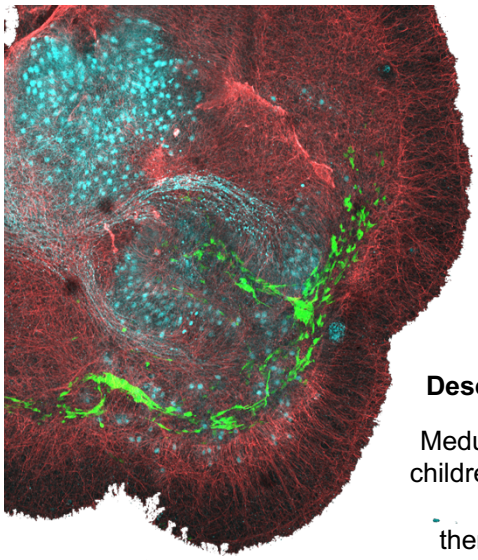
University of Zurich[UZH]

UNIVERSITY CHILDREN'S HOSPITAL ZURICH
Children's Research Center CRC



MASTER'S THESIS PROJECT:

Functional and Molecular Characterization of Novel Invasion-inhibitory Compounds in Medulloblastoma

Description of research theme:

Medulloblastoma (MB) is the most common malignant brain tumor in children. Its aggressive behavior and high invasiveness together with a lack of targeted therapy options represent a major therapeutical challenge. In collaboration with the Gisbert Schneider Group at ETHZ and using *de novo* compound design and functional validation, we have identified compound A024 and its structural analogs A153 and T006 that repress growth factor-driven invasion. Molecular target identification approaches and functional assays indicated the implication of A024 in controlling the ARP2/3 complex, a central regulator of actin polymerization, cell migration and cell invasion. The working hypothesis is that A024 and its analogs interfere with ARP2/3 complex function, which mechanistically underlies repressed motility and invasion. In this thesis project, the candidate will test this hypothesis and clarify the mode of action of A024, A153 and T006.

The aims of the Master's thesis project are:

- To validate the predicted regulation of the ARP2/3 complex by A024 and its analogs using biochemical and microscopy-based approaches
- To test whether A153 and T006 also affect ARP2/3 complex function
- To determine the functional consequences of ARP2/3 complex interference for actin polymerization, motility and invasion

What you will learn:

- Design, experimental testing and analysis of hypothesis-driven research questions
- State-of-the-art microscopy approaches to study mammalian cell dynamics and molecular functions
- Biochemical approaches to study compound effects at molecular and cellular levels

Supervisors:	Marc Thomas Schönholzer (direct), Prof. Dr. Martin Baumgartner
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Links:	https://pediatric-molecular-neurooncology.ch/
Requirements:	Genuine interest in the cell biology of cancer cells, and in the molecular processes that govern cell motility and invasiveness. Strong motivation to work in a wet-lab environment. Experience in microscopy and/or protein biochemistry is an asset.
Starting date:	Immediately or upon agreement

PeMNOR lab
Pediatric Molecular Neuro-Oncology Research