Similar but Not the Same, the Fission Yeast Processing Bodies

Abstract

Processing bodies (P-bodies) are cytoplasmic RNA granules containing the Dcp1-Dcp2 decapping-enzymes where mRNA decay can occur. We have used the fission yeast Schizosaccharomyces pombe as a model system to study their structures and compositions. Because several components of P-bodies, such as the decapping enzyme and its co-activators, are found in both yeast and mammalian cells, it is believed that P-bodies are evolutionarily conserved among eukaryotes. However, we found that species diversity has developed; the protein compositions and underlying molecular mechanisms for their function can be distinct between species. These results led us to suggest that the whole complex including the decapping enzyme and its co-activators might have coevolved together and acquired additional proteins and different mechanisms for their function highlighting the importance of cross-species studies of this sort. Furthermore, we found that, although predominantly present in the cytoplasm, components of P-bodies also function in the nucleus. A function of Pdc2, the fission yeast ortholog of Pat1 protein, and the decapping enzyme Dcp1-Dcp2 function together with the 5'-3' exonuclease Dhp1 in the nucleus to regulate lincRNA by promoting its decapping/destruction was suggested.

Keywords: Fission Yeast; Decapping; P-bodies

Mini Review

Cytoplasmic processing bodies (P-bodies) are RNA protein granules containing un translating mRNAs complexes with a set of translation repressors, the mRNA decapping machinery Dcp1-Dcp2 and the 5'-3' exonuclease Xrn1 where mRNA decay can occur and have merged as important sub cellular structures that are involved in mRNA metabolism. Although components of P-bodies have been described in Schizosaccharomyces pombe, a detailed description of P-bodies is still lacking. To this end, we have initiated a study to characterize the fission yeast P-bodies and several interesting aspects with regard to the protein composition between different species and underlying molecular mechanisms for their function were identified (Figure 1) [1,2]. Because of its importance, several model systems have been applied to study the structure of P-bodies, and studies in the budding yeast Saccharomyces cerevisiae have been crucial in unravelling P-body biology. However, there is a clear difference in terms of the decapping proteins presence in different organisms. In yeast, the catalytic subunit of decapping enzyme Dcp2 interacts directly with its cofactor Dcp1 [3]. This complex has low intrinsic decapping activity and requires additional proteins including the enhancer of decapping 1-3 (Edc1-3), the heptametrical Lsm1-7 complex, the DExH/D-box RNA heli case 1 (Dhh1, RCK/p54 in mammals) and Pat1 for its full activity. All of these proteins concentrate in P-bodies and function differentially in activating decapping [4].

In metazoans, Dcp1 and Dcp2 form direct but weak interactions that are facilitated by the decapping activator Edc4 (also known as Ge-1 or Hedls, Human enhancer of decapping large subunit) [5]. Edc4 is required for Dcp1-Dcp2 catalytic activity [6], which is not present in S. cerevisiae, indicating that species diversity has developed. The different protein composition of P-bodies between different species was highlighted by our recent study with the identification of the fission yeast Pdc1 (partner of decapping enzyme protein 1) as the functional homologue of Edc4 [1], a third component of the decapping enzymes that is thought to be absent from fungi. Pdc1 forms a complex with Dcp2. Similar to Edc4, Pdc1 is an enhancer of decapping and plays a vital role in the formation of P-bodies. The protein composition and structure organization of fission yeast P-bodies is therefore more closely related to high eukaryote than that of S. cerevisiae, making S. pombe an ideal model for studying P-body biology. Intriguingly, our studies of characterization of Pdc2 (partner of decapping enzyme protein 2), the fission yeast ortholog of Pat1 protein complexing with Lsm1-7 to couple deadenylation and decapping, further reveal that even though species sharing similar protein composition, the underlying molecular mechanisms for their function can be distinct [10]. Pat1 was first identified as a protein associated with topoisomerase II [7]. Since then, no other studies have focused on this nuclear function. Rather, Pat1 has been reported to play important roles in translational control and mRNA decay [8]. It has been suggested that, in addition to facilitate decapping, S. cerevisiae Pat1 seems to play additional roles at earlier steps involving translational repression and mRNA rearrangement that set the stage for decapping [4]. Translational repression activity has also been noted for Pat1 homolog’s in Xenopus but in human [8,9]. It is of interest to note that, as in the case of Pdc1, we found that the role of Pdc2 is similar to the Pat1 homolog in human but not in S. cerevisiae, which appears to be involved
In different species, the requirement of Pat1 proteins plays a role in P-body formation. Consistent with the proposed model, deadenylation in the assembly of P-bodies diverged, too. While Pat1 proteins only have minor role in the assembly of P-bodies, we found that Pdc2 interacts with the nuclear 5′-3′ exonuclease Dhp1, the ortholog of budding yeast Rat1 protein, and may function together with the decapping enzyme Dcp1-Dcp2 to regulate long non-coding RNA (lncRNA) in the nucleus. At present, the biological functions of the lncRNAs regulated by Pdc2 remain unclear as most of them located between previously uncharacterized-genes that required further attention. Regardless of this, our study adds significantly to the versatility and complexity of the pathway and the mechanism in which decapping enzyme and its co-activators participated.

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Conflict of Interest

The author declares that he have no conflict of interest.

References

