

A genome-based study of the habu snake *Protobothrops flavoviridis* reveals an extensive alternative splicing of mRNA to produce highly divergent venom proteins

Speaker: Dr. Tomohisa Ogawa
Tohoku University



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Snake venoms are complex protein mixtures encoded by various gene families that function synergistically to incapacitate the prey. A genome-wide survey of the repertoire and molecular mechanisms of highly divergent venom proteins including decoded approximately 1.8-Gb genome of the *Protobothrops flavoviridis* and the high-throughput Iso-Seq transcriptomic analyses of the venom gland revealed the extensive alternative splicing in the production of venom mRNA variants in addition to the accelerated evolution of venom-related genes. For example, the genome of the habu *Protobothrops flavoviridis* contains 11 genes that encode venom metalloproteinase (*svMP01* to *svMP11*) consist of 13 to 17 exons depending on members. Transcriptome analysis including Iso-Seq reads identified a total 55 transcriptome variants of *svMP*. Furthermore, we analyzed the molecular functions of disintegrin and Cys-rich domains of svMPs such as integrin adhesion activities and the effects on cell migration and invasion. Our results indicate a great contribution of alternative splicing in the production of transcript variants of the habu snake venom genes and their unique diverse activities.

All Welcome

Correspondence: Marine Genomics Unit, OIST

Tel: (098) 966-8653

POC: Koki Nishitsuji / koki.nishitsuji@oist.jp