grated molecular approach, and utilized preclinical models to validate our findings. RESULTS: Meningiomas with either CDKN2A/B deletions (partial or homozygous loss) or an intact CDKN2A gene locus but elevated mRNA expression (CDKN2Ahigh) both had poor clinical outcomes. Increased CDKN2A mRNA expression was a poor prognostic factor independent of deletion status. CDKN2A expression and p16 protein also progressively increased with tumor grade and more aggressive molecular and methylation groups. CDKN2Ahigh meningiomas and meningiomas with CDKN2A deletions were enriched for similar cell cycling pathways but dysregulated at different checkpoints (G1/S vs G2/M). p16 immunohistochemistry was unreliable in differentiating between meningiomas with and without CDKN2A deletions, but increased positivity was associated with mRNA expression. CDKN2Ahigh meningiomas were associated with gene hypermethylation, Rb-deficiency, and lack of response to CDK inhibition. CONCLUSIONS: In meningiomas, CDKN2A mRNA expression consistently increases with biological aggressiveness, is prognostic independent of copy number loss, and may be used as an important prognostic biomarker with therapeutic implications for resistance to CDK4/6 inhibitors clinically.

YOUNG INVESTIGATOR PRESENTATIONS

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1525-1540 Basic/Translational Young Investigator Award Presentation, Abstract 2

COMPREHENSIVE MULTIPLATFORM ANALYSIS OF CDKN2A ALTERATIONS IN MENINGIOMAS

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In meningiomas, CDKN2A/B deletions are associated with poor clinical outcomes but are exceeding rare in most cohorts (1-5% of cases). Large molecular datasets are therefore required to explore these deletions and their relationship to other CDKN2A alterations that may be more common, but also prognostic on a transcriptomic, epigenomic, and/or copy number level.

METHODS: We used multidimensional molecular data of 560 meningioma samples from 5 independent cohorts to comprehensively interrogate the spectrum of CDKN2A alterations through DNA methylation, copy number variation, transcriptomics, and proteomics using an inte-