Junior Science Communications
Faculty of Applied Sciences, UiTM Shah Alam
https://journal.uitm.edu.my/ojs/index.php/JSC

E-ISSN 2637-0689
Vol 64 2026

Colloquium on Applied Sciences 2 2025
7-12 July 2025, Faculty of Applied Sciences, UiTM Shah Alam, Malaysia

Structural Conservation of Hypertrophic Cardiomyopathy Associated Proteins in Zebrafish as a Model for Human Heart Disease

Nur A'in Farhana Hairil Azwar, Norfatimah Mohamed Yunus

Structured Abstract

Background: Hypertrophic cardiomyopathy (HCM) is the most common inherited cardiac disorder, typically caused by mutations in genes encoding sarcomeric proteins responsible for force generation and contraction in the heart. While the genetic basis of HCM is well established in humans, understanding the conservation and functional relevance of these genes across model organisms remains a challenge. Zebrafish (*Danio rerio*) are increasingly used as a cardiovascular model due to their conserved heart structure, rapid development, and amenability to genetic studies. Evaluating which human HCM-associated genes are functionally conserved in zebrafish is crucial for leveraging this model in mechanistic and translational studies**.**

Methods: To assess cross-species conservation at the structural level, three core sarcomeric proteins, MYBPC3, MYH7, and TTN, were analyzed for comparative domain architecture between humans and zebrafish. Protein domain arrangements were schematically illustrated, highlighting the presence, absence, or positional shifts of functional domains. For MYBPC3, modular architecture including tri-helix bundles (THB), immunoglobulin-like (Ig) repeats, and fibronectin type III (FN3) domains were compared. MYH7 domains, including SH3, myosin head, and tail regions, were assessed for sequence and positional conservation. For TTN, only a representative portion of the protein was analyzed, focusing on Ig-like and FN3 repeats, the central PEVK region, and the C-terminal protein kinase (PK) domain. This approach enabled a clear visualization of structural conservation and divergence between species.

Results: Analysis revealed that MYH7 domains were highly conserved between humans and zebrafish, reflecting strong structural preservation of this core contractile protein. MYBPC3 showed modular conservation with slight positional shifts in THB and FN3 domains, suggesting functional conservation despite minor differences. TTN exhibited partial representation of Ig-like repeats and FN3 domains, as well as the PEVK and PK regions, indicating conserved structural elements within an otherwise highly repetitive protein.

Conclusion: Comparative domain analysis of key sarcomeric proteins demonstrates that zebrafish orthologs retain essential structural features necessary for sarcomere function. These findings support the use of zebrafish as a functional model to study HCM-related genes and provide a framework for further mechanistic studies of cardiac contractile proteins.

Keywords: Hypertrophic cardiomyopathy, Zebrafish ortholog, Sarcomere, Protein domain architecture, Comparative genomics.

*Correspondence: fatim423@uitm.edu.my

[a] School of Biology, Faculty of Applied Sciences, Universiti Teknologi MARA, Shah Alam, Malaysia