Investigation of osteosarcoma genomics and its impact on targeted therapy*

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Abstract

Osteosarcoma is a genetically unstable malignancy that most frequently occurs in children and young adults. The lack of progress in managing this devastating disease in the clinic has prompted international researchers to collaborate to profile key genomic alterations that define osteosarcoma. A team of researchers and clinicians from China, Finland, and the United States investigated human osteosarcoma by integrating Whole genomic sequencing (WGS), transcriptome sequencing (RNA-seq), high-density genome-wide array comparative genomic hybridization (aCGH), fluorescence in situ hybridization (FISH), reverse transcription-polymerase chain reaction (RT-PCR), Sanger sequencing, cell culture, and molecular biological approaches. Systematic analysis of genetic/genomic alterations and further functional studies have led to several important findings, including novel rearrangement hotspots, osteosarcoma-specific *LRP1-SNRNP25* fusion genes, VEGF and WNT signaling pathway alterations, deletion of the *WWOX* gene, and amplification of the *APEX1* and *RUNX2* genes. Importantly, these genetic events correlate significantly with pathogenesis, prognosis, progression, and therapeutic activity in osteosarcoma, suggesting their potential impact on improved managements of human osteosarcoma patients.

Key words:

Osteosarcoma, Whole genomic sequencing, transcriptome sequencing, aCGH, *LRP1-SNRNP25 fusion gene*, VEGF pathway, WNT pathway, *WWOX* gene, *RUNX2* gene, *APEX1* gene