A JOURNEY OF INTERNATIONAL COLLABORATIONS TO UNDERSTAND DENGUE INFECTIONS

Aruna Dharshan De Silva
Director - KDU CARE, Department of Paraclinical Sciences,
Faculty of Medicine, General Sir John Kotelawala Defence University, Sri Lanka
dslv90@yahoo.com

Dengue infections have been common in Sri Lankan since 1989 when the first epidemic of >1200 cases, was reported by the Ministry of Health (MoH). My work in dengue began after I returned to Sri Lanka in 2007 and oversaw the laboratory component of the Pediatric Dengue Surveillance project in collaboration with the MoH. Then in collaboration with Prof Alex Sette and Prof Aravinda de Silva of the US, a National Institutes of Health (NIH)- USA, funded project was initiated to expand the knowledge of the human T cell response against dengue in the context of the larger immune response. Lymphocytes being discarded from blood donors at the National Blood Bank, Sri Lanka, were used after ethical review committee and MoH approvals to identify possible new epitopes in the context of the Sri Lankan population. The lymphocytes were screened for past dengue infections and used to validate the 8000+ potential peptide pool generated using bioinformatics. Validating the peptides by testing lymphocytes from past dengue infected blood donors added ~300 new dengue T cell epitope peptides to the literature. One major discovery highlighted the importance of the dengue non-structural proteins in the T cell immune response against dengue infections. This new pool of peptides has been used to study the immune responses being generated by new dengue vaccines. Our data suggest that the non-structural (NS) proteins of dengue are largely responsible for the human T cell response and this may explain the lack of protection in the recently WHO approved Dengvaxia dengue vaccine, which lacks the dengue NS proteins. Furthermore, our data show that the immune response from the yet to be approved NIH/Butantan vaccine is similar to the natural infection and may provide better protection. In addition, this international project has helped understand the role of T cells in the overall human immune response in controlling a dengue infection.