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REVIEW

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Regulation of processing bodies: From viruses to cancer epigenetic machinery

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Abstract

Processing bodies (PBs) are 100–300 nm cytoplasmic messenger ribonucleoprotein particle (mRNP) granules that regulate eukaryotic gene expression. These cytoplasmic compartments harbor messenger RNAs (mRNAs) and several proteins involved in mRNA decay, microRNA silencing, nonsense-mediated mRNA decay, and splicing. Though membrane-less, PB structures are maintained by RNA-protein and protein-protein interactions. PB proteins have intrinsically disordered regions and low complexity domains, which account for its liquid to liquid phase separation. In addition to being dynamic and actively involved in the exchange of materials with other mRNPs and organelles, they undergo changes on various cellular cues and environmental stresses, including viral infections. Interestingly, several PB proteins are individually implicated in cancer development, and no study has addressed the effects on PB dynamics after epigenetic modifications of cancer-associated PB genes. In the current review, we summarize modulations undergone by P bodies or P body components upon viral infections. Furthermore, we discuss the selective and widely investigated PB proteins that undergo methylation changes in cancer and their potential as biomarkers.

KEYWORDS
biomarker, cancer, epigenetics, methylation, processing-body, stress granules

1 | INTRODUCTION

Eukaryotic cellular RNA statis involves sequestering of messenger RNAs (mRNAs) into larger RNA granules called messenger ribonucleoprotein particles (mRNPs). mRNPs are nonmembranous bodies present in both the nucleus and cytoplasm and contain RNA binding proteins (Tauber et al., 2020). Nuclear RNA granules include nucleolus, Cajal bodies, histone locus bodies, and para-speckles, whereas cytoplasmic RNA granules include processing bodies (PBs), stress granules (SGs), and neuronal granules (Buchan & Parker, 2009; Thomas et al., 2011). PBs are 100–300 nm and were first identified as XRN1 (5′-3′ exoribonuclease 1) foci due to the presence of exoribonuclease XRN1 (Yang et al., 2004). Further studies revealed that it is rich in RNA decay machineries, such as decapping enzymes DCP1 (mRNA-decapping enzyme 1)/DCP2 (mRNA-decapping enzyme 2) and decapping activators Hedls, Edc3, Pat1, LSm1–7, and RCK (Rock-N-Rollers-DNA helicase). Hence, it was featured as an mRNA degrading complex (Anderson & Roche, 2015). Eventually, its functions have been associated with nonsense-mediated mRNA decay (Durand et al., 2007; Merai et al., 2012) and RNA interference (RNAi; Eulalio et al., 2008). Additionally, they are rich in argonautes, translation regulating factors, such as eIF4E (eukaryotic translation initiation factor 4E), the translational silencer/RNA helicase p54/RCK, and GW body component GW182 (glycine-tryptophan protein of 182 kDa; Zhang & Herman, 2020).

Abbreviations: Ago1, argonaute RISC component 1; APOBEC3G, apolipoprotein B mRNA editing enzyme catalytic subunit 3G; CPEB1, cytoplasmic polyadenylation element-binding protein 1; KSHV, Kaposi's sarcoma-associated herpes virus; mRNP, messenger ribonucleoprotein; P body, processing body; RISC, RNA induces silencing complex; SG, stress granules; TNRC6B, trinucleotide repeat-containing gene 6B; TOB1, transducer of ERBB2; TTP, tristetraprolin; XRN1, 5′-3′ exoribonuclease 1; ZAR1, Human zygote arrest 1.

