“Methods and strategies for discovering copy number variation with next-generation sequencing”

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Copy number variations (CNVs) are important contributors to human genetic heterozygosity. Systematic and comprehensive assessment of CNVs has been problematic owing to its complexity and multifaceted features. Array-based approaches (array CGH and SNP microarrays) have successfully identified CNVs. However, their power is limited to detecting copy-number differences of sequences present in the reference assembly used to design the probes, and being unable to resolve breakpoints at single-base-pair level. More recently, next-generation sequencing (NGS) technologies have been successfully used to discover CNVs at a much higher resolution than array-based methods. However, NGS approaches present substantial computational and bioinformatics challenges, including inconsistent results from existing algorithms, inappropriate application of array-based methods, and storage and analysis of huge NGS data. This project aims at developing an integrated workflow that overcomes current computational and bioinformatics challenges for CNV discovery using NGS data. We will apply the built CNV detection workflow to the NGS coupling with whole exome enrichment in the five cases collected from the National Taiwan University Hospital. It is hoped that this workflow is able to detect the microdeletion and small nucleotide changes, and it may provide an alternative and efficient tool for the genetic diagnosis of genetically heterogeneous diseases.

Keywords: Copy number variation; Next-generation sequencing; Parallel computing; Whole exome sequencing