predominance of fatal cases in children, usually in the first 3 hours after sting, and the failure in early antivenom and supportive treatment. Multidisciplinary studies analyzing biological aspects of the causative agent, climate factors, and social economic indicators are needed to fully understand the determinants for the increase of scorpion population in urban zones and the impacts of scorpion sting envenoming for the health systems.

THE NEGLECTED TROPICAL DISEASE BURULI ULCER; TIME TO TEAM UP

Ymkje Stienstra. *University of Groningen, the Netherlands*

Buruli ulcer is a neglected tropical disease caused by a toxin produced by *Mycobacterium ulcerans*. The infection leads to ulcers, especially on the limbs. Mortality in Buruli ulcer is low, but morbidity is high. Patients with Buruli ulcer need antimicrobial treatment and wound care. The long term burden mainly consists of permanent disabilities caused by contractures, stigma and subsequent socioeconomic problems. In this presentation I will talk about the Buruli ulcer research agenda and its challenges. I will relate these challenges to the priorities in snakebite envenoming research.

LONG READS DNA SEQUENCING IN GENOMICS AND VENOM GLAND TRANSCRIPTOMICS

Vincent Viala. *Laboratório Especial de Toxinologia Aplicada, Instituto Butantan, São Paulo, Brazil*

Knowledge about the genomic organization of toxin genes is fundamental to better understand venom variation and evolution. State-of-the-art sequencing technologies, such as Illumina, generate high throughput short-reads data that allows to produce *de novo* draft genomes, as for the *Bothrops jararaca* (Serpentes:Viperidae) genome. However, it failed to generate long contiguous sequences at some multigenic toxin family *loci*. The high similarity between paralogue genes and the repetitive content of some genomic regions might be puzzling the genomic assemblers resulting in fragmented data independently from the sequencing depth. Long-reads sequencing technologies, also known as the 3rd generation of DNA sequencing, have shown the ability to overcome the issue by generating reads (> 30 kb) that span long repetitive regions. The same concept applies to transcriptomic analysis: data from short-reads can generate false-positive chimeric transcripts (i.e. mixture of sequences from distinct real mRNAs) which is the case for several multigenic toxin families. Long-reads can overcome this issue by sequencing full-length transcripts and excluding the step of assembly. In this presentation, I discuss the benefits and limitations of DNA long-reads sequencing technologies applied to the field of Toxinology. The discussion is supported with experimental data generated from the MinION sequencer of Bacterial Artificial Clones (BAC) containing ~200 kb regions of the *Bothrops jararaca* genome encoding for Snake Venom Metalloproteases (SVMP). The MinION technology generated ultra-long reads that allowed the assembly of 11 full BACs and the identification of 28 full SVMP genes. The data evidence that SVMP genes are organized in tandem clusters. 3rd generation sequencing technologies have proven to generate reads long enough (> 30 kb) to increase assembly statistics and to obtain full-length transcripts. Long-reads technologies have just emerged and some technical limitations will be quickly overcome turning it into a basic toolbox for molecular biology research.

VENOM WITHOUT GLANDS: NOVEL METHODS TO INVESTIGATE TOXIN DIVERSITY, FUNCTION AND EVOLUTION IN RIBBON WORMS (NEMERTEA)

Aida Verdes. *Departamento de Biología, Universidad Autónoma de Madrid, Spain; Department of Life Sciences, Natural History Museum of London, United Kingdom*

Nemerteans, also known as ribbon worms, are active predators characterized by an eversible proboscis used to administer venom and subdue prey. There are approximately 1,300 species, mostly marine, that belong to three lineages (Palaeonemertea, Pilidiophora and Hoplonemertea) with important differences in the proboscis morphology. Hoplonemerteans have a calcareous stylet used to stab prey and possibly inject toxins, whereas palaeonemerteans and pilidiophorans contain rod-shaped structures that might puncture prey facilitating envenomation. Investigating nemertean venom is specially challenging because they don't have distinct multicellular glands, instead, toxins are produced by secretory cells lining the body wall and the proboscis epithelium, hypothesized to have defensive and predatory roles respectively. As a consequence, there is no empirical evidence supporting these hypotheses and our knowledge on nemertean venom is very limited. To overcome these obstacles, we implemented an RNA-Seq differential gene expression (DGE) analysis to identify putative toxin genes differentially expressed in the proboscis and the body wall, and performed the first proteotranscroptomic profiling of an hoplonemertean, the species *Antarctonemertes valida*. We identified numerous putative toxins, some of them differentially expressed in the body wall, and recovered parborlysin homologs, previously only known from two heteronemertean species. We also tested the toxic mucus of the heteronemertean *Lineus longissimus* for anticancer activity. Preliminary analyses show the mucus effectively reduced the viability of two melanoma cell lines whereas it had no deleterious effects on healthy fibroblasts. Our studies indicate there is a hidden diversity of nemertean toxins and suggest that ribbon worm venoms are an untapped source of novel bioactive compounds with biomedical potential. We discuss future steps to elucidate venom delivery mechanisms and sources of toxin production and storage, illustrating the value of nemerteans as model organisms to investigate poorly-known, challenging venom systems, such as those without distinct venom glands or where venom cannot be milked.

THE ANTIPROLIFERATIVE PROFILE OF A LINEAR OCTOPUS-DERIVED PEPTIDE IN MELANOMA OF BRAF-MUTATION

Manuel A. Fernandez-Rojo, Andreas Brust, Jeremy Potriquet, Joshua Daley, Lotten Ragnarsson, Asa Andersson, Pamela Mukhopadhyay, Patrick Wilhelm, Yanni Chin, Taylor Smallwood, Richard Clark, Glenn King, Grant Ramm, Nic Waddell, Richard Lewis, Glen Boyle, Bryan Fry, Paul Alewood, Jason Mulvenna, John Miles, Maria P. Ikonomopoulou. *Madrid Institute for Advanced Studies in Food, Madrid, E28049, Spain; QIMR Berghofer MRI, Queensland, 4006, Australia; Institute for Molecular Bioscience, The University of Queensland, Queensland, 4072, Australia; School of Biomedical Sciences, The University of Queensland, Queensland, 4072, Australia; School of Biological Sciences, The University of Queensland, Queensland, 4072, Australia; James Cook University, Centre for Biodiscovery and Molecular Development of Therapeutics and Centre for Biosecurity in Tropical Infectious Diseases, Cairns, 4811, Australia*

Over 50% of melanoma patients bear BRAF mutation, prompting us to identify novel compounds with therapeutic applications against it. Here, we describe the antiproliferative profile of an octopus-derived peptide (MI1) in melanoma BRAF-mutated cells and in melanoma xenograft tumours. MI1 reduced the viability of melanoma BRAF-mutated cells of approximately 40% and had minimum effect on the neonatal foreskin fibroblasts. This was followed by an increase in reactive oxygen species while no change was observed on the mitochondrial membrane potential or cell cycle phases in melanoma cells. Interestingly, MI1 did not lead to apoptosis after 48 h. Due to the high homology of MI1 with tachykinin peptides, we examined its relationship with neurokinin receptors, but we found no obvious link with its antiproliferative capacity. Hence, to enlighten further on the mode of action of MI1 in melanoma cells, we performed in parallel proteomics and RNAseq analysis during a time-course. PI3K/AKT/mTOR pathway, a major driver of metabolism and cell proliferation, was one of the main affected signalling cascades, which was validated further by western-blotting. RNAseq also revealed alterations in other cancer, metabolic and immune-related pathways. *In vivo*, MI1 reduced the progression of melanoma-xenograft mouse tumours in comparison to the vehicle-treated mouse group. In conclusion, our results suggest that the antiproliferative profile of MI1 in melanoma of BRAF-mutation could be regulated by metabolic changes. .