Is their fate phosphonate? A cryptic pathway for cell surface tailoring in human pathogen *Trypanosoma cruzi*

Eva Horáková[1], *Roberto Docampo*[2] & *Jan Janouškovec*[1,3]

[1]Institute of Microbiology, Czech Academy of Sciences, Třeboň, Czech Republic
[2]Center for Tropical and Emerging Global Diseases and Department of Cellular Biology, University of Georgia, Athens, Georgia, USA
[3]University of Southhampton, Southhampton, United Kingdom

Trypanosoma cruzi is a medically and economically important agent of human Chagas disease, with over 7 million people infected. *T. cruzi* evades host immunity by displaying glycolipids on its surface, which are crucial for host-pathogen interactions. A previously unstudied component of these glycolipids is aminoethylphosphonate (AEP), a molecule carrying the rare carbon-phosphorus bond. Discovered over six decades ago, phosphonates have long been considered biological oddities. Recent studies found phosphonates on surfaces of diverse cells from bacteria to eukaryotes, yet little is known about their physiological role. Our *in silico* searches suggest that many eukaryotic phosphonate enzymes carry mitochondrial targeting pre-sequences. It seems to be also the case in *T. cruzi* where we found a complete pathway for AEP synthesis in the mitochondrion. *T. cruzi* represents an ideal model to understand what role AEP has in surface glycolipid tailoring which is needed during the whole *T. cruzi* life cycle. Combining molecular methods such as *in situ* tagging and gene knock-out we aim to illuminate the enigmatic role of AEP which represents a promising drug target.