Impacts of retroelements in tumorigenesis

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Abstract

Colorectal cancer (CRC) is the third most common cancer in the world, with nearly 1 million new cases annually diagnosed. Of these, about 50% of the patients evolve to death mainly due to the development of metastatic (secondary) tumors originated from primary colorectal tumors. Thus, studying genetic variations in secondary tumors is central to better understand tumor progression and to provide treatments that are more effective for CRC-affected patients. Here, we are using whole genome sequencing (WGS) data - matched normal tissue, primary and secondary tumor tissues from 5 CRC-affected patients - and bioinformatics methodologies to study genomic variation present CRC. Among genomic variations, we are developing methods to identify and evaluate the functional role from those caused by LINE-1, retrocopies of protein-coding genes and Alu elements, these latter two unexplored genomic variations with great potential to be functional. Three of five patients (60%) were stage IV when diagnosed. When comparing early-stage patients with late-stage in the progression of CRC, we found that the number of (likely) novels LINE-1 insertions are (10x) higher in the late stages of the disease. However, these numbers are not the same while looking for retrocopies of coding genes. Patients that were stage IV had on average 40 retrotransposition events, while one patient stage II had 95 retrotransposition events from coding genes and the stage III patient had only three. Thereby, our work aims to investigate two types of variations poorly studied, mostly in secondary/metastatic tumors, and contribute to an understanding of the frequency and importance of these variations in tumorigenesis and metastasis of a very relevant type of cancer, colorectal cancer.

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