J Astrophys Aerospace Technol 2017, 5:2 (Suppl)
DOI: 10.4172/2329-6542-C1-009

Evaluating RNA exosomes function in non-coding RNA metabolism at 3D nuclear space

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Strand specific DNA mutations determine whether programmed DNA rearrangements diversify antigen receptor loci genes. However, patients with various malignancies demonstrate DNA mutagenesis skewed toward the sense strand genome wide. Using single-molecule super-resolution microscopy, we have identified subnuclear compartments in B cells where biologically programmed strand-specific DNA mutagenesis are engineered at focal DNA/RNA hybrid structures. The strand specific distribution of DNA mutations is determined by the coupled activities of two RNA helicases, Mtr4 and Senataxin, along with the noncoding RNA processing function of RNA exosome. Our study envisions that the regulatory mechanism of strand specific DNA mutagenesis in subnuclear compartments during programmed and aberrant DNA mutagenesis events will play a major role in other undiscovered aspects of organismic development.

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