Journal and Proceedings of the Royal Society of New South Wales, vol. 145, nos. 443 & 444, pp. 97-98.
ISSN 0035-9173/12/010097-2

Thesis abstract

Investigation into the molecular function of the neuronal Hu RNA binding protein, HuCsv1

Peter McCarthy

Abstract of a thesis for a Doctorate of Philosophy submitted to the University of Adelaide, Adelaide, South Australia

Of the four Hu genes found in most vertebrates (HuA, HuB, HuC and HuD), all except HuA exhibit mRNA and protein expression that is essentially restricted to post-mitotic neurons of the developing and adult nervous systems. Spatial and temporal examination of individual "neuronal Hu" (nHu = HuB, HuC and HuD) proteins in brain tissue suggests nHu proteins may play a functional role during neuronal differentiation; as RNA-binding proteins, the nHu proteins may participate in gene regulatory events that are essential for acquisition of the neuronal phenotype.

We have identified a number of candidate mRNA targets of the nHu proteins. Our data suggest that the majority of these mRNAs interact with nHu proteins through sequences present in their 3' untranslated regions (UTRs). From this 3'UTR target subset, several mRNAs were selected for further examination based on reported roles for their encoded proteins during axonogenesis, a critical developmental process during which nascent neurons grow and extend axons that eventually connect to and form synaptic connections with other neurons. The mRNAs chosen encode for cytoskeleton-modifying proteins; Cofilin, Vasodilator-Stimulated Phosphoprotein (VASP) and the Rho GTPase Cdc42.

The primary aim of the work reported in this thesis was to characterise the effect of interactions between the neuronal Hu protein HuC, and the CLIP-identified 3'UTRs listed above. To do this, the 3'UTR sequences were cloned into reporter vectors (both fluorescent and luciferase reporter-based) to produce reporter protein-encoding messages that included a putative target 3'UTR. These vectors were then used in co-transfection experiments with or without HuC and measurements of reporter protein and mRNA abundance obtained. Interestingly, despite initial speculation that HuC might be involved in directly regulating protein expression from target mRNAs, no significant effect of HuC on protein production from any of the 3'UTR-reporter mRNAs tested was observed. However and quite unexpectedly, measurement of 3'UTR-reporter mRNA abundance from co-

transfection assays revealed a potential role for HuC in modulating alternative polyadenylation site choice for one of the CLIP-identified 3'UTR sequences. Regulation of mRNA polyadenylation site choice may be a novel mechanism by which nHu proteins post-transcriptionally control gene expression during neuronal development.

Dr Peter McCarthy,
School of Molecular & Biomedical Science,
University of Adelaide,
Adelaide SA 5005
AUSTRALIA

E-mail: peter.mccarthy@adelaide.edu.au