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GROWTH AND DEVELOPMENT

Poly(A) tail-based regulation of cardiac hypertrophy

Protein synthesis in the heart is a dynamic process, characterized by low synthesis rates in the adult heart that can increase substantially in periods of hypertrophy; however the regulatory mechanisms involved are unclear. New research now reveals that the dynamic regulation of *PABPC1* translation, via changes in its poly(A) tail length, modulates global protein synthesis during postnatal heart development and in response to hypertrophic triggers such as endurance exercise and heart disease.

Poly(A)-binding protein 1 (PABPC1) promotes mRNA translation by binding to the poly(A) tail, a sequence of 250–300 adenosine residues that contribute to mRNA stability and translational regulation. Chorghade *et al.* found that PABPC1 protein, but not mRNA, was absent in adult human and mouse hearts. Suppression of *PABPC1* translation was mediated by shortening of its poly(A) tail, and led to reduced global protein synthesis rates. Notably, *PABPC1* poly(A) tail length and translation were partially restored during hypertrophy triggered by endurance exercise or thoracic aortic constriction in mice. "These findings provide an example of poly(A) tail-based regulation in a physiological context at a time when the field is debating whether poly(A) tail length of specific transcripts matters," explain authors Sandip Chorghade, Joseph Seimetz, and Auinash Kalsotra.

The researchers further showed that cardiomyocyte-specific upregulation of PABPC1 induced global protein synthesis and physiological hypertrophy in adult mice. "We are excited to pursue the therapeutic potential of targeting PABPC1 in promoting healthy cardiac growth and preventing disease," comment Seimetz and Kalsotra.

Irene Fernández-Ruiz

> "upregulation of PABPC1 induced global protein synthesis and physiological hypertrophy in adult mice"

ORIGINAL ARTICLE Chorghade, S. *et al.* Poly(A) tail length regulates PABPC1 expression to tune translation in the heart. *eLife* **6**, e24139 (2017)
FURTHER READING Henning, R. H. & Brundel, B. J. J.M. Proteostasis in cardiac health and disease. *Nat. Rev. Cardiol.* http://dx.doi.org/10.1038/nrcardio.2017.89 (2017)