

## Eawag Seminar Invitation

# Hunting down the eagle killer - A novel cyanobacterial neurotoxin causes a mysterious wildlife disease

Speakers **Prof Timo Niedermeyer, University of Halle-Wittenberg, Germany**

When **October 21, 16:00 – 17:00, CEST**

Where **Online via Zoom, contact [seminars@eawag.ch](mailto:seminars@eawag.ch) for access details.**

Abstract Vacuolar Myelinopathy (VM) is a fatal neurological disease characterized by widespread vacuolization in the white matter of the brain. First diagnosed in 1994 in bald eagles, it has since spread in wildlife throughout the south-eastern United States. Its cause has been unclear for many years, but recently, occurrence of VM has been linked to the cyanobacterium *Aetokthonos hydrillicola*, which grows on the leaves of the invasive aquatic plant *Hydrilla verticillata*. Cyanobacteria are known as toxin producers, thus we hypothesized that a neurotoxin from the epiphytic cyanobacterium causes VM.

Laboratory cultures of the cyanobacterium, however, did not elicit VM. Thus, colonized *H. verticillata* leaves collected at VM positive reservoirs were analyzed by mass spectrometry imaging, revealing that cyanobacteria colonies are co-localized with a pentabrominated metabolite. Supplementation of an *A. hydrillicola* lab culture with bromides resulted in pronounced biosynthesis of this metabolite. Isolation and structure elucidation revealed a structurally intriguing biindole alkaloid, which we named aetokthonotoxin (AETX). Genome sequencing of *A. hydrillicola* allowed the identification of the AETX biosynthetic gene cluster, which was subsequently confirmed by biochemical studies with recombinant enzymes. AETX is highly toxic to *C. elegans* (LC50 40 nM) and *D. rerio* (LC50 275 nM). Chickens gavaged with AETX developed characteristic brain lesions, proving that AETX is the long sought-after cause of VM.

AETX biosynthesis relies on the availability of bromide. Consequences of elevated bromide from geologic and anthropogenic sources, e.g. from chemical plant management to control *H. verticillata*, must be reassessed to avoid the use of bromide containing chemicals (e.g. the herbicide diquat dibromide). AETX is lipophilic with potential for bioaccumulation during transfer through food webs. Monitoring should be implemented for *A. hydrillicola* and AETX to protect wildlife and human health.