UNIVERSITÄT AUGSBURG
Universitätsbibliothek

OPEN ACCESS
OPUS AUGSBURG

ID #523 Comparative analyses of human AT/RT-TYR and murine Smarcb1-deficient choroid plexus cells implicate the choroid plexus of the fourth ventricle as potential cellular origin for AT/RT-TYR [Abstract]

Lea Altendorf, Alicia Johler, Levke-Sophie Peter, Karoline Hack, Beatrix Mahnke, Alina Klein, Matthias Dottermusch, Svenja Tonn, Rajanya Roy, Michael Holtzman, Michael Frühwald, Christian Thomas, Kornelius Kerl, Melanie Schoof, Martin Hasselblatt, Ulrich Schüller

Angaben zur Veröffentlichung / Publication details:

Altendorf, Lea, Alicia Johler, Levke-Sophie Peter, Karoline Hack, Beatrix Mahnke, Alina Klein, Matthias Dottermusch, et al. 2026. "ID #523 Comparative analyses of human AT/RT-TYR and murine Smarcb1-deficient choroid plexus cells implicate the choroid plexus of the fourth ventricle as potential cellular origin for AT/RT-TYR [Abstract]." *Neuro-Oncology Pediatrics* 2 (Supplement_1): i62. https://doi.org/10.1093/neuped/wuag026.191.

Nutzungsbedingungen / Terms of use:

CC BY-NC 4.0

Dieses Dokument wird unter folgenden Bedingungen zur Verfügung gestellt: / This document is made available under these conditions:
CC-BY-NC 4.0: Creative Commons: Namensnennung - Nicht kommerziell
Weitere Informationen finden Sie unter: / For more information see:
https://creativecommons.org/licenses/by-nc/4.0/deed.de

ABSTRACT CITATION ID: WUAG026.191

ID #523 COMPARATIVE ANALYSES OF HUMAN AT/RT-TYR AND MURINE SMARCB1-DEFICIENT CHOROID PLEXUS CELLS IMPLICATE THE CHOROID PLEXUS OF THE FOURTH VENTRICLE AS POTENTIAL CELLULAR ORIGIN FOR AT/RT-TYR

Lea Altendorf[1,2], Alicia Johler[1,2], Levke-Sophie Peter[1,2], Karoline Hack[1,2], Beatrix Mahnke[1,2], Alina Klein[1,2], Matthias Dottermusch[3], Svenja Tonn[1,2], Rajanya Roy[4], Michael Holtzman[5], Michael Frühwald[6], Christian Thomas[7], Kornelius Kerl[4], Melanie Schoof[1,2], Martin Hasselblatt[7], Ulrich Schüller[1,2,3]; [1]Department of Pediatric Hematology and Oncology, University Medical Center Hamburg-Eppendorf, Germany, Department of Pediatric Hematology and Oncology, Hamburg, Hamburg, Germany; [2]Research Institute Children's Cancer Hamburg, Germany, Research Institute Children's Cancer Center, Hamburg, Hamburg, Germany; [3]Institute of Neuropathology, University Medical Center Hamburg-Eppendorf, Germany, Institute of Neuropathology, Hamburg, Hamburg, Germany; [4]Department of Pediatric Hematology and Oncology, University Medical Center Münster, Germany, Department of Pediatric Hematology and Oncology, Münster, Nordrhein-Westfalen, Germany; [5]Pulmonary and Critical Care Medicine, Department of Medicine, Washington University, St. Louis, MO, USA, Pulmonary and Critical Care Medicine, St. Louis, Missouri, United States; [6]Pediatrics and Adolescent Medicine, Swabian Children's Cancer Center, University Hospital Augsburg, Germany, Pediatrics and Adolescent Medicine, Augsburg, Bayern, Germany; [7]Institute of Neuropathology, University Hospital Münster, Germany, Institute of Neuropathology, Münster, Nordrhein-Westfalen, Germany

Atypical teratoid/rhabdoid tumors (AT/RT) belong to the most common malignant tumors of the central nervous system during infancy. They split into four major DNA methylation subtypes: AT/RT-TYR, AT/RT-SHH, AT/RT-MYC, and AT/RT-SMARCA4. Each of these subtypes demonstrates distinct molecular fingerprints and clinical characteristics, with AT/RT-TYR most frequently occurring in the fourth ventricle. However, details on the cellular origins and tumor initiation of AT/RT-TYR remain largely unknown and mouse models providing insights into tumor development are completely missing. Therefore, we performed histopathological examination as well as bulk- and single-nucleus RNA sequencing analyses in human AT/RT. Additionally, genetically engineered mouse models with a conditional Cre/*loxP*-induced Smarcb1 loss were generated. Here, we show that AT/RT-TYR very often appear intermingled with fourth ventricle choroid plexus (CP) tissue and that tumor cells express CP markers on a gene expression and protein level. In addition, we observed a general resemblance of AT/RT-TYR to the CP of the fourth ventricle by analyzing bulk- and single-nucleus RNA sequencing data. Finally, *Foxj1-cre*::*Smarcb1*$^{fl/fl}$ mice showing loss of Smarcb1 in early CP progenitors gave rise to large, atypical CP cells with gene expression most similar to human AT/RT-TYR. Further investigation of the CP phenotype via ARL13B immunohistochemistry and transmission electron microscopy demonstrated reduced cilia numbers in *Foxj1-cre*::*Smarcb1*$^{fl/fl}$ mice compared to control mice, which was also observed in human AT/RT-TYR compared to healthy CP of the same patient. In conclusion, analyses of human AT/RT-TYR as well as murine CP cells lacking Smarcb1 point towards the CP of the fourth ventricle as a potential cellular origin of AT/RT-TYR.

Downloaded from https://academic.oup.com/neuro-onc-peds/article/2/Supplement_1/wuag026.191/8714856 by Augsburg University Library user on 09 July 2026