Retrovirology

Poster presentation

Identification of the 'basal' human LINE-1 retrotransposition complex

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Mobile elements such as transposons and retrotransposons constitute a substantial fraction of eukaryotic genomes. Such elements represent ~45% of the human genome. Long INterspersed Element-1 (LINE-1 or L1) constitutes about 17% of human DNA and is the only known autonomously active human retrotransposon. L1s are bi-cistronic elements that encode two proteins, ORF1p and ORF2p, which are essential for retrotransposition. These proteins associate with the RNA from which they were translated to form an L1 ribonucleoprotein particle (L1-RNP), which is a hypothesized retrotransposition intermediate. The insertion of a new L1 copy occurs by a mechanism known as target-site primed reverse transcription (TPRT), which is performed by the endonuclease and reverse-transcriptase activities of ORF2p and possibly other cellular factors. About 80 to 100 L1s per human genome retain the ability to retrotranspose by this mechanism, and therefore the ongoing mobility of L1 elements contin! ues to impact the evolution of our genome.

Here, we developed new molecular tools to detect retrotransposition-competent L1 RNA and proteins through an epitope-tagging strategy. We used a biochemical approach to identify the 'basal' retrotransposition complex containing L1 RNA, epitope-tagged ORF1p and epitope-tagged ORF2p. We also tested retrotransposition-deficient L1s for their ability to form RNPs and to encode an ORF2p-specific reverse transcriptase activity. Using immunocytochemistry coupled with FISH, we observed a cytoplasmic accumulation of L1 RNPs in perinuclear foci in association with stress granules (SG). Interestingly, we observed that the SG protein markers consistently surrounded the L1 RNP foci. Point mutations in the RNA binding domain of ORF1p decreased the ability of the L1 proteins to form cytoplasmic aggregates, and confirmed the role of this domain in L1 RNP formation. Thus, these results further our understanding of the L1 RNP complex and the general mechanism of L1 retrotransposition.