DURIAN: a brain-specific secreted peptide impacting behaviour

Grace GOH1, Pui Mun WONG1, Marta GARCIA-MIRALLES2, Mahmoud POULADI2, Lena HO1, Bruno REVERSADE1

1 Institute of Medical Biology, A*STAR, Singapore, 2 Translational Laboratory in Genetic Medicine, National University of Singapore/A*STAR, Singapore

Introduction

In recent years, several groups including our lab have reported long non-coding RNAs (lncRNAs) that encode biologically active short peptides smaller than 100 residues (e.g. ELABELA1 and Myoregulin2). Here, we report that an annotated lncRNA containing a putative open reading frame produces in fact a secreted peptide of less than 80 residues, which is conserved in all vertebrates species. To understand the physiological function of this peptide, which we named DURIAN, we developed gain-of-function assays in Xenopus embryos, and generated DURIAN-null mice. Our first results point towards a neuro-modulatory role for DURIAN, with implications in anxiety-like phenotypes and motor performance.

DURIAN is a highly conserved secreted peptide

Transfected 293T cells express and secrete DURIAN protein recognized by a custom antibody with no apparent cleavage of a signal peptide. Secretion of overexpressed DURIAN protein is inhibited by Brefeldin A (BFA) in dissociated Xenopus embryos, indicating that DURIAN undergoes Golgi-mediated trafficking and secretion.

Expression of endogenous durian in Xenopus

Durian developmental qPCR

qPCR analysis indicates that durian transcripts are expressed in the early embryonic development and the late tailbud stages. Wholemount in situ hybridization reveals restricted durian expression in the spinal cord and CNS (red arrows) at stage 28.

References


Conclusions

• DURIAN is a novel and conserved secreted peptide that is translated from a transcript annotated as a lncRNA.
• The phenotypes exhibited in Xenopus and mouse assays indicate a neuro-modulatory role of DURIAN, possibly involving serotonergic or GABA-ergic signaling4.
• Our current efforts aim to identify DURIAN’s cell surface receptor(s), establish its molecular and physiological function, and possible clinical indications.