MECHANISM AND REGULATION OF NONSENSE-MEDIATED MRNA DECAY (NMD), AN ESSENTIAL QUALITY CONTROL SYSTEM OF PLANTS

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In eukaryotic cell, various quality control mechanisms have evolved to ensure that only perfect mRNAs could be translated. Nonsense-mediated mRNA decay (NMD) is a quality control system that identifies and eliminates mRNAs containing premature termination codons, thereby preventing the accumulation of potentially harmful truncated proteins. While NMD is well-characterized in yeast, in invertebrates and in mammals, plant NMD is poorly understood. In yeast and in invertebrates unusually long 3'untranslated regions (3'UTRs) render an mRNA subject to NMD, while in mammals' 3'UTR located introns trigger NMD. UPF1, 2 and 3 are the key trans-acting NMD factors in yeast as well as in animals. However, in mammals, the core components of the Exon Junction Complex (Mago, Y14, eIF4A3 and MLN51) are also required for NMD. It was proposed that long 3'UTR-induced NMD is the ancient type and that it was changed to a more complex intron-based NMD in mammals. To better understand the evolution of eukaryotic NMD systems, we have studied the NMD machinery of plants, as plants are outgroup relative to fungi and animals. We have elaborated various transient assays to analyze plant NMD. Using these assays we defined the cis elements of plant NMD and characterized several trans-acting plant NMD factors. We demonstrated that two plant NMD pathways co-exist, one pathway, as yeast or invertebrate NMD systems, eliminates mRNAs with long 3'UTRs, while a distinct pathway, like mammalian NMD, degrades mRNAs harbouring 3'UTR-located introns. We showed that UPF1, UPF2, and SMG-7 are involved in both plant NMD pathways, whereas Mago and Y14 are required only for intron-based NMD. We also provide evidence that the molecular mechanism of long 3'UTR-based plant NMD resembles yeast NMD, while the intron-based NMD is similar to mammalian NMD. Moreover we have found that the SMG-7 component of plant NMD is targeted by NMD suggesting that plant NMD is autoregulated. We propose that in the common ancestors of extant eukaryotes (stem eukaryotes) both systems, the long 3'UTR-based and intron-based NMD operated and that this complex NMD mechanism was autoregulated, We also propose that despite aspect of the mechanism being simplified in different lineages, for instance intron-based NMD was lost in intron-loss dominated lineages, feedback-regulation was retained in all kingdoms. Our data also support previous theory that intron-based NMD facilitated the spreading of introns in stem eukaryotes.