

Deciphering the Role of RNA-Binding Proteins in Human Cardiac Development and Diseases

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Abstract

Sarcomeres are fundamental to cardiac muscle contraction. Their impairment can elicit cardiomyopathies, leading causes of death worldwide. However, the molecular mechanism underlying sarcomere assembly remains obscure.

Apart from the scaffold proteins that assemble into the building blocks of sarcomeres, the sarcomere assembly process is modulated by multiple regulatory factors, such as RNA-binding proteins (RBPs) and molecular chaperones. Our previous study demonstrated that the RBP RBM24 mediates alternative splicing of core myofibrillogenesis genes in a stage-specific manner and that ACTN2 interacts with the N-terminus of TTN (TTN-N), allowing MYH6 to bind the C-terminus of TTN (TTN-C). Notably, our unpublished data suggests that RBM24 may play a role in cardiomyocyte maturation by regulating the expression of a novel long non-coding RNA, LINC C.

In summary, our research leveraged human pluripotent stem cell (hPSC)-derived cardiomyocytes (CMs) to unveil the stepwise spatiotemporal regulation of core cardiac myofibrillogenesis-associated proteins. Furthermore, we discovered a novel regulator, LINC C, which potentially participates in cardiac maturation. This investigation holds the promise of shedding light on the potential applications of hPSC-CMs in cell therapeutics.