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Presenter Information

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Airway smooth muscle pathology in Pompe Disease

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Pompe disease is a rare autosomal recessive disease which results from a deficiency of acid α -glucosidase (GAA) - an enzyme that degrades lysosomal glycogen. Patients with Pompe disease develop intra-lysosomal accumulation of glycogen in multiple tissues including skeletal muscle, CNS and smooth muscle.

Pulmonary dysfunction is a hallmark of Pompe disease and has classically been attributed to muscle weakness and CNS neuropathology. However, the potential role of respiratory smooth muscles in the respiratory pathology is unknown. Therefore we postulated that GAA deficiency results in airway smooth muscle glycogen accumulation that leads to airway smooth muscle dysfunction.

Using the Pompe mouse model, the *Gaa*^{-/-} mouse, we examined the airway smooth muscle structure and function. We used in vivo forced oscillometry measurements (N=7WT, N=7 *Gaa*^{-/-}) to examine pulmonary physiology and administered methacholine challenges to assess in vivo airway resistance. Also, we used ex-vivo contraction testing (N=6WT, N=5 *Gaa*^{-/-}) to determine bronchi contractility. In response to the highest dose methacholine challenge (100mg/ml), there was a significant decrease in conducting airway resistance in *Gaa*^{-/-} versus WT mice (p=0.007). Also, ex vivo bronchi contraction testing demonstrated a significantly weaker response to potassium chloride (p=0.008) and methacholine (2-way ANOVA p=0.005) in Pompe mice compared to WT mice, suggesting impaired smooth muscle contraction. Furtherly, we performed PAS staining on fresh-frozen tissue to examine the degree of glycogen accumulation as a result of GAA deficiency. PAS staining revealed robust glycogen accumulation in the trachea and bronchi of Pompe mice and a disruption of the airway smooth muscle architecture.

In conclusion, GAA deficiency results in glycogen accumulation and a disruption of the architecture in the airway smooth muscles of *Gaa*^{-/-} mice. Furthermore, both in vivo and ex vivo tests reveal that *Gaa*^{-/-} murine airways have impaired function as evidenced by decreased contractility and a decreased response to methacholine.

I'm submitting my abstract for the 6th Annual Research Retreat on May 20th, 2016. My contact information is as follows: name - Lang Xiong, email address - Lang.Xiong@umassmed.edu, lab phone number - 774 455 3506, mobile phone number - 508 373 3189.