Nature Reviews Neuroscience | AOP, published online 15 August 2007; doi:10.1038/nrn2219

AXONAL TRANSPORT

SUMmOned back to the nucleus

DOI:
10.1038/nrn2219

Over the past few years a crucial role for local protein translation in axon guidance and synaptic plasticity has emerged. However, relatively little is known about how the translation machinery is targeted to axons and dendrites or how it is regulated. La (also known as Sjogren syndrome antigen B (SSB)) is an RNA-binding protein that associates with mRNAs and small (non-coding) RNAs, protecting them from exonucleases and thus aiding translation. Twiss and colleagues have found that La undergoes anterograde transport to distal neuronal processes, where many of its target mRNAs are localized, and that addition of small ubiquitin-like modifying polypeptide (SUMO) is required for retrograde transport back to the cell body.

In this study, the authors used immunofluorescence and immunoprecipitates from lysates prepared from the axons of dorsal root ganglion (DRG) neurons to show that endogenous sumoylated La interacts with the retrograde microtubule motor protein dynein, but not with the anterograde motor protein kinesin. In agreement with these findings, mutant La–green fluorescent protein (GFP) fusion contructs in which high-probability sumoylation sites had been mutated to arginine (K41R, K185R and/or K208R) did not co-precipitate with dynein, indicating that sumoylation is required for La's interaction with this motor protein. Furthermore, live cell imaging of transfected DRG neurons showed that mutant La–GFP moved only in an anterograde direction (and accumulated in distal processes), whereas wild-type La-GFP moved bidirectionally.

BANANASTOCK

To determine whether sumoylation regulates La retrograde transport *in vivo*, the authors carried out sciatic nerve ligations in adult rats, thereby blocking both anterograde and retrograde transport within the nerve. They found that, indeed, sumoylated La accumulated distal to the ligation site, as its transport back to the cell body was interrupted. These results suggest that sumoylation targets La for nuclear transport and, possibly, recycling.

Sumoylation was originally thought to target only nuclear proteins, but a growing number of substrates have been found in the cytoplasm and the plasma membrane, suggesting that it has wider-ranging actions. In neurons, sumoylation of ion channels, neurotransmitter receptors and transcription factors has been shown to control neuronal excitability, synaptic function and differentiation, respectively. Relatively few RNA-binding proteins have been shown to undergo sumoylation, but this study suggests that, by modifying their protein–protein interactions and changing the directionality of transport, sumoylation could constitute a major regulatory mechanism of local translation in axons.

Monica Hoyos Flight

ORIGINAL RESEARCH PAPER van Niekerk, E. A. *et al.* Sumoylation in axons triggers retrograde transport of the RNA binding protein La. *Proc. Natl Acad. Sci. USA* **104**, 12913–12918 (2007)