Evaluating leukemic structural variations using optical genome mapping

Saeam Shin

Yonsei University College of Medicine, Korea

Among various genetic variations, structural variations of chromosomes play an essential role in the pathogenesis of cancer development and progression. Especially in hematologic malignancies, it is well known that one of the major mechanisms of oncogenesis is the formation of fusion genes due to chromosomal rearrangements, which induces the loss of control of cell division and proliferation. Thus, structural variations are dealt with as important markers of diagnosis, selecting target therapy, and predicting prognosis through risk stratification in hematologic malignancies. Conventional methods for detecting structural variations, including G-banding karyotyping, fluorescence in situ hybridization, chromosomal microarray, and reverse-transcription polymerase chain reaction, have limitations. The short-read next-generation sequencing platform has limitations in precisely analyzing structural variations that are large in size and homologous elements such as repetitive sequences and pseudogenes. There is growing interest in single-molecule strategies, exploring long reads from tens to hundreds of kilobases. Optical mapping is a technique for constructing ordered, genome-wide, high-resolution maps from ultra-high-molecular-weight DNA labeled fluorescent probes. This mapping technique enables de novo assembly and gap filling, and it can detect structural variations that are up to tens of kilobases long. Optical mapping can overcome the limitations of conventional methods and detect structural variations with higher resolution in much less time. Moreover, the optical mapping may uncover novel chromosomal aberrations used as additional diagnosis markers, target therapy, and prognosis prediction.