BRD4-LEUTX fusion

CNS Embryonal Tumor with BRD4-LEUTX Fusion.

Decock et al. assessed the performance of mRNA capture sequencing to identify fusion transcripts in FFPE tissue of different sarcoma types, followed by RT-qPCR confirmation. To validate the workflow, six positive control tumors with a specific chromosomal rearrangement were analyzed using the TruSight RNA Pan-Cancer Panel. Fusion transcript calling by FusionCatcher confirmed these aberrations and enabled the identification of both fusion gene partners and breakpoints. Next, whole-transcriptome TruSeq RNA Exome sequencing was applied to 17 fusion gene-negative alveolar rhabdomyosarcoma (ARMS) or undifferentiated round cell sarcoma (URCS) tumors, for whom fluorescence in situ hybridization (FISH) did not identify the classical pathognomonic rearrangements. For six patients, a pathognomonic fusion transcript was readily detected, i.e., PAX3-FOXO1 in two ARMS patients, and EWSR1-FLI1, EWSR1-ERG, or EWSR1-NFATC2 in four URCS patients. For the 11 remaining patients, 11 newly identified fusion transcripts were confirmed by RT-qPCR, including COPS3-TOM1L2, NCOA1-DTNB, WWTR1-LINC01986, PLAA-MOB3B, AP1B1-CHEK2, and BRD4-LEUTX fusion transcripts in ARMS patients. Additionally, recurrently detected secondary fusion transcripts in patients diagnosed with EWSR1-NFATC2-positive sarcoma were confirmed (COPS4-TBC1D9, PICALM-SYTL2, SMG6-VPS53, and UBE2F-ALS2). In conclusion, this study shows that mRNA capture sequencing enhances the detection rate of pathognomonic fusions and enables the identification of novel and secondary fusion transcripts in sarcomas [1].

Malignant epithelioid soft tissue tumors encompass a wide spectrum of lesions. Among them, Epithelioid Malignant Peripheral Nerve Sheath Tumors (MPNST) constitute a distinct subgroup, accounting for <5% of all MPNSTs. Epithelioid MPNST is infrequently associated with neurofibromatosis type 1, occasionally arises in schwannoma, and shows diffuse S100 and CD34 expression, often combined with INI-1 loss. However, the molecular mechanisms underlying the tumorigenesis of epithelioid MPNST remain largely unknown. We describe a case of a 10-year-old girl with an epithelioid malignancy of the orbit. The tumor proved positive for S100, CD34, and SOX10, and, although INI-1 expression was maintained, the overall features suggested the possibility of an epithelioid MPNST, arising in an unusual location. NGS analysis revealed a novel in-frame BRD4-LEUTX fusion gene. LEUTX plays an important role in embryonal genome activation and its expression is mostly suppressed postnatally. We were able to detect increased levels of LEUTX transcript in the tumor, indicating that BRD4-LEUTX fusion leads to LEUTX re-activation. To our knowledge, this fusion has never been reported previously. Whether the current case represents an example of epithelioid MPNST or a distinct tumor entity remains to be determined [2].

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2)
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