CENTER FOR RNA BIOMEDICINE

RNA Innovation Seminar

Monday, November 19th at 3:00pm
ABC Seminar rooms, Biomedical Research Science Building (BSRB), 109 Zina Pitcher

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"Dual Leucine Zipper Kinase: Elucidating the local role of a major player of axon regeneration"

Abstract: Axons spontaneously regenerate following injury in the adult mammalian peripheral nervous system (PNS), but fail to do so in the central nervous system (CNS). This dichotomy stems from both extrinsic and intrinsic factors, that either aid in or block regeneration. Through manipulation of these factors, axons of the CNS can be coaxed to regenerate. A classical way to do this is through a conditioning injury (CI) of dorsal root ganglion (DRG) sensory neurons. DRG neurons feature two axons one projecting peripherally, the other centrally including axons in the dorsal columns of the spinal cord. Injury to the sciatic nerve prior to injury of the dorsal columns will enhance regeneration of dorsal column axons. The CI stimulates an intrinsic growth response in DRG neurons and this can be observed in primary sensory DRG neuron cultures. . An important regulator of this response is the dual leucine zipper kinase (DLK), a member of the map kinase family (MAP3K12). DLK protein levels rapidly increase in axotomized DRG axons and form a retrograde signaling complex that leads to increased transcription of regeneration-associated genes. However, it is not well understood how DLK is regulated at the axon after injury. Here, we show that DLK mRNA is transported to CI cultured DRG axons and this is through its 5' untranslated region (UTR). Two DLK splice variants have been detected that differ in their 5'UTR. One of the two 5'UTR variants is preferentially regulated in the axon and we have evidence that DLK can be translated locally within axons. We suspect that local translation of DLK is a key component of its function and ultimately the successful regeneration response in injured peripheral nerves.