal shelf elevation and mandibular development and answer the long-standing and unanswered question of how mandibular dysmorphology contributes to cleft palate in PRS.

3. Statement on benefit to orthodontic education

Orthodontics is a critical component of the care for individuals with craniofacial anomalies, including cleft palate and PRS, from birth to adulthood. Improved understanding of the mandibular hypoplasia and how it contributes to cleft palate at the cellular and molecular level in mouse will lay the foundation for improved therapies for PRS patients. Additionally, this work will increase our understanding of mandibular hypoplasia and the mechanisms involved, which affects not only individuals with clefts but the general population as well. Thus, this work understanding the mechanisms of mandibular hypoplasia and cleft palate in mouse may ultimately reveal candidate genes and signaling pathways and potential therapeutic targets to treat mandibular hypoplasia and clefting in PRS and the spectrum of mandibular hypoplasia in orthodontic patients.

4. Why the Foundation is important to the project

AAOF funding will provide crucial resources to support a technician and purchase reagents for experiments to complete this project. In particular, the funds will support the proposed RNA sequencing experiment which will identify gene targets of Sox9 important in mandibular development and provide new avenues of research for future funding.

5. How Foundation funding has benefited my career

I am very grateful for the support AAOF has provided me. The PFA gave me time and support as a postdoc to develop my research project, obtain NIDCR funding (K08), and attain a faculty position. The BRA will provide resources to complete and publish this project and generate preliminary data for R level funding applications.