

## Biomedical Research Award

### Dr. Eung-Kwon Pae, *The University of Maryland School of Dentistry*

Dr. Pae is a board-certified orthodontist currently an associate professor at the University of Maryland Baltimore, School of Dentistry. His research has long focused on the impacts that breathing insufficiency exerts on the neuro-musculoskeletal system, principally as a consequence of accompanying autonomic dysfunction. He hypothesizes that apnea of prematurity and periodic breathing accompanying premature birth results in long-term changes in autonomic neural circuitry and targeted organs, including osteogenesis as a consequence of exaggerated sympathetic tone and oxidative stress. The disrupted neural circuitry will disturb homeostasis in autonomic balance associated with orofacial growth.



#### **Project Synopsis:**

Long-term increased sympathetic discharge leads to facial skeletal defects during rapid growth of the perinatal period. An animal model, using spontaneously hypertensive rats, examined this premise by several research groups; moreover, a non-selective  $\beta$ -adrenergic antagonist, propranolol, can reverse the bone growth deficiencies. This proposal aims to demonstrate 1) sympathetic tone is elevated in our preterm-equivalent rat pups after a one-time brief repetitive intermittent hypoxic challenge; 2) this immediate postnatal IH challenge leads to orofacial skeletal defects, including fragile bones and a small jaw.

#### **Benefit to Orthodontic Education:**

More than ten percent of infants in the US are born prematurely. Preterm infants born between 34 and 36 weeks gestation are as much as 17 times more likely to have respiratory distress than full-term infants, with that distress including periodic breathing, the very definition of intermittent hypoxia. Those preterm infants who survive face a risk of lifelong health consequences, such as potential malocclusions due to skeletal mismatch, in addition to other health problems. Clinical reports suggest that individuals born preterm tend to have an increased (~30% higher than full-term) occurrence of malocclusions with a small mandible and a narrow palate in the absence of conspicuous craniofacial dysmorphic features. Although numerous explanations are conceivable, a mechanistic pathophysiological explanation for these orofacial skeletal mismatches due to preterm birth has not been examined. If the cause-effect relationship between early respiratory distress and skeletal malocclusions in later age were revealed, our field could develop interceptive modalities as a preemptive measure before skeletal malocclusions fully develop.

#### **Importance of AAOF Funding:**

When a part of this proposal submitted to NIH for NIDCR funding, one of the reviewers' comments was as quoted "Even if the extent of malocclusion is such that orthognathic surgery is needed, that still might be the best option to treat the patients, ...". I believe this comment demonstrates the importance of AAOF funding. The importance rests with the importance of demonstrating the need to attack the cause of malocclusions, namely preventing the failure of jaw growth management by reducing sympathetic drive initiated from the respiratory issues.