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Establishment of a primary orthotopic patient-derived osteosarcoma mouse model

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Introduction: Osteosarcoma (OS) is the most common primary malignant bone tumor in children. Because outcome of patients following standard treatment has not shown major improvement over almost three decades, functional preclinical models that closely reflect important clinical cancer characteristics are urgently needed to develop new treatment strategies. The objective of this study was to establish an orthotopic xenotransplanted mouse model using patient-derived tumor tissue.

Methods: Fresh tumor tissue from an adolescent female patient with osteosarcoma relapse was surgically xenografted into the right tibia of 6 immunodeficient BALB/c Nu/Nu mice as well as cultured into medium. Tumor growth was serially assessed by palpation and with magnetic resonance imaging (MRI). In parallel, a primary cell line of the same tumor was established. Histology and high-resolution array-based comparative genomic hybridization (aCGH) were used to investigate both phenotypic and genotypic characteristics of different passages of human xenografts and the cell line compared to the tissue of origin.

Results: We established a primary OS cell line and a primary patient-derived orthotopic xenotranplanted mouse model. MRI analyses and histopathology revealed the same architecture in the primary tumor and in the xenografts. Array-CGH analyses of the cell line and all xenografts showed similar patterns of genomic alterations as the primary tumor.

Conclusion: We report the first orthotopic OS mouse model established by transplantation of tumor pieces directly harvested from the patient.