May 20th, 12:30 PM

Characterization of Respiratory Phenotype in Very Long-chain Acyl-CoA Dehydrogenase Deficient Mice.

Allison M. Keeler
University of Massachusetts Medical School

Et al.

Let us know how access to this document benefits you.
Follow this and additional works at: https://escholarship.umassmed.edu/cts_retreat

Part of the Congenital, Hereditary, and Neonatal Diseases and Abnormalities Commons, Enzymes and Coenzymes Commons, Genetics and Genomics Commons, and the Respiratory Tract Diseases Commons

Repository Citation

Creative Commons License
This work is licensed under a Creative Commons Attribution-Noncommercial-Share Alike 3.0 License. This material is brought to you by eScholarship@UMMS. It has been accepted for inclusion in UMass Center for Clinical and Translational Science Research Retreat by an authorized administrator of eScholarship@UMMS. For more information, please contact Lisa.Palmer@umassmed.edu.
Characterization of Respiratory Phenotype in Very Long-chain Acyl-CoA Dehydrogenase Deficient Mice.

Allison Keeler, PhD. Kaitlyn Desrochers, BS. Mai ElMallah, MD

Department of Pediatrics, Gene Therapy Center, University of Massachusetts Medical School, Worcester MA.

Rationale: Very Long-chain Acyl-CoA dehydrogenase (VLCAD) deficiency is the most common inherited long-chain fatty acid disorder. The VLCAD enzyme catalyzes the first step of mitochondrial fatty acid oxidation and loss of the enzyme results in energy deficiency as well as accumulation of long chain fatty acids. Recently, a related enzyme, Long-chain Acyl-CoA dehydrogenase (LCAD), which unlike VLCAD is not highly expressed in metabolic tissues like liver, heart and skeletal muscle, was found to be expressed in the lung and surfactant and lung dysfunction were observed in LCAD deficient mice. Respiratory distress syndrome has been described in other fatty acid oxidation disorders. VLCAD is expressed in lung, and likely plays an important role in lung compliance.

Methods: VLCAD deficient mice and litter-mate controls were fasted for 18 hours, then exercised on a treadmill for 2 hours. Breathing was immediately assessed using whole body plethysmography in unanaesthetized spontaneously breathing mice. After a stable baseline was achieved, mice were given a “respiratory” challenge with 7% hypercapnia. In a subgroup of animals, pulmonary mechanics were assessed using Flexivent (Scireq).

Results: Following exercise, VLCAD deficient mice had a decreased tidal volume and minute ventilation compared to their wild type controls. However, post-exercise VLCAD deficient mice were able to stabilize to similar levels as wild-type during baseline. The VLCAD deficient mice had a decreased response to a respiratory challenge with 7% hypercapnia. Early preliminary results suggest that VLCAD deficient animals have lower airway resistance.

Conclusions: Respiratory insufficiency was demonstrated in a fasted and exercise challenged VLCAD deficient mice.

My contact information is Kaitlyn Desrochers (Wetmore), Lab phone number is 774 455 3506, and my email is Kaitlyn.wetmore@umassmed.edu.