Chromoplexy Rearrangements: Investigating the Functional and Diagnostic Role of Novel Mutational Mechanisms Uncovered In Cancer Genomes

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Conventionally, tumorigenesis is understood as a gradual accumulation of genetic mutations. Yet, chromoplexy rearrangements (ChRs) are a mutational phenomenon characterized by highly complex, genomic rearrangements which rapidly fragment and restitch across a genome. Though these mutational mechanisms suggest a distinct form of cancer progression, ChRs lack comprehensive analysis across cancers due to their extremely complex, interchromosomal mechanisms genome-wide. These biological complexities drive genomic heterogeneity and instability, which in turn hinder the computational accuracy of deciphering these mechanisms. As a result, there exists no systematic analysis of the significance of this phenomenon in cancer pathogenesis. This research presents a novel computational paradigm towards unraveling complex, interchromosomal patterns of ChRs, revealing high fidelity in reconstructing and uncovering complex mutational patterns across cancer genomes. Using the models developed, 301 instances of ChRs were discovered across 23 cancers. To examine their significance as mutational mechanisms in genomes, ChRs were analyzed on a genetic, genomic, and clinical scale. Bioinformatics analyses revealed the pan-cancer significance of ChRs in driving oncogenic amplification, inactivation of tumor-suppressor genes, and genomic instability as well as significance in lower clinical survival, as observed in a case-study ChR. The interchromosomal, sporadic patterns of ChRs have hindered a comprehensive analysis of their significance in cancer genomes. Yet, this research reveals a novel computational framework for uncovering these mutational mechanisms as well as discovering the key genetic, genomic, and clinical significance of ChRs in cancer pathogenesis.

Awards Won:
Second Award of $2,000