For the Development of Cancer DNA Biomarker

Yong Sung Kim

Genome Research Center, KRIBB, Daejon, Korea

Cancer development is associated with the progressive accumulation of genetic and epigenetic alterations. Loss of heterozygosity (LOH) is one of the most frequently described genetic alterations associated with solid tumors and detectable in precancerous regions as well as cancer cells, thus representing one of the most promising biomarkers for the early detection of cancer. Microsatellite analysis for LOH has been performed with short tandem repeat (STR) markers that map to every chromosome. However, owing to the relative low abundance of microsatellite markers, the resolution for whole genome scanning is limited to 5 cM with commercially available sets of primers, and the process for whole genome analysis is long and tedious. With the discovery of more than 1.4 million single-nucleotide polymorphisms (SNPs) distributed throughout the human genome, high-resolution genome-wide allelotyping became a reality by using high-density SNP array. To ensure accurate data interpretation for the development of cancer biomarker, it is desirable to use laser capture microdissection (LCM) to separate cancer cells or precancerous region from surrounding normal cells in tumor lesions, but cell number from LCM is limited for genome-wide allelotyping. Thus, a whole genome amplification (WGA) method that amplifies DNA a small number of LCM cells while maintaining locus and allele balances is necessary. Recently, whole genome multiple strand displacement amplification (MDA) demonstrated a high-amplification potential up to 10^4-fold, but we found that DNA from MDA showed more pronounced allelic bias than non-amplified DNA and that this bias seemed to inversely correlate with template quantity. Here we will demonstrate how much DNA is needed for maintaining locus and allele balances during MDA or how many cell is captured by LCM for genome-wide allelotyping, such as high-density SNP array.