Overlapping High Resolution Copy Number Alterations in Cancer Genomes Identified Putative Cancer Genes in Hepatocellular Carcinoma


Recurrent cancer genome alterations are indicators of residing crucial cancer genes. To facilitate searches of cancer genes in human hepatocellular carcinoma (HCC), we established a comprehensive protocol to analyze copy number alterations (CNA) in cancer genomes using high density single nucleotide polymorphism (SNP) arrays with non-paired reference genomes. A total of 653 amplicons and 57 homozygous deletions (HDs) were identified in 23 cancer cell lines. By overlapping the shared aberrant loci in cancer genomes, 6 HDs and 126 amplicons were revealed in at least two cell lines. We selected two novel genes, FNDC3B at 3q26.3 and SLC29A2 at 11q13.2 overlapped amplicons, to investigate their aberrations in HCC tumorigenesis. Knockdown of these genes in amplified cells decreased cell proliferation, anchorage independent growth and tumor formation in xenograft models. Importantly, up regulation of SLC29A2 in HCC tissues was significantly associated with advanced stages (P =0.0031), vascular invasion (P =0.0353) and poor patient survival (P =0.0325). These results indicated our protocol could facilitate high-throughput detection of cancer genes as significant target genes and biomarkers for cancer diagnosis and therapy.