LIÈGE université
Médecine Vétérinaire

LIÈGE université

FARAH

Proceedings of the 10th FARAH-Day

Faculty of Veterinary Medicine
(University of Liège - Belgium)

December 21, 2023

One Health

L'Animal et l'Homme, une même santé

Zebrafish embryos as alternative model to study intoxication by Acer pseudoplatanus toxins: Hypoglycin A, Methylenecyclopropylglycine and Methylenecyclopropylacetate

Wouters C. P.[1], Klein B.[1], Price N.[2], Boemer F.[3], Joris M. [1,4], Voz M. L.[5], and Votion D.-M.[1]

1. Dept of Functional Sciences, Faculty of veterinary Medicine, Pharmacology and Toxicology, FARAH, ULiège,; *2. Dept of Biochemistry, University of Alberta, Edmonton, Alberta, Canada* ; *3. Biochemical Genetics Laboratory, Human Genetics, CHU, ULiège*; *4. Centre de Recherches (CRIG), Haute Ecole Libre Mosane (HELMo), Mont Saint-Martin 45, 4000 Liège Belgium* ; *5. Laboratory of Zebrafish Development and Disease Models (ZDDM), GIGA, University of Liège, Sart Tilman, 4000 Liège, Belgium*
Corresponding author: *clovis.wouters@uliege.be*

Hypoglycin A (HGA) and methylenecyclopropylglycine (MCPrG) are protoxins synthesised by plants of the *Sapindaceae* family notably *Acer pseudoplatanus. A. pseudoplatanus* poisoning is a recognised emerging pasture-associated intoxication leading to atypical myopathy (AM) in equids. Once ingested the protoxins are metabolised into toxic compounds including methylenecyclopropylacetate-CoA (MCPA-CoA) that impairs lipid metabolism and induces a severe rhabdomyolysis syndrome. Currently, there are limited laboratory models for studying AM under controlled conditions, with few existing cell culture models utilising MCPA alone. In this study, zebrafish embryos were used to evaluate the toxicity of AM protoxins (*i.e.* HGA and MCPrG) and the toxic metabolite MCPA. Zebrafish embryos of 1 day post fertilisation were individually exposed during 72 hours to several concentrations of HGA, MCPrG and MCPA. The experiment was performed in triplicate using 20 larvae per concentration, E3 medium and 3,4 dichloroaniline as negative and positive control, respectively. Every 24 hours, four endpoints based on OECD guidelines were recorded as indicator of lethality as well as sublethal effects to determine the LC_{50} and EC_{50} using a four parameters log-logistic model. Markedly, MCPrG did not induce mortality or sublethal effects, even after 72h at 5 mM. Conversely, HGA-induced toxicity appeared after 48 hours with mainly a reduced heartbeat. After 72h of intoxication, the LC_{50} and EC_{50} of MCPA were 0.98 and 1.33 µM, respectively, while those for HGA were 1.66 and 2.07 µM. This study suggests that zebrafish embryos could be used as an alternative intoxication model for studying HGA toxicity, particularly as cell culture models did not exhibit cytotoxicity with this protoxin.

Development of a Systems Immunology Approach to Explore Factors Influencing Vaccination Response in Belgian Blue Cattle

Darimont C.[1], Li S.[1], Watillon A.[1], Javaux J.[1], Pathammavong M.[1], Tang L.[2], Gualdruón Duarte JL.[2], Druet T.[2], Georges M.[2], Mayeres P.[3], Charlier C.[2], Myster F.[1], Gillet L.[1]

1.Immunology-vaccinology, Department of infectious and parasitic diseases, Veterinary public health, FARAH, ULiège, Belgium ; 2.Unit of Animal Genomics, Uliège, Belgium ; 3.Elevéo, Ciney, Belgium

Corresponding author : *celia.darimont@uliege.be*

Response to vaccination varies significantly among individuals and is influenced by various factors, including genetic and environment. In particular, persistent viruses, such as herpesviruses, appear to profoundly impact the immune response of their host. While these factors have been largely studied in humans, nothing is known in domestic animals. Here, we investigated the effect of genetics and of Bovine Herpesvirus 4 (BoHV4) infection on the responses of calves to vaccination. Briefly, 227 Belgian Blue calves, aged 1 to 6 months and housed under uniform conditions at the Ciney cattle selection center, were vaccinated against *Mannheimia haemolytica*, BRSV, BPI3, and *Clostridium perfringens* (ε and β toxins). Antibody levels were measured four weeks post-vaccination using commercial ELISA kits. BoHV-4 infection status was determined through serology and qPCR. Genotyping was conducted for all calves, and a genome-wide association study (GWAS) was performed to identify genetic factors associated with variation in the responses to vaccination. The findings unveiled significant variations, particularly in response to *Clostridium perfringens* ε and β toxins vaccination, with BoHV4-infected calves exhibiting a more robust response. Moreover, the GWAS pinpointed a specific region on chromosome 23 linked to the response to *Clostridium perfringens* ε-toxin. This region encompassed genes related to the TNF family and MHC classes I and III. Further research is essential to establish causal links between these identified factors and response to vaccination. Nevertheless, this study paves the way for a detailed understanding of immune response variability in Belgian Blue cattle.