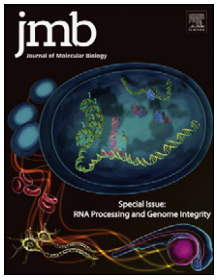

Molecular Regulation of Alternative Polyadenylation (APA) within the *Drosophila* Nervous System

Raul Vallejos Baier, Joao Picao-Osorio and Claudio R. Alonso

Sussex Neuroscience, *School of Life Sciences, University of Sussex, Brighton BN1 9QG, UK*

Correspondence to Claudio R. Alonso: *c.alonso@sussex.ac.uk*
http://dx.doi.org/10.1016/j.jmb.2017.03.028
Edited by Lori A Passmore

Abstract

Alternative polyadenylation (APA) is a widespread gene regulatory mechanism that generates mRNAs with different 3′-ends, allowing them to interact with different sets of RNA regulators such as microRNAs and RNA-binding proteins. Recent studies have shown that during development, neural tissues produce mRNAs with particularly long 3′UTRs, suggesting that such extensions might be important for neural development and function. Despite this, the mechanisms underlying neural APA are not well understood. Here, we investigate this problem within the *Drosophila* nervous system, focusing on the roles played by general cleavage and polyadenylation factors (CPA factors). In particular, we examine the model that modulations in CPA factor concentration may affect APA during development. For this, we first analyse the expression of the *Drosophila* orthologues of all mammalian CPA factors and note that their expression decreases during embryogenesis. In contrast to this global developmental decrease in CPA factor expression, we see that cleavage factor I (CFI) expression is actually elevated in the late embryonic central nervous system, suggesting that CFI might play a special role in neural tissues. To test this, we use the UAS/Gal4 system to deplete CFI proteins from neural tissue and observe that in this condition, multiple genes switch their APA patterns, demonstrating a role of CFI in APA control during *Drosophila* neural development. Furthermore, analysis of genes with 3′UTR extensions of different length leads us to suggest a novel relation between 3′UTR length and sensitivity to CPA factor expression. Our work thus contributes to the understanding of the mechanisms of APA control within the developing central nervous system.

© 2017 The Authors. Published by Elsevier Ltd. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/).

Introduction

Alternative polyadenylation (APA) is an RNA processing mechanism that leads to the generation of mRNA forms bearing different 3′ untranslated regions (3′UTRs; Fig. 1a) [1–3]. APA is a very prevalent mechanism that affects the majority of genes in a wide variety of metazoans including mammals and insects. Given that 3′UTR sequence composition and structure determine the nature of physical interactions between mRNAs and RNA modulators such as microRNAs (miRNAs) and RNA-binding proteins (RBPs), APA-dependent variations in 3′UTR length and composition are thought to have a significant impact on mRNA dynamics within the cell through effects on mRNA degradation, localisation, and translation (Fig. 1a) [4,5]. Accurate control of APA patterns may therefore be critical to the organism, particularly within the physiological context of animal development when gene activity must be closely coordinated with complex cell patterning and differentiation processes.

The end point of a given mRNA is determined by two concerted biochemical reactions that involve the endonucleolytic cleavage of the RNA transcript 3′ end and the concomitant synthesis of a string of adenosine nucleotides (poly-adenylation) on the free 3′ terminus [1]. These reactions are commonly referred to as the process of cleavage and polyadenylation (CPA), which is controlled by a multiprotein complex composed of CPA factors [6–8]. The definition of the site for CPA [i.e., the polyadenylation site (PAS)] is achieved through contacts of the CPAs with specific *cis*-elements present in the RNA

0022-2836/© 2017 The Authors. Published by Elsevier Ltd. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/).

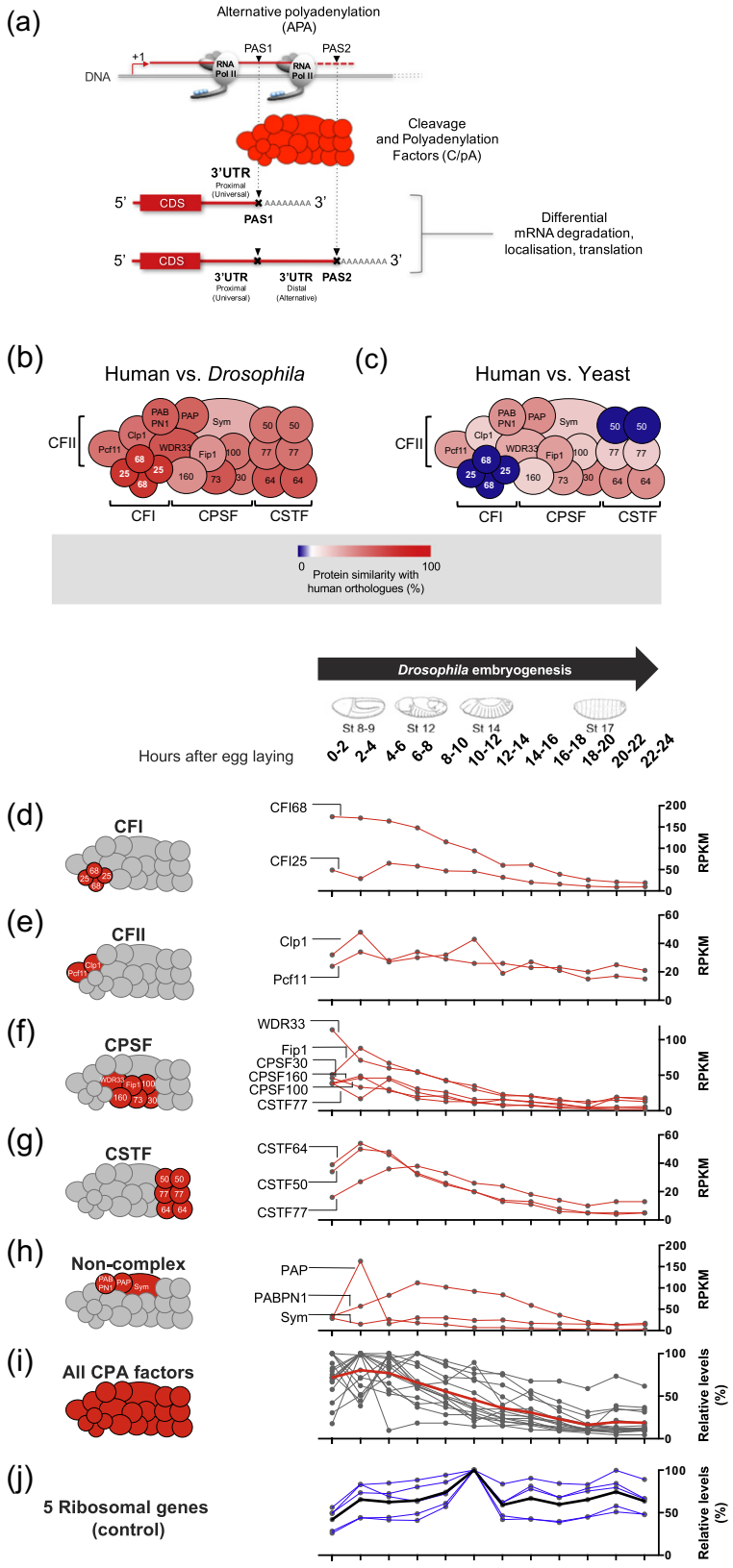

Fig. 1. (*legend on next page*)

Download English Version:

https://daneshyari.com/en/article/5533108

Download Persian Version:

https://daneshyari.com/article/5533108

Daneshyari.com