

Votion 2012 Abstract Bioblast

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Reference

Votion DM (2012) The cause of atypical myopathy in grazing European horses revealed. Mitochondr Physiol Network 17.12.

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Authors: Votion DM

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Abstract

Atypical myopathy (AM) is a frequently fatal pasture myopathy that emerges in Europe. More than one thousand European cases have been communicated to the AM Alert Group (AMAG) since autumn 2006. This seasonal condition kills 75% of affected horses within 72 hours with signs resulting from acute degeneration in postural and respiratory muscles.

From epidemiological studies performed on European cases [1] and by elucidating the pathophysiological mechanism [2], using several samples collected through the AMAG network, the assumption of a toxin of environmental origin that would alter the energy metabolism has been hypothesized. Indeed, affected horses have acquired deficiencies in multiple acyl-CoA dehydrogenases resulting, among others, from defects in several mitochondrial dehydrogenases [2].

Recently, it was shown that Seasonal Pasture Myopathy (SPM) in the US was caused by the toxic amino acid hypoglycin A present in the seeds of box elder trees (*Acer negundo*) [3]. Once ingested, hypoglycin A is metabolized into methylenecyclopropyl acetic acid (MCPA) that disrupts energetic metabolism leading to the biochemical derangements seen in both, SPM and AM.

In a preliminary study, the mitochondrial respiration in cultured equine skeletal myoblasts was monitored with high-resolution respirometry with or without addition of serum of AM-affected horses. We observed a dose-dependent inhibition of the mitochondrial respiration (up to the full inhibition) which was not induced by serum of healthy controls but that was similar to the one obtained with MCPA.

Hypoglycin A may be contained in seeds of *Acer pseudoplatanus* (maple tree; *Aceraceae*) that was consistently present in pastures of affected horses and currently, sera from European cases are being analyzed to search for MCPA-conjugates in blood. We should know soon if AM is due to the same toxin than SPM in the US.



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2. Westermann CM, de Sain-van der Velden MG, van der Kolk JH, Berger R, Wijnberg ID, Koeman JP, Wanders RJ, Lenstra JA, Testerink N, Vaandrager AB, Vianey-Saban C, Acquaviva-Bourdain C, Dorland L (2007) Acquired multiple Acyl-CoA dehydrogenase deficiency in 10 horses with atypical myopathy. *Neuromuscular Disorders* 91: 362-369. (<http://hdl.handle.net/2268/4440>)
3. Valberg SJ, Sponseller BT, Hegeman AD, Earing J, Bender JB, Martinson KL, Patterson SE, Sweetman L (2012) Seasonal Pasture Myopathy/atypical myopathy in North America associated with ingestion of Hypoglycin A within seeds of the box elder tree. *Equine Veterinary Journal*. (<http://onlinelibrary.wiley.com/doi/10.1111/j.2042-3306.2012.00684.x/pdf>)

Keywords: Horse, Myopathy, Rhabdomyolysis, Pasture, Multiple acyl-CoA dehydrogenase deficiency

MiPNetLab: BE Liege Votion DM

Labels: High-Resolution Respirometry: Oxygraph-2k, Protocol **Injuries and Adaptations:** Mitochondrial Disease; Degenerative Disease and Defect **Organism:** Other Mammal **Tissues and Cells:** Skeletal muscle **Preparations:** Permeabilized cells **Coupling states:** OXPHOS **Substrate states:** CI, CII, CI+II **Enzymes:** TCA Cycle and Matrix Dehydrogenases

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