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Expression of YAP and TAZ in brain tumors from different age groups

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Introduction

Brain tumors from different age groups come with variable characteristics. They differ in their molecular characteristics and in the patients' outcome. There is few research on the underlying mechanisms[1]. Yes-associated Protein (YAP) and the homologous protein Transcriptional Co-Activator With PDZ-Binding Motif (TAZ) are transcriptional co-activators and control proliferation and apoptosis of the cell[2,3]. There is evidence, that YAP and TAZ play a role in both pediatric and adult brain tumors, especially gliomas.[3,4,6] They have an impact on proliferation, invasion and metastasis of cancer cells and thereby affect the tumorigenesis and survival of patients.[2,4,5] In contrast YAP also applies as a positive prognostic marker in a subtype of pediatric ependymoma, leading to better outcome of patients.[7] Tumors in young adults often show a heterogenous pattern, displaying not only molecular characteristics from adult, but also from pediatric brain tumors.[1]

Our goal was to identify differences among these age groups in YAP and TAZ expression in low- and high-grade brain tumors.

Methods

We analyzed a total of 63 patients divided into three cohorts by age. Patients from the pediatric group were not older than 18 years, young adults are defined from 18 to 25 years and the adult group contains patients older than 25 years. After neurosurgical resection diagnoses including pilocytic astrocytoma (WHO Grade, n=28), ependymoma (EPN, n=25), medulloblastoma (MED, n=20) and glioblastoma multiforme (GBM, n=24) were histologically assessed and classified with WHO 2007 classification. Levels of YAP and TAZ gene and protein expression were measured via PCR and Western Blotting.

Results

Increased levels of YAP in adult astrocytoma

In pilocytic astrocytoma YAP mRNA expression shows significantly higher rates in the adult group than in the pediatric group (z=3.828, adjusted p=0.0004, Kruskal Wallis test, Fig. 1B). There is a tendency of higher YAP mRNA levels with increasing age, which however is not significant. YAP protein expression also shows the tendency of higher expression in the adult group.

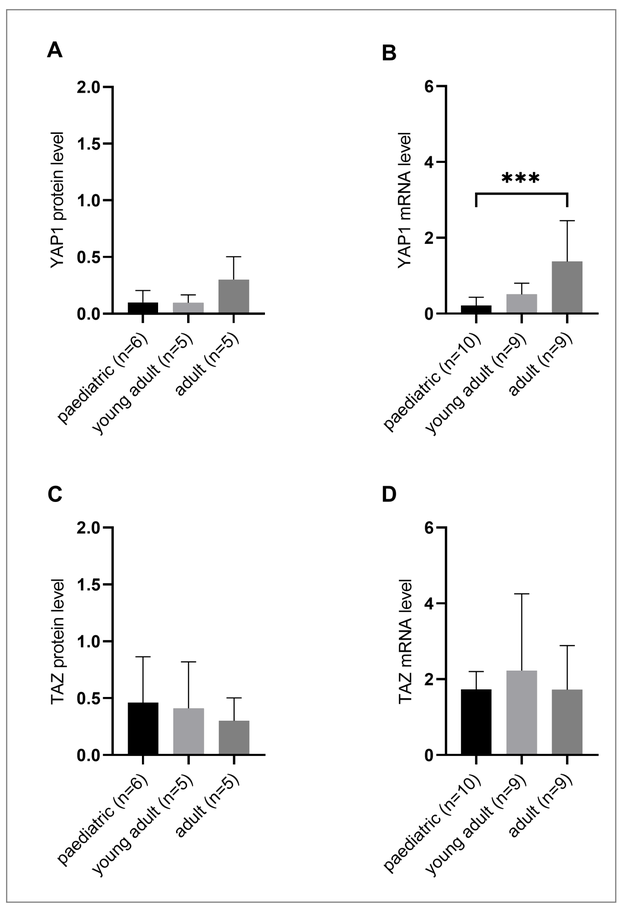

Fig. 1: YAP and TAZ expression in astrocytomas

Higher levels of TAZ in pediatric ependymoma

We found high mRNA expression of YAP and TAZ in pediatric ependymoma. TAZ mRNA expression was significant to both young adults (z=3.083, adjusted p=0.0061, Kruskal Wallis test, Fig. 2D) and the adult group (z=3.794, adjusted p=0.0004, Kruskal Wallis test, Fig. 2D).

YAP and TAZ expression tends to increase with older age in high-grade tumors

YAP and TAZ expression levels in medulloblastoma tend to increase with older age. Both YAP and TAZ mRNA expression in the adult group is thereby significant compared to the pediatric group (YAP: z=3.087, adjusted p=0.0061, Kruskal Wallis test; TAZ: q=4.095, adjusted p=0.0258, One-way ANOVA, Fig. 3B and 3D).

Glioblastoma multiforme shows the same tendency as pilocytic astrocytoma in YAP expression, but only YAP protein expression was significantly higher in adults compared to the pediatric group (q=3.859, adjusted p=0.0375, One-way ANOVA, Fig. 4A).

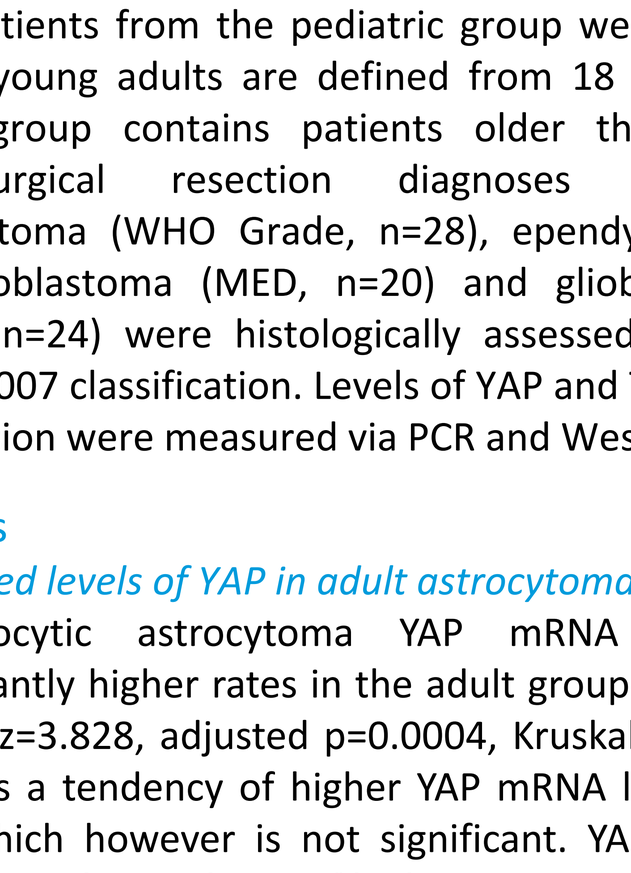

Fig. 2: YAP and TAZ expression in ependymomas

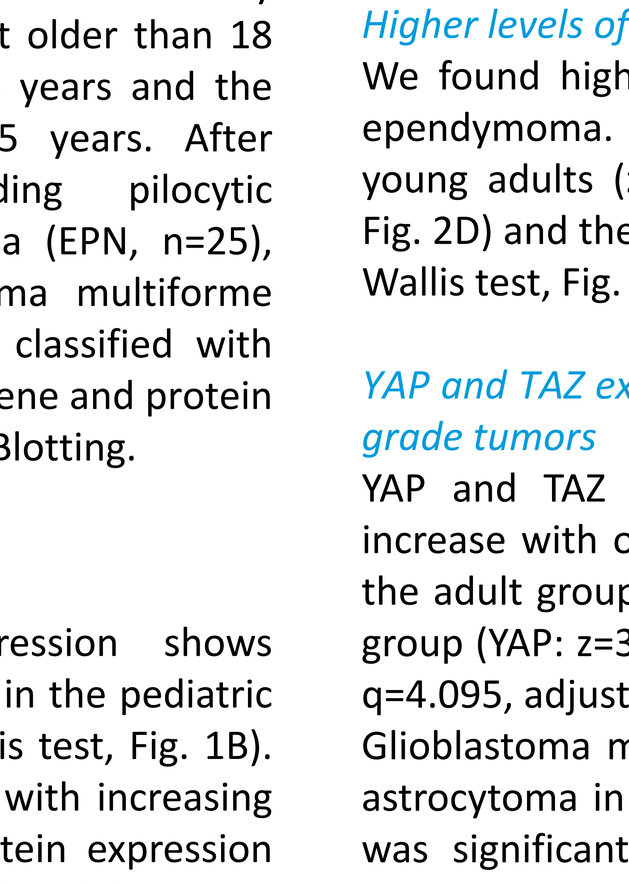

Fig. 3: YAP and TAZ expression in medulloblastomas

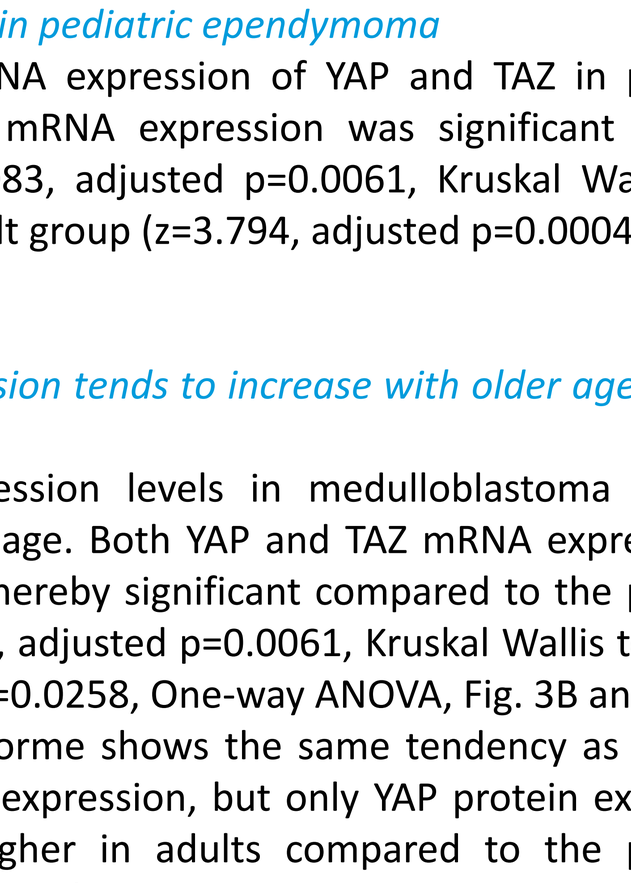

Fig. 4: YAP and TAZ expression in glioblastomas

Conclusion

We found distinct relations between age and expression of YAP and TAZ in the different entities. Differences in expression rates of YAP and TAZ could display a possible reason for the variable outcome between the three cohorts. In the following our findings must be linked to clinical data to confirm this hypothesis.

References

1. Hafeez U et al. Young adults diagnosed with high grade gliomas: Patterns of care, outcomes, and impact on employment. J Clin Neurosci 2019; 68: 45-50.
2. Cobbaut M, Karagil S, Bruno L, et al. Dysfunctional Mechanotransduction through the YAP/TAZ/Hippo Pathway as a Feature of Chronic Disease. Cells. 2020;9(1).
3. Li P-D, Wang X-J, Shan Q, Wu Y-H, Wang Z. Evaluation of TAZ expression and its effect on tumor invasion and metastasis in human glioma. Asian Pacific Journal of Tropical Medicine. 2014;7(10):757-760.
4. Li W, Dong S, Wei W, et al. The role of transcriptional coactivator TAZ in gliomas. Oncotarget. 2016;7(50):82686-82699.
5. Piccolo S, Dupont S, Cordenonsi M. The biology of YAP/TAZ: Hippo signaling and beyond. Physiol Rev. 2014;94:1287-1312.
6. Liu M, Lin Y, Zhang X-C, et al. Phosphorylated mTOR and YAP serve as prognostic markers and therapeutic targets in gliomas. Lab Invest. 2017;97(11):1354-1363.
7. Jones DTW, Banito A, Grünewald TGP, et al. Molecular characteristics and therapeutic vulnerabilities across paediatric solid tumours. Nat Rev Cancer. 2019;19(8):420-438.

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