Mechanistic investigation of Linc-p27 function in skeletal muscle satellite cell and muscle regeneration

Abstract: Skeletal muscle allows voluntary movement and plays a key role in regulating metabolism and homeostasis in the organism. Meanwhile it has a remarkable ability to regenerate after injury thus provides an excellent model to study tissue regeneration. Muscle regeneration relies on its resident muscle stem cells (also called satellite cells, SCs) which normally lie quiescently beneath muscle fiber. SCs can quickly activate and proliferate following injury, then differentiate and fuse into myofiber; meanwhile a subset of SCs undergoes self-renewal and returns to quiescent state to replenish the adult stem cell pool. Each state of the myogenic lineage progression is orchestrated by complex regulatory networks of intrinsic and extrinsic factors/mechanisms. Disruption of the regulations may render their loss of ability to regenerate, contributing to muscle wasting conditions such as muscular dystrophy, cachexia, and sarcopenia that are prevalent in our society. As a recently discovered family of cellular regulators, long noncoding RNAs (>200nt non-protein coding RNAs, lncRNAs) are remarkably powerful, flexible, and pervasive in controlling major biological processes. Despite efforts from our groups and others in the past few years, our understanding of lncRNA participation in SC activities remains largely elusive. Here in this study we investigate the function of a previously uncharacterized lncRNA, *Linc-p27* in promoting myogenic lineage progression. *Linc-p27* is induced during SC activation/proliferation. Subsequent loss- and gain-of-function assays demonstrated a potential role of *Linc-p27* in promoting SC activation and proliferation. Mechanistic elucidation revealed it binds with RNA helicase Dhx36 and facilitates mRNA translation by unwinding 5'UTR quadruplex (rG4) structures. Together, our study uncovers *Linc-p27* as a novel regulator of SC function and muscle regeneration; it enhances our knowledge foundation in the intrinsic regulatory mechanisms underlying skeletal muscle regeneration for future therapeutic development of treating muscle damages and diseases.