

Mitochondrial Physiology Network



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Bioblast 2012 Conference on Mitochondrial Competence A Mitochondrial Festival in the Spirit of Gentle Science

Editors
Erich Gnaiger
Barbara Meißner
Verena Laner

Mitochondr Physiol Network 17.12

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OROBOROS INSTRUMENTS Corp. high-resolution respirometry Schöpfstr. 18
A-6020 Innsbruck, Austria erich.gnaiger@oroboros.at www.bioblast.at



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supercomplexes (respirosomes) is abnormal in some of these patients; alterations are still being explored in others.



Votion 2012 Abstract Bioblast

The cause of atypical myopathy in grazing European horses revealed.

Dominique M Votion
Equine Clinic - Faculty of Veterinary Medicine, University of Liège,
Belgium. - <u>dominique.votion@ulg.ac.be</u>

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 hypothetised. 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 <u>high-resolution respirometry</u> 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 obtain 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.

- 1. Votion D-M (2012) The story of equine atypical myopathy: a review from the beginning to a possible end. ISRN Veterinary Science 1-14.
- 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.
- 3. Valberg SJ, Sponseller BT, Hegeman AD, Earing J, Bender JB, Martinson KL, PattersonSE, 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 (in press).

