Overexpression of *TEAD4* in AT/RT; New Insight to the Pathophysiology of an Aggressive Brain Tumor

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Atypical teratoid/rhabdoid tumor (AT/RT) is a highly malignant brain tumor in early childhood. The median overall survival is 6 to 18 months despite of intensive multimodal therapy including surgery, chemotherapy, high-dose chemotherapy with or without stem cell rescue, and, radiation therapy. Though the most of tumor is characterized by inactivation of *SMARCB1* gene, much of the biological contribution to the development and aggressiveness of this tumor is still poorly understood. We have investigated new molecular pathways involved in AT/RT formation and progression. Tumor samples were collected from patients diagnosed with AT/RT. Copy number variation (CNV) study was performed to investigate the characteristic in one patient using primary and relapsed tumors. The data was verified in a large set of samples by gene expression analysis, Q-PCR, and immunohistochemistry. Total of 22 tumor samples and two cell lines, which were established from each of primary and relapsed tumor in one patient, were investigated. Amplification of *TEAD4* was observed in the patient by CNV study and *in situ hybridization*. In a large set of samples, gene expression of *TEAD4* and its co-activator *YAP1* were significantly higher in AT/RT when compared with medulloblastoma. *MYC* and *CCND1*, both of which are downstream targets of Hippo pathway, were overexpressed in AT/RT when compared with medulloblastoma. By immunohistochemistry, *TEAD4* was overexpressed in mainly nucleus and *YAP1* was in both nucleus and cytoplasm. We report the overexpression of *TEAD4* and *YAP1* in AT/RT, both of which are key components of Hippo pathway. Hippo pathway plays an important role in biological processes, including organ size control, cancer development, and stem cell self-renewal and differentiation. Dysregulation of the pathway is considered to contribute tumor progression and poor prognosis. Our results may be supposed to be new insight to the pathophysiology on AT/RT. Further study is needed to reveal the role and function of Hippo pathway in this lethal tumor.