

ID #748 Single-cell profiling of CSF-circulating tumor cells reveals distinct invasion and stemness programs in pediatric brain tumors [Abstract]

Victoria Fincke, Katrin Mauch-Mauchmücke, Jasmin Hager, Stefanie Volz, Markus Metzler, Irene von Luettichau, Michael Frühwald, Kendra Maass, Markus Riemenschneider, Pascal Johann

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NK/T-cells (~10%). Pilot experiments analyzing matched tumor tissue specimens and CSF-derived cellular material from atypical teratoid/rhabdoid tumor (ATRT) and medulloblastoma revealed that CSF-circulating tumor cells co-clustered with primary tumor cells but exhibited a distinct transcriptional signature enriched for stemness and plasticity markers (*SOX2+*, *OLIG2+*) alongside invasion and motility-associated genes (*CYRIB+*, *ELMO1+*). Notably, these CSF-specific programs were absent in matched primary tumor populations, indicating selective pressure within the CSF microenvironment. These findings suggest that tumor cells within the CSF microenvironment activate specialized survival and dissemination programs. Ongoing analyses determine whether pan-entity molecular programs characterize circulating tumor cells across pediatric CNS tumor subtypes and whether these programs harbor therapeutically actionable vulnerabilities in this clinically aggressive cell population.

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ID #748 SINGLE-CELL PROFILING OF CSF-CIRCULATING
TUMOR CELLS REVEALS DISTINCT INVASION AND STEMNESS
PROGRAMS IN PEDIATRIC BRAIN TUMORS

Victoria Fincke^{1,2}, Katrin Mauch-Mauchmücke³, Jasmin Hager⁴, Stefanie Volz⁵, Markus Metzler⁶, Irene von Luettichau⁷, Michael Frühwald¹, Kendra Maass⁸, Markus Riemenschneider^{3,2}, Pascal Johann^{1,2}; ¹Pediatrics and Adolescent Medicine, Swabian Children's Cancer Center, University Hospital Augsburg, Augsburg, Germany, Augsburg, Bayern, Germany; ²Bavarian Cancer Research Center (BZKF) and Pediatric Oncology Network, KIONET BAVARIA, Bavaria, Germany, Bayern, Germany; ³Department of Neuropathology, Regensburg University Hospital, Regensburg, Germany, Regensburg, Bayern, Germany; ⁴TUM School of Medicine, Children's Hospital Munich Schwabing, Technical University of Munich, 2Department of Pediatrics and Children's Cancer Research Center, Bayern, Germany; ⁵Hopp Children's Cancer Center Heidelberg (KiTZ), Baden-Württemberg, Germany; ⁶University Hospital Erlangen, Department of Pediatrics and Adolescent Medicine, Bayern, Germany; ⁷TUM School of Medicine, Children's Hospital Munich Schwabing, Technical University of Munich, Department of Pediatrics and Children's Cancer Research Center, Bayern, Germany; ⁸Hopp Children's Cancer Center Heidelberg (KiTZ), Heidelberg, Baden-Württemberg, Germany

CNS tumors represent a leading cause of cancer-related mortality in children, asking for precise molecular profiling and longitudinal disease surveillance for optimal therapeutic management. In particular, intensified investigation into the biological mechanisms underlying metastatic dissemination is essential, as leptomeningeal spread confers poor prognosis in pediatric brain tumors.

Through a multicenter initiative within the Bavarian Center for Cancer Research within the KIONET network, we analyzed CSF samples from 36 brain tumor patients, comprising ATRT, medulloblastoma, and other high-grade entities. We performed single-cell transcriptomic profiling of the cellular fraction of cerebrospinal fluid (CSF) and integrated these data with matched primary tumor profiles to identify molecular programs specific to circulating versus tissue-resident tumor cells. As anticipated, tumor cell content was sparse (<5%) within CSF samples, with the cellular landscape dominated by macrophages/microglia (~60%) and