Abstract

Myeloma is a genetically heterogeneous disease and is sub-classified based on the presence of structural variants and genetic mutations. Structural variants/copy number changes are historically identified by traditional methods such as karyotyping and fluorescence in situ hybridization (FISH). Although microarray based genome wide analyses greatly improve the resolution of structural variation, they may be limited by probe density. Consequently, identification of structural variation may be insensitive to specific disrupted gene(s), neglecting the sequence complexity that might underlie these rearrangements. Determination of the specific breakpoints of structural variants at the nucleotide level is required for a better understanding of the genetic causes and to enhance the development of therapeutics for patients. The emergence of Next-Generation Sequencing (NGS) technology has led to the identification of structural variants in the genome at a higher resolution relative to currently used cytogenetic methods. We analyzed DNA extracted from a set of patients with multiple myeloma, who had Affymetrix SNP array (~2.7 million probes) data, by both whole exome sequencing (WES) and whole genome sequencing (WGS) on the Illumina HiSeq® platform to identify the full spectrum of associated genomic aberrations. Sequence data was mapped to the hg19 reference sequence and analyzed by various in-house developed and open source data analytic tools. RNA extracted from a subset of the multiple myeloma patients was also analyzed by RNA-Seq with the goal of identifying fusion events. Additionally, a custom sequence analysis pipeline was written to interrogate chromosomal deletions and translocations in these samples. Our analysis showed that ~43% (6/14) of patients have deletions in chr17p and/or chr13q. We further confirmed structural variants using the Integrative Genomics Viewer (IGV). These data indicate large areas of gain, while losses are present on chr 6 and chr X.

Methods

- 11 multiple-myeloma samples have been analyzed by both whole exome sequencing (100X coverage) and whole genome sequencing (30X coverage) on the Illumina HiSeq® platform (Illumina) - Sequencing data was aligned to hg19 with bwa1 and variants were called using Pindel.2
- Additional normalized coverage at a resolution of 14b was calculated using the Reference Coverage Profile3 method to examine copy-number variants.

Concordance with Array Data

9 of the 11 patient samples have also been analyzed by RNA-sequencing on the Illumina HiSeq® platform

Multi-Platform Analysis

![Multi-platform analysis](image)

**DNA Analysis**

- Whole Genome Analysis
- RNA-Seq Analysis
- WGS Analysis

**RNA Analysis**

- Myeloma RNASeq
- Whole Transcriptome Analysis
- RNA-Seq Analysis

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