

News: \$1.5 million Aus.D. Awarded for Phase I&II Antivenom Studies.

Great progress has been made in the University of Papua New Guinea (UPNG) School of Medicine and Health Sciences in the development of new antivenoms for some of the most lethal snakes in Papua New Guinea. This work was headed by Professor Teatulohi Matainaho and David J. Williams, and funded through the Australian Venom Research Unit at the University of Melbourne and UPNG. Mr. Williams is completing his Ph.D. studies with the Australian Venom Research Unit, and he has been directly overseeing the project. Mr. Williams and a UPNG student, Mr. Owen Paiva, performed most of the research. This Work has culminated to this point with a \$1,500,000 award to the University of Melbourne Australian Venom Research Unit (AVRU) and Co-Investigators Dr. K. Winkel, Mr. D. Williams and Dr. T.K. Matainaho for phase I & II clinical trials of UPNG developed antivenom! See the clinical trial application pdf here.

Mr. Paiva presented his work at the 2009 PNG Medical Symposium: # 78; “Successful Development of a New Equine Whole IgG Monovalent Antivenom for use in the Treatment of Bites by the Papuan taipan (*Oxyuranus scutellatus*)” and # 80; “A Clinical Study of Snake Bite at Port Moresby General Hospita (2006-2008): Renal Impairment, Cardiac Enzyme Release, Antivenom Efficacy and Causes of Death”. The scientific manuscript detailing this work has recently been published: PLoS Neglected Tropical Diseases: “Preclinical evaluation of caprylic acid-fractionated IgG antivenom for the treatment of taipan (*Oxyuranus scutellatus*) envenoming in Papua New Guinea”.



Papuan Taipan

Mr. Owen Paiva has been supported for his Honors and Masters projects by the ICBG. In addition, much of the work has been conducted within the UPNG BioAssay Lab that was established with Fogarty funds and maintained with ICBG support, and within the new Herpetarium that is located next to the BioAssay Lab at the School of Medicine and Health Sciences, to which some minor ICBG funds also contributed.

This AVRU work generated a new equine - whole IgG monovalent Papuan taipan antivenom that is currently in GMP production at Instituto Clodomiro Picado, San Jose, Costa Rica. The exciting lyophilized anti-venom product shows superior venom binding affinity and potency when compared to the commercial CSL Ltd. product. In addition, the new antivenom has passed preclinical assessment of neutralization of specific neurotoxic, procoagulant, myotoxic and platelet aggregating activities of venom and it is ready for clinical testing. In addition, the lyophilized Instituto Clodomiro Picado antivenom has superior stability and shelf life to the current product.



UPNG Herpetarium

Probably the most important practical issue addressed by this new antivenom is cost. The projected cost for the Instituto Clodomiro Picado antivenom is ~\$250 USD per vial. This compares favorably to the current cost of \$1,500-1,650 USD per vial for the current antivenom. In fact, the high cost of the current CSL Ltd. taipan antivenom, and its instability, limits access to this essential medicine in PNG since the National Department of Health only maintains a fraction of the stock needed to treat snake bites annually.

To quote Mr. Williams: “In the Australasian region, southern PNG has some of the highest localised snakebite incidence rates in the world (up to 526-562 per 100,000 per year). Papuan taipans (*Oxyuranus scutellatus*) cause more than 90% of all cases of envenoming admitted to Port Moresby General Hospital (PMGH), including 60% of all ventilator bed-days. This high injury burden reflects the fact that envenoming by this snake is very common throughout southern PNG. Taipans thrive on in rural areas cleared for farming, oil palm, cassava, and village gardens, and even in peri-urban areas of Port Moresby. Envenoming produces consumption coagulopathy, bleeding, irreversible presynaptic neurotoxicity, myotoxicity, arrhythmias and acute kidney injury. Case fatality rates as high as 14.6% for adults and 25.9% for children have been reported at PMGH. Early antivenom administration is critical in preventing potentially fatal paralysis; patients who receive antivenom late (>4 hours post-bite) have a significantly increased risk of airway compromise and respiratory failure, requiring intubation and ventilation. Only 13.3% of patients given antivenom within 4 hours post-bite subsequently developed severe paralysis necessitating intubation, whereas 26.8% of those treated up to 6 hours post-bite, and 63% treated more than 6 hours post-bite, required ventilation. All patients treated within 6 hours post-bite survived, whereas 7.8% of patients treated more than 6 hours post-bite died.”

This isn't all, either. Mr. Williams and Mr. Paiva are working on a similar antivenom for the Small Eyed snake (*Micropechis ikaheka*). This antivenom will soon be ready for production. The success of the Taipan work has led other ICBG supported student projects to focus on venom research as well. Rosemary Benjamin completed her Honors project studying snake venom phospholipase A₂. Julius L Jacobs is currently comparing venom components between closely related Australian and New Guinean snakes.

Congratulations to Professor Matainaho, Dave Williams, Owen Paiva, the AVRU and their colleagues at Instituto Clodomiro Picado for successfully addressing some of the most important neglected diseases in PNG. From the ICBG's perspective, this is clear evidence that student training and infrastructure building can contribute to unanticipated breakthroughs.



Owen Paiva (seated) and Lothe Stanley in the FIRCA BioAssay Lab